Acute and Persistent Effects from Environmental Toxicant Exposure on the Gut-Liver Axis

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Abstract

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Persistent environmental pollutants (POPs), such as polybrominated diphenyl ethers (PBDEs), and polychlorinated biphenyls (PCBs), are ubiquitously detected in the environment despite removal from commercial and industrial use. Due to their lipophilic and bioaccumulative nature, POPs have been found in close proximity to the human environment, including food (i.e. milk, eggs, meat, seafood), soil and water. In humans, such exposures have been linked to metabolic diseases and developmental disorders. The liver is as an essential organ for xenobiotic metabolism and nutrient homeostasis. Specifically, the liver serves as a central hub for digestion and homeostatic signaling, metabolism of carbohydrates, amino acids, nucleotides, fatty acids, cholesterol, hormones, and importantly, xenobiotics such as drugs, and chemicals present in our environment such as POPs. Interacting with the liver, the gut microbiome can modify xenobiotic biotransformation activities of the host and dysbiosis of the gut microbiome is appreciated as a critical regulator of disease susceptibility. However, little is known regarding how environmental toxicants and

the gut microbiome interact to modulate the interface between xenobiotic and intermediary metabolism. Furthermore, it is increasingly recognized that there is a sensitive developmental time window for toxic exposures that may have life-long impacts on disease risk. Therefore, the goal of my thesis is to investigate, in an unbiased way, the acute effects of PCBs on the gut microbiome and liver (Aim 1), as well as the persistent effects from acute exposure to PBDEs, or PCBs, as compared to bisphenol A (BPA), a well-known epigenetic modifier (Aim 2). I hypothesized that the gut microbiome regulates PCB-mediated changes in the liver's metabolic signatures and transcriptome, and that acute exposure to PBDEs and PCBs have persistent effects on the liver transcriptome. To achieve Aim 1, ninety-day-old female conventional (CV) and germ-free (GF) C57BL/6 mice were orally exposed to the PCB Fox River Mixture (an environmentally relevant synthetic PCB mixture, 6 or 30 mg/kg, respectively representing the low and high dose) or corn oil (vehicle control, 10 ml/kg), once daily for 3 consecutive days. Organs were collected 24 hours after the final dose. RNA-Seq was conducted on liver, and endogenous aqueous metabolites (i.e. amino acids, carbohydrates, and nucleotides) were measured in liver and serum by LC-MS. For Aim 2, two-day-old male and female C57BL/6 mice were supralingually exposed to corn oil, BPA (250 µg/kg), BDE-99 (an enriched PBDE congener found in the diet and in human tissues, 57 mg/kg), or the PCB Fox River Mixture (30 mg/kg), once daily for three days. RNA-Seq was conducted in mouse livers at postnatal (PND) day 5 (acute response) and PND 60 (persistent response). The prototypical target genes of the major xenobiotic-sensing transcription factors aryl hydrocarbon receptor (AhR), pregnane X receptor (PXR), and constitutive androstane receptor (CAR) were more readily up-regulated by PCBs in CV than in GF conditions, indicating that the effect of PCBs on the hepatic transcriptome act partly through the gut microbiome. Xenobiotic and steroid metabolism pathways were up-regulated, whereas the response to incorrectly folded proteins pathway (unfolded protein response – UPR; also

commonly called the endoplasmic reticulum (ER) stress response) was down-regulated by PCBs in a gut microbiome-dependent manner. At the high PCB dose, NADP and arginine appear to interact with genes that encode drug-metabolizing enzymes (Cyp1-3 family, DhcR7, and Nqo1), which are highly correlated with the presence of *Anaerotruncus* and *Roseburia* bacteria in CV mice, providing a novel explanation of gut-liver interaction from PCB exposure. In GF exposure groups, hepatic glucose was down-regulated, whereas fructose 6-phosphate and glucose 6-phosphate were up-regulated, indicating increased glucose utilization potentiated by the lack of gut microbiota. Through querying the LINCS L1000 chemical database, I predicted that therapeutic drugs targeting the anti-inflammatory and ER stress pathways are potential remedies to mitigate PCB toxicity. Interestingly, as opposed to Aim 1, the chemical effects on the hepatic transcriptomic changes were minimal in PND5 and were markedly amplified by PND60 (young adults), indicating that early life toxicant exposure shifted the developmental trajectory of the liver. The acute response showed signs of active metabolism of the exposed contaminants; these responses were then greatly amplified in young adults. In these young adults, all three chemicals persistently altered the expression of hepatic genes involved in the metabolism of drugs, carbohydrates, and lipids, oxidative stress and inflammation, as well as epigenetic modifications, with males being more susceptible than females. At the doses given, BPA and BDE-99 had more prominent effects compared to PCBs. The top most persistently altered predicted upstream transcriptional and cell signaling regulators include essential cell cycle genes (*Trp53*, *Cdkn1a*, *E2f1* and *E2f3*), sterol biosynthesis (*Scap*), bile acid synthesis (*Fgf15*), as well as the nuclear receptors that regulate lipids (PPARs) and drug metabolism (RORs, CAR, PXR). In accordance with these observations, other notable trends included persistent down-regulation of genes that encode phase-I and phase-II drug-metabolizing enzymes, up-regulation of many membrane transporters, and up-regulation of oxidative stress and inflammation-related genes in young

adults exposed neonatally to BPA and BDE-99. In addition, the expression of cancer-related lncRNAs and genes (i.e. *H19*, *Snhg1* and *Snhg4*, *Gsts*) were persistently dysregulated following neonatal exposure to BPA or BDE-99. In conclusion, my findings demonstrate that the gut microbiota dramatically influence PCB-mediated hepatic responses, possibly due to crosstalk between the gut and liver. Furthermore, my results demonstrate that neonatal exposure to these environmental chemicals (especially BDE-99 and BPA) leads to persistent and amplified hepatic transcriptomic changes in young adulthood, with males being more sensitive than females. Persistent dysbiosis in the colon and potentially altered gut-liver axis were observed. Most notably, dysregulation of cell cycle, inflammation, oxidative stress, as well as lipid and drug metabolism pathways were observed, possibly due to cross-talk between epigenetic reprogramming and nuclear receptors/transcription factors.

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I would like to take this opportunity to thank all those who helped me during my MS journey. I am grateful to be a part in such a diverse lab with members having different interests and specialties. This experience enabled me to broaden my views and have a deeper understanding of the toxicology field. Openly discussing ideas about science and technology lead to asking “so what can we do?” and opened doors to new experiments and long-term planning. Senior members in the lab, as well as my committee members, guided me when I was lost, as if I was left alone in a dark space. As I gained more experience, on my path to becoming a more senior member myself, the junior members in the lab shared with me their excitement and pure curiosity.

I am fortunate to have a supportive family in Seattle, Guam, and Korea who helped me focus on work and provide a place to relax. Having a family whose occupation and field of expertise that range from end-to-end helped me think about the broader aspects in the application of my work. The hospitable and cheerful environment changed my viewpoint of what a home should be from a mere place to sleep to a warm shelter, although this change of thought lead to acceptable laziness from time to time. Being and spending time together often made me feel better after failed experiments. I would not have accomplished as much without their support.

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CHAPTER 1. Introduction

Persistent environmental pollutants: polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs)

Environmental contaminants, often from anthropogenic sources, such as polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs), are ubiquitously present in the environment and linked to multiple diseases in humans and other animals. Polychlorinated biphenyls (PCBs) were widely used as electric coolants and insulators due to their chemical stability and fire resistance and were banned from production in the United States in 1979 due to their toxicity (Korrick and Sagiv, 2008). PCBs bio-accumulate and are environmentally persistent with an estimated 150 million pounds of PCBs dispersed in the environment (Korrick and Sagiv, 2008). PCBs can be detected in food, soil, water, human tissues, and serum (Boesen et al., 2019; Ellsworth et al., 2015; Grimm et al., 2015; Jahnke and Hornbuckle, 2019; Jin et al., 2019; Stremy et al., 2019; Weber et al., 2018). There are several known adverse health effects of PCB exposure; epidemiological and animal models have demonstrated dysregulation in neurodevelopment (Klocke and Lein, 2020; Schug et al., 2015; Zhang et al., 2017), interference of thyroid hormone signaling (Li et al., 2018), perturbation of the gut microbiome (Cheng et al., 2018; Petriello et al., 2018), and development of type II diabetes (Dzierlenga et al., 2019; Meek et al., 2019; Rahman et al., 2019; Tornevi et al., 2019) and cancer (Leng et al., 2016; He et al., 2017; Ghosh et al., 2018; Georgiadis et al., 2019).

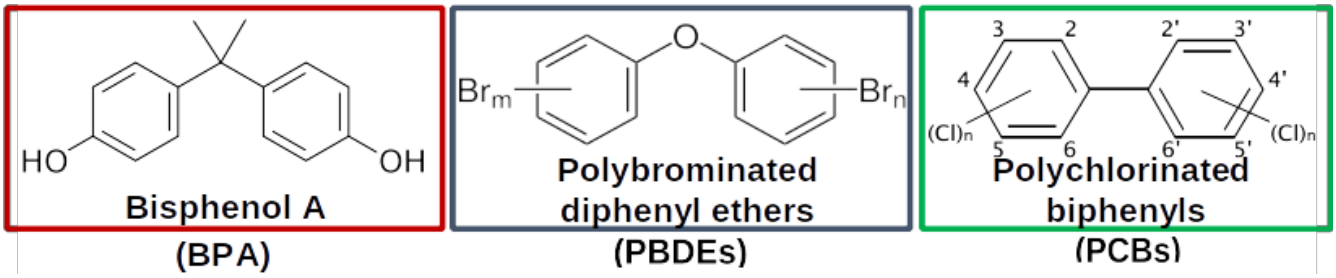

Figure 1.2. Chemical structure of BPA, PBDEs, and PCBs.

Polybrominated diphenyl ethers (PBDEs) are used as flame retardants in construction, plastics, furniture, and upholstery, electronics, and other household products (Vojta et al., 2017; Xu et al., 2019). Due to their lipophilic nature and resistance to breakdown, PBDEs are persistent in the environment and are found in meats, fish, dairy, human milk, and household dust (Babalola and Adeyi, 2018; Cade et al., 2018; Pietron et al., 2019). PBDEs were detected in serum of nearly all people who participated in the National Health and Nutrition Examination Survey (NHANES) data from 2003 to 2004 (Sjodin et al., 2008). PBDEs are linked to thyroid hormone disorders, neurotoxicity, oxidative stress in the liver, and carcinogenesis in both animal models and humans (Blanco et al., 2014; Bruchajzer et al., 2014; Yuan et al., 2017; Albert et al., 2018; Dorman et al., 2018; Dunnick et al., 2018; Gibson et al., 2018; Cowell et al., 2019; de Water et al., 2019; Hurley et al., 2019). Among the numerous congeners, PBDE-99 (BDE-99) was one of the most predominantly found xenobiotic compounds in breast milk, raising concerns for infant exposures (Hooper et al., 2007, Abdallah and Harrad, 2011).

Although multiple outcomes were reported and measured regarding acute and chronic exposures to PCBs and PBDEs, it is not known to what extent early life exposure to these two chemical classes persistently modulate the expression of important liver genes involved in xenobiotic and intermediary metabolism pathways, and how these two chemical classes

compare to the effect of early life exposure to bisphenol A (BPA), which is well-known to produce delayed onset of liver tumors in rodent models. Therefore, the goal of the present study was to test our hypothesis that similar to BPA, early life exposure to environmental contaminants PCBs or PBDEs also persistently dysregulates the transcriptome of the liver, leading to detrimental effects such as a perturbed cell cycle, as well as dysregulated drug metabolism pathways.

Gut microbiome

The gut microbiome is comprised of an estimated 38 trillion bacteria, and millions of microbial genes functionally exist in the human body (Yang et al., 2009; Sender et al., 2016; Kho and Lal, 2018). Altered gut microbiome composition may indicate altered microbial function that affects the host, and gut dysbiosis may serve as a biomarker for toxic exposure and diseases. The gut microbiome contributes to xenobiotic biotransformation via reactions including reduction and hydrolysis reactions. In addition, the gut microbiome may also indirectly modify xenobiotic biotransformation activities of the host via microbial metabolites, which can enter circulation and remotely regulate host signaling in target organs (Fu and Cui, 2017; Klaassen and Cui, 2015; Spanogiannopoulos et al., 2016). In addition to xenobiotic biotransformation, gut microbiota modulate host intermediary metabolism by producing distinct microbial metabolites such as secondary bile acids and short chain fatty acids, and modifying host metabolites such as amino acids, carbohydrates, and nucleotides (den Besten et al., 2013; LeBlanc et al., 2017; Prawitt et al., 2011, Scoville et al., 2019). It is increasingly recognized that these intermediary metabolites can be essential signaling molecules in complex human diseases. Quantifying altered endogenous metabolites in biological systems can lead to detailed physiologically-relevant biochemical status during diseases and xenobiotic exposure (Ramirez et al., 2013). Integrating microbial and metabolomic changes from toxic exposures

can provide additional insights for understanding the mechanisms of toxicity or diseases related to dysbiosis.

Liver and gut-liver axis

The liver is an essential organ for drug metabolism and nutrient homeostasis (Rui, 2014; Robey et al., 2015). Specifically, the liver serves as a central hub for bile production and excretion, and metabolism of various substances such as carbohydrates, amino acids, cholesterol, lipids, hormones, and drugs (Bechmann et al., 2012). Dysregulated inflammatory, proliferative, and apoptotic signaling are closely linked to disrupted liver function, and can lead to complex diseases, such as metabolic syndrome, obesity, type 2 diabetes, alchoholic and non-alcoholic fatty liver disease (NAFLD), fibrosis (cirrhosis), and cancer (Bechmann et al., 2012; Heindel et al., 2017). The individual steps in liver function are delicately regulated by the interplay of hormones, cellular signaling pathways, and nuclear receptors and other transcription factors, all of which having key roles in the complex functions of the liver (Bechmann et al., 2012). In response to various exposures, nuclear receptors and other transcription factors are activated in the liver, which lead to cascades of downstream transcriptional responses, including both protein-coding mRNAs and non-coding RNAs, all of which then can influence the transcription and translation of further responses (Wang and Chang, 2011; Dempsey and Cui, 2017).

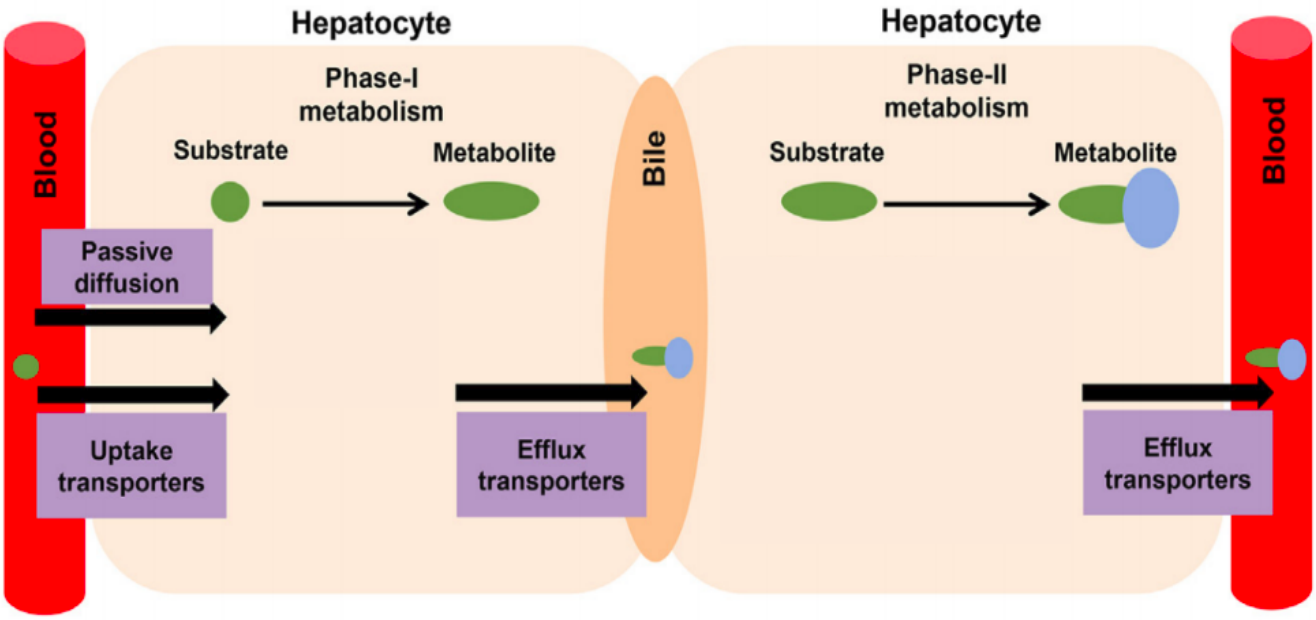

Figure 1.2. Metabolism of xenobiotics in the liver. Modified from Cui, J. Y., & Li, C. Y. (2018) Regulation of Xenobiotic Metabolism in the Liver. Ch 2. in: McQueen, C. A., Comprehensive Toxicology, Third Edition. Vol. 2, pp.168–214. Oxford: Elsevier Ltd.

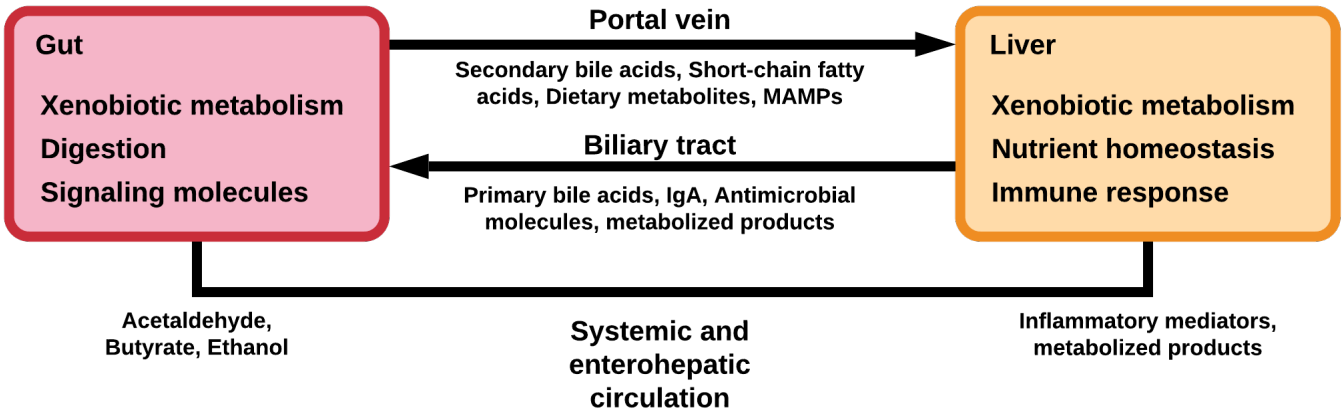

Figure 1.3. The role of the gut and liver and their interactions. Adapted from: Tripathi, A., Debelius, J., Brenner, D.A. et al. The gut–liver axis and the intersection with the microbiome. Nat Rev Gastroenterol Hepatol 15, 397–411 (2018).

Furthermore, through the biliary tract, portal vein, and systemic mediators, the gut and liver extensively communicate with one another. It has been increasingly recognized that the gut microbiome, through microbial metabolites, mediate liver functions and play a role in intermediary metabolism modification and progression of toxicant-induced liver diseases (Kolodziejczyk et al., 2019; Scoville et al., 2019; Zhang et al., 2020). Less is known regarding the interactions between the gut-microbiome and the liver from exposure to environmental contaminants, and the potential acute and persistent effect on the host xenobiotic biotransformation and intermediary metabolism.

Thesis Outline

The overall goal of this thesis is to identify the effect of environmental contaminant exposure, using PCBs and PBDEs, on the gut-liver axis and characterize the acute and persistent responses from acute exposure to these agents. Using an unbiased approach, such as RNA sequencing (RNA-Seq), the transcriptomic signatures following toxic exposure can reveal the perturbed biological pathways, which serve as an initial step in predicting the mechanisms of toxification. A primary objective of this thesis is to investigate the transcriptional changes in the liver using an unbiased RNA sequencing approach after exposure to PCBs and PBDEs, and the role of the microbiome in these changes. My central hypotheses are that the microbiome serves as a primary regulator of hepatic responses to PCB exposure; and that early life exposure to PBDEs and PCBs persistently dysregulates the transcriptome of the liver, leading to detrimental effects such as purturbed cell cycle regulation as well as dysregulated drug metabolism pathways.

Chapter 1. Introduction

Chapter 2. Polychlorinated biphenyls (PCBs), although banned for production and use since the late 1970s, are ubiquitously detected in the environment and have been linked to metabolic diseases. The gut microbiome is recognized as a critical regulator of disease susceptibility. However, little is known how PCBs and the gut microbiome interact to modulate hepatic xenobiotic and intermediary metabolism. In this chapter, to investigate the global effect of the gut microbiome on PCB mediated changes in liver gene expression and metabolism, I compared the liver transcriptomic and metabolomic and serum metabolomic responses comparing conventional (CV) and germ-free (GF) mice exposed to PCBs. In addition, I utilized 16s rDNA sequencing on CV mice to study the potential regulatory

relationships between differentially abundant bacteria and dysregulated genes and metabolites after PCB exposure.

Chapter 3. Polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs), which are classes of persistent organic pollutants, are linked to many human diseases. These chemicals are easily detected in meat, water, soil, and serum, and worrisome levels have been found in breastmilk. It is increasingly recognized that there is a sensitive developmental time window for toxic exposures that may have a life-long impact on disease risk. Although the acute and chronic responses from exposure to PBDEs and PCBs are well-established, little is known whether these contaminants have long-term effects in the xenobiotic metabolism capabilities of the liver. In this chapter, I compared the acute and persistent transcriptomic responses in livers of mice that were neonatally exposed to BDE-99 or PCBs for three consecutive days, and compared the results with those of bisphenol A, a well-known chemical that has been associated with epigenetic modification in rodent models.

Chapter 4. Conclusion and future work

Specific Aims and Hypotheses

Chapter 2.

Specific Aim: Investigate the role of the gut microbiome on the hepatic responses to PCB exposure.

Hypothesis: The gut microbiome regulates PCB-mediated changes in liver metabolic signatures and the liver transcriptome.

Chapter 3.

Specific Aim: Characterize the acute and persistent transcriptomic responses following acute neonatal exposure to environmental contaminants (BPA, PBDEs, and PCBs).

Hypothesis: Neonatal exposure to PBDEs and PCBs persistently dysregulates the transcriptome of the liver, which is the major organ for xenobiotic metabolism and nutrient homeostasis.

Chapter 2.

Gut Microbiome Critically Impacts PCB-induced Changes in Metabolic Fingerprints and the Hepatic Transcriptome in Mice

This chapter was published in Toxicological Sciences on 6/2020.

ABSTRACT

Polychlorinated biphenyls (PCBs) are ubiquitously detected and have been linked to metabolic diseases. The gut microbiome is recognized as a critical regulator of disease susceptibility, however, little is known how PCBs and the gut microbiome interact to modulate hepatic xenobiotic and intermediary metabolism. We hypothesized the gut microbiome regulates PCB-mediated changes in liver metabolic signatures and the liver transcriptome. Ninety-day-old female conventional (CV) and germ-free (GF) mice were orally exposed to the Fox River Mixture (synthetic PCB mixture, 6 or 30 mg/kg) or corn oil (vehicle control, 10 ml/kg), once daily for 3 consecutive days. RNA-Seq was conducted in liver, and endogenous metabolites were measured in liver and serum by LC-MS. Prototypical target genes of AhR, PXR, and CAR were more readily up-regulated by PCBs in CV conditions, indicating PCB-mediated changes in the hepatic transcriptome act partly through the gut microbiome. In a gut microbiome-dependent manner, xenobiotic and steroid metabolism pathways were up-regulated, whereas pathways related to the unfolded protein response (UPR; ER Stress pathway) were down-regulated by PCBs. At the high PCB dose, NADP and arginine appear to interact with drug-metabolizing enzymes (i.e. *Cyp1-3* family), which are highly correlated with the presence of *Ruminiclostridium* and *Roseburia* bacteria, providing a novel explanation of gut-liver interaction with PCB exposure. Utilizing the LINCS L1000 database, therapeutics targeting anti-inflammatory and ER stress pathways are predicted to be remedies that can mitigate PCB toxicity. Our findings demonstrate that the gut microbiota modulate PCB-mediated hepatic responses. Our study adds knowledge of physiological response differences from PCB exposure and considerations for further investigations for gut microbiome-dependent therapeutics.

INTRODUCTION

Polychlorinated biphenyls (PCBs) were widely used as electric coolants and insulators due to their chemical stability and fire resistance and were banned from production in the United States in 1979 due to their toxicity (Korrick and Sagiv, 2008). Certain congeners of PCBs bio-accumulate and are environmentally persistent with an estimated 150 million pounds of PCBs dispersed in the environment (Korrick and Sagiv, 2008). PCBs can be detected in food, soil, water, human tissues, and serum (Boesen et al., 2019; Ellsworth et al., 2015; Grimm et al., 2015; Jahnke and Hornbuckle, 2019; Jin et al., 2019; Stremy et al., 2019; Weber et al., 2018). There are several known adverse health effects of PCB exposure. Epidemiological and animal models have demonstrated dysregulation in neurodevelopment (Klocke and Lein, 2020; Schug et al., 2015; Zhang et al., 2017), interference of thyroid hormone signaling (Li et al., 2018), perturbation of the gut microbiome (Cheng et al., 2018; Petriello et al., 2018), development of type II diabetes (Dzierlenga et al., 2019; Meek et al., 2019; Rahman et al., 2019; Tornevi et al., 2019) and cancer (Leng et al., 2016; He et al., 2017; Ghosh et al., 2018; Georgiadis et al., 2019).

The microbiome is comprised of an estimated 38 trillion bacteria in the gut; millions of microbial genes functionally exist in the human body (Yang et al., 2009; Sender et al., 2016; Kho and Lal, 2018). Altered gut microbiome composition may indicate altered microbial function that affects the host, and gut dysbiosis may serve as a biomarker for toxic exposure and diseases. The gut microbiome contributes to xenobiotic biotransformation via reactions including reduction and hydrolysis reactions. In addition, the gut microbiome may also indirectly modify xenobiotic biotransformation activities of the host via microbial metabolites, which can enter the circulation and remotely regulate host signaling in target organs (Fu and Cui, 2017; Klaassen and Cui, 2015; Spanogiannopoulos et al., 2016). In addition to xenobiotic biotransformation, the gut microbiota modulates host intermediary metabolism by

producing distinct microbial metabolites such as secondary bile acids and short chain fatty acids, and modifying host metabolites such as amino acids, carbohydrates, and nucleotides (den Besten et al., 2013; LeBlanc et al., 2017; Prawitt et al., 2011, Scoville et al., 2019). It is increasingly recognized that these intermediary metabolites can be essential signaling molecules in complex human diseases. Quantifying altered endogenous metabolites in biological systems can lead to detailed physiologically-relevant biochemical status during diseases and xenobiotic exposure (Ramirez et al., 2013). Integrating microbial and metabolomic changes from toxic exposures can provide additional insights toward understanding the mechanisms of toxicity or diseases related to dysbiosis.

The liver is a critical organ in xenobiotic metabolism and nutrient homeostasis. The individual steps in liver function are delicately regulated by the interplay of hormones, cellular signaling pathways, and nuclear receptors and other transcription factors (Bechmann et al., 2012). Through the biliary tract, portal vein, and systemic mediators, the gut and liver extensively communicate with one another. The gut microbiome, through microbial metabolites, can mediate liver function and play an important role in intermediary metabolism modification and progression of toxicant-induced liver diseases (Kolodziejczyk et al., 2019; Scoville et al., 2019; Zhang et al., 2020). Using RNA-Seq, transcriptomic signatures following toxic exposure can reveal the perturbed biological pathways, which can serve as an initial step for predicting the mechanism(s) of toxicant-induced adverse outcomes. Furthermore, through comparing the transcriptomic signatures following toxicant exposure and xenobiotic-induced transcriptomic cellular responses, one may predict the potential therapeutic remedies that may mitigate the toxicity of these chemicals.

Previously, using the same PCB-exposed mice, our group has shown that PCBs produce dysbiosis and modulate bile acid metabolism in a gut microbiome-dependent manner (Cheng et al., 2018). However, the global effect of PCB exposure and gut microbiome

interactions on the hepatic transcriptome has not been characterized. Therefore, we tested our hypothesis that the gut microbiome is a critical regulator of the interface between xenobiotic biotransformation and intermediary metabolic signatures following PCB exposure.

MATERIALS AND METHODS

Chemical preparation

The Fox River PCB mixture was prepared from technical PCB mixtures as described previously (Cheng et al., 2018). Briefly, Aroclor 1242, 1248, 1254, and 1260 were prepared in pesticide grade acetone (50 mg/ml acetone) (purchased from Fisher Scientific, Far Lawn, New Jersey) and mixed at a ratio of 35:35:15:15, respectively, by weight. The acetone was then evaporated and the solute PCB mixture was used in the study upon successful congener-specific analysis as described previously (Cheng et al., 2018).

Animals and chemical exposure

The experimental design is summarized in Fig. 1A. All mice were housed according to the Association for Assessment and Accreditation of Laboratory Animal Care International guidelines (https://aaalac.org/resources/theguide.cfm). All experiments were approved by Institutional Animal Care and Use Committee (IACUC) at the University of Washington. Three-month-old conventional (CV) specific pathogen free (SPF) female C57BL/6J mice were purchased from the Jackson Laboratory (Bar Harbor, Maine) and were acclimated to the animal facility at the University of Washington at 74 degrees Fahrenheit, 26 percent humidity, and 12-hour light and dark cycle for one week prior to the experiment. Germ-free (GF) C57BL/6 breeder mice were purchased from the National Gnotobiotic Rodent Resource Center (University of North Carolina, Chapel Hill). Pups born from GF mice were raised in the Gnotobiotic Animal Core (GNAC) Facility at the University of Washington. All mice had *ad*

libitum access to standard laboratory autoclaved rodent diet (LabDiet #5010 after weaning and LabDiet #5021 for breeding; LabDiet, St. Louis, MO) and water (non-acidified autoclaved water). Animals were housed with autoclaved bedding (autoclaved Enrich-N'Pure; Andersons, Maumee, OH). Animals were monitored daily by the University of Washington Department of Comparative Medicine technicians.

Female mice were used in this study to compare results and as a follow-up with a previous publication on PCB-mediated developmental neurotoxicity, which used female mice (Kania-Korwel et al., 2010; Kania-Korwel et al., 2008a, b; Kania-Korwel et al., 2008c; Wu et al., 2015; Wu et al., 2013). Mice were exposed to corn oil (vehicle control; 10 ml/kg body weight), or Fox River mixture low dose (6 mg/kg body weight) or high dose (30 mg/kg body weight), once daily between 8 and 10 AM for 3 consecutive days. Doses of PCBs were chosen to compare results from a previous study (Cheng et al., 2018). Similar doses of PCBs have been used to identify the induction of hepatic xenobiotic metabolism-related expression, PCB disposition, and developmental neurotoxicity (Kania-Korwel et al., 2012; Kania-Korwel et al., 2008; Poon et al., 2013; Sable et al., 2011; Yang et al., 2009). The higher doses of PCBs used in this study was to detect alterations in the gut microbiome in a short time to connect to the hepatic responses to add to future mechanistic studies. These PCB doses are also below the dose of another human health relevant PCB mixture that have been found in contaminated food, namely PCB-138, PCB-153, and PCB-180 (150 μmol/kg or 43 mg/kg), which has been shown to result in a PCB plasma level of 5 μM (Choi et al., 2010), and is comparable to PCB plasma levels in an acutely exposed human population (Jensen 1989; Wassermann et al., 1979).

Mice were anesthetized with carbon dioxide narcosis, and then sacrificed via cervical dislocation 24 hours after the final dose. Whole blood was collected via cardiac puncture and transferred to a MiniCollect serum separator (Greiner Bio-One, Kremsmunster, Austria), and

was kept on ice for at least 30 min to allow sufficient time for coagulation. Serum was collected by centrifugation at 4000 rpm (1503 g) at 4°C for 20 min and was stored at −80°C until use. Tissues were harvested immediately after blood collection. Large intestinal contents was flushed out in 15 ml of ice-cold phosphate-buffered saline (PBS) that contains 0.1% dithiothreitol (DTT) (Sigma Aldrich, St. Louis, Missouri), and immediately frozen on dry ice. Microbial DNA was extracted as previously described (Cheng et al., 2018). All tissues were immediately frozen after disection in liquid nitrogen and stored at −80°C until further analysis.

RNA Isolation

Total RNA was extracted from frozen livers using RNA-Bee reagent (Tel-Test Inc., Friendswood, Texas) following the manufacturer's protocol. RNA concentrations were quantified using a NanoDrop 1000 Spectrophotometer (Thermo Scientific, Waltham, MA) at 260 nm. The integrity of total RNA samples was evaluated by agarose gel electrophoresis with visualization of 18S and 28S rRNA bands under UV light, and confirmed by an Agilent 2100 Bioanalyzer (Agilent Technologies Inc., Santa Clara, CA). Samples with RNA integrity numbers above 8.0 were used for RNA-Seq in triplicates.

RNA Sequencing

The cDNA library was constructed using a ribosomal depletion method, and reads were sequenced using a 75 bp paired end sequencing per the manufacturer's protocol (Illumina, San Diego, CA). FASTQ files were de-multiplexed and concatenated for each sample. Quality control of the FASTQ files was performed using FastQC analysis (http://www.bioinformatics.babraham.ac.uk/projects/fastqc/). Sequenced reads from the FASTQ files were then mapped to the mouse reference genome (National Center for Biotechnology Information [NCBI GRCm38/mm10]) using HISAT2 version 2.1 (Kim et al.,

2019). The sequencing alignment/map (SAM) files were converted to binary alignment/map (BAM) format using SAMtools version 1.8 (Li et al., 2009) and were analyzed by Cufflinks version 2.2.1 to estimate the transcript abundance (Trapnell et al., 2012) using Gencode mouse version 22 (vM22) gene transfer format (GTF). The abundance was expressed as fragments per kilobase of transcript per million mapped reads (FPKM) and was converted to transcripts per million (TPM). Genes were considered expressed if the transcripts per million (TPM) of each gene were greater than the total sample number and if the variance was greater than 1. Differential expression analysis was performed using Cuffdiff (Trapnell et al., 2012). The differentially expressed genes were defined as false discovery rate Benjamini-Hotchberg adjusted *p* value (FDR-BH) <0.05 in the chemical-exposed groups compared with the vehicle-exposed control group. Differentially expressed genes were also categorized and matched with genes in categories of interest (xenobiotic biotransformation, epigenetic modifiers, nuclear receptors, oxidative stress and inflammation). Gene categories were generated based on literature and gene sets from the Gene Ontology Consortium and Kyoto Encyclopedia of Genes and Genomes. If the absolute value of a transcript was greater than 1.5 fold change from controls, it was considered as an up- or down-regulated gene. Dysregulation was defined as transcripts that were either up- or down-regulated in treated vs. control mice, and/or by enterotype (CV vs. GF mice). Venn diagrams were plotted for differentially regulated genes for exposure group and enterotype using the R package VennDiagram (Chen and Boutros, 2011). Hierarchical clustering was performed using R package ComplexHeatmap (Gu et al., 2016). Lists of differentially up- and down-regulated genes were used as input for gene ontology enrichment using the R package topGO (https://bioconductor.org/packages/release/bioc/vignettes/topGO/inst/doc/topGO.pdf) for all groups with the list of genes in the unfiltered expression table was used as the background. Box and whiskers plots were created using ggplot2 (Wickham. ggplot2: Elegant Graphics for

Data Analysis. Springer-Verlag New York, 2016, http://ggplot2.org). The raw and analyzed RNA-Seq data are available Dryad: https://doi.org/10.5061/dryad.wwpzgmsgf.

Potential therapeutics were inferred by Enrichr (https://amp.pharm.mssm.edu/Enrichr/) using the Library of Integrated Network-based Cellular Signatures (LINCS) L1000 database as a reference, which is a National Institutes of Health-driven database catalog containing around 28,000 drug and small molecule induced gene expressions at different doses and time points ((Subramanian et al., 2017; Wang et al., 2016). The Enrichr analysis using the LINCS database is a computational prediction through comparing the gene expression signatures from published datasets and the dataset from the present study. Specifically, genes that were up-regulated by PCBs in a gut microbiome-dependent manner were queried against the chemicals that down-regulated the same genes; whereas genes that were down-regulated by PCBs in a gut microbiome-dependent manner were queried against the chemicals that down-regulated the same genes. The fundamental assumption of this analysis is that chemicals that reverse the PCB-mediated gene expression signatures may serve as candidate therapies to mitigate PCB toxicity in liver. The top 15 hits were shown, with a false discovery rate (FDR) below 0.05.

Serum and Liver Preparation for Aqueous Metabolite Measurements

Frozen serum samples stored at −80°C were thawed overnight at 4 °C. Fifty μL of each serum sample were placed in a 2 mL Eppendorf tube. Two hundred fifty μL of MeOH were added for the initial step for protein precipitation and metabolite extraction. Each liver sample (10 mg) was homogenized in 200 μL water in an Eppendorf tube using a Bullet Blender homogenizer (Next Advance, Averill Park, NY). Eight hundred μL of MeOH were added, and after vortexing for 10 seconds, the samples were stored on dry ice for 30 minutes. The samples were then sonicated in an ice bath for 10 minutes. Each serum and liver sample was

then vortexed for 10 seconds and stored at −20 °C for 30 minutes, followed by centrifugation at 14,000 rpm for 10 minutes at 4 °C. The supernatants (200 µL for serum and 800 µL for liver) were collected into a new Eppendorf vial and dried under vacuum using an Eppendorf Vacufuge (Eppendorf, Hauppauge, NY). The dried samples were reconstituted in 200 µL of 40% PBS/60% acrylonitrile (ACN). Liver and serum metabolomics analyses were performed in quadruplicates.

The targeted LC-MS/MS method used here was modeled after that developed and used in a growing number of studies (Carroll et al., 2015; Shi et al., 2019; Zhu et al., 2014). Briefly, all LC-MS/MS experiments were performed on an Agilent 1290 UPLC-6490 QQQ-MS system (Santa Clara, CA). Each sample was injected twice for analysis, with 10 µL using the negative ionization mode and 4 µL using the positive ionization mode. Both chromatographic separations were performed using the hydrophilic interaction chromatography (HILIC) mode on a Waters XBridge BEH Amide column (150 x 2.1 mm, 2.5 µm particle size, Waters Corporation, Milford, MA). The flow rate was set to 0.3 mL/min, auto-sampler temperature was kept at 4 ℃, and the column compartment was set at 40 ℃. The mobile phase was composed of Solvents A (10 mM ammonium acetate, 10 mM ammonium hydroxide in 95% H_2O/5% ACN) and B (10 mM ammonium acetate, 10 mM ammonium hydroxide in 95% ACN/5% H_2O). After the initial 1 min isocratic elution of 90% B, the percentage of Solvent B decreased to 40% at t=11 min. The composition of Solvent B was maintained at 40% for 4 min (t=15 min). The percentage of B gradually went back to 90%, and the next injection was prepared.

The mass spectrometer is equipped with an electrospray ionization (ESI) source. Targeted data acquisition was performed in multiple-reaction-monitoring (MRM) mode. We monitored 118 and 160 MRM transitions in negative and positive mode, respectively (278 transitions in total). The whole LC-MS system was controlled by Agilent Masshunter

Workstation software (Santa Clara, CA). The extracted MRM peaks were integrated using Agilent MassHunter Quantitative Data Analysis (Santa Clara, CA).

Relative abundance values for each metabolite in liver and serum were compared using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test using base R (R Core Team, 2019). Venn Diagrams and heat maps were built using differentially abundant metabolites in liver and serum using packages available in VennDiagram (Chen and Boutros, 2011). Gene-metabolite network analysis was performed using differentially abundant metabolites and differentially regulated genes per each exposure group and enterotype using Network explorer function in MetaboAnalyst (Chong et al., 2018). Spearman correlation for differentially abundant metabolites and differentially regulated genes were plotted using ComplexHeatmap in R (Gu et al., 2016) for germ-free groups. Box and whiskers plots were created using ggplot2 (Wickham. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York, 2016).

16S rDNA Sequencing and data analysis

The V4-amplified rDNA sequencing FASTQ files were obtained as described previously (Cheng et al., 2018, Dryad: https://doi.org/10.5061/dryad.wwpzgmsgf). The paired-end sequence reads, in triplicate, were merged, de-multiplexed, quality-checked, and chimera-filtered using QIIME 2 (Vazquez-Baeza et al., 2013; Mandal et al., 2015; Callahan et al., 2016; Vazquez-Baeza et al., 2017; Hall and Beiko, 2018). Community composition and (Bokulich et al., 2013) the Silva 99 version 132 reference (Quast et al., 2013) using QIIME2 (Hall and Beiko, 2018). The OTU table annotated with classified bacteria information was read into R for further analysis (R Core Team, 2019). Negative binomial differential abundance testing was performed using the R package DESeq2 (Love et al., 2014) following pipelines in phyloseq (McMurdie and Holmes, 2013). Differentially abundant bacteria and correlation

tables of differentially abundant bacteria (relative abundance of OTU) and metabolites, and differentially regulated hepatic genes (Spearman correlation) were plotted using ComplexHeatmap (Gu et al., 2016).

RESULTS

Effect of PCB exposure on the hepatic transcriptome as well as hepatic and serum metabolome in CV and GF mice

Principal component analysis (PCA) was performed on the Z-normalized expression and abundance matrix and was labeled by enterotype and exposure group (Fig. 1B). Clusters on normalized expression levels on the principal component space showed that enterotype (i.e. presence or absence of the gut microbiome) was the primary factor in grouping the transcriptomic and metabolomic signatures within the same exposure. Although the coordinates of GF mice exposed to the PCB high dose were distinct in the first principal component from the other GF exposure groups, overall, no clear clusters were formed among PCB-exposed groups within the same enterotype.

Venn diagrams were used to visualize the commonly and differentially regulated genes and abundant metabolites between PCB-exposed group and the vehicle-expose group of the same dose and enterotype (Fig. 1C). Regarding the liver transcriptome, exposure to PCBs had a greater effect on the CV mice, having more differentially regulated genes than the GF mice (Fig. 1C top panel). Regarding the effect of the two PCB doses, the number of differentially regulated genes was higher in the high PCB dose group than the low PCB dose group in livers of CV mice; however, in livers of the GF mice, the low PCB dose differentially regulated more genes than the high PCB dose. The majority of genes were uniquely regulated by PCBs in different enterotype and PCB dose groups, with only five genes commonly differentially regulated, namely *Cyp1a2*, *Arntl*, *G6pc*, and *Sult2a1* (Table S1a-Table

S1d). In the liver transcriptome of CV mice, most genes were commonly regulated between the low and high PCB doses (e.g. *Cyp2a5*, *Mt1*, *Mt2*, *Slc16a1*). Interestingly, the bile acid metabolizing enzyme *Cyp8b1* was differentially regulated by both of the two PCB doses only in GF conditions (Table S6).

Regarding the liver metabolome of amino acids, carbohydrates, and nucleotides, in general, GF mice had more differentially regulated metabolites following PCB exposure than CV mice that were exposed to the same dose of PCBs. The differentially regulated metabolites were not shared between the two enterotypes or the two PCB doses (Fig. 1C middle panel, Fig. S2A, and Table S6B). Specifically, the high PCB dose exposed GF mice had the most differentially regulated metabolites (18), followed by the high PCB dose exposed CV mice (8), whereas the PCB low dose exposed CV and GF mice both had only 3 differentially regulated metabolites. Aminoisobutyric acid and dimethylglycine were commonly regulated by PCB exposure in the livers of CV mice, as well as raffinose, glucose-6 phosphate and fructose-6 phosphate in the livers of GF mice (Fig. 1C middle panel, Fig. S2A, and Table S6A).

The serum metabolome, similar to the liver metabolome, showed no commonly regulated metabolites in CV and GF mice (Fig. 1C bottom panel, Fig. S2B, and Table S6C). In CV mice, the low PCB dose did not alter any serum metabolites, whereas the high PCB dose altered 6 serum metabolites (levulinic acid, 6-methyl-DL-tryptophan, serine, asparagine, proline, and urocanic acid). In GF mice, the low PCB dose uniquely altered 4 serum metabolites, namely mucic acid, mannose, norvaline, and cytosine and the high PCB dose uniquely altered 1 serum metabolite, 2-hydroxyphenylacetic acid. Glucuronic acid was commonly regulated in serum of low and high PCB dose exposed GF mice.

PCB-mediated functional changes predicted from the transcriptomic response in livers of CV and GF groups

As shown in Figures 2A-2B, Gene Ontology (GO) enrichment was performed to determine the transcriptional change of biological functions using up- and down-regulated genes. For both the low and high PCB doses, up- and down-regulated GO terms were more highly enriched in livers of the CV than GF mice, indicating that the presence of the gut microbiome facilitates PCB mediated effects. As shown in Figure 2A, up-regulated GO terms were mostly comprised of steroid or xenobiotic metabolism related pathways, and there appeared to be similarities in the predicted changes in pathways between the low PCB dose exposure. For both CV (Fig. 2A top) and GF (Fig. 2A bottom) mice, the enrichment significance ($-\log_{10}$P-value) followed a dose-response pattern. For the down-regulated GO terms, responses to misfolded protein (UPR) were the top enriched terms, and this enrichment disappeared in the GF group (Fig. 2B), suggesting that the gut microbiome may promote PCB-induced ER-stress (Cybulsky, 2017; Gardner et al., 2013; Rashid et al., 2015). For the GF group exposed to the low dose PCBs (Fig. 2A bottom left), temperature homeostasis was the only significantly down-regulated enriched term due to the down-regulation in heat shock protein encoding genes and no significantly down-regulated GO terms were found for GF mice exposed to the PCB high dose (Fig. 2A bottom right).

Effect of PCB exposure on the hepatic expression of xenobiotic-sensing transcription factor target genes in CV and GF mice

As shown in Fig. 2C, the prototypical target genes of the major xenobiotic-sensing transcription factors aryl hydrocarbon receptor (AhR), constitutive androstane receptor (CAR), and pregnane X receptor (PXR), were more readily up-regulated by PCBs in livers of the CV mice as compared to the GF mice (Fig 2C). Specifically, the mRNA transcripts of *Cyp1a1* and

Cyp1a2, which are the prototypical target genes of AhR (Flaveny et al., 2010; Lo and Matthews, 2012), were more up-regulated by PCBs in the livers of CV mice than in GF mice; this trend was more prominent at the high PCB dose. Similarly, the mRNAs of the CAR prototypical target genes in the *Cyp2* family (i.e. *Cyp2b10*, *Cyp2c50*) (Cui and Klaassen, 2016; Kiyosawa et al., 2008; Maglich et al., 2003) had higher PCB-mediated fold induction in livers of CV mice, and the induction change was also more prominent at the high PCB dose. The mRNAs of the prototypical target genes for PXR in the *Cyp3* family (Cui and Klaassen, 2016; Kiyosawa et al., 2008; Maglich et al., 2003), including *Cyp3a16* and *Cyp3a41a*, were more induced by the low PCB dose in CV mice than in GF mice, whereas the high PCB dose did not alter these *Cyp3a* gene isoforms in CV livers, but moderately up-regulated these genes in GF livers.

Taken together, our data at the mRNA level showed that the presence of the gut microbiome is necessary for PCB-mediated up-regulation of the prototypical target genes of major xenobiotic-sensing transcription factors.

Differentially abundant bacteria from exposure to PCBs

V4-amplified 16s rDNA sequencing was conducted to study the gut microbiota changes in the large intestinal fecal pellets of CV mice in response to exposure to PCBs as we described before (Cheng et al., 2018). Overall, as seen in Figure 3B, the PCB low dose had a larger effect on bacterial abundance than the PCB high dose. The low PCB dose uniquely down-regulated Ruminococcaceae, Muribaculaceae, Lachnospiraceae *ASF356*, and two taxa in Lachnospiraceae *UCG-001,* while it uniquely up-regulated *Akkermansia muciniphila*, *Erysipelatoclostridium*, *Ruminiclostridium* 6, *Enterohabdus*, and *Clostridiales* bacterium CIEAF 016. The high PCB dose uniquely down-regulated *Dubosiella newyorkensis*, *Anaerotruncus*, *Acetatifactor*, *Turicibacter*, and Muribaculaceae, while it uniquely up-regulated

Ruminococcaceae, *Clostridium sp.* Clone-44, *Lachnospiraceae* GCA-900066575, and *Lachnospiraceae A2*. *Clostridium scindens*, *Ruminococcaceae* UCG-013, *Oscillibacter*, *Roseburia*, Family XIII UCG-001, *Clostridium sp*. Culture-1 were up-regulated by both the low and the high PCB doses. There were no bacterial species that were commonly down-regulated by the low and the high PCB dose, or regulated in opposite directions by the two PCB doses.

Comparison between CV and conventionalized mice

Figure S3 shows the microbiome composition for the top 15 most abundant bacteria in the colon at the family level for CV (n = 3) and conventionalized mice (GF mice bred in CV conditions for 2 weeks for microbiome colonization, n = 2). The top family included *Clostridlaceae*, *Eryslpelotrichaceae*, *Lachnospiraceae*, *Lactobacillaceae*, *Ruminococcaceae*, *S24-7*, *Staphylococcaceae*, and an unidentified family in the *Clostridales* order.

Metabolite changes in response to PCBs for CV and GF groups

Endogenous metabolites in liver (Fig. 3C, 4A, and Fig. S2A) and serum (Fig. 3D, 4B, and Fig. S2B) were measured and analyzed to investigate the effect of the gut microbiome on PCB-mediated changes on essential endogenous metabolites for energy metabolism. In general, the PCB-mediated differences in relative abundances for metabolites were greater in liver than serum in both CV and GF mice. Dysregulated liver metabolites for the CV group exposed to PCBs were mainly from the amino acid metabolism pathways, including acetylcarnitine, adenylosuccinate, 3-hydroxybutyric acid, aminoisobutyric acid, and dimethylglycine (Fig 3C). Specifically, in livers of CV mice exposed to the PCB high dose, arginine was down-regulated and acetylcarnitine was up-regulated, dose-dependently. Adenylosuccinate, which is involved in nucleotide metabolism, and shikimic acid, which is a

metabolite from bacteria, were up-regulated by PCB exposure dose-dependently in the CV mice and were significant in the PCB high dose group. The cofactor NADP dose-dependently increased with exposure to PCBs in CV mice. The abundances of two liver metabolites from butyric acid metabolism, namely 3-hydroxybutyric acid (down-regulated in CV PCB low) and aminoisobutyric acid (up-regulated in CV mice in either doses) were altered only in CV mice. Dimethylglycine, a derivative of glycine, was up-regulated by PCBs only in livers of CV mice (Fig. 3C).

In serum, as shown in Figure 3D, amino acid metabolism-related serum metabolites, namely, 6-methyl-DL-tryptophan, serine, asparagine, proline, and urocanic acid were up-regulated in CV mice exposed to the PCB high dose. Levulinic acid, a metabolite from cellulose degradation, was up-regulated from PCB high dose in CV mice in serum. Asparagine was up-regulated in CV mice exposed to the PCB high dose (Fig. S2B). No metabolites were dysregulated from PCB low exposure in the CV group.

To establish the regulatory relationships between differentially expressed genes and differentially abundant metabolites (Fig. 3C and D, and Fig. 5A and B), gene-metabolite integrated analysis on MetaboAnalyst was used as described previously (Chong et al., 2018). Links between significantly altered hepatic gene expression and liver metabolites by PCB exposure were only found in CV mice exposed to the PCB high dose (Fig. 3E). The up-regulation of many P450s and other phase-I xenobiotic biotransformation enzymes (except for *Cyp3a44*), through the utilization of NADPH, induced the abundance of NADP. In addition, an association between arginine abundance and the pro-inflammatory cytokine Il1b gene expression was observed (El-Sayed et al., 2019; Fultang et al., 2019; Pulugulla et al., 2018, Weldy et al., 2012).

In GF mice, altered hepatic metabolites were mostly from carbohydrate metabolism or nucleotide metabolism (Fig 4A). Uridine, adenosine, and 2-deoxycytidine were up-regulated

in GF mice exposed to the PCB high dose in the liver. Uridine diphosphate N-acetylglucosamine (UDP-GlcNAc), a nucleotide sugar and a coenzyme involved in cell maintenance regulation (Love and Hanover, 2005), was up-regulated in the livers of GF group exposed to the PCB high dose. The relative abundance for dextrose (also known as D-glucose) in the liver was lower for both PCB doses in GF mice, but only down-regulated in the GF PCB high group. The relative abundance of the hepatic glucose-6 phosphate (G6P) and fructose-6 phosphate (F6P) were up-regulated for both PCB doses in the GF group. In addition, NAD, an essential cofactor, was significantly greater for PCB high dose in the GF group. Adenosyl-L-homocysteine, dopamine, inosine, and nicotinamide were up-regulated in GF mice exposed to the PCB high dose (Fig. 4A). Guanosine triphosphate (GDP), 2,3-dihydroxybenzoic acid, 4-methylvaleric acid, and allantoin were up-regulated by GF mice exposed to the PCB high dose and raffinose was down-regulated by GF mice exposed to either PCB dose (Fig. S2).

In serum, cytosine was up-regulated by the low PCB dose in GF mice (Fig. S2A). Carbohydrate metabolism-related metabolites were up-regulated only in GF mice, including mucic acid and mannose (up-regulated in GF PCB low) and glucuronic acid (up-regulated in GF PCB low or high) (Fig. 4B and Fig. S2B). Norvaline (isomer of valine) was up-regulated in GF mice exposed to the low PCB dose and 2-hydroxyphenylacetic acid, a metabolite of phenyalanine, was down-regulated in GF mice exposed to the PCB high dose (Fig. 4B and Fig. S2B).

Highly correlated changes between differentially abundant bacteria and metabolites from exposure to PCBs

Spearman's correlation analysis was conducted to determine the association between gut dysbiosis and differentially regulated metabolites by PCB exposure in CV mice (Fig. 3B

and Table S5A and B). Only the highly correlated relationships with an absolute value of ρ > 0.8 with FDR-adjusted *p*-value < 0.1 were considered significant correlations (indicated by the pink background in the cell).

In the liver, Family XIII UCG-001 (-0.81) and *Clostridium sp.* Culture-1 (-0.83) were both negatively associated with 3-hydroxybutyric acid. In addition, Family XIII UCG-001 was positively correlated with aminosobuturic acid (0.88) and dimethylglycine (0.81). *Clostridium sp.* Culture-1 was negatively associated with the hepatic 3-hydroxybutyric acid (-0.83). *Lachnospiraceae A2* was positively associated with arginine (0.90), which was negatively associated with *Clostridium sp.* Clone-44 (-0.82). Interestingly, *Anaerotruncus* was negatively associated with the majority (6 out of 9 in CV mice) of dysregulated liver metabolites, namely acetylcarnitine (-0.80), adenylosuccinate (-0.84), aminoisobutyric acid (-0.85), dimethylglycine (-0.86), NADP (-0.85), and shikimic acid (-0.82). In addition, *Turicibacter* was negatively associated with shikimic acid (-0.84).

As seen in Figure 5B and Table S5A, in serum, *Roseburia* was positively associated with serine (0.87). *Roseburia* was positively correlated and *Lachnospiraceae* A2 was negatively correlated with levulinic acid (0.83 and -0.80, respectively). *Clostricium sp.* Clone-44 was positively associated with 6-methyl-DL-tryptophan (0.82), and proline (0.84). Furthermore, *Clostridium sp.* Clone-44 was positively associated and *Dubosiella newyorkensis* was negatively associated with serum urocanic acid (0.82 and -0.86, respectively). *Anaerotruncus* was negatively associated with proline (-0.82), serine (-0.86), and urocanic acid (-0.82).

Transcriptomic response involved in critical pathways in livers of CV and GF groups following PCB exposure

Specific examples of important hepatic pathways are presented in Figure 5A and 5B. Dysregulated genes were grouped into categories to determine the regulation of the following pathways: epigenetic modification factors (Epi.), inflammation and oxidative stress, nuclear receptors (NR), phase-I and –II drug metabolizing enzymes, and transporters. In general, unique expression patterns were observed comparing each enterotype (Fig. 5A and 5B). The mRNA of *Nr0b2* (also known as SHP) was down-regulated by the high PCB dose in both CV and GF mice; however, the degree of decrease was greater for the GF group (Fig. 5A). None of the gene categories shown in Figure 3C were commonly regulated by both enterotypes and doses, and no genes in these categories were uniquely regulated for GF mice. Most of the genes were dysregulated for the CV group exposed to PCBs for both doses in the inflammation and oxidative stress, and nuclear receptor categories, which included *Il6ra*, *Mt1*, *Mt2*, *Il1b*, *Nr1d1*, and *Nr1d2* (Fig. 5A).

For genes that are important in xenobiotic biotransformation (Fig. 5B), similar to the gene expression pattern shown in Figure 3C, gene induction by PCBs occurred more readily in CV mice than in GF mice. Specifically, as shown in Fig. 4D top cluster, genes that encode transporters in liver were more regulated by PCBs of CV mice than the GF mice. In the CV group exposed to PCBs, manganese efflux transporter (*Slc30a10*) and proton-coupled monocarboxylate transporter (*Slc16a1*) were commonly down-regulated in livers of CV mice by either dose of PCBs. The membrane glycoprotein transporter involved in neutral amino acid transport (*Slc3a1*) and sodium/bile acid cotransporter (*Slc10a2* [*Ntcp*]) were up-regulated by the PCB high dose in livers of the CV mice. Sodium-dependent phosphate transporter (*Slc17a2*) and proton-coupled peptide transporter (*Slc15a2*) were uniquely down-regulated by PCB high dose and PCB low dose in CV mice, respectively. ATP-binding cassette subfamily G, member 8 (*Abcg8* [sterolin-2]), which is important for sterol regulation and excretion, cationic amino acid transporter 2 (*Slc7a2*), multidrug resistance-associated protein 4 (*Abcc4*

[*Mrp4*]), and lysosomal catabolite transporter (*Slc46a3*) were up-regulated in CV mice exposed to the PCB high dose. Sodium-independent organic anion transporter *Slco1a1* (Oatp1a1) was down-regulated in CV mice exposed to the PCB high dose and GF mice exposed to PCB low dose. The lysosomal proton pump *Atp6v0d2* was up-regulated for CV mice exposed to either PCB dose, however it was down-regulated in GF mice exposed to the PCB high dose.

For genes that encode phase-I enzymes (Fig 5B middle cluster), in general, genes in the *Cyp1*, *Cyp2*, and *Cyp3* families are known to be important for drug metabolism and *Cyp4* families are involved in fatty acid metabolism. Except for *Cyp1a2* (prototypical target gene for AhR), *Cyp2c29*, and *Cyp2b10* (prototypical target gene for CAR), most of the genes in the *Cyp1* and *Cyp2* families were uniquely differentially regulated in the CV group, including *Cyp1a1*, *Cyp2c54*, *Cyp17a1*, and *Cyp2a5*. Other phase-I drug metabolizing enzymes, such as aldehyde dehydrogenase (*Aldh1a7*), P450 oxidoreductase (*Por*), NAD(P)H dehydrogenase [quinone] (Nqo1), carboxylesterase (*Ces1b* and *Ces2c*), and short chain dehydrogenase/reductase (*Sdr9c7*) followed the same trend as *Cyp1* and *Cyp2* families, being more up-regulated by PCBs in livers of CV mice than in livers of GF mice. *Cyp26b1* (involved in retinoic acid metabolism) and *Cyp4a14* were down-regulated in CV mice exposed to the PCB high dose and *Cyp2j9* (involved in arachidonic acid metabolism) was down-regulated for CV mice exposed to either PCB dose. Genes in the *Cyp3* family (*Cyp3a16* and *Cyp3a41a*) were up-regulated in CV mice exposed to the low dose PCBs and either dose for GF mice. *Cyp26a1* was up-regulated for mice exposed to the PCB low dose for both enterotypes.

Interestingly, as seen in the bottom cluster on Figure 5B, for the phase-II conjugation enzymes, genes in the glutathione-*S*-transferase (*Gst*) category were uniquely up-regulated by CV mice, with the exception of *Gstm3* (up-regulated by CV mice in either PCB dose and

GF mice exposed to PCB low dose), whereas genes in the sulfotransferase (*Sult*) 1 and 2 categories, except the *Sult2a1* mRNA (up-regulated by either enterotype or dose) were up-regulated by GF mice. The *Gstp1* mRNA was up-regulated by the PCB high dose in both enterotypes. For the up-regulated phase-II enzymes that are shared between enterotypes, baseline relative expression (mice exposed to corn oil control) and the degree of induction were also different, such that the *Gstm3* mRNA was lower, while *Gstp1* and *Sult2a1* mRNAs were higher in CV than GF mice. In summary, the dysregulated genes show that the PCB-mediated liver transcriptome is regulated in part by the gut microbiome.

Correlation of differentially regulated intestinal bacteria and expression of hepatic xenobiotic-biotransformation related genes following PCB exposure

To investigate to what extent the gut microbiome regulates xenobiotic biotransformation-related functions upon responses to PCB toxic exposure, we focused on the potential relationship between differentially regulated genes and differentially abundant bacteria as examined using Spearman's correlation (Fig. 5C and D, and Table S5C and D). In the phase-I category (Fig. 5C left panel), *Clostridium scindens* was negatively associated with *Cyp2b10* and *Cyp2c50* (-0.85 for both genes). *Ruminiclostridium* 9 was positively associated with *Cyp1a2*, *Cyp2c54*, and *Nqo1* (0.82, 0.83, and 0.85, respectively). *Roseburia* was positively associated with *Ces2c*, *Cyp1a2*, *Cyp2c54*, *Cyp2c50*, *Nqo1*, and *Por* (0.93, 0.87, 0.88, 0.82, 0.9, and 0.85, respectively). *Anaerotruncus* was negatively associated with *Ces2c*, *Cyp1a2*, *Cyp2c29*, *Ces1b*, and *Cyp1a1* (-9.84, -0.86, -0.91, -0.83, and -0.91, respectively), and positively associated with *Sdr9c7* (0.91). *Lachnospiraceae* A2 was negatively associated with *Cyp2c54*, *Cyp2c50*, and *Por* (-0.81, -0.85, and -0.84, respectively). *Dubosiella newyorkensis* was negatively associated with *Cyp2c29*, *Ces1b*, *Cyp1a1* (-0.85 for all three genes), but positively associated with *Cyp26b1* and *Sdr9c7* (0.81 for both genes). *Clostridium sp.* Clone-

44 was positively associated with *Ces1b*, *Cyp1a1*, and *Cyp2c55* (0.82, 0.82, and 0.84, respectively).

In the Phase-II category (Fig. 5C right panel), *Dubosiella newyorkensis* was negatively associated with *Gstm2* (-0.83) and *Gstm1* (-0.81). In addition, *Anaerotruncus* was negatively associated with *Gstm1* (-0.84).

For transporters (Fig. 5D left panel), *Roseburia* was negatively associated with *Atp2b2* (-0.93) and both *Roseburia* and *Ruminiclostridium* 9 were negatively associated with *Slc16a1* (-0.87 and -0.82, respectively) and *Slc30a10* (0.87 for both). However, *Anaerotruncus* was associated with both genes (0.86 and 0.80, respectively), in addition to *Atp2a2*, *Atp2b2*, *Atp6v0d2*, *Slc17a2*, and *Slc3a1* (0.91, 0.84, -0.82, 0.89, and -0.86, respectively). Family XIII UCG-001 was associated positively with *Atp6v0d2* (0.85), and negatively with *Slc17a2* and *Atp2a2* (-0.88 and -0.90, respectively). *Dubosiella newyorkensis* was positively associated with *Slc17a2*. *Turicibacter* was positively associated with *Atp2b2* (0.85) and *Clostridium sp.* Clone-44 was positively associated with *Slc10a2* (0.82).

In the immune response, oxidative stress, and nuclear receptors categories (Fig. 5D right panel), *Roseburia* and Family XIII UCG-001 were negatively associated with *Cldn1* (-0.88 and -0.85, respectively). *Ruminococcaceae* and *Clostridium sp.* Clone-44 were positively association with *Socs2* (0.87 and 0.84, respectively). *Lachnospiraceae* UCG-001 Ambiguous was associated negatively with *Cebpb* (0.83) and positively with *Hmox1* (0.81). *Clostridium scindens* was positively associated with *Icam1* (0.87) and *Il1b* (0.9). *Oscillibacter* uncultured was negatively associated with *Il1b* (-0.95) and *Clostridium sp.* Culture-1 was negatively associated with *Il6ra* (-0.87).

Potential therapeutics to target gut microbiome-dependent PCB-induced toxicity

To find potential therapeutics against the gut microbiome-dependent PCB effects, we performed an inverse correlation analysis between dysregulated genes from PCB low or high dose exposure and drugs and small molecule response were done using the LINCS L1000 database (Fig. 6). For example, up-regulated genes unique to CV mice exposed to the PCB low dose compared to GF PCB low were associated with target genes that were down-regulated from drugs and other small molecule exposure to human cell lines (inverse association). The top drugs ranked by the combined score in the up-regulated signatures using down-regulated genes from PCB exposure in both doses included geldanamycin, radicicol, and NVP-AUY922, which are antitumor compounds that potently inhibit HSP90 function to regulate cell and growth, and angiogenesis (He et al., 2013; Jensen et al., 2008; Schulte et al., 1998)(Fig. 6A and C). In addition, as seen in Fig. 6A, tanespimycin, another drug that inhibits HSP90, was observed in the top drug list for the CV PCB low dose (Yang et al., 2009). Other top compounds for down-regulated gene expression signatures for CV PCB low included ABT-737 (Bcl-2 and Bcl-XL inhibitor), celastrol (sitruin 1 inhibitor), PD-0325901 (MEK inhibitor), AS-601245 (JNK inhibitor), PF-477736 (cell cycle checkpoint kinase 1 [chk1] inhibitor), lapatinib (epidermal growth factor receptor [EGFR] inhibitor), QL-XII-47 (BTK kinase inhibitor), as well as KIN001-043, NRD-K41859756 and NCGC00183401-01, for which the mechanism of actions are not defined (Bryant et al., 2014; Cerbone et al., 2012; de Wispelaere et al., 2017; Huang et al., 2009; Medina and Goodin, 2008; Parrondo et al., 2013; Venkatesha and Moudgil, 2016). Drugs targeting the gut microbiome-dependent down-regulated genes from PCB high exposure included QS11 (GTPase activating protein of ADP-ribosylation factors [ARFGAPs] inhibitor), tipifarnib (farnesyltransferase inhibitor), ZSTK-474 (IFNg and IL-17 proliferation inhibitor), GSK690692 (pan-AKT inhibitor), CAY10594 (phospholipase D2 inhibitor), as well as PF-43758309, BRD-K84203638, and BRD-

K31706415 (unknown mechanisms) (Kong and Yamori, 2010; Lee et al., 2019; Levy et al., 2009; Reid and Beese, 2004; Zhang et al., 2007).

Down-regulated drug response signatures using up-regulated genes from PCB exposure were the same for both PCB doses (Fig. 6B and D). Nilitinib, a transduction inhibitor targeting BCR-ABL oncogene, c-kit (CD117), and platelet-derived growth factor receptor (PDGF), was among the top potential therapeutics to counter-regulate up-regulated genes related to actin function (i.e. actin alpha2 [*Acta2*], Gelsolin [*Gsn*]), xenobiotic biotransformation (i.e. nicotinamide N-methyltransferase [*Nnmt*]), immune response (i.e. immunoglobulin kappa constant [*Igkc*]), and lipid/steroid metabolism (i.e. squalene epoxidase [*Sqle*], hydromethylglutaryl-CoA synthase [*Hmgcs1*], methylsterol monooxygenase 1 [*Msmo1*], 7-dehydrocholesterol reductase [*Dhcr7*]) from PCB low and high exposure groups (Blay and von Mehren, 2011) (Fig. 6B and D). Additionally, neratinib (human epidermal growth factor inhibitor 2 [Her2] and EGFR inhibitor), dasatinib (dual BCR-ABL and Src family tyrosine kinase inhibitor), sorafenib (Raf kinase, PDGF, VEGFR, and c-kit inhibitor), GW-843682X (ATP-competitive polo-like kinase 1 and 3[PLK1 and 3] inhibitor), sunitinib (multi-receptor tyrosine kinase inhibitor), WYE-125132, AZD-8055, torin 1, and sirolimus (ATP-competitive mTOR inhibitor), RAF265 (B-raf kinase and VEGFR2 phosphorylation inhibitor), CX-5461 (p53 stabilizer), QL-XII-47 (selective BTK inhibitor), and GSK-429286A (selective Rho-kinase inhibitor) were inversely correlated with the up-regulated gene expression signatures from PCB exposure at both doses (Chresta et al., 2010; Dumont and Su, 1996; Huang et al., 2017; Mena et al., 2010; Schade et al., 2008; Segovia-Mendoza et al., 2015; Thompson et al., 2017).

DISCUSSION

The present study demonstrates that the gut microbiome is a necessary component in mediating PCB-induced effects on the liver transcriptome and metabolome of liver and serum in mice (Fig. 7 and Table S7). The presence of the gut microbiome drives PCB-mediated activation of xenobiotic-sensing transcription factors AhR, CAR, and PXR, evidenced by a more prominent increase in the expression of their prototypical target genes, as well as a more up-regulated GO involved in xenobiotic biotransformation. In addition, the presence of the gut microbiome lead to the down-regulation of the GO terms involved in response to misfolded proteins, which indicates the contribution of the gut microbiome in PCB-mediated ER stress. Regarding intermediary metabolism, the presence of the gut microbiome promotes PCB-mediated up-regulation of amino acid metabolites, but suppresses the metabolites involved in nucleotide metabolism. In particular, the genus *Anaerotruncus* as well as the short-chain fatty acid-producing bacteria *Roseburia* and *Ruminiclostridium* were highly associated with hepatic xenobiotic biotransformation enzymes and metabolites in liver and serum. Taken together, our findings demonstrate that the presence of the gut microbiota drives PCBs-mediated toxic responses including bioactivation of xenobiotics, ER stress, and dysregulation of intermediary metabolism.

Gut microbiome-mediated transcriptomic responses from PCB exposure

The gut microbiome mediates the activation of transcription factors and their targets (Bjorkholm et al., 2009; Richards et al., 2019), which is possibly due to the metabolite interaction with the biochemical environment (Venkatesh et al., 2014). The PCB-mediated up-regulation of the prototypical target genes of AhR, CAR, and PXR act partly through the gut microbiome, indicating that PCBs may increase microbial metabolites that can further activate these host receptors, or the gut microbiome may convert PCBs to more potent

ligands for these host receptors. In contrast to PCBs, we have previously shown that the absence of gut microbiota potentiated the liver to PBDE congeners (PBDE-47 and 99), and mediated up-regulation of the prototypical target genes of these host receptors (Li et al., 2017a), suggesting that the two classes of persistent environmental toxicants (PCBs and PBDEs) may modify the gut-liver axis through two distinct mechanisms.

To note, the xenobiotic-sensing transcription factor genes themselves were not altered in livers of GF mice. Previous studies have shown that the activity of host xenobiotic-sensing transcription factors, such as AhR, PXR, and CAR can alter the composition of the gut microbiome (Dempsey et al., 2019; Hudson et al., 2017). To the best of our knowledge, the microbial AhR and CAR receptors have not been known in the literature. Even if these microbial receptors do exist, it is unlikely they will contribute to the up-regulation of host hepatic AhR- and CAR-target genes, because these receptors are expected to interact with portions of the PCB mixtures. The present study provides novel findings that the absence of the gut microbiome greatly attenuated the expression of the prototypical targets, which indicates that the effect of PCBs in host transcription factor activation acts partly through the gut microbiome, likely due to the microbial biotransformation of PCBs or host-derived PCB metabolites into more potent ligands for theses host receptors. The relative abundance for the most abundant bacteria for the conventionalized exGF mice resemble those of the CV mice (Fig. S3). This result indicates that re-colonization of the gut microbiome reaches a similar microbial abundance level as the CV mice. In addition, previous studies have shown that the conventionalization of GF mice have restored xenobiotic metabolism signatures to similar levels of those of the CV mice and conventionalization of GF mice led to the induction of host xenobiotic-sensing transcription factors, indicating that the gut microbiome, through bacterial metabolites, can regulate the activation of these receptors (Claus et al., 2011; Selwyn et al., 2016). Therefore, the attenuation effects are likely due to the lack of gut microbiome. Although

CV and GF mice have different physiology, colonization of healthy bacteria to PCB-exposed GF mice may result in responses similar to the CV mice.

PCBs are well-known to activate host transcription factors, including AhR, PXR, CAR, and PPARα (Wahlang et al., 2014), which are known to up-regulate their prototypical target genes following a dose response curve, and this may subsequently lead to changes in endogenous metabolites in a dose-dependent manner. In the present study, although the hepatic transcriptome and metabolome tended to have a dose-response relationship from exposure to the two different PCB doses, the effect of PCBs on the gut microbiome is not monotonic, possibly involving different regulatory mechanisms. It has been shown that the PCB low dose tended to lower the richness of the gut microbiota to a greater extent than the PCB high dose (Cheng et al., 2018). It is possible that the PCB high dose may overwhelm the system and involve less specific regulatory pathways.

The gut microbiome appears to have fundamental roles in PCB-mediated up-regulation of P450 activities, because the two genes that encode essential enzymes that sustain P450 reactions, namely *Cyb5b* (regulates P450 activity through P450-dependent monooxygenase system) and *Por* (transfers electrons from NADPH to P450s) were up-regulated by PCBs in a gut microbiome-dependent manner; thus, PCB-exposed GF mice may have less efficiency and decreased hepatic P450 activity than PCB-exposed CV mice. In addition, the gut microbiome-dependent up-regulation of *Gst*s may be due to epigenetic modification from the gut microbial metabolites, such as butyrate, succinate, and acetate (Fellows et al., 2018; Hullar and Fu, 2014; Xu et al., 2018). The lack of *Gst* up-regulation in PCB-exposed GF mice may send a stress signal to up-regulate other phase-II detoxification pathways such as sulfonation, evidenced by a PCB-mediated up-regulation of multiple *Sult*s only in livers of GF mice.

Differences in PCB-induced metabolism changes between CV and GF mice

ER stress has been shown to be one of the key mechanisms of PCB-mediated hepatotoxicity (Xu et al., 2015; Ruan et al., 2020), but little is known to what extent gut microbiome contributes to this mechanism. The present study is the first to show that the presence of the gut microbiome is linked to PCB-mediated down-regulation of pathways related to response to misfolded proteins, which is a hallmark for ER stress. Oxidative damage and impaired amino acid metabolism are known to cause ER stress, which involves Ca^{2+} signaling (Harding et al., 2003; Bahar et al., 2016; Chong et al., 2017). Altered amino acid metabolites were found primarily in the livers of PCB-exposed CV mice, including acetylcarnitine, adenylosuccinate, 3-hydroxybutyric acid, aminoisobutyric acid, and dimethylglycine (Fig. 3C). Furthermore, numerous liver genes related to oxidative stress were up-regulated in CV mice exposed to PCBs, such as *Arntl*, *Atp2a2*, *Jun*, *Mt1*, *Mt2*, and *Cebpb* (Han et al., 2008; Kujiraoka et al., 2013; Moloney and Cotter, 2018; Wilking et al., 2013). These results suggest that oxidative damage and altered amino acid metabolism from PCB exposure possibly drive hepatic ER stress as suggested by down-regulation GO terms in CV mice (Fig. 2B), down-regulation of heat shock proteins, as well as Ca^{2+} transporters involved in intrinsic apoptotic signaling pathways in response to ER stress (Concilli et al., 2016; Xu et al., 2018; Yang et al., 2015) (Fig. 2B and 5B, and Table S1A and B).

Regarding the microbial signatures, the PCB low dose up-regulated *Ruminiclostridium* 6 and Family XIII UCG-013, and both of them were positively associated with dimethylglycine and aminoisobutyric acid (Fig. 3B). The abundance of the genus *Ruminiclostridium* is increased by immune response and oxidative damage, and PCBs are known to produce inflammation and oxidative stress (Sarkar et al., 2019; Petriello et al., 2018; Phillips et al., 2018). The Family XIII UCG-013 was negatively correlated with *Atp2a2* (sarco/endoplasmic reticulum $Ca2^{+}$-ATPase [SERCA2]). *Atp2a2* has been shown to be down-

regulated in oxidative damage and ER stress (Kujiraoka et al., 2013). Dimethylglycine is generated from homocysteine metabolism, which is related to protein degradation and ER stress. Therefore, the up-regulation of *Ruminiclostridium* 6 and dimethylglycine may reflect PCB-mediated oxidative damage, ER stress, and inflammation. Aminoisobutyric acid is one of the end products of pyrimidine metabolism (van Kuilenburg et al., 2006). Multiple species of *Ruminiclostridium*, such as *Ruminiclostridium cellulolyticum*, have enzymes that contribute to generating aminoisobutyric acid, such as pyrimidine-nucleoside phosphorylase (Dumitrache et al., 2017). Aminoisobutyric acid concentration has been suggested to be protective against metabolic disorder (Roberts et al., 2014). In turn, the up-regulated oxidative stress elements may have up-regulated aminoisobutyric acid, as a compensatory response, to alleviate the PCB responses in liver. In summary, the oxidative damage and immune response pathways as regulated by the PCB low dose, associated with up-regulated *Ruminiclostridium* 6 and Family XIII UCG-013, may have contribute to the gut microbiome-dependent ER stress, and modulating amino acid metabolites may have a therapeutic value in alleviating adverse health effects from PCB exposures.

The absence of gut microbiome potentiated PCB-mediated dysregulation of metabolites involved in carbohydrate metabolism and nucleotide metabolism (Fig. 4 and S2). Specifically, hepatic G6P and F6P were up-regulated in GF mice exposed to both PCB doses, whereas D-glucose was down-regulated. This may indicate that the glucose utilization in the liver is impaired in GF mice exposed to PCBs. It is known that the lack of gut microbiome impairs liver regeneration (Liu et al., 2015; Wu et al., 2015), suggesting the importance of the gut microbiome in providing key regenerative signals to the host liver.

Clostridium sp. Clone-44 was positively associated with genes involved in inflammation and oxidative stress (*Ces1b*, *Cyp1a1*, *Cyp2c55*, *Slc10a2*, and *Socs2*), but was negatively associated with arginine levels (Fig. 3 and 5). Through its contribution to the formation of

nitric oxide, arginine can reduce inflammatory responses and oxidative stress by inhibiting cytokine secretion and inducing glutathione synthesis (Hnia et al., 2008; Liang et al., 2018; Wu et al., 2016). Multiple species in the *Clostridium* genus have been shown to metabolize arginine (Mitruka and Costilow, 1967; Neumann-Schaal et al., 2019). The gut microbiome-dependent decrease of arginine may be due to increased abundance of *Clostridium sp.* Clone-44, which may explain the up-regulated pathways involved in inflammation and oxidative stress. Arachidonic acid is suggested to interact with arginine by sharing the nitric oxide pathway. Milner and Perkins showed that rats deficient in arginine had increased levels of arachidonic acid (Milner and Perkins, 1978). In CV mice exposed to the high dose PCB, more arachidonic acid metabolizing P450s were up-regulated, such as *Cyp1a1* and *Cyp2c55*, which metabolizes arachidonic acid to eicosanoids, suggesting a rapid inflammation-mediating transition, compared to the GF state.

Anaerotruncus, a butyrate producer, is a normal gut inhabitant in mice with enhanced growth in the presence of mucin (Wang et al., 2019; Wlodarska et al., 2017). Following PCB exposure, *Anaerotruncus* was negatively associated with amino acid metabolites, such as asacetylcarnitine, adenylosuccinate, aminoisobutyric acid, and dimethylglycine in liver, as well as proline, serine, and urocanic acid in serum (Fig. 5A and B). *Anaerotruncus* was also negatively associated with expression of *Ces2c*, *Cyp1a2*, *Cyp2c29*, *Ces1b*, *Cyp1a1* and positively associated with *Atp1a2*, *Atp2b2*, *Slc16a1*, *Slc30a10*, and *Slc17a2* (Fig. 6C and D). It has been reported that *Anaerotruncus* has the capabilities to metabolize fatty acids and its abundance was negatively correlated with xenobiotic exposure, such as dipeptidyl peptidase 4 inhibitors, which reduces blood glucose levels (Olivares et al., 2018; Visconti et al., 2019; Yan et al., 2016; Zhang et al., 2017). *Anaerotruncus* has been linked to glucose intolerance, gut permeability, muscle lipid content, and type 2 diabetes in humans, cats, and rats, which suggests that *Anaerotruncus* may have a protective role in oxidative damage, and the

decrease in the abundance of *Anaerotruncus* may have contributed to PCB-induced toxicities (Everard et al., 2011; Kieler et al., 2019; Li et al., 2017b).

Potential therapeutics to limit impact of exposure to PCBs via gut microbiome-dependent signatures

Results from the inverse relationships between transcriptomic signatures from the LINCS L1000 database and the gut microbiome-dependent gene expression signatures following PCB exposure highlighted the potential remedy to mitigate gut microbiome-potentiated PCB toxicity. The majority of the drugs and other small compounds that were identified to have opposite gene expression signatures as compared to PCB-exposed conditions are anti-cancer drugs. These results may indicate that the gut microbiome contributes to tumorigenesis mechanisms associated with PCB exposure. Geldanmycin, which inhibits the function of HSP90 and regulates cell cycle, growth, and apoptosis, was the top inversely correlated drug that up-regulates the genes that make up the down-regulated signatures, such as *Hyou1* and *Hspa5*, from PCB exposure. In addition, other top drugs and small molecules that could restore expression of down-regulated genes included ABT-737, celastrol, and KIN001-043, which may reverse the ER damage and oxidative stress signatures, such as *Hyou1*, *Hspa5*, *Hspa13*, and *Atp2b2*, which are potentially due to and closely related with changes in altered bacteria, such as *Ruminiclostridium*, *Roseburia*, and *Anaerotruncus* (Fig. 3B, 5C and D, and 6A and C). Similarly, the top inversely correlated drug that could inhibit the gut microbiome-dependent up-regulated genes from PCB exposure was shown to be nilotinib, which may normalize the levels of up-regulated lipid and sterol metabolism- and actin function-related genes (Fig. 6B and D). Interestingly, compounds inhibiting the mTOR pathway (i.e. WYE-125132, AZD-8055, torin 1, and sirolimus) were repeatedly observed (Fig. 6B and D). It has been shown that PCB-95 activated mTOR in

primary rat hippocampal neurons and developing zebrafish (Frank et al., 2017; Keil et al., 2018). Activation of the mTOR pathway in the liver has been linked to liver tumors, NASH, and liver damage from autophagy in both mouse models and humans (Okuno et al., 2018; Saxton and Sabatini, 2017). The inhibition of the mTOR signaling pathway using therapeutics may reduce the risk of liver cancer and metabolic disease development from the activation of the mTOR from PCB exposure.

The present study has limitations, such as not having information on all of the dysregulated bacteria at the species level and metabolites in specific pathways, and a small sample size for the transcriptomic responses and 16S bacteria changes. Species and strain levels of dysregulated bacteria through deeper sequencing methods, such as from using shotgun metagenomics, and anaerobic culturing-coupled sequencing may give more mechanistic evidence of how bacteria regulate and respond with the gut and liver during PCB exposure. However, with the given breadth of data, we showed that the higher induction of xenobiotic biotransformation, immune response and oxidative stress-related mRNA signatures, and ER stress-mediated damage is unique to mice with a normal gut microbiome.

Future investigations should focus on the specific metabolic capacities of the dysregulated microbiome to study the mechanisms of biochemical perturbation from PCB exposure. Furthermore, despite the limitations, our study identifies the gut microbiome as a key player in biochemical regulation. To delineate whether the transcription factor signaling pathway is modified by the presence of the gut microbiome, an *in vitro* experiment using primary hepatocytes from CV and GF mice can be planned. However, the in vitro hepatocytes loses many in vivo features within hours after plating, including down-regulation of many transporters as well as drug-metabolizing enzymes; in addition, the in *in vitro* system lacks the gut-liver axis and is not exposed to gut-derived microbial metabolites. The gut-liver axis is the key focus of the present study and can only be assessed *in vivo*. When cells are isolated from

an organism, the resulting responses are likely not directly comparable from the introduction of an artificial environment to cells, which may not function as equivalent. Furthermore, using isolated cells exposed to PCBs would drastically alter the mode of exposure, which the exposed cells would lack intestinal biotransformation pathways. In order for this approach to be comparable to *in vivo* results, a cell battery consisting of multiple bio-compartments, including enterocytes colonized with key microbiota and liver, should be used.

For people with severe dysbiotic states (e.g., from antibiotics treatment), our study adds knowledge of potential differences in physiological responses from ubiquitous environmental contaminants, such as PCBs and potential considerations for further investigations regarding therapeutics.

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Figure legends

Figure 1. Experimental design of the study and summary of data.

A. 90-day-old female conventional (CV) and germ-free (GF) mice were orally exposed to the Fox River PCB mixture (6 or 30 mg/kg) or corn oil (vehicle control, 10 ml/kg). Twenty four hours after the final dosing, organs were collected. RNA-seq, 16s rDNA-seq, LC-MS were performed on the liver, large intestinal fecal pellets, and liver and serum, respectively. B. Principal component analysis (PCA) of the liver transcriptome and liver and serum metabolome. Individual points on the principal components scale are labeled by enterotype and exposure. C. Venn diagrams of differentially expressed genes of the liver and differentially abundant metabolites in the liver and serum.

Figure 2. Gene ontology enrichment of differentially regulated genes and gene expression of prototypical target genes of xenobiotic-sensing transcription factors.

A. Top 5 down-regulated gene ontology enrichment terms for CV (top) and GF (bottom) mice. The red dotted lines represent -log10(FDR) = 0.1. **B.** Box plots of differentially regulated prototypical target genes of the transcription factors, Aryl hydrocarbon receptor (AhR), constitutive androstane receptor (CAR), and pragnane X receptor (PXR). The pound signs and asterisks represent differential expression in the CV and GF groups, respectively.

Figure 3. Differentially abundant bacteria and correlation with differentially abundant liver and serum metabolites in conventional mice.

A. Scaled relative abundance of bacteria for CV mice. Differential abundance (Significant) information is provided on the colored bar (i.e. blue shows differential expression for conventional mice exposed to PCB 6 mg/kg and grey indicates genes that are not differentially regulated). **B.** Spearman correlation for differentially abundant bacteria (rows)

and liver and serum metabolites (columns). Green-orange color scale represents the direction of correlation and sizes of circles show strength of correlation. Differential abundant bacteria and metabolites are shown as blue and green colored bars, representing significance for mice exposed to PCB 6 and 30 mg/kg, respectively. Pink filled box indicates significant correlation at FDR < 0.1 with absolute spearman's ρ >0.8. Box plots of differentially abundant metabolites in liver **(C)** and serum **(D)** for CV mice exposed to PCBs. Data are shown as relative abundance. The asterisks represent differential abundance in CV groups exposed to PCBs. **E.** Differentially abundant metabolites are shown as triangles and differentially regulated genes are represented in circles. Colors indicate metabolite abundance and gene expression relative to the control (blue = lower abundance or expression; red = higher abundance or expression).

Figure 4. Selected liver and serum metabolites differentially abundant in germ-free mice exposed to PCBs.

Box plots of differentially abundant metabolites in liver **(A)** and serum **(B)**. Data are shown as relative abundance. The asterisks represent differential abundance in GF groups exposed to PCBs.

Figure 5. Relative expression of differentially regulated genes grouped by functional categories and correlation of differentially abundant bacteria and differentially regulated genes in conventional mice.

A. Scaled expression of genes in epigenetic modification (Epi.), inflammation and oxidative stress, and nuclear receptor (NR) categories for CV and GF mice. Differential regulation (Significant) information is provided on the colored bar (i.e. blue shows differential expression for CV mice exposed to PCB 6 mg/kg and grey indicates genes that are not differentially

regulated). **B.** Scaled expression of genes in phase-I, -II, and transporter categories for CV and GF mice. Differential regulation (Significant) information is provided on the colored bar (i.e. blue shows differential expression for CV mice exposed to PCB 6 mg/kg and grey indicates genes that are not differentially regulated). Spearman correlation for differentially abundant bacteria (rows) and differentially regulated genes (columns) in phase-I and II **(C)**, and transporters, inflammation and oxidative stress, and nuclear receptor categories **(D)**. Green-orange color scale represents the direction of correlation and sizes of circles show strength of association. Differential abundant bacteria and metabolites are shown as blue and green colored bars, representing significance for mice exposed to PCB 6 and 30 mg/kg, respectively. Pink filled box indicates significant correlation at FDR < 0.1 with absolute spearman's ρ >0.8.

Figure 6. Potential therapeutics from gut microbiome-dependent PCB exposure.

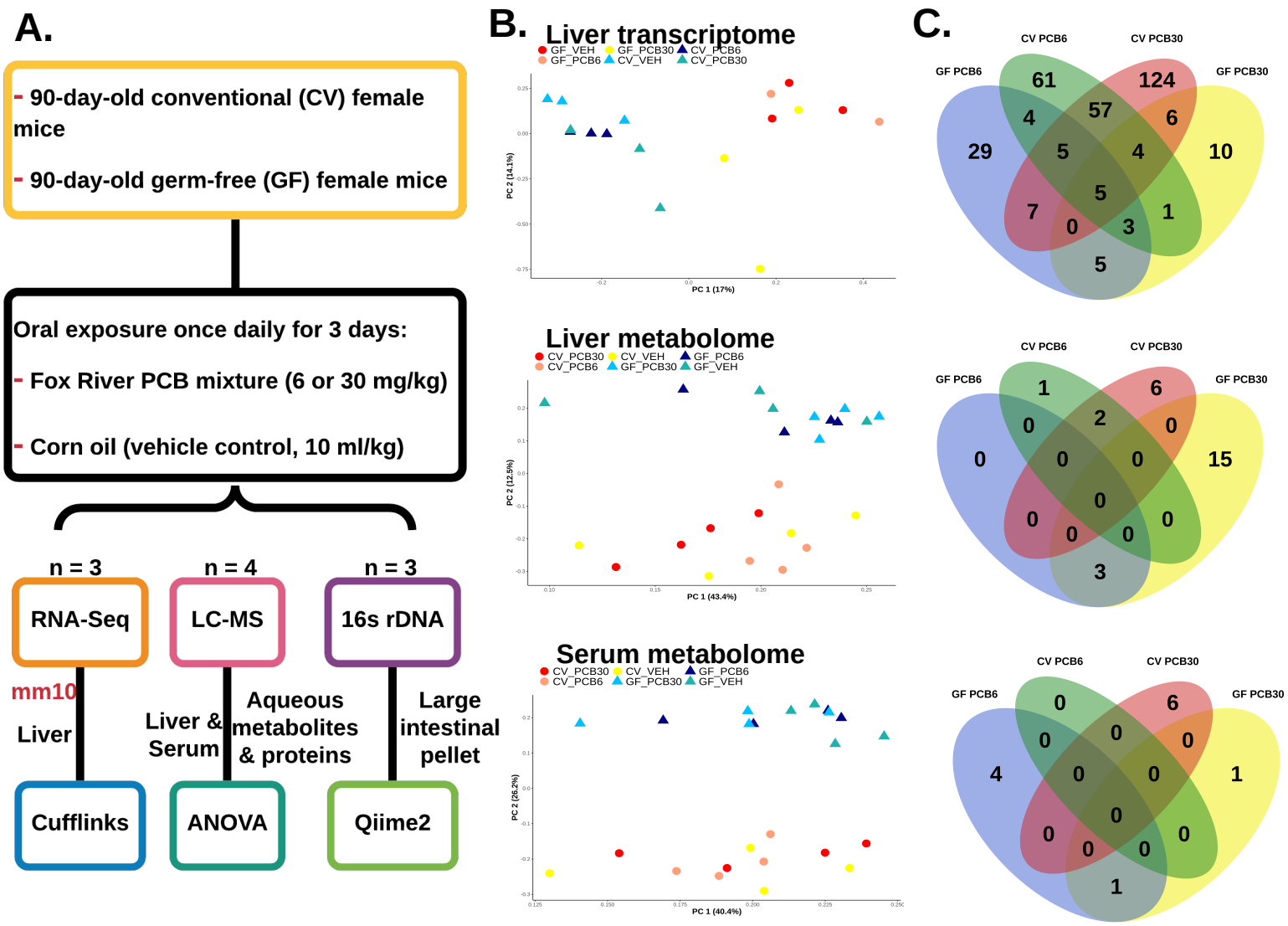
Drugs and small molecule (columns) and their respective target genes (rows) in human cell lines. Top bar plot represents the combined score using the adjusted p-value and odds ratio. Top 15 inversely correlated target signatures with the differentially regulated genes from PCB exposure are shown. Up-regulated target genes from exposure to drugs and small molecules (down-regulated from PCB low and or high exposure) are highlighted in orange (A and B, respectively). Down-regulated target genes from exposure to drugs and small compounds (up-regulated from PCB low or high exposure) are highlighted in blue (C and D, respectively).

Figure 7. Summary of study findings.

From PCB exposure, in livers of CV mice, higher induction of prototypical target genes of AhR, CAR, and PXR were observed, compared to the GF mice. In CV mice, xenobiotic biotransformation-related GO terms were more enriched and ER stress-related GO terms

were uniquely down-regulated. Most *Gstm*s were up-regulated in CV mice, whereas most *Sult*s were up-regulated in GF mice exposed to PCBs. In addition, CV mice exposed to PCBs had differentially regulated transporters; however, less change in transporter expression was observed in GF mice. In the liver and serum, amino acid metabolism-related metabolites were preferably up-regulated in CV mice. Conversely, nucleotide and carbohydrate metabolism-related metabolites were up-regulated in GF mice. Short-chain fatty acid-producing bacteria, such as *Roseburia* (PCB both doses) and *Ruminiclostridium* (PCB low dose) were up-regulated and *Anaerotruncus* was down-regulated in the PCB high dose following PCB exposure and were correlated with metabolites, such as aminoisobutyric acid, dimethylglycine, and arginine, and genes important in xenobiotic biotransformation, such as *Cyp1a1*, *Cyp1a2*, and *Atp2a2*, showing the possible role of these bacteria in mediating PCB-induced toxicity. Therapeutics that target critical pathways, such as mTOR and Bcl-2, have the potential to resolve signatures from PCB exposure.

Fig. 1


A.
- 90-day-old conventional (CV) female mice
- 90-day-old germ-free (GF) female mice
Oral exposure once daily for 3 days:
- Fox River PCB mixture (6 or 30 mg/kg)
- Corn oil (vehicle control, 10 ml/kg)
n = 3
n = 4
n = 3
RNA-Seq
LC-MS
16s rDNA
mm10
Liver
Liver & Serum
Aqueous metabolites & proteins
Large intestinal pellet
Cufflinks
ANOVA
Qiime2
B.
Liver transcriptome
GF_VEH GF_PCB30 CV_PCB6
GF_PCB6 CV_VEH CV_PCB30
PC 2 (14.1%)
PC 1 (17%)
Liver metabolome
CV_PCB30 CV_VEH GF_PCB6
CV_PCB6 GF_PCB30 GF_VEH
PC 2 (12.5%)
PC 1 (43.4%)
Serum metabolome
CV_PCB30 CV_VEH GF_PCB6
CV_PCB6 GF_PCB30 GF_VEH
PC 2 (26.2%)
PC 1 (40.4%)
C.
CV PCB6
CV PCB30
GF PCB6
GF PCB30
61
124
29
10
4
57
6
5
4
5
7
0
3
1
5
CV PCB6
CV PCB30
GF PCB6
GF PCB30
1
6
0
2
0
0
0
0
15
0
0
0
0
0
3
CV PCB6
CV PCB30
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1

Fig. 2

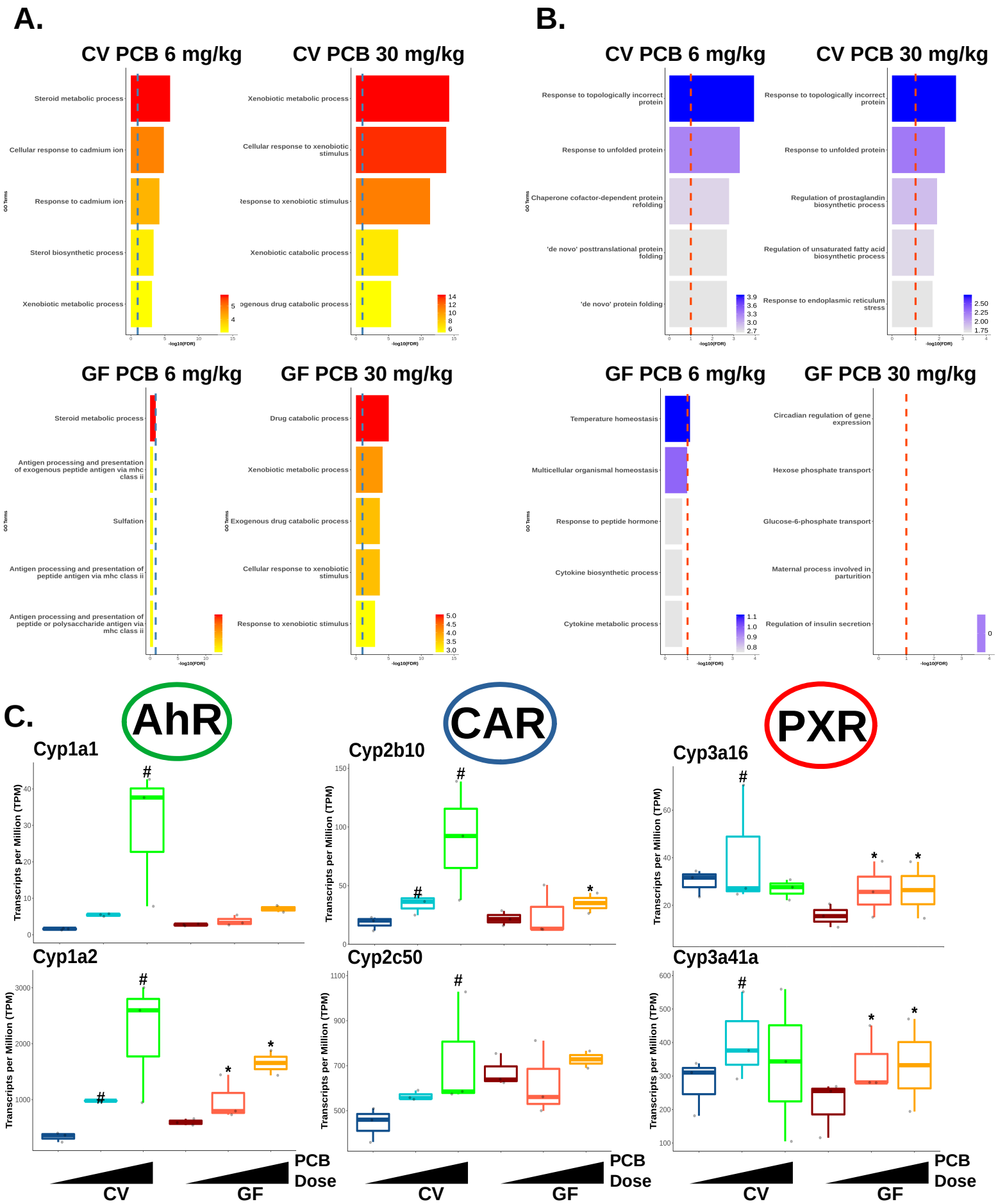

A.
CV PCB 6 mg/kg
Steroid metabolic process
Cellular response to cadmium ion
Response to cadmium ion
Sterol biosynthetic process
Xenobiotic metabolic process
GO Terms
-log10(FDR)
CV PCB 30 mg/kg
Xenobiotic metabolic process
Cellular response to xenobiotic stimulus
Response to xenobiotic stimulus
Xenobiotic catabolic process
ogenous drug catabolic process
GF PCB 6 mg/kg
Steroid metabolic process
Antigen processing and presentation of exogenous peptide antigen via mhc class ii
Sulfation
Antigen processing and presentation of peptide antigen via mhc class ii
Antigen processing and presentation of peptide or polysaccharide antigen via mhc class ii
GF PCB 30 mg/kg
Drug catabolic process
Xenobiotic metabolic process
Exogenous drug catabolic process
Cellular response to xenobiotic stimulus
Response to xenobiotic stimulus
B.
CV PCB 6 mg/kg
Response to topologically incorrect protein
Response to unfolded protein
Chaperone cofactor-dependent protein refolding
'de novo' posttranslational protein folding
'de novo' protein folding
CV PCB 30 mg/kg
Response to topologically incorrect protein
Response to unfolded protein
Regulation of prostaglandin biosynthetic process
Regulation of unsaturated fatty acid biosynthetic process
Response to endoplasmic reticulum stress
GF PCB 6 mg/kg
Temperature homeostasis
Multicellular organismal homeostasis
Response to peptide hormone
Cytokine biosynthetic process
Cytokine metabolic process
GF PCB 30 mg/kg
Circadian regulation of gene expression
Hexose phosphate transport
Glucose-6-phosphate transport
Maternal process involved in parturition
Regulation of insulin secretion
C.
AhR
CAR
PXR
Cyp1a1
Cyp1a2
Cyp2b10
Cyp2c50
Cyp3a16
Cyp3a41a
Transcripts per Million (TPM)
CV
GF
PCB Dose

Fig. 3

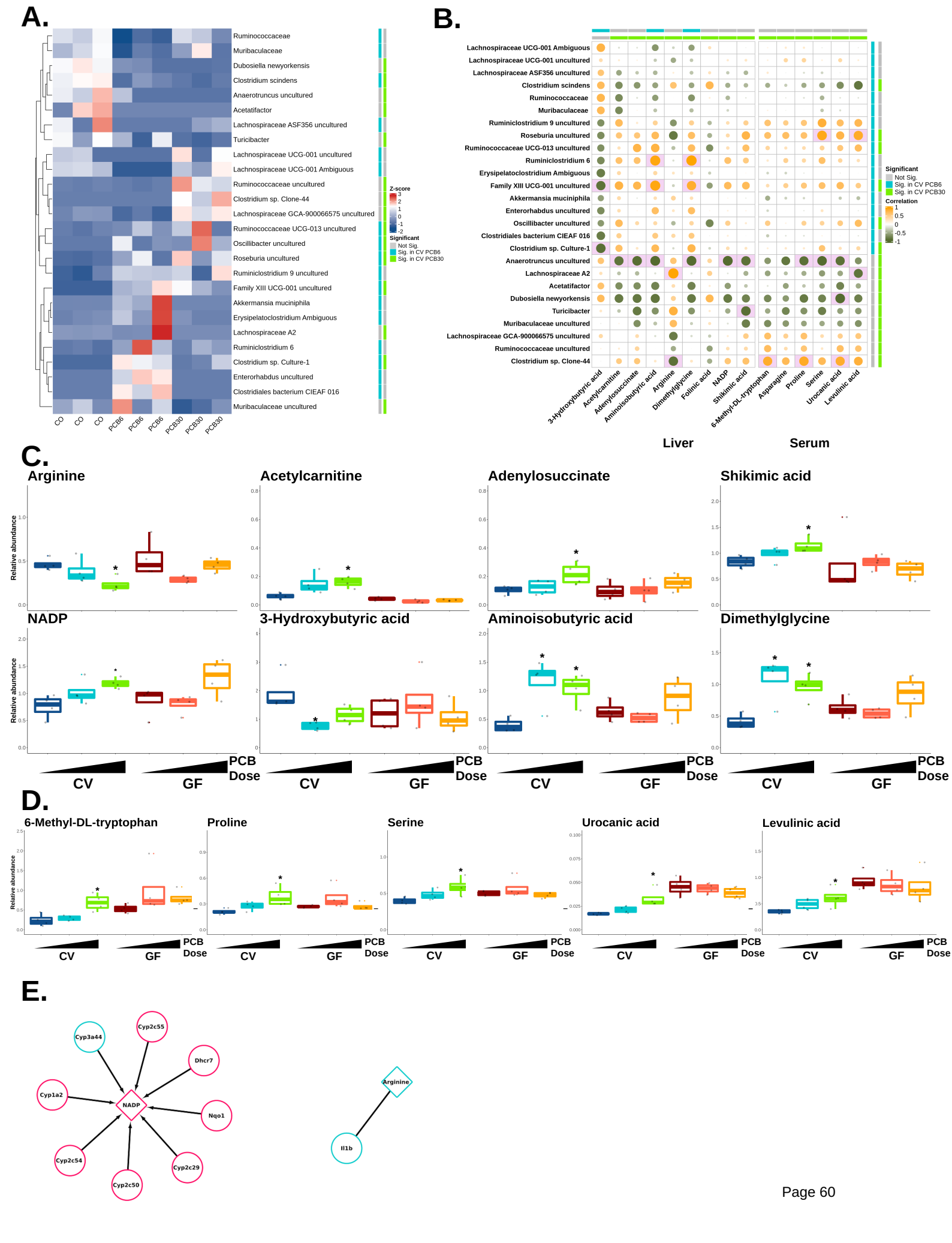
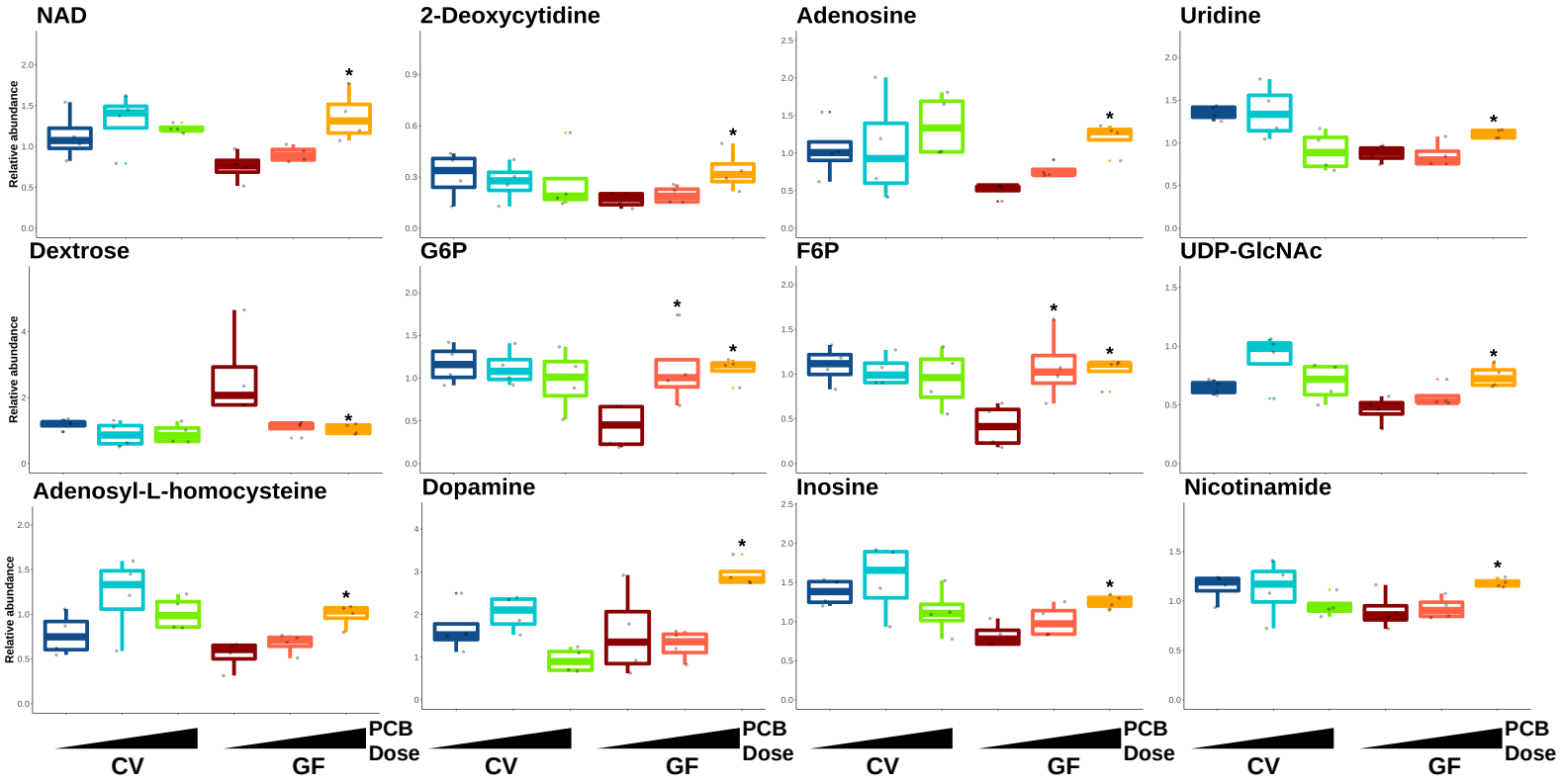

A.
Ruminococcaceae
Muribaculaceae
Dubosiella newyorkensis
Clostridium scindens
Anaerotruncus uncultured
Acetatifactor
Lachnospiraceae ASF356 uncultured
Turicibacter
Lachnospiraceae UCG-001 uncultured
Lachnospiraceae UCG-001 Ambiguous
Ruminococcaceae uncultured
Clostridium sp. Clone-44
Lachnospiraceae GCA-900066575 uncultured
Ruminococcaceae UCG-013 uncultured
Oscillibacter uncultured
Roseburia uncultured
Ruminiclostridium 9 uncultured
Family XIII UCG-001 uncultured
Akkermansia muciniphila
Erysipelatoclostridium Ambiguous
Lachnospiraceae A2
Ruminiclostridium 6
Clostridium sp. Culture-1
Enterorhabdus uncultured
Clostridiales bacterium CIEAF 016
Muribaculaceae uncultured
CO CO CO PCB6 PCB6 PCB6 PCB30 PCB30 PCB30
Z-score
Significant
Not Sig.
Sig. in CV PCB6
Sig. in CV PCB30
B.
Lachnospiraceae UCG-001 Ambiguous
Lachnospiraceae UCG-001 uncultured
Lachnospiraceae ASF356 uncultured
Clostridium scindens
Ruminococcaceae
Muribaculaceae
Ruminiclostridium 9 uncultured
Roseburia uncultured
Ruminococcaceae UCG-013 uncultured
Ruminiclostridium 6
Erysipelatoclostridium Ambiguous
Family XIII UCG-001 uncultured
Akkermansia muciniphila
Enterorhabdus uncultured
Oscillibacter uncultured
Clostridiales bacterium CIEAF 016
Clostridium sp. Culture-1
Anaerotruncus uncultured
Lachnospiraceae A2
Acetatifactor
Dubosiella newyorkensis
Turicibacter
Muribaculaceae uncultured
Lachnospiraceae GCA-900066575 uncultured
Ruminococcaceae uncultured
Clostridium sp. Clone-44
3-Hydroxybutyric acid
Acetylcarnitine
Adenylosuccinate
Aminoisobutyric acid
Arginine
Dimethylglycine
Folinic acid
NADP
Shikimic acid
6-Methyl-DL-tryptophan
Asparagine
Proline
Serine
Urocanic acid
Levulinic acid
Liver
Serum
Significant
Not Sig.
Sig. in CV PCB6
Sig. in CV PCB30
Correlation
C.
Arginine
Acetylcarnitine
Adenylosuccinate
Shikimic acid
NADP
3-Hydroxybutyric acid
Aminoisobutyric acid
Dimethylglycine
Relative abundance
CV GF PCB Dose
D.
6-Methyl-DL-tryptophan
Proline
Serine
Urocanic acid
Levulinic acid
Relative abundance
CV GF PCB Dose
E.
Cyp3a44
Cyp2c55
Dhcr7
Cyp1a2
NADP
Nqo1
Cyp2c54
Cyp2c50
Cyp2c29
Arginine
Il1b

Fig. 4

A.


NAD
2-Deoxycytidine
Adenosine
Uridine
Dextrose
G6P
F6P
UDP-GlcNAc
Adenosyl-L-homocysteine
Dopamine
Inosine
Nicotinamide
Relative abundance
CV
GF
PCB Dose

B.

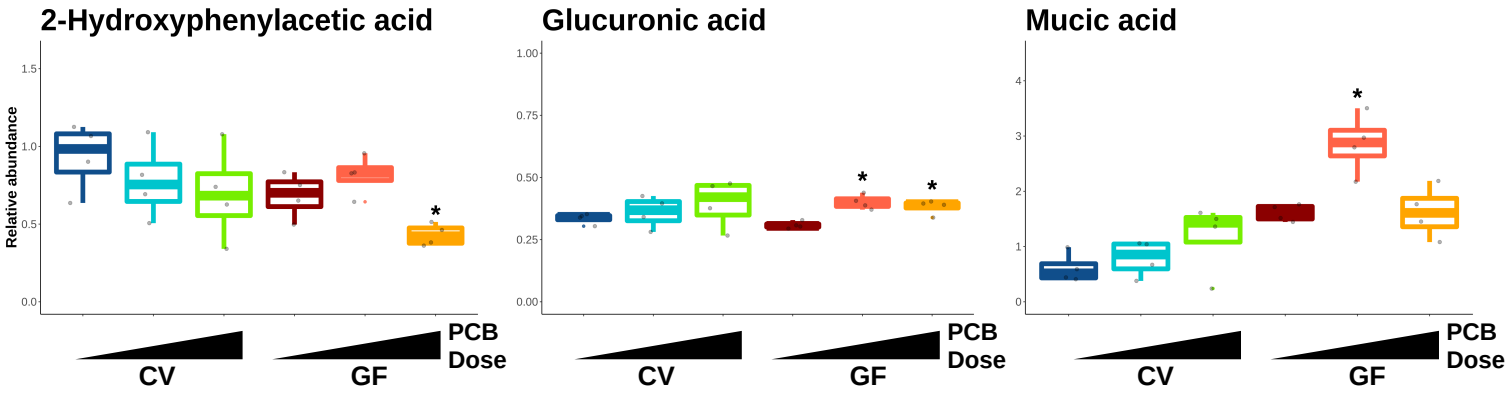

2-Hydroxyphenylacetic acid
Glucuronic acid
Mucic acid
Relative abundance
CV
GF
PCB Dose

Fig. 5

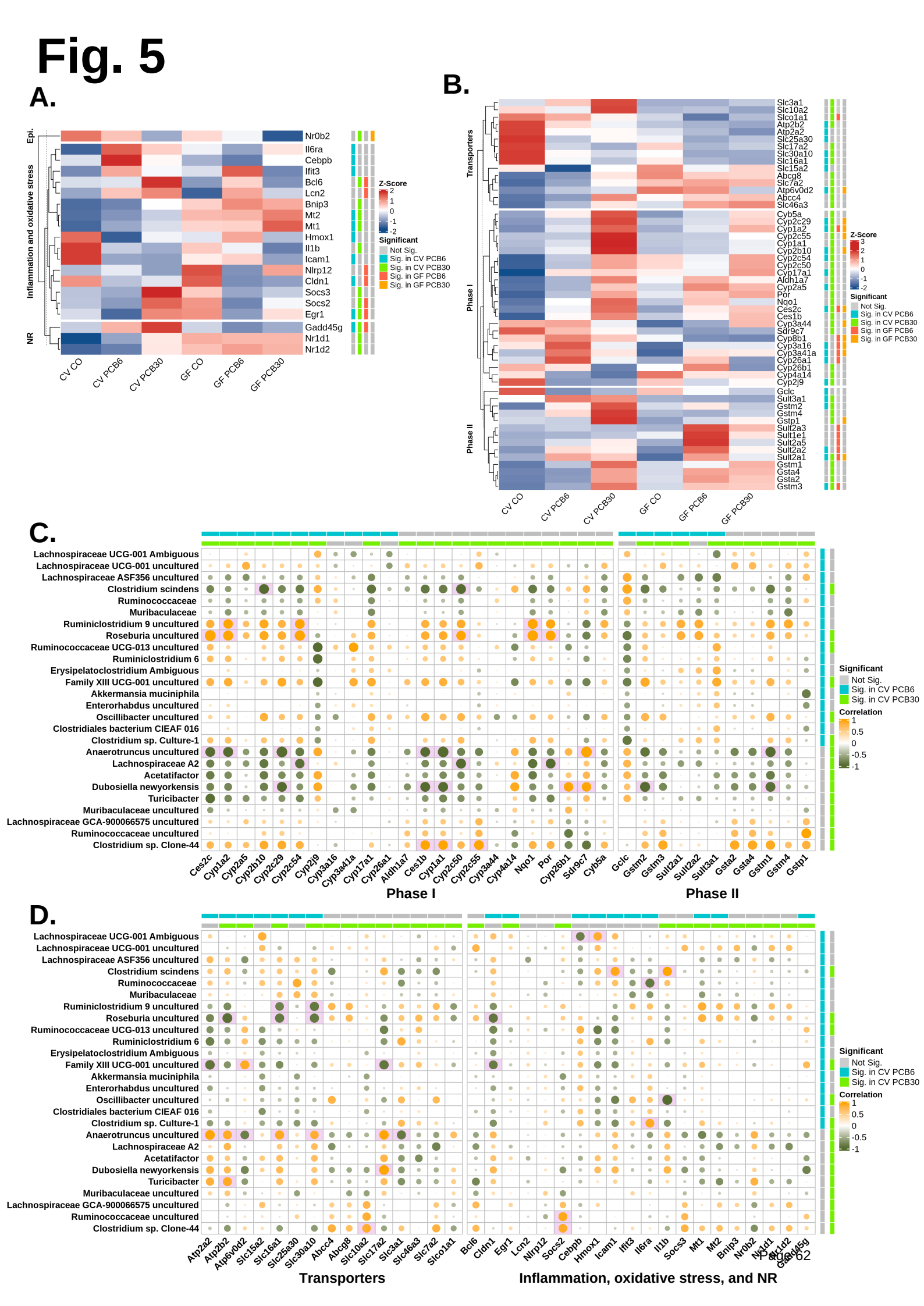

A.
Epi.
Inflammation and oxidative stress
NR
Nr0b2
Il6ra
Cebpb
Ifit3
Bcl6
Lcn2
Bnip3
Mt2
Mt1
Hmox1
Il1b
Icam1
Nlrp12
Cldn1
Socs3
Socs2
Egr1
Gadd45g
Nr1d1
Nr1d2
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in CV PCB6
Sig. in CV PCB30
Sig. in GF PCB6
Sig. in GF PCB30
CV CO
CV PCB6
CV PCB30
GF CO
GF PCB6
GF PCB30
B.
Transporters
Phase I
Phase II
Slc3a1
Slc10a2
Slco1a1
Atp2b2
Atp2a2
Slc25a30
Slc17a2
Slc30a10
Slc16a1
Slc15a2
Abcg8
Slc7a2
Atp6v0d2
Abcc4
Slc46a3
Cyb5a
Cyp2c29
Cyp1a2
Cyp2c55
Cyp1a1
Cyp2b10
Cyp2c54
Cyp2c50
Cyp17a1
Aldh1a7
Cyp2a5
Por
Nqo1
Ces2c
Ces1b
Cyp3a44
Sdr9c7
Cyp8b1
Cyp3a16
Cyp3a41a
Cyp26a1
Cyp26b1
Cyp4a14
Cyp2j9
Gclc
Sult3a1
Gstm2
Gstm4
Gstp1
Sult2a3
Sult1e1
Sult2a5
Sult2a2
Sult2a1
Gstm1
Gsta4
Gsta2
Gstm3
Z-Score
3
2
1
0
-1
-2
Significant
Not Sig.
Sig. in CV PCB6
Sig. in CV PCB30
Sig. in GF PCB6
Sig. in GF PCB30
CV CO
CV PCB6
CV PCB30
GF CO
GF PCB6
GF PCB30
C.
Lachnospiraceae UCG-001 Ambiguous
Lachnospiraceae UCG-001 uncultured
Lachnospiraceae ASF356 uncultured
Clostridium scindens
Ruminococcaceae
Muribaculaceae
Ruminiclostridium 9 uncultured
Roseburia uncultured
Ruminococcaceae UCG-013 uncultured
Ruminiclostridium 6
Erysipelatoclostridium Ambiguous
Family XIII UCG-001 uncultured
Akkermansia muciniphila
Enterorhabdus uncultured
Oscillibacter uncultured
Clostridiales bacterium CIEAF 016
Clostridium sp. Culture-1
Anaerotruncus uncultured
Lachnospiraceae A2
Acetatifactor
Dubosiella newyorkensis
Turicibacter
Muribaculaceae uncultured
Lachnospiraceae GCA-900066575 uncultured
Ruminococcaceae uncultured
Clostridium sp. Clone-44
Ces2c
Cyp1a2
Cyp2a5
Cyp2b10
Cyp2c29
Cyp2c54
Cyp2j9
Cyp3a16
Cyp3a41a
Cyp17a1
Cyp26a1
Aldh1a7
Ces1b
Cyp1a1
Cyp2c50
Cyp2c55
Cyp3a44
Cyp4a14
Nqo1
Por
Cyp26b1
Sdr9c7
Cyb5a
Gclc
Gstm2
Gstm3
Sult2a1
Sult2a2
Sult3a1
Gsta2
Gsta4
Gstm1
Gstm4
Gstp1
Phase I
Phase II
Significant
Not Sig.
Sig. in CV PCB6
Sig. in CV PCB30
Correlation
1
0.5
0
-0.5
-1
D.
Lachnospiraceae UCG-001 Ambiguous
Lachnospiraceae UCG-001 uncultured
Lachnospiraceae ASF356 uncultured
Clostridium scindens
Ruminococcaceae
Muribaculaceae
Ruminiclostridium 9 uncultured
Roseburia uncultured
Ruminococcaceae UCG-013 uncultured
Ruminiclostridium 6
Erysipelatoclostridium Ambiguous
Family XIII UCG-001 uncultured
Akkermansia muciniphila
Enterorhabdus uncultured
Oscillibacter uncultured
Clostridiales bacterium CIEAF 016
Clostridium sp. Culture-1
Anaerotruncus uncultured
Lachnospiraceae A2
Acetatifactor
Dubosiella newyorkensis
Turicibacter
Muribaculaceae uncultured
Lachnospiraceae GCA-900066575 uncultured
Ruminococcaceae uncultured
Clostridium sp. Clone-44
Atp2a2
Atp2b2
Atp6v0d2
Slc15a2
Slc16a1
Slc25a30
Slc30a10
Abcc4
Abcg8
Slc10a2
Slc17a2
Slc3a1
Slc46a3
Slc7a2
Slco1a1
Bcl6
Cldn1
Egr1
Lcn2
Nlrp12
Socs2
Cebpb
Hmox1
Icam1
Ifit3
Il6ra
Il1b
Socs3
Mt1
Mt2
Bnip3
Nr0b2
Nr1d1
Nr1d2
Gadd45g
Transporters
Inflammation, oxidative stress, and NR
Significant
Not Sig.
Sig. in CV PCB6
Sig. in CV PCB30
Correlation
1
0.5
0
-0.5
-1

Fig. 6

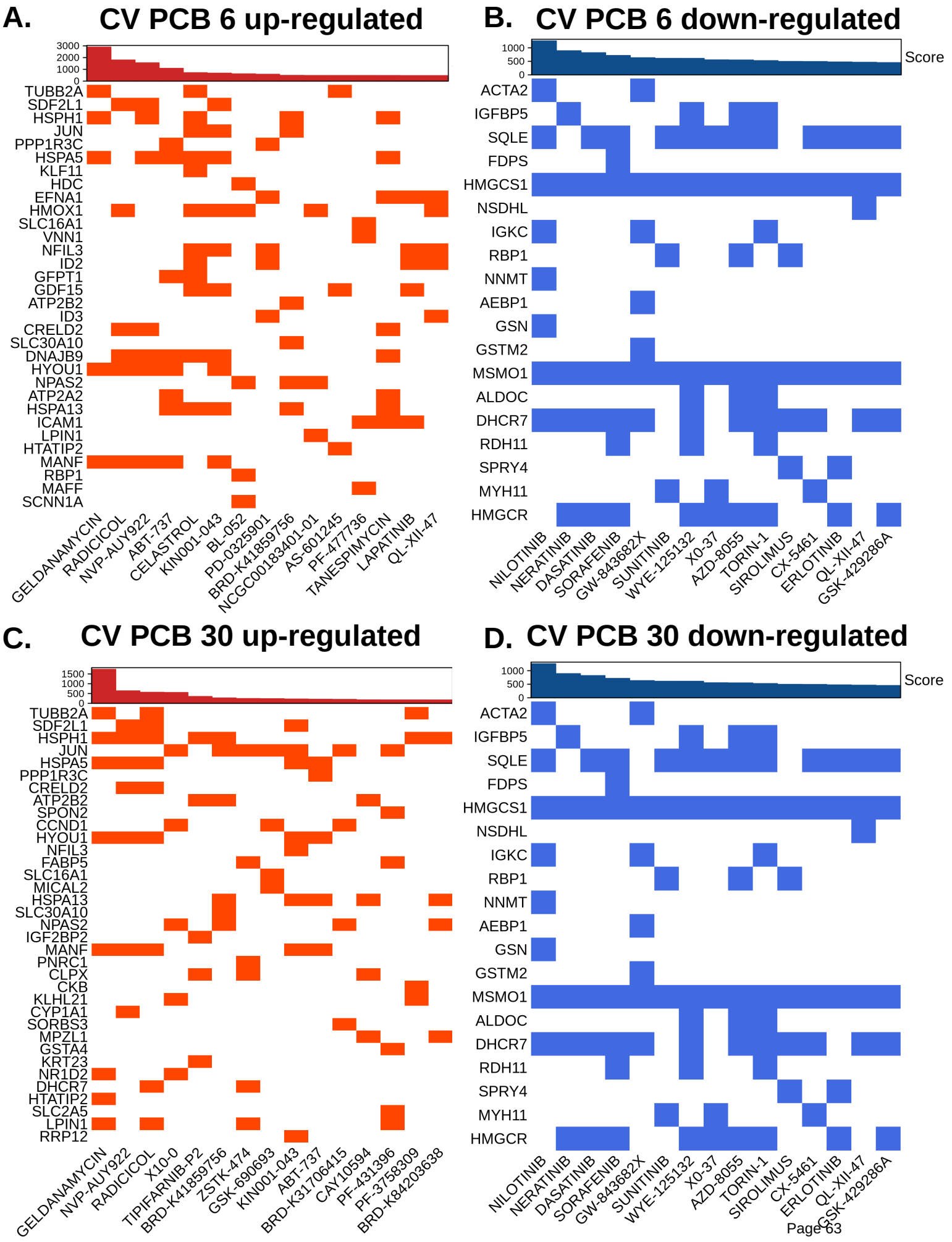
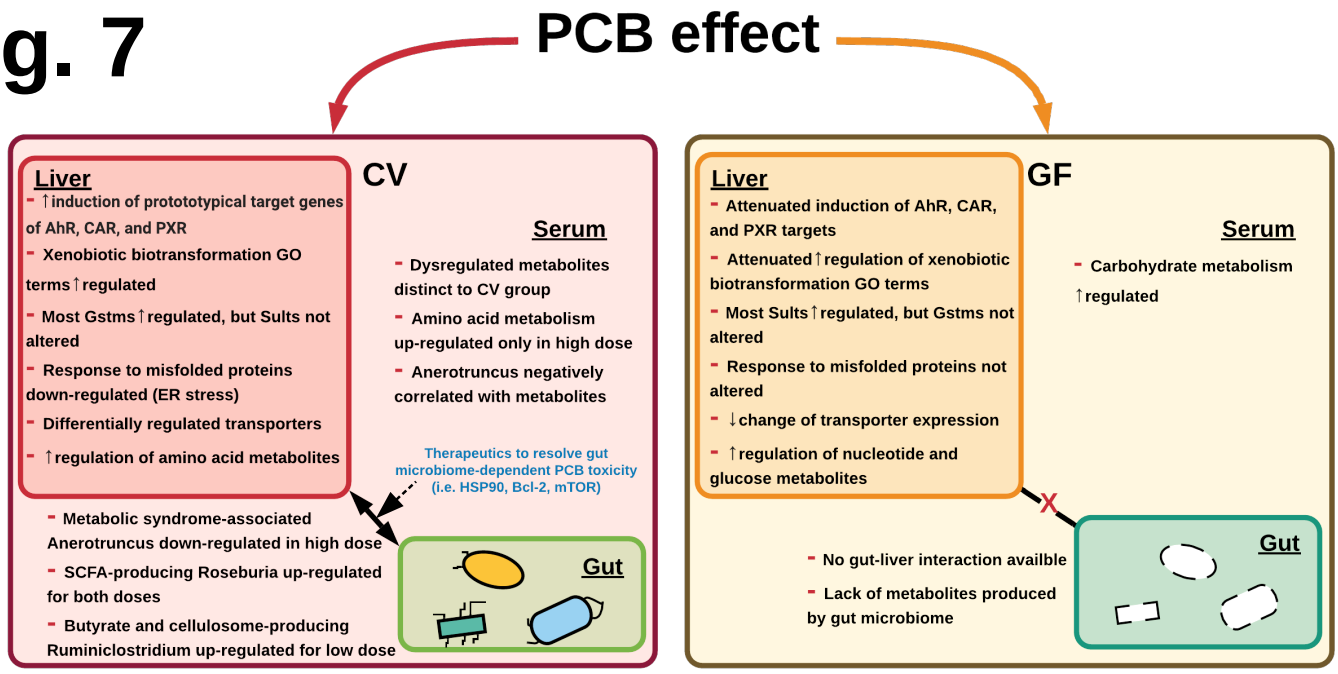

A.
CV PCB 6 up-regulated
3000
2000
1000
0
TUBB2A
SDF2L1
HSPH1
JUN
PPP1R3C
HSPA5
KLF11
HDC
EFNA1
HMOX1
SLC16A1
VNN1
NFIL3
ID2
GFPT1
GDF15
ATP2B2
ID3
CRELD2
SLC30A10
DNAJB9
HYOU1
NPAS2
ATP2A2
HSPA13
ICAM1
LPIN1
HTATIP2
MANF
RBP1
MAFF
SCNN1A
GELDANAMYCIN
RADICICOL
NVP-AUY922
ABT-737
CELASTROL
KIN001-043
BL-052
PD-0325901
BRD-K41859756
NCGC00183401-01
AS-601245
PF-477736
TANESPIMYCIN
LAPATINIB
QL-XII-47
B.
CV PCB 6 down-regulated
1000
500
0
Score
ACTA2
IGFBP5
SQLE
FDPS
HMGCS1
NSDHL
IGKC
RBP1
NNMT
AEBP1
GSN
GSTM2
MSMO1
ALDOC
DHCR7
RDH11
SPRY4
MYH11
HMGCR
NILOTINIB
NERATINIB
DASATINIB
SORAFENIB
GW-843682X
SUNITINIB
WYE-125132
X0-37
AZD-8055
TORIN-1
SIROLIMUS
CX-5461
ERLOTINIB
QL-XII-47
GSK-429286A
C.
CV PCB 30 up-regulated
1500
1000
500
0
TUBB2A
SDF2L1
HSPH1
JUN
HSPA5
PPP1R3C
CRELD2
ATP2B2
SPON2
CCND1
HYOU1
NFIL3
FABP5
SLC16A1
MICAL2
HSPA13
SLC30A10
NPAS2
IGF2BP2
MANF
PNRC1
CLPX
CKB
KLHL21
CYP1A1
SORBS3
MPZL1
GSTA4
KRT23
NR1D2
DHCR7
HTATIP2
SLC2A5
LPIN1
RRP12
GELDANAMYCIN
NVP-AUY922
RADICICOL
X10-0
TIPIFARNIB-P2
BRD-K41859756
ZSTK-474
GSK-690693
KIN001-043
ABT-737
BRD-K31706415
CAY10594
PF-431396
PF-3758309
BRD-K84203638
D.
CV PCB 30 down-regulated
1000
500
0
Score
ACTA2
IGFBP5
SQLE
FDPS
HMGCS1
NSDHL
IGKC
RBP1
NNMT
AEBP1
GSN
GSTM2
MSMO1
ALDOC
DHCR7
RDH11
SPRY4
MYH11
HMGCR
NILOTINIB
NERATINIB
DASATINIB
SORAFENIB
GW-843682X
SUNITINIB
WYE-125132
X0-37
AZD-8055
TORIN-1
SIROLIMUS
CX-5461
ERLOTINIB
QL-XII-47
GSK-429286A

Fig. 7


PCB effect
Liver
- ↑induction of prototypical target genes of AhR, CAR, and PXR
- Xenobiotic biotransformation GO terms↑regulated
- Most Gstms↑regulated, but Sults not altered
- Response to misfolded proteins down-regulated (ER stress)
- Differentially regulated transporters
- ↑regulation of amino acid metabolites
CV
Serum
- Dysregulated metabolites distinct to CV group
- Amino acid metabolism up-regulated only in high dose
- Anerotruncus negatively correlated with metabolites
Therapeutics to resolve gut microbiome-dependent PCB toxicity (i.e. HSP90, Bcl-2, mTOR)
- Metabolic syndrome-associated Anerotruncus down-regulated in high dose
- SCFA-producing Roseburia up-regulated for both doses
- Butyrate and cellulosome-producing Ruminiclostridium up-regulated for low dose
Gut
Liver
- Attenuated induction of AhR, CAR, and PXR targets
- Attenuated↑regulation of xenobiotic biotransformation GO terms
- Most Sults↑regulated, but Gstms not altered
- Response to misfolded proteins not altered
- ↓change of transporter expression
- ↑regulation of nucleotide and glucose metabolites
GF
Serum
- Carbohydrate metabolism ↑regulated
X
- No gut-liver interaction availble
- Lack of metabolites produced by gut microbiome
Gut

SUPPLEMENTAL FIGURE LEGENDS

Figure S1. Venn diagrams for the liver transcriptome, and liver and serum metabolome for CV (A) and GF (B) mice.

Figure S2. Box plots of differentially abundant metabolites in liver and serum. Data are shown as relative abundance. The pound signs and asterisks represent differential abundance in the CV and GF groups, respectively.

Fig. S1

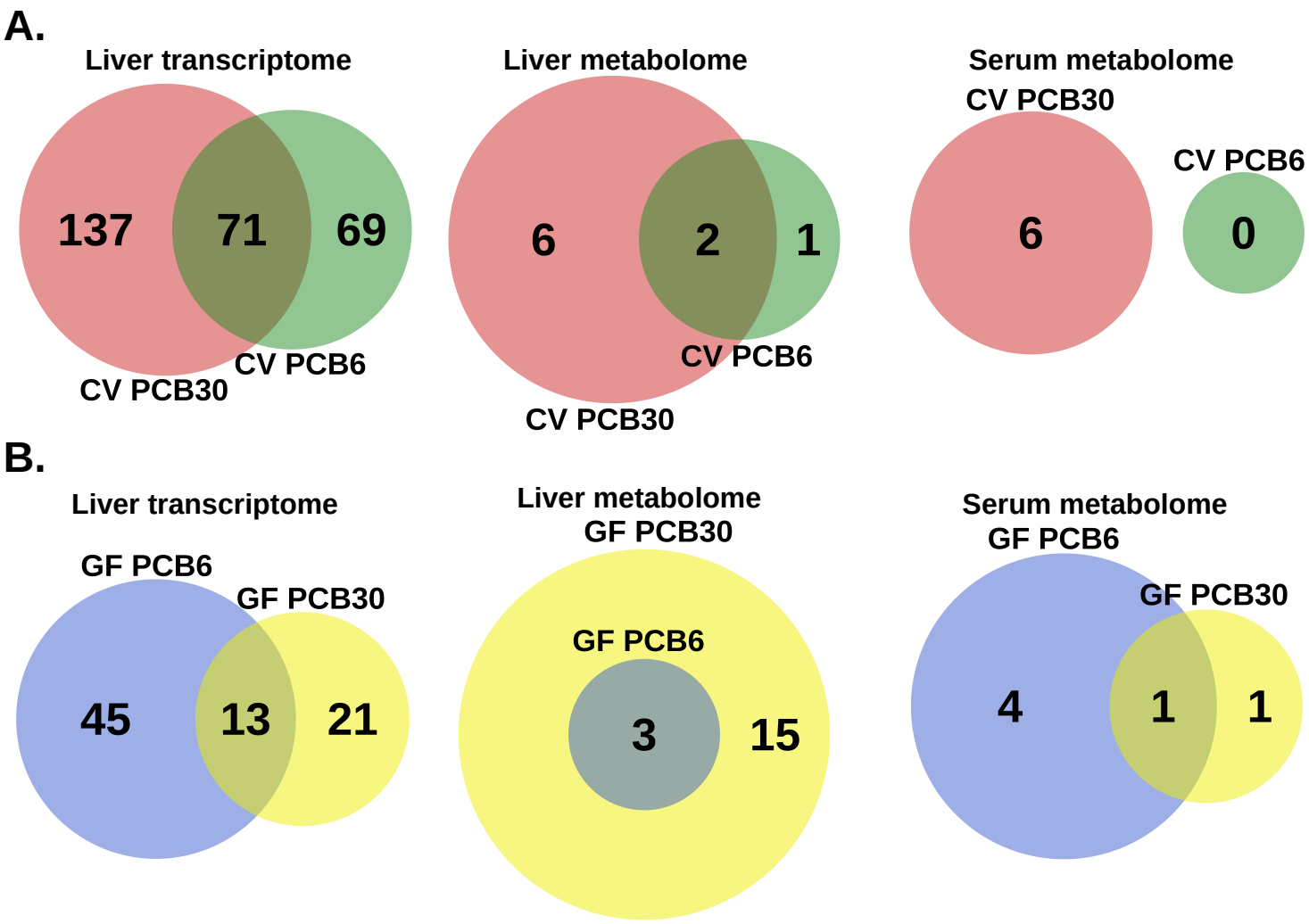
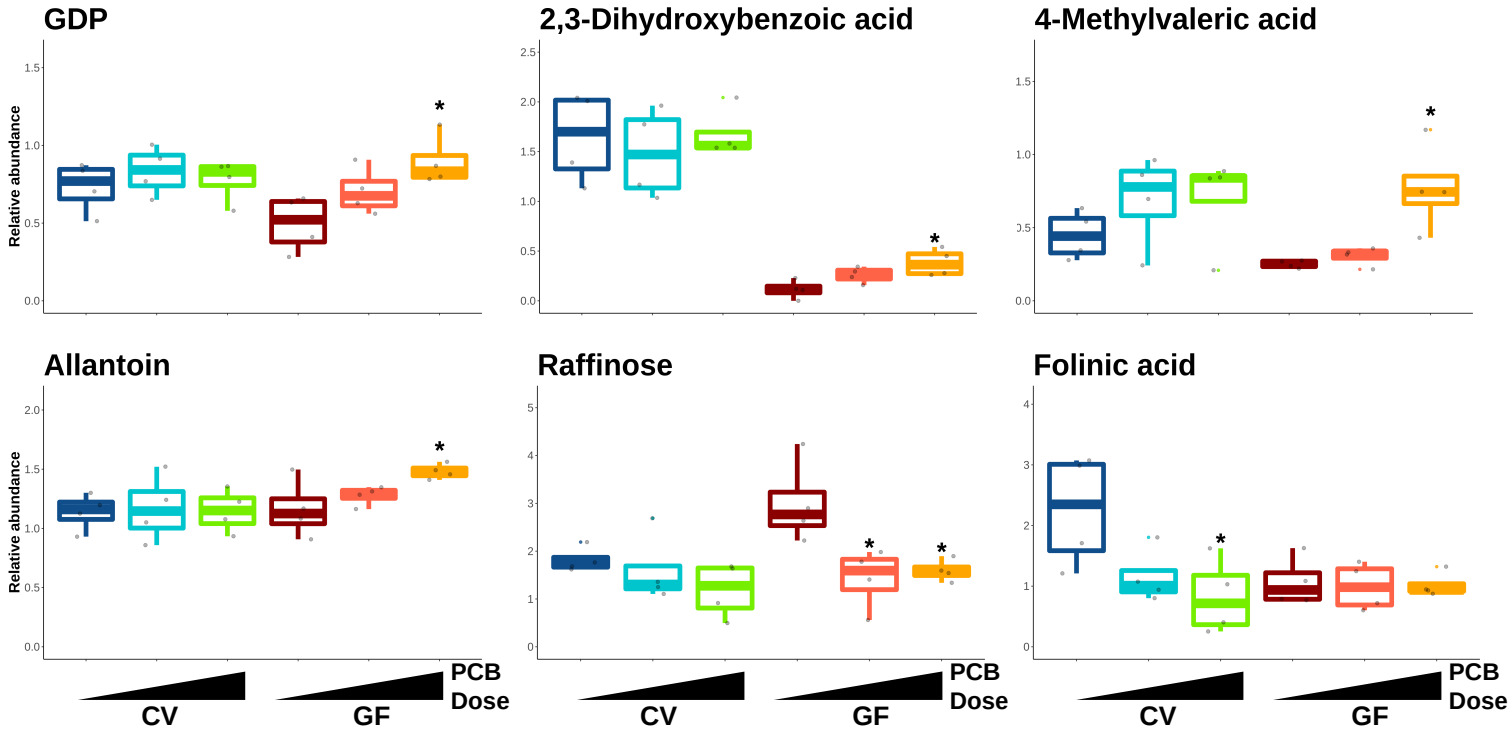
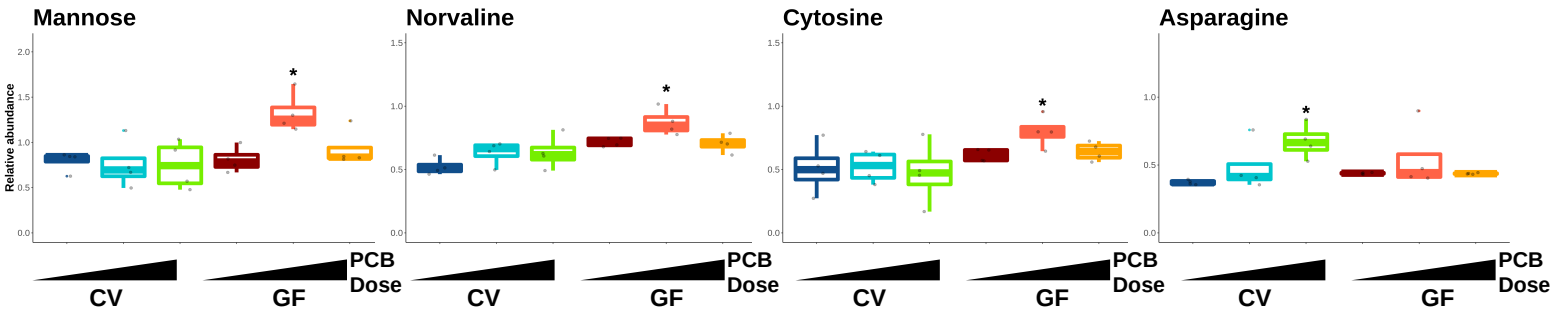

A.
Liver transcriptome
137
71
69
CV PCB6
CV PCB30
Liver metabolome
6
2
1
CV PCB6
CV PCB30
Serum metabolome
CV PCB30
6
CV PCB6
0
B.
Liver transcriptome
GF PCB6
GF PCB30
45
13
21
Liver metabolome
GF PCB30
GF PCB6
3
15
Serum metabolome
GF PCB6
GF PCB30
4
1
1

Fig. S2

A.


GDP
2,3-Dihydroxybenzoic acid
4-Methylvaleric acid
Allantoin
Raffinose
Folinic acid
Relative abundance
CV
GF
PCB Dose

B.


Mannose
Norvaline
Cytosine
Asparagine
Relative abundance
CV
GF
PCB Dose

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001082.12	Mfsd10	6.27489	1.7969	-1.80408	-1.666	0.00005	0.00761968
ENSMUSG00000003053.17	Cyp2c29	505.17	834.73	0.72454	2.77488	0.00005	0.00761968
ENSMUSG00000003555.8	Cyp17a1	30.7127	66.9781	1.12485	3.97657	0.00005	0.00761968
ENSMUSG00000004038.9	Gstm3	20.5927	33.851	0.717065	2.92459	0.00005	0.00761968
ENSMUSG00000005413.8	Hmox1	10.8956	7.33838	-0.570219	-2.05123	0.00035	0.037983
ENSMUSG00000005547.14	Cyp2a5	430.556	721.13	0.744058	2.24398	0.00015	0.0193581
ENSMUSG00000007872.3	Id3	27.5332	13.3798	-1.04111	-3.69018	0.00005	0.00761968
ENSMUSG00000014905.4	Dnajb9	24.6827	16.6976	-0.563856	-2.44755	0.00005	0.00761968
ENSMUSG00000015224.10	Cyp2j9	8.84831	4.99311	-0.825464	-2.92044	0.00005	0.00761968
ENSMUSG00000015357.10	Clpx	78.2269	50.077	-0.643518	-2.64475	0.00005	0.00761968
ENSMUSG00000017390.15	Aldoc	3.30235	6.26799	0.924508	1.8897	0.00045	0.0460446
ENSMUSG00000018427.7	Ypel2	9.95094	5.96948	-0.737227	-3.14699	0.00005	0.00761968
ENSMUSG00000018830.10	Myh11	0.856366	1.92082	1.16542	2.76044	0.00005	0.00761968
ENSMUSG00000020175.15	Rab36	7.24259	4.05831	-0.835627	-2.23857	0.00005	0.00761968
ENSMUSG00000020190.13	Mknk2	16.502	34.2124	1.05188	2.706	0.00005	0.00761968
ENSMUSG00000020473.13	Aebp1	0.537474	1.24369	1.21036	1.91027	0.00015	0.0193581
ENSMUSG00000020593.15	Lpin1	23.3481	63.294	1.43876	4.53512	0.00005	0.00761968
ENSMUSG00000020623.11	Map2k6	2.79563	4.8047	0.781271	2.25429	0.00015	0.0193581
ENSMUSG00000020644.9	Id2	65.4148	42.2437	-0.630882	-2.77822	0.00005	0.00761968
ENSMUSG00000020653.12	Klf11	4.00267	1.83482	-1.12533	-2.16824	0.00005	0.00761968
ENSMUSG00000021453.2	Gadd45g	4.23384	9.3219	1.13866	3.01194	0.00005	0.00761968
ENSMUSG00000021670.14	Hmgcr	42.2238	98.0346	1.21523	3.29717	0.00005	0.00761968
ENSMUSG00000022003.7	Slc25a30	21.1229	8.85161	-1.2548	-2.70092	0.00005	0.00761968
ENSMUSG00000022351.14	Sqle	14.4701	22.8969	0.662076	2.85745	0.00005	0.00761968
ENSMUSG00000022512.3	Cldn1	25.5877	18.7521	-0.448393	-2.02615	0.00035	0.037983
ENSMUSG00000022769.9	Sdf2l1	44.9273	25.0223	-0.844377	-3.54758	0.00005	0.00761968
ENSMUSG00000022899.9	Slc15a2	3.0659	0.37101	-3.04678	-1.38684	0.00005	0.00761968
ENSMUSG00000023087.15	Noct	3.11413	6.68196	1.10144	2.47459	0.00005	0.00761968
ENSMUSG00000023272.4	Creld2	42.1392	14.3552	-1.55359	-6.28154	0.00005	0.00761968
ENSMUSG00000024427.7	Spry4	3.84589	5.82326	0.598512	2.37281	0.00005	0.00761968
ENSMUSG00000024548.11	Setbp1	0.571063	0.898115	0.65325	2.01298	0.0004	0.0421324
ENSMUSG00000024807.18	Syvn1	26.659	12.2223	-1.12511	-3.46232	0.00005	0.00761968
ENSMUSG00000024843.15	Chka	45.983	21.79	-1.07743	-2.35525	0.00025	0.028881
ENSMUSG00000024987.6	Cyp26a1	11.1487	24.2118	1.11883	3.82575	0.00005	0.00761968
ENSMUSG00000025185.14	Loxl4	3.94432	2.11188	-0.90125	-2.33915	0.00005	0.00761968
ENSMUSG00000025190.13	Got1	73.9132	114.605	0.632762	2.52771	0.00005	0.00761968
ENSMUSG00000026077.15	Npas2	8.47762	1.95208	-2.11865	-2.21209	0.0001	0.0140441
ENSMUSG00000026185.8	Igfbp5	5.37805	8.0981	0.590499	2.46113	0.00005	0.00761968
ENSMUSG00000026348.7	Acmsd	7.9453	11.3608	0.515893	2.05887	0.00025	0.028881
ENSMUSG00000026390.7	Marco	4.51252	2.20537	-1.03291	-2.38186	0.00005	0.00761968
ENSMUSG00000026614.7	Slc30a10	12.8976	7.77189	-0.730768	-3.05461	0.00005	0.00761968
ENSMUSG00000026839.17	Upp2	61.1429	142.443	1.22013	4.83935	0.00005	0.00761968
ENSMUSG00000026864.13	Hspa5	838.917	453.702	-0.886781	-2.47163	0.00005	0.00761968
ENSMUSG00000026879.14	Gsn	5.39704	11.4131	1.08046	3.81852	0.00005	0.00761968
ENSMUSG00000027346.15	Gpcpd1	23.3608	40.7371	0.802254	2.42579	0.0001	0.0140441
ENSMUSG00000027360.5	Hdc	3.45119	1.89382	-0.865796	-1.76936	0.00045	0.0460446
ENSMUSG00000027947.11	Il6ra	12.7959	19.116	0.579098	2.29486	0.00025	0.028881
ENSMUSG00000027954.9	Efna1	27.2749	14.7794	-0.883989	-3.61654	0.00005	0.00761968
ENSMUSG00000028238.6	Atp6v0d2	5.28464	8.4326	0.674173	2.16648	0.0001	0.0140441
ENSMUSG00000028680.14	Plk3	10.5138	6.01814	-0.804897	-3.05136	0.00005	0.00761968
ENSMUSG00000029009.17	Mthfr	7.1591	3.44294	-1.05613	-2.20818	0.00035	0.037983

ENSMUSG00000029188.14	Slc34a2	1.56037	0.365782	-2.09283	-2.78098	0.00005	0.00761968
ENSMUSG00000029467.15	Atp2a2	86.4356	60.473	-0.515334	-1.97184	0.00035	0.037983
ENSMUSG00000029657.15	Hsph1	47.3595	28.792	-0.717988	-2.07578	0.00015	0.0193581
ENSMUSG00000029992.14	Gfpt1	13.4599	9.01933	-0.577579	-1.84116	0.00045	0.0460446
ENSMUSG00000030302.16	Atp2b2	4.38644	2.77593	-0.66008	-2.11664	0.0002	0.0244872
ENSMUSG00000030483.14	Cyp2b10	17.3823	34.9186	1.00638	4.20068	0.00005	0.00761968
ENSMUSG00000030917.13	Tmem159	0.899211	4.33785	2.27025	1.53715	0.0004	0.0421324
ENSMUSG00000031349.4	Nsdhl	10.9891	18.7202	0.768519	3.05432	0.00005	0.00761968
ENSMUSG00000031604.10	Msmo1	88.8162	141.341	0.67029	2.3651	0.0002	0.0244872
ENSMUSG00000031762.7	Mt2	14.6712	30.7685	1.06847	2.79551	0.00005	0.00761968
ENSMUSG00000031765.8	Mt1	41.5758	103.19	1.31148	4.86124	0.00005	0.00761968
ENSMUSG00000032115.14	Hyou1	67.4029	46.7624	-0.527462	-2.28962	0.00005	0.00761968
ENSMUSG00000032271.13	Nnmt	56.8868	84.4939	0.570754	2.3728	0.00005	0.00761968
ENSMUSG00000032310.4	Cyp1a2	347.498	1061.1	1.61048	5.9896	0.00005	0.00761968
ENSMUSG00000032350.9	Gclc	79.3815	50.4684	-0.653422	-2.42429	0.00005	0.00761968
ENSMUSG00000032575.16	Manf	239.221	135.412	-0.820986	-2.2734	0.0001	0.0140441
ENSMUSG00000032902.1	Slc16a1	19.0525	12.3003	-0.631283	-2.79129	0.00005	0.00761968
ENSMUSG00000032932.15	Hspa13	14.3906	9.10349	-0.660639	-2.73434	0.00005	0.00761968
ENSMUSG00000033107.6	Rnf125	123.021	61.7043	-0.995457	-4.47951	0.00005	0.00761968
ENSMUSG00000035686.8	Thrsp	108.608	275.462	1.34273	5.6328	0.00005	0.00761968
ENSMUSG00000035783.9	Acta2	1.51116	4.87177	1.68878	2.67871	0.00005	0.00761968
ENSMUSG00000035828.11	Pim3	5.49715	9.06074	0.720943	2.54131	0.00005	0.00761968
ENSMUSG00000037405.8	Icam1	7.588	5.10752	-0.571098	-2.12615	0.0004	0.0421324
ENSMUSG00000037440.8	Vnn1	26.6312	18.1146	-0.555968	-2.3665	0.0001	0.0140441
ENSMUSG00000038418.7	Egr1	8.5935	4.36381	-0.977659	-3.36242	0.00005	0.00761968
ENSMUSG00000038508.7	Gdf15	2.87642	1.396	-1.04298	-2.33349	0.00035	0.037983
ENSMUSG00000038656.5	Cyp3a16	15.6662	29.4555	0.910887	3.44256	0.00005	0.00761968
ENSMUSG00000039633.6	Lonrf1	1.73883	1.02745	-0.759046	-2.12834	0.0004	0.0421324
ENSMUSG00000039801.7	Cplane1	1.57608	11.8302	2.90806	2.79653	0.00015	0.0193581
ENSMUSG00000040128.9	Pnrc1	65.8791	42.2407	-0.641185	-2.71807	0.00005	0.00761968
ENSMUSG00000040562.12	Gstm2	44.5903	65.892	0.563373	2.4444	0.00005	0.00761968
ENSMUSG00000041324.14	Inhba	9.92684	4.22896	-1.23103	-2.8545	0.00005	0.00761968
ENSMUSG00000045287.6	Rtn4rl1	6.73191	4.46	-0.593973	-2.31529	0.00015	0.0193581
ENSMUSG00000045776.3	Lrtm1	4.59023	7.84042	0.772364	2.57822	0.00005	0.00761968
ENSMUSG00000046402.10	Rbp1	2.24938	3.8182	0.763363	2.38685	0.00005	0.00761968
ENSMUSG00000047777.9	Phf13	2.44905	1.25344	-0.966331	-2.7493	0.00005	0.00761968
ENSMUSG00000047822.8	Angptl8	82.3516	37.7627	-1.12484	-2.15144	0.00045	0.0460446
ENSMUSG00000049164.7	Zfp518a	3.42441	2.24797	-0.607233	-2.21996	0.00005	0.00761968
ENSMUSG00000049580.12	Tsku	7.78541	17.2903	1.15112	2.39263	0.0002	0.0244872
ENSMUSG00000052684.4	Jun	8.02239	3.56567	-1.16986	-4.3468	0.00005	0.00761968
ENSMUSG00000054277.8	Arfgap3	4.98675	2.38411	-1.06465	-2.77345	0.00005	0.00761968
ENSMUSG00000055116.8	Arntl	9.47854	4.66962	-1.02136	-3.41105	0.00005	0.00761968
ENSMUSG00000056313.5	Tcim	6.3628	10.6007	0.736431	2.63227	0.00005	0.00761968
ENSMUSG00000056501.3	Cebpb	33.2417	49.8658	0.585055	2.15225	0.0002	0.0244872
ENSMUSG00000056749.7	Nfil3	11.4209	6.76087	-0.756389	-2.86792	0.00005	0.00761968
ENSMUSG00000057068.15	Fam47e	6.37728	11.3884	0.836547	2.00781	0.00025	0.028881
ENSMUSG00000057069.7	Ero1lb	12.8374	8.73738	-0.555077	-2.29919	0.0001	0.0140441
ENSMUSG00000058454.15	Dhcr7	16.3576	28.6402	0.808075	2.67257	0.00005	0.00761968
ENSMUSG00000058672.7	Tubb2a	60.3828	42.6623	-0.501177	-2.22162	0.0002	0.0244872
ENSMUSG00000059060.15	Rad51b	2.98263	1.00564	-1.56846	-2.7696	0.00005	0.00761968
ENSMUSG00000059743.12	Fdps	68.1418	100.306	0.557798	2.3204	0.00005	0.00761968

ENSMUSG00000061825.10	Ces2c	4.32809	7.73435	0.837552	2.81141	0.00005	0.00761968
ENSMUSG00000064213.5	Defa24	1.36432	0	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000064354.1	mt-Co2	6.53406	11.5824	0.825885	2.28304	0.00015	0.0193581
ENSMUSG00000066441.14	Rdh11	16.5169	23.867	0.531074	2.24242	0.00005	0.00761968
ENSMUSG00000066687.5	Zbtb16	17.6103	35.1446	0.996886	3.99134	0.00005	0.00761968
ENSMUSG00000067225.2	Cyp2c54	162.272	224.41	0.467721	2.06478	0.00025	0.028881
ENSMUSG00000067279.3	Ppp1r3c	27.6268	14.325	-0.947532	-4.13342	0.00005	0.00761968
ENSMUSG00000069324.6	Gm5096	15.1526	23.2798	0.619511	2.53681	0.00005	0.00761968
ENSMUSG00000069668.4	Sult3a1	97.163	160.62	0.725176	3.28788	0.00005	0.00761968
ENSMUSG00000070644.13	Etnk2	62.5601	96.255	0.621618	2.63482	0.00005	0.00761968
ENSMUSG00000070811.6	Sult2a2	47.5462	75.7986	0.672841	2.07079	0.0003	0.03438
ENSMUSG00000072949.6	Acot1	33.817	19.1723	-0.818729	-2.60084	0.00005	0.00761968
ENSMUSG00000074063.10	Osgin1	93.9424	49.382	-0.927792	-4.03213	0.00005	0.00761968
ENSMUSG00000074768.6	Bhmt	276.248	458.526	0.731038	2.73971	0.00005	0.00761968
ENSMUSG00000074896.3	Ifit3	4.81246	7.59939	0.659108	2.2256	0.00025	0.028881
ENSMUSG00000075551.4	Cyp3a41a	33.4333	57.9428	0.793345	3.43636	0.00005	0.00761968
ENSMUSG00000075552.4	Cyp3a41b	4.55117	8.51163	0.903198	3.06479	0.00005	0.00761968
ENSMUSG00000076609.2	Igkc	9.38561	17.1417	0.868984	2.35993	0.00005	0.00761968
ENSMUSG00000078650.2	G6pc	118.654	70.8163	-0.744612	-3.34005	0.00005	0.00761968
ENSMUSG00000078798.4	Sult2a1	56.4787	97.1215	0.782085	3.19123	0.00005	0.00761968
ENSMUSG00000078866.10	Zfp970	11.5288	17.8725	0.632507	2.15652	0.00015	0.0193581
ENSMUSG00000081207.4	Gm13775	12.4872	21.3006	0.770447	2.48423	0.00005	0.00761968
ENSMUSG00000084923.1	Gm15611	21.2021	5.05847	-2.06744	-4.28501	0.00005	0.00761968
ENSMUSG00000085445.1	Gm16348	0.998651	2.12188	1.08729	2.36459	0.00005	0.00761968
ENSMUSG00000090298.2	Sult3a2	3.39104	7.38886	1.12362	2.81264	0.00005	0.00761968
ENSMUSG00000090877.3	Hspa1b	1.21104	0.49013	-1.305	-2.62497	0.0002	0.0244872
ENSMUSG00000090942.1	F830016B	18.3992	13.1678	-0.482627	-2.08238	0.00035	0.037983
ENSMUSG00000092075.1	Serpina4-	21.4399	5.39866	-1.98962	-6.65923	0.00005	0.00761968
ENSMUSG00000093930.2	Hmgcs1	79.4702	111.752	0.491821	1.79112	0.00015	0.0193581
ENSMUSG00000096674.1	Mup15	16.0544	25.2402	0.652756	2.36601	0.00005	0.00761968
ENSMUSG00000096688.1	Mup17	35.5827	61.429	0.787745	3.16456	0.00005	0.00761968
ENSMUSG00000099032.2	Tcf24	4.46246	2.40791	-0.890059	-2.74594	0.00005	0.00761968
ENSMUSG00000100277.8	1810053B	0.732602	2.66094	1.86084	1.18658	0.0001	0.0140441
ENSMUSG00000102888.1	Ighv1-11	0	6.24986	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000106397.1	Gm21049	4.52985	7.62193	0.750694	2.11318	0.00035	0.037983
ENSMUSG00000110384.1	Gm45301	1.01899	2.77951	1.44769	2.41211	0.00025	0.028881
ENSMUSG00000115388.2	Eppk1	5.00691	7.2053	0.525136	2.22729	0.0001	0.0140441
ENSMUSG00000115919.1	Gm31583	2.90438	5.0658	0.802558	2.71184	0.00005	0.00761968

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001270.9	Ckb	4.9592	2.82251	-0.813128	-1.925	0.00055	0.0404152
ENSMUSG00000003053.17	Cyp2c29	502.057	1871.49	1.89827	4.7931	0.00005	0.00618632
ENSMUSG00000003555.8	Cyp17a1	30.523	69.3286	1.18355	3.76365	0.00005	0.00618632
ENSMUSG00000003849.8	Nqo1	4.13848	8.59917	1.05509	3.10818	0.00005	0.00618632
ENSMUSG00000004038.9	Gstm3	20.4693	75.9074	1.89078	6.88927	0.00005	0.00618632
ENSMUSG00000005514.14	Por	143.718	286.806	0.996833	2.93999	0.00005	0.00618632
ENSMUSG00000005547.14	Cyp2a5	427.875	1202.66	1.49096	3.44719	0.00005	0.00618632
ENSMUSG00000005779.12	Psmb4	57.871	84.627	0.548278	1.92037	0.00065	0.0456767
ENSMUSG00000006777.7	Krt23	1.02612	5.09059	2.31064	4.50613	0.00005	0.00618632
ENSMUSG00000007950.9	Abhd8	1.46653	0.490162	-1.58107	-2.25758	0.0002	0.0194309
ENSMUSG00000011305.11	Plin5	16.8478	11.2536	-0.582169	-2.14557	0.00015	0.0159662
ENSMUSG00000015224.10	Cyp2j9	8.79124	5.13102	-0.776822	-2.50401	0.00005	0.00618632
ENSMUSG00000015357.10	Clpx	77.7399	44.4332	-0.807017	-2.76713	0.00005	0.00618632
ENSMUSG00000016239.11	Lonrf3	2.78045	1.06184	-1.38874	-2.97987	0.00005	0.00618632
ENSMUSG00000020027.18	Socs2	8.61402	16.6749	0.952916	2.06	0.00005	0.00618632
ENSMUSG00000020123.6	Avpr1a	24.1839	14.3293	-0.755076	-2.41315	0.00005	0.00618632
ENSMUSG00000020175.15	Rab36	7.19819	4.01968	-0.840554	-2.06135	0.00035	0.029457
ENSMUSG00000020190.13	Mknk2	16.398	38.746	1.24053	2.84633	0.00005	0.00618632
ENSMUSG00000020593.15	Lpin1	23.2003	40.0422	0.78738	2.19992	0.00055	0.0404152
ENSMUSG00000020889.11	Nr1d1	17.095	37.493	1.13305	2.42106	0.0005	0.0385
ENSMUSG00000021453.2	Gadd45g	4.2085	13.5086	1.6825	4.46078	0.00005	0.00618632
ENSMUSG00000021775.11	Nr1d2	18.5393	32.2923	0.800601	2.14163	0.0001	0.0113094
ENSMUSG00000022025.13	Cnmd	2.94353	7.12175	1.27469	2.30779	0.0001	0.0113094
ENSMUSG00000022091.6	Sorbs3	8.7422	15.3301	0.810301	2.61385	0.00005	0.00618632
ENSMUSG00000022270.16	Retreg1	33.766	64.9642	0.944073	2.71635	0.00005	0.00618632
ENSMUSG00000022346.15	Myc	1.47519	5.7052	1.95138	3.05112	0.00005	0.00618632
ENSMUSG00000022508.5	Bcl6	3.5485	6.1976	0.804501	2.72117	0.00005	0.00618632
ENSMUSG00000022679.13	Mpv17l	3.4023	7.38539	1.11816	2.33264	0.00005	0.00618632
ENSMUSG00000022769.9	Sdf2l1	44.6531	24.9449	-0.840016	-3.10498	0.00005	0.00618632
ENSMUSG00000023073.2	Slc10a2	3.87084	6.00992	0.634701	2.23853	0.0002	0.0194309
ENSMUSG00000023272.4	Creld2	41.8868	10.7104	-1.96748	-6.82395	0.00005	0.00618632
ENSMUSG00000024131.8	Slc3a1	16.845	27.1766	0.690046	1.95102	0.00055	0.0404152
ENSMUSG00000024254.15	Abcg8	23.9899	44.5496	0.892986	2.2514	0.00005	0.00618632
ENSMUSG00000024427.7	Spry4	3.8216	7.52294	0.977118	3.54048	0.00005	0.00618632
ENSMUSG00000024548.11	Setbp1	0.567395	0.943684	0.733949	2.09591	0.00035	0.029457
ENSMUSG00000024646.14	Cyb5a	1372.68	2262.27	0.720771	2.28567	0.00005	0.00618632
ENSMUSG00000024747.3	Aldh1a7	74.5145	106.783	0.519085	1.98059	0.0006	0.043428
ENSMUSG00000024807.18	Syvn1	26.4973	12.6676	-1.0647	-2.99172	0.00005	0.00618632
ENSMUSG00000025002.5	Cyp2c55	5.11	22.678	2.1499	7.12158	0.00005	0.00618632
ENSMUSG00000025185.14	Loxl4	3.92033	1.51462	-1.37202	-2.71184	0.00005	0.00618632
ENSMUSG00000025190.13	Got1	73.4621	143.402	0.964996	3.33157	0.00005	0.00618632
ENSMUSG00000026077.15	Npas2	8.42746	1.66594	-2.33876	-3.01011	0.0001	0.0113094
ENSMUSG00000026226.16	Spata3	2.63728	0.875213	-1.59135	-1.67117	0.0001	0.0113094
ENSMUSG00000026259.14	Ngef	11.0126	17.9847	0.707619	2.38152	0.00005	0.00618632
ENSMUSG00000026272.6	Agxt	102.981	151.74	0.559222	2.16773	0.00005	0.00618632
ENSMUSG00000026348.7	Acmsd	7.89756	21.2665	1.42911	4.87646	0.00005	0.00618632
ENSMUSG00000026390.7	Marco	4.48507	2.16164	-1.05301	-2.28692	0.00005	0.00618632
ENSMUSG00000026566.15	Mpzl1	6.70294	2.77735	-1.27108	-2.14427	0.00025	0.0235
ENSMUSG00000026614.7	Slc30a10	12.8176	6.44774	-0.991257	-3.4987	0.00005	0.00618632
ENSMUSG00000026839.17	Upp2	60.7617	218.9	1.84904	6.12168	0.00005	0.00618632
ENSMUSG00000026864.13	Hspa5	833.809	437.932	-0.929011	-2.08676	0.00015	0.0159662

ENSMUSG00000027253.15	Lrp4	4.77798	7.06684	0.564666	2.03091	0.0002	0.0194309
ENSMUSG00000027331.15	Knstrn	0.217572	1.42377	2.71015	1.00013	0.00015	0.0159662
ENSMUSG00000027346.15	Gpcpd1	23.2178	53.4558	1.20312	3.25032	0.00005	0.00618632
ENSMUSG00000027398.13	Il1b	3.56328	1.05211	-1.75992	-2.14464	0.0001	0.0113094
ENSMUSG00000027533.10	Fabp5	26.5272	16.0182	-0.727761	-2.43622	0.00005	0.00618632
ENSMUSG00000027890.17	Gstm4	22.8624	40.384	0.820811	3.1403	0.00005	0.00618632
ENSMUSG00000028019.9	Pdgfc	2.88046	1.70807	-0.753934	-1.99822	0.0006	0.043428
ENSMUSG00000028238.6	Atp6v0d2	5.25254	9.46139	0.849037	2.4918	0.00005	0.00618632
ENSMUSG00000028383.17	Hsdl2	27.8303	19.1411	-0.539983	-2.08801	0.0003	0.0264805
ENSMUSG00000028479.18	Gne	79.8364	128.18	0.683054	2.04104	0.00065	0.0456767
ENSMUSG00000028715.2	Cyp4a14	391.915	237.782	-0.720899	-2.27606	0.00015	0.0159662
ENSMUSG00000028957.12	Per3	1.72562	11.0867	2.68365	4.12698	0.00005	0.00618632
ENSMUSG00000028976.10	Slc2a5	0.440546	1.76822	2.00493	1.65217	0.00065	0.0456767
ENSMUSG00000029009.17	Mthfr	7.11418	2.70437	-1.3954	-2.97286	0.00005	0.00618632
ENSMUSG00000029188.14	Slc34a2	1.55125	0.246171	-2.65571	-2.62671	0.00005	0.00618632
ENSMUSG00000029650.10	Slc46a3	31.8414	52.3096	0.71617	2.06244	0.0003	0.0264805
ENSMUSG00000029657.15	Hsph1	47.0702	27.7613	-0.761739	-2.01922	0.00025	0.0235
ENSMUSG00000030244.7	Gys2	36.9491	64.0714	0.794143	2.09027	0.00055	0.0404152
ENSMUSG00000030302.16	Atp2b2	4.35972	2.18107	-0.999203	-2.83779	0.00005	0.00618632
ENSMUSG00000030340.16	Scnn1a	6.11295	9.11203	0.575904	2.05878	0.00065	0.0456767
ENSMUSG00000030364.6	Clec2h	1.55662	4.31177	1.46986	2.18053	0.00005	0.00618632
ENSMUSG00000030483.14	Cyp2b10	17.2776	94.9368	2.45806	8.74658	0.00005	0.00618632
ENSMUSG00000031271.14	Serpina7	9.22525	4.97408	-0.891158	-2.09026	0.0004	0.033088
ENSMUSG00000031596.15	Slc7a2	85.9182	171.302	0.995503	2.42586	0.00005	0.00618632
ENSMUSG00000031762.7	Mt2	14.5776	52.8041	1.8569	4.62578	0.00005	0.00618632
ENSMUSG00000031765.8	Mt1	41.3184	148.541	1.84601	6.05154	0.00005	0.00618632
ENSMUSG00000031775.5	Pllp	6.14127	2.78882	-1.13888	-2.14469	0.00045	0.0359901
ENSMUSG00000032012.8	Nectin1	24.696	17.389	-0.506108	-1.94543	0.00055	0.0404152
ENSMUSG00000032115.14	Hyou1	66.9891	43.0138	-0.639125	-2.34774	0.00005	0.00618632
ENSMUSG00000032271.13	Nnmt	56.5371	127.246	1.17034	4.24758	0.00005	0.00618632
ENSMUSG00000032310.4	Cyp1a2	345.376	2354.78	2.76935	6.42721	0.00005	0.00618632
ENSMUSG00000032315.6	Cyp1a1	0.408235	21.3863	5.71114	10.8865	0.00005	0.00618632
ENSMUSG00000032348.6	Gsta4	52.469	81.8235	0.641049	2.47242	0.00005	0.00618632
ENSMUSG00000032575.16	Manf	237.772	126.916	-0.905701	-2.11863	0.0003	0.0264805
ENSMUSG00000032715.9	Trib3	3.62747	8.68618	1.25976	2.03279	0.00035	0.029457
ENSMUSG00000032724.5	Abtb2	5.87529	3.77695	-0.637439	-2.04753	0.0004	0.033088
ENSMUSG00000032849.14	Abcc4	1.71548	3.77068	1.13622	2.61385	0.00005	0.00618632
ENSMUSG00000032902.1	Slc16a1	18.9328	10.1797	-0.8952	-3.40735	0.00005	0.00618632
ENSMUSG00000032932.15	Hspa13	14.303	9.86525	-0.535886	-1.97593	0.00025	0.0235
ENSMUSG00000033107.6	Rnf125	122.257	74.8678	-0.707494	-2.81318	0.00005	0.00618632
ENSMUSG00000033581.17	Igf2bp2	1.66105	0.509047	-1.70623	-1.12591	0.0003	0.0264805
ENSMUSG00000034774.6	Dsg1c	1.07675	2.19221	1.0257	2.76946	0.0001	0.0113094
ENSMUSG00000034837.12	Gnat1	12.5088	21.0651	0.751915	2.1181	0.00035	0.029457
ENSMUSG00000035049.4	Rrp12	2.74802	1.48642	-0.886549	-2.6113	0.00005	0.00618632
ENSMUSG00000035372.2	1810055G	6.32408	10.8725	0.781761	1.96938	0.00035	0.029457
ENSMUSG00000035686.8	Thrsp	107.955	205.081	0.925768	3.34836	0.00005	0.00618632
ENSMUSG00000035828.11	Pim3	5.46211	9.62427	0.81722	2.71331	0.00005	0.00618632
ENSMUSG00000035944.17	Ttc38	14.0742	20.1391	0.516941	1.96377	0.00055	0.0404152
ENSMUSG00000036110.14	Slc17a2	47.9669	31.78	-0.59392	-2.07519	0.00015	0.0159662
ENSMUSG00000036957.8	Lrfn3	2.96637	1.17429	-1.33691	-3.36685	0.00005	0.00618632
ENSMUSG00000037095.8	Lrg1	67.2168	47.361	-0.505121	-1.98627	0.00065	0.0456767

ENSMUSG00000037157.8	Il22ra1	3.93685	2.30756	-0.770677	-2.21827	0.0002	0.0194309
ENSMUSG00000037379.7	Spon2	4.43994	1.82471	-1.28287	-2.45754	0.00005	0.00618632
ENSMUSG00000037583.2	Nr0b2	25.807	16.3589	-0.657683	-2.30236	0.0002	0.0194309
ENSMUSG00000037679.9	Inf2	14.5959	21.2562	0.542318	1.95943	0.0005	0.0385
ENSMUSG00000038244.14	Mical2	7.57323	4.32506	-0.808189	-2.30005	0.00005	0.00618632
ENSMUSG00000038415.10	Foxq1	3.1372	4.80063	0.613744	2.07957	0.00045	0.0359901
ENSMUSG00000038418.7	Egr1	8.53806	14.7592	0.789639	2.33622	0.00015	0.0159662
ENSMUSG00000038550.10	Ciart	0.635327	4.26202	2.74597	2.5058	0.00005	0.00618632
ENSMUSG00000038702.6	Dsel	0.318647	1.1368	1.83495	1.59147	0.0005	0.0385
ENSMUSG00000038768.8	9130409I	1.69012	3.3601	0.991375	2.38357	0.0002	0.0194309
ENSMUSG00000039395.8	Mreg	31.446	22.0227	-0.513883	-2.00407	0.0005	0.0385
ENSMUSG00000039533.8	Mmd2	1.90734	4.59768	1.26934	2.91012	0.00005	0.00618632
ENSMUSG00000039745.8	Htatip2	13.6124	21.7983	0.679289	2.28578	0.0001	0.0113094
ENSMUSG00000039886.8	Tmem12(	16.7696	27.8392	0.731267	2.68188	0.00005	0.00618632
ENSMUSG00000040127.13	Sdr9c7	19.4072	11.0266	-0.815607	-2.73366	0.00005	0.00618632
ENSMUSG00000040128.9	Pnrc1	65.4718	42.3024	-0.630135	-2.33326	0.00005	0.00618632
ENSMUSG00000040264.10	Gbp2b	2.41906	1.40646	-0.782373	-1.95544	0.0007	0.0487173
ENSMUSG00000040562.12	Gstm2	44.3194	85.0048	0.939604	3.60356	0.00005	0.00618632
ENSMUSG00000041324.14	Inhba	9.86411	3.40919	-1.53276	-3.38139	0.00005	0.00618632
ENSMUSG00000041698.11	Slco1a1	51.4801	33.2839	-0.62919	-2.3143	0.00005	0.00618632
ENSMUSG00000042115.4	Klhdc8a	0.80677	0.334395	-1.2706	-2.44981	0.00025	0.0235
ENSMUSG00000042363.14	Lgalsl	8.00763	4.41853	-0.857811	-2.18413	0.00005	0.00618632
ENSMUSG00000042622.14	Maff	1.85114	4.3513	1.23303	2.48105	0.00005	0.00618632
ENSMUSG00000043445.7	Pgp	4.53206	2.65663	-0.770568	-2.30203	0.00005	0.00618632
ENSMUSG00000044071.8	Tafa2	0.48376	1.16023	1.26205	2.303	0.0003	0.0264805
ENSMUSG00000044847.13	Lsm11	0.880467	0.334164	-1.39771	-2.60413	0.00005	0.00618632
ENSMUSG00000045287.6	Rtn4rl1	6.68976	3.11675	-1.10191	-3.68259	0.00005	0.00618632
ENSMUSG00000046402.10	Rbp1	2.23594	3.74793	0.745215	2.09243	0.0003	0.0264805
ENSMUSG00000046541.9	Zfp526	1.73728	3.00717	0.791579	2.28551	0.0001	0.0113094
ENSMUSG00000047617.11	Paxx	39.0765	17.0249	-1.19866	-2.96755	0.00005	0.00618632
ENSMUSG00000052305.6	Hbb-bs	63.8974	36.6592	-0.80158	-2.85373	0.00005	0.00618632
ENSMUSG00000052496.5	Pkdrej	0.475661	1.0218	1.10311	2.72703	0.00005	0.00618632
ENSMUSG00000052676.16	Zmat1	4.08129	6.4258	0.654851	2.13824	0.00025	0.0235
ENSMUSG00000052684.4	Jun	7.97305	4.26725	-0.901823	-3.1051	0.00005	0.00618632
ENSMUSG00000053113.3	Socs3	2.49474	5.38121	1.10904	2.11745	0.0003	0.0264805
ENSMUSG00000053559.13	Smagp	31.1285	19.9458	-0.642154	-2.13389	0.00035	0.029457
ENSMUSG00000054191.8	Klf1	1.62248	3.2131	0.985766	2.18554	0.00045	0.0359901
ENSMUSG00000054277.8	Arfgap3	4.95607	2.07293	-1.25753	-2.8446	0.00005	0.00618632
ENSMUSG00000054417.5	Cyp3a44	25.8573	17.1078	-0.595916	-2.16753	0.0002	0.0194309
ENSMUSG00000054659.13	Pm20d2	3.10156	1.32451	-1.22753	-2.48902	0.0002	0.0194309
ENSMUSG00000054827.12	Cyp2c50	357.009	627.067	0.812659	2.57099	0.00005	0.00618632
ENSMUSG00000055116.8	Arntl	9.41997	3.72741	-1.33755	-3.70408	0.00005	0.00618632
ENSMUSG00000055254.15	Ntrk2	1.32876	2.94734	1.14933	1.80865	0.0003	0.0264805
ENSMUSG00000056666.13	Retsat	163.179	84.9098	-0.942452	-2.9787	0.00005	0.00618632
ENSMUSG00000056749.7	Nfil3	11.3496	6.37484	-0.832181	-2.80945	0.00005	0.00618632
ENSMUSG00000057069.7	Ero1lb	12.7588	7.57204	-0.752743	-2.69188	0.00005	0.00618632
ENSMUSG00000057933.10	Gsta2	14.8876	36.6186	1.29846	4.13678	0.00005	0.00618632
ENSMUSG00000058135.12	Gstm1	591.115	1077.86	0.866655	2.73107	0.00005	0.00618632
ENSMUSG00000058454.15	Dhcr7	16.2573	24.4437	0.588377	1.73799	0.00045	0.0359901
ENSMUSG00000058569.8	Tmed9	27.8989	18.8487	-0.565745	-2.03359	0.00055	0.0404152
ENSMUSG00000058571.11	Gpc6	0.925695	2.30111	1.31372	2.76731	0.00005	0.00618632

ENSMUSG00000058672.7	Tubb2a	60.0095	29.3901	-1.02986	-3.68327	0.00005	0.00618632
ENSMUSG00000059060.15	Rad51b	2.96318	0.790659	-1.90602	-2.70012	0.00005	0.00618632
ENSMUSG00000060317.9	Acnat2	62.994	36.0946	-0.803432	-3.04246	0.00005	0.00618632
ENSMUSG00000060550.16	H2-Q7	26.9214	17.4807	-0.622989	-2.11728	0.0002	0.0194309
ENSMUSG00000060803.6	Gstp1	52.2482	94.5054	0.855015	3.20267	0.00005	0.00618632
ENSMUSG00000060807.7	Serpina6	169.985	262.86	0.628886	2.32333	0.00005	0.00618632
ENSMUSG00000061080.11	Lsamp	1.22575	0.291018	-2.07448	-1.14479	0.0001	0.0113094
ENSMUSG00000061601.15	Pclo	0.57566	0.977399	0.763729	2.10847	0.00035	0.029457
ENSMUSG00000061825.10	Ces2c	4.3022	11.1216	1.37022	4.14522	0.00005	0.00618632
ENSMUSG00000063415.12	Cyp26b1	6.19951	2.65142	-1.22539	-4.09556	0.00005	0.00618632
ENSMUSG00000064225.6	Paqr9	57.3054	30.826	-0.894525	-3.17638	0.00005	0.00618632
ENSMUSG00000064605.3	Gm22220	0	7.00551	#NUM!	#NUM!	0.00005	0.00618632
ENSMUSG00000066154.11	Mup3	2026.5	1252.6	-0.694063	-2.02644	0.00045	0.0359901
ENSMUSG00000067199.4	Frat1	3.39578	1.93858	-0.808739	-2.24788	0.0002	0.0194309
ENSMUSG00000067219.9	Nipal1	4.44909	8.25715	0.892133	2.59416	0.00005	0.00618632
ENSMUSG00000067225.2	Cyp2c54	161.282	296.593	0.878904	3.09255	0.00005	0.00618632
ENSMUSG00000067279.3	Ppp1r3c	27.4578	14.4551	-0.925639	-3.55848	0.00005	0.00618632
ENSMUSG00000069668.4	Sult3a1	96.5726	152.327	0.657483	2.4394	0.00005	0.00618632
ENSMUSG00000069917.7	Hba-a2	15.9522	7.92925	-1.0085	-2.53543	0.00005	0.00618632
ENSMUSG00000069919.7	Hba-a1	123.857	80.1852	-0.627271	-2.30735	0.0002	0.0194309
ENSMUSG00000070348.5	Ccnd1	28.8011	18.0061	-0.677632	-2.00581	0.00015	0.0159662
ENSMUSG00000070644.13	Etnk2	62.1735	97.5737	0.650192	2.3878	0.00005	0.00618632
ENSMUSG00000072949.6	Acot1	33.5979	19.9522	-0.751821	-2.2701	0.0002	0.0194309
ENSMUSG00000073700.3	Klhl21	4.84991	8.7584	0.85271	3.05752	0.00005	0.00618632
ENSMUSG00000074240.4	Cib3	0.143641	2.40529	4.06566	2.29099	0.00035	0.029457
ENSMUSG00000074277.4	Phldb3	4.05555	2.40923	-0.751325	-1.90668	0.00045	0.0359901
ENSMUSG00000075602.10	Ly6a	9.16001	4.67716	-0.969716	-2.31759	0.00005	0.00618632
ENSMUSG00000078566.8	Bnip3	89.9067	133.144	0.566486	1.97231	0.00055	0.0404152
ENSMUSG00000078650.2	G6pc	117.921	34.0649	-1.79147	-6.18411	0.00005	0.00618632
ENSMUSG00000078672.2	Mup20	28.4851	45.4009	0.672516	2.49254	0.00005	0.00618632
ENSMUSG00000078798.4	Sult2a1	56.1121	88.0628	0.650222	2.29294	0.0002	0.0194309
ENSMUSG00000078964.2	Ces1b	38.6623	59.9889	0.633769	2.50962	0.00005	0.00618632
ENSMUSG00000081207.4	Gm13775	12.4095	21.5678	0.797432	2.15377	0.00005	0.00618632
ENSMUSG00000083409.1	Gm11340	7.21515	2.24671	-1.68321	-2.46551	0.00055	0.0404152
ENSMUSG00000083832.1	Gm13771	1.8277	0	#NUM!	#NUM!	0.0005	0.0385
ENSMUSG00000084923.1	Gm15611	21.0683	6.28033	-1.74616	-3.69593	0.00005	0.00618632
ENSMUSG00000085445.1	Gm16348	0.992266	3.40219	1.77767	3.9325	0.00005	0.00618632
ENSMUSG00000090298.2	Sult3a2	3.37105	7.75229	1.20143	2.72803	0.00005	0.00618632
ENSMUSG00000090877.3	Hspa1b	1.20366	0.247192	-2.28373	-3.46215	0.00005	0.00618632
ENSMUSG00000092075.1	Serpina4-	21.3086	5.73997	-1.89232	-5.72874	0.00005	0.00618632
ENSMUSG00000093183.2	Gm25687	30.7806	63.7545	1.0505	2.67769	0.00005	0.00618632
ENSMUSG00000099021.1	Rn7s1	700.234	447.929	-0.644568	-2.2057	0.0003	0.0264805
ENSMUSG00000100277.8	1810053E	0.727864	4.99681	2.77927	2.15033	0.00005	0.00618632
ENSMUSG00000106069.1	Gm6135	34.0333	18.6619	-0.866848	-2.29436	0.00015	0.0159662
ENSMUSG00000106397.1	Gm21049	4.50211	8.69691	0.949903	2.48844	0.0001	0.0113094
ENSMUSG00000107369.1	Gstm2-ps	5.28283	9.53136	0.851371	2.01229	0.0007	0.0487173
ENSMUSG00000107451.1	Gm44421	1.80148	3.62615	1.00925	2.14888	0.0006	0.043428
ENSMUSG00000108822.1	Gm44787	1.69451	5.98364	1.82015	2.27612	0.00005	0.00618632
ENSMUSG00000110353.1	Gm33543	7.64038	13.1396	0.782206	2.39977	0.00005	0.00618632
ENSMUSG00000110439.1	Mup22	99.9007	68.6497	-0.541243	-2.05099	0.00065	0.0456767
ENSMUSG00000111923.1	Gm34777	2.67348	4.37875	0.711799	2.03435	0.0005	0.0385

ENSMUSG00000113387.1	Gm31508	1.24582	0.612387	-1.02458	-2.20024	0.0004	0.033088
ENSMUSG00000115509.1	Gm49012	1.8745	0.444212	-2.07719	-3.09822	0.0001	0.0113094
ENSMUSG00000117879.1	AC138228	8.67119	4.72504	-0.875903	-2.12505	0.0003	0.0264805
ENSMUSG00000118017.1	AC15791(	211.714	108.509	-0.964301	-1.99521	0.0005	0.0385

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000004038.9	Gstm3	38.0431	58.9022	0.630687	2.46013	0.00005	0.0145745
ENSMUSG00000017119.19	Nbr1	76	156.094	1.03834	3.08994	0.00005	0.0145745
ENSMUSG00000018427.7	Ypel2	5.3982	3.31232	-0.704637	-2.41028	0.00005	0.0145745
ENSMUSG00000020027.18	Socs2	13.2242	6.3375	-1.0612	-2.2998	0.00005	0.0145745
ENSMUSG00000020429.7	Igfbp1	53.6002	26.8102	-0.999456	-3.89039	0.00005	0.0145745
ENSMUSG00000020893.17	Per1	3.68334	6.25289	0.76351	2.15347	0.00005	0.0145745
ENSMUSG00000021288.18	Klc1	12.9409	6.37187	-1.02214	-2.07132	0.00015	0.0387736
ENSMUSG00000021453.2	Gadd45g	4.11008	1.45737	-1.4958	-2.59523	0.00005	0.0145745
ENSMUSG00000022508.5	Bcl6	2.65652	4.42275	0.735406	2.26063	0.0002	0.0472414
ENSMUSG00000022512.3	Cldn1	26.1421	15.2533	-0.777248	-3.02367	0.00005	0.0145745
ENSMUSG00000024987.6	Cyp26a1	7.22284	16.3768	1.18101	3.76685	0.00005	0.0145745
ENSMUSG00000026822.14	Lcn2	3.61183	6.99576	0.953752	2.06076	0.0002	0.0472414
ENSMUSG00000026839.17	Upp2	141.068	212.088	0.588275	2.19764	0.0002	0.0472414
ENSMUSG00000026980.15	Ly75	1.02455	1.86615	0.865078	2.35758	0.0001	0.0268627
ENSMUSG00000027533.10	Fabp5	20.9053	11.7917	-0.826097	-2.64221	0.00005	0.0145745
ENSMUSG00000027796.2	Smad9	3.96217	1.89784	-1.06193	-3.47194	0.00005	0.0145745
ENSMUSG00000028445.7	Enho	5.8256	2.52464	-1.20633	-2.74623	0.00005	0.0145745
ENSMUSG00000029272.8	Sult1e1	3.01955	12.0294	1.99416	4.46773	0.00005	0.0145745
ENSMUSG00000032310.4	Cyp1a2	580.244	1032.94	0.832029	2.805	0.00005	0.0145745
ENSMUSG00000035686.8	Thrsp	75.4226	108.929	0.530321	2.11579	0.00015	0.0387736
ENSMUSG00000036594.15	H2-Aa	12.3664	24.7286	0.999753	3.13856	0.00005	0.0145745
ENSMUSG00000037847.14	Nmrk1	8.65751	16.9132	0.966125	2.32446	0.00005	0.0145745
ENSMUSG00000038418.7	Egr1	13.1471	6.28833	-1.064	-3.7676	0.00005	0.0145745
ENSMUSG00000038656.5	Cyp3a16	7.12851	15.836	1.15154	3.67862	0.00005	0.0145745
ENSMUSG00000039457.4	Ppl	4.08077	7.12185	0.803411	2.80195	0.00005	0.0145745
ENSMUSG00000041698.11	Slco1a1	21.356	5.97873	-1.83673	-5.94679	0.00005	0.0145745
ENSMUSG00000050423.11	Ppp1r3g	2.1755	0.629848	-1.78827	-2.64187	0.00005	0.0145745
ENSMUSG00000050445.4	Cyp8b1	29.9766	12.9283	-1.2133	-3.83764	0.00005	0.0145745
ENSMUSG00000055116.8	Arntl	4.50112	1.45834	-1.62596	-3.46099	0.00005	0.0145745
ENSMUSG00000057346.12	Apol9a	19.3931	32.688	0.753217	2.48492	0.00005	0.0145745
ENSMUSG00000057897.14	Camk2b	0.84208	2.11891	1.33129	1.48241	0.0002	0.0472414
ENSMUSG00000061825.10	Ces2c	4.35545	8.60041	0.981582	2.97034	0.00005	0.0145745
ENSMUSG00000063388.5	BC023105	3.59428	6.85076	0.930563	2.34984	0.0001	0.0268627
ENSMUSG00000064225.6	Paqr9	35.9574	23.9919	-0.583741	-2.37141	0.00005	0.0145745
ENSMUSG00000070811.6	Sult2a2	45.0135	98.3588	1.12769	3.25888	0.00005	0.0145745
ENSMUSG00000072849.10	Serpina1e	78.1579	34.9136	-1.1626	-4.35291	0.00005	0.0145745
ENSMUSG00000073421.6	H2-Ab1	23.9638	51.1132	1.09284	2.55741	0.00005	0.0145745
ENSMUSG00000074375.3	Sult2a3	0.913931	5.76955	2.6583	3.99495	0.0001	0.0268627
ENSMUSG00000075551.4	Cyp3a41a	26.1917	45.374	0.79276	3.08305	0.00005	0.0145745
ENSMUSG00000075552.4	Cyp3a41b	2.76118	6.39617	1.21192	3.37149	0.00005	0.0145745
ENSMUSG00000078650.2	G6pc	83.6587	38.114	-1.1342	-4.05012	0.00005	0.0145745
ENSMUSG00000078798.4	Sult2a1	36.972	91.5233	1.30771	4.24884	0.00005	0.0145745
ENSMUSG00000078799.5	Sult2a5	2.28821	5.90122	1.36679	2.19044	0.0002	0.0472414
ENSMUSG00000078817.4	Nlrp12	6.13793	3.48939	-0.814775	-2.95155	0.00005	0.0145745
ENSMUSG00000082008.1	Gm12390	0	2.18739	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000086316.8	Nbdy	0.965126	9.08573	3.23481	2.3883	0.00005	0.0145745
ENSMUSG00000092674.2	Gm24105	94.9427	153.292	0.691157	2.26807	0.00005	0.0145745
ENSMUSG00000093183.2	Gm25687	16.9584	55.347	1.7065	3.05133	0.00005	0.0145745
ENSMUSG00000096768.8	Gm47283	21.0555	8.4086	-1.32426	-3.46356	0.00005	0.0145745
ENSMUSG00000099901.1	Zbed4-ps2	3.94207	10.8342	1.45857	2.99773	0.00005	0.0145745
ENSMUSG00000101397.6	Mug-ps1	34.2915	22.1456	-0.630835	-2.52439	0.00005	0.0145745

ENSMUSG00000105192.1	Gm42796	9.81164	3.82683	-1.35835	-2.85412	0.00005	0.0145745
ENSMUSG00000107185.1	Gm42642	1.32544	0	#NUM!	#NUM!	0.0001	0.0268627
ENSMUSG00000109089.1	4833411C	13.8725	7.63832	-0.860895	-2.57638	0.00005	0.0145745
ENSMUSG00000110439.1	Mup22	64.7271	39.1905	-0.723867	-2.61227	0.00005	0.0145745
ENSMUSG00000110838.1	Gm47789	1.24793	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000111253.1	Gm34654	1.07187	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000117780.1	AC127342	13.9016	5.9063	-1.23493	-4.21178	0.00005	0.0145745

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000003053.17	Cyp2c29	673.766	1232.86	0.871696	2.7636	0.00005	0.0237172
ENSMUSG00000025002.5	Cyp2c55	5.10794	9.57033	0.905826	2.8894	0.00005	0.0237172
ENSMUSG00000026185.8	Igfbp5	4.14362	7.52489	0.860778	3.06263	0.00005	0.0237172
ENSMUSG00000028238.6	Atp6v0d2	14.2949	8.46584	-0.755773	-2.57671	0.0001	0.0404588
ENSMUSG00000030428.16	Ttyh1	7.83723	20.5459	1.39044	3.46049	0.00005	0.0237172
ENSMUSG00000030483.14	Cyp2b10	18.4894	34.553	0.902114	3.34575	0.00005	0.0237172
ENSMUSG00000032310.4	Cyp1a2	573.897	1767.5	1.62285	4.7819	0.00005	0.0237172
ENSMUSG00000033107.6	Rnf125	119.634	73.9456	-0.694086	-2.68283	0.00005	0.0237172
ENSMUSG00000035202.8	Lars2	37.9931	16.2798	-1.22265	-3.96694	0.00005	0.0237172
ENSMUSG00000037583.2	Nr0b2	19.8513	11.5096	-0.786389	-2.59725	0.0001	0.0404588
ENSMUSG00000038656.5	Cyp3a16	7.05363	15.3354	1.12043	3.49577	0.00005	0.0237172
ENSMUSG00000050445.4	Cyp8b1	29.6178	11.0736	-1.41934	-4.51314	0.00005	0.0237172
ENSMUSG00000054417.5	Cyp3a44	19.7219	34.2151	0.794836	3.04706	0.00005	0.0237172
ENSMUSG00000055116.8	Arntl	4.44971	1.11565	-1.99583	-4.29871	0.00005	0.0237172
ENSMUSG00000060803.6	Gstp1	38.6763	66.8057	0.788521	2.91206	0.00005	0.0237172
ENSMUSG00000061825.10	Ces2c	4.30826	10.0339	1.21971	3.75254	0.00005	0.0237172
ENSMUSG00000069917.7	Hba-a2	12.5054	28.9749	1.21225	3.16461	0.00005	0.0237172
ENSMUSG00000069919.7	Hba-a1	161.435	257.664	0.674535	2.60695	0.00005	0.0237172
ENSMUSG00000072849.10	Serpina1e	77.2634	33.2336	-1.21714	-4.58994	0.00005	0.0237172
ENSMUSG00000073940.3	Hbb-bt	11.4866	32.257	1.48966	4.17862	0.00005	0.0237172
ENSMUSG00000075551.4	Cyp3a41a	25.9157	41.7969	0.689571	2.51749	0.0001	0.0404588
ENSMUSG00000075552.4	Cyp3a41b	2.73222	5.71036	1.06351	2.88173	0.00005	0.0237172
ENSMUSG00000078650.2	G6pc	82.715	52.4814	-0.656343	-2.57516	0.0001	0.0404588
ENSMUSG00000078798.4	Sult2a1	36.5984	71.0306	0.95666	3.13829	0.00005	0.0237172
ENSMUSG00000083563.1	Gm13340	22.2303	36.8976	0.731	2.47186	0.0001	0.0404588
ENSMUSG00000092674.2	Gm24105	93.8984	264.708	1.49523	4.56281	0.00005	0.0237172
ENSMUSG00000096768.8	Gm47283	20.8212	9.60095	-1.1168	-3.03589	0.00005	0.0237172
ENSMUSG00000096887.2	Gm20594	84.8472	147.632	0.799063	2.84097	0.00005	0.0237172
ENSMUSG00000098973.1	Mir6236	2424.83	1036.7	-1.22589	-4.1389	0.00005	0.0237172
ENSMUSG00000100131.1	Gm28439	7.92885	17.6712	1.15622	2.9385	0.00005	0.0237172
ENSMUSG00000101111.1	Gm28437	27.3548	48.503	0.826281	2.816	0.00005	0.0237172
ENSMUSG00000102189.1	Gm37194	1.33501	3.28318	1.29824	3.26943	0.00005	0.0237172
ENSMUSG00000115420.1	Rmrp	783.954	1427.45	0.864595	2.95006	0.00005	0.0237172
ENSMUSG00000117780.1	AC127342	13.7433	7.49599	-0.874538	-3.05459	0.00005	0.0237172

Table S2A. Liver metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	0.6417779	0.7530381	0.8854124	1.3165750	1.0407458	0.7608884	0.9882787	0.7862970	1.0625771	1.1283548	1.2155264	1.1977029	1.1177079	1.0111845	0.9166488	1.1527351	0.5878772	1.3592881	0.8895624	1.4278042	0.6871709	0.9504117	0.5052311	0.9326832
Indole-3-acetic.acid	0.7860392	1.9509565	0.5580886	1.5278171	1.0873190	0.7463817	0.1771168	0.3526087	0.4630552	0.5291279	0.7148218	0.4862421	0.5835993	0.4962891	0.7906378	1.5020283	0.6540461	1.0075090	1.0404164	0.8920219	0.2602962	0.5700573	0.5769496	0.6458184
Indole-3-pyruvic.acid	0.06424609	1.10713323	0.19021050	0.33843027	0.11897162	0.46282540	0.37132059	0.22765562	0.18087326	0.38830899	0.02884164	0.26659506	0.14896618	0.51208752	0.16279090	0.28747783	0.37848709	0.37283283	0.00000000	0.14392771	0.29731054	1.18302681	0.16473559	0.51285387
Kynurenine	1.5130420	1.8160458	1.1177367	3.3235912	1.4236657	1.8332443	0.4968082	0.4627796	1.0845344	1.1908755	0.8681831	1.3064311	1.4310919	1.0449380	0.7998276	2.0758060	0.9268621	1.9954938	1.5519350	2.5454728	1.1179864	2.3883236	0.7527254	1.1935632
2-Deoxycytidine	0.1456107	0.2046070	0.1144417	0.2018454	0.2570833	0.1523639	0.1548636	0.2199208	0.2156768	0.4964199	0.3365320	0.2922682	0.4379804	0.2772534	0.1278656	0.3985392	0.1284519	0.4021005	0.3026561	0.2529262	0.1450090	0.1766973	0.2007113	0.5602648
2-aminoadipic.acid	0.4075929	1.8351217	0.9447126	1.2758676	0.8124402	0.8410186	0.4128866	0.5227665	1.3971905	0.9069514	1.2938552	0.6817271	0.8004980	0.8948402	0.7905779	1.0971095	1.0229457	1.4079170	1.8391106	1.8948830	5.3693974	5.3069206	0.8495688	1.1904178
2-deoxyguanosine	0.58479568	0.00000000	0.00000000	0.44162009	0.58363951	0.00000000	1.63457253	0.37970606	0.00000000	0.38769672	0.06838577	0.19997020	0.80554615	0.29129296	0.00000000	0.23430805	0.06706320	1.46333000	0.00000000	0.15525769	0.00000000	0.00000000	0.00000000	0.52384648
3-Aminoisobutyric.acid	0.3103612	0.2316226	0.2791112	0.3631104	0.2398946	0.2452838	0.2880905	0.1962715	0.3782312	0.3797402	0.3751967	0.2140135	0.2781475	0.3356190	0.1825315	0.3856304	0.1752509	0.4551243	0.3276935	0.3667051	0.3028023	0.3385240	0.2649583	0.2924743
3-Hydroxybutyric.acid	1.7156741	0.6825009	1.6340875	0.7728069	0.6845594	3.0031276	1.4763494	1.4043569	1.8066952	0.5647619	0.8475344	1.0578820	1.6273289	2.9045689	1.5403997	1.5944642	0.5934880	0.8834803	0.6819804	0.8640724	0.8097863	0.9743788	1.3148739	1.5162630
4-Aminobutyric.acid	0.5156079	0.9141045	1.1005954	2.3476444	1.3140889	0.7357734	0.6096718	0.4719302	1.4989862	1.1886618	1.0745111	1.6027557	1.1806124	1.5513006	1.0620008	0.9948536	1.2875127	1.3189201	2.1056291	2.6841771	1.0229754	1.3207144	0.4810400	1.0543936
5-Aminolevulinic.acid	0.2867715	0.8398926	0.2810464	0.2019449	0.1020569	0.1164548	0.2761496	0.1963395	0.2273984	0.1812200	0.3716822	0.2694858	0.2225276	0.2574289	0.3098547	0.4189624	0.1705895	0.4910491	0.4734825	0.3410167	0.8565262	0.8064531	0.3156030	0.4568366
5-Methylcytidine	2.6366484	2.3470198	0.7913250	3.1443083	4.0459524	1.9228826	0.8837537	2.5323469	0.7833072	1.5051036	2.2849148	2.9870170	2.6811237	2.1907469	1.9084163	3.1802859	1.1070842	2.1720066	2.3003041	2.3661019	1.8300040	3.8581447	1.5396344	1.0123362
7-ketocholesterol	1.2891896	1.0073455	0.8360030	0.4664388	1.2795914	1.3383909	1.0546935	1.9164554	0.4051727	0.6767182	0.4498655	0.7065973	0.6043564	1.3701550	1.0951610	1.3300680	1.3873236	1.1263964	0.3944428	0.9683976	0.9645003	0.7742208	0.6170155	2.0484274
Acetyl-L-glutamine	0.4553014	0.4776746	0.4556176	1.1360893	0.4899839	0.4115659	0.4724127	0.3995740	0.7519312	0.7612600	0.5757849	0.8012261	0.9084725	0.7581108	0.5658879	0.6871090	0.4090363	0.6004718	0.4349892	0.7548255	0.3635997	0.5794367	0.3717956	0.6783111
Acetylcarnitine	0.02915257	0.05742605	0.04085568	0.04646320	0.01610918	0.02863787	0.02092485	0.04034642	0.02849962	0.03521710	0.03001347	0.03903095	0.06032182	0.06379381	0.03554116	0.08904216	0.13924858	0.08820948	0.25276956	0.11555283	0.15110799	0.11136802	0.18095977	0.19759626
Acetylglucosamine	1.3115664	1.2280059	1.0550751	1.8277008	1.5382448	0.8317039	0.9006399	0.7437013	0.8639561	1.1169542	1.2680750	1.4683521	0.8830023	1.0020359	1.2230501	1.0899670	0.6023287	1.6330727	1.0205687	1.5326382	0.7522740	0.9907671	0.6387737	1.1292635
Acetylglycine	0.2617616	1.5929109	1.2342161	2.1902251	2.0066785	1.0029190	1.9138947	0.8145704	1.6919136	2.5442625	2.4643134	1.7957466	0.2814305	0.3470204	1.2344673	0.8244505	0.2272679	2.3645095	0.3638673	0.9529061	1.4823383	0.8343840	1.0978394	0.7816405
Acetylornithine	0.23480651	0.10218698	0.15858941	0.19771777	0.62851733	0.05134179	0.18836825	0.08521779	0.11193669	0.26567215	0.32023260	0.26012605	0.47490123	1.12893094	0.14985087	0.74458555	0.45819030	1.06512125	0.75622866	0.72796858	0.76879026	0.70500716	0.82648159	0.71440786
Adenosine	0.3581978	0.5481528	0.5538759	0.5637655	0.7135748	0.7417769	0.9125724	0.7036831	1.2996513	1.2692738	1.3658697	0.8970467	0.9973923	1.5460150	0.6196735	1.0165961	0.6620103	2.0082194	1.1925067	0.4137528	1.0192838	1.0090414	1.8101009	1.6507011
Adenosyl-L-homocysteine	0.3163094	0.6499900	0.5642770	0.6660210	0.7347727	0.6880711	0.7655124	0.5100250	1.0084109	1.0896944	1.0674588	0.8004986	0.6242744	1.0607179	0.5468198	0.8729612	0.5892073	1.5979238	1.2145764	1.4491398	0.8496154	1.1124521	0.8608683	1.2268764
Adenylosuccinate	0.03907467	0.10987980	0.07196339	0.18365262	0.02049657	0.18750397	0.10259660	0.10153863	0.17733045	0.22357127	0.13469431	0.08656620	0.13093812	0.10786607	0.06330485	0.11795322	0.09404531	0.17072564	0.16554603	0.07081627	0.25297802	0.31067335	0.16538933	0.14309574
Alanine	0.8571079	0.8937346	1.2829469	1.2536040	1.3312153	1.0258898	0.9927881	0.8043505	1.3840192	1.2575998	1.3394220	1.3339071	1.3476500	1.2322631	0.9589156	1.1416117	0.9940162	1.2597832	1.1339764	1.4759244	1.1721014	1.4205798	0.6686826	0.9158186
Aminoisobutyric.acid	0.4493258	0.5828958	0.6461483	0.8794325	0.4539889	0.6068997	0.5862818	0.4553500	0.4213689	1.0816655	0.7381336	1.2356525	0.4183226	0.2992163	0.3076177	0.5605960	0.5548940	1.4832715	1.2783811	1.3008123	1.1644110	1.2625703	1.0386166	0.6530749
Arginine	0.5230813	0.8326213	0.3829666	0.3855671	0.2697902	0.3039470	0.3348270	0.2517091	0.3584439	0.5363771	0.4821799	0.4340597	0.5603556	0.3996499	0.4430393	0.4462321	0.3594968	0.3102111	0.5864398	0.2758807	0.1643636	0.2102865	0.2007999	0.3539812
Asparagine	0.8842260	0.8152583	0.9024042	1.3833165	1.2449474	0.9768765	1.1941756	0.9351111	0.9971121	1.3182055	1.2117728	1.3431893	1.1858922	0.9978230	1.2058328	1.2294066	0.6536824	1.4452643	1.2063691	1.3491411	0.8293748	1.0875278	0.7053539	0.9158058
Aspartic.acid	0.3762233	0.4292970	0.2857379	0.5451212	0.4423451	0.3255798	0.4889660	0.4377361	0.4992604	0.6124258	0.6449889	0.4799587	0.5048493	0.4952580	0.4067786	0.5631700	0.2476733	0.7353890	0.5144635	0.4634559	0.2357814	0.3112372	0.4857510	0.4860391
Betaine	0.7509563	0.7301263	0.6645387	0.8280204	0.7483555	0.7586245	0.6799378	0.7332552	0.5995388	1.1140138	0.9279227	1.0862676	0.7167985	0.4884979	0.8491893	1.0252541	0.6586413	1.5355912	0.9498598	1.0125740	0.7907893	0.8387790	1.0066512	1.0111870
Carnitine	0.4638704	0.6540949	0.5326691	1.0417368	0.7563746	0.5297869	0.5900569	0.5139531	0.7313478	0.9329322	0.8872217	0.9785690	1.1477622	0.8874642	0.6541203	1.1244702	0.7064974	1.6744503	1.3159400	1.4626136	0.9617662	1.2497777	0.6554014	1.3367312
Carnosine	0.1379304	0.1837529	0.1527487	0.3168994	0.2416656	0.1920351	0.2827001	0.2258543	0.2003689	0.5326479	0.2786935	0.3996725	0.3411534	0.1948664	0.1848126	0.3064725	0.2054774	0.4477849	0.3000470	0.4893805	0.2089623	0.2489793	0.1568765	0.2635589
Choline	0.7764507	0.8191480	0.6335699	0.6340663	0.8203244	0.6701257	0.8159180	0.6395891	0.6805273	0.9335008	0.9493801	1.0877272	0.6584530	0.8890556	0.3250131	0.9338085	0.6925649	1.0695122	1.0062782	1.0230024	0.8411477	0.9132406	0.4218052	1.0180560
Citrulline	0.4214526	1.4571427	0.4513969	0.6357133	0.5489945	0.4507589	0.3650552	0.3008129	0.3946912	0.7066947	0.6170127	0.5663506	0.3569724	0.5146847	0.4069223	0.6087197	0.3548486	0.4907301	0.6420626	0.6432533	1.0133808	0.8909440	0.3728396	0.6870457
Creatine	0.4086522	1.8336104	0.4751913	0.5582335	0.5536743	0.4931385	0.5850576	0.4867122	0.5313360	0.7563221	0.6526906	0.7692563	0.5293707	0.6098790	0.4726509	0.7157762	0.6398291	0.8875395	0.8520455	0.9165180	0.5239349	0.6135616	0.4791432	0.8448273
Creatinine	0.5057162	0.8707744	0.4629378	0.6562094	0.6613873	0.5594884	0.5854751	0.4851771	0.5782317	0.7563661	0.8161167	0.8193643	0.8426159	1.0442179	0.6368156	0.9255601	0.6743669	0.9832099	1.0984917	1.1851292	1.0670715	1.4789607	0.5438834	1.0728971
Cystathionine	0.2459859	0.3683612	0.3431268	0.4048110	0.2935433	0.4965935	0.3682411	0.2695575	0.3493903	0.4215621	0.3267381	0.3072462	0.2838443	0.2927669	0.2830256	0.3648586	0.1816999	0.2010483	0.2689415	0.2830604	0.4150128	0.3916642	0.1232459	0.2743187
Cytidine	1.0704769	1.1045405	0.5452250	1.1143852	2.2242367	0.8437256	0.8379310	0.7302953	0.8250596	1.2351377	1.2415660	1.4356379	1.0721686	1.3694450	1.1486803	1.3431894	0.5011534	1.7333319	1.2794172	1.8635491	0.4951477	0.7534005	0.9403074	1.1735831
D2-phosphoglyceric.acid	0.3310944	0.5996730	0.5421477	0.5783187	0.4516969	0.6160839	0.5869482	0.8026354	0.5160980	1.7919010	1.3227615	0.7696889	0.8412157	0.9673621	0.5756555	0.7466133	0.4928834	0.5637712	1.2022054	1.3578467	0.5968598	0.8221555	0.7988284	1.3712116
Dimethylarginine	0.9740189	1.0761789	0.9286955	1.7805238	1.3582373	0.9595825	0.9619014	0.7611321	0.8233580	1.2680150	1.1986943	1.4689141	1.1321591	0.7743156	1.1449154	1.2622517	0.5733991	1.5776915	1.3679222	1.4523821	0.6839601	1.0027647	0.7136403	0.9098727
Dimethylglycine	0.4607362	0.6099623	0.5798673	0.8415445	0.4800336	0.5956410	0.6211296	0.4700505	0.4793892	0.9944620	0.7717746	1.1394720	0.4232337	0.3249359	0.3335234	0.5717760	0.5680419	1.2948865	1.2641046	1.2082976	0.9839331	1.1826156	0.9984687	0.6824968
Dopamine	0.6221969	0.9233208	1.7799437	2.9220513	0.8243819	1.2029912	1.5160785	1.6078648	2.8711232	2.7599863	3.4069383	2.7410775	2.4948055	1.5058086	1.1234065	1.5403673	1.5234156	1.8589505	2.4006292	2.3461096	1.2409628	0.7001368	0.6745019	1.0942887
Folic.acid	0.2239471	0.7487736	1.0598652	1.7528520	0.5643385	0.1206645	2.1591450	1.4651981	1.3696177	1.7913465	0.6001736	1.0758190	1.3699781	2.3413983	1.4799907	1.6345688	1.0877975	3.9654829	0.6068767	2.1335282	1.1901542	1.7785697	2.3565170	0.7551478
Folinic.acid	0.7674852	1.6268925	1.0852252	0.7893310	1.2473922	0.7184188	1.4028261	0.6030513	0.9306193	0.9450751	1.3213389	0.8735870	3.0728728	1.7100075	1.2098770	2.9880290	0.8017804	1.8047687	1.0751854	0.9404757	0.2533398	0.4022695	1.6236487	1.0310206
GDP	0.2824551	0.4104324	0.6581356	0.6326138	0.5607096	0.6279206	0.9077773	0.7229344	0.7825835	1.1341158	0.8687443	0.7987579	0.8721362	0.8370757	0.5121924	0.7037107	0.6499428	0.7694018	0.9147735	1.0046965	0.7964523	0.8625709	0.5791299	0.8675360
Glucosamine	2.0459784	1.8586589	0.9763065	2.3173203	2.7368014	1.2832705	1.5635184	1.1995193	0.8349244	1.1213999	1.3293286	1.9080310	0.7805758	1.1948329	2.3484920	1.5326383	0.5317680	2.6586547	0.9757728	1.2297610	0.5173460	1.3240417	0.6768534	1.0608675
Glutamic.acid	0.3867288	0.6585914	0.2594397	0.6983488	0.4513374	0.4237792	0.2899086	0.2583647	0.4606375	0.4076183	0.4274454	0.4655869	0.5175806	0.6526626	0.7723591	0.7010507	0.4853293	1.0569855	0.8696258	0.9357680	0.3399974	0.5327368	0.6822027	0.9084132
Glutathione.oxidized	0.8428468	0.9934283	0.8284747	1.2904800	1.1288540	0.9433971	0.9309067	0.8341607	0.7050951	1.7922744	1.5380908	1.2666532	1.1660800	1.1961860	0.7966210	1.7078418	1.1142226	1.7799967	1.4630840	1.4101672	0.9523861	1.1156960	0.7591486	2.1125401
Glutathione.reduced	0.8328146	0.9973012	0.9263039	1.1861743	1.0307202	0.9995192	0.8701441	0.8078348	0.7663752	1.5181023	1.4216837	1.1157582	1.0358050	1.2074976	0.8834492	1.4707737	1.1736260	1.5332945	1.3728646	1.2931630	0.9865631	0.9085870	0.8146667	1.6901167
Glycerol.3-phosphate	0.4728707	0.9220561	0.5403641	0.4929494	1.1101013	0.6136874	0.5507888	0.5474192	0.5800091	0.8919979	0.6383870	0.8603690	0.9634107	1.0130460	1.1563273	0.9250990	1.3260552	2.9327821	1.8083472	1.8427419	0.4780161	0.5059864	2.0318877	0.9390341
Glycine	0.8730863	1.3705099	0.9158263	1.2231668	1.3027717	0.9159551	1.0228547	0.7828555	1.2443312	1.3262574	1.2728658	1.2074510	0.8440967	0.9126339	0.8707803	0.9282927	0.6426631	1.1847707	0.9643004	1.1552033	1.0063595	1.2029528	0.7578952	0.9970674
Glycocyamine	0.4700012	1.6812018	0.8093291	0.8862727	0.6447139	0.6131750	0.7258364	0.4538833	1.4261794	0.9214418	0.9556441	0.9071715	0.5539589	0.7430127	0.6726305	0.7824019	0.6505485	0.9903394	0.9944325	1.4137428	1.1282637	1.3375366	0.6221903	0.5836888
Glycylproline	1.8354316	2.4923578	2.6578428	3.1714119	2.4727788	1.9152073	1.8255724	1.7998914	1.5739886	2.8731885	2.3700045	2.6665893	2.2624526	1.4006515	1.9016969	1.9771679	0.8534983	2.6499820	2.2516603	2.3700619	1.9364397	2.2477298	0.8725860	1.5342976
Guanine	0.17621558	0.02278745	0.15415498	0.29704774	0.21663483	0.08342667	0.18120350	0.32614899	0.24036579	0.20259922	0.38402340	0.28300992	0.43238992	0.27333795	0.16728693	0.38415723	0.22893049	0.42081721	0.22346236	0.41695774	0.20548302	0.27833217	0.47305873	0.55053296
Guanosine	0.3246598	0.7685011	0.5047241	0.6499907	0.5206282	0.6397830	0.6747621	0.6381834	0.8289680	0.7105909	1.0300515	0.7829405	0.9793604	1.3265568	0.7543370	1.1106217	0.7258154	1.5540844	0.7140582	1.4509617	0.4875484	0.7297572	0.8773832	1.3040662
HIAA	2.4412992	2.6983910	0.8340145	3.2664718	1.4622671	0.6602276	0.6127725	0.4979979	1.9400444	0.9404046	0.9567780	2.4501998	1.1286798	0.4954157	1.8092108	1.3313670	0.6916914	2.1301379	0.9272512	2.2856990	1.5603747	3.5012040	0.4755159	1.8120372
Homoserine	0.8509122	0.8893932	0.7896290	1.2645999	1.2080315	0.8902052	1.0056840	0.7481959	0.9495331	1.1548321	1.1279660	1.1857805	0.9891440	0.8623097	0.9327528	1.0666565	0.5662173	1.0695083	0.9945852	1.1881665	0.8156957	1.0217079	0.5884026	0.8560951
Hydroxyproline	0.2787770	0.4799966	0.2375902	0.3059802	0.3431303	0.2190838	0.2147382	0.1216726	0.2352834	0.1174432	0.3323629	0.3495331	0.2464465	0.3174669	0.3419158	0.4244054	0.3477392	0.3852723	0.4589917	0.6555311	0.6199176	0.9536136	0.2041111	0.4815902
Hypoxanthine	0.9974282	1.0928235	0.8876036	1.2570637	1.4171350	0.9833092	0.8904424	0.8622482	0.9724418	1.0087576	1.1682902	1.2436913	1.1114261	1.1937916	1.1325733	1.3134446	0.7104519	1.3286557	1.0959749	1.3218071	0.8378953	1.0824028	0.8661801	1.1903877
Inosine	0.7073993	0.8391119	0.7140293	1.0391484	1.2535338	0.8420802	1.1015346	0.8319424	1.1457617	1.2143153	1.3476063	1.2969553	1.2625817	1.5320379	1.1991691	1.5026616	0.9335940	1.9186397	1.4259257	1.8834052	0.7778325	1.0904168	1.1187931	1.5236756
Isoleucine	0.8528558	0.9125115	1.0217673	1.5496715	1.2388609	1.0109370	1.1912526	0.9214470	1.1406629	1.2647698	1.2625838	1.3054733	1.2786902	1.0450159	1.0627395	1.1645459	0.6330773	1.4210589	1.0894039	1.3649646	0.9157909	1.1766452	0.7847429	0.9943086
L-Alloisoleucine	0.8517790	0.9111445	1.0125399	1.5249889	1.2311331	1.0197709	1.1902293	0.9271793	1.1383725	1.2737694	1.2513103	1.3068848	1.2579197	1.0529558	1.0765331	1.1544872	0.6385982	1.4168104	1.0940247	1.3688610	0.9093086	1.1719494	0.7768059	0.9903981
Leucine	0.8476465	0.8962709	1.0266517	1.5385229	1.2401560	1.0079082	1.2035426	0.9227276	1.1359438	1.2795848	1.2575548	1.3011260	1.2710841	1.0653769	1.0637925	1.1611670	0.6377768	1.4253318	1.0888724	1.3837039	0.9196804	1.1688058	0.7811297	1.0016315
Lysine	1.4482072	1.0568177	1.1645744	1.8665608	1.4198726	1.0589478	1.4302917	1.0602397	1.1560245	1.7148566	1.6197058	1.6151634	1.4481528	1.2386714	1.1956266	1.5964858	0.7940763	1.7900829	1.5315174	1.4456983	1.2263541	1.3774511	0.9487037	1.6550266
Methionine	0.8972607	0.9251098	0.9370634	1.6825585	1.3009507	0.9540860	1.2933955	0.9654324	1.0819269	1.3994877	1.3717682	1.5317663	1.4078088	1.1686087	1.2161785	1.3539391	0.7224215	1.6457019	1.4097348	1.6598803	1.0329937	1.4074516	0.8338763	1.0874213
N-Acetylneuraminic.acid	0.6206421	0.8199069	0.5600818	1.0237435	0.6379889	0.5087411	0.5873233	0.5743446	0.6651696	0.9633031	0.8905661	0.8053625	0.4815686	0.4091472	0.4826958	0.6580611	0.4163223	0.8383301	0.9182577	0.9383752	0.5135255	0.5525025	0.4070563	0.6223561
NAD	0.5189115	0.7432001	0.7848089	0.9723333	1.0264845	0.8151934	0.9443994	0.8430001	1.0739810	1.7751225	1.4312229	1.1960606	1.1191554	1.5435374	0.8247645	1.0287660	0.7932043	1.3737844	1.6242790	1.4497317	1.2129971	1.2927545	1.2158123	1.1611846
NADP	0.4645545	1.0033445	0.9597302	1.0300501	0.5523697	0.9305444	0.8770339	0.8463191	1.1799497	1.6125850	1.5100842	0.8503701	0.8669583	0.9652894	0.4649232	0.7248484	0.8139846	0.9654545	1.3477053	0.9537815	1.0817424	1.1563229	1.1929342	1.3127996
Nicotinamide	0.7178230	0.8810389	0.8387394	1.1619439	1.0747429	0.8485019	0.9581953	0.8306311	1.1420243	1.1893909	1.1554375	1.2419390	1.2246746	1.2373342	0.9347814	1.1588332	0.7229536	1.2618774	1.0789894	1.4088462	0.8409249	1.1128264	0.9288390	0.9164444
Norleucine	0.8518739	0.9031989	1.0352939	1.5405561	1.2409032	1.0051005	1.2031724	0.9123117	1.1186044	1.2682845	1.2530081	1.3082198	1.2709141	1.0547923	1.0632294	1.1498179	0.6271827	1.4302944	1.0885495	1.3559512	0.9163913	1.1671295	0.7881985	0.9965756
Norvaline	0.9124836	0.9298527	1.0368697	1.6448278	1.1552369	1.0535945	1.1661068	0.8477787	1.1226926	1.1524275	1.1425004	1.2132199	1.2447680	1.0239704	1.0882174	1.2925641	0.6011751	1.3398496	1.0437265	1.2117027	1.0259126	1.1945400	0.9568618	0.9967921
Ornithine	1.0332296	0.8179956	0.7856410	1.3515693	0.9279344	0.7778656	0.9067942	0.6364167	0.7778348	1.0385131	1.0756493	0.9922528	1.2363026	0.9490234	0.9931245	1.3358021	0.6026925	1.4751211	1.2747343	1.1052278	1.2221460	1.3833450	0.8267835	1.4047324
Pantothenic.acid	0.5843001	0.7413393	0.6365224	0.9997849	0.8483685	0.7045172	0.6561683	0.6052149	0.7990996	0.8561870	0.8310670	0.8831817	0.8910804	0.7766499	0.7562383	0.9005148	0.4408332	1.1369992	0.7531680	0.8794983	0.4826726	0.7702197	0.6456869	0.7288907
Phenylalanine	0.8266777	0.9186807	1.0043263	1.5735330	1.3371442	0.9285578	1.2423992	0.9631628	1.1908843	1.3133446	1.3050369	1.4669236	1.4456966	1.1005134	1.1502301	1.2907528	0.7015021	1.6027515	1.1682306	1.6519843	0.9048820	1.2502029	0.7999375	1.0173964
Pipecolinic.acid	0.3294063	1.0094060	0.3818550	0.5711961	0.4551660	0.3332365	0.4550962	0.3707791	0.4427522	0.6345462	0.4652044	0.5736943	0.5446118	0.6177807	0.4724979	0.6498503	0.4190516	0.8724576	0.6294419	0.8597367	0.5914717	0.7777559	0.5766327	0.5802869
Proline	0.5141562	0.6178646	0.5822266	1.3063838	0.7457581	0.5776894	0.7298739	0.5105093	0.6245210	0.8541810	0.6404874	0.9124592	0.7089632	0.6439353	0.6385716	0.7810780	0.3922450	0.9376606	0.7503399	1.0259594	0.7327704	0.9253374	0.5640057	0.5703749
Pyroglutamic.acid	0.3082117	0.8843707	0.4362193	0.5921241	0.4758751	0.4111866	0.4229338	0.3914758	0.4400848	0.5739163	0.4679617	0.5115939	0.5537708	0.6806015	0.4737140	0.5919037	0.4162531	0.8276363	0.6802242	0.8473929	0.4889404	0.6901764	0.5664578	0.5789078
Sarcosine	1.0084766	1.0659462	1.4043571	1.3180316	1.3173108	0.9578035	1.0446095	0.8087390	1.2527798	1.4248970	1.4078169	1.4296566	1.4621763	1.4146250	1.1970317	1.2222388	0.9605841	1.4551496	1.1998666	1.4855036	1.1753213	1.1102789	0.7256942	0.9738131
Serine	0.9631746	0.7482507	0.8027561	1.4342633	1.2503764	0.9510122	1.1738940	0.8230972	0.9846277	1.2222407	1.2662427	1.2908321	1.1188887	0.8060649	1.1238529	1.1654594	0.5992233	1.2091939	1.1286308	1.2184897	0.7885404	1.0498191	0.6902211	0.8701550
TMAO	0.09437101	0.43303428	0.27471777	0.11216410	0.77217358	0.46438820	0.18648344	0.22312431	0.83269885	0.48161575	0.14550246	0.22655480	2.34051394	0.79755627	7.29396053	7.28121795	0.61150801	0.84295022	2.54722104	1.89654121	2.66298055	2.24567385	0.86779300	1.35080682
Taurine	0.7178835	0.8336343	0.8542148	1.1605061	1.0823282	0.8895874	1.1038355	0.9200192	1.0612253	1.3159387	1.2440577	1.2424510	0.5820055	1.3399539	0.6293543	0.8610343	0.6677345	1.4970880	1.0986328	1.0589133	0.8018202	1.0684514	1.1126616	1.4430778
Threonine	0.8232457	0.8706377	0.7730140	1.2312086	1.2037216	0.8912114	0.9660505	0.7585548	0.9620484	1.1447777	1.0785856	1.1441714	0.9735837	0.8573386	0.9307297	1.0386725	0.5642106	1.0126094	1.0241260	1.2153759	0.7968829	1.0072283	0.6001133	0.8525195
Tyrosine	0.9150162	1.0841190	1.0359367	2.4642402	1.2867226	0.9170167	1.3293614	1.0450251	1.2348882	1.6267038	1.1748098	1.7505491	1.3043186	1.1454333	1.0372301	1.3440036	0.6115674	1.8582848	1.1087729	1.8802615	0.6253943	1.0400158	0.8149456	0.8355209
UDP-GlcNAc	0.2934447	0.5004356	0.4652797	0.5732223	0.7177815	0.5265830	0.5310480	0.5149530	0.6552245	0.8666439	0.7747757	0.6714735	0.5809566	0.6796868	0.6131760	0.7155939	0.5540551	1.0615481	1.0151025	0.9471085	0.4996689	0.6153224	0.8202686	0.8398630
Uracil	0.8606104	1.1405109	0.9367328	1.1936004	1.0690069	0.8014622	0.9855269	1.0904810	0.9049300	1.1703200	0.9967556	1.3101537	0.6560391	0.7866817	0.8377139	0.9379920	0.6340143	1.5360757	0.7688687	1.2509321	0.8756824	1.2854795	0.7315423	1.0174820
Uridine	0.8463357	0.9289961	0.7456293	0.9695010	1.0747293	0.7520132	0.8439773	0.7566538	1.0583116	1.0561338	1.1516558	1.1443289	1.3153369	1.4348080	1.2522523	1.4124399	1.1748731	1.0449634	1.4928727	1.7468186	0.7417218	1.0299351	0.6787251	1.1677144
Urocanic.acid	0.8638117	0.3212854	0.2892404	1.7392963	1.1278006	1.1803694	4.6323495	0.8480094	0.1972440	1.0285895	0.5361097	1.2196895	0.9425947	0.2852366	0.4181020	0.3113765	0.3851985	0.4109156	0.4547907	0.4721768	0.2222827	0.3274246	0.3922131	0.4958654
Valine	0.9146230	0.9386614	1.0100753	1.5698269	1.1371203	1.0416494	1.1706341	0.8330754	1.1107848	1.1486198	1.1281245	1.1790151	1.2029580	0.9875298	1.0709863	1.2544596	0.6194352	1.3227468	1.0324728	1.1931394	1.0201331	1.1820476	0.9588230	0.9909290
Xanthosine	1.1578918	1.0963044	1.8140309	2.5780088	1.6815118	0.7748606	1.4037110	1.4535702	1.6892207	2.5296336	1.9151461	2.4928248	1.8328610	1.4805901	1.0967489	1.4175627	1.0784961	1.4506998	1.4556784	2.4213394	0.9455076	1.1696542	0.6661710	0.9053000
3-Indoxylsulfate	0.0014066653	0.0004189127	0.0010537000	0.0083676171	0.0142302571	0.0009821833	0.0053553740	0.0037918780	0.0099701690	0.0018319320	0.0000000000	0.0032034815	1.6957355303	1.7628992518	1.6905300705	2.6690102670	2.6662227663	1.2041302524	2.8159077618	3.9225468829	1.4879194492	1.2193387223	0.5481725665	0.6420550854
4-Methoxyphenylacetic.acid	0.6466108	0.8747982	0.6853639	0.4635535	0.6923135	0.9081214	0.3864574	0.5932554	0.8592044	0.7749379	0.6144890	1.6048136	1.3247088	1.9877733	0.5777823	0.4745502	0.6657401	0.7476548	1.1156824	0.3347995	0.4634213	0.4693551	0.7580660	0.8725201
2,3-Dihydroxybenzoic.acid	0.2284087	0.0000000	0.1073506	0.1197521	0.3433866	0.2394200	0.2957455	0.1572915	0.2597474	0.4494817	0.2776771	0.5415174	1.1314134	2.0412582	1.3909532	2.0095700	1.0359663	1.9621842	1.1671127	1.7748041	1.5807294	1.5394085	2.0435920	1.5376939
2-Hydroxybenzoic.acid	0.9912718	1.0984016	0.8859903	2.9777668	1.2496739	0.8263873	0.4437614	0.6297594	0.7991838	1.2558908	0.4339783	1.1235803	1.7674413	2.4987940	1.7318874	3.3508043	2.1025498	1.1283852	1.9534964	2.6782763	3.6617174	2.3740483	1.5164736	2.3913293
2-Methylbutyric.acid	0.7510326	0.0000000	0.5933317	0.4652210	0.8170571	0.6277748	0.5667496	1.2758309	0.4076446	0.6058693	0.5857997	0.7638084	0.5694005	0.5361239	5.5609744	0.6463784	0.8742257	0.6882732	0.5173637	0.7346524	1.1216587	0.9157327	0.5570880	1.4616018

Table S2A. Liver metabolites

4-Hydroxybenzoic.acid	0.9001782	1.0560988	0.5165869	1.6783153	0.5699435	0.8027474	0.7099929	0.9605478	0.4151053	0.8681392	0.5752243	1.0260255	1.6784020	2.1886534	2.2593682	3.0059774	1.4193347	1.8491539	1.9264320	2.0369756	2.6518981	1.4725679	0.8501041	2.2330271
4-Methoxyphenylacetic.acid.1	1.9877733	2.0373450	0.8337383	1.6048136	2.0658340	1.2979754	1.1156824	1.9172275	0.7001501	1.3116874	0.6853639	0.7476548	0.9081214	0.7218465	1.3247088	0.6144890	1.4894123	0.3347995	0.6466108	0.9913256	2.3431603	1.4964245	0.8747982	0.5932554
4-Methylvaleric.acid	0.2696367	0.2186943	0.2389721	0.2746247	0.3590760	0.3322700	0.3165805	0.2152099	1.1698982	0.4311654	0.7466173	0.7422495	0.6337153	0.3439619	0.5406916	0.2775697	0.2417917	0.6953245	0.8615943	0.9623980	0.8432549	0.8873891	0.8374581	0.2084494
Acetoacetate	0.9898180	0.8188094	0.9803567	0.9251530	0.9654123	0.9608998	0.9271387	1.0024227	0.8747964	0.9635099	0.9376343	1.0259165	0.9012016	0.9546399	1.0628470	1.0269441	0.9713463	0.9222361	0.9781181	0.8887658	0.9629445	0.9882867	0.9223725	1.0056272
Allantoin	0.9081038	1.1675675	1.0835233	1.4973499	1.3482714	1.1630004	1.2846565	1.3128294	1.4097008	1.5623482	1.4565717	1.4920634	1.3007490	1.1960430	0.9304598	1.1245904	0.8584241	1.5205353	1.0506660	1.2419266	1.0761671	1.2260110	1.3543364	0.9334865
Benzoic.acid	1.5878079	1.6902164	0.4250484	0.9203602	1.8134949	0.8459258	0.8249963	1.2637116	0.2394484	1.2308995	0.5166132	0.3333922	1.2684222	0.5741011	1.0986724	0.5265405	1.6702033	0.4627586	1.1916263	1.1436699	3.5990895	2.2423102	1.1203569	0.9979186
Citraconic.acid	1.3647653	2.2112889	0.8797576	1.4538588	1.7578296	1.5525089	0.7205279	1.0104727	0.5281336	2.3166094	0.4419381	0.6244150	0.9155004	0.7162225	0.9572177	0.5355094	1.0329688	0.2687801	0.5441814	1.9064968	2.0203813	0.9108907	0.8113292	0.5437640
Dextrose	1.7685669	4.6572716	2.3556058	1.7827129	1.1974816	1.1544892	1.2490300	0.7734221	0.9285326	0.8872297	1.2075044	1.1579873	1.2059183	0.9654718	1.2255272	1.3560641	0.5118914	1.3100008	0.6316051	1.1003823	0.6802550	1.0078298	0.6595299	1.2910940
Ethylmalonic.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
F6P	0.6739597	0.2447394	0.1826924	0.5818162	0.6716709	0.9746235	1.6123935	1.0723225	1.1070088	1.1154111	1.1312938	0.8015774	0.8302518	1.1814138	1.0512689	1.3252791	0.9051761	1.2707456	1.0729524	0.9041556	0.5528828	0.8035899	1.1194059	1.3061925
Fumarate	1.4192990	0.9868137	0.8213347	1.4978703	1.0743669	0.7292620	1.0526249	0.6276190	1.0221781	1.3314953	1.0614763	0.9885643	1.1486085	1.1050599	1.0235470	1.4572782	0.8988348	1.4704258	1.0546681	1.0817807	0.7715662	0.9892307	1.4595397	1.6709555
G1P	0.6752635	0.8029834	0.7627249	0.6158372	0.6249657	1.1037194	1.7901152	1.1289605	1.1985437	1.2173511	1.2187953	0.7115492	0.8453992	1.3293391	0.9983102	1.4457266	1.0017281	1.3487788	1.1853711	1.0712144	0.5663022	0.8982037	1.1802936	1.3657570
G6P	0.6688839	0.2380527	0.1925240	0.6659184	0.6797407	0.9710578	1.7391819	1.0406175	1.1499232	1.1649878	1.2167404	0.8868503	0.9159730	1.2787757	1.0400833	1.4203444	0.9207098	1.4076844	1.1534235	1.0067520	0.5166500	0.8859144	1.1368587	1.3662755
Galactose	1.5341257	5.2179303	2.3947257	1.5528834	1.3580207	1.1063219	1.1401609	0.8658799	0.9155313	0.9234025	1.1114644	1.1004973	1.1229601	1.0896220	1.1545220	1.3138040	0.6990620	1.1046280	0.7290189	1.1359700	0.7966584	1.1953606	0.7623118	1.0896942
Gentisic.acid	0.3546276	0.0000000	0.4713781	0.7467572	0.3560114	0.5168665	0.7327730	0.4047499	0.3646098	0.3597696	0.4111592	0.9474256	1.0461493	2.6593919	1.7835470	2.1266823	0.8074980	2.2794278	1.0550036	1.2916958	1.2224337	1.0283997	1.5228155	1.2681876
Glucuronic.acid	0.8618951	1.2635837	0.3914980	0.5864809	0.7149729	0.8905112	0.6466698	0.4523792	0.8934652	0.5236532	0.5877000	0.5639786	1.8837233	1.5606799	1.5985878	1.6699945	1.0047435	1.2180814	1.2296122	1.6472588	2.2245028	3.2449828	1.3460268	1.4921735
Glutaric.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
Glyceric.acid	1.1496164	2.5195502	1.1739954	1.3951672	1.4599438	0.8746264	0.9923443	1.2507857	0.8864898	1.5545627	0.9987718	0.9439196	0.7221400	1.4318077	0.8648158	1.2905391	1.3513554	0.8347342	0.9936521	0.7147244	0.7321524	0.8865097	0.8960178	1.4822709
Isobutyric.acid	0.00000000	0.05244963	0.50898333	0.82647449	0.00000000	0.65901154	0.56581734	0.71041992	1.32707167	0.56170639	1.01099565	1.18177968	0.84196243	1.21985165	0.69521063	1.08410990	1.63819382	0.52221008	2.05200836	1.27874196	1.92633325	1.10015048	1.10209239	1.01358025
Isovaleric.acid	0.7155741	0.0000000	1.0151671	0.4655771	0.9275040	0.4950023	0.7486756	1.0320418	0.8385003	0.7539450	0.5534565	0.6301668	0.4893295	0.5065836	5.2080493	0.7206219	0.7182304	0.4833982	0.6210143	0.8176440	1.0377181	1.1049437	0.3567986	1.2920695
Lactose	1.7278542	12.3361306	3.5970124	1.6204874	1.3170386	1.1452639	0.9148891	0.7427353	0.8165284	0.7769225	0.9731502	1.0814995	1.1334146	0.9947503	1.0370356	1.3653067	0.6670843	1.2811463	0.6614136	1.0377394	0.5529015	1.0834332	0.5707073	1.3489137
Levulinic.acid	1.5570665	1.2926634	0.7031304	0.6362157	0.7702267	0.6458151	0.4586144	0.6789458	1.2085580	0.9497924	0.8597124	0.6798147	0.8956509	0.6319326	0.9339435	0.5457088	0.9271357	0.9459671	1.2397537	1.8196988	0.9844683	0.8069519	0.7865500	0.4809240
Mannose	1.4952340	1.0294612	1.1193161	2.1812875	1.5518865	1.0888375	1.4574358	1.2740713	1.5870256	1.4937340	1.4813516	1.7636578	2.0195185	1.3265372	1.5246655	1.5385679	1.2863063	1.3664471	1.2684240	1.7166670	0.8845929	1.3531122	0.9221497	1.3065198
Methyl.alpha-D-glucopyranoside	0.7022848	1.3289890	0.7121133	0.9536818	1.1250414	0.6308415	1.1896947	0.8454161	1.2042655	0.9617926	0.8191024	1.0102836	0.9483462	1.1641299	0.6849502	1.0440661	0.6582924	1.3262151	0.9590109	0.8453300	0.8214475	1.1854478	1.1363926	1.0440430
Myoinositol	0.8694791	1.1178407	1.3772587	1.7509144	1.7419164	1.1912207	0.7806327	1.1023066	1.0258326	1.0494177	1.3554179	0.9649657	1.4025886	1.1070176	0.9472456	0.8104337	1.1539989	0.8418495	0.9136361	1.4517492	0.8450081	1.6781317	0.7083603	1.0566861
Nonadecanoic.acid	0.8291083	0.4843062	0.7006170	0.6379930	0.6590255	0.7834945	0.6717061	0.6468235	0.6136272	0.6344273	0.5468030	0.7088714	0.5691938	0.8135633	0.7518102	0.7726551	0.7042177	0.6471807	0.5237051	0.3273494	0.4570268	0.4718718	0.5502521	0.7504966
OAA	0.4706844	1.4768433	0.9478751	0.9480796	0.7043471	1.0231675	0.7729994	0.5138535	0.8686459	0.6839295	0.7601366	0.4938531	0.7716700	0.7003961	0.7052642	0.7108140	0.7430833	1.2272501	0.7375726	0.8898757	2.6271150	2.4659336	0.8769646	0.6642809
Palmitic.acid	0.6576104	2.4876173	1.1086988	0.9933969	0.6654050	0.5312395	0.7647661	0.7191476	0.6994420	0.7180929	0.5547641	0.8033647	0.6966770	0.8559372	0.7094591	0.7680809	0.5930325	0.8984361	0.5270847	0.9339967	0.4984569	0.6610013	0.5752758	0.5048961
Pentadecanoic.acid	1.1427298	0.5870484	0.6274741	0.6752754	0.6227439	0.7262631	0.5656418	0.5217017	0.6089249	0.4430046	0.4323494	0.7093060	0.4577233	0.5140927	0.6343803	0.6179902	0.4894114	0.5277205	0.3626343	0.3959666	0.4648136	0.3559489	0.5488784	0.4773791
Phthalic.acid	2.2467277	2.8811973	0.9590323	1.4759390	2.5516393	1.2665585	1.1557750	3.2708233	0.9187764	1.8053250	1.1865923	1.0920811	1.5253343	1.5010486	1.5789988	1.0036075	1.6275219	0.6693168	1.1291957	0.9520331	4.1384040	1.7908762	1.4875792	0.9633425
Raffinose	4.2406534	2.6381289	2.8986832	2.2229446	1.4063470	1.9821988	1.7797267	0.5603099	1.5427157	1.3383924	1.8955090	1.5934417	1.6822064	2.1903529	1.6188200	1.7642422	1.2483946	2.6886577	1.1058582	1.3579173	0.4961662	0.9152473	1.6370885	1.6808395
Shikimic.acid	0.4566439	1.6953687	0.4436559	0.5014321	0.9789059	0.6421197	0.8611503	0.8154816	0.4553175	0.8477968	0.7800669	0.6293811	0.6921569	0.9635854	0.7885012	0.8913415	0.7719212	1.1031032	1.0271294	1.0289196	1.1278543	1.0499156	1.0467217	1.3644345
Sorbitol	1.585376	2.068789	2.017347	2.935154	2.439898	1.695450	1.235273	0.948883	1.877812	1.083459	1.648626	2.228505	2.471795	1.821555	3.012169	1.975258	2.174246	2.263342	2.427025	4.434080	1.370861	1.535353	1.067649	1.186329
Stearic.acid	0.7809648	2.2287310	1.2442121	1.0303458	0.9092352	0.7524102	0.7931729	0.8663392	0.7608388	0.7868036	0.6238720	0.8245983	0.8188588	0.8765730	0.8958090	0.8963560	0.7338885	0.8893772	0.7047385	0.9714868	0.8025889	0.8111246	0.7017546	0.7680203
Trehalose	2.1142004	13.2894395	3.9071349	2.2777436	1.5761671	1.0666695	1.5014004	0.6787332	0.8279424	0.7812906	1.2507457	1.4231432	1.3643417	0.9935851	1.1759800	1.3869828	0.5431801	1.0142042	0.8030972	0.9663495	0.5082489	1.0376458	0.7117123	1.6965194
Urate	1.3406364	1.5250610	0.8473836	1.1140390	2.4907067	1.2353838	1.7609205	1.1875856	1.5123852	1.3022075	1.4339406	1.0269305	0.6765105	1.0893236	0.6584594	0.7040288	0.7428215	1.9296033	0.8196379	1.6574426	0.8632615	0.8101919	1.2833077	2.1605345
Valeric.acid	0.70749133	0.09470111	0.98921146	0.46459669	0.91370278	0.47580163	0.74021893	1.03119080	0.81706168	0.75332329	0.55229107	0.62304875	0.48829916	0.49363134	5.14922195	0.71910449	0.69037095	0.47793804	0.60513635	0.78592837	1.03686237	1.08850223	0.34767608	1.28934875
X5P	1.201143	1.276757	1.413303	1.653952	1.267569	1.278849	1.780746	1.354567	1.779299	1.577205	1.707360	1.920431	1.580249	1.517633	1.585497	2.195201	1.459374	1.733696	1.705658	2.215318	1.187748	1.478072	1.491918	1.627948
Xanthine	1.479659	1.481760	1.402484	1.887153	1.778127	1.252138	1.518562	1.382384	1.521875	1.459015	1.538795	1.813552	1.511328	1.476498	1.470618	1.495125	1.065810	1.728239	1.406754	1.589197	1.155761	1.426024	1.365320	1.292267
alpha-Hydroxyisovaleric.acid	0.22652691	0.06324408	0.24138572	0.38533503	0.40858595	0.08999759	0.13680320	0.24739137	0.67448423	0.27068110	0.05595278	0.38246377	1.40021748	0.40581075	0.59413534	0.16162409	0.14820324	0.80589746	0.45462266	0.50294160	0.51224833	0.62746522	0.94315331	0.27787725
alpha-ketoisovaleric.acid	1.6450600	1.9676816	0.9101139	0.7138070	0.8190894	0.5382239	0.4271922	0.7849076	1.1082485	0.9436748	0.6605273	0.5106391	1.2123041	0.5905675	0.8120547	0.5422817	0.3049550	1.0403584	1.1329032	1.8615979	0.9017435	0.8825711	0.9590286	0.7871725

Table S2B. Serum metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	1.0317667	1.0303621	0.9847637	0.9921081	0.9160872	1.0764221	1.0336387	1.4405943	0.7765993	0.9986675	1.0874466	1.0637402	0.6305017	0.5213879	0.7407689	0.8465473	0.6182256	0.6951432	1.0381927	0.6869308	1.1003884	0.7616520	0.7266176	0.6292298
3-Indolepropionic.acid	0.01904275	0.00000000	0.00000000	0.01174865	0.00000000	0.03955007	0.06561667	0.03874387	0.00000000	0.00000000	0.00000000	0.00000000	0.55859613	0.47659752	0.71442760	0.27750775	0.61415979	1.10075666	0.37694018	1.13900959	0.22864990	0.44264462	0.75318881	2.27604977
6-Methyl-DL-tryptophan	0.41570933	0.55659384	0.67931578	0.49104472	0.80584709	1.93103976	0.63320850	0.66146933	1.08739075	0.65511807	0.75366381	0.74293619	0.09812646	0.17093453	0.45117283	0.25733516	0.22503132	0.36726015	0.26036736	0.33192057	0.59247137	0.78618775	0.94471496	0.45148486
Indole-3-acetic.acid	0.5580839	0.5380495	0.5656663	0.5636264	0.4919839	0.4800485	0.4241354	0.6233548	0.3343458	0.5122234	0.6933088	0.4484751	0.7917882	0.9824133	1.0578317	1.1315136	0.6962389	1.0884141	1.7883287	1.4874967	1.2532215	1.2294161	2.2210241	1.7300960
Indole-3-lactic.acid	1.1092210	0.8554817	0.8354971	1.1621817	0.7877591	1.0869508	0.8945694	1.5749362	0.6616183	1.0120818	1.0766544	0.9578828	0.6190572	0.4244500	0.7577282	0.8598728	0.5966954	0.7057665	1.0638820	0.6138955	1.0639085	0.6896377	0.6855773	0.5902174
Kynurenine	1.0909688	0.8734492	0.3294966	0.7872656	0.2680286	0.8604749	1.0273913	0.9765153	0.8797466	0.7120567	0.7678117	0.9076418	0.3653122	0.6868505	0.6065237	0.7695144	0.5623107	0.3753020	0.5503452	0.4305640	0.3471962	0.5665617	0.6669201	0.4597565
Serotonin	0.8442799	0.9014375	0.7353003	0.7508531	0.8737883	1.3184758	0.8002665	0.7634158	0.7392552	0.8125640	0.8092775	0.8531453	0.4321848	0.5080711	0.4937651	0.5775824	0.5864579	0.5811751	0.6443621	0.5838568	0.7712975	0.5235457	0.8569040	0.5515420
2-Deoxycytidine	0.3174848	0.2913996	0.2822617	0.3026962	0.2133915	0.3491761	0.2773496	0.3324238	0.2194807	0.2744738	0.2549853	0.2950616	0.2459364	0.2298095	0.3028967	0.3110092	0.2116033	0.3872227	0.2877459	0.3042525	0.2941973	0.2165142	0.3662207	0.3591027
213C-Glutamic.acid	0.9844852	0.9950125	0.9327800	1.0003609	0.9661615	0.9508437	0.9988592	0.9277253	1.0146637	0.9506263	1.0051244	1.0134514	1.0141268	1.0258431	1.0099926	1.0166979	0.9702272	1.0188772	0.9572153	0.9783577	0.9923269	0.9244512	0.9319085	1.0222706
5-Aminolevulinic.acid	0.7795518	0.7610577	0.6979264	0.6854502	0.9618818	1.2366398	0.7757380	0.8759584	0.7565268	0.8750895	0.6972154	0.5884368	0.5317662	0.4935351	0.5312805	0.6134248	0.6264979	0.4866220	0.6992055	0.7625584	0.7390534	0.5473003	0.6652192	0.5197771
6-Hydroxynicotinic.acid	0.028878300	0.053021903	0.055377422	0.067188470	0.069876473	0.033207796	0.050327910	0.064691863	0.057382380	0.066923263	0.050205179	0.020650789	0.023744369	0.012478698	0.008996055	0.025685372	0.020600780	0.016676094	0.009066213	0.020656543	0.027477553	0.000000000	0.038251691	0.035514356
7-ketocholesterol	0.2924918	0.2284840	0.4863401	0.3812536	0.5532410	0.2924774	0.4050716	0.6754374	0.3572131	0.5246027	0.4581334	0.5209997	1.3684958	2.2957026	0.9383200	10.2231564	0.3468779	0.7566915	5.0969810	0.5870745	0.6553080	0.5284319	0.9099085	2.8210692
Acetylcarnitine	0.9441641	0.9762040	0.8584805	0.8966743	0.8083222	1.2599501	0.9270292	1.1218529	0.6377153	0.9340284	0.9575799	1.0547174	0.8179229	0.7078616	1.3668700	1.1744102	0.8729917	1.4676838	1.0122209	1.3667082	0.8370880	0.5816249	0.8944781	1.2286137
Acetylglucosamine	0.40392903	0.20460270	0.40498773	0.42430252	0.40644811	0.73773239	0.37272404	0.36942373	0.34369816	0.43376192	0.32548500	0.30721539	0.31563018	0.10564735	0.17228083	0.24874233	0.24854459	0.28460983	0.31103168	0.36955219	0.19195022	0.09980531	0.34108868	0.20726354
Acetylglycine	1.4991894	1.2571867	1.4613053	1.3676502	0.8618283	0.8963021	1.3151055	1.5117083	1.2874666	1.2558855	2.0225116	2.1556291	0.3764896	0.1361418	0.9900842	0.7101797	0.3881535	0.8370687	0.1611271	0.3595276	0.5242699	0.2188906	0.2776544	1.1418755
Adenosine	0.2140969	0.2102831	0.2204731	0.2183226	0.1923837	0.1817932	0.2516306	0.3133118	0.3362446	0.5335153	0.2711058	0.2710070	0.1909757	0.1598037	0.3264152	0.1133139	0.9777930	0.2111847	0.2169560	1.1616375	0.2937814	0.2245176	0.2665889	0.2164441
Adenosyl-L-homocysteine	0.6714422	0.4308204	1.5075238	1.2276340	1.5873233	1.2629599	1.1093691	2.1367804	1.2361365	2.0044919	0.7645900	0.3509771	0.7865940	0.3838238	0.4334325	0.8561266	0.8834433	0.3909437	0.7933884	1.1344111	1.2445698	0.8234503	0.2881118	0.3432706
Alanine	0.8039607	0.7589530	1.5213952	0.7050528	2.4600018	1.6993623	0.7328026	0.5635759	0.9061994	1.0124162	0.8918277	1.1135432	0.6239487	1.1980224	0.4809799	0.8274591	1.5761646	1.5665982	1.4870625	0.8288178	2.1276307	0.8214103	1.1012487	0.6655912
Allopurinol	0.03371837	0.03982831	0.07967565	0.09631134	0.29066584	0.43212536	0.10127359	0.13557639	0.15064015	0.43628029	0.07268631	0.04541401	0.18894061	0.15836448	0.86294382	0.35844435	0.26588665	0.01586960	0.21502325	0.77772557	0.23225748	0.19562593	0.24672431	0.21442101
Asparagine	0.4449370	0.4373391	0.4302286	0.4423950	0.4736336	0.8986803	0.4141668	0.4037197	0.4344819	0.4441081	0.4378873	0.4320793	0.3776924	0.3610497	0.3550619	0.3946823	0.3544344	0.7584599	0.4232461	0.4070500	0.6391954	0.5276892	0.8365307	0.6913280
Aspartic.acid	0.4152065	0.4430707	0.5818116	0.5320270	0.7732795	0.5713789	0.3907554	0.5394307	0.3698395	0.6125440	0.4739644	0.9147199	0.6267113	0.6123835	0.5933458	1.0165807	0.6299843	0.7023535	0.7167973	0.5597980	0.7913604	0.5099731	0.8173880	0.5713535
Betaine	0.7234086	0.7048656	0.6882660	0.7301375	1.0328520	1.0547873	0.8330171	0.7567204	0.8401010	1.0007066	0.7405565	0.6415822	0.4648153	0.6546769	0.6748845	0.7449814	0.5910158	0.7913117	0.6501385	0.9196811	0.5226326	0.4670694	0.8190514	1.0041040
Carnitine	1.0364532	0.9510847	0.6900549	0.7823069	0.8722678	1.4882140	1.0155252	1.0430504	0.7671293	1.1915917	0.9239250	0.6549932	1.2215885	1.1295841	1.0461135	1.1959042	1.1850933	1.0845366	1.4431300	1.6938279	1.3330664	1.1024471	1.5497510	1.0555476
Creatinine	2.0182532	3.1826911	0.6806979	1.3364505	1.0357324	1.0650838	0.9285776	1.0191995	2.2516750	1.1956444	1.5971185	0.8120371	1.4682139	1.1740891	1.8848313	1.5277349	0.4602601	1.4305611	1.3358876	1.8145411	1.3705444	1.2221740	1.0911130	1.7973037
Cystathionine	0.28309420	0.22951454	0.19001737	0.36697649	0.24784214	0.79328559	0.51016562	0.33012475	0.19901532	0.36555136	0.24005707	0.43611053	0.11324349	0.25762183	0.16868932	0.20845813	0.14641402	0.22658746	0.15482380	0.16571156	0.18506241	0.09193353	0.33018113	0.17725964
Cystine	0.2811702	0.2796157	0.2622289	0.4158454	0.2951822	0.4626571	0.2329457	0.4313985	0.3481685	0.7131780	0.1786220	0.1504858	0.4354672	0.3925378	0.7481704	1.2502132	0.5341248	0.2328273	0.3078212	1.0104342	0.6121067	0.7567378	1.1014113	0.2250691
Cytidine	0.5210576	0.5032761	0.5765483	0.5981420	0.6814616	0.8751241	0.6748009	0.6019237	0.5428900	0.7095091	0.5425272	0.7119897	0.4274866	0.2924270	0.6648767	0.5449437	0.3117971	0.5249493	0.3719328	0.5661403	0.4281487	0.2193708	0.5383064	0.6722130
Cytosine	0.5724007	0.5687503	0.6540320	0.6572037	0.7955865	0.9571722	0.7971547	0.6449386	0.5586945	0.6774215	0.6049335	0.7243051	0.4699204	0.2732985	0.7717965	0.5282462	0.3810730	0.6414866	0.4522232	0.6106754	0.4545835	0.1679954	0.4922570	0.7779320
Decanoylcarnitine	1.03977434	0.99283216	0.43905377	1.23286038	0.21996057	1.66219197	1.14613326	1.16848327	0.86426812	0.72083633	1.21367682	0.93209662	0.40954643	0.77981803	2.03456776	0.62146441	1.09213349	2.43900461	0.36883592	1.46662126	0.38505780	0.09040753	0.38388122	1.57232054
Glutamic.acid	0.5190196	0.5011747	0.4923732	0.4956872	0.6323800	0.5782931	0.3782653	0.4835876	0.3689661	0.6442815	0.4484648	0.6992172	0.6507610	0.4443386	0.6106565	0.6727734	0.4415760	0.6311273	0.4996465	0.5072568	0.5993526	0.4951351	0.6628929	0.6303698
Glutathione.oxidized	0.05294285	0.07759938	0.29613676	0.37270704	1.55391661	0.73383892	0.28143294	0.37137794	0.38844261	0.74461270	0.14097362	0.19893314	0.53946391	0.77446884	0.80577163	2.06643648	0.20456022	0.49325699	1.32663578	0.77536742	0.29639357	0.38259976	0.67550784	0.48181953
Glutathione.reduced	1.1026759	0.8923498	1.1151582	0.5953181	1.6980991	0.6901809	0.7222110	1.1313823	0.7949924	1.5343012	0.7254251	0.4263253	0.1457852	0.1639876	0.3207433	0.3435307	0.5711687	0.6251995	0.2651110	0.2859727	0.5322789	0.5886255	0.2908863	0.3738287
Glycine	0.7725024	0.9251390	0.8940421	0.7024416	0.9043963	1.0035431	0.8484915	0.9572646	0.8936362	0.7776883	1.1724503	0.9329527	0.3696696	0.4106501	0.5924033	0.5879735	0.5078564	0.7956602	0.4571842	0.5517679	0.7122945	0.4886854	0.6821170	0.7807791
Glycocyamine	0.8074463	0.3146842	0.4313919	0.7983406	0.7402149	0.9057195	0.2322731	0.3787078	0.4721578	0.9536144	0.6623463	0.1779486	0.3463183	0.2636901	0.4921304	0.4061054	0.6702330	1.0676197	0.2848171	0.6642394	0.7265750	0.6081363	0.6230967	1.7139250
Guanine	0.02532942	0.05454220	0.44570051	0.44655817	0.75594909	0.43156865	0.31297704	0.65911714	0.11930541	0.99610076	0.14866761	0.15196284	0.03857490	0.02812718	0.64312146	0.13858959	0.30982399	0.00000000	0.08996413	0.61969980	0.04445479	0.10089361	0.11101912	0.10465782
Guanosine	0.041368434	0.027223213	0.439538214	0.393871216	0.755126475	0.359767631	0.387946879	0.525422776	0.131452859	0.908707699	0.114507263	0.107079476	0.038413887	0.043984439	0.470480486	0.110833692	0.298855593	0.005636157	0.076048250	0.663438323	0.119137456	0.048801513	0.090631906	0.058864363
HIAA	0.4614215	0.4563886	0.5361250	0.6674289	0.5526476	0.7528907	0.6618530	0.8154046	0.3770931	0.5050472	0.8687341	1.0162924	0.5355136	0.4474822	0.5572884	0.7506275	0.2775017	0.3348267	0.5920746	0.4323071	0.8289809	0.4134172	0.6647502	0.4651709
Homoserine	0.6983023	0.7018378	0.7149072	0.7242009	0.6649812	0.8189758	0.7640266	0.6782549	0.5256616	0.7163832	0.6410018	0.4788504	0.4438158	0.5528304	0.3849193	0.6326310	0.6478078	0.3654759	0.5773910	0.6299180	0.7322205	0.5901563	0.8331537	0.3790520
Hydroxyproline	0.7868130	0.7673889	0.6748305	0.6843264	0.9174251	1.2313570	0.7636354	0.8520473	0.7546107	0.9010612	0.7151542	0.6026010	0.5303085	0.4746016	0.5074172	0.6101571	0.6367897	0.4844010	0.6824918	0.7603418	0.7412404	0.5531942	0.6457549	0.5127148
Hypoxanthine	0.03108008	0.03295078	0.07230745	0.10605112	0.24210361	0.46310881	0.10167784	0.14625749	0.16616489	0.51041860	0.06533173	0.04225448	0.24245563	0.13432216	0.87837180	0.36355552	0.25734567	0.01519113	0.21277908	0.74516568	0.21031964	0.20654750	0.27581957	0.22056332
Inosine	0.02600116	0.02615317	0.07605084	0.07720853	0.24970896	0.38404333	0.09108355	0.12666396	0.13240581	0.36308907	0.06973492	0.04524077	0.16349696	0.16517816	0.90361214	0.37945644	0.29174887	0.01648628	0.22917311	0.71077105	0.24821758	0.17251436	0.22439895	0.20742862
Isoleucine	0.7734905	0.7720793	0.6809624	0.7169639	0.9427465	1.2809432	0.7698176	0.8840363	0.7578946	0.9174449	0.6951529	0.5988584	0.5521642	0.4869889	0.5300929	0.6111975	0.6246363	0.4812083	0.6819774	0.7716538	0.7384486	0.5738182	0.6861106	0.5234358
L-Alloisoleucine	0.7816351	0.7675873	0.6931879	0.7254023	0.9586529	1.2948073	0.7777563	0.8893020	0.7541538	0.9230311	0.6862217	0.5978543	0.5540295	0.4943954	0.5348676	0.6202152	0.6324164	0.4872354	0.6973422	0.7748112	0.7349445	0.5754398	0.6966434	0.5213951
Leucine	0.7762630	0.7700904	0.6859590	0.7049883	0.9531758	1.2854569	0.7691488	0.8836390	0.7621739	0.9174278	0.7043351	0.6034554	0.5525940	0.4889069	0.5287984	0.6207396	0.6323462	0.4784675	0.6888833	0.7697485	0.7440186	0.5678910	0.6857679	0.5269246
Methionine	0.4595065	0.4579772	0.4746533	0.4885255	0.4920350	0.6604720	0.4462489	0.4727000	0.4003232	0.4848580	0.4535979	0.4214641	0.3289654	0.4052902	0.3049758	0.4320432	0.4224938	0.3929081	0.5814995	0.4638038	0.7436927	0.5635675	0.7926240	0.3739858
Methylguanidine	0.6083126	0.5991099	0.7510126	0.7478605	0.6616402	0.7147471	0.7355709	0.7186135	0.5271701	0.7047024	0.6328199	0.3575302	0.4456060	0.4159211	0.3919142	0.5690907	0.6021682	0.2794409	0.6075165	0.5859735	0.8534668	0.5224783	0.8782036	0.3948659
N,N'-Dicyclohexylurea	0.4491116	0.7786632	1.0568974	0.8605733	0.3151338	0.2683889	0.8111300	0.8860459	0.9300668	0.6072164	0.7132078	0.7497717	0.5024905	0.3967395	0.3895438	0.4417970	0.4784667	0.7943685	0.4818193	0.5755309	0.3671177	0.5808789	0.8349089	1.5812582
N-Acetylethanolamine	0.1837007	0.3351524	0.1712734	0.1999842	0.1839945	0.3390010	0.3605331	0.4625985	0.1857110	0.2160144	0.1688903	0.1901620	0.1246755	0.1620703	0.3036458	0.2729194	0.3908199	0.4101847	0.3189875	0.2665719	0.3897250	0.1503872	0.4816167	0.3320829
N-Acetylneuraminic.acid	0.06720457	0.11616575	0.06952991	0.06068203	0.14038777	0.16392413	0.06753194	0.15396054	0.07783408	0.20979568	0.16580744	0.18465772	0.09179428	0.11928544	0.17453190	0.10237460	0.08390267	0.17293004	0.09089243	0.13104024	0.08846533	0.08536574	0.14463525	0.10738479
Nicotinamide	1.1086306	1.0155569	0.9927073	1.0139620	1.7020512	2.0952281	1.2648053	1.1001351	1.0931990	2.0225090	1.1455333	1.2253957	0.8691954	0.8242333	1.0545029	1.3757596	0.9047593	0.6271669	1.1229611	1.3799018	0.8479625	0.6773855	1.0690791	0.7598487
Norleucine	0.7688610	0.7655194	0.6721997	0.7120115	0.9469902	1.2760697	0.7667306	0.8749643	0.7609668	0.9137877	0.6953367	0.5920285	0.5545982	0.4870829	0.5265577	0.6099556	0.6318839	0.4853943	0.6818889	0.7537906	0.7431439	0.5691091	0.6839599	0.5239574
Normetanephrine	0.4602634	0.7922858	1.0278972	1.1844420	1.1925011	1.0998287	1.4460477	1.2505234	0.8085146	0.8390345	0.7908881	0.6272976	0.7473370	0.6527553	0.9018705	0.9717988	1.1085613	0.6866956	1.8133871	0.7053081	1.5459995	0.7414323	0.8043796	0.5152777
Norvaline	0.7456426	0.7479910	0.6948016	0.6796876	0.8187685	1.0167348	0.7761884	0.8805773	0.7022088	0.7862304	0.7152055	0.6146859	0.4932867	0.5133007	0.4637410	0.6137076	0.6419375	0.4975852	0.6883464	0.7023230	0.8132069	0.6068848	0.6269995	0.4917820
Phenylalanine	0.6926250	0.7008467	0.6459153	0.6778132	0.8648654	1.2378989	0.6956844	0.8330104	0.7424098	0.8759900	0.6224442	0.5904636	0.5133810	0.4601704	0.5379103	0.5883836	0.5392128	0.6769541	0.6840378	0.7221243	0.7056662	0.5232141	0.7153008	0.6231087
Proline	0.2536354	0.2665351	0.2729979	0.2910349	0.3455349	0.5739777	0.2744232	0.3060478	0.2541320	0.3370148	0.2492915	0.2561445	0.1759309	0.2077588	0.2071730	0.2544563	0.2057017	0.2743556	0.2967707	0.3282657	0.4057957	0.2971243	0.5417059	0.3029315
Sarcosine	0.7972464	0.6285018	1.1937639	0.6966922	2.1649467	1.8733796	0.6445680	0.5183578	0.7599217	0.8395287	0.5969229	1.3593589	0.5837919	1.1513682	0.4793732	0.7341413	1.3038976	1.6908640	1.6649814	0.7639477	2.0942908	0.5273449	0.8220729	0.6044479
Serine	0.5353581	0.5267698	0.4793458	0.4622670	0.5259625	0.7771565	0.5041540	0.4785595	0.4262779	0.5054402	0.5073924	0.4689129	0.3561538	0.3706829	0.4047429	0.4597577	0.4136697	0.5811335	0.4466357	0.4885491	0.5757121	0.4545363	0.7522944	0.5896785
TMAO	0.85451078	0.65696505	1.21903340	0.39266798	1.48554668	0.47086960	0.40870485	0.92978038	0.64500025	1.40691014	0.49913503	0.04325557	0.00000000	0.33761085	0.18429464	0.25384521	0.63396713	0.61949213	0.26769308	0.25273734	0.31276815	0.33318616	0.14893635	0.28665877
Threonine	0.7150959	0.7015677	0.7629955	0.7761223	0.6462053	0.8520302	0.7351514	0.6963445	0.5208669	0.7185048	0.6479620	0.4750623	0.4655190	0.5523690	0.3989872	0.6481275	0.5915996	0.3782476	0.5667950	0.6336898	0.7189485	0.6165406	0.9114231	0.3670283
Tyrosine	0.6030869	0.6125875	0.7887788	0.8232557	1.0062731	1.2490204	0.6071225	0.8777774	0.6561377	0.8893080	0.6613815	0.6228148	0.3730047	0.3463561	0.4792403	0.4594995	0.3938609	0.5973173	0.5438654	0.5633916	0.6423756	0.4651992	0.6423144	0.4970374
UDP-GlcNAc	0.000000000	0.000000000	0.000000000	0.004592017	0.193086076	0.040915595	0.004539314	0.145934213	0.178034558	0.116639623	0.000000000	0.070587210	0.149759237	0.000000000	0.055340246	0.339265912	0.000000000	0.018765855	0.038192797	0.065482356	0.000000000	0.000000000	0.070706147	0.000000000
Uracil	0.8457426	0.8495759	1.0951227	1.2036762	2.6855035	3.3864430	1.5948670	1.2708232	1.4810583	2.7345165	0.0000000	0.5702306	1.3042441	0.5982922	1.2443398	0.8348638	0.7037339	0.5697256	0.7155200	1.7113136	0.5957357	0.4716715	0.6942587	0.6309362
Uridine	0.8880025	0.8636672	0.9870649	1.0857023	2.5189912	3.0324660	1.5176027	1.2631859	1.6074507	2.5373434	1.0135393	0.6157471	1.2844979	0.6318885	1.2363457	0.8629738	0.7619592	0.5965804	0.7071004	1.7040465	0.6145321	0.4385381	0.6160858	0.6436844
Urocanic.acid	0.03376918	0.04254745	0.05724673	0.04831958	0.04635670	0.04936237	0.03685679	0.04165554	0.04238366	0.03293443	0.03548771	0.04557768	0.01823145	0.01534968	0.01744506	0.01649835	0.01764671	0.02310776	0.02532258	0.01928040	0.04746682	0.02773702	0.03005870	0.02772801
Valine	0.7459956	0.7503615	0.7026255	0.7024037	0.8202731	1.0275209	0.7588466	0.8909467	0.7097040	0.7982574	0.7008425	0.6146873	0.5054868	0.5030490	0.4737987	0.6111390	0.6462739	0.5020537	0.6864407	0.6854861	0.8229823	0.6217540	0.6254272	0.4997380
Xanthosine	0.4577110	0.4849641	0.6241970	0.6766769	4.2558855	7.7630219	1.5764167	1.0264283	4.2477904	7.8442639	1.0624214	0.1908877	0.8124879	0.1524969	1.8590245	0.6193012	0.4041642	0.1813820	0.2700349	2.3332162	0.1061311	0.1309162	0.1285644	0.3067931
methyl-a-D-galactopyranoside	1.3477293	0.9038175	0.7205699	0.5291660	1.0640751	1.5175823	0.9536713	0.7824787	1.0652578	0.6404905	1.0459692	1.1463473	0.6403432	0.7595554	1.0700229	0.9111508	0.7905356	0.9514611	0.9061882	1.0269884	1.2904433	0.9006732	1.4165315	0.9374045
3-Indoxylsulfate	0.0039742006	0.0023391308	0.0353740607	0.0016464954	0.0022620914	0.0031716151	0.0032944106	0.0030293134	0.0014770960	0.0010762186	0.0009190207	0.0016898664	1.6172315346	2.2955004825	3.8331504617	1.8889801044	2.9435636983	1.0289100428	1.5241429637	4.5331715267	1.5340171634	1.4178092065	2.0482161824	0.6584347506
2,3-Dihydroxybenzoic.acid	0.48998087	0.45925943	0.20171275	0.11165078	0.40996557	0.48016548	0.38672610	0.54687554	0.11396917	0.11675343	0.11986621	0.07671945	1.24635923	1.42578176	1.18469069	2.02295701	1.50349511	2.05013084	1.32332791	1.94655749	1.59277083	1.10832205	1.72193673	1.59378286
2-Hydroxybenzoic.acid	0.7965871	0.7728044	0.3218101	0.2447120	0.6136844	0.3744148	0.4319101	0.7563006	0.3510303	0.2609883	0.2320656	0.3058933	2.2558602	2.5915402	1.5055872	4.0838144	2.3711602	1.4305851	2.8694710	3.5659023	3.3476204	3.0332858	3.9963234	1.7222825
2-Hydroxyphenylacetic.acid	0.8336771	0.7515347	0.6511527	0.4969051	0.6434132	0.9558337	0.8266350	0.8324308	0.3614684	0.4623572	0.5138190	0.3820153	1.1250300	0.9010148	1.0660509	0.6361450	0.8173596	0.5060616	0.6922646	1.0914150	0.6260436	0.7397448	1.0785493	0.3409159
2-Methylbutyric.acid	0.9162436	0.7647800	0.8114202	0.6791095	0.5724590	0.7517002	0.3763115	1.2930302	0.9617106	0.9124321	0.8012958	0.5613845	0.4573325	0.4679710	0.4829717	0.7781003	0.8911581	0.3806420	0.3924137	0.6863296	0.4486746	0.7857104	0.3367745	0.6051235
3-Hydroxyphenylacetic.acid	0.6300611	0.8019803	0.4395543	0.3531513	0.5712445	0.7262196	0.5517035	0.7293511	0.4730190	0.6674977	0.4150897	0.2773652	0.9234166	0.9577731	1.4031874	0.7612582	0.9709512	0.7315022	1.3207369	1.7982472	1.0991215	0.8245665	1.2208213	0.7844164
3-Indoleacrylic.acid	0.06863647	0.07993838	0.29599954	0.01919182	0.00000000	0.13184064	0.03164545	0.14464441	0.09467593	0.11117823	0.01868143	0.01239224	0.92060183	0.61627943	0.93140097	0.66541385	0.56434471	1.32301774	1.42618439	1.99700779	0.37785536	0.20324056	0.60686634	1.64759696
3-Methyl-2-oxovaleric.acid	0.7284818	0.7998605	0.8214719	0.7937070	0.4602629	0.6143488	0.5652290	0.8385703	0.5941437	0.4562508	0.6723339	0.7837716	0.3804015	0.3810327	0.5773716	0.7591478	0.7364682	0.4953530	0.4704629	0.6691918	0.4352169	0.4875276	0.4163757	0.3738398
3-Phenyllactic.acid	0.1588272	0.1628897	0.1481714	0.2012786	0.1907786	0.3345011	0.1358782	0.2337874	0.1476731	0.1240542	0.1009023	0.1153669	0.3804044	0.5534323	0.1483201	0.6223141	0.3725672	0.1412559	0.6140716	0.9084644	0.3132405	0.3880331	0.2251292	0.3031758
4-Hydroxybenzaldehyde	0.2899898	0.4539353	0.2719443	0.1845166	0.4342202	0.1635672	0.3338587	0.3637891	0.3575433	0.3653502	0.3196463	0.1567934	0.1617343	0.6138772	0.2441290	0.4573647	0.5656350	0.4557670	0.6785351	0.7462931	1.9606845	1.3874968	0.6191694	0.2239879
4-Hydroxybenzoic.acid	0.7415720	0.6427323	0.3418409	0.2771368	0.5039981	0.4729974	0.4056269	0.8144809	0.2511309	0.2701269	0.2969636	0.2283418	2.4564177	2.5600532	1.7188250	3.7086417	2.5128617	1.5046030	3.0486985	3.3705885	3.2851761	3.2291628	4.4785681	1.5404096
4-Hydroxyphenylacetic.acid	1.0741901	0.9484975	0.6531368	0.4162101	0.6926568	0.7114619	0.7534805	0.7216074	0.8789581	0.6506508	0.8736327	0.2907721	1.0987438	0.8528024	0.9308913	1.0528581	0.7804062	0.4420478	0.9035063	1.3928209	0.8826471	0.8112688	1.0836423	0.7085074
4-Hydroxyphenylpyruvic.acid	1.14921842	0.98845607	1.98099909	1.72171599	1.23177289	1.72876545	0.83944057	2.56334937	1.38221909	0.52593743	1.12397307	1.22757429	0.24319700	0.39547674	0.44914055	0.12458038	0.68509201	0.18949878	0.47693233	0.48118769	2.00381191	1.66541921	0.79929192	0.08403531
4-Methyl-2-oxopentanoic.acid	0.5350964	0.7260103	0.8990688	0.8404178	0.5670097	0.4391739	0.5110427	0.6475787	0.4532219	0.3383676	0.7675285	0.6123645	0.4158343	0.4958764	0.5988977	0.8790783	0.7914478	0.4360865	0.6702444	0.6582298	0.4875331	0.4562112	0.4409016	0.5753140
4-Methylvaleric.acid	1.2193120	1.1373415	1.2803601	1.2649514	0.7155701	1.2545237	1.0279050	1.3477962	1.2666246	0.6921735	1.1916585	0.9646052	0.5288983	0.4787545	0.5958022	0.8224816	0.8099802	0.6323150	0.5876209	0.7061165	0.6493778	0.6388923	0.6152713	0.6383928
Acetyl-L-tyrosine	1.3823909	1.5654071	2.4631201	1.8466601	2.5207747	1.8986028	1.1913219	2.1991471	1.1217505	1.2484589	1.8941245	1.1053379	0.7384137	0.6968520	1.0445795	0.9093524	0.7819208	3.3148925	1.3974540	0.6655445	2.4891795	1.5615589	1.2013689	1.0886114
Allantoin	0.4179758	0.3920830	0.4618506	0.5288154	0.4099781	0.9940990	0.5244163	0.5888625	0.3894575	0.4465263	0.4335474	0.5277082	0.3798188	0.4607883	0.4766550	0.5942443	0.5207472	0.4367983	0.6263660	0.3932992	0.6471256	0.5786775	0.7884335	0.3839070

Table S2B. Serum metabolites

Benzoic.acid	0.5137459	0.8011919	0.8700612	0.7071747	0.7833871	0.5132784	0.9021533	1.0397754	0.6048753	0.4560824	0.7378836	0.9754978	1.1409319	1.1780068	0.7153125	1.3047273	0.8824771	0.6084236	1.1787358	0.6067928	1.2885574	0.9537052	0.9203954	0.6804284
Citraconic.acid	1.1832005	0.8655313	0.8829787	0.9384341	0.7149742	0.9088399	0.8197862	0.9260997	0.7828447	0.6176995	0.8662048	1.0564296	0.6012591	0.5014137	0.6816109	0.8420866	0.9668129	0.6730451	0.7962384	1.0701069	0.6463906	0.4847092	0.6272626	0.4146637
F6P	0.6148911	0.6397381	0.4180315	0.4791333	0.8018948	1.0489481	0.5600311	0.4700166	0.5596413	0.7723185	0.5416507	0.8945571	1.3691818	0.9980324	0.7388595	2.4056484	0.4272504	1.0292442	1.8827413	1.0846360	1.0310069	0.7883688	1.5219983	1.0737757
G6P	0.5960554	0.6725720	0.5424209	0.4639696	0.7149186	1.0277904	0.6028397	0.4610059	0.5065798	0.6587487	0.6167404	0.6808418	1.2350843	1.1748242	0.8482595	2.0001126	0.6219998	1.0504048	1.8062061	1.1607852	0.8258928	0.6993957	1.1175112	1.3118745
Gentisic.acid	0.5139415	0.4151858	0.1699240	0.1634507	0.4950193	0.5381677	0.4975664	0.4815131	0.1646657	0.1868625	0.1272859	0.1044369	1.2590846	1.5629216	1.2770249	2.0023922	1.5103748	1.8111364	1.2449566	2.1445328	1.5509669	1.2755833	1.7910363	1.3444712
Glucuronic.acid	0.2943072	0.3285132	0.3076357	0.3028917	0.4062023	0.3879114	0.3706921	0.4386659	0.3901433	0.3952716	0.3387479	0.4035722	0.3447072	0.3041804	0.3525938	0.3387238	0.4254461	0.2811051	0.3409680	0.3958022	0.2665106	0.3763200	0.4654544	0.4758465
Glutaconic.acid	0.8936806	0.7301086	0.9696221	0.8526519	0.5442453	0.5880147	0.5992676	0.9477549	0.6377112	0.4061179	0.7163246	0.8437270	0.5472146	0.4245548	0.7144656	0.9034756	0.8900980	0.5316449	0.6503364	0.7681063	0.4747078	0.4802786	0.3834784	0.3985794
Isobutyric.acid	1.2611450	1.0617315	1.2009763	1.0144702	1.6725007	1.3712387	0.9813562	1.1676435	1.0259964	1.1891182	1.1904247	1.0942924	1.5989614	1.4913369	1.5619882	2.1045380	1.2262023	2.0379971	1.5637909	1.3742913	1.7912535	2.4635205	2.4077597	0.8333862
Isocitrate	0.9363562	0.9694145	1.8275446	1.6172730	1.9900427	5.4531547	0.8358172	2.2995017	0.9928619	1.4021071	1.0910185	1.6178133	0.6324479	0.5417913	1.1534480	1.0034652	0.4038732	1.0685027	0.8624940	1.8233722	0.7640728	0.5662017	1.4586538	1.0827235
Isovaleric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
Ketoisoleucine	0.6320128	0.6428483	0.8286818	0.8677048	0.5299760	0.6119989	0.6528786	0.9677705	0.5359146	0.4973663	0.6318207	0.7465316	0.4568074	0.5057830	0.6968982	0.8765001	0.8146209	0.5613216	0.6569281	0.7444931	0.5323563	0.4600245	0.4162702	0.4342382
Ketoleucine	0.7407093	0.6770491	0.8666374	0.8526344	0.4862419	0.6715415	0.6274490	0.9300686	0.5821689	0.4755816	0.6434545	0.7973945	0.4390582	0.4554591	0.6420511	0.8235266	0.8422553	0.5404413	0.5446198	0.7969653	0.5417458	0.5267113	0.3870948	0.4680990
Leucic.acid	0.07332520	0.05691064	0.16240462	0.13844880	0.00000000	0.13192383	0.18425088	0.09091516	0.09485068	0.09601863	0.12344032	0.07552676	0.07950051	0.18992066	0.18504689	0.23065715	0.09115326	0.08444802	0.03149924	0.39720394	0.12766977	0.17789873	0.05538901	0.09050159
Levulinic.acid	0.8733528	0.7773803	1.1885660	0.9115188	0.7639572	0.6718761	0.8896795	1.1401628	0.7158665	0.5367945	0.7854932	1.2883168	0.3414807	0.3001495	0.3850537	0.3747144	0.5945561	0.5645422	0.3800352	0.4273772	0.8644449	0.6055051	0.5948493	0.3990532
Mannose	0.6683804	0.7490577	0.9983012	0.8180795	1.3001285	1.6448997	1.1464313	1.2114073	0.8301304	1.2382297	0.8439367	0.8125773	0.6266621	0.8626987	0.8407750	0.8446483	0.6687708	0.4966768	0.7226429	1.1309506	1.0346696	0.5709434	0.9154449	0.4778395
Mucic.acid	1.4449558	1.5175796	1.7136174	1.7628124	2.9718829	3.5026565	2.1747000	2.7953622	1.7672312	2.1885316	1.4510821	1.0805201	0.9881322	0.4407361	0.5894630	0.4070065	1.0587811	0.3780752	1.0418203	0.6686453	1.6099692	1.3606473	1.4986516	0.2406813
Myoinositol	0.9158956	1.0903492	1.0132274	0.7188772	1.0656828	1.1381421	1.0394161	1.4046805	0.7925365	1.0714162	0.8230511	1.0257722	0.9557425	0.9178068	1.1749202	0.9482438	0.8227359	0.9848646	0.8354734	1.0013812	1.1290946	0.6984916	0.7774978	0.6192854
Nonadecanoic.acid	0.7597794	1.0984831	1.0566841	0.6869035	0.7567158	0.6152611	1.1422799	0.7788149	0.9910287	0.5742253	0.6355600	0.7711078	0.6560131	0.6744979	0.6686692	0.4608864	0.5979236	0.7173817	0.5101773	0.4252656	0.8019144	0.5360187	0.6069391	0.7542067
Palmitic.acid	1.1697404	1.1289978	1.0746644	1.0579965	1.0081349	1.0744314	1.1476871	1.1941974	0.8681928	1.2085481	0.9326418	1.0318683	0.8677152	0.6149741	1.0140553	0.7505703	0.9214058	0.8712176	0.6402457	0.9742409	0.8439879	0.7187422	0.7523927	0.6433307
Pentadecanoic.acid	1.0416191	1.0968575	1.2484225	1.3574081	1.1434541	1.0799144	1.1658474	1.1948132	1.3305186	1.2054729	1.2713009	1.5459406	0.8983497	0.5198255	0.6073550	0.4853418	0.5751780	1.0182041	0.5896763	0.4666398	0.7345063	0.5951775	0.7111444	1.3217963
Phenylglyoxylic.acid	0.6505425	0.7622024	0.4309066	0.4541979	0.2762495	0.7508618	0.5632261	0.6586299	0.5866884	0.5445800	0.4662587	0.1722703	0.7744946	0.6864339	0.7886320	1.3051016	0.5019615	0.4552686	0.6690830	1.0880316	0.3913430	0.4653460	0.7296399	0.4115943
Phenylpyruvic.acid	1.6837193	1.1946551	1.2117800	1.4134552	1.2954706	2.1709991	1.1442532	2.6172624	1.0717084	1.3957800	1.0979073	1.1359335	1.1605814	1.1434987	1.1531757	0.9821010	1.4858917	0.9080724	1.9169820	1.1176169	2.5614484	2.4989341	1.3980044	0.5780909
Phthalic.acid	0.8312283	1.6718001	1.6295232	0.6950160	0.9813302	0.7106078	1.0632694	0.8647620	0.8410628	0.7436008	0.7956362	1.1354350	0.8725004	0.8293501	1.0938052	0.5822359	1.4563201	0.5690216	0.9613559	0.6940954	1.4272887	0.7233408	0.5024063	0.4871232
Pregnenolone.sulfate	0.15109681	0.06450606	0.07824688	0.11139556	0.16581628	0.10776864	0.25053390	0.01274011	0.18073139	0.11896680	0.04564024	0.04885158	0.01195747	0.02402525	0.01011219	0.17572145	0.13117700	0.39292133	0.39154295	0.10137071	0.05705211	0.00000000	0.16982081	0.79087325
Sorbitol	0.5263006	1.1125334	0.8735987	1.0204774	1.8649705	2.9610703	1.1785228	1.5158011	2.0153651	1.8722321	1.1390051	0.8823096	1.0456780	0.9890519	1.3129599	1.0471344	0.9181730	0.6389121	0.9514893	1.4349702	0.5031007	0.5956122	1.2551092	1.2870245
Stearic.acid	1.0184713	1.0750990	1.2224773	1.0051354	0.9065094	0.7811735	1.1789520	0.8386794	0.7374513	0.8942426	0.7940715	1.0533583	0.9066691	0.8976884	0.9911621	0.7727796	1.1123866	0.8484215	0.7059182	0.8682556	1.0533575	0.7744590	0.7948777	0.6558604
Suberic.acid	0.6717550	0.7711379	1.0687371	1.0001316	1.0048246	0.9080725	0.9082036	1.1276302	0.8134137	0.8582683	0.7563850	0.8792998	0.7326972	0.6036770	0.8775342	0.9730880	0.7433058	0.9116463	0.9155839	0.7838742	0.8153078	0.6814005	0.7289064	0.8155878
Valeric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
X5P	0.5027232	0.5146277	0.3386513	0.4047086	0.8736686	0.7205287	0.3494380	0.3850901	0.2681374	1.0155902	0.3328307	0.5785047	2.9203121	2.3234867	2.2986260	4.6446462	1.7533107	2.0129461	3.7469756	2.2407628	2.3747651	1.7961056	2.2261729	2.3189625
alpha-Hydroxyisovaleric.acid	0.2371994	0.2527587	0.3991637	0.3119418	0.2179633	0.4664979	0.3021191	0.2406591	0.1822040	0.2528320	0.4813419	0.2408560	0.1477089	0.1300373	0.2515798	0.1820547	0.2035981	0.1894338	0.3520112	0.1956317	0.1405861	0.1275436	0.3147498	0.1255165
alpha-ketoisovaleric.acid	1.1483537	0.9211920	1.0424223	1.1143107	0.6507956	0.7640291	0.9224072	1.3979542	0.8386406	0.5159111	1.0674584	1.1048148	0.5318858	0.4081003	0.6895266	0.8388138	0.6593168	0.4917263	0.4880581	0.7309270	0.7401869	0.6986751	0.6619629	0.5088614
p-Coumaric.acid	0.8884362	2.5429656	0.8671267	0.3814133	0.4828513	0.4830849	0.3138755	1.1793190	1.9050500	0.2601965	1.4171255	0.5975559	0.5928540	0.5256743	0.5782154	0.6462564	0.6272135	0.2994134	0.7650979	0.6735591	1.3843546	0.5536971	4.3952783	2.8617781

Constructed from biom file

#OTU ID	CO.1	CO.2	CO.3	PCB6.1	PCB6.2	PCB6.3	PCB30.1	PCB30.2	PCB30.3
D_0__Bacteria;D_1__Actinobacteria;D_2__Actinobacteria;D_3__Bifidobacteriales;D_4__Bifidobacteriaceae;D_5__Bifidobacterium;__	0	0	18	0	0	0	0	0	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;Ambiguous_taxa	19	26	15	43	0	0	0	37	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium	0	0	0	74	122	109	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Barnesiellaceae;D_5__uncultured;D_6__Bacteroides sp. Tilapia9	0	12	0	0	16	0	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	9296	10607	8015	13871	7845	10279	6933	7367	10551
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;__;__	8115	8838	9280	5390	6298	5799	7923	10196	7843
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Rikenellaceae;D_5__Alistipes;__	2588	2712	2528	1387	2374	1818	3313	2397	2808
D_0__Bacteria;D_1__Cyanobacteria;D_2__Oxyphotobacteria;D_3__Chloroplast;__;__;__	8	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Bacillales;D_4__Bacillaceae;D_5__Bacillus;__	0	0	0	0	0	0	61	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Lactobacillaceae;D_5__Lactobacillus;D_6__Lactobacillus gasseri	329	316	457	795	190	685	1548	189	1114
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Streptococcaceae;D_5__Lactococcus;__	39	0	30	35	59	37	0	0	40
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiaceae 1;D_5__Clostridium sensu stricto 1;D_6__uncultured bacterium	62	58	55	18	0	0	0	0	254
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;Ambiguous_taxa;Ambiguous_taxa	0	57	0	0	103	0	109	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;D_5__uncultured bacterium;D_6__uncultured bacterium	46	228	28	41	198	39	178	80	188
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;__;__	94	120	0	127	141	161	65	180	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Defluviitaleaceae;D_5__Defluviitaleaceae UCG-011;Ambiguous_taxa	131	154	92	70	0	188	0	0	159
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium	0	0	0	55	60	105	106	57	41
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] brachy group;D_6__uncultured bacterium	0	0	0	0	0	7	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured bacterium	0	16	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured organism	0	3	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;__	67	62	63	0	185	0	94	208	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;D_6__uncultured bacterium	1455	1296	1162	1122	1580	431	1767	1383	1644
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;__	121	91	123	0	17	1803	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium	109	0	162	0	0	0	0	37	64
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;Ambiguous_taxa	303	293	302	0	287	0	278	0	279
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;D_6__uncultured bacterium	0	362	472	585	226	498	237	393	324
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;__	0	106	114	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetitomaculum;D_6__Firmicutes bacterium CAG_194_44_15	262	245	321	454	304	0	319	241	294
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;D_6__Lachnospiraceae bacterium 609	203	0	320	0	1693	0	0	0	128
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;__	257	183	319	222	0	250	83	117	206
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium	331	388	366	244	287	206	757	591	869
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens	486	530	520	91	214	151	130	84	161
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__uncultured bacterium	244	0	512	0	0	572	0	631	636
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;__	905	727	990	1994	843	1142	628	1336	656
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae FCS020 group;__	143	117	105	173	98	92	183	212	147
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;D_6__uncultured bacterium	4489	4932	2051	4199	4272	3122	2789	1700	3057
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;__	8765	8865	8624	6923	9399	7884	12717	12190	11786
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa	718	738	571	0	0	0	668	406	1198
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium	466	499	0	0	0	0	858	0	897
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;__	1120	848	1065	0	313	0	0	878	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;D_6__uncultured bacterium	112	142	0	1124	150	150	218	226	821
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;__	0	0	70	0	0	193	0	287	154
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;Ambiguous_taxa	0	0	0	0	0	36	51	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;D_6__uncultured bacterium	297	293	243	425	252	0	106	231	208
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44	0	0	0	0	0	0	74	43	109
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium	474	445	507	945	1516	529	2001	861	1832
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;__	0	0	129	0	0	0	27	126	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella 3;D_6__uncultured bacterium	183	31	283	415	0	5	37	703	431
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella;D_6__uncultured bacterium	57	67	0	72	58	72	84	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;D_6__uncultured bacterium	226	227	201	0	825	0	912	291	295
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;__	0	0	0	0	0	0	181	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016	0	0	0	159	97	171	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Clone-47	234	331	135	0	112	195	68	73	541

D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture Jar-19	0	0	0	93	0	0	0	0	94
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-27	0	0	164	0	118	0	125	0	72
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-54	0	0	0	0	0	71	50	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__uncultured bacterium	3274	2630	2983	2961	2110	2254	3683	2587	3054
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;__	350	385	616	511	297	410	584	497	381
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;__;__	6804	5724	7057	7593	6563	4562	6732	5530	11105
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptococcaceae;D_5__uncultured;Ambiguous_taxa	89	70	66	64	43	104	88	128	132
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptostreptococcaceae;D_5__Romboutsia;__	0	0	0	0	0	0	0	62	84
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium	149	111	197	98	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;__	76	0	54	127	88	175	51	0	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__GCA-900066225;__	64	0	95	0	104	0	0	84	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Harryflintia;D_6__uncultured bacterium	0	0	0	0	0	0	0	30	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	258	141	349	112	119	391	0	129	155
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	227	254	153	0	320	0	0	265	432
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;D_6__uncultured bacterium	101	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium	0	0	0	270	0	58	51	440	164
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__unidentified	1602	1557	1495	1500	1279	920	524	1258	1403
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;__	436	440	421	340	213	176	800	266	354
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;Ambiguous_taxa	501	564	356	762	366	492	415	540	394
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;D_6__uncultured bacterium	387	58	461	124	290	213	335	405	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 6;__	91	104	64	190	562	242	118	235	218
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium	232	220	248	325	308	299	351	238	463
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;__	1161	1127	873	1270	1378	1155	1290	1131	1291
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium;D_6__uncultured bacterium	2409	2239	2033	1913	1367	1784	2656	2134	2415
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae NK4A214 group;D_6__uncultured bacterium	0	0	0	0	0	25	0	81	34
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-005;Ambiguous_taxa	0	95	0	164	116	212	35	180	114
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-009;Ambiguous_taxa	454	473	388	283	552	265	684	622	611
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-010;D_6__uncultured organism	77	53	70	79	59	134	59	54	112
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium	94	48	118	158	437	187	502	1052	104
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;__	0	0	0	0	0	70	0	0	60
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;D_6__uncultured bacterium	0	32	0	72	183	75	0	72	264
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;__	277	280	352	51	163	136	95	57	731
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcus 1;__	1370	1132	1457	263	1098	139	1583	2721	1531
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__[Eubacterium] coprostanoligenes group;__	401	231	489	14	315	34	134	85	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1	0	0	0	980	816	685	110	176	785
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__unidentified	120	139	147	108	144	110	421	134	140
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;__	37	22	42	21	0	24	653	394	406
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;__;__	1109	1025	1157	441	580	499	1166	1030	902
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis	556	613	516	135	106	0	0	0	20
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa	0	23	37	200	63	530	55	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Turicibacter;__	471	277	460	329	133	421	191	149	237
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	0	0	0	39	31	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured;D_6__uncultured bacterium	0	55	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Anaeroplasmatales;D_4__Anaeroplasmataceae;D_5__Anaeroplasma;Ambiguous_taxa	275	338	0	562	1369	786	922	665	625
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;Ambiguous_taxa;Ambiguous_taxa;Ambiguous_taxa	0	0	16	0	0	0	0	0	50
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;D_4__uncultured bacterium;D_5__uncultured bacterium;D_6__uncultured bacterium	138	137	0	100	147	87	44	87	66
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;__;__;__	245	479	91	42	203	0	417	216	279
D_0__Bacteria;D_1__Verrucomicrobia;D_2__Verrucomicrobiae;D_3__Verrucomicrobiales;D_4__Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium	0	20	0	2363	1475	7608	0	0	0

#Differentially abundant for PCB6

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
316.7182704	-11.65082862	1.236665352	-9.421165231	0	0	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa
153.3172368	-10.60410763	3.148390595	-3.368104215	0.0007568698067	0.005710926723	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium
41.03072715	-8.702464375	3.274032281	-2.658026442	0.007859972585	0.04077360779	Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium
319.3213166	-1.580215074	0.3616598924	-4.369340109	0.00001246225466	0.0001292958921	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
781.7386176	-0.9207800117	0.1196190574	-7.69760297	0	0	Ruminococcaceae;__;__
7200.677116	-0.3902585448	0.08636488756	-4.518717685	0.000006221528614	0.00007376955357	Muribaculaceae;__;__
275.8941433	0.6171854875	0.2015178394	3.062684124	0.002193614783	0.01517250225	Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium
754.2569069	1.264658563	0.4337143845	2.915878763	0.003546882969	0.02102794903	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
177.0232909	1.776599012	0.6062650277	2.930399958	0.003385259774	0.02102794903	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
214.5092189	2.099707756	0.5666020505	3.705789194	0.0002107335238	0.001749088248	Ruminococcaceae;D_5__Ruminiclostridium 6;__
149.9534028	3.917624073	1.51816477	2.580499923	0.009865737835	0.04816801414	Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa
38.92808467	8.824512079	1.427806771	6.180466614	0.0000000006391241199	0.000000008841216991	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
2019.466775	9.269818825	2.203252554	4.207333747	0.00002584013765	0.0002383034916	Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium
53.84095289	9.292598686	1.328101098	6.996906108	0	0	Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium
62.8067954	9.514101089	3.293079828	2.889119482	0.003863222531	0.02137649801	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
76.87108532	9.805534228	1.36829318	7.166252356	0	0	Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016
447.5479333	12.34718529	1.245794989	9.911089227	0	0	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

#Differentially abundant bacteria for PCB30

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
83.46976574	-9.948696447	1.426866799	-6.972407274	0	0.0000000001386455415	Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium
61.1174388	-9.499046883	1.511973717	-6.282547625	0.0000000003330691888	0.000000005928631561	Lachnospiraceae;D_5__A2;__
39.30425587	-8.862241275	2.96685731	-2.987080385	0.002816556532	0.01790525224	Lachnospiraceae;D_5__Acetatifactor;__
307.8175697	-6.935230581	1.27412215	-5.443144191	0.00000005234823872	0.0000006655704638	Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis
334.6713868	-2.313158666	0.3287417297	-7.036401093	0	0.0000000001386455415	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
308.0630698	-1.346206268	0.4204681762	-3.201684084	0.001366267468	0.009353677279	Erysipelotrichaceae;D_5__Turicibacter;__
8798.415146	-0.4334527046	0.1329022528	-3.261439858	0.001108479444	0.008968606407	Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium
532.8390926	0.7735398016	0.2396538735	3.227737529	0.001247734027	0.009254027366	Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium
965.8942038	1.446139973	0.3454244671	4.186559179	0.00002832151155	0.0002800682809	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
332.2258696	2.576372032	0.9118396441	2.825466132	0.004721187874	0.02801238138	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
246.2103261	3.623458987	0.5613278261	6.455156539	0.0000000001081070969	0.000000002405382905	Ruminococcaceae;D_5__uncultured;__
32.70775081	8.350701175	2.012224217	4.149985427	0.00003324964435	0.0002959218347	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
33.11545623	8.369454039	1.915893281	4.36843436	0.00001251404163	0.0001392187131	Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44
107.2867183	10.06452036	1.673272351	6.014872807	0.000000001800279971	0.0000000267041529	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
144.5866908	10.49616302	1.535432272	6.835966137	0	0.0000000002416474138	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

Table S5-a. Correlation between differentially abundant bacteria and metabolties

Biocompartment	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Serum	Serum	Serum	Serum	Serum	Serum
Taxa	3-Hydroxybutyric acid	Acetylcarnitine	Adenylosuccinate	Aminoisobutyric acid	Arginine	Dimethylglycine	Folinic acid	NADP	Shikimic acid	6-Methyl-DL-tryptophan	Asparagine	Proline	Serine	Urocanic acid	Levulinic acid
Lachnospiraceae UCG-001 Ambiguous	0.745869854	-0.1695158759	-0.1525642883	-0.5933055657	-0.2373222263	-0.5424508029	0.288176989	0.01695158759	-0.08475793795	0.1186611131	0.2034190511	0.2034190511	-0.1017095255	0.05085476277	-0.1017095255
Lachnospiraceae UCG-001 uncultured	0.3286335345	0.1825741858	0.1278019301	-0.2921186973	-0.4746928832	-0.3103761159	0.01825741858	0.2008316044	0.2373464416	0.1460593487	0.3834057903	0.4016632088	0.1460593487	0.3651483717	0.1643167673
Lachnospiraceae ASF356 uncultured	0.5659799761	-0.4929503018	-0.3103761159	-0.4016632088	0.1643167673	-0.3286335345	0.2738612788	-0.2921186973	-0.4016632088	0.2008316044	-0.07302967433	-0.1825741858	-0.2373464416	-0.09128709292	-0.07302967433
Clostridium scindens	0.6666666667	-0.65	-0.5833333333	-0.5166666667	0.5833333333	-0.5	0.7	-0.45	-0.4	-0.45	-0.2833333333	-0.4666666667	-0.5166666667	-0.65	-0.7833333333
Ruminococcaceae	0.7166666667	-0.6666666667	-0.1666666667	-0.55	0.05	-0.6	0.1666666667	-0.4	-0.1333333333	0	-0.1166666667	-0.1666666667	-0.4166666667	-0.15	-0.15
Muribaculaceae	0.6833333333	-0.6666666667	0.1	-0.3333333333	-0.03333333333	-0.3666666667	0.03333333333	-0.2333333333	0.05	0.1333333333	-0.08333333333	-0.05	-0.3166666667	-0.1833333333	-0.06666666667
Ruminiclostridium 9 uncultured	-0.6333333333	0.6666666667	0.2	0.4333333333	-0.6	0.45	-0.3833333333	0.3166666667	0.45	0.5833333333	0.4833333333	0.55	0.7833333333	0.6333333333	0.7
Roseburia uncultured	-0.65	0.55	0.55	0.6666666667	-0.7666666667	0.6333333333	-0.4333333333	0.35	0.7333333333	0.6166666667	0.6333333333	0.6	0.8666666667	0.7333333333	0.8333333333
Ruminococcaceae UCG-013 uncultured rumen bacterium	-0.6333333333	0.2833333333	0.7333333333	0.75	-0.35	0.65	-0.6333333333	0.3	0.6166666667	0.4	0.2833333333	0.3333333333	0.4333333333	0.55	0.65
Ruminiclostridium 6	-0.6666666667	0.6	0.6	0.8833333333	-0.1833333333	0.9	-0.1833333333	0.6	0.5166666667	0.2166666667	0.45	0.3833333333	0.6166666667	0.4	0.3
Erysipelatoclostridium Ambiguous	-0.745869854	0.3559833394	-0.08475793795	0.372934927	0.2542738139	0.3051285766	-0.2712254014	0	0.08475793795	-0.2373222263	-0.2373222263	-0.1186611131	0.08475793795	-0.1017095255	-0.05085476277
Family XIII UCG-001 uncultured	-0.8136762043	0.745869854	0.7119666788	0.8814825547	-0.2542738139	0.8136762043	-0.5424508029	0.661111916	0.6780635036	0.3220801642	0.4576928649	0.5424508029	0.6102571533	0.661111916	0.4915960401
Akkermansia muciniphila	-0.5477225575	0.3468909531	-0.1278019301	0.3103761159	0.4199206274	0.3103761159	0.03651483717	0.1095445115	-0.1095445115	-0.4564354646	-0.2556038602	-0.219089023	-0.03651483717	-0.2921186973	-0.3468909531
Enterorhabdus uncultured	-0.6534973784	0.3168472138	0.0990147543	0.6336944275	0.2475368857	0.6336944275	0.0990147543	0.1485221314	0.1188177052	-0.2277339349	0.04950737715	-0.1188177052	0.2574383612	-0.04950737715	-0.1089162297
Oscillibacter uncultured	-0.5744562647	0.6614950926	0.3568591947	0.3568591947	-0.3916747259	0.3916747259	-0.687606741	0.4613057883	0.1914854216	0.4874174367	0.130558242	0.4438980227	0.4177863743	0.5048252023	0.644087327
Clostridiales bacterium CIEAF 016	-0.7525121327	0.4554678698	-0.01980295086	0.5148767223	0.3663545909	0.5148767223	-0.07921180344	0.1683250823	-0.05940885258	-0.2871427875	-0.1485221314	-0.1584236069	0.1188177052	-0.06931032801	-0.1287191806
Clostridium sp. Culture-1	-0.8306277919	0.6272087408	0.2373222263	0.6780635036	-0.2034190511	0.7119666788	-0.2373222263	0.3220801642	0.2542738139	0.1695158759	0.2203706387	0.2034190511	0.5763539781	0.288176989	0.372934927
Anaerotruncus uncultured	0.5659799761	-0.8033264177	-0.8398412548	-0.8580986734	0.5659799761	-0.8580986734	0.4016632088	-0.8580986734	-0.8215838363	-0.5842373947	-0.7850689991	-0.8215838363	-0.8580986734	-0.8215838363	-0.6207522318
Lachnospiraceae A2	0.2872281323	-0.3307475463	-0.3829708431	-0.174077656	0.8964999282	-0.174077656	0.4526019055	-0.1479660076	-0.4351941399	-0.5135290851	-0.3568591947	-0.4526019055	-0.5570484991	-0.4961213195	-0.8007572174
Acetatifactor	0.593366104	-0.6390096504	-0.6390096504	-0.7074749701	0.3195048252	-0.7074749701	0.1825741858	-0.5477225575	-0.3195048252	-0.1597524126	-0.5249007843	-0.3195048252	-0.502079011	-0.7074749701	-0.4792572378
Dubosiella newyorkensis	0.661111916	-0.7628214416	-0.7797730292	-0.7967246168	0.4407412774	-0.7628214416	0.6950150912	-0.7628214416	-0.7119666788	-0.6780635036	-0.5763539781	-0.7628214416	-0.7119666788	-0.8645309671	-0.7289182664
Turicibacter	0.2333333333	-0.3166666667	-0.7666666667	-0.6166666667	0.7666666667	-0.6	0.2	-0.4666666667	-0.8333333333	-0.4833333333	-0.7	-0.6166666667	-0.7333333333	-0.5333333333	-0.5833333333
Muribaculaceae uncultured	-0.1	0.1166666667	-0.6333333333	-0.3333333333	0.65	-0.2666666667	0.2666666667	-0.1666666667	-0.7333333333	-0.65	-0.5833333333	-0.5166666667	-0.4833333333	-0.55	-0.6166666667
Lachnospiraceae GCA-900066575 uncultured	0.3666666667	0.01666666667	0.3333333333	-0.1833333333	-0.75	-0.2	-0.2833333333	0.1833333333	0.4833333333	0.6166666667	0.45	0.6	0.3333333333	0.4666666667	0.5333333333
Ruminococcaceae uncultured	0.1166666667	0.1833333333	0.4	-0.01666666667	-0.4666666667	-0.05	-0.5333333333	0.3166666667	0.35	0.65	0.3333333333	0.5666666667	0.2333333333	0.6333333333	0.5833333333
Clostridium sp. Clone-44	-0.06931032801	0.5049752469	0.5445811486	0.2277339349	-0.8218224607	0.2475368857	-0.4554678698	0.5544826241	0.6039900012	0.8218224607	0.6832018047	0.8416254115	0.6832018047	0.8218224607	0.782216559

Table S5-a. Correlation between differentially abundant bacteria and metabolties

Biocompartment	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Serum	Serum	Serum	Serum	Serum	Serum
Taxa	3-Hydroxybutyric acid	Acetylcarnitine	Adenylosuccinate	Aminoisobutyric acid	Arginine	Dimethylglycine	Folinic acid	NADP	Shikimic acid	6-Methyl-DL-tryptophan	Asparagine	Proline	Serine	Urocanic acid	Levulinic acid
Lachnospiraceae UCG-001 Ambiguous	0.189	0.894	0.894	0.394	0.894	0.394	0.894	0.965	0.932	0.897	0.897	0.897	0.897	0.897	0.897
Lachnospiraceae UCG-001 uncultured	0.821	0.821	0.836	0.821	0.821	0.821	0.963	0.821	0.821	0.708	0.668	0.668	0.708	0.668	0.708
Lachnospiraceae ASF356 uncultured	0.535	0.535	0.535	0.535	0.673	0.535	0.535	0.535	0.535	0.852	0.852	0.852	0.852	0.852	0.852
Clostridium scindens	0.194	0.194	0.194	0.228	0.194	0.228	0.194	0.259	0.291	0.276	0.463	0.276	0.276	0.2	0.103
Ruminococcaceae	0.265	0.265	0.836	0.299	0.912	0.29	0.836	0.524	0.836	1	0.931	0.931	0.931	0.931	0.931
Muribaculaceae	0.265	0.265	0.948	0.867	0.948	0.867	0.948	0.948	0.948	0.912	0.912	0.912	0.912	0.912	0.912
Ruminiclostridium 9 uncultured	0.29	0.29	0.613	0.375	0.29	0.375	0.402	0.461	0.375	0.159	0.194	0.159	0.103	0.152	0.13
Roseburia uncultured	0.137	0.171	0.171	0.137	0.137	0.137	0.281	0.359	0.137	0.097	0.097	0.097	0.025	0.062	0.025
Ruminococcaceae UCG-013 uncultured rumen bacterium	0.129	0.463	0.129	0.129	0.461	0.129	0.129	0.463	0.129	0.437	0.463	0.462	0.437	0.398	0.398
Ruminiclostridium 6	0.145	0.145	0.145	0.014	0.644	0.014	0.644	0.145	0.208	0.581	0.469	0.469	0.469	0.469	0.524
Erysipelatoclostridium Ambiguous	0.189	0.764	0.932	0.764	0.764	0.764	0.764	1	0.932	0.897	0.897	0.897	0.897	0.897	0.897
Family XIII UCG-001 uncultured	0.023	0.047	0.057	0.015	0.509	0.023	0.148	0.068	0.067	0.398	0.258	0.258	0.243	0.243	0.258
Akkermansia muciniphila	0.749	0.749	0.876	0.749	0.749	0.749	0.926	0.876	0.876	0.685	0.685	0.685	0.926	0.685	0.685
Enterorhabdus uncultured	0.201	0.8	0.8	0.201	0.8	0.201	0.8	0.8	0.8	0.899	0.899	0.899	0.899	0.899	0.899
Oscillibacter uncultured	0.317	0.235	0.389	0.389	0.389	0.389	0.235	0.389	0.622	0.316	0.738	0.316	0.316	0.316	0.316
Clostridiales bacterium CIEAF 016	0.174	0.49	0.96	0.468	0.598	0.468	0.96	0.96	0.96	0.859	0.859	0.859	0.859	0.859	0.859
Clostridium sp. Culture-1	0.05	0.159	0.6	0.134	0.6	0.134	0.6	0.6	0.6	0.663	0.663	0.663	0.626	0.663	0.663
Anaerotruncus uncultured	0.126	0.014	0.01	0.009	0.126	0.009	0.284	0.009	0.012	0.099	0.018	0.013	0.013	0.013	0.089
Lachnospiraceae A2	0.68	0.68	0.68	0.704	0.01	0.704	0.68	0.704	0.68	0.262	0.346	0.265	0.262	0.262	0.057
Acetatifactor	0.166	0.144	0.144	0.144	0.452	0.144	0.638	0.19	0.452	0.681	0.288	0.482	0.288	0.198	0.288
Dubosiella newyorkensis	0.059	0.03	0.03	0.03	0.235	0.03	0.048	0.03	0.047	0.054	0.104	0.047	0.047	0.016	0.047
Turicibacter	0.613	0.527	0.064	0.174	0.064	0.174	0.613	0.319	0.064	0.194	0.13	0.162	0.13	0.177	0.162
Muribaculaceae uncultured	0.81	0.81	0.228	0.74	0.228	0.74	0.74	0.81	0.228	0.194	0.194	0.194	0.194	0.194	0.194
Lachnospiraceae GCA-900066575 uncultured	0.724	0.982	0.724	0.724	0.229	0.724	0.724	0.724	0.724	0.276	0.276	0.276	0.385	0.276	0.276
Ruminococcaceae uncultured	0.982	0.965	0.738	0.982	0.738	0.982	0.738	0.738	0.738	0.181	0.462	0.181	0.552	0.181	0.181
Clostridium sp. Clone-44	0.859	0.298	0.291	0.625	0.059	0.625	0.327	0.291	0.291	0.013	0.042	0.013	0.042	0.013	0.019

	Phase-I Ces2c	Phase-I Cyp1a2	Phase-I Cyp2a5	Phase-I Cyp2b10	Phase-I Cyp2c29	Phase-I Cyp2c54	Phase-I Cyp2j9	Phase-I Cyp3a16	Phase-I Cyp3a41a	Phase-I Cyp17a1	Phase-I Cyp26a1	Phase-I Aldh1a7	Phase-I Ces1b	Phase-I Cyp1a1	Phase-I Cyp2c50	Phase-I Cyp2c55	Phase-I Cyp3a44	Phase-I Cyp4a14	Phase-I Nqo1
Lachnospiraceae UCG-001 Ambiguous	-0.1356127007	-0.06780635036	0.3051285766	-0.01695158759	0	-0.03390317518	0.6272087408	-0.3898865146	-0.5254992153	-0.2712254014	-0.5424508029	0.1525642883	0	0.03390317518	-0.1186611131	0.4576928649	-0.288176989	0.050854762	-0.05085476277
Lachnospiraceae UCG-001 uncultured	0.2921186973	0.4016632088	0.6937819062	0.3834057903	0.4016632088	0.4016632088	0.3468909531	-0.3651483717	-0.1460593487	0.219089023	-0.5477225575	0.4564354646	0.3468909531	0.4016632088	0.3103761159	0.6390096504	-0.1460593487	-0.2738612788	0.3834057903
Lachnospiraceae ASF356 uncultured	-0.4199206274	-0.5477225575	-0.6024948133	-0.3468909531	-0.438178046	-0.4929503018	0.4564354646	0.219089023	-0.3468909531	-0.6390096504	-0.09128709292	-0.4199206274	-0.3651483717	-0.3834057903	-0.5112077203	-0.1278019301	0.1278019301	0.1825741858	-0.4016632088
Clostridium scindens	-0.6666666667	-0.55	-0.3	-0.85	-0.6666666667	-0.7333333333	0.6833333333	0.3166666667	-0.2	-0.7833333333	-0.3666666667	-0.4666666667	-0.7666666667	-0.7333333333	-0.85	-0.4833333333	0.2666666667	0.6333333333	-0.75
Ruminococcaceae	-0.3666666667	-0.4833333333	-0.2833333333	-0.4333333333	-0.4	-0.4833333333	0.5166666667	0.4	0.01666666667	-0.6	-0.1333333333	-0.08333333333	-0.3666666667	-0.35	-0.5	-0.06666666667	0.3833333333	0.06666666667	-0.45
Muribaculaceae	-0.3333333333	-0.5666666667	-0.3833333333	-0.4833333333	-0.3833333333	-0.5166666667	0.1666666667	0.3333333333	0.03333333333	-0.6333333333	0.1	-0.01666666667	-0.2833333333	-0.2666666667	-0.4666666667	-0.03333333333	0.1666666667	0.03333333333	-0.5333333333
Ruminiclostridium 9 uncultured	0.7166666667	0.8166666667	0.5666666667	0.7833333333	0.6833333333	0.8333333333	-0.1333333333	-0.1666666667	0.1	0.7	-0.15	0.06666666667	0.7	0.65	0.75	0.3333333333	-0.1666666667	-0.2333333333	0.85
Roseburia uncultured	0.9333333333	0.8666666667	0.5833333333	0.7833333333	0.7333333333	0.8833333333	-0.4333333333	0.1166666667	0.45	0.6833333333	-0.1333333333	0.15	0.7333333333	0.75	0.8166666667	0.35	0.08333333333	-0.4333333333	0.9
Ruminococcaceae UCG-013 uncultured	0.5833333333	0.3666666667	-0.03333333333	0.4166666667	0.45	0.3666666667	-0.8333333333	0.45	0.8166666667	0.45	0.4166666667	0.3166666667	0.4833333333	0.5	0.45	0.1333333333	0.3833333333	-0.6333333333	0.4
Ruminiclostridium 6	0.5833333333	0.5666666667	0.2333333333	0.4	0.5333333333	0.4666666667	-0.8166666667	-0.03333333333	0.4	0.5	0.01666666667	0.2	0.45	0.5166666667	0.45	0.2	-0.06666666667	-0.35	0.45
Erysipelatoclostridium Ambiguous	0.1017095255	0.288176989	0.1017095255	0.08475793795	0.1356127007	0.1695158759	-0.288176989	0.1356127007	0.4068381022	0.4576928649	0.3390317518	0	0.08475793795	0.01695158759	0.1864674635	-0.3559833394	0.1356127007	0.08475793795	0.1356127007
Family XIII UCG-001 uncultured	0.6780635036	0.7289182664	0.3390317518	0.5933055657	0.7628214416	0.5763539781	-0.8306277919	0.08475793795	0.7289182664	0.745869854	0.1356127007	0.5424508029	0.6780635036	0.7119666788	0.5763539781	0.372934927	0.1525642883	-0.661111916	0.5763539781
Akkermansia muciniphila	-0.05477225575	0.1460593487	0.07302967433	-0.05477225575	0.01825741858	0.03651483717	-0.3103761159	-0.1643167673	0.09128709292	0.3103761159	0.2008316044	-0.01825741858	-0.07302967433	-0.09128709292	0.05477225575	-0.3103761159	-0.1278019301	0.2008316044	-0.01825741858
Enterorhabdus uncultured	0.2376354103	0.3069457383	0.01980295086	0.02970442629	0.1089162297	0.1584236069	-0.4851722961	0.207930984	0.3663545909	0.277241312	0.03960590172	-0.1980295086	-0.01980295086	0.01980295086	0.1188177052	-0.3366501646	0.1881280332	0.06931032801	0.1584236069
Oscillibacter uncultured	0.3829708431	0.3568591947	0.1218543592	0.7137183894	0.5483446163	0.5396407335	-0.5222329679	-0.5222329679	-0.09574271078	0.6614950926	0.4700096711	0.3916747259	0.6963106238	0.600567913	0.6701989754	0.4438980227	-0.5309368507	-0.4438980227	0.5396407335
Clostridiales bacterium CIEAF 016	0.0990147543	0.2475368857	-0.03960590172	0.1089162297	0.1287191806	0.138620656	-0.4653693452	-0.00990147543	0.2475368857	0.4158619681	0.2574383612	-0.05940885258	0.03960590172	0.01980295086	0.1584236069	-0.2970442629	0.02970442629	0.02970442629	0.138620656
Clostridium sp. Culture-1	0.5424508029	0.5763539781	0.2542738139	0.5254992153	0.4407412774	0.5933055657	-0.5594023905	-0.1525642883	0.1525642883	0.6272087408	0.1356127007	-0.05085476277	0.4237896898	0.4068381022	0.5933055657	0	-0.1864674635	-0.1186611131	0.5933055657
Anaerotruncus uncultured	-0.8398412548	-0.8580986734	-0.5659799761	-0.7302967433	-0.9128709292	-0.7485541619	0.7485541619	0.1825741858	-0.438178046	-0.6937819062	0.1825741858	-0.5659799761	-0.8398412548	-0.9128709292	-0.6937819062	-0.6937819062	0.1460593487	0.6755244876	-0.7302967433
Lachnospiraceae A2	-0.7050145066	-0.5396407335	-0.5657523819	-0.7659416862	-0.5135290851	-0.8094611002	0.2175970699	0.3220436635	0.07833494518	-0.5570484991	-0.04351941399	-0.1914854216	-0.6527912098	-0.6266795614	-0.8529805142	-0.4351941399	0.3568591947	0.3046358979	-0.7920533346
Acetatifactor	-0.7302967433	-0.6390096504	-0.2738612788	-0.7302967433	-0.6390096504	-0.6390096504	0.7302967433	0.06846531969	-0.3879701449	-0.6390096504	0.1369306394	-0.3651483717	-0.5249007843	-0.6390096504	-0.6390096504	-0.4564354646	-0.1597524126	0.7302967433	-0.7302967433
Dubosiella newyorkensis	-0.6780635036	-0.6780635036	-0.2542738139	-0.7119666788	-0.8475793795	-0.5933055657	0.7628214416	0.03390317518	-0.5594023905	-0.6950150912	-0.1695158759	-0.6102571533	-0.8475793795	-0.8475793795	-0.6102571533	-0.6102571533	0.01695158759	0.7797730292	-0.6102571533
Turicibacter	-0.8166666667	-0.65	-0.6	-0.5	-0.6	-0.6666666667	0.55	0	-0.35	-0.3833333333	0.25	-0.2833333333	-0.5833333333	-0.6833333333	-0.6166666667	-0.4666666667	0.08333333333	0.4	-0.6166666667
Muribaculaceae uncultured	-0.5333333333	-0.2833333333	-0.1666666667	-0.2166666667	-0.3333333333	-0.2666666667	0.2333333333	-0.5	-0.5333333333	0.01666666667	0.1666666667	-0.1666666667	-0.3666666667	-0.4333333333	-0.2166666667	-0.3333333333	-0.3666666667	0.4333333333	-0.2833333333
Lachnospiraceae GCA-900066575 uncultured	0.35	0.2666666667	0.4666666667	0.3666666667	0.3833333333	0.3666666667	0.2	-0.1833333333	-0.08333333333	0.08333333333	-0.25	0.3666666667	0.4833333333	0.4833333333	0.3333333333	0.6333333333	-0.2166666667	-0.3	0.3333333333
Ruminococcaceae uncultured	0.2333333333	0.1666666667	0.08333333333	0.4166666667	0.4333333333	0.2166666667	-0.05	-0.06666666667	0.1333333333	0.1833333333	0.06666666667	0.5166666667	0.5333333333	0.5	0.25	0.6333333333	-0.03333333333	-0.5833333333	0.25
Clostridium sp. Clone-44	0.6435959029	0.6138914766	0.5445811486	0.7525121327	0.7525121327	0.6832018047	-0.1485221314	-0.34655164	-0.00990147543	0.4653693452	-0.2277339349	0.4950737715	0.8218224607	0.8218224607	0.6435959029	0.8416254115	-0.3267486892	-0.5643840995	0.6832018047

Phase-I	Phase-I	Phase-I	Phase-I	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter
Por	Cyp26b1	Sdr9c7	Cyb5a	Gclc	Gstm2	Gstm3	Sult2a1	Sult2a2	Sult3a1	Gsta2	Gsta4	Gstm1	Gstm4	Gstp1	Atp2a2	Atp2b2	Atp6v0d2	Slc15a2	Slc16a1	Slc25a30	Slc30a10
0.03390317518	-0.08475793795	-0.05085476277	0.1356127007	0.5424508029	-0.1017095255	0.3051285766	-0.1017095255	-0.1525642883	-0.6441603284	0.4068381022	0.4068381022	0.03390317518	0.1525642883	0.4576928649	0.4237896898	0.1525642883	-0.2373222263	0.7967246168	0.06780635036	0.06780635036	0.01695158759
0.4199206274	-0.3103761159	-0.3834057903	0.5477225575	0.07302967433	0.2921186973	0.5477225575	0.3103761159	0.3103761159	-0.1278019301	0.6207522318	0.6207522318	0.3651483717	0.5294651389	0.4564354646	-0.01825741858	-0.2556038602	0.1825741858	0.6207522318	-0.4016632088	-0.03651483717	-0.3834057903
-0.4746928832	-0.01825741858	0.3651483717	-0.5477225575	0.7302967433	-0.5294651389	-0.09128709292	-0.5659799761	-0.6755244876	-0.7120393248	-0.09128709292	-0.09128709292	-0.2738612788	-0.5294651389	0.6024948133	0.657267069	0.4929503018	-0.6755244876	0.4564354646	0.5477225575	0.5477225575	0.4746928832
-0.65	0.45	0.65	-0.6166666667	0.7833333333	-0.7333333333	-0.6	-0.2666666667	-0.3333333333	-0.5333333333	-0.4333333333	-0.4333333333	-0.7333333333	-0.5166666667	-0.15	0.5166666667	0.6166666667	-0.5	0.4833333333	0.55	0.3833333333	0.5833333333
-0.4	-0.1333333333	0.45	-0.45	0.6666666667	-0.4	-0.2	-0.3166666667	-0.4333333333	-0.4166666667	-0.08333333333	-0.08333333333	-0.45	-0.5333333333	0.4333333333	0.5166666667	0.3833333333	-0.3166666667	0.5666666667	0.4833333333	0.8166666667	0.55
-0.4	-0.15	0.4166666667	-0.5666666667	0.5166666667	-0.3	-0.3166666667	-0.4833333333	-0.5833333333	-0.4166666667	-0.1666666667	-0.1666666667	-0.4833333333	-0.6833333333	0.08333333333	0.35	0.2833333333	-0.1166666667	0.2333333333	0.5666666667	0.6666666667	0.6166666667
0.8	-0.25	-0.7	0.6833333333	-0.5666666667	0.45	0.5	0.7166666667	0.7333333333	0.2833333333	0.3833333333	0.3833333333	0.7333333333	0.75	0.4833333333	-0.5	-0.7333333333	0.2333333333	0.15	-0.8166666667	-0.35	-0.8666666667
0.85	-0.4166666667	-0.7	0.5666666667	-0.75	0.5	0.4	0.7166666667	0.7333333333	0.4833333333	0.35	0.35	0.6833333333	0.5833333333	0.3166666667	-0.7666666667	-0.9333333333	0.4833333333	-0.05	-0.8666666667	-0.1666666667	-0.8666666667
0.3	-0.5833333333	-0.35	0.1	-0.6333333333	0.5	0.15	0.1333333333	0.1666666667	0.6833333333	0.1166666667	0.1166666667	0.35	-0.03333333333	0.03333333333	-0.6833333333	-0.5666666667	0.6333333333	-0.6333333333	-0.3666666667	0.2666666667	-0.25
0.3666666667	-0.2333333333	-0.55	0.2666666667	-0.6666666667	0.4666666667	0.2	0.1833333333	0.3	0.4666666667	0.2	0.2	0.4833333333	0.3166666667	-0.3833333333	-0.8166666667	-0.5833333333	0.6	-0.6833333333	-0.5666666667	-0.4666666667	-0.55
0.1356127007	0.1864674635	-0.06780635036	0.2203706387	-0.5085476277	0.2203706387	-0.1864674635	0.4576928649	0.5254992153	0.6780635036	-0.2712254014	-0.2712254014	0.05085476277	0.2373222263	-0.4068381022	-0.4068381022	-0.1864674635	0.3051285766	-0.4746444525	-0.288176989	-0.2542738139	-0.2034190511
0.4576928649	-0.5933055657	-0.6950150912	0.4915960401	-0.7119666788	0.7628214416	0.4407412774	0.3220801642	0.4407412774	0.745869854	0.4237896898	0.4237896898	0.661111916	0.4407412774	-0.03390317518	-0.8984341423	-0.6780635036	0.8475793795	-0.6272087408	-0.7289182664	-0.1525642883	-0.5933055657
-0.01825741858	0.3834057903	-0.01825741858	0.1460593487	-0.4016632088	0.1278019301	-0.2008316044	0.2008316044	0.3103761159	0.4564354646	-0.2556038602	-0.2556038602	-0.01825741858	0.219089023	-0.7302967433	-0.3103761159	0	0.219089023	-0.5842373947	-0.1460593487	-0.5842373947	-0.1278019301
0.06931032801	0.207930984	-0.1089162297	0.00990147543	-0.4950737715	0.04950737715	-0.2178324595	0.2475368857	0.3366501646	0.4950737715	-0.2475368857	-0.2475368857	0.06931032801	0.1188177052	-0.5544826241	-0.5445811486	-0.2376354103	0.2376354103	-0.6039900012	-0.3069457383	-0.3663545909	-0.2871427875
0.4787135539	-0.3307475463	-0.5831601475	0.5483446163	-0.5483446163	0.6614950926	0.5831601475	0.07833494518	0.1392621248	0.2698203667	0.3916747259	0.3916747259	0.6789028582	0.4700096711	0.1914854216	-0.2698203667	-0.3829708431	0.3133397807	-0.4177863743	-0.3568591947	-0.4787135539	-0.4264902571
0.02970442629	0.207930984	-0.1287191806	0.1485221314	-0.4950737715	0.1881280332	-0.07921180344	0.1881280332	0.2970442629	0.5544826241	-0.1881280332	-0.1881280332	0.1485221314	0.2178324595	-0.4950737715	-0.4059604926	-0.0990147543	0.2178324595	-0.6832018047	-0.2475368857	-0.4653693452	-0.2277339349
0.5085476277	0.05085476277	-0.4746444525	0.4068381022	-0.7628214416	0.3559833394	0.1695158759	0.4407412774	0.5254992153	0.4915960401	0.03390317518	0.03390317518	0.4915960401	0.4915960401	-0.2542738139	-0.6102571533	-0.5424508029	0.288176989	-0.5254992153	-0.5763539781	-0.6441603284	-0.6441603284
-0.657267069	0.657267069	0.9128709292	-0.6024948133	0.6390096504	-0.7850689991	-0.6390096504	-0.3103761159	-0.4199206274	-0.4016632088	-0.6755244876	-0.6755244876	-0.8398412548	-0.6024948133	-0.09128709292	0.9128709292	0.8398412548	-0.8215838363	0.3651483717	0.8580986734	0.3468909531	0.8033264177
-0.8442766314	0.1914854216	0.5135290851	-0.5918640302	0.6527912098	-0.4264902571	-0.4090824915	-0.5483446163	-0.5309368507	-0.2175970699	-0.3046358979	-0.3046358979	-0.5396407335	-0.5483446163	-0.2175970699	0.3394514291	0.7050145066	-0.2350048355	-0.08703882798	0.5396407335	0.3829708431	0.6527912098
-0.4336136914	0.502079011	0.6390096504	-0.4564354646	0.6390096504	-0.5477225575	-0.6390096504	-0.1141088661	-0.2282177323	-0.5249007843	-0.5477225575	-0.5477225575	-0.7302967433	-0.4564354646	-0.1369306394	0.6390096504	0.5249007843	-0.4564354646	0.5249007843	0.6390096504	0.2738612788	0.6390096504
-0.4915960401	0.8136762043	0.8136762043	-0.5085476277	0.5424508029	-0.8306277919	-0.661111916	-0.1525642883	-0.2373222263	-0.4746444525	-0.6272087408	-0.6272087408	-0.8136762043	-0.4237896898	-0.3559833394	0.745869854	0.6780635036	-0.7628214416	0.4407412774	0.6780635036	0.03390317518	0.5763539781
-0.6833333333	0.3666666667	0.5833333333	-0.35	0.6166666667	-0.4333333333	-0.2333333333	-0.4166666667	-0.45	-0.2666666667	-0.3333333333	-0.3333333333	-0.45	-0.35	0.15	0.7833333333	0.85	-0.6333333333	0.15	0.65	0.25	0.65
-0.3166666667	0.6166666667	0.2666666667	0.05	0.1	-0.1666666667	-0.1166666667	-0.1333333333	-0.06666666667	-0.03333333333	-0.25	-0.25	-0.1833333333	0.1333333333	-0.4333333333	0.4	0.55	-0.3666666667	-0.2	0.2833333333	-0.5833333333	0.2
0.4666666667	-0.4666666667	-0.3666666667	0.3333333333	0.06666666667	0.2833333333	0.4166666667	0.2	0.1333333333	-0.2666666667	0.5	0.5	0.3166666667	0.25	0.5833333333	-0.03333333333	-0.4	0.2	0.6	-0.2666666667	0.2	-0.2666666667
0.2166666667	-0.75	-0.4	0.2666666667	0.1166666667	0.45	0.6	-0.1166666667	-0.15	-0.1	0.6	0.6	0.45	0.1166666667	0.8166666667	0	-0.2166666667	0.25	0.2666666667	-0.1666666667	0.4333333333	-0.1
0.6832018047	-0.6733003292	-0.7723150835	0.6138914766	-0.2277339349	0.6039900012	0.7723150835	0.2574383612	0.2574383612	-0.07921180344	0.7723150835	0.7723150835	0.7723150835	0.5643840995	0.7030047555	-0.3366501646	-0.6435959029	0.3861575418	0.3168472138	-0.6138914766	-0.07921180344	-0.6336944275

Table S5D. Bacteria-gene significance

	Phase-I Ces2c	Phase-I Cyp1a2	Phase-I Cyp2a5	Phase-I Cyp2b10	Phase-I Cyp2c29	Phase-I Cyp2c54	Phase-I Cyp2j9	Phase-I Cyp3a16	Phase-I Cyp3a41a	Phase-I Cyp17a1	Phase-I Cyp26a1	Phase-I Aldh1a7	Phase-I Ces1b	Phase-I Cyp1a1	Phase-I Cyp2c50	Phase-I Cyp2c55	Phase-I Cyp3a44	Phase-I Cyp4a14	Phase-I Nqo1	Phase-I Por	Phase-I Cyp26b1	Phase-I Sdr9c7	Phase-I Cyb5a	Phase-II Gclc	Phase-II Gstm2	Phase-II Gstm3	Phase-II Sult2a1	Phase-II Sult2a2	Phase-II Sult3a1	Phase-II Gsta2	Phase-II Gsta4	Phase-II Gstm1
Lachnospiraceae UCG-001 Ambiguous	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.61	0.874	0.778	0.874	0.874	0.61	0.61	0.61	0.931
Lachnospiraceae UCG-001 uncultured	0.539	0.518	0.518	0.518	0.518	0.518	0.518	0.518	0.708	0.626	0.518	0.518	0.518	0.518	0.532	0.518	0.708	0.547	0.518	0.518	0.532	0.518	0.518	0.852	0.545	0.392	0.545	0.545	0.817	0.392	0.392	0.545
Lachnospiraceae ASF356 uncultured	0.488	0.488	0.488	0.488	0.488	0.488	0.488	0.73	0.488	0.488	0.852	0.488	0.488	0.488	0.488	0.814	0.814	0.773	0.488	0.488	0.963	0.488	0.488	0.168	0.224	0.815	0.224	0.168	0.168	0.815	0.815	0.654
Clostridium scindens	0.128	0.204	0.478	0.07	0.128	0.102	0.128	0.472	0.613	0.102	0.407	0.288	0.102	0.102	0.07	0.279	0.516	0.135	0.102	0.128	0.294	0.128	0.141	0.114	0.114	0.266	0.543	0.471	0.297	0.344	0.344	0.114
Ruminococcaceae	0.515	0.515	0.626	0.515	0.515	0.515	0.515	0.515	0.982	0.515	0.9	0.92	0.515	0.515	0.515	0.92	0.515	0.92	0.515	0.515	0.9	0.515	0.515	0.458	0.458	0.75	0.564	0.458	0.458	0.843	0.843	0.458
Muribaculaceae	0.682	0.653	0.653	0.653	0.653	0.653	0.905	0.682	0.982	0.653	0.981	0.982	0.756	0.756	0.653	0.982	0.905	0.982	0.653	0.653	0.905	0.653	0.653	0.426	0.6	0.6	0.426	0.426	0.494	0.746	0.746	0.426
Ruminiclostridium 9 uncultured	0.096	0.079	0.198	0.079	0.096	0.079	0.814	0.814	0.847	0.096	0.814	0.88	0.096	0.118	0.096	0.591	0.814	0.746	0.079	0.079	0.746	0.096	0.096	0.265	0.316	0.305	0.101	0.101	0.463	0.344	0.344	0.101
Roseburia uncultured	0.017	0.026	0.191	0.057	0.072	0.024	0.338	0.811	0.338	0.096	0.811	0.811	0.072	0.072	0.041	0.434	0.843	0.338	0.023	0.028	0.344	0.09	0.198	0.135	0.305	0.394	0.135	0.135	0.305	0.394	0.394	0.138
Ruminococcaceae UCG-013 uncultured	0.455	0.455	0.948	0.455	0.455	0.455	0.124	0.455	0.124	0.455	0.455	0.496	0.455	0.455	0.455	0.814	0.455	0.455	0.455	0.502	0.455	0.458	0.847	0.418	0.651	0.948	0.948	0.948	0.418	0.948	0.948	0.948
Ruminiclostridium 6	0.481	0.481	0.705	0.515	0.481	0.481	0.248	0.982	0.515	0.481	0.982	0.705	0.481	0.481	0.481	0.705	0.964	0.55	0.481	0.55	0.705	0.481	0.705	0.584	0.584	0.644	0.644	0.644	0.584	0.644	0.644	0.584
Erysipelatoclostridium Ambiguous	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	1	0.945	1	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.592	0.694	0.694	0.592	0.592	0.492	0.694	0.694	0.897
Family XIII UCG-001 uncultured	0.114	0.114	0.428	0.16	0.114	0.16	0.114	0.828	0.114	0.114	0.761	0.189	0.114	0.114	0.16	0.391	0.761	0.121	0.16	0.275	0.16	0.114	0.242	0.115	0.115	0.312	0.438	0.312	0.115	0.312	0.312	0.144
Akkermansia muciniphila	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.739	0.817	0.739	0.739	0.739	0.739	0.739	0.739	0.963
Enterorhabdus uncultured	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.643	0.899	0.788	0.788	0.788	0.643	0.788	0.788	0.899
Oscillibacter uncultured	0.374	0.398	0.789	0.264	0.264	0.264	0.264	0.264	0.806	0.264	0.309	0.374	0.264	0.264	0.264	0.313	0.264	0.313	0.264	0.309	0.421	0.264	0.264	0.347	0.288	0.347	0.841	0.793	0.664	0.467	0.467	0.288
Clostridiales bacterium CIEAF 016	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.643	0.767	0.839	0.767	0.767	0.643	0.767	0.767	0.773
Clostridium sp. Culture-1	0.414	0.414	0.781	0.414	0.455	0.414	0.414	0.875	0.875	0.414	0.875	0.937	0.455	0.455	0.414	1	0.875	0.875	0.414	0.414	0.937	0.452	0.455	0.185	0.545	0.81	0.431	0.394	0.394	0.931	0.931	0.394
Anaerotruncus uncultured	0.018	0.018	0.136	0.059	0.005	0.058	0.058	0.667	0.274	0.068	0.667	0.136	0.018	0.005	0.068	0.068	0.708	0.075	0.059	0.078	0.078	0.005	0.116	0.117	0.067	0.117	0.458	0.347	0.347	0.117	0.117	0.051
Lachnospiraceae A2	0.13	0.256	0.249	0.074	0.258	0.063	0.681	0.539	0.879	0.249	0.911	0.681	0.186	0.204	0.048	0.371	0.497	0.544	0.063	0.048	0.681	0.258	0.238	0.311	0.431	0.431	0.311	0.311	0.574	0.52	0.52	0.311
Acetatifactor	0.117	0.123	0.547	0.117	0.123	0.123	0.117	0.861	0.386	0.123	0.758	0.404	0.26	0.123	0.123	0.312	0.746	0.117	0.117	0.33	0.277	0.123	0.312	0.231	0.231	0.231	0.77	0.678	0.231	0.231	0.231	0.231
Dubosiella newyorkensis	0.093	0.093	0.585	0.09	0.03	0.132	0.055	0.965	0.159	0.093	0.726	0.124	0.03	0.03	0.124	0.124	0.965	0.051	0.124	0.217	0.035	0.035	0.207	0.241	0.042	0.155	0.695	0.593	0.309	0.155	0.155	0.042
Turicibacter	0.226	0.226	0.226	0.314	0.226	0.226	0.254	1	0.434	0.434	0.57	0.532	0.226	0.226	0.226	0.349	0.882	0.434	0.226	0.226	0.434	0.226	0.434	0.53	0.53	0.607	0.53	0.53	0.603	0.53	0.53	0.53
Muribaculaceae uncultured	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.982	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.953	0.948	0.948	0.948	0.948	0.948	0.948	0.948	0.948	0.948
Lachnospiraceae GCA-900066575 uncultured	0.591	0.665	0.591	0.591	0.591	0.591	0.705	0.705	0.843	0.843	0.665	0.591	0.591	0.591	0.591	0.591	0.703	0.628	0.591	0.591	0.591	0.591	0.591	0.88	0.716	0.716	0.75	0.818	0.716	0.651	0.651	0.716
Ruminococcaceae uncultured	0.891	0.917	0.948	0.744	0.744	0.891	0.948	0.948	0.948	0.917	0.948	0.681	0.681	0.681	0.891	0.681	0.948	0.681	0.891	0.891	0.586	0.744	0.891	0.81	0.421	0.266	0.81	0.81	0.81	0.266	0.266	0.421
Clostridium sp. Clone-44	0.118	0.129	0.186	0.074	0.074	0.108	0.735	0.437	0.98	0.264	0.609	0.237	0.05	0.05	0.118	0.05	0.449	0.174	0.108	0.108	0.108	0.074	0.129	0.611	0.156	0.04	0.611	0.611	0.839	0.04	0.04	0.04

Table S5D. Bacteria-gene significance

Phase-II Gstm4	Phase-II Gstp1	Transporter Atp2a2	Transporter Atp2b2	Transporter Atp6v0d2	Transporter Slc15a2	Transporter Slc16a1	Transporter Slc25a30	Transporter Slc30a10	Transporter Abcc4	Transporter Abcg8	Transporter Slc10a2	Transporter Slc17a2	Transporter Slc3a1	Transporter Slc46a3	Transporter Slc7a2	Transporter Slco1a1	NR, immune response and oxidative stress, epi Bcl6	NR, immune response and oxidative stress, epi Cldn1
0.874	0.61	0.869	0.869	0.869	0.152	0.924	0.924	0.965	0.869	0.869	0.869	0.869	0.869	0.869	0.869	0.869	0.666	0.405
0.392	0.477	0.963	0.845	0.957	0.727	0.727	0.963	0.727	0.727	0.727	0.727	0.963	0.963	0.963	0.727	0.727	0.248	0.815
0.224	0.224	0.361	0.361	0.361	0.361	0.361	0.361	0.361	0.577	0.963	0.557	0.361	0.577	0.361	0.541	0.557	0.555	0.473
0.297	0.708	0.264	0.257	0.264	0.264	0.264	0.391	0.264	0.216	0.903	0.601	0.216	0.221	0.264	0.216	0.912	0.546	0.482
0.458	0.458	0.484	0.538	0.559	0.484	0.484	0.162	0.484	0.538	1	0.637	0.538	0.442	0.579	0.538	0.759	1	0.484
0.426	0.843	0.642	0.673	0.776	0.69	0.603	0.603	0.603	0.642	0.776	0.642	0.743	0.642	0.642	0.642	0.673	0.982	0.77
0.101	0.305	0.296	0.13	0.591	0.708	0.081	0.448	0.068	0.13	0.13	0.504	0.345	0.296	0.397	0.147	0.163	0.415	0.268
0.238	0.41	0.08	0.011	0.242	0.912	0.023	0.726	0.023	0.181	0.108	0.534	0.108	0.181	0.108	0.18	0.18	0.295	0.062
0.948	0.948	0.257	0.301	0.257	0.257	0.721	0.781	0.781	0.817	0.805	0.805	0.207	0.722	0.257	0.831	0.912	0.948	0.156
0.644	0.644	0.129	0.249	0.249	0.249	0.249	0.354	0.249	0.69	0.69	0.982	0.249	0.129	0.375	0.69	0.631	0.904	0.36
0.694	0.61	0.946	0.946	0.946	0.946	0.946	0.946	0.946	0.965	0.965	0.946	0.946	0.965	0.946	0.965	0.965	0.922	0.922
0.312	0.931	0.013	0.134	0.02	0.177	0.097	0.695	0.196	0.434	0.409	0.695	0.013	0.244	0.196	0.459	0.353	0.599	0.078
0.739	0.28	1	1	1	0.561	1	0.561	1	1	1	0.561	1	1	1	1	1	0.858	0.858
0.899	0.643	0.767	0.767	0.767	0.767	0.767	0.767	0.767	0.767	0.98	0.767	0.767	0.767	0.767	0.767	0.857	0.897	0.78
0.444	0.76	0.603	0.519	0.561	0.519	0.519	0.519	0.519	0.241	0.977	0.519	0.501	0.241	0.812	0.241	0.982	0.929	0.703
0.767	0.643	0.914	0.96	0.914	0.637	0.914	0.914	0.914	0.96	0.96	0.914	0.914	0.914	0.914	0.96	0.96	0.769	0.769
0.394	0.7	0.304	0.313	0.565	0.313	0.313	0.304	0.304	0.473	0.663	0.663	0.392	0.304	0.392	0.473	0.663	0.944	0.224
0.135	0.815	0.008	0.014	0.017	0.358	0.012	0.36	0.02	0.173	0.168	0.25	0.008	0.012	0.25	0.164	0.12	0.224	0.219
0.311	0.574	0.557	0.186	0.626	0.824	0.334	0.515	0.212	0.186	0.626	0.619	0.415	0.334	0.415	0.143	0.632	0.321	0.457
0.298	0.77	0.16	0.275	0.361	0.275	0.16	0.595	0.16	0.548	0.923	0.954	0.16	0.16	0.16	0.548	0.889	0.556	0.461
0.352	0.424	0.105	0.134	0.105	0.271	0.134	0.931	0.174	0.174	0.219	0.174	0.008	0.153	0.346	0.244	0.269	0.679	0.175
0.53	0.708	0.129	0.091	0.163	0.708	0.163	0.558	0.163	0.504	0.341	0.504	0.163	0.163	0.291	0.291	0.291	0.214	0.492
0.948	0.948	0.63	0.498	0.63	0.767	0.694	0.498	0.767	0.843	0.498	0.498	0.581	0.817	0.694	0.831	0.63	0.926	0.926
0.716	0.651	0.948	0.624	0.767	0.581	0.767	0.767	0.767	0.581	0.581	0.467	0.767	0.895	0.948	0.581	0.624	0.482	0.978
0.81	0.118	1	0.871	0.871	0.871	0.924	0.781	0.977	0.781	0.781	0.207	0.781	0.977	0.977	0.781	0.871	0.982	0.982
0.178	0.076	0.469	0.167	0.415	0.469	0.169	0.839	0.167	0.074	0.167	0.074	0.182	0.182	0.774	0.074	0.182	0.212	0.651

Table S5D. Bacteria-gene significance

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Egr1	Lcn2	Nlrp12	Socs2	Cebpb	Hmox1	Icam1
0.666	0.789	0.809	0.679	0.076	0.076	0.405
0.595	0.595	0.595	0.595	0.317	0.248	0.595
0.963	0.473	0.963	0.473	0.473	0.555	0.473
0.88	0.787	0.88	0.546	0.482	0.393	0.045
0.937	0.937	0.511	0.788	0.484	0.484	0.484
0.953	0.822	0.77	0.929	0.822	0.904	0.82
0.546	0.81	0.546	0.294	0.715	0.81	0.296
0.982	0.446	0.96	0.327	0.327	0.456	0.295
0.554	0.873	0.728	0.873	0.156	0.156	0.156
0.868	0.904	0.912	0.912	0.36	0.36	0.36
0.944	0.922	0.922	0.922	0.922	0.922	0.922
0.599	0.599	0.599	0.599	0.391	0.224	0.224
0.858	0.858	0.858	0.858	0.858	0.858	0.858
0.796	0.796	0.796	0.796	0.78	0.78	0.796
0.703	0.703	0.764	0.703	0.703	0.423	0.109
0.769	0.837	0.769	0.769	0.769	0.769	0.769
0.965	0.884	0.479	0.92	0.245	0.307	0.224
0.852	0.672	0.708	0.366	0.49	0.296	0.219
0.457	0.694	0.813	0.549	0.549	0.813	0.321
0.549	0.487	0.653	0.653	0.481	0.461	0.481
0.766	0.965	0.646	0.175	0.62	0.175	0.175
0.982	0.517	0.826	0.826	0.517	0.658	0.517
0.926	0.926	0.926	0.926	0.926	0.926	0.926
0.529	0.978	0.728	0.482	0.529	0.529	0.978
0.982	0.982	0.969	0.09	0.982	0.982	0.982
0.554	0.821	0.739	0.089	0.696	0.899	0.651

Table S5D. Bacteria-gene significance

NR, immune response and oxidative stress, epi Ifit3	NR, immune response and oxidative stress, epi Il6ra	NR, immune response and oxidative stress, epi Il1b	NR, immune response and oxidative stress, epi Socs3	NR, immune response and oxidative stress, epi Mt1	NR, immune response and oxidative stress, epi Mt2	NR, immune response and oxidative stress, epi Bnip3
0.897	0.679	0.666	0.666	0.897	0.679	0.679
0.786	0.786	0.595	0.248	0.434	0.317	0.248
0.473	0.473	0.929	0.963	0.473	0.473	0.473
0.492	0.508	0.041	0.546	0.546	0.546	0.722
0.484	0.09	0.484	0.937	0.484	0.746	0.788
0.507	0.507	0.82	0.982	0.507	0.82	0.77
0.268	0.268	0.294	0.546	0.268	0.268	0.268
0.456	0.323	0.295	0.456	0.214	0.288	0.295
0.948	0.948	0.443	0.948	0.948	0.948	0.948
0.868	0.36	0.36	0.912	0.462	0.82	0.912
0.922	0.922	0.944	0.922	0.922	0.965	0.922
0.599	0.599	0.418	0.588	0.369	0.599	0.599
0.858	0.858	0.858	0.858	0.858	0.963	0.858
0.98	0.78	0.897	0.796	0.796	0.98	0.98
0.322	0.423	0.001	0.703	0.703	0.731	0.831
0.769	0.769	0.769	0.769	0.769	0.933	0.96
0.366	0.078	0.224	0.92	0.335	0.694	0.875
0.417	0.219	0.219	0.219	0.219	0.219	0.411
0.457	0.423	0.321	0.694	0.423	0.321	0.423
0.653	0.487	0.461	0.487	0.481	0.653	0.907
0.62	0.62	0.175	0.175	0.366	0.646	0.766
0.982	0.517	0.517	0.624	0.492	0.246	0.517
0.926	0.926	0.926	0.926	0.926	0.926	0.926
0.982	0.968	0.982	0.482	0.849	0.529	0.529
0.982	0.982	0.982	0.433	0.982	0.982	0.982
0.555	0.651	0.39	0.193	0.284	0.223	0.392

Table S5D. Bacteria-gene significance

NR, immune response and oxidative stress, epi Nr0b2	NR, immune response and oxidative stress, epi Nr1d1	NR, immune response and oxidative stress, epi Nr1d2	NR, immune response and oxidative stress, epi Gadd45g
0.679	0.679	0.666	0.809
0.317	0.248	0.248	0.815
0.473	0.473	0.554	0.963
0.546	0.546	0.546	0.546
0.788	0.717	0.858	1
0.904	0.77	0.894	0.978
0.268	0.268	0.268	0.683
0.295	0.295	0.295	0.456
0.948	0.948	0.948	0.432
0.82	0.904	0.912	0.82
0.944	0.944	0.944	0.944
0.599	0.599	0.862	0.224
0.858	0.858	0.858	0.858
0.98	0.98	0.897	0.98
0.731	0.703	0.703	0.703
0.879	0.96	0.769	0.933
0.849	0.772	0.884	0.92
0.219	0.296	0.411	0.219
0.321	0.321	0.321	0.894
0.653	0.757	0.907	0.461
0.522	0.711	0.766	0.175
0.214	0.517	0.492	0.826
0.926	0.948	0.926	0.926
0.482	0.529	0.482	0.978
0.982	0.982	0.982	0.885
0.212	0.284	0.223	0.506

Transporter Abcc4	Transporter Abcg8	Transporter Slc10a2	Transporter Slc17a2	Transporter Slc3a1	Transporter Slc46a3	Transporter Slc7a2	Transporter Slco1a1	NR, immune response and oxidative stress, epi Bcl6	NR, immune response and oxidative stress, epi Cldn1	NR, immune response and oxidative stress, epi Egr1	NR, immune response and oxidative stress, epi Lcn2	NR, immune response and oxidative stress, epi Nlrp12
0.1695158759	0.1525642883	0.4068381022	0.3051285766	-0.1525642883	-0.3898865146	0.2203706387	-0.2203706387	0.4407412774	0.6102571533	0.4576928649	-0.1864674635	-0.1356127007
0.4016632088	0.3286335345	0.3468909531	-0.1095445115	-0.05477225575	0.09128709292	0.4746928832	-0.4746928832	0.7302967433	0.1095445115	0.3651483717	0.2738612788	-0.3286335345
-0.2373464416	-0.01825741858	0.2921186973	0.4564354646	-0.2556038602	-0.4929503018	-0.3468909531	0.2921186973	-0.3103761159	0.5659799761	-0.01825741858	-0.5842373947	0.05477225575
-0.7	-0.08333333333	-0.25	0.75	-0.6666666667	-0.5333333333	-0.7	0.05	-0.3	0.6	-0.06666666667	-0.15	0.06666666667
-0.35	0	0.2333333333	0.35	-0.6666666667	-0.2833333333	-0.3833333333	0.15	0	0.4833333333	-0.08333333333	-0.1	-0.45
-0.35	-0.1166666667	0.3333333333	0.1833333333	-0.3333333333	-0.35	-0.3333333333	0.2666666667	-0.03333333333	0.4833333333	-0.1	-0.2666666667	-0.4166666667
0.7	0.7	0.3	-0.45	0.5	0.4	0.6666666667	-0.6333333333	0.4166666667	-0.7	0.3	0.1166666667	0.3333333333
0.55	0.6833333333	0.2833333333	-0.7	0.5666666667	0.6833333333	0.5833333333	-0.6	0.6	-0.8833333333	0.01666666667	0.3833333333	0.05
0.15	0.2	0.1833333333	-0.8	0.3333333333	0.6166666667	0.1166666667	-0.05	0.1	-0.7666666667	-0.4833333333	0.3	-0.4
0.1833333333	0.2	-0.01666666667	-0.65	0.7833333333	0.4333333333	0.2333333333	-0.2833333333	0.1666666667	-0.6333333333	-0.2666666667	0.2	0.1
0.01695158759	0.05085476277	-0.4237896898	-0.1864674635	-0.05085476277	0.3051285766	-0.03390317518	-0.1356127007	-0.288176989	-0.6102571533	-0.1356127007	0.3051285766	0.2034190511
0.3559833394	0.3898865146	0.1695158759	-0.8814825547	0.5254992153	0.5763539781	0.3220801642	-0.4407412774	0.2203706387	-0.8475793795	-0.3220801642	0.3559833394	-0.2712254014
-0.09128709292	-0.2373464416	-0.5659799761	-0.03651483717	0.1460593487	0.1278019301	-0.07302967433	0.01825741858	-0.3103761159	-0.2921186973	-0.09128709292	0.2008316044	0.3286335345
-0.1881280332	0.00990147543	-0.4950737715	-0.2178324595	0.3069457383	0.3762560663	-0.1683250823	-0.0990147543	-0.1881280332	-0.5544826241	-0.3663545909	0.3069457383	0.2970442629
0.7485339206	0.04351941399	0.3568591947	-0.5396407335	0.6701989754	0.1479660076	0.687606741	0.008703882798	0.03481553119	-0.3481553119	0.2698203667	-0.2524126011	0.1566698904
-0.02970442629	-0.1287191806	-0.4950737715	-0.1980295086	0.2475368857	0.277241312	-0.06931032801	0.01980295086	-0.3663545909	-0.4950737715	-0.2475368857	0.1881280332	0.3168472138
0.3559833394	0.1695158759	-0.1864674635	-0.4407412774	0.6780635036	0.4576928649	0.372934927	-0.2034190511	0.05085476277	-0.6950150912	-0.01695158759	0.1695158759	0.4576928649
-0.5477225575	-0.5659799761	-0.4564354646	0.8946135106	-0.8580986734	-0.4564354646	-0.5842373947	0.6390096504	-0.5659799761	0.6755244876	0.07302967433	-0.2008316044	0.1643167673
-0.6963106238	-0.2524126011	-0.2872281323	0.4526019055	-0.5396407335	-0.4700096711	-0.8007572174	0.2088931871	-0.6527912098	0.4264902571	-0.3916747259	-0.2088931871	-0.1131504764
-0.3195048252	-0.06846531969	0.02282177323	0.7302967433	-0.6390096504	-0.7302967433	-0.3423265984	0.1141088661	-0.3651483717	0.593366104	0.3879701449	-0.4564354646	0.2282177323
-0.5763539781	-0.5254992153	-0.5763539781	0.9153857299	-0.6441603284	-0.372934927	-0.4915960401	0.4576928649	-0.2542738139	0.6950150912	0.1525642883	-0.01695158759	0.288176989
-0.3166666667	-0.4333333333	-0.3	0.6666666667	-0.7	-0.5166666667	-0.4833333333	0.4833333333	-0.7666666667	0.5333333333	0.01666666667	-0.3666666667	0.1333333333
-0.08333333333	-0.5666666667	-0.5833333333	0.4833333333	-0.15	-0.3	-0.1166666667	0.3666666667	-0.5333333333	0.3333333333	0.2	-0.15	0.4666666667
0.4833333333	0.4833333333	0.7333333333	-0.2333333333	0.1166666667	-0.03333333333	0.5333333333	-0.4166666667	0.6833333333	0.06666666667	0.4166666667	-0.06666666667	-0.3
0.4833333333	0.3833333333	0.8	-0.4	0.06666666667	-0.05	0.3833333333	-0.2166666667	0.2833333333	-0.01666666667	0.1333333333	-0.2333333333	-0.4833333333
0.7723150835	0.6336944275	0.8218224607	-0.5643840995	0.5544826241	0.138620656	0.7723150835	-0.5643840995	0.6832018047	-0.2475368857	0.3663545909	-0.1089162297	-0.1683250823

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Socs2	Cebpb	Hmox1	Icam1	Ifit3	Il6ra	Il1b	Socs3
0.3051285766	-0.8306277919	0.8136762043	0.6272087408	-0.05085476277	-0.2542738139	0.3898865146	0.4068381022
0.3468909531	-0.5294651389	0.6207522318	0.3103761159	0.1643167673	-0.1460593487	0.2738612788	0.6390096504
0.4199206274	-0.4929503018	0.3103761159	0.4929503018	-0.4199206274	-0.4016632088	0.1278019301	-0.05477225575
-0.35	-0.5666666667	0.6666666667	0.8666666667	-0.5333333333	-0.5	0.9	-0.3333333333
0.25	-0.5	0.5166666667	0.6166666667	-0.6166666667	-0.8666666667	0.6	0.1
0.1333333333	-0.2666666667	0.1833333333	0.35	-0.65	-0.6666666667	0.3166666667	-0.01666666667
0.5166666667	0.1833333333	-0.1	-0.5	0.6	0.6166666667	-0.5333333333	0.3166666667
0.4666666667	0.4666666667	-0.3166666667	-0.6166666667	0.3166666667	0.5	-0.5333333333	0.3333333333
0.3	0.75	-0.8333333333	-0.7333333333	-0.06666666667	0.03333333333	-0.55	0.2
-0.05	0.6	-0.7	-0.6166666667	0.25	0.7	-0.5833333333	0.1
-0.3559833394	0.5254992153	-0.4068381022	-0.4576928649	0.3559833394	0.2712254014	-0.1017095255	-0.2542738139
0.2542738139	0.5594023905	-0.7119666788	-0.6950150912	0.3220801642	0.372934927	-0.5254992153	0.4407412774
-0.6390096504	0.4199206274	-0.3651483717	-0.3103761159	0.3651483717	0.4746928832	-0.09128709292	-0.3468909531
-0.4257634435	0.6039900012	-0.5148767223	-0.3663545909	0.1287191806	0.5148767223	-0.1881280332	-0.3168472138
0.3829708431	0.3394514291	-0.5918640302	-0.7920533346	0.6701989754	0.5744562647	-0.9574271078	0.2611164839
-0.4059604926	0.5643840995	-0.5742855749	-0.4653693452	0.3663545909	0.5148767223	-0.3069457383	-0.277241312
-0.08475793795	0.6441603284	-0.5933055657	-0.7119666788	0.5254992153	0.8475793795	-0.6780635036	-0.1186611131
-0.438178046	-0.3103761159	0.4929503018	0.5842373947	-0.3651483717	-0.6024948133	0.6207522318	-0.6207522318
-0.3133397807	-0.3220436635	0.130558242	0.5744562647	-0.4090824915	-0.4613057883	0.600567913	-0.2088931871
-0.2510395055	-0.502079011	0.593366104	0.502079011	-0.2282177323	-0.4336136914	0.593366104	-0.4336136914
-0.661111916	-0.3390317518	0.661111916	0.6950150912	-0.3559833394	-0.3390317518	0.7289182664	-0.6441603284
-0.1666666667	-0.3833333333	0.2666666667	0.4333333333	-0.03333333333	-0.45	0.3666666667	-0.3
-0.6	-0.08333333333	0.06666666667	0.1	0.4166666667	0.2666666667	0.06666666667	-0.4
0.6333333333	-0.4	0.4	0.06666666667	0.01666666667	-0.1666666667	-0.03333333333	0.5666666667
0.8666666667	-0.3	0.01666666667	-0.1	0.05	-0.3166666667	-0.2666666667	0.7
0.8416254115	-0.207930984	0.04950737715	-0.277241312	0.34655164	0.2574383612	-0.4950737715	0.7525121327

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Mt1	Mt2	Bnip3	Nr0b2	Nr1d1	Nr1d2	Gadd45g
0.05085476277	0.2542738139	0.288176989	-0.288176989	0.3220801642	0.4068381022	-0.1525642883
0.4564354646	0.5477225575	0.6390096504	-0.5477225575	0.6207522318	0.6207522318	0.09128709292
-0.5294651389	-0.4564354646	-0.5294651389	0.4016632088	-0.5112077203	-0.3468909531	-0.01825741858
-0.4166666667	-0.35	-0.2	0.3166666667	-0.3166666667	-0.3166666667	-0.4
-0.5166666667	-0.3166666667	-0.2333333333	0.2333333333	-0.35	-0.1833333333	-0.01666666667
-0.6333333333	-0.3166666667	-0.4166666667	0.1666666667	-0.4333333333	-0.2166666667	-0.06666666667
0.8	0.6666666667	0.6333333333	-0.5666666667	0.6333333333	0.5833333333	0.2166666667
0.7666666667	0.7	0.5333333333	-0.65	0.5333333333	0.5333333333	0.3166666667
0.1333333333	0.03333333333	-0.1333333333	-0.1166666667	-0.15	-0.1333333333	0.5833333333
0.5166666667	0.3166666667	0.06666666667	-0.3666666667	0.1833333333	0.05	0.3166666667
0.2542738139	0.01695158759	0.2203706387	0.06780635036	0.1017095255	-0.08475793795	0.05085476277
0.5933055657	0.3051285766	0.2373222263	-0.3898865146	0.2373222263	0.06780635036	0.6780635036
0.2008316044	-0.01825741858	0.09128709292	0.09128709292	0.09128709292	-0.1278019301	-0.1278019301
0.3069457383	0.03960590172	-0.01980295086	0.00990147543	-0.01980295086	-0.1980295086	0.03960590172
0.2785242495	0.2088931871	0.1044465936	-0.1914854216	0.2524126011	0.2437087183	0.3133397807
0.2475368857	-0.07921180344	-0.01980295086	0.1485221314	-0.01980295086	-0.2376354103	0.0990147543
0.5594023905	0.3559833394	0.2203706387	-0.2542738139	0.3051285766	0.1864674635	0.08475793795
-0.7850689991	-0.6207522318	-0.3834057903	0.7302967433	-0.4929503018	-0.3834057903	-0.5842373947
-0.4787135539	-0.6789028582	-0.4961213195	0.5657523819	-0.5918640302	-0.7224222722	0.05222329679
-0.5477225575	-0.2510395055	-0.04564354646	0.2510395055	-0.1597524126	-0.04564354646	-0.593366104
-0.5254992153	-0.3051285766	-0.1695158759	0.4407412774	-0.2203706387	-0.1356127007	-0.7967246168
-0.5833333333	-0.7166666667	-0.3833333333	0.7666666667	-0.4833333333	-0.5333333333	-0.1333333333
-0.1333333333	-0.3	-0.06666666667	0.4333333333	-0.03333333333	-0.2	-0.35
0.2333333333	0.5166666667	0.4333333333	-0.5833333333	0.45	0.6166666667	0.1
0.05	0.1	0.08333333333	-0.2333333333	0.08333333333	0.1833333333	0.55
0.5643840995	0.6336944275	0.4752708206	-0.7030047555	0.5643840995	0.6336944275	0.4059604926

#CV PCB6 & CV PCB30 & GF PCB6 & GF PCB30 COMMON	#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB6 COMMON	#CV PCB6 & GF PCB6 & GF PCB30 COMMOn	#CV PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB30 & CV PCB30 COMMON
Cyp1a2	Cyp17a1	Cyp8b1	Ypel2	Cyp3a16	Igfbp5	Cyp2c29
Arntl	Cyp2a5	Serpina1e	Cldn1	Cyp3a41a		Atp6v0d2
Ces2c	Cyp2j9	Gm24105	Cyp26a1	Cyp3a41b		Cyp2b10
G6pc	Clpx	Gm47283	Sult2a2			Rnf125
Sult2a1	Rab36	AC127342.1				
	Mknk2					
	Lpin1					
	Sdf2l1					
	Creld2					
	Spry4					
	Setbp1					
	Syvn1					
	Loxl4					
	Got1					
	Npas2					
	Acmsd					
	Marco					
	Slc30a10					
	Hspa5					
	Gpcpd1					
	Mthfr					
	Slc34a2					
	Hsph1					
	Atp2b2					
	Mt2					
	Mt1					
	Hyou1					
	Nnmt					
	Manf					
	Slc16a1					
	Hspa13					
	Pim3					
	Pnrc1					
	Gstm2					
	Inhba					
	Rtn4rl1					
	Rbp1					
	Jun					
	Arfgap3					
	Nfil3					
	Ero1lb					
	Dhcr7					
	Tubb2a					
	Rad51b					
	Cyp2c54					
	Ppp1r3c					
	Sult3a1					
	Etnk2					
	Acot1					
	Gm13775					
	Gm15611					
	Gm16348					
	Sult3a2					
	Hspa1b					
	Serpina4-ps1					
	1810053B23Rik					
	Gm21049					

#CV PCB30 & GF PCB6 COMMON	#CV PCB30 & GF PCB6 & CV PCB30 COMMON	#CV PCB30 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only GF PCB6	#only GF PCB30
Socs2	Gstm3	Cyp2c55	Mfsd10	Ckb	Nbr1	Ttyh1
Bcl6	Gadd45g	Nr0b2	Hmox1	Nqo1	Igfbp1	Lars2
Fabp5	Upp2	Cyp3a44	Id3	Por	Per1	Hbb-bt
Slco1a1	Thrsp	Gstp1	Dnajb9	Psmb4	Klc1	Gm13340
Paqr9	Egr1	Hba-a2	Aldoc	Krt23	Lcn2	Gm20594
Gm25687		Hba-a1	Myh11	Abhd8	Ly75	Mir6236
Mup22			Aebp1	Plin5	Smad9	Gm28439
			Map2k6	Lonrf3	Enho	Gm28437
			Id2	Avpr1a	Sult1e1	Gm37194
			Klf11	Nr1d1	H2-Aa	Rmrp
			Hmgcr	Nr1d2	Nmrk1	
			Slc25a30	Cnmd	Ppl	
			Sqle	Sorbs3	Ppp1r3g	
			Slc15a2	Retreg1	Apol9a	
			Noct	Myc	Camk2b	
			Chka	Mpv17l	BC023105	
			Gsn	Slc10a2	H2-Ab1	
			Hdc	Slc3a1	Sult2a3	
			Il6ra	Abcg8	Sult2a5	
			Efna1	Cyb5a	Nlrp12	
			Plk3	Aldh1a7	Gm12390	
			Atp2a2	Spata3	Nbdy	
			Gfpt1	Ngef	Zbed4-ps2	
			Tmem159	Agxt	Mug-ps1	
			Nsdhl	Mpzl1	Gm42796	
			Msmo1	Lrp4	Gm42642	
			Gclc	Knstrn	4833411C07Rik	
			Acta2	Il1b	Gm47789	
			Icam1	Gstm4	Gm34654	
			Vnn1	Pdgfc		
			Gdf15	Hsdl2		
			Lonrf1	Gne		
			Cplane1	Cyp4a14		
			Lrtm1	Per3		
			Phf13	Slc2a5		
			Angptl8	Slc46a3		
			Zfp518a	Gys2		
			Tsku	Scnn1a		
			Tcim	Clec2h		
			Cebpb	Serpina7		
			Fam47e	Slc7a2		
			Fdps	Pllp		
			Defa24	Nectin1		
			mt-Co2	Cyp1a1		
			Rdh11	Gsta4		
			Zbtb16	Trib3		
			Gm5096	Abtb2		
			Osgin1	Abcc4		
			Bhmt	Igf2bp2		
			Ifit3	Dsg1c		
			Igkc	Gnat1		
			Zfp970	Rrp12		
			F830016B08Rik	1810055G02Rik		
			Hmgcs1	Ttc38		
			Mup15	Slc17a2		
			Mup17	Lrfn3		
			Tcf24	Lrg1		
			Ighv1-11	Il22ra1		
			Gm45301	Spon2		
			Eppk1	Inf2		
			Gm31583	Mical2		
				Foxq1		
				Ciart		
				Dsel		

9130409I23Rik
Mreg
Mmd2
Htatip2
Tmem120a
Sdr9c7
Gbp2b
Klhdc8a
Lgalsl
Maff
Pgp
Tafa2
Lsm11
Zfp526
Paxx
Hbb-bs
Pkdrej
Zmat1
Socs3
Smagp
Klf1
Pm20d2
Cyp2c50
Ntrk2
Retsat
Gsta2
Gstm1
Tmed9
Gpc6
Acnat2
H2-Q7
Serpina6
Lsamp
Pclo
Cyp26b1
Gm22220
Mup3
Frat1
Nipal1
Ccnd1
Klhl21
Cib3
Phldb3
Ly6a
Bnip3
Mup20
Ces1b
Gm11340
Gm13771
Rn7s1
Gm6135
Gstm2-ps1
Gm44421
Gm44787
Gm33543
Gm34777
Gm31508
Gm49012
AC138228.1
AC157910.3

#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only CV PCB30
Aminosobutyric acid	G6P	3-Hydroxybutyric acid	Folinic acid	Dopamine
2,3-Dihydroxybenzoic acid	F6P		Shikimic acid	Dextrose
	Raffinose		NADP	Allantoin
			Arginine	Inosine
			Adenylosuccinate	NAD
			Acetylcarnitine	Uridine
				Nicotinamide
				Taurine
				Adenosine
				Adenosyl-L-homocysteine
				UDP-GlcNAc
				3-Methylvaleric acid
				2,3-Dihydroxybenzoic acid
				2-Deoxycytidine

#GF PCB6 & GF PCB30 COMMON	#only CV PCB30	#only CV PCB6	#only CV PCB30
Glucuronic acid	Levulinic acid	Mucic acid	2-Hydroxyphenylacetic acid
	6-Methyl-DL-tryptophan	Mannose	
	Serine	Norvaline	
	Asparagine	Cytosine	
	Proline		
	Urocanic acid		

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001082.12	Mfsd10	6.27489	1.7969	-1.80408	-1.666	0.00005	0.00761968
ENSMUSG00000003053.17	Cyp2c29	505.17	834.73	0.72454	2.77488	0.00005	0.00761968
ENSMUSG00000003555.8	Cyp17a1	30.7127	66.9781	1.12485	3.97657	0.00005	0.00761968
ENSMUSG00000004038.9	Gstm3	20.5927	33.851	0.717065	2.92459	0.00005	0.00761968
ENSMUSG00000005413.8	Hmox1	10.8956	7.33838	-0.570219	-2.05123	0.00035	0.037983
ENSMUSG00000005547.14	Cyp2a5	430.556	721.13	0.744058	2.24398	0.00015	0.0193581
ENSMUSG00000007872.3	Id3	27.5332	13.3798	-1.04111	-3.69018	0.00005	0.00761968
ENSMUSG00000014905.4	Dnajb9	24.6827	16.6976	-0.563856	-2.44755	0.00005	0.00761968
ENSMUSG00000015224.10	Cyp2j9	8.84831	4.99311	-0.825464	-2.92044	0.00005	0.00761968
ENSMUSG00000015357.10	Clpx	78.2269	50.077	-0.643518	-2.64475	0.00005	0.00761968
ENSMUSG00000017390.15	Aldoc	3.30235	6.26799	0.924508	1.8897	0.00045	0.0460446
ENSMUSG00000018427.7	Ypel2	9.95094	5.96948	-0.737227	-3.14699	0.00005	0.00761968
ENSMUSG00000018830.10	Myh11	0.856366	1.92082	1.16542	2.76044	0.00005	0.00761968
ENSMUSG00000020175.15	Rab36	7.24259	4.05831	-0.835627	-2.23857	0.00005	0.00761968
ENSMUSG00000020190.13	Mknk2	16.502	34.2124	1.05188	2.706	0.00005	0.00761968
ENSMUSG00000020473.13	Aebp1	0.537474	1.24369	1.21036	1.91027	0.00015	0.0193581
ENSMUSG00000020593.15	Lpin1	23.3481	63.294	1.43876	4.53512	0.00005	0.00761968
ENSMUSG00000020623.11	Map2k6	2.79563	4.8047	0.781271	2.25429	0.00015	0.0193581
ENSMUSG00000020644.9	Id2	65.4148	42.2437	-0.630882	-2.77822	0.00005	0.00761968
ENSMUSG00000020653.12	Klf11	4.00267	1.83482	-1.12533	-2.16824	0.00005	0.00761968
ENSMUSG00000021453.2	Gadd45g	4.23384	9.3219	1.13866	3.01194	0.00005	0.00761968
ENSMUSG00000021670.14	Hmgcr	42.2238	98.0346	1.21523	3.29717	0.00005	0.00761968
ENSMUSG00000022003.7	Slc25a30	21.1229	8.85161	-1.2548	-2.70092	0.00005	0.00761968
ENSMUSG00000022351.14	Sqle	14.4701	22.8969	0.662076	2.85745	0.00005	0.00761968
ENSMUSG00000022512.3	Cldn1	25.5877	18.7521	-0.448393	-2.02615	0.00035	0.037983
ENSMUSG00000022769.9	Sdf2l1	44.9273	25.0223	-0.844377	-3.54758	0.00005	0.00761968
ENSMUSG00000022899.9	Slc15a2	3.0659	0.37101	-3.04678	-1.38684	0.00005	0.00761968
ENSMUSG00000023087.15	Noct	3.11413	6.68196	1.10144	2.47459	0.00005	0.00761968
ENSMUSG00000023272.4	Creld2	42.1392	14.3552	-1.55359	-6.28154	0.00005	0.00761968
ENSMUSG00000024427.7	Spry4	3.84589	5.82326	0.598512	2.37281	0.00005	0.00761968
ENSMUSG00000024548.11	Setbp1	0.571063	0.898115	0.65325	2.01298	0.0004	0.0421324
ENSMUSG00000024807.18	Syvn1	26.659	12.2223	-1.12511	-3.46232	0.00005	0.00761968
ENSMUSG00000024843.15	Chka	45.983	21.79	-1.07743	-2.35525	0.00025	0.028881
ENSMUSG00000024987.6	Cyp26a1	11.1487	24.2118	1.11883	3.82575	0.00005	0.00761968
ENSMUSG00000025185.14	Loxl4	3.94432	2.11188	-0.90125	-2.33915	0.00005	0.00761968
ENSMUSG00000025190.13	Got1	73.9132	114.605	0.632762	2.52771	0.00005	0.00761968
ENSMUSG00000026077.15	Npas2	8.47762	1.95208	-2.11865	-2.21209	0.0001	0.0140441
ENSMUSG00000026185.8	Igfbp5	5.37805	8.0981	0.590499	2.46113	0.00005	0.00761968
ENSMUSG00000026348.7	Acmsd	7.9453	11.3608	0.515893	2.05887	0.00025	0.028881
ENSMUSG00000026390.7	Marco	4.51252	2.20537	-1.03291	-2.38186	0.00005	0.00761968
ENSMUSG00000026614.7	Slc30a10	12.8976	7.77189	-0.730768	-3.05461	0.00005	0.00761968
ENSMUSG00000026839.17	Upp2	61.1429	142.443	1.22013	4.83935	0.00005	0.00761968
ENSMUSG00000026864.13	Hspa5	838.917	453.702	-0.886781	-2.47163	0.00005	0.00761968
ENSMUSG00000026879.14	Gsn	5.39704	11.4131	1.08046	3.81852	0.00005	0.00761968
ENSMUSG00000027346.15	Gpcpd1	23.3608	40.7371	0.802254	2.42579	0.0001	0.0140441
ENSMUSG00000027360.5	Hdc	3.45119	1.89382	-0.865796	-1.76936	0.00045	0.0460446
ENSMUSG00000027947.11	Il6ra	12.7959	19.116	0.579098	2.29486	0.00025	0.028881
ENSMUSG00000027954.9	Efna1	27.2749	14.7794	-0.883989	-3.61654	0.00005	0.00761968
ENSMUSG00000028238.6	Atp6v0d2	5.28464	8.4326	0.674173	2.16648	0.0001	0.0140441
ENSMUSG00000028680.14	Plk3	10.5138	6.01814	-0.804897	-3.05136	0.00005	0.00761968
ENSMUSG00000029009.17	Mthfr	7.1591	3.44294	-1.05613	-2.20818	0.00035	0.037983

ENSMUSG00000029188.14	Slc34a2	1.56037	0.365782	-2.09283	-2.78098	0.00005	0.00761968
ENSMUSG00000029467.15	Atp2a2	86.4356	60.473	-0.515334	-1.97184	0.00035	0.037983
ENSMUSG00000029657.15	Hsph1	47.3595	28.792	-0.717988	-2.07578	0.00015	0.0193581
ENSMUSG00000029992.14	Gfpt1	13.4599	9.01933	-0.577579	-1.84116	0.00045	0.0460446
ENSMUSG00000030302.16	Atp2b2	4.38644	2.77593	-0.66008	-2.11664	0.0002	0.0244872
ENSMUSG00000030483.14	Cyp2b10	17.3823	34.9186	1.00638	4.20068	0.00005	0.00761968
ENSMUSG00000030917.13	Tmem159	0.899211	4.33785	2.27025	1.53715	0.0004	0.0421324
ENSMUSG00000031349.4	Nsdhl	10.9891	18.7202	0.768519	3.05432	0.00005	0.00761968
ENSMUSG00000031604.10	Msmo1	88.8162	141.341	0.67029	2.3651	0.0002	0.0244872
ENSMUSG00000031762.7	Mt2	14.6712	30.7685	1.06847	2.79551	0.00005	0.00761968
ENSMUSG00000031765.8	Mt1	41.5758	103.19	1.31148	4.86124	0.00005	0.00761968
ENSMUSG00000032115.14	Hyou1	67.4029	46.7624	-0.527462	-2.28962	0.00005	0.00761968
ENSMUSG00000032271.13	Nnmt	56.8868	84.4939	0.570754	2.3728	0.00005	0.00761968
ENSMUSG00000032310.4	Cyp1a2	347.498	1061.1	1.61048	5.9896	0.00005	0.00761968
ENSMUSG00000032350.9	Gclc	79.3815	50.4684	-0.653422	-2.42429	0.00005	0.00761968
ENSMUSG00000032575.16	Manf	239.221	135.412	-0.820986	-2.2734	0.0001	0.0140441
ENSMUSG00000032902.1	Slc16a1	19.0525	12.3003	-0.631283	-2.79129	0.00005	0.00761968
ENSMUSG00000032932.15	Hspa13	14.3906	9.10349	-0.660639	-2.73434	0.00005	0.00761968
ENSMUSG00000033107.6	Rnf125	123.021	61.7043	-0.995457	-4.47951	0.00005	0.00761968
ENSMUSG00000035686.8	Thrsp	108.608	275.462	1.34273	5.6328	0.00005	0.00761968
ENSMUSG00000035783.9	Acta2	1.51116	4.87177	1.68878	2.67871	0.00005	0.00761968
ENSMUSG00000035828.11	Pim3	5.49715	9.06074	0.720943	2.54131	0.00005	0.00761968
ENSMUSG00000037405.8	Icam1	7.588	5.10752	-0.571098	-2.12615	0.0004	0.0421324
ENSMUSG00000037440.8	Vnn1	26.6312	18.1146	-0.555968	-2.3665	0.0001	0.0140441
ENSMUSG00000038418.7	Egr1	8.5935	4.36381	-0.977659	-3.36242	0.00005	0.00761968
ENSMUSG00000038508.7	Gdf15	2.87642	1.396	-1.04298	-2.33349	0.00035	0.037983
ENSMUSG00000038656.5	Cyp3a16	15.6662	29.4555	0.910887	3.44256	0.00005	0.00761968
ENSMUSG00000039633.6	Lonrf1	1.73883	1.02745	-0.759046	-2.12834	0.0004	0.0421324
ENSMUSG00000039801.7	Cplane1	1.57608	11.8302	2.90806	2.79653	0.00015	0.0193581
ENSMUSG00000040128.9	Pnrc1	65.8791	42.2407	-0.641185	-2.71807	0.00005	0.00761968
ENSMUSG00000040562.12	Gstm2	44.5903	65.892	0.563373	2.4444	0.00005	0.00761968
ENSMUSG00000041324.14	Inhba	9.92684	4.22896	-1.23103	-2.8545	0.00005	0.00761968
ENSMUSG00000045287.6	Rtn4rl1	6.73191	4.46	-0.593973	-2.31529	0.00015	0.0193581
ENSMUSG00000045776.3	Lrtm1	4.59023	7.84042	0.772364	2.57822	0.00005	0.00761968
ENSMUSG00000046402.10	Rbp1	2.24938	3.8182	0.763363	2.38685	0.00005	0.00761968
ENSMUSG00000047777.9	Phf13	2.44905	1.25344	-0.966331	-2.7493	0.00005	0.00761968
ENSMUSG00000047822.8	Angptl8	82.3516	37.7627	-1.12484	-2.15144	0.00045	0.0460446
ENSMUSG00000049164.7	Zfp518a	3.42441	2.24797	-0.607233	-2.21996	0.00005	0.00761968
ENSMUSG00000049580.12	Tsku	7.78541	17.2903	1.15112	2.39263	0.0002	0.0244872
ENSMUSG00000052684.4	Jun	8.02239	3.56567	-1.16986	-4.3468	0.00005	0.00761968
ENSMUSG00000054277.8	Arfgap3	4.98675	2.38411	-1.06465	-2.77345	0.00005	0.00761968
ENSMUSG00000055116.8	Arntl	9.47854	4.66962	-1.02136	-3.41105	0.00005	0.00761968
ENSMUSG00000056313.5	Tcim	6.3628	10.6007	0.736431	2.63227	0.00005	0.00761968
ENSMUSG00000056501.3	Cebpb	33.2417	49.8658	0.585055	2.15225	0.0002	0.0244872
ENSMUSG00000056749.7	Nfil3	11.4209	6.76087	-0.756389	-2.86792	0.00005	0.00761968
ENSMUSG00000057068.15	Fam47e	6.37728	11.3884	0.836547	2.00781	0.00025	0.028881
ENSMUSG00000057069.7	Ero1lb	12.8374	8.73738	-0.555077	-2.29919	0.0001	0.0140441
ENSMUSG00000058454.15	Dhcr7	16.3576	28.6402	0.808075	2.67257	0.00005	0.00761968
ENSMUSG00000058672.7	Tubb2a	60.3828	42.6623	-0.501177	-2.22162	0.0002	0.0244872
ENSMUSG00000059060.15	Rad51b	2.98263	1.00564	-1.56846	-2.7696	0.00005	0.00761968
ENSMUSG00000059743.12	Fdps	68.1418	100.306	0.557798	2.3204	0.00005	0.00761968

ENSMUSG00000061825.10	Ces2c	4.32809	7.73435	0.837552	2.81141	0.00005	0.00761968
ENSMUSG00000064213.5	Defa24	1.36432	0	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000064354.1	mt-Co2	6.53406	11.5824	0.825885	2.28304	0.00015	0.0193581
ENSMUSG00000066441.14	Rdh11	16.5169	23.867	0.531074	2.24242	0.00005	0.00761968
ENSMUSG00000066687.5	Zbtb16	17.6103	35.1446	0.996886	3.99134	0.00005	0.00761968
ENSMUSG00000067225.2	Cyp2c54	162.272	224.41	0.467721	2.06478	0.00025	0.028881
ENSMUSG00000067279.3	Ppp1r3c	27.6268	14.325	-0.947532	-4.13342	0.00005	0.00761968
ENSMUSG00000069324.6	Gm5096	15.1526	23.2798	0.619511	2.53681	0.00005	0.00761968
ENSMUSG00000069668.4	Sult3a1	97.163	160.62	0.725176	3.28788	0.00005	0.00761968
ENSMUSG00000070644.13	Etnk2	62.5601	96.255	0.621618	2.63482	0.00005	0.00761968
ENSMUSG00000070811.6	Sult2a2	47.5462	75.7986	0.672841	2.07079	0.0003	0.03438
ENSMUSG00000072949.6	Acot1	33.817	19.1723	-0.818729	-2.60084	0.00005	0.00761968
ENSMUSG00000074063.10	Osgin1	93.9424	49.382	-0.927792	-4.03213	0.00005	0.00761968
ENSMUSG00000074768.6	Bhmt	276.248	458.526	0.731038	2.73971	0.00005	0.00761968
ENSMUSG00000074896.3	Ifit3	4.81246	7.59939	0.659108	2.2256	0.00025	0.028881
ENSMUSG00000075551.4	Cyp3a41a	33.4333	57.9428	0.793345	3.43636	0.00005	0.00761968
ENSMUSG00000075552.4	Cyp3a41b	4.55117	8.51163	0.903198	3.06479	0.00005	0.00761968
ENSMUSG00000076609.2	Igkc	9.38561	17.1417	0.868984	2.35993	0.00005	0.00761968
ENSMUSG00000078650.2	G6pc	118.654	70.8163	-0.744612	-3.34005	0.00005	0.00761968
ENSMUSG00000078798.4	Sult2a1	56.4787	97.1215	0.782085	3.19123	0.00005	0.00761968
ENSMUSG00000078866.10	Zfp970	11.5288	17.8725	0.632507	2.15652	0.00015	0.0193581
ENSMUSG00000081207.4	Gm13775	12.4872	21.3006	0.770447	2.48423	0.00005	0.00761968
ENSMUSG00000084923.1	Gm15611	21.2021	5.05847	-2.06744	-4.28501	0.00005	0.00761968
ENSMUSG00000085445.1	Gm16348	0.998651	2.12188	1.08729	2.36459	0.00005	0.00761968
ENSMUSG00000090298.2	Sult3a2	3.39104	7.38886	1.12362	2.81264	0.00005	0.00761968
ENSMUSG00000090877.3	Hspa1b	1.21104	0.49013	-1.305	-2.62497	0.0002	0.0244872
ENSMUSG00000090942.1	F830016B	18.3992	13.1678	-0.482627	-2.08238	0.00035	0.037983
ENSMUSG00000092075.1	Serpina4-	21.4399	5.39866	-1.98962	-6.65923	0.00005	0.00761968
ENSMUSG00000093930.2	Hmgcs1	79.4702	111.752	0.491821	1.79112	0.00015	0.0193581
ENSMUSG00000096674.1	Mup15	16.0544	25.2402	0.652756	2.36601	0.00005	0.00761968
ENSMUSG00000096688.1	Mup17	35.5827	61.429	0.787745	3.16456	0.00005	0.00761968
ENSMUSG00000099032.2	Tcf24	4.46246	2.40791	-0.890059	-2.74594	0.00005	0.00761968
ENSMUSG00000100277.8	1810053B	0.732602	2.66094	1.86084	1.18658	0.0001	0.0140441
ENSMUSG00000102888.1	Ighv1-11	0	6.24986	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000106397.1	Gm21049	4.52985	7.62193	0.750694	2.11318	0.00035	0.037983
ENSMUSG00000110384.1	Gm45301	1.01899	2.77951	1.44769	2.41211	0.00025	0.028881
ENSMUSG00000115388.2	Eppk1	5.00691	7.2053	0.525136	2.22729	0.0001	0.0140441
ENSMUSG00000115919.1	Gm31583	2.90438	5.0658	0.802558	2.71184	0.00005	0.00761968

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001270.9	Ckb	4.9592	2.82251	-0.813128	-1.925	0.00055	0.0404152
ENSMUSG00000003053.17	Cyp2c29	502.057	1871.49	1.89827	4.7931	0.00005	0.00618632
ENSMUSG00000003555.8	Cyp17a1	30.523	69.3286	1.18355	3.76365	0.00005	0.00618632
ENSMUSG00000003849.8	Nqo1	4.13848	8.59917	1.05509	3.10818	0.00005	0.00618632
ENSMUSG00000004038.9	Gstm3	20.4693	75.9074	1.89078	6.88927	0.00005	0.00618632
ENSMUSG00000005514.14	Por	143.718	286.806	0.996833	2.93999	0.00005	0.00618632
ENSMUSG00000005547.14	Cyp2a5	427.875	1202.66	1.49096	3.44719	0.00005	0.00618632
ENSMUSG00000005779.12	Psmb4	57.871	84.627	0.548278	1.92037	0.00065	0.0456767
ENSMUSG00000006777.7	Krt23	1.02612	5.09059	2.31064	4.50613	0.00005	0.00618632
ENSMUSG00000007950.9	Abhd8	1.46653	0.490162	-1.58107	-2.25758	0.0002	0.0194309
ENSMUSG00000011305.11	Plin5	16.8478	11.2536	-0.582169	-2.14557	0.00015	0.0159662
ENSMUSG00000015224.10	Cyp2j9	8.79124	5.13102	-0.776822	-2.50401	0.00005	0.00618632
ENSMUSG00000015357.10	Clpx	77.7399	44.4332	-0.807017	-2.76713	0.00005	0.00618632
ENSMUSG00000016239.11	Lonrf3	2.78045	1.06184	-1.38874	-2.97987	0.00005	0.00618632
ENSMUSG00000020027.18	Socs2	8.61402	16.6749	0.952916	2.06	0.00005	0.00618632
ENSMUSG00000020123.6	Avpr1a	24.1839	14.3293	-0.755076	-2.41315	0.00005	0.00618632
ENSMUSG00000020175.15	Rab36	7.19819	4.01968	-0.840554	-2.06135	0.00035	0.029457
ENSMUSG00000020190.13	Mknk2	16.398	38.746	1.24053	2.84633	0.00005	0.00618632
ENSMUSG00000020593.15	Lpin1	23.2003	40.0422	0.78738	2.19992	0.00055	0.0404152
ENSMUSG00000020889.11	Nr1d1	17.095	37.493	1.13305	2.42106	0.0005	0.0385
ENSMUSG00000021453.2	Gadd45g	4.2085	13.5086	1.6825	4.46078	0.00005	0.00618632
ENSMUSG00000021775.11	Nr1d2	18.5393	32.2923	0.800601	2.14163	0.0001	0.0113094
ENSMUSG00000022025.13	Cnmd	2.94353	7.12175	1.27469	2.30779	0.0001	0.0113094
ENSMUSG00000022091.6	Sorbs3	8.7422	15.3301	0.810301	2.61385	0.00005	0.00618632
ENSMUSG00000022270.16	Retreg1	33.766	64.9642	0.944073	2.71635	0.00005	0.00618632
ENSMUSG00000022346.15	Myc	1.47519	5.7052	1.95138	3.05112	0.00005	0.00618632
ENSMUSG00000022508.5	Bcl6	3.5485	6.1976	0.804501	2.72117	0.00005	0.00618632
ENSMUSG00000022679.13	Mpv17l	3.4023	7.38539	1.11816	2.33264	0.00005	0.00618632
ENSMUSG00000022769.9	Sdf2l1	44.6531	24.9449	-0.840016	-3.10498	0.00005	0.00618632
ENSMUSG00000023073.2	Slc10a2	3.87084	6.00992	0.634701	2.23853	0.0002	0.0194309
ENSMUSG00000023272.4	Creld2	41.8868	10.7104	-1.96748	-6.82395	0.00005	0.00618632
ENSMUSG00000024131.8	Slc3a1	16.845	27.1766	0.690046	1.95102	0.00055	0.0404152
ENSMUSG00000024254.15	Abcg8	23.9899	44.5496	0.892986	2.2514	0.00005	0.00618632
ENSMUSG00000024427.7	Spry4	3.8216	7.52294	0.977118	3.54048	0.00005	0.00618632
ENSMUSG00000024548.11	Setbp1	0.567395	0.943684	0.733949	2.09591	0.00035	0.029457
ENSMUSG00000024646.14	Cyb5a	1372.68	2262.27	0.720771	2.28567	0.00005	0.00618632
ENSMUSG00000024747.3	Aldh1a7	74.5145	106.783	0.519085	1.98059	0.0006	0.043428
ENSMUSG00000024807.18	Syvn1	26.4973	12.6676	-1.0647	-2.99172	0.00005	0.00618632
ENSMUSG00000025002.5	Cyp2c55	5.11	22.678	2.1499	7.12158	0.00005	0.00618632
ENSMUSG00000025185.14	Loxl4	3.92033	1.51462	-1.37202	-2.71184	0.00005	0.00618632
ENSMUSG00000025190.13	Got1	73.4621	143.402	0.964996	3.33157	0.00005	0.00618632
ENSMUSG00000026077.15	Npas2	8.42746	1.66594	-2.33876	-3.01011	0.0001	0.0113094
ENSMUSG00000026226.16	Spata3	2.63728	0.875213	-1.59135	-1.67117	0.0001	0.0113094
ENSMUSG00000026259.14	Ngef	11.0126	17.9847	0.707619	2.38152	0.00005	0.00618632
ENSMUSG00000026272.6	Agxt	102.981	151.74	0.559222	2.16773	0.00005	0.00618632
ENSMUSG00000026348.7	Acmsd	7.89756	21.2665	1.42911	4.87646	0.00005	0.00618632
ENSMUSG00000026390.7	Marco	4.48507	2.16164	-1.05301	-2.28692	0.00005	0.00618632
ENSMUSG00000026566.15	Mpzl1	6.70294	2.77735	-1.27108	-2.14427	0.00025	0.0235
ENSMUSG00000026614.7	Slc30a10	12.8176	6.44774	-0.991257	-3.4987	0.00005	0.00618632
ENSMUSG00000026839.17	Upp2	60.7617	218.9	1.84904	6.12168	0.00005	0.00618632
ENSMUSG00000026864.13	Hspa5	833.809	437.932	-0.929011	-2.08676	0.00015	0.0159662

ENSMUSG00000027253.15	Lrp4	4.77798	7.06684	0.564666	2.03091	0.0002	0.0194309
ENSMUSG00000027331.15	Knstrn	0.217572	1.42377	2.71015	1.00013	0.00015	0.0159662
ENSMUSG00000027346.15	Gpcpd1	23.2178	53.4558	1.20312	3.25032	0.00005	0.00618632
ENSMUSG00000027398.13	Il1b	3.56328	1.05211	-1.75992	-2.14464	0.0001	0.0113094
ENSMUSG00000027533.10	Fabp5	26.5272	16.0182	-0.727761	-2.43622	0.00005	0.00618632
ENSMUSG00000027890.17	Gstm4	22.8624	40.384	0.820811	3.1403	0.00005	0.00618632
ENSMUSG00000028019.9	Pdgfc	2.88046	1.70807	-0.753934	-1.99822	0.0006	0.043428
ENSMUSG00000028238.6	Atp6v0d2	5.25254	9.46139	0.849037	2.4918	0.00005	0.00618632
ENSMUSG00000028383.17	Hsdl2	27.8303	19.1411	-0.539983	-2.08801	0.0003	0.0264805
ENSMUSG00000028479.18	Gne	79.8364	128.18	0.683054	2.04104	0.00065	0.0456767
ENSMUSG00000028715.2	Cyp4a14	391.915	237.782	-0.720899	-2.27606	0.00015	0.0159662
ENSMUSG00000028957.12	Per3	1.72562	11.0867	2.68365	4.12698	0.00005	0.00618632
ENSMUSG00000028976.10	Slc2a5	0.440546	1.76822	2.00493	1.65217	0.00065	0.0456767
ENSMUSG00000029009.17	Mthfr	7.11418	2.70437	-1.3954	-2.97286	0.00005	0.00618632
ENSMUSG00000029188.14	Slc34a2	1.55125	0.246171	-2.65571	-2.62671	0.00005	0.00618632
ENSMUSG00000029650.10	Slc46a3	31.8414	52.3096	0.71617	2.06244	0.0003	0.0264805
ENSMUSG00000029657.15	Hsph1	47.0702	27.7613	-0.761739	-2.01922	0.00025	0.0235
ENSMUSG00000030244.7	Gys2	36.9491	64.0714	0.794143	2.09027	0.00055	0.0404152
ENSMUSG00000030302.16	Atp2b2	4.35972	2.18107	-0.999203	-2.83779	0.00005	0.00618632
ENSMUSG00000030340.16	Scnn1a	6.11295	9.11203	0.575904	2.05878	0.00065	0.0456767
ENSMUSG00000030364.6	Clec2h	1.55662	4.31177	1.46986	2.18053	0.00005	0.00618632
ENSMUSG00000030483.14	Cyp2b10	17.2776	94.9368	2.45806	8.74658	0.00005	0.00618632
ENSMUSG00000031271.14	Serpina7	9.22525	4.97408	-0.891158	-2.09026	0.0004	0.033088
ENSMUSG00000031596.15	Slc7a2	85.9182	171.302	0.995503	2.42586	0.00005	0.00618632
ENSMUSG00000031762.7	Mt2	14.5776	52.8041	1.8569	4.62578	0.00005	0.00618632
ENSMUSG00000031765.8	Mt1	41.3184	148.541	1.84601	6.05154	0.00005	0.00618632
ENSMUSG00000031775.5	Pllp	6.14127	2.78882	-1.13888	-2.14469	0.00045	0.0359901
ENSMUSG00000032012.8	Nectin1	24.696	17.389	-0.506108	-1.94543	0.00055	0.0404152
ENSMUSG00000032115.14	Hyou1	66.9891	43.0138	-0.639125	-2.34774	0.00005	0.00618632
ENSMUSG00000032271.13	Nnmt	56.5371	127.246	1.17034	4.24758	0.00005	0.00618632
ENSMUSG00000032310.4	Cyp1a2	345.376	2354.78	2.76935	6.42721	0.00005	0.00618632
ENSMUSG00000032315.6	Cyp1a1	0.408235	21.3863	5.71114	10.8865	0.00005	0.00618632
ENSMUSG00000032348.6	Gsta4	52.469	81.8235	0.641049	2.47242	0.00005	0.00618632
ENSMUSG00000032575.16	Manf	237.772	126.916	-0.905701	-2.11863	0.0003	0.0264805
ENSMUSG00000032715.9	Trib3	3.62747	8.68618	1.25976	2.03279	0.00035	0.029457
ENSMUSG00000032724.5	Abtb2	5.87529	3.77695	-0.637439	-2.04753	0.0004	0.033088
ENSMUSG00000032849.14	Abcc4	1.71548	3.77068	1.13622	2.61385	0.00005	0.00618632
ENSMUSG00000032902.1	Slc16a1	18.9328	10.1797	-0.8952	-3.40735	0.00005	0.00618632
ENSMUSG00000032932.15	Hspa13	14.303	9.86525	-0.535886	-1.97593	0.00025	0.0235
ENSMUSG00000033107.6	Rnf125	122.257	74.8678	-0.707494	-2.81318	0.00005	0.00618632
ENSMUSG00000033581.17	Igf2bp2	1.66105	0.509047	-1.70623	-1.12591	0.0003	0.0264805
ENSMUSG00000034774.6	Dsg1c	1.07675	2.19221	1.0257	2.76946	0.0001	0.0113094
ENSMUSG00000034837.12	Gnat1	12.5088	21.0651	0.751915	2.1181	0.00035	0.029457
ENSMUSG00000035049.4	Rrp12	2.74802	1.48642	-0.886549	-2.6113	0.00005	0.00618632
ENSMUSG00000035372.2	1810055G	6.32408	10.8725	0.781761	1.96938	0.00035	0.029457
ENSMUSG00000035686.8	Thrsp	107.955	205.081	0.925768	3.34836	0.00005	0.00618632
ENSMUSG00000035828.11	Pim3	5.46211	9.62427	0.81722	2.71331	0.00005	0.00618632
ENSMUSG00000035944.17	Ttc38	14.0742	20.1391	0.516941	1.96377	0.00055	0.0404152
ENSMUSG00000036110.14	Slc17a2	47.9669	31.78	-0.59392	-2.07519	0.00015	0.0159662
ENSMUSG00000036957.8	Lrfn3	2.96637	1.17429	-1.33691	-3.36685	0.00005	0.00618632
ENSMUSG00000037095.8	Lrg1	67.2168	47.361	-0.505121	-1.98627	0.00065	0.0456767

ENSMUSG00000037157.8	Il22ra1	3.93685	2.30756	-0.770677	-2.21827	0.0002	0.0194309
ENSMUSG00000037379.7	Spon2	4.43994	1.82471	-1.28287	-2.45754	0.00005	0.00618632
ENSMUSG00000037583.2	Nr0b2	25.807	16.3589	-0.657683	-2.30236	0.0002	0.0194309
ENSMUSG00000037679.9	Inf2	14.5959	21.2562	0.542318	1.95943	0.0005	0.0385
ENSMUSG00000038244.14	Mical2	7.57323	4.32506	-0.808189	-2.30005	0.00005	0.00618632
ENSMUSG00000038415.10	Foxq1	3.1372	4.80063	0.613744	2.07957	0.00045	0.0359901
ENSMUSG00000038418.7	Egr1	8.53806	14.7592	0.789639	2.33622	0.00015	0.0159662
ENSMUSG00000038550.10	Ciart	0.635327	4.26202	2.74597	2.5058	0.00005	0.00618632
ENSMUSG00000038702.6	Dsel	0.318647	1.1368	1.83495	1.59147	0.0005	0.0385
ENSMUSG00000038768.8	9130409I	1.69012	3.3601	0.991375	2.38357	0.0002	0.0194309
ENSMUSG00000039395.8	Mreg	31.446	22.0227	-0.513883	-2.00407	0.0005	0.0385
ENSMUSG00000039533.8	Mmd2	1.90734	4.59768	1.26934	2.91012	0.00005	0.00618632
ENSMUSG00000039745.8	Htatip2	13.6124	21.7983	0.679289	2.28578	0.0001	0.0113094
ENSMUSG00000039886.8	Tmem12(	16.7696	27.8392	0.731267	2.68188	0.00005	0.00618632
ENSMUSG00000040127.13	Sdr9c7	19.4072	11.0266	-0.815607	-2.73366	0.00005	0.00618632
ENSMUSG00000040128.9	Pnrc1	65.4718	42.3024	-0.630135	-2.33326	0.00005	0.00618632
ENSMUSG00000040264.10	Gbp2b	2.41906	1.40646	-0.782373	-1.95544	0.0007	0.0487173
ENSMUSG00000040562.12	Gstm2	44.3194	85.0048	0.939604	3.60356	0.00005	0.00618632
ENSMUSG00000041324.14	Inhba	9.86411	3.40919	-1.53276	-3.38139	0.00005	0.00618632
ENSMUSG00000041698.11	Slco1a1	51.4801	33.2839	-0.62919	-2.3143	0.00005	0.00618632
ENSMUSG00000042115.4	Klhdc8a	0.80677	0.334395	-1.2706	-2.44981	0.00025	0.0235
ENSMUSG00000042363.14	Lgalsl	8.00763	4.41853	-0.857811	-2.18413	0.00005	0.00618632
ENSMUSG00000042622.14	Maff	1.85114	4.3513	1.23303	2.48105	0.00005	0.00618632
ENSMUSG00000043445.7	Pgp	4.53206	2.65663	-0.770568	-2.30203	0.00005	0.00618632
ENSMUSG00000044071.8	Tafa2	0.48376	1.16023	1.26205	2.303	0.0003	0.0264805
ENSMUSG00000044847.13	Lsm11	0.880467	0.334164	-1.39771	-2.60413	0.00005	0.00618632
ENSMUSG00000045287.6	Rtn4rl1	6.68976	3.11675	-1.10191	-3.68259	0.00005	0.00618632
ENSMUSG00000046402.10	Rbp1	2.23594	3.74793	0.745215	2.09243	0.0003	0.0264805
ENSMUSG00000046541.9	Zfp526	1.73728	3.00717	0.791579	2.28551	0.0001	0.0113094
ENSMUSG00000047617.11	Paxx	39.0765	17.0249	-1.19866	-2.96755	0.00005	0.00618632
ENSMUSG00000052305.6	Hbb-bs	63.8974	36.6592	-0.80158	-2.85373	0.00005	0.00618632
ENSMUSG00000052496.5	Pkdrej	0.475661	1.0218	1.10311	2.72703	0.00005	0.00618632
ENSMUSG00000052676.16	Zmat1	4.08129	6.4258	0.654851	2.13824	0.00025	0.0235
ENSMUSG00000052684.4	Jun	7.97305	4.26725	-0.901823	-3.1051	0.00005	0.00618632
ENSMUSG00000053113.3	Socs3	2.49474	5.38121	1.10904	2.11745	0.0003	0.0264805
ENSMUSG00000053559.13	Smagp	31.1285	19.9458	-0.642154	-2.13389	0.00035	0.029457
ENSMUSG00000054191.8	Klf1	1.62248	3.2131	0.985766	2.18554	0.00045	0.0359901
ENSMUSG00000054277.8	Arfgap3	4.95607	2.07293	-1.25753	-2.8446	0.00005	0.00618632
ENSMUSG00000054417.5	Cyp3a44	25.8573	17.1078	-0.595916	-2.16753	0.0002	0.0194309
ENSMUSG00000054659.13	Pm20d2	3.10156	1.32451	-1.22753	-2.48902	0.0002	0.0194309
ENSMUSG00000054827.12	Cyp2c50	357.009	627.067	0.812659	2.57099	0.00005	0.00618632
ENSMUSG00000055116.8	Arntl	9.41997	3.72741	-1.33755	-3.70408	0.00005	0.00618632
ENSMUSG00000055254.15	Ntrk2	1.32876	2.94734	1.14933	1.80865	0.0003	0.0264805
ENSMUSG00000056666.13	Retsat	163.179	84.9098	-0.942452	-2.9787	0.00005	0.00618632
ENSMUSG00000056749.7	Nfil3	11.3496	6.37484	-0.832181	-2.80945	0.00005	0.00618632
ENSMUSG00000057069.7	Ero1lb	12.7588	7.57204	-0.752743	-2.69188	0.00005	0.00618632
ENSMUSG00000057933.10	Gsta2	14.8876	36.6186	1.29846	4.13678	0.00005	0.00618632
ENSMUSG00000058135.12	Gstm1	591.115	1077.86	0.866655	2.73107	0.00005	0.00618632
ENSMUSG00000058454.15	Dhcr7	16.2573	24.4437	0.588377	1.73799	0.00045	0.0359901
ENSMUSG00000058569.8	Tmed9	27.8989	18.8487	-0.565745	-2.03359	0.00055	0.0404152
ENSMUSG00000058571.11	Gpc6	0.925695	2.30111	1.31372	2.76731	0.00005	0.00618632

ENSMUSG00000058672.7	Tubb2a	60.0095	29.3901	-1.02986	-3.68327	0.00005	0.00618632
ENSMUSG00000059060.15	Rad51b	2.96318	0.790659	-1.90602	-2.70012	0.00005	0.00618632
ENSMUSG00000060317.9	Acnat2	62.994	36.0946	-0.803432	-3.04246	0.00005	0.00618632
ENSMUSG00000060550.16	H2-Q7	26.9214	17.4807	-0.622989	-2.11728	0.0002	0.0194309
ENSMUSG00000060803.6	Gstp1	52.2482	94.5054	0.855015	3.20267	0.00005	0.00618632
ENSMUSG00000060807.7	Serpina6	169.985	262.86	0.628886	2.32333	0.00005	0.00618632
ENSMUSG00000061080.11	Lsamp	1.22575	0.291018	-2.07448	-1.14479	0.0001	0.0113094
ENSMUSG00000061601.15	Pclo	0.57566	0.977399	0.763729	2.10847	0.00035	0.029457
ENSMUSG00000061825.10	Ces2c	4.3022	11.1216	1.37022	4.14522	0.00005	0.00618632
ENSMUSG00000063415.12	Cyp26b1	6.19951	2.65142	-1.22539	-4.09556	0.00005	0.00618632
ENSMUSG00000064225.6	Paqr9	57.3054	30.826	-0.894525	-3.17638	0.00005	0.00618632
ENSMUSG00000064605.3	Gm22220	0	7.00551	#NUM!	#NUM!	0.00005	0.00618632
ENSMUSG00000066154.11	Mup3	2026.5	1252.6	-0.694063	-2.02644	0.00045	0.0359901
ENSMUSG00000067199.4	Frat1	3.39578	1.93858	-0.808739	-2.24788	0.0002	0.0194309
ENSMUSG00000067219.9	Nipal1	4.44909	8.25715	0.892133	2.59416	0.00005	0.00618632
ENSMUSG00000067225.2	Cyp2c54	161.282	296.593	0.878904	3.09255	0.00005	0.00618632
ENSMUSG00000067279.3	Ppp1r3c	27.4578	14.4551	-0.925639	-3.55848	0.00005	0.00618632
ENSMUSG00000069668.4	Sult3a1	96.5726	152.327	0.657483	2.4394	0.00005	0.00618632
ENSMUSG00000069917.7	Hba-a2	15.9522	7.92925	-1.0085	-2.53543	0.00005	0.00618632
ENSMUSG00000069919.7	Hba-a1	123.857	80.1852	-0.627271	-2.30735	0.0002	0.0194309
ENSMUSG00000070348.5	Ccnd1	28.8011	18.0061	-0.677632	-2.00581	0.00015	0.0159662
ENSMUSG00000070644.13	Etnk2	62.1735	97.5737	0.650192	2.3878	0.00005	0.00618632
ENSMUSG00000072949.6	Acot1	33.5979	19.9522	-0.751821	-2.2701	0.0002	0.0194309
ENSMUSG00000073700.3	Klhl21	4.84991	8.7584	0.85271	3.05752	0.00005	0.00618632
ENSMUSG00000074240.4	Cib3	0.143641	2.40529	4.06566	2.29099	0.00035	0.029457
ENSMUSG00000074277.4	Phldb3	4.05555	2.40923	-0.751325	-1.90668	0.00045	0.0359901
ENSMUSG00000075602.10	Ly6a	9.16001	4.67716	-0.969716	-2.31759	0.00005	0.00618632
ENSMUSG00000078566.8	Bnip3	89.9067	133.144	0.566486	1.97231	0.00055	0.0404152
ENSMUSG00000078650.2	G6pc	117.921	34.0649	-1.79147	-6.18411	0.00005	0.00618632
ENSMUSG00000078672.2	Mup20	28.4851	45.4009	0.672516	2.49254	0.00005	0.00618632
ENSMUSG00000078798.4	Sult2a1	56.1121	88.0628	0.650222	2.29294	0.0002	0.0194309
ENSMUSG00000078964.2	Ces1b	38.6623	59.9889	0.633769	2.50962	0.00005	0.00618632
ENSMUSG00000081207.4	Gm13775	12.4095	21.5678	0.797432	2.15377	0.00005	0.00618632
ENSMUSG00000083409.1	Gm11340	7.21515	2.24671	-1.68321	-2.46551	0.00055	0.0404152
ENSMUSG00000083832.1	Gm13771	1.8277	0	#NUM!	#NUM!	0.0005	0.0385
ENSMUSG00000084923.1	Gm15611	21.0683	6.28033	-1.74616	-3.69593	0.00005	0.00618632
ENSMUSG00000085445.1	Gm16348	0.992266	3.40219	1.77767	3.9325	0.00005	0.00618632
ENSMUSG00000090298.2	Sult3a2	3.37105	7.75229	1.20143	2.72803	0.00005	0.00618632
ENSMUSG00000090877.3	Hspa1b	1.20366	0.247192	-2.28373	-3.46215	0.00005	0.00618632
ENSMUSG00000092075.1	Serpina4-	21.3086	5.73997	-1.89232	-5.72874	0.00005	0.00618632
ENSMUSG00000093183.2	Gm25687	30.7806	63.7545	1.0505	2.67769	0.00005	0.00618632
ENSMUSG00000099021.1	Rn7s1	700.234	447.929	-0.644568	-2.2057	0.0003	0.0264805
ENSMUSG00000100277.8	1810053E	0.727864	4.99681	2.77927	2.15033	0.00005	0.00618632
ENSMUSG00000106069.1	Gm6135	34.0333	18.6619	-0.866848	-2.29436	0.00015	0.0159662
ENSMUSG00000106397.1	Gm21049	4.50211	8.69691	0.949903	2.48844	0.0001	0.0113094
ENSMUSG00000107369.1	Gstm2-ps	5.28283	9.53136	0.851371	2.01229	0.0007	0.0487173
ENSMUSG00000107451.1	Gm44421	1.80148	3.62615	1.00925	2.14888	0.0006	0.043428
ENSMUSG00000108822.1	Gm44787	1.69451	5.98364	1.82015	2.27612	0.00005	0.00618632
ENSMUSG00000110353.1	Gm33543	7.64038	13.1396	0.782206	2.39977	0.00005	0.00618632
ENSMUSG00000110439.1	Mup22	99.9007	68.6497	-0.541243	-2.05099	0.00065	0.0456767
ENSMUSG00000111923.1	Gm34777	2.67348	4.37875	0.711799	2.03435	0.0005	0.0385

ENSMUSG00000113387.1	Gm31508	1.24582	0.612387	-1.02458	-2.20024	0.0004	0.033088
ENSMUSG00000115509.1	Gm49012	1.8745	0.444212	-2.07719	-3.09822	0.0001	0.0113094
ENSMUSG00000117879.1	AC138228	8.67119	4.72504	-0.875903	-2.12505	0.0003	0.0264805
ENSMUSG00000118017.1	AC15791(	211.714	108.509	-0.964301	-1.99521	0.0005	0.0385

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000004038.9	Gstm3	38.0431	58.9022	0.630687	2.46013	0.00005	0.0145745
ENSMUSG00000017119.19	Nbr1	76	156.094	1.03834	3.08994	0.00005	0.0145745
ENSMUSG00000018427.7	Ypel2	5.3982	3.31232	-0.704637	-2.41028	0.00005	0.0145745
ENSMUSG00000020027.18	Socs2	13.2242	6.3375	-1.0612	-2.2998	0.00005	0.0145745
ENSMUSG00000020429.7	Igfbp1	53.6002	26.8102	-0.999456	-3.89039	0.00005	0.0145745
ENSMUSG00000020893.17	Per1	3.68334	6.25289	0.76351	2.15347	0.00005	0.0145745
ENSMUSG00000021288.18	Klc1	12.9409	6.37187	-1.02214	-2.07132	0.00015	0.0387736
ENSMUSG00000021453.2	Gadd45g	4.11008	1.45737	-1.4958	-2.59523	0.00005	0.0145745
ENSMUSG00000022508.5	Bcl6	2.65652	4.42275	0.735406	2.26063	0.0002	0.0472414
ENSMUSG00000022512.3	Cldn1	26.1421	15.2533	-0.777248	-3.02367	0.00005	0.0145745
ENSMUSG00000024987.6	Cyp26a1	7.22284	16.3768	1.18101	3.76685	0.00005	0.0145745
ENSMUSG00000026822.14	Lcn2	3.61183	6.99576	0.953752	2.06076	0.0002	0.0472414
ENSMUSG00000026839.17	Upp2	141.068	212.088	0.588275	2.19764	0.0002	0.0472414
ENSMUSG00000026980.15	Ly75	1.02455	1.86615	0.865078	2.35758	0.0001	0.0268627
ENSMUSG00000027533.10	Fabp5	20.9053	11.7917	-0.826097	-2.64221	0.00005	0.0145745
ENSMUSG00000027796.2	Smad9	3.96217	1.89784	-1.06193	-3.47194	0.00005	0.0145745
ENSMUSG00000028445.7	Enho	5.8256	2.52464	-1.20633	-2.74623	0.00005	0.0145745
ENSMUSG00000029272.8	Sult1e1	3.01955	12.0294	1.99416	4.46773	0.00005	0.0145745
ENSMUSG00000032310.4	Cyp1a2	580.244	1032.94	0.832029	2.805	0.00005	0.0145745
ENSMUSG00000035686.8	Thrsp	75.4226	108.929	0.530321	2.11579	0.00015	0.0387736
ENSMUSG00000036594.15	H2-Aa	12.3664	24.7286	0.999753	3.13856	0.00005	0.0145745
ENSMUSG00000037847.14	Nmrk1	8.65751	16.9132	0.966125	2.32446	0.00005	0.0145745
ENSMUSG00000038418.7	Egr1	13.1471	6.28833	-1.064	-3.7676	0.00005	0.0145745
ENSMUSG00000038656.5	Cyp3a16	7.12851	15.836	1.15154	3.67862	0.00005	0.0145745
ENSMUSG00000039457.4	Ppl	4.08077	7.12185	0.803411	2.80195	0.00005	0.0145745
ENSMUSG00000041698.11	Slco1a1	21.356	5.97873	-1.83673	-5.94679	0.00005	0.0145745
ENSMUSG00000050423.11	Ppp1r3g	2.1755	0.629848	-1.78827	-2.64187	0.00005	0.0145745
ENSMUSG00000050445.4	Cyp8b1	29.9766	12.9283	-1.2133	-3.83764	0.00005	0.0145745
ENSMUSG00000055116.8	Arntl	4.50112	1.45834	-1.62596	-3.46099	0.00005	0.0145745
ENSMUSG00000057346.12	Apol9a	19.3931	32.688	0.753217	2.48492	0.00005	0.0145745
ENSMUSG00000057897.14	Camk2b	0.84208	2.11891	1.33129	1.48241	0.0002	0.0472414
ENSMUSG00000061825.10	Ces2c	4.35545	8.60041	0.981582	2.97034	0.00005	0.0145745
ENSMUSG00000063388.5	BC023105	3.59428	6.85076	0.930563	2.34984	0.0001	0.0268627
ENSMUSG00000064225.6	Paqr9	35.9574	23.9919	-0.583741	-2.37141	0.00005	0.0145745
ENSMUSG00000070811.6	Sult2a2	45.0135	98.3588	1.12769	3.25888	0.00005	0.0145745
ENSMUSG00000072849.10	Serpina1e	78.1579	34.9136	-1.1626	-4.35291	0.00005	0.0145745
ENSMUSG00000073421.6	H2-Ab1	23.9638	51.1132	1.09284	2.55741	0.00005	0.0145745
ENSMUSG00000074375.3	Sult2a3	0.913931	5.76955	2.6583	3.99495	0.0001	0.0268627
ENSMUSG00000075551.4	Cyp3a41a	26.1917	45.374	0.79276	3.08305	0.00005	0.0145745
ENSMUSG00000075552.4	Cyp3a41b	2.76118	6.39617	1.21192	3.37149	0.00005	0.0145745
ENSMUSG00000078650.2	G6pc	83.6587	38.114	-1.1342	-4.05012	0.00005	0.0145745
ENSMUSG00000078798.4	Sult2a1	36.972	91.5233	1.30771	4.24884	0.00005	0.0145745
ENSMUSG00000078799.5	Sult2a5	2.28821	5.90122	1.36679	2.19044	0.0002	0.0472414
ENSMUSG00000078817.4	Nlrp12	6.13793	3.48939	-0.814775	-2.95155	0.00005	0.0145745
ENSMUSG00000082008.1	Gm12390	0	2.18739	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000086316.8	Nbdy	0.965126	9.08573	3.23481	2.3883	0.00005	0.0145745
ENSMUSG00000092674.2	Gm24105	94.9427	153.292	0.691157	2.26807	0.00005	0.0145745
ENSMUSG00000093183.2	Gm25687	16.9584	55.347	1.7065	3.05133	0.00005	0.0145745
ENSMUSG00000096768.8	Gm47283	21.0555	8.4086	-1.32426	-3.46356	0.00005	0.0145745
ENSMUSG00000099901.1	Zbed4-ps2	3.94207	10.8342	1.45857	2.99773	0.00005	0.0145745
ENSMUSG00000101397.6	Mug-ps1	34.2915	22.1456	-0.630835	-2.52439	0.00005	0.0145745

ENSMUSG00000105192.1	Gm42796	9.81164	3.82683	-1.35835	-2.85412	0.00005	0.0145745
ENSMUSG00000107185.1	Gm42642	1.32544	0	#NUM!	#NUM!	0.0001	0.0268627
ENSMUSG00000109089.1	4833411C	13.8725	7.63832	-0.860895	-2.57638	0.00005	0.0145745
ENSMUSG00000110439.1	Mup22	64.7271	39.1905	-0.723867	-2.61227	0.00005	0.0145745
ENSMUSG00000110838.1	Gm47789	1.24793	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000111253.1	Gm34654	1.07187	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000117780.1	AC127342	13.9016	5.9063	-1.23493	-4.21178	0.00005	0.0145745

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000003053.17	Cyp2c29	673.766	1232.86	0.871696	2.7636	0.00005	0.0237172
ENSMUSG00000025002.5	Cyp2c55	5.10794	9.57033	0.905826	2.8894	0.00005	0.0237172
ENSMUSG00000026185.8	Igfbp5	4.14362	7.52489	0.860778	3.06263	0.00005	0.0237172
ENSMUSG00000028238.6	Atp6v0d2	14.2949	8.46584	-0.755773	-2.57671	0.0001	0.0404588
ENSMUSG00000030428.16	Ttyh1	7.83723	20.5459	1.39044	3.46049	0.00005	0.0237172
ENSMUSG00000030483.14	Cyp2b10	18.4894	34.553	0.902114	3.34575	0.00005	0.0237172
ENSMUSG00000032310.4	Cyp1a2	573.897	1767.5	1.62285	4.7819	0.00005	0.0237172
ENSMUSG00000033107.6	Rnf125	119.634	73.9456	-0.694086	-2.68283	0.00005	0.0237172
ENSMUSG00000035202.8	Lars2	37.9931	16.2798	-1.22265	-3.96694	0.00005	0.0237172
ENSMUSG00000037583.2	Nr0b2	19.8513	11.5096	-0.786389	-2.59725	0.0001	0.0404588
ENSMUSG00000038656.5	Cyp3a16	7.05363	15.3354	1.12043	3.49577	0.00005	0.0237172
ENSMUSG00000050445.4	Cyp8b1	29.6178	11.0736	-1.41934	-4.51314	0.00005	0.0237172
ENSMUSG00000054417.5	Cyp3a44	19.7219	34.2151	0.794836	3.04706	0.00005	0.0237172
ENSMUSG00000055116.8	Arntl	4.44971	1.11565	-1.99583	-4.29871	0.00005	0.0237172
ENSMUSG00000060803.6	Gstp1	38.6763	66.8057	0.788521	2.91206	0.00005	0.0237172
ENSMUSG00000061825.10	Ces2c	4.30826	10.0339	1.21971	3.75254	0.00005	0.0237172
ENSMUSG00000069917.7	Hba-a2	12.5054	28.9749	1.21225	3.16461	0.00005	0.0237172
ENSMUSG00000069919.7	Hba-a1	161.435	257.664	0.674535	2.60695	0.00005	0.0237172
ENSMUSG00000072849.10	Serpina1e	77.2634	33.2336	-1.21714	-4.58994	0.00005	0.0237172
ENSMUSG00000073940.3	Hbb-bt	11.4866	32.257	1.48966	4.17862	0.00005	0.0237172
ENSMUSG00000075551.4	Cyp3a41a	25.9157	41.7969	0.689571	2.51749	0.0001	0.0404588
ENSMUSG00000075552.4	Cyp3a41b	2.73222	5.71036	1.06351	2.88173	0.00005	0.0237172
ENSMUSG00000078650.2	G6pc	82.715	52.4814	-0.656343	-2.57516	0.0001	0.0404588
ENSMUSG00000078798.4	Sult2a1	36.5984	71.0306	0.95666	3.13829	0.00005	0.0237172
ENSMUSG00000083563.1	Gm13340	22.2303	36.8976	0.731	2.47186	0.0001	0.0404588
ENSMUSG00000092674.2	Gm24105	93.8984	264.708	1.49523	4.56281	0.00005	0.0237172
ENSMUSG00000096768.8	Gm47283	20.8212	9.60095	-1.1168	-3.03589	0.00005	0.0237172
ENSMUSG00000096887.2	Gm20594	84.8472	147.632	0.799063	2.84097	0.00005	0.0237172
ENSMUSG00000098973.1	Mir6236	2424.83	1036.7	-1.22589	-4.1389	0.00005	0.0237172
ENSMUSG00000100131.1	Gm28439	7.92885	17.6712	1.15622	2.9385	0.00005	0.0237172
ENSMUSG00000101111.1	Gm28437	27.3548	48.503	0.826281	2.816	0.00005	0.0237172
ENSMUSG00000102189.1	Gm37194	1.33501	3.28318	1.29824	3.26943	0.00005	0.0237172
ENSMUSG00000115420.1	Rmrp	783.954	1427.45	0.864595	2.95006	0.00005	0.0237172
ENSMUSG00000117780.1	AC127342	13.7433	7.49599	-0.874538	-3.05459	0.00005	0.0237172

Table S2A. Liver metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	0.6417779	0.7530381	0.8854124	1.3165750	1.0407458	0.7608884	0.9882787	0.7862970	1.0625771	1.1283548	1.2155264	1.1977029	1.1177079	1.0111845	0.9166488	1.1527351	0.5878772	1.3592881	0.8895624	1.4278042	0.6871709	0.9504117	0.5052311	0.9326832
Indole-3-acetic.acid	0.7860392	1.9509565	0.5580886	1.5278171	1.0873190	0.7463817	0.1771168	0.3526087	0.4630552	0.5291279	0.7148218	0.4862421	0.5835993	0.4962891	0.7906378	1.5020283	0.6540461	1.0075090	1.0404164	0.8920219	0.2602962	0.5700573	0.5769496	0.6458184
Indole-3-pyruvic.acid	0.06424609	1.10713323	0.19021050	0.33843027	0.11897162	0.46282540	0.37132059	0.22765562	0.18087326	0.38830899	0.02884164	0.26659506	0.14896618	0.51208752	0.16279090	0.28747783	0.37848709	0.37283283	0.00000000	0.14392771	0.29731054	1.18302681	0.16473559	0.51285387
Kynurenine	1.5130420	1.8160458	1.1177367	3.3235912	1.4236657	1.8332443	0.4968082	0.4627796	1.0845344	1.1908755	0.8681831	1.3064311	1.4310919	1.0449380	0.7998276	2.0758060	0.9268621	1.9954938	1.5519350	2.5454728	1.1179864	2.3883236	0.7527254	1.1935632
2-Deoxycytidine	0.1456107	0.2046070	0.1144417	0.2018454	0.2570833	0.1523639	0.1548636	0.2199208	0.2156768	0.4964199	0.3365320	0.2922682	0.4379804	0.2772534	0.1278656	0.3985392	0.1284519	0.4021005	0.3026561	0.2529262	0.1450090	0.1766973	0.2007113	0.5602648
2-aminoadipic.acid	0.4075929	1.8351217	0.9447126	1.2758676	0.8124402	0.8410186	0.4128866	0.5227665	1.3971905	0.9069514	1.2938552	0.6817271	0.8004980	0.8948402	0.7905779	1.0971095	1.0229457	1.4079170	1.8391106	1.8948830	5.3693974	5.3069206	0.8495688	1.1904178
2-deoxyguanosine	0.58479568	0.00000000	0.00000000	0.44162009	0.58363951	0.00000000	1.63457253	0.37970606	0.00000000	0.38769672	0.06838577	0.19997020	0.80554615	0.29129296	0.00000000	0.23430805	0.06706320	1.46333000	0.00000000	0.15525769	0.00000000	0.00000000	0.00000000	0.52384648
3-Aminoisobutyric.acid	0.3103612	0.2316226	0.2791112	0.3631104	0.2398946	0.2452838	0.2880905	0.1962715	0.3782312	0.3797402	0.3751967	0.2140135	0.2781475	0.3356190	0.1825315	0.3856304	0.1752509	0.4551243	0.3276935	0.3667051	0.3028023	0.3385240	0.2649583	0.2924743
3-Hydroxybutyric.acid	1.7156741	0.6825009	1.6340875	0.7728069	0.6845594	3.0031276	1.4763494	1.4043569	1.8066952	0.5647619	0.8475344	1.0578820	1.6273289	2.9045689	1.5403997	1.5944642	0.5934880	0.8834803	0.6819804	0.8640724	0.8097863	0.9743788	1.3148739	1.5162630
4-Aminobutyric.acid	0.5156079	0.9141045	1.1005954	2.3476444	1.3140889	0.7357734	0.6096718	0.4719302	1.4989862	1.1886618	1.0745111	1.6027557	1.1806124	1.5513006	1.0620008	0.9948536	1.2875127	1.3189201	2.1056291	2.6841771	1.0229754	1.3207144	0.4810400	1.0543936
5-Aminolevulinic.acid	0.2867715	0.8398926	0.2810464	0.2019449	0.1020569	0.1164548	0.2761496	0.1963395	0.2273984	0.1812200	0.3716822	0.2694858	0.2225276	0.2574289	0.3098547	0.4189624	0.1705895	0.4910491	0.4734825	0.3410167	0.8565262	0.8064531	0.3156030	0.4568366
5-Methylcytidine	2.6366484	2.3470198	0.7913250	3.1443083	4.0459524	1.9228826	0.8837537	2.5323469	0.7833072	1.5051036	2.2849148	2.9870170	2.6811237	2.1907469	1.9084163	3.1802859	1.1070842	2.1720066	2.3003041	2.3661019	1.8300040	3.8581447	1.5396344	1.0123362
7-ketocholesterol	1.2891896	1.0073455	0.8360030	0.4664388	1.2795914	1.3383909	1.0546935	1.9164554	0.4051727	0.6767182	0.4498655	0.7065973	0.6043564	1.3701550	1.0951610	1.3300680	1.3873236	1.1263964	0.3944428	0.9683976	0.9645003	0.7742208	0.6170155	2.0484274
Acetyl-L-glutamine	0.4553014	0.4776746	0.4556176	1.1360893	0.4899839	0.4115659	0.4724127	0.3995740	0.7519312	0.7612600	0.5757849	0.8012261	0.9084725	0.7581108	0.5658879	0.6871090	0.4090363	0.6004718	0.4349892	0.7548255	0.3635997	0.5794367	0.3717956	0.6783111
Acetylcarnitine	0.02915257	0.05742605	0.04085568	0.04646320	0.01610918	0.02863787	0.02092485	0.04034642	0.02849962	0.03521710	0.03001347	0.03903095	0.06032182	0.06379381	0.03554116	0.08904216	0.13924858	0.08820948	0.25276956	0.11555283	0.15110799	0.11136802	0.18095977	0.19759626
Acetylglucosamine	1.3115664	1.2280059	1.0550751	1.8277008	1.5382448	0.8317039	0.9006399	0.7437013	0.8639561	1.1169542	1.2680750	1.4683521	0.8830023	1.0020359	1.2230501	1.0899670	0.6023287	1.6330727	1.0205687	1.5326382	0.7522740	0.9907671	0.6387737	1.1292635
Acetylglycine	0.2617616	1.5929109	1.2342161	2.1902251	2.0066785	1.0029190	1.9138947	0.8145704	1.6919136	2.5442625	2.4643134	1.7957466	0.2814305	0.3470204	1.2344673	0.8244505	0.2272679	2.3645095	0.3638673	0.9529061	1.4823383	0.8343840	1.0978394	0.7816405
Acetylornithine	0.23480651	0.10218698	0.15858941	0.19771777	0.62851733	0.05134179	0.18836825	0.08521779	0.11193669	0.26567215	0.32023260	0.26012605	0.47490123	1.12893094	0.14985087	0.74458555	0.45819030	1.06512125	0.75622866	0.72796858	0.76879026	0.70500716	0.82648159	0.71440786
Adenosine	0.3581978	0.5481528	0.5538759	0.5637655	0.7135748	0.7417769	0.9125724	0.7036831	1.2996513	1.2692738	1.3658697	0.8970467	0.9973923	1.5460150	0.6196735	1.0165961	0.6620103	2.0082194	1.1925067	0.4137528	1.0192838	1.0090414	1.8101009	1.6507011
Adenosyl-L-homocysteine	0.3163094	0.6499900	0.5642770	0.6660210	0.7347727	0.6880711	0.7655124	0.5100250	1.0084109	1.0896944	1.0674588	0.8004986	0.6242744	1.0607179	0.5468198	0.8729612	0.5892073	1.5979238	1.2145764	1.4491398	0.8496154	1.1124521	0.8608683	1.2268764
Adenylosuccinate	0.03907467	0.10987980	0.07196339	0.18365262	0.02049657	0.18750397	0.10259660	0.10153863	0.17733045	0.22357127	0.13469431	0.08656620	0.13093812	0.10786607	0.06330485	0.11795322	0.09404531	0.17072564	0.16554603	0.07081627	0.25297802	0.31067335	0.16538933	0.14309574
Alanine	0.8571079	0.8937346	1.2829469	1.2536040	1.3312153	1.0258898	0.9927881	0.8043505	1.3840192	1.2575998	1.3394220	1.3339071	1.3476500	1.2322631	0.9589156	1.1416117	0.9940162	1.2597832	1.1339764	1.4759244	1.1721014	1.4205798	0.6686826	0.9158186
Aminoisobutyric.acid	0.4493258	0.5828958	0.6461483	0.8794325	0.4539889	0.6068997	0.5862818	0.4553500	0.4213689	1.0816655	0.7381336	1.2356525	0.4183226	0.2992163	0.3076177	0.5605960	0.5548940	1.4832715	1.2783811	1.3008123	1.1644110	1.2625703	1.0386166	0.6530749
Arginine	0.5230813	0.8326213	0.3829666	0.3855671	0.2697902	0.3039470	0.3348270	0.2517091	0.3584439	0.5363771	0.4821799	0.4340597	0.5603556	0.3996499	0.4430393	0.4462321	0.3594968	0.3102111	0.5864398	0.2758807	0.1643636	0.2102865	0.2007999	0.3539812
Asparagine	0.8842260	0.8152583	0.9024042	1.3833165	1.2449474	0.9768765	1.1941756	0.9351111	0.9971121	1.3182055	1.2117728	1.3431893	1.1858922	0.9978230	1.2058328	1.2294066	0.6536824	1.4452643	1.2063691	1.3491411	0.8293748	1.0875278	0.7053539	0.9158058
Aspartic.acid	0.3762233	0.4292970	0.2857379	0.5451212	0.4423451	0.3255798	0.4889660	0.4377361	0.4992604	0.6124258	0.6449889	0.4799587	0.5048493	0.4952580	0.4067786	0.5631700	0.2476733	0.7353890	0.5144635	0.4634559	0.2357814	0.3112372	0.4857510	0.4860391
Betaine	0.7509563	0.7301263	0.6645387	0.8280204	0.7483555	0.7586245	0.6799378	0.7332552	0.5995388	1.1140138	0.9279227	1.0862676	0.7167985	0.4884979	0.8491893	1.0252541	0.6586413	1.5355912	0.9498598	1.0125740	0.7907893	0.8387790	1.0066512	1.0111870
Carnitine	0.4638704	0.6540949	0.5326691	1.0417368	0.7563746	0.5297869	0.5900569	0.5139531	0.7313478	0.9329322	0.8872217	0.9785690	1.1477622	0.8874642	0.6541203	1.1244702	0.7064974	1.6744503	1.3159400	1.4626136	0.9617662	1.2497777	0.6554014	1.3367312
Carnosine	0.1379304	0.1837529	0.1527487	0.3168994	0.2416656	0.1920351	0.2827001	0.2258543	0.2003689	0.5326479	0.2786935	0.3996725	0.3411534	0.1948664	0.1848126	0.3064725	0.2054774	0.4477849	0.3000470	0.4893805	0.2089623	0.2489793	0.1568765	0.2635589
Choline	0.7764507	0.8191480	0.6335699	0.6340663	0.8203244	0.6701257	0.8159180	0.6395891	0.6805273	0.9335008	0.9493801	1.0877272	0.6584530	0.8890556	0.3250131	0.9338085	0.6925649	1.0695122	1.0062782	1.0230024	0.8411477	0.9132406	0.4218052	1.0180560
Citrulline	0.4214526	1.4571427	0.4513969	0.6357133	0.5489945	0.4507589	0.3650552	0.3008129	0.3946912	0.7066947	0.6170127	0.5663506	0.3569724	0.5146847	0.4069223	0.6087197	0.3548486	0.4907301	0.6420626	0.6432533	1.0133808	0.8909440	0.3728396	0.6870457
Creatine	0.4086522	1.8336104	0.4751913	0.5582335	0.5536743	0.4931385	0.5850576	0.4867122	0.5313360	0.7563221	0.6526906	0.7692563	0.5293707	0.6098790	0.4726509	0.7157762	0.6398291	0.8875395	0.8520455	0.9165180	0.5239349	0.6135616	0.4791432	0.8448273
Creatinine	0.5057162	0.8707744	0.4629378	0.6562094	0.6613873	0.5594884	0.5854751	0.4851771	0.5782317	0.7563661	0.8161167	0.8193643	0.8426159	1.0442179	0.6368156	0.9255601	0.6743669	0.9832099	1.0984917	1.1851292	1.0670715	1.4789607	0.5438834	1.0728971
Cystathionine	0.2459859	0.3683612	0.3431268	0.4048110	0.2935433	0.4965935	0.3682411	0.2695575	0.3493903	0.4215621	0.3267381	0.3072462	0.2838443	0.2927669	0.2830256	0.3648586	0.1816999	0.2010483	0.2689415	0.2830604	0.4150128	0.3916642	0.1232459	0.2743187
Cytidine	1.0704769	1.1045405	0.5452250	1.1143852	2.2242367	0.8437256	0.8379310	0.7302953	0.8250596	1.2351377	1.2415660	1.4356379	1.0721686	1.3694450	1.1486803	1.3431894	0.5011534	1.7333319	1.2794172	1.8635491	0.4951477	0.7534005	0.9403074	1.1735831
D2-phosphoglyceric.acid	0.3310944	0.5996730	0.5421477	0.5783187	0.4516969	0.6160839	0.5869482	0.8026354	0.5160980	1.7919010	1.3227615	0.7696889	0.8412157	0.9673621	0.5756555	0.7466133	0.4928834	0.5637712	1.2022054	1.3578467	0.5968598	0.8221555	0.7988284	1.3712116
Dimethylarginine	0.9740189	1.0761789	0.9286955	1.7805238	1.3582373	0.9595825	0.9619014	0.7611321	0.8233580	1.2680150	1.1986943	1.4689141	1.1321591	0.7743156	1.1449154	1.2622517	0.5733991	1.5776915	1.3679222	1.4523821	0.6839601	1.0027647	0.7136403	0.9098727
Dimethylglycine	0.4607362	0.6099623	0.5798673	0.8415445	0.4800336	0.5956410	0.6211296	0.4700505	0.4793892	0.9944620	0.7717746	1.1394720	0.4232337	0.3249359	0.3335234	0.5717760	0.5680419	1.2948865	1.2641046	1.2082976	0.9839331	1.1826156	0.9984687	0.6824968
Dopamine	0.6221969	0.9233208	1.7799437	2.9220513	0.8243819	1.2029912	1.5160785	1.6078648	2.8711232	2.7599863	3.4069383	2.7410775	2.4948055	1.5058086	1.1234065	1.5403673	1.5234156	1.8589505	2.4006292	2.3461096	1.2409628	0.7001368	0.6745019	1.0942887
Folic.acid	0.2239471	0.7487736	1.0598652	1.7528520	0.5643385	0.1206645	2.1591450	1.4651981	1.3696177	1.7913465	0.6001736	1.0758190	1.3699781	2.3413983	1.4799907	1.6345688	1.0877975	3.9654829	0.6068767	2.1335282	1.1901542	1.7785697	2.3565170	0.7551478
Folinic.acid	0.7674852	1.6268925	1.0852252	0.7893310	1.2473922	0.7184188	1.4028261	0.6030513	0.9306193	0.9450751	1.3213389	0.8735870	3.0728728	1.7100075	1.2098770	2.9880290	0.8017804	1.8047687	1.0751854	0.9404757	0.2533398	0.4022695	1.6236487	1.0310206
GDP	0.2824551	0.4104324	0.6581356	0.6326138	0.5607096	0.6279206	0.9077773	0.7229344	0.7825835	1.1341158	0.8687443	0.7987579	0.8721362	0.8370757	0.5121924	0.7037107	0.6499428	0.7694018	0.9147735	1.0046965	0.7964523	0.8625709	0.5791299	0.8675360
Glucosamine	2.0459784	1.8586589	0.9763065	2.3173203	2.7368014	1.2832705	1.5635184	1.1995193	0.8349244	1.1213999	1.3293286	1.9080310	0.7805758	1.1948329	2.3484920	1.5326383	0.5317680	2.6586547	0.9757728	1.2297610	0.5173460	1.3240417	0.6768534	1.0608675
Glutamic.acid	0.3867288	0.6585914	0.2594397	0.6983488	0.4513374	0.4237792	0.2899086	0.2583647	0.4606375	0.4076183	0.4274454	0.4655869	0.5175806	0.6526626	0.7723591	0.7010507	0.4853293	1.0569855	0.8696258	0.9357680	0.3399974	0.5327368	0.6822027	0.9084132
Glutathione.oxidized	0.8428468	0.9934283	0.8284747	1.2904800	1.1288540	0.9433971	0.9309067	0.8341607	0.7050951	1.7922744	1.5380908	1.2666532	1.1660800	1.1961860	0.7966210	1.7078418	1.1142226	1.7799967	1.4630840	1.4101672	0.9523861	1.1156960	0.7591486	2.1125401
Glutathione.reduced	0.8328146	0.9973012	0.9263039	1.1861743	1.0307202	0.9995192	0.8701441	0.8078348	0.7663752	1.5181023	1.4216837	1.1157582	1.0358050	1.2074976	0.8834492	1.4707737	1.1736260	1.5332945	1.3728646	1.2931630	0.9865631	0.9085870	0.8146667	1.6901167
Glycerol.3-phosphate	0.4728707	0.9220561	0.5403641	0.4929494	1.1101013	0.6136874	0.5507888	0.5474192	0.5800091	0.8919979	0.6383870	0.8603690	0.9634107	1.0130460	1.1563273	0.9250990	1.3260552	2.9327821	1.8083472	1.8427419	0.4780161	0.5059864	2.0318877	0.9390341
Glycine	0.8730863	1.3705099	0.9158263	1.2231668	1.3027717	0.9159551	1.0228547	0.7828555	1.2443312	1.3262574	1.2728658	1.2074510	0.8440967	0.9126339	0.8707803	0.9282927	0.6426631	1.1847707	0.9643004	1.1552033	1.0063595	1.2029528	0.7578952	0.9970674
Glycocyamine	0.4700012	1.6812018	0.8093291	0.8862727	0.6447139	0.6131750	0.7258364	0.4538833	1.4261794	0.9214418	0.9556441	0.9071715	0.5539589	0.7430127	0.6726305	0.7824019	0.6505485	0.9903394	0.9944325	1.4137428	1.1282637	1.3375366	0.6221903	0.5836888
Glycylproline	1.8354316	2.4923578	2.6578428	3.1714119	2.4727788	1.9152073	1.8255724	1.7998914	1.5739886	2.8731885	2.3700045	2.6665893	2.2624526	1.4006515	1.9016969	1.9771679	0.8534983	2.6499820	2.2516603	2.3700619	1.9364397	2.2477298	0.8725860	1.5342976
Guanine	0.17621558	0.02278745	0.15415498	0.29704774	0.21663483	0.08342667	0.18120350	0.32614899	0.24036579	0.20259922	0.38402340	0.28300992	0.43238992	0.27333795	0.16728693	0.38415723	0.22893049	0.42081721	0.22346236	0.41695774	0.20548302	0.27833217	0.47305873	0.55053296
Guanosine	0.3246598	0.7685011	0.5047241	0.6499907	0.5206282	0.6397830	0.6747621	0.6381834	0.8289680	0.7105909	1.0300515	0.7829405	0.9793604	1.3265568	0.7543370	1.1106217	0.7258154	1.5540844	0.7140582	1.4509617	0.4875484	0.7297572	0.8773832	1.3040662
HIAA	2.4412992	2.6983910	0.8340145	3.2664718	1.4622671	0.6602276	0.6127725	0.4979979	1.9400444	0.9404046	0.9567780	2.4501998	1.1286798	0.4954157	1.8092108	1.3313670	0.6916914	2.1301379	0.9272512	2.2856990	1.5603747	3.5012040	0.4755159	1.8120372
Homoserine	0.8509122	0.8893932	0.7896290	1.2645999	1.2080315	0.8902052	1.0056840	0.7481959	0.9495331	1.1548321	1.1279660	1.1857805	0.9891440	0.8623097	0.9327528	1.0666565	0.5662173	1.0695083	0.9945852	1.1881665	0.8156957	1.0217079	0.5884026	0.8560951
Hydroxyproline	0.2787770	0.4799966	0.2375902	0.3059802	0.3431303	0.2190838	0.2147382	0.1216726	0.2352834	0.1174432	0.3323629	0.3495331	0.2464465	0.3174669	0.3419158	0.4244054	0.3477392	0.3852723	0.4589917	0.6555311	0.6199176	0.9536136	0.2041111	0.4815902
Hypoxanthine	0.9974282	1.0928235	0.8876036	1.2570637	1.4171350	0.9833092	0.8904424	0.8622482	0.9724418	1.0087576	1.1682902	1.2436913	1.1114261	1.1937916	1.1325733	1.3134446	0.7104519	1.3286557	1.0959749	1.3218071	0.8378953	1.0824028	0.8661801	1.1903877
Inosine	0.7073993	0.8391119	0.7140293	1.0391484	1.2535338	0.8420802	1.1015346	0.8319424	1.1457617	1.2143153	1.3476063	1.2969553	1.2625817	1.5320379	1.1991691	1.5026616	0.9335940	1.9186397	1.4259257	1.8834052	0.7778325	1.0904168	1.1187931	1.5236756
Isoleucine	0.8528558	0.9125115	1.0217673	1.5496715	1.2388609	1.0109370	1.1912526	0.9214470	1.1406629	1.2647698	1.2625838	1.3054733	1.2786902	1.0450159	1.0627395	1.1645459	0.6330773	1.4210589	1.0894039	1.3649646	0.9157909	1.1766452	0.7847429	0.9943086
L-Alloisoleucine	0.8517790	0.9111445	1.0125399	1.5249889	1.2311331	1.0197709	1.1902293	0.9271793	1.1383725	1.2737694	1.2513103	1.3068848	1.2579197	1.0529558	1.0765331	1.1544872	0.6385982	1.4168104	1.0940247	1.3688610	0.9093086	1.1719494	0.7768059	0.9903981
Leucine	0.8476465	0.8962709	1.0266517	1.5385229	1.2401560	1.0079082	1.2035426	0.9227276	1.1359438	1.2795848	1.2575548	1.3011260	1.2710841	1.0653769	1.0637925	1.1611670	0.6377768	1.4253318	1.0888724	1.3837039	0.9196804	1.1688058	0.7811297	1.0016315
Lysine	1.4482072	1.0568177	1.1645744	1.8665608	1.4198726	1.0589478	1.4302917	1.0602397	1.1560245	1.7148566	1.6197058	1.6151634	1.4481528	1.2386714	1.1956266	1.5964858	0.7940763	1.7900829	1.5315174	1.4456983	1.2263541	1.3774511	0.9487037	1.6550266
Methionine	0.8972607	0.9251098	0.9370634	1.6825585	1.3009507	0.9540860	1.2933955	0.9654324	1.0819269	1.3994877	1.3717682	1.5317663	1.4078088	1.1686087	1.2161785	1.3539391	0.7224215	1.6457019	1.4097348	1.6598803	1.0329937	1.4074516	0.8338763	1.0874213
N-Acetylneuraminic.acid	0.6206421	0.8199069	0.5600818	1.0237435	0.6379889	0.5087411	0.5873233	0.5743446	0.6651696	0.9633031	0.8905661	0.8053625	0.4815686	0.4091472	0.4826958	0.6580611	0.4163223	0.8383301	0.9182577	0.9383752	0.5135255	0.5525025	0.4070563	0.6223561
NAD	0.5189115	0.7432001	0.7848089	0.9723333	1.0264845	0.8151934	0.9443994	0.8430001	1.0739810	1.7751225	1.4312229	1.1960606	1.1191554	1.5435374	0.8247645	1.0287660	0.7932043	1.3737844	1.6242790	1.4497317	1.2129971	1.2927545	1.2158123	1.1611846
NADP	0.4645545	1.0033445	0.9597302	1.0300501	0.5523697	0.9305444	0.8770339	0.8463191	1.1799497	1.6125850	1.5100842	0.8503701	0.8669583	0.9652894	0.4649232	0.7248484	0.8139846	0.9654545	1.3477053	0.9537815	1.0817424	1.1563229	1.1929342	1.3127996
Nicotinamide	0.7178230	0.8810389	0.8387394	1.1619439	1.0747429	0.8485019	0.9581953	0.8306311	1.1420243	1.1893909	1.1554375	1.2419390	1.2246746	1.2373342	0.9347814	1.1588332	0.7229536	1.2618774	1.0789894	1.4088462	0.8409249	1.1128264	0.9288390	0.9164444
Norleucine	0.8518739	0.9031989	1.0352939	1.5405561	1.2409032	1.0051005	1.2031724	0.9123117	1.1186044	1.2682845	1.2530081	1.3082198	1.2709141	1.0547923	1.0632294	1.1498179	0.6271827	1.4302944	1.0885495	1.3559512	0.9163913	1.1671295	0.7881985	0.9965756
Norvaline	0.9124836	0.9298527	1.0368697	1.6448278	1.1552369	1.0535945	1.1661068	0.8477787	1.1226926	1.1524275	1.1425004	1.2132199	1.2447680	1.0239704	1.0882174	1.2925641	0.6011751	1.3398496	1.0437265	1.2117027	1.0259126	1.1945400	0.9568618	0.9967921
Ornithine	1.0332296	0.8179956	0.7856410	1.3515693	0.9279344	0.7778656	0.9067942	0.6364167	0.7778348	1.0385131	1.0756493	0.9922528	1.2363026	0.9490234	0.9931245	1.3358021	0.6026925	1.4751211	1.2747343	1.1052278	1.2221460	1.3833450	0.8267835	1.4047324
Pantothenic.acid	0.5843001	0.7413393	0.6365224	0.9997849	0.8483685	0.7045172	0.6561683	0.6052149	0.7990996	0.8561870	0.8310670	0.8831817	0.8910804	0.7766499	0.7562383	0.9005148	0.4408332	1.1369992	0.7531680	0.8794983	0.4826726	0.7702197	0.6456869	0.7288907
Phenylalanine	0.8266777	0.9186807	1.0043263	1.5735330	1.3371442	0.9285578	1.2423992	0.9631628	1.1908843	1.3133446	1.3050369	1.4669236	1.4456966	1.1005134	1.1502301	1.2907528	0.7015021	1.6027515	1.1682306	1.6519843	0.9048820	1.2502029	0.7999375	1.0173964
Pipecolinic.acid	0.3294063	1.0094060	0.3818550	0.5711961	0.4551660	0.3332365	0.4550962	0.3707791	0.4427522	0.6345462	0.4652044	0.5736943	0.5446118	0.6177807	0.4724979	0.6498503	0.4190516	0.8724576	0.6294419	0.8597367	0.5914717	0.7777559	0.5766327	0.5802869
Proline	0.5141562	0.6178646	0.5822266	1.3063838	0.7457581	0.5776894	0.7298739	0.5105093	0.6245210	0.8541810	0.6404874	0.9124592	0.7089632	0.6439353	0.6385716	0.7810780	0.3922450	0.9376606	0.7503399	1.0259594	0.7327704	0.9253374	0.5640057	0.5703749
Pyroglutamic.acid	0.3082117	0.8843707	0.4362193	0.5921241	0.4758751	0.4111866	0.4229338	0.3914758	0.4400848	0.5739163	0.4679617	0.5115939	0.5537708	0.6806015	0.4737140	0.5919037	0.4162531	0.8276363	0.6802242	0.8473929	0.4889404	0.6901764	0.5664578	0.5789078
Sarcosine	1.0084766	1.0659462	1.4043571	1.3180316	1.3173108	0.9578035	1.0446095	0.8087390	1.2527798	1.4248970	1.4078169	1.4296566	1.4621763	1.4146250	1.1970317	1.2222388	0.9605841	1.4551496	1.1998666	1.4855036	1.1753213	1.1102789	0.7256942	0.9738131
Serine	0.9631746	0.7482507	0.8027561	1.4342633	1.2503764	0.9510122	1.1738940	0.8230972	0.9846277	1.2222407	1.2662427	1.2908321	1.1188887	0.8060649	1.1238529	1.1654594	0.5992233	1.2091939	1.1286308	1.2184897	0.7885404	1.0498191	0.6902211	0.8701550
TMAO	0.09437101	0.43303428	0.27471777	0.11216410	0.77217358	0.46438820	0.18648344	0.22312431	0.83269885	0.48161575	0.14550246	0.22655480	2.34051394	0.79755627	7.29396053	7.28121795	0.61150801	0.84295022	2.54722104	1.89654121	2.66298055	2.24567385	0.86779300	1.35080682
Taurine	0.7178835	0.8336343	0.8542148	1.1605061	1.0823282	0.8895874	1.1038355	0.9200192	1.0612253	1.3159387	1.2440577	1.2424510	0.5820055	1.3399539	0.6293543	0.8610343	0.6677345	1.4970880	1.0986328	1.0589133	0.8018202	1.0684514	1.1126616	1.4430778
Threonine	0.8232457	0.8706377	0.7730140	1.2312086	1.2037216	0.8912114	0.9660505	0.7585548	0.9620484	1.1447777	1.0785856	1.1441714	0.9735837	0.8573386	0.9307297	1.0386725	0.5642106	1.0126094	1.0241260	1.2153759	0.7968829	1.0072283	0.6001133	0.8525195
Tyrosine	0.9150162	1.0841190	1.0359367	2.4642402	1.2867226	0.9170167	1.3293614	1.0450251	1.2348882	1.6267038	1.1748098	1.7505491	1.3043186	1.1454333	1.0372301	1.3440036	0.6115674	1.8582848	1.1087729	1.8802615	0.6253943	1.0400158	0.8149456	0.8355209
UDP-GlcNAc	0.2934447	0.5004356	0.4652797	0.5732223	0.7177815	0.5265830	0.5310480	0.5149530	0.6552245	0.8666439	0.7747757	0.6714735	0.5809566	0.6796868	0.6131760	0.7155939	0.5540551	1.0615481	1.0151025	0.9471085	0.4996689	0.6153224	0.8202686	0.8398630
Uracil	0.8606104	1.1405109	0.9367328	1.1936004	1.0690069	0.8014622	0.9855269	1.0904810	0.9049300	1.1703200	0.9967556	1.3101537	0.6560391	0.7866817	0.8377139	0.9379920	0.6340143	1.5360757	0.7688687	1.2509321	0.8756824	1.2854795	0.7315423	1.0174820
Uridine	0.8463357	0.9289961	0.7456293	0.9695010	1.0747293	0.7520132	0.8439773	0.7566538	1.0583116	1.0561338	1.1516558	1.1443289	1.3153369	1.4348080	1.2522523	1.4124399	1.1748731	1.0449634	1.4928727	1.7468186	0.7417218	1.0299351	0.6787251	1.1677144
Urocanic.acid	0.8638117	0.3212854	0.2892404	1.7392963	1.1278006	1.1803694	4.6323495	0.8480094	0.1972440	1.0285895	0.5361097	1.2196895	0.9425947	0.2852366	0.4181020	0.3113765	0.3851985	0.4109156	0.4547907	0.4721768	0.2222827	0.3274246	0.3922131	0.4958654
Valine	0.9146230	0.9386614	1.0100753	1.5698269	1.1371203	1.0416494	1.1706341	0.8330754	1.1107848	1.1486198	1.1281245	1.1790151	1.2029580	0.9875298	1.0709863	1.2544596	0.6194352	1.3227468	1.0324728	1.1931394	1.0201331	1.1820476	0.9588230	0.9909290
Xanthosine	1.1578918	1.0963044	1.8140309	2.5780088	1.6815118	0.7748606	1.4037110	1.4535702	1.6892207	2.5296336	1.9151461	2.4928248	1.8328610	1.4805901	1.0967489	1.4175627	1.0784961	1.4506998	1.4556784	2.4213394	0.9455076	1.1696542	0.6661710	0.9053000
3-Indoxylsulfate	0.0014066653	0.0004189127	0.0010537000	0.0083676171	0.0142302571	0.0009821833	0.0053553740	0.0037918780	0.0099701690	0.0018319320	0.0000000000	0.0032034815	1.6957355303	1.7628992518	1.6905300705	2.6690102670	2.6662227663	1.2041302524	2.8159077618	3.9225468829	1.4879194492	1.2193387223	0.5481725665	0.6420550854
4-Methoxyphenylacetic.acid	0.6466108	0.8747982	0.6853639	0.4635535	0.6923135	0.9081214	0.3864574	0.5932554	0.8592044	0.7749379	0.6144890	1.6048136	1.3247088	1.9877733	0.5777823	0.4745502	0.6657401	0.7476548	1.1156824	0.3347995	0.4634213	0.4693551	0.7580660	0.8725201
2,3-Dihydroxybenzoic.acid	0.2284087	0.0000000	0.1073506	0.1197521	0.3433866	0.2394200	0.2957455	0.1572915	0.2597474	0.4494817	0.2776771	0.5415174	1.1314134	2.0412582	1.3909532	2.0095700	1.0359663	1.9621842	1.1671127	1.7748041	1.5807294	1.5394085	2.0435920	1.5376939
2-Hydroxybenzoic.acid	0.9912718	1.0984016	0.8859903	2.9777668	1.2496739	0.8263873	0.4437614	0.6297594	0.7991838	1.2558908	0.4339783	1.1235803	1.7674413	2.4987940	1.7318874	3.3508043	2.1025498	1.1283852	1.9534964	2.6782763	3.6617174	2.3740483	1.5164736	2.3913293
2-Methylbutyric.acid	0.7510326	0.0000000	0.5933317	0.4652210	0.8170571	0.6277748	0.5667496	1.2758309	0.4076446	0.6058693	0.5857997	0.7638084	0.5694005	0.5361239	5.5609744	0.6463784	0.8742257	0.6882732	0.5173637	0.7346524	1.1216587	0.9157327	0.5570880	1.4616018

Table S2A. Liver metabolites

4-Hydroxybenzoic.acid	0.9001782	1.0560988	0.5165869	1.6783153	0.5699435	0.8027474	0.7099929	0.9605478	0.4151053	0.8681392	0.5752243	1.0260255	1.6784020	2.1886534	2.2593682	3.0059774	1.4193347	1.8491539	1.9264320	2.0369756	2.6518981	1.4725679	0.8501041	2.2330271
4-Methoxyphenylacetic.acid.1	1.9877733	2.0373450	0.8337383	1.6048136	2.0658340	1.2979754	1.1156824	1.9172275	0.7001501	1.3116874	0.6853639	0.7476548	0.9081214	0.7218465	1.3247088	0.6144890	1.4894123	0.3347995	0.6466108	0.9913256	2.3431603	1.4964245	0.8747982	0.5932554
4-Methylvaleric.acid	0.2696367	0.2186943	0.2389721	0.2746247	0.3590760	0.3322700	0.3165805	0.2152099	1.1698982	0.4311654	0.7466173	0.7422495	0.6337153	0.3439619	0.5406916	0.2775697	0.2417917	0.6953245	0.8615943	0.9623980	0.8432549	0.8873891	0.8374581	0.2084494
Acetoacetate	0.9898180	0.8188094	0.9803567	0.9251530	0.9654123	0.9608998	0.9271387	1.0024227	0.8747964	0.9635099	0.9376343	1.0259165	0.9012016	0.9546399	1.0628470	1.0269441	0.9713463	0.9222361	0.9781181	0.8887658	0.9629445	0.9882867	0.9223725	1.0056272
Allantoin	0.9081038	1.1675675	1.0835233	1.4973499	1.3482714	1.1630004	1.2846565	1.3128294	1.4097008	1.5623482	1.4565717	1.4920634	1.3007490	1.1960430	0.9304598	1.1245904	0.8584241	1.5205353	1.0506660	1.2419266	1.0761671	1.2260110	1.3543364	0.9334865
Benzoic.acid	1.5878079	1.6902164	0.4250484	0.9203602	1.8134949	0.8459258	0.8249963	1.2637116	0.2394484	1.2308995	0.5166132	0.3333922	1.2684222	0.5741011	1.0986724	0.5265405	1.6702033	0.4627586	1.1916263	1.1436699	3.5990895	2.2423102	1.1203569	0.9979186
Citraconic.acid	1.3647653	2.2112889	0.8797576	1.4538588	1.7578296	1.5525089	0.7205279	1.0104727	0.5281336	2.3166094	0.4419381	0.6244150	0.9155004	0.7162225	0.9572177	0.5355094	1.0329688	0.2687801	0.5441814	1.9064968	2.0203813	0.9108907	0.8113292	0.5437640
Dextrose	1.7685669	4.6572716	2.3556058	1.7827129	1.1974816	1.1544892	1.2490300	0.7734221	0.9285326	0.8872297	1.2075044	1.1579873	1.2059183	0.9654718	1.2255272	1.3560641	0.5118914	1.3100008	0.6316051	1.1003823	0.6802550	1.0078298	0.6595299	1.2910940
Ethylmalonic.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
F6P	0.6739597	0.2447394	0.1826924	0.5818162	0.6716709	0.9746235	1.6123935	1.0723225	1.1070088	1.1154111	1.1312938	0.8015774	0.8302518	1.1814138	1.0512689	1.3252791	0.9051761	1.2707456	1.0729524	0.9041556	0.5528828	0.8035899	1.1194059	1.3061925
Fumarate	1.4192990	0.9868137	0.8213347	1.4978703	1.0743669	0.7292620	1.0526249	0.6276190	1.0221781	1.3314953	1.0614763	0.9885643	1.1486085	1.1050599	1.0235470	1.4572782	0.8988348	1.4704258	1.0546681	1.0817807	0.7715662	0.9892307	1.4595397	1.6709555
G1P	0.6752635	0.8029834	0.7627249	0.6158372	0.6249657	1.1037194	1.7901152	1.1289605	1.1985437	1.2173511	1.2187953	0.7115492	0.8453992	1.3293391	0.9983102	1.4457266	1.0017281	1.3487788	1.1853711	1.0712144	0.5663022	0.8982037	1.1802936	1.3657570
G6P	0.6688839	0.2380527	0.1925240	0.6659184	0.6797407	0.9710578	1.7391819	1.0406175	1.1499232	1.1649878	1.2167404	0.8868503	0.9159730	1.2787757	1.0400833	1.4203444	0.9207098	1.4076844	1.1534235	1.0067520	0.5166500	0.8859144	1.1368587	1.3662755
Galactose	1.5341257	5.2179303	2.3947257	1.5528834	1.3580207	1.1063219	1.1401609	0.8658799	0.9155313	0.9234025	1.1114644	1.1004973	1.1229601	1.0896220	1.1545220	1.3138040	0.6990620	1.1046280	0.7290189	1.1359700	0.7966584	1.1953606	0.7623118	1.0896942
Gentisic.acid	0.3546276	0.0000000	0.4713781	0.7467572	0.3560114	0.5168665	0.7327730	0.4047499	0.3646098	0.3597696	0.4111592	0.9474256	1.0461493	2.6593919	1.7835470	2.1266823	0.8074980	2.2794278	1.0550036	1.2916958	1.2224337	1.0283997	1.5228155	1.2681876
Glucuronic.acid	0.8618951	1.2635837	0.3914980	0.5864809	0.7149729	0.8905112	0.6466698	0.4523792	0.8934652	0.5236532	0.5877000	0.5639786	1.8837233	1.5606799	1.5985878	1.6699945	1.0047435	1.2180814	1.2296122	1.6472588	2.2245028	3.2449828	1.3460268	1.4921735
Glutaric.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
Glyceric.acid	1.1496164	2.5195502	1.1739954	1.3951672	1.4599438	0.8746264	0.9923443	1.2507857	0.8864898	1.5545627	0.9987718	0.9439196	0.7221400	1.4318077	0.8648158	1.2905391	1.3513554	0.8347342	0.9936521	0.7147244	0.7321524	0.8865097	0.8960178	1.4822709
Isobutyric.acid	0.00000000	0.05244963	0.50898333	0.82647449	0.00000000	0.65901154	0.56581734	0.71041992	1.32707167	0.56170639	1.01099565	1.18177968	0.84196243	1.21985165	0.69521063	1.08410990	1.63819382	0.52221008	2.05200836	1.27874196	1.92633325	1.10015048	1.10209239	1.01358025
Isovaleric.acid	0.7155741	0.0000000	1.0151671	0.4655771	0.9275040	0.4950023	0.7486756	1.0320418	0.8385003	0.7539450	0.5534565	0.6301668	0.4893295	0.5065836	5.2080493	0.7206219	0.7182304	0.4833982	0.6210143	0.8176440	1.0377181	1.1049437	0.3567986	1.2920695
Lactose	1.7278542	12.3361306	3.5970124	1.6204874	1.3170386	1.1452639	0.9148891	0.7427353	0.8165284	0.7769225	0.9731502	1.0814995	1.1334146	0.9947503	1.0370356	1.3653067	0.6670843	1.2811463	0.6614136	1.0377394	0.5529015	1.0834332	0.5707073	1.3489137
Levulinic.acid	1.5570665	1.2926634	0.7031304	0.6362157	0.7702267	0.6458151	0.4586144	0.6789458	1.2085580	0.9497924	0.8597124	0.6798147	0.8956509	0.6319326	0.9339435	0.5457088	0.9271357	0.9459671	1.2397537	1.8196988	0.9844683	0.8069519	0.7865500	0.4809240
Mannose	1.4952340	1.0294612	1.1193161	2.1812875	1.5518865	1.0888375	1.4574358	1.2740713	1.5870256	1.4937340	1.4813516	1.7636578	2.0195185	1.3265372	1.5246655	1.5385679	1.2863063	1.3664471	1.2684240	1.7166670	0.8845929	1.3531122	0.9221497	1.3065198
Methyl.alpha-D-glucopyranoside	0.7022848	1.3289890	0.7121133	0.9536818	1.1250414	0.6308415	1.1896947	0.8454161	1.2042655	0.9617926	0.8191024	1.0102836	0.9483462	1.1641299	0.6849502	1.0440661	0.6582924	1.3262151	0.9590109	0.8453300	0.8214475	1.1854478	1.1363926	1.0440430
Myoinositol	0.8694791	1.1178407	1.3772587	1.7509144	1.7419164	1.1912207	0.7806327	1.1023066	1.0258326	1.0494177	1.3554179	0.9649657	1.4025886	1.1070176	0.9472456	0.8104337	1.1539989	0.8418495	0.9136361	1.4517492	0.8450081	1.6781317	0.7083603	1.0566861
Nonadecanoic.acid	0.8291083	0.4843062	0.7006170	0.6379930	0.6590255	0.7834945	0.6717061	0.6468235	0.6136272	0.6344273	0.5468030	0.7088714	0.5691938	0.8135633	0.7518102	0.7726551	0.7042177	0.6471807	0.5237051	0.3273494	0.4570268	0.4718718	0.5502521	0.7504966
OAA	0.4706844	1.4768433	0.9478751	0.9480796	0.7043471	1.0231675	0.7729994	0.5138535	0.8686459	0.6839295	0.7601366	0.4938531	0.7716700	0.7003961	0.7052642	0.7108140	0.7430833	1.2272501	0.7375726	0.8898757	2.6271150	2.4659336	0.8769646	0.6642809
Palmitic.acid	0.6576104	2.4876173	1.1086988	0.9933969	0.6654050	0.5312395	0.7647661	0.7191476	0.6994420	0.7180929	0.5547641	0.8033647	0.6966770	0.8559372	0.7094591	0.7680809	0.5930325	0.8984361	0.5270847	0.9339967	0.4984569	0.6610013	0.5752758	0.5048961
Pentadecanoic.acid	1.1427298	0.5870484	0.6274741	0.6752754	0.6227439	0.7262631	0.5656418	0.5217017	0.6089249	0.4430046	0.4323494	0.7093060	0.4577233	0.5140927	0.6343803	0.6179902	0.4894114	0.5277205	0.3626343	0.3959666	0.4648136	0.3559489	0.5488784	0.4773791
Phthalic.acid	2.2467277	2.8811973	0.9590323	1.4759390	2.5516393	1.2665585	1.1557750	3.2708233	0.9187764	1.8053250	1.1865923	1.0920811	1.5253343	1.5010486	1.5789988	1.0036075	1.6275219	0.6693168	1.1291957	0.9520331	4.1384040	1.7908762	1.4875792	0.9633425
Raffinose	4.2406534	2.6381289	2.8986832	2.2229446	1.4063470	1.9821988	1.7797267	0.5603099	1.5427157	1.3383924	1.8955090	1.5934417	1.6822064	2.1903529	1.6188200	1.7642422	1.2483946	2.6886577	1.1058582	1.3579173	0.4961662	0.9152473	1.6370885	1.6808395
Shikimic.acid	0.4566439	1.6953687	0.4436559	0.5014321	0.9789059	0.6421197	0.8611503	0.8154816	0.4553175	0.8477968	0.7800669	0.6293811	0.6921569	0.9635854	0.7885012	0.8913415	0.7719212	1.1031032	1.0271294	1.0289196	1.1278543	1.0499156	1.0467217	1.3644345
Sorbitol	1.585376	2.068789	2.017347	2.935154	2.439898	1.695450	1.235273	0.948883	1.877812	1.083459	1.648626	2.228505	2.471795	1.821555	3.012169	1.975258	2.174246	2.263342	2.427025	4.434080	1.370861	1.535353	1.067649	1.186329
Stearic.acid	0.7809648	2.2287310	1.2442121	1.0303458	0.9092352	0.7524102	0.7931729	0.8663392	0.7608388	0.7868036	0.6238720	0.8245983	0.8188588	0.8765730	0.8958090	0.8963560	0.7338885	0.8893772	0.7047385	0.9714868	0.8025889	0.8111246	0.7017546	0.7680203
Trehalose	2.1142004	13.2894395	3.9071349	2.2777436	1.5761671	1.0666695	1.5014004	0.6787332	0.8279424	0.7812906	1.2507457	1.4231432	1.3643417	0.9935851	1.1759800	1.3869828	0.5431801	1.0142042	0.8030972	0.9663495	0.5082489	1.0376458	0.7117123	1.6965194
Urate	1.3406364	1.5250610	0.8473836	1.1140390	2.4907067	1.2353838	1.7609205	1.1875856	1.5123852	1.3022075	1.4339406	1.0269305	0.6765105	1.0893236	0.6584594	0.7040288	0.7428215	1.9296033	0.8196379	1.6574426	0.8632615	0.8101919	1.2833077	2.1605345
Valeric.acid	0.70749133	0.09470111	0.98921146	0.46459669	0.91370278	0.47580163	0.74021893	1.03119080	0.81706168	0.75332329	0.55229107	0.62304875	0.48829916	0.49363134	5.14922195	0.71910449	0.69037095	0.47793804	0.60513635	0.78592837	1.03686237	1.08850223	0.34767608	1.28934875
X5P	1.201143	1.276757	1.413303	1.653952	1.267569	1.278849	1.780746	1.354567	1.779299	1.577205	1.707360	1.920431	1.580249	1.517633	1.585497	2.195201	1.459374	1.733696	1.705658	2.215318	1.187748	1.478072	1.491918	1.627948
Xanthine	1.479659	1.481760	1.402484	1.887153	1.778127	1.252138	1.518562	1.382384	1.521875	1.459015	1.538795	1.813552	1.511328	1.476498	1.470618	1.495125	1.065810	1.728239	1.406754	1.589197	1.155761	1.426024	1.365320	1.292267
alpha-Hydroxyisovaleric.acid	0.22652691	0.06324408	0.24138572	0.38533503	0.40858595	0.08999759	0.13680320	0.24739137	0.67448423	0.27068110	0.05595278	0.38246377	1.40021748	0.40581075	0.59413534	0.16162409	0.14820324	0.80589746	0.45462266	0.50294160	0.51224833	0.62746522	0.94315331	0.27787725
alpha-ketoisovaleric.acid	1.6450600	1.9676816	0.9101139	0.7138070	0.8190894	0.5382239	0.4271922	0.7849076	1.1082485	0.9436748	0.6605273	0.5106391	1.2123041	0.5905675	0.8120547	0.5422817	0.3049550	1.0403584	1.1329032	1.8615979	0.9017435	0.8825711	0.9590286	0.7871725

Table S2B. Serum metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	1.0317667	1.0303621	0.9847637	0.9921081	0.9160872	1.0764221	1.0336387	1.4405943	0.7765993	0.9986675	1.0874466	1.0637402	0.6305017	0.5213879	0.7407689	0.8465473	0.6182256	0.6951432	1.0381927	0.6869308	1.1003884	0.7616520	0.7266176	0.6292298
3-Indolepropionic.acid	0.01904275	0.00000000	0.00000000	0.01174865	0.00000000	0.03955007	0.06561667	0.03874387	0.00000000	0.00000000	0.00000000	0.00000000	0.55859613	0.47659752	0.71442760	0.27750775	0.61415979	1.10075666	0.37694018	1.13900959	0.22864990	0.44264462	0.75318881	2.27604977
6-Methyl-DL-tryptophan	0.41570933	0.55659384	0.67931578	0.49104472	0.80584709	1.93103976	0.63320850	0.66146933	1.08739075	0.65511807	0.75366381	0.74293619	0.09812646	0.17093453	0.45117283	0.25733516	0.22503132	0.36726015	0.26036736	0.33192057	0.59247137	0.78618775	0.94471496	0.45148486
Indole-3-acetic.acid	0.5580839	0.5380495	0.5656663	0.5636264	0.4919839	0.4800485	0.4241354	0.6233548	0.3343458	0.5122234	0.6933088	0.4484751	0.7917882	0.9824133	1.0578317	1.1315136	0.6962389	1.0884141	1.7883287	1.4874967	1.2532215	1.2294161	2.2210241	1.7300960
Indole-3-lactic.acid	1.1092210	0.8554817	0.8354971	1.1621817	0.7877591	1.0869508	0.8945694	1.5749362	0.6616183	1.0120818	1.0766544	0.9578828	0.6190572	0.4244500	0.7577282	0.8598728	0.5966954	0.7057665	1.0638820	0.6138955	1.0639085	0.6896377	0.6855773	0.5902174
Kynurenine	1.0909688	0.8734492	0.3294966	0.7872656	0.2680286	0.8604749	1.0273913	0.9765153	0.8797466	0.7120567	0.7678117	0.9076418	0.3653122	0.6868505	0.6065237	0.7695144	0.5623107	0.3753020	0.5503452	0.4305640	0.3471962	0.5665617	0.6669201	0.4597565
Serotonin	0.8442799	0.9014375	0.7353003	0.7508531	0.8737883	1.3184758	0.8002665	0.7634158	0.7392552	0.8125640	0.8092775	0.8531453	0.4321848	0.5080711	0.4937651	0.5775824	0.5864579	0.5811751	0.6443621	0.5838568	0.7712975	0.5235457	0.8569040	0.5515420
2-Deoxycytidine	0.3174848	0.2913996	0.2822617	0.3026962	0.2133915	0.3491761	0.2773496	0.3324238	0.2194807	0.2744738	0.2549853	0.2950616	0.2459364	0.2298095	0.3028967	0.3110092	0.2116033	0.3872227	0.2877459	0.3042525	0.2941973	0.2165142	0.3662207	0.3591027
213C-Glutamic.acid	0.9844852	0.9950125	0.9327800	1.0003609	0.9661615	0.9508437	0.9988592	0.9277253	1.0146637	0.9506263	1.0051244	1.0134514	1.0141268	1.0258431	1.0099926	1.0166979	0.9702272	1.0188772	0.9572153	0.9783577	0.9923269	0.9244512	0.9319085	1.0222706
5-Aminolevulinic.acid	0.7795518	0.7610577	0.6979264	0.6854502	0.9618818	1.2366398	0.7757380	0.8759584	0.7565268	0.8750895	0.6972154	0.5884368	0.5317662	0.4935351	0.5312805	0.6134248	0.6264979	0.4866220	0.6992055	0.7625584	0.7390534	0.5473003	0.6652192	0.5197771
6-Hydroxynicotinic.acid	0.028878300	0.053021903	0.055377422	0.067188470	0.069876473	0.033207796	0.050327910	0.064691863	0.057382380	0.066923263	0.050205179	0.020650789	0.023744369	0.012478698	0.008996055	0.025685372	0.020600780	0.016676094	0.009066213	0.020656543	0.027477553	0.000000000	0.038251691	0.035514356
7-ketocholesterol	0.2924918	0.2284840	0.4863401	0.3812536	0.5532410	0.2924774	0.4050716	0.6754374	0.3572131	0.5246027	0.4581334	0.5209997	1.3684958	2.2957026	0.9383200	10.2231564	0.3468779	0.7566915	5.0969810	0.5870745	0.6553080	0.5284319	0.9099085	2.8210692
Acetylcarnitine	0.9441641	0.9762040	0.8584805	0.8966743	0.8083222	1.2599501	0.9270292	1.1218529	0.6377153	0.9340284	0.9575799	1.0547174	0.8179229	0.7078616	1.3668700	1.1744102	0.8729917	1.4676838	1.0122209	1.3667082	0.8370880	0.5816249	0.8944781	1.2286137
Acetylglucosamine	0.40392903	0.20460270	0.40498773	0.42430252	0.40644811	0.73773239	0.37272404	0.36942373	0.34369816	0.43376192	0.32548500	0.30721539	0.31563018	0.10564735	0.17228083	0.24874233	0.24854459	0.28460983	0.31103168	0.36955219	0.19195022	0.09980531	0.34108868	0.20726354
Acetylglycine	1.4991894	1.2571867	1.4613053	1.3676502	0.8618283	0.8963021	1.3151055	1.5117083	1.2874666	1.2558855	2.0225116	2.1556291	0.3764896	0.1361418	0.9900842	0.7101797	0.3881535	0.8370687	0.1611271	0.3595276	0.5242699	0.2188906	0.2776544	1.1418755
Adenosine	0.2140969	0.2102831	0.2204731	0.2183226	0.1923837	0.1817932	0.2516306	0.3133118	0.3362446	0.5335153	0.2711058	0.2710070	0.1909757	0.1598037	0.3264152	0.1133139	0.9777930	0.2111847	0.2169560	1.1616375	0.2937814	0.2245176	0.2665889	0.2164441
Adenosyl-L-homocysteine	0.6714422	0.4308204	1.5075238	1.2276340	1.5873233	1.2629599	1.1093691	2.1367804	1.2361365	2.0044919	0.7645900	0.3509771	0.7865940	0.3838238	0.4334325	0.8561266	0.8834433	0.3909437	0.7933884	1.1344111	1.2445698	0.8234503	0.2881118	0.3432706
Alanine	0.8039607	0.7589530	1.5213952	0.7050528	2.4600018	1.6993623	0.7328026	0.5635759	0.9061994	1.0124162	0.8918277	1.1135432	0.6239487	1.1980224	0.4809799	0.8274591	1.5761646	1.5665982	1.4870625	0.8288178	2.1276307	0.8214103	1.1012487	0.6655912
Allopurinol	0.03371837	0.03982831	0.07967565	0.09631134	0.29066584	0.43212536	0.10127359	0.13557639	0.15064015	0.43628029	0.07268631	0.04541401	0.18894061	0.15836448	0.86294382	0.35844435	0.26588665	0.01586960	0.21502325	0.77772557	0.23225748	0.19562593	0.24672431	0.21442101
Asparagine	0.4449370	0.4373391	0.4302286	0.4423950	0.4736336	0.8986803	0.4141668	0.4037197	0.4344819	0.4441081	0.4378873	0.4320793	0.3776924	0.3610497	0.3550619	0.3946823	0.3544344	0.7584599	0.4232461	0.4070500	0.6391954	0.5276892	0.8365307	0.6913280
Aspartic.acid	0.4152065	0.4430707	0.5818116	0.5320270	0.7732795	0.5713789	0.3907554	0.5394307	0.3698395	0.6125440	0.4739644	0.9147199	0.6267113	0.6123835	0.5933458	1.0165807	0.6299843	0.7023535	0.7167973	0.5597980	0.7913604	0.5099731	0.8173880	0.5713535
Betaine	0.7234086	0.7048656	0.6882660	0.7301375	1.0328520	1.0547873	0.8330171	0.7567204	0.8401010	1.0007066	0.7405565	0.6415822	0.4648153	0.6546769	0.6748845	0.7449814	0.5910158	0.7913117	0.6501385	0.9196811	0.5226326	0.4670694	0.8190514	1.0041040
Carnitine	1.0364532	0.9510847	0.6900549	0.7823069	0.8722678	1.4882140	1.0155252	1.0430504	0.7671293	1.1915917	0.9239250	0.6549932	1.2215885	1.1295841	1.0461135	1.1959042	1.1850933	1.0845366	1.4431300	1.6938279	1.3330664	1.1024471	1.5497510	1.0555476
Creatinine	2.0182532	3.1826911	0.6806979	1.3364505	1.0357324	1.0650838	0.9285776	1.0191995	2.2516750	1.1956444	1.5971185	0.8120371	1.4682139	1.1740891	1.8848313	1.5277349	0.4602601	1.4305611	1.3358876	1.8145411	1.3705444	1.2221740	1.0911130	1.7973037
Cystathionine	0.28309420	0.22951454	0.19001737	0.36697649	0.24784214	0.79328559	0.51016562	0.33012475	0.19901532	0.36555136	0.24005707	0.43611053	0.11324349	0.25762183	0.16868932	0.20845813	0.14641402	0.22658746	0.15482380	0.16571156	0.18506241	0.09193353	0.33018113	0.17725964
Cystine	0.2811702	0.2796157	0.2622289	0.4158454	0.2951822	0.4626571	0.2329457	0.4313985	0.3481685	0.7131780	0.1786220	0.1504858	0.4354672	0.3925378	0.7481704	1.2502132	0.5341248	0.2328273	0.3078212	1.0104342	0.6121067	0.7567378	1.1014113	0.2250691
Cytidine	0.5210576	0.5032761	0.5765483	0.5981420	0.6814616	0.8751241	0.6748009	0.6019237	0.5428900	0.7095091	0.5425272	0.7119897	0.4274866	0.2924270	0.6648767	0.5449437	0.3117971	0.5249493	0.3719328	0.5661403	0.4281487	0.2193708	0.5383064	0.6722130
Cytosine	0.5724007	0.5687503	0.6540320	0.6572037	0.7955865	0.9571722	0.7971547	0.6449386	0.5586945	0.6774215	0.6049335	0.7243051	0.4699204	0.2732985	0.7717965	0.5282462	0.3810730	0.6414866	0.4522232	0.6106754	0.4545835	0.1679954	0.4922570	0.7779320
Decanoylcarnitine	1.03977434	0.99283216	0.43905377	1.23286038	0.21996057	1.66219197	1.14613326	1.16848327	0.86426812	0.72083633	1.21367682	0.93209662	0.40954643	0.77981803	2.03456776	0.62146441	1.09213349	2.43900461	0.36883592	1.46662126	0.38505780	0.09040753	0.38388122	1.57232054
Glutamic.acid	0.5190196	0.5011747	0.4923732	0.4956872	0.6323800	0.5782931	0.3782653	0.4835876	0.3689661	0.6442815	0.4484648	0.6992172	0.6507610	0.4443386	0.6106565	0.6727734	0.4415760	0.6311273	0.4996465	0.5072568	0.5993526	0.4951351	0.6628929	0.6303698
Glutathione.oxidized	0.05294285	0.07759938	0.29613676	0.37270704	1.55391661	0.73383892	0.28143294	0.37137794	0.38844261	0.74461270	0.14097362	0.19893314	0.53946391	0.77446884	0.80577163	2.06643648	0.20456022	0.49325699	1.32663578	0.77536742	0.29639357	0.38259976	0.67550784	0.48181953
Glutathione.reduced	1.1026759	0.8923498	1.1151582	0.5953181	1.6980991	0.6901809	0.7222110	1.1313823	0.7949924	1.5343012	0.7254251	0.4263253	0.1457852	0.1639876	0.3207433	0.3435307	0.5711687	0.6251995	0.2651110	0.2859727	0.5322789	0.5886255	0.2908863	0.3738287
Glycine	0.7725024	0.9251390	0.8940421	0.7024416	0.9043963	1.0035431	0.8484915	0.9572646	0.8936362	0.7776883	1.1724503	0.9329527	0.3696696	0.4106501	0.5924033	0.5879735	0.5078564	0.7956602	0.4571842	0.5517679	0.7122945	0.4886854	0.6821170	0.7807791
Glycocyamine	0.8074463	0.3146842	0.4313919	0.7983406	0.7402149	0.9057195	0.2322731	0.3787078	0.4721578	0.9536144	0.6623463	0.1779486	0.3463183	0.2636901	0.4921304	0.4061054	0.6702330	1.0676197	0.2848171	0.6642394	0.7265750	0.6081363	0.6230967	1.7139250
Guanine	0.02532942	0.05454220	0.44570051	0.44655817	0.75594909	0.43156865	0.31297704	0.65911714	0.11930541	0.99610076	0.14866761	0.15196284	0.03857490	0.02812718	0.64312146	0.13858959	0.30982399	0.00000000	0.08996413	0.61969980	0.04445479	0.10089361	0.11101912	0.10465782
Guanosine	0.041368434	0.027223213	0.439538214	0.393871216	0.755126475	0.359767631	0.387946879	0.525422776	0.131452859	0.908707699	0.114507263	0.107079476	0.038413887	0.043984439	0.470480486	0.110833692	0.298855593	0.005636157	0.076048250	0.663438323	0.119137456	0.048801513	0.090631906	0.058864363
HIAA	0.4614215	0.4563886	0.5361250	0.6674289	0.5526476	0.7528907	0.6618530	0.8154046	0.3770931	0.5050472	0.8687341	1.0162924	0.5355136	0.4474822	0.5572884	0.7506275	0.2775017	0.3348267	0.5920746	0.4323071	0.8289809	0.4134172	0.6647502	0.4651709
Homoserine	0.6983023	0.7018378	0.7149072	0.7242009	0.6649812	0.8189758	0.7640266	0.6782549	0.5256616	0.7163832	0.6410018	0.4788504	0.4438158	0.5528304	0.3849193	0.6326310	0.6478078	0.3654759	0.5773910	0.6299180	0.7322205	0.5901563	0.8331537	0.3790520
Hydroxyproline	0.7868130	0.7673889	0.6748305	0.6843264	0.9174251	1.2313570	0.7636354	0.8520473	0.7546107	0.9010612	0.7151542	0.6026010	0.5303085	0.4746016	0.5074172	0.6101571	0.6367897	0.4844010	0.6824918	0.7603418	0.7412404	0.5531942	0.6457549	0.5127148
Hypoxanthine	0.03108008	0.03295078	0.07230745	0.10605112	0.24210361	0.46310881	0.10167784	0.14625749	0.16616489	0.51041860	0.06533173	0.04225448	0.24245563	0.13432216	0.87837180	0.36355552	0.25734567	0.01519113	0.21277908	0.74516568	0.21031964	0.20654750	0.27581957	0.22056332
Inosine	0.02600116	0.02615317	0.07605084	0.07720853	0.24970896	0.38404333	0.09108355	0.12666396	0.13240581	0.36308907	0.06973492	0.04524077	0.16349696	0.16517816	0.90361214	0.37945644	0.29174887	0.01648628	0.22917311	0.71077105	0.24821758	0.17251436	0.22439895	0.20742862
Isoleucine	0.7734905	0.7720793	0.6809624	0.7169639	0.9427465	1.2809432	0.7698176	0.8840363	0.7578946	0.9174449	0.6951529	0.5988584	0.5521642	0.4869889	0.5300929	0.6111975	0.6246363	0.4812083	0.6819774	0.7716538	0.7384486	0.5738182	0.6861106	0.5234358
L-Alloisoleucine	0.7816351	0.7675873	0.6931879	0.7254023	0.9586529	1.2948073	0.7777563	0.8893020	0.7541538	0.9230311	0.6862217	0.5978543	0.5540295	0.4943954	0.5348676	0.6202152	0.6324164	0.4872354	0.6973422	0.7748112	0.7349445	0.5754398	0.6966434	0.5213951
Leucine	0.7762630	0.7700904	0.6859590	0.7049883	0.9531758	1.2854569	0.7691488	0.8836390	0.7621739	0.9174278	0.7043351	0.6034554	0.5525940	0.4889069	0.5287984	0.6207396	0.6323462	0.4784675	0.6888833	0.7697485	0.7440186	0.5678910	0.6857679	0.5269246
Methionine	0.4595065	0.4579772	0.4746533	0.4885255	0.4920350	0.6604720	0.4462489	0.4727000	0.4003232	0.4848580	0.4535979	0.4214641	0.3289654	0.4052902	0.3049758	0.4320432	0.4224938	0.3929081	0.5814995	0.4638038	0.7436927	0.5635675	0.7926240	0.3739858
Methylguanidine	0.6083126	0.5991099	0.7510126	0.7478605	0.6616402	0.7147471	0.7355709	0.7186135	0.5271701	0.7047024	0.6328199	0.3575302	0.4456060	0.4159211	0.3919142	0.5690907	0.6021682	0.2794409	0.6075165	0.5859735	0.8534668	0.5224783	0.8782036	0.3948659
N,N'-Dicyclohexylurea	0.4491116	0.7786632	1.0568974	0.8605733	0.3151338	0.2683889	0.8111300	0.8860459	0.9300668	0.6072164	0.7132078	0.7497717	0.5024905	0.3967395	0.3895438	0.4417970	0.4784667	0.7943685	0.4818193	0.5755309	0.3671177	0.5808789	0.8349089	1.5812582
N-Acetylethanolamine	0.1837007	0.3351524	0.1712734	0.1999842	0.1839945	0.3390010	0.3605331	0.4625985	0.1857110	0.2160144	0.1688903	0.1901620	0.1246755	0.1620703	0.3036458	0.2729194	0.3908199	0.4101847	0.3189875	0.2665719	0.3897250	0.1503872	0.4816167	0.3320829
N-Acetylneuraminic.acid	0.06720457	0.11616575	0.06952991	0.06068203	0.14038777	0.16392413	0.06753194	0.15396054	0.07783408	0.20979568	0.16580744	0.18465772	0.09179428	0.11928544	0.17453190	0.10237460	0.08390267	0.17293004	0.09089243	0.13104024	0.08846533	0.08536574	0.14463525	0.10738479
Nicotinamide	1.1086306	1.0155569	0.9927073	1.0139620	1.7020512	2.0952281	1.2648053	1.1001351	1.0931990	2.0225090	1.1455333	1.2253957	0.8691954	0.8242333	1.0545029	1.3757596	0.9047593	0.6271669	1.1229611	1.3799018	0.8479625	0.6773855	1.0690791	0.7598487
Norleucine	0.7688610	0.7655194	0.6721997	0.7120115	0.9469902	1.2760697	0.7667306	0.8749643	0.7609668	0.9137877	0.6953367	0.5920285	0.5545982	0.4870829	0.5265577	0.6099556	0.6318839	0.4853943	0.6818889	0.7537906	0.7431439	0.5691091	0.6839599	0.5239574
Normetanephrine	0.4602634	0.7922858	1.0278972	1.1844420	1.1925011	1.0998287	1.4460477	1.2505234	0.8085146	0.8390345	0.7908881	0.6272976	0.7473370	0.6527553	0.9018705	0.9717988	1.1085613	0.6866956	1.8133871	0.7053081	1.5459995	0.7414323	0.8043796	0.5152777
Norvaline	0.7456426	0.7479910	0.6948016	0.6796876	0.8187685	1.0167348	0.7761884	0.8805773	0.7022088	0.7862304	0.7152055	0.6146859	0.4932867	0.5133007	0.4637410	0.6137076	0.6419375	0.4975852	0.6883464	0.7023230	0.8132069	0.6068848	0.6269995	0.4917820
Phenylalanine	0.6926250	0.7008467	0.6459153	0.6778132	0.8648654	1.2378989	0.6956844	0.8330104	0.7424098	0.8759900	0.6224442	0.5904636	0.5133810	0.4601704	0.5379103	0.5883836	0.5392128	0.6769541	0.6840378	0.7221243	0.7056662	0.5232141	0.7153008	0.6231087
Proline	0.2536354	0.2665351	0.2729979	0.2910349	0.3455349	0.5739777	0.2744232	0.3060478	0.2541320	0.3370148	0.2492915	0.2561445	0.1759309	0.2077588	0.2071730	0.2544563	0.2057017	0.2743556	0.2967707	0.3282657	0.4057957	0.2971243	0.5417059	0.3029315
Sarcosine	0.7972464	0.6285018	1.1937639	0.6966922	2.1649467	1.8733796	0.6445680	0.5183578	0.7599217	0.8395287	0.5969229	1.3593589	0.5837919	1.1513682	0.4793732	0.7341413	1.3038976	1.6908640	1.6649814	0.7639477	2.0942908	0.5273449	0.8220729	0.6044479
Serine	0.5353581	0.5267698	0.4793458	0.4622670	0.5259625	0.7771565	0.5041540	0.4785595	0.4262779	0.5054402	0.5073924	0.4689129	0.3561538	0.3706829	0.4047429	0.4597577	0.4136697	0.5811335	0.4466357	0.4885491	0.5757121	0.4545363	0.7522944	0.5896785
TMAO	0.85451078	0.65696505	1.21903340	0.39266798	1.48554668	0.47086960	0.40870485	0.92978038	0.64500025	1.40691014	0.49913503	0.04325557	0.00000000	0.33761085	0.18429464	0.25384521	0.63396713	0.61949213	0.26769308	0.25273734	0.31276815	0.33318616	0.14893635	0.28665877
Threonine	0.7150959	0.7015677	0.7629955	0.7761223	0.6462053	0.8520302	0.7351514	0.6963445	0.5208669	0.7185048	0.6479620	0.4750623	0.4655190	0.5523690	0.3989872	0.6481275	0.5915996	0.3782476	0.5667950	0.6336898	0.7189485	0.6165406	0.9114231	0.3670283
Tyrosine	0.6030869	0.6125875	0.7887788	0.8232557	1.0062731	1.2490204	0.6071225	0.8777774	0.6561377	0.8893080	0.6613815	0.6228148	0.3730047	0.3463561	0.4792403	0.4594995	0.3938609	0.5973173	0.5438654	0.5633916	0.6423756	0.4651992	0.6423144	0.4970374
UDP-GlcNAc	0.000000000	0.000000000	0.000000000	0.004592017	0.193086076	0.040915595	0.004539314	0.145934213	0.178034558	0.116639623	0.000000000	0.070587210	0.149759237	0.000000000	0.055340246	0.339265912	0.000000000	0.018765855	0.038192797	0.065482356	0.000000000	0.000000000	0.070706147	0.000000000
Uracil	0.8457426	0.8495759	1.0951227	1.2036762	2.6855035	3.3864430	1.5948670	1.2708232	1.4810583	2.7345165	0.0000000	0.5702306	1.3042441	0.5982922	1.2443398	0.8348638	0.7037339	0.5697256	0.7155200	1.7113136	0.5957357	0.4716715	0.6942587	0.6309362
Uridine	0.8880025	0.8636672	0.9870649	1.0857023	2.5189912	3.0324660	1.5176027	1.2631859	1.6074507	2.5373434	1.0135393	0.6157471	1.2844979	0.6318885	1.2363457	0.8629738	0.7619592	0.5965804	0.7071004	1.7040465	0.6145321	0.4385381	0.6160858	0.6436844
Urocanic.acid	0.03376918	0.04254745	0.05724673	0.04831958	0.04635670	0.04936237	0.03685679	0.04165554	0.04238366	0.03293443	0.03548771	0.04557768	0.01823145	0.01534968	0.01744506	0.01649835	0.01764671	0.02310776	0.02532258	0.01928040	0.04746682	0.02773702	0.03005870	0.02772801
Valine	0.7459956	0.7503615	0.7026255	0.7024037	0.8202731	1.0275209	0.7588466	0.8909467	0.7097040	0.7982574	0.7008425	0.6146873	0.5054868	0.5030490	0.4737987	0.6111390	0.6462739	0.5020537	0.6864407	0.6854861	0.8229823	0.6217540	0.6254272	0.4997380
Xanthosine	0.4577110	0.4849641	0.6241970	0.6766769	4.2558855	7.7630219	1.5764167	1.0264283	4.2477904	7.8442639	1.0624214	0.1908877	0.8124879	0.1524969	1.8590245	0.6193012	0.4041642	0.1813820	0.2700349	2.3332162	0.1061311	0.1309162	0.1285644	0.3067931
methyl-a-D-galactopyranoside	1.3477293	0.9038175	0.7205699	0.5291660	1.0640751	1.5175823	0.9536713	0.7824787	1.0652578	0.6404905	1.0459692	1.1463473	0.6403432	0.7595554	1.0700229	0.9111508	0.7905356	0.9514611	0.9061882	1.0269884	1.2904433	0.9006732	1.4165315	0.9374045
3-Indoxylsulfate	0.0039742006	0.0023391308	0.0353740607	0.0016464954	0.0022620914	0.0031716151	0.0032944106	0.0030293134	0.0014770960	0.0010762186	0.0009190207	0.0016898664	1.6172315346	2.2955004825	3.8331504617	1.8889801044	2.9435636983	1.0289100428	1.5241429637	4.5331715267	1.5340171634	1.4178092065	2.0482161824	0.6584347506
2,3-Dihydroxybenzoic.acid	0.48998087	0.45925943	0.20171275	0.11165078	0.40996557	0.48016548	0.38672610	0.54687554	0.11396917	0.11675343	0.11986621	0.07671945	1.24635923	1.42578176	1.18469069	2.02295701	1.50349511	2.05013084	1.32332791	1.94655749	1.59277083	1.10832205	1.72193673	1.59378286
2-Hydroxybenzoic.acid	0.7965871	0.7728044	0.3218101	0.2447120	0.6136844	0.3744148	0.4319101	0.7563006	0.3510303	0.2609883	0.2320656	0.3058933	2.2558602	2.5915402	1.5055872	4.0838144	2.3711602	1.4305851	2.8694710	3.5659023	3.3476204	3.0332858	3.9963234	1.7222825
2-Hydroxyphenylacetic.acid	0.8336771	0.7515347	0.6511527	0.4969051	0.6434132	0.9558337	0.8266350	0.8324308	0.3614684	0.4623572	0.5138190	0.3820153	1.1250300	0.9010148	1.0660509	0.6361450	0.8173596	0.5060616	0.6922646	1.0914150	0.6260436	0.7397448	1.0785493	0.3409159
2-Methylbutyric.acid	0.9162436	0.7647800	0.8114202	0.6791095	0.5724590	0.7517002	0.3763115	1.2930302	0.9617106	0.9124321	0.8012958	0.5613845	0.4573325	0.4679710	0.4829717	0.7781003	0.8911581	0.3806420	0.3924137	0.6863296	0.4486746	0.7857104	0.3367745	0.6051235
3-Hydroxyphenylacetic.acid	0.6300611	0.8019803	0.4395543	0.3531513	0.5712445	0.7262196	0.5517035	0.7293511	0.4730190	0.6674977	0.4150897	0.2773652	0.9234166	0.9577731	1.4031874	0.7612582	0.9709512	0.7315022	1.3207369	1.7982472	1.0991215	0.8245665	1.2208213	0.7844164
3-Indoleacrylic.acid	0.06863647	0.07993838	0.29599954	0.01919182	0.00000000	0.13184064	0.03164545	0.14464441	0.09467593	0.11117823	0.01868143	0.01239224	0.92060183	0.61627943	0.93140097	0.66541385	0.56434471	1.32301774	1.42618439	1.99700779	0.37785536	0.20324056	0.60686634	1.64759696
3-Methyl-2-oxovaleric.acid	0.7284818	0.7998605	0.8214719	0.7937070	0.4602629	0.6143488	0.5652290	0.8385703	0.5941437	0.4562508	0.6723339	0.7837716	0.3804015	0.3810327	0.5773716	0.7591478	0.7364682	0.4953530	0.4704629	0.6691918	0.4352169	0.4875276	0.4163757	0.3738398
3-Phenyllactic.acid	0.1588272	0.1628897	0.1481714	0.2012786	0.1907786	0.3345011	0.1358782	0.2337874	0.1476731	0.1240542	0.1009023	0.1153669	0.3804044	0.5534323	0.1483201	0.6223141	0.3725672	0.1412559	0.6140716	0.9084644	0.3132405	0.3880331	0.2251292	0.3031758
4-Hydroxybenzaldehyde	0.2899898	0.4539353	0.2719443	0.1845166	0.4342202	0.1635672	0.3338587	0.3637891	0.3575433	0.3653502	0.3196463	0.1567934	0.1617343	0.6138772	0.2441290	0.4573647	0.5656350	0.4557670	0.6785351	0.7462931	1.9606845	1.3874968	0.6191694	0.2239879
4-Hydroxybenzoic.acid	0.7415720	0.6427323	0.3418409	0.2771368	0.5039981	0.4729974	0.4056269	0.8144809	0.2511309	0.2701269	0.2969636	0.2283418	2.4564177	2.5600532	1.7188250	3.7086417	2.5128617	1.5046030	3.0486985	3.3705885	3.2851761	3.2291628	4.4785681	1.5404096
4-Hydroxyphenylacetic.acid	1.0741901	0.9484975	0.6531368	0.4162101	0.6926568	0.7114619	0.7534805	0.7216074	0.8789581	0.6506508	0.8736327	0.2907721	1.0987438	0.8528024	0.9308913	1.0528581	0.7804062	0.4420478	0.9035063	1.3928209	0.8826471	0.8112688	1.0836423	0.7085074
4-Hydroxyphenylpyruvic.acid	1.14921842	0.98845607	1.98099909	1.72171599	1.23177289	1.72876545	0.83944057	2.56334937	1.38221909	0.52593743	1.12397307	1.22757429	0.24319700	0.39547674	0.44914055	0.12458038	0.68509201	0.18949878	0.47693233	0.48118769	2.00381191	1.66541921	0.79929192	0.08403531
4-Methyl-2-oxopentanoic.acid	0.5350964	0.7260103	0.8990688	0.8404178	0.5670097	0.4391739	0.5110427	0.6475787	0.4532219	0.3383676	0.7675285	0.6123645	0.4158343	0.4958764	0.5988977	0.8790783	0.7914478	0.4360865	0.6702444	0.6582298	0.4875331	0.4562112	0.4409016	0.5753140
4-Methylvaleric.acid	1.2193120	1.1373415	1.2803601	1.2649514	0.7155701	1.2545237	1.0279050	1.3477962	1.2666246	0.6921735	1.1916585	0.9646052	0.5288983	0.4787545	0.5958022	0.8224816	0.8099802	0.6323150	0.5876209	0.7061165	0.6493778	0.6388923	0.6152713	0.6383928
Acetyl-L-tyrosine	1.3823909	1.5654071	2.4631201	1.8466601	2.5207747	1.8986028	1.1913219	2.1991471	1.1217505	1.2484589	1.8941245	1.1053379	0.7384137	0.6968520	1.0445795	0.9093524	0.7819208	3.3148925	1.3974540	0.6655445	2.4891795	1.5615589	1.2013689	1.0886114
Allantoin	0.4179758	0.3920830	0.4618506	0.5288154	0.4099781	0.9940990	0.5244163	0.5888625	0.3894575	0.4465263	0.4335474	0.5277082	0.3798188	0.4607883	0.4766550	0.5942443	0.5207472	0.4367983	0.6263660	0.3932992	0.6471256	0.5786775	0.7884335	0.3839070

Table S2B. Serum metabolites

Benzoic.acid	0.5137459	0.8011919	0.8700612	0.7071747	0.7833871	0.5132784	0.9021533	1.0397754	0.6048753	0.4560824	0.7378836	0.9754978	1.1409319	1.1780068	0.7153125	1.3047273	0.8824771	0.6084236	1.1787358	0.6067928	1.2885574	0.9537052	0.9203954	0.6804284
Citraconic.acid	1.1832005	0.8655313	0.8829787	0.9384341	0.7149742	0.9088399	0.8197862	0.9260997	0.7828447	0.6176995	0.8662048	1.0564296	0.6012591	0.5014137	0.6816109	0.8420866	0.9668129	0.6730451	0.7962384	1.0701069	0.6463906	0.4847092	0.6272626	0.4146637
F6P	0.6148911	0.6397381	0.4180315	0.4791333	0.8018948	1.0489481	0.5600311	0.4700166	0.5596413	0.7723185	0.5416507	0.8945571	1.3691818	0.9980324	0.7388595	2.4056484	0.4272504	1.0292442	1.8827413	1.0846360	1.0310069	0.7883688	1.5219983	1.0737757
G6P	0.5960554	0.6725720	0.5424209	0.4639696	0.7149186	1.0277904	0.6028397	0.4610059	0.5065798	0.6587487	0.6167404	0.6808418	1.2350843	1.1748242	0.8482595	2.0001126	0.6219998	1.0504048	1.8062061	1.1607852	0.8258928	0.6993957	1.1175112	1.3118745
Gentisic.acid	0.5139415	0.4151858	0.1699240	0.1634507	0.4950193	0.5381677	0.4975664	0.4815131	0.1646657	0.1868625	0.1272859	0.1044369	1.2590846	1.5629216	1.2770249	2.0023922	1.5103748	1.8111364	1.2449566	2.1445328	1.5509669	1.2755833	1.7910363	1.3444712
Glucuronic.acid	0.2943072	0.3285132	0.3076357	0.3028917	0.4062023	0.3879114	0.3706921	0.4386659	0.3901433	0.3952716	0.3387479	0.4035722	0.3447072	0.3041804	0.3525938	0.3387238	0.4254461	0.2811051	0.3409680	0.3958022	0.2665106	0.3763200	0.4654544	0.4758465
Glutaconic.acid	0.8936806	0.7301086	0.9696221	0.8526519	0.5442453	0.5880147	0.5992676	0.9477549	0.6377112	0.4061179	0.7163246	0.8437270	0.5472146	0.4245548	0.7144656	0.9034756	0.8900980	0.5316449	0.6503364	0.7681063	0.4747078	0.4802786	0.3834784	0.3985794
Isobutyric.acid	1.2611450	1.0617315	1.2009763	1.0144702	1.6725007	1.3712387	0.9813562	1.1676435	1.0259964	1.1891182	1.1904247	1.0942924	1.5989614	1.4913369	1.5619882	2.1045380	1.2262023	2.0379971	1.5637909	1.3742913	1.7912535	2.4635205	2.4077597	0.8333862
Isocitrate	0.9363562	0.9694145	1.8275446	1.6172730	1.9900427	5.4531547	0.8358172	2.2995017	0.9928619	1.4021071	1.0910185	1.6178133	0.6324479	0.5417913	1.1534480	1.0034652	0.4038732	1.0685027	0.8624940	1.8233722	0.7640728	0.5662017	1.4586538	1.0827235
Isovaleric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
Ketoisoleucine	0.6320128	0.6428483	0.8286818	0.8677048	0.5299760	0.6119989	0.6528786	0.9677705	0.5359146	0.4973663	0.6318207	0.7465316	0.4568074	0.5057830	0.6968982	0.8765001	0.8146209	0.5613216	0.6569281	0.7444931	0.5323563	0.4600245	0.4162702	0.4342382
Ketoleucine	0.7407093	0.6770491	0.8666374	0.8526344	0.4862419	0.6715415	0.6274490	0.9300686	0.5821689	0.4755816	0.6434545	0.7973945	0.4390582	0.4554591	0.6420511	0.8235266	0.8422553	0.5404413	0.5446198	0.7969653	0.5417458	0.5267113	0.3870948	0.4680990
Leucic.acid	0.07332520	0.05691064	0.16240462	0.13844880	0.00000000	0.13192383	0.18425088	0.09091516	0.09485068	0.09601863	0.12344032	0.07552676	0.07950051	0.18992066	0.18504689	0.23065715	0.09115326	0.08444802	0.03149924	0.39720394	0.12766977	0.17789873	0.05538901	0.09050159
Levulinic.acid	0.8733528	0.7773803	1.1885660	0.9115188	0.7639572	0.6718761	0.8896795	1.1401628	0.7158665	0.5367945	0.7854932	1.2883168	0.3414807	0.3001495	0.3850537	0.3747144	0.5945561	0.5645422	0.3800352	0.4273772	0.8644449	0.6055051	0.5948493	0.3990532
Mannose	0.6683804	0.7490577	0.9983012	0.8180795	1.3001285	1.6448997	1.1464313	1.2114073	0.8301304	1.2382297	0.8439367	0.8125773	0.6266621	0.8626987	0.8407750	0.8446483	0.6687708	0.4966768	0.7226429	1.1309506	1.0346696	0.5709434	0.9154449	0.4778395
Mucic.acid	1.4449558	1.5175796	1.7136174	1.7628124	2.9718829	3.5026565	2.1747000	2.7953622	1.7672312	2.1885316	1.4510821	1.0805201	0.9881322	0.4407361	0.5894630	0.4070065	1.0587811	0.3780752	1.0418203	0.6686453	1.6099692	1.3606473	1.4986516	0.2406813
Myoinositol	0.9158956	1.0903492	1.0132274	0.7188772	1.0656828	1.1381421	1.0394161	1.4046805	0.7925365	1.0714162	0.8230511	1.0257722	0.9557425	0.9178068	1.1749202	0.9482438	0.8227359	0.9848646	0.8354734	1.0013812	1.1290946	0.6984916	0.7774978	0.6192854
Nonadecanoic.acid	0.7597794	1.0984831	1.0566841	0.6869035	0.7567158	0.6152611	1.1422799	0.7788149	0.9910287	0.5742253	0.6355600	0.7711078	0.6560131	0.6744979	0.6686692	0.4608864	0.5979236	0.7173817	0.5101773	0.4252656	0.8019144	0.5360187	0.6069391	0.7542067
Palmitic.acid	1.1697404	1.1289978	1.0746644	1.0579965	1.0081349	1.0744314	1.1476871	1.1941974	0.8681928	1.2085481	0.9326418	1.0318683	0.8677152	0.6149741	1.0140553	0.7505703	0.9214058	0.8712176	0.6402457	0.9742409	0.8439879	0.7187422	0.7523927	0.6433307
Pentadecanoic.acid	1.0416191	1.0968575	1.2484225	1.3574081	1.1434541	1.0799144	1.1658474	1.1948132	1.3305186	1.2054729	1.2713009	1.5459406	0.8983497	0.5198255	0.6073550	0.4853418	0.5751780	1.0182041	0.5896763	0.4666398	0.7345063	0.5951775	0.7111444	1.3217963
Phenylglyoxylic.acid	0.6505425	0.7622024	0.4309066	0.4541979	0.2762495	0.7508618	0.5632261	0.6586299	0.5866884	0.5445800	0.4662587	0.1722703	0.7744946	0.6864339	0.7886320	1.3051016	0.5019615	0.4552686	0.6690830	1.0880316	0.3913430	0.4653460	0.7296399	0.4115943
Phenylpyruvic.acid	1.6837193	1.1946551	1.2117800	1.4134552	1.2954706	2.1709991	1.1442532	2.6172624	1.0717084	1.3957800	1.0979073	1.1359335	1.1605814	1.1434987	1.1531757	0.9821010	1.4858917	0.9080724	1.9169820	1.1176169	2.5614484	2.4989341	1.3980044	0.5780909
Phthalic.acid	0.8312283	1.6718001	1.6295232	0.6950160	0.9813302	0.7106078	1.0632694	0.8647620	0.8410628	0.7436008	0.7956362	1.1354350	0.8725004	0.8293501	1.0938052	0.5822359	1.4563201	0.5690216	0.9613559	0.6940954	1.4272887	0.7233408	0.5024063	0.4871232
Pregnenolone.sulfate	0.15109681	0.06450606	0.07824688	0.11139556	0.16581628	0.10776864	0.25053390	0.01274011	0.18073139	0.11896680	0.04564024	0.04885158	0.01195747	0.02402525	0.01011219	0.17572145	0.13117700	0.39292133	0.39154295	0.10137071	0.05705211	0.00000000	0.16982081	0.79087325
Sorbitol	0.5263006	1.1125334	0.8735987	1.0204774	1.8649705	2.9610703	1.1785228	1.5158011	2.0153651	1.8722321	1.1390051	0.8823096	1.0456780	0.9890519	1.3129599	1.0471344	0.9181730	0.6389121	0.9514893	1.4349702	0.5031007	0.5956122	1.2551092	1.2870245
Stearic.acid	1.0184713	1.0750990	1.2224773	1.0051354	0.9065094	0.7811735	1.1789520	0.8386794	0.7374513	0.8942426	0.7940715	1.0533583	0.9066691	0.8976884	0.9911621	0.7727796	1.1123866	0.8484215	0.7059182	0.8682556	1.0533575	0.7744590	0.7948777	0.6558604
Suberic.acid	0.6717550	0.7711379	1.0687371	1.0001316	1.0048246	0.9080725	0.9082036	1.1276302	0.8134137	0.8582683	0.7563850	0.8792998	0.7326972	0.6036770	0.8775342	0.9730880	0.7433058	0.9116463	0.9155839	0.7838742	0.8153078	0.6814005	0.7289064	0.8155878
Valeric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
X5P	0.5027232	0.5146277	0.3386513	0.4047086	0.8736686	0.7205287	0.3494380	0.3850901	0.2681374	1.0155902	0.3328307	0.5785047	2.9203121	2.3234867	2.2986260	4.6446462	1.7533107	2.0129461	3.7469756	2.2407628	2.3747651	1.7961056	2.2261729	2.3189625
alpha-Hydroxyisovaleric.acid	0.2371994	0.2527587	0.3991637	0.3119418	0.2179633	0.4664979	0.3021191	0.2406591	0.1822040	0.2528320	0.4813419	0.2408560	0.1477089	0.1300373	0.2515798	0.1820547	0.2035981	0.1894338	0.3520112	0.1956317	0.1405861	0.1275436	0.3147498	0.1255165
alpha-ketoisovaleric.acid	1.1483537	0.9211920	1.0424223	1.1143107	0.6507956	0.7640291	0.9224072	1.3979542	0.8386406	0.5159111	1.0674584	1.1048148	0.5318858	0.4081003	0.6895266	0.8388138	0.6593168	0.4917263	0.4880581	0.7309270	0.7401869	0.6986751	0.6619629	0.5088614
p-Coumaric.acid	0.8884362	2.5429656	0.8671267	0.3814133	0.4828513	0.4830849	0.3138755	1.1793190	1.9050500	0.2601965	1.4171255	0.5975559	0.5928540	0.5256743	0.5782154	0.6462564	0.6272135	0.2994134	0.7650979	0.6735591	1.3843546	0.5536971	4.3952783	2.8617781

Constructed from biom file

#OTU ID	CO.1	CO.2	CO.3	PCB6.1	PCB6.2	PCB6.3	PCB30.1	PCB30.2	PCB30.3
D_0__Bacteria;D_1__Actinobacteria;D_2__Actinobacteria;D_3__Bifidobacteriales;D_4__Bifidobacteriaceae;D_5__Bifidobacterium;__	0	0	18	0	0	0	0	0	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;Ambiguous_taxa	19	26	15	43	0	0	0	37	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium	0	0	0	74	122	109	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Barnesiellaceae;D_5__uncultured;D_6__Bacteroides sp. Tilapia9	0	12	0	0	16	0	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	9296	10607	8015	13871	7845	10279	6933	7367	10551
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;__;__	8115	8838	9280	5390	6298	5799	7923	10196	7843
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Rikenellaceae;D_5__Alistipes;__	2588	2712	2528	1387	2374	1818	3313	2397	2808
D_0__Bacteria;D_1__Cyanobacteria;D_2__Oxyphotobacteria;D_3__Chloroplast;__;__;__	8	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Bacillales;D_4__Bacillaceae;D_5__Bacillus;__	0	0	0	0	0	0	61	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Lactobacillaceae;D_5__Lactobacillus;D_6__Lactobacillus gasseri	329	316	457	795	190	685	1548	189	1114
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Streptococcaceae;D_5__Lactococcus;__	39	0	30	35	59	37	0	0	40
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiaceae 1;D_5__Clostridium sensu stricto 1;D_6__uncultured bacterium	62	58	55	18	0	0	0	0	254
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;Ambiguous_taxa;Ambiguous_taxa	0	57	0	0	103	0	109	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;D_5__uncultured bacterium;D_6__uncultured bacterium	46	228	28	41	198	39	178	80	188
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;__;__	94	120	0	127	141	161	65	180	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Defluviitaleaceae;D_5__Defluviitaleaceae UCG-011;Ambiguous_taxa	131	154	92	70	0	188	0	0	159
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium	0	0	0	55	60	105	106	57	41
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] brachy group;D_6__uncultured bacterium	0	0	0	0	0	7	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured bacterium	0	16	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured organism	0	3	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;__	67	62	63	0	185	0	94	208	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;D_6__uncultured bacterium	1455	1296	1162	1122	1580	431	1767	1383	1644
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;__	121	91	123	0	17	1803	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium	109	0	162	0	0	0	0	37	64
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;Ambiguous_taxa	303	293	302	0	287	0	278	0	279
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;D_6__uncultured bacterium	0	362	472	585	226	498	237	393	324
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;__	0	106	114	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetitomaculum;D_6__Firmicutes bacterium CAG_194_44_15	262	245	321	454	304	0	319	241	294
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;D_6__Lachnospiraceae bacterium 609	203	0	320	0	1693	0	0	0	128
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;__	257	183	319	222	0	250	83	117	206
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium	331	388	366	244	287	206	757	591	869
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens	486	530	520	91	214	151	130	84	161
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__uncultured bacterium	244	0	512	0	0	572	0	631	636
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;__	905	727	990	1994	843	1142	628	1336	656
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae FCS020 group;__	143	117	105	173	98	92	183	212	147
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;D_6__uncultured bacterium	4489	4932	2051	4199	4272	3122	2789	1700	3057
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;__	8765	8865	8624	6923	9399	7884	12717	12190	11786
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa	718	738	571	0	0	0	668	406	1198
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium	466	499	0	0	0	0	858	0	897
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;__	1120	848	1065	0	313	0	0	878	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;D_6__uncultured bacterium	112	142	0	1124	150	150	218	226	821
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;__	0	0	70	0	0	193	0	287	154
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;Ambiguous_taxa	0	0	0	0	0	36	51	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;D_6__uncultured bacterium	297	293	243	425	252	0	106	231	208
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44	0	0	0	0	0	0	74	43	109
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium	474	445	507	945	1516	529	2001	861	1832
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;__	0	0	129	0	0	0	27	126	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella 3;D_6__uncultured bacterium	183	31	283	415	0	5	37	703	431
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella;D_6__uncultured bacterium	57	67	0	72	58	72	84	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;D_6__uncultured bacterium	226	227	201	0	825	0	912	291	295
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;__	0	0	0	0	0	0	181	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016	0	0	0	159	97	171	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Clone-47	234	331	135	0	112	195	68	73	541

D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture Jar-19	0	0	0	93	0	0	0	0	94
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-27	0	0	164	0	118	0	125	0	72
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-54	0	0	0	0	0	71	50	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__uncultured bacterium	3274	2630	2983	2961	2110	2254	3683	2587	3054
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;__	350	385	616	511	297	410	584	497	381
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;__;__	6804	5724	7057	7593	6563	4562	6732	5530	11105
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptococcaceae;D_5__uncultured;Ambiguous_taxa	89	70	66	64	43	104	88	128	132
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptostreptococcaceae;D_5__Romboutsia;__	0	0	0	0	0	0	0	62	84
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium	149	111	197	98	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;__	76	0	54	127	88	175	51	0	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__GCA-900066225;__	64	0	95	0	104	0	0	84	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Harryflintia;D_6__uncultured bacterium	0	0	0	0	0	0	0	30	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	258	141	349	112	119	391	0	129	155
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	227	254	153	0	320	0	0	265	432
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;D_6__uncultured bacterium	101	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium	0	0	0	270	0	58	51	440	164
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__unidentified	1602	1557	1495	1500	1279	920	524	1258	1403
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;__	436	440	421	340	213	176	800	266	354
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;Ambiguous_taxa	501	564	356	762	366	492	415	540	394
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;D_6__uncultured bacterium	387	58	461	124	290	213	335	405	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 6;__	91	104	64	190	562	242	118	235	218
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium	232	220	248	325	308	299	351	238	463
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;__	1161	1127	873	1270	1378	1155	1290	1131	1291
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium;D_6__uncultured bacterium	2409	2239	2033	1913	1367	1784	2656	2134	2415
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae NK4A214 group;D_6__uncultured bacterium	0	0	0	0	0	25	0	81	34
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-005;Ambiguous_taxa	0	95	0	164	116	212	35	180	114
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-009;Ambiguous_taxa	454	473	388	283	552	265	684	622	611
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-010;D_6__uncultured organism	77	53	70	79	59	134	59	54	112
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium	94	48	118	158	437	187	502	1052	104
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;__	0	0	0	0	0	70	0	0	60
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;D_6__uncultured bacterium	0	32	0	72	183	75	0	72	264
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;__	277	280	352	51	163	136	95	57	731
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcus 1;__	1370	1132	1457	263	1098	139	1583	2721	1531
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__[Eubacterium] coprostanoligenes group;__	401	231	489	14	315	34	134	85	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1	0	0	0	980	816	685	110	176	785
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__unidentified	120	139	147	108	144	110	421	134	140
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;__	37	22	42	21	0	24	653	394	406
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;__;__	1109	1025	1157	441	580	499	1166	1030	902
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis	556	613	516	135	106	0	0	0	20
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa	0	23	37	200	63	530	55	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Turicibacter;__	471	277	460	329	133	421	191	149	237
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	0	0	0	39	31	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured;D_6__uncultured bacterium	0	55	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Anaeroplasmatales;D_4__Anaeroplasmataceae;D_5__Anaeroplasma;Ambiguous_taxa	275	338	0	562	1369	786	922	665	625
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;Ambiguous_taxa;Ambiguous_taxa;Ambiguous_taxa	0	0	16	0	0	0	0	0	50
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;D_4__uncultured bacterium;D_5__uncultured bacterium;D_6__uncultured bacterium	138	137	0	100	147	87	44	87	66
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;__;__;__	245	479	91	42	203	0	417	216	279
D_0__Bacteria;D_1__Verrucomicrobia;D_2__Verrucomicrobiae;D_3__Verrucomicrobiales;D_4__Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium	0	20	0	2363	1475	7608	0	0	0

#Differentially abundant for PCB6

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
316.7182704	-11.65082862	1.236665352	-9.421165231	0	0	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa
153.3172368	-10.60410763	3.148390595	-3.368104215	0.0007568698067	0.005710926723	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium
41.03072715	-8.702464375	3.274032281	-2.658026442	0.007859972585	0.04077360779	Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium
319.3213166	-1.580215074	0.3616598924	-4.369340109	0.00001246225466	0.0001292958921	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
781.7386176	-0.9207800117	0.1196190574	-7.69760297	0	0	Ruminococcaceae;__;__
7200.677116	-0.3902585448	0.08636488756	-4.518717685	0.000006221528614	0.00007376955357	Muribaculaceae;__;__
275.8941433	0.6171854875	0.2015178394	3.062684124	0.002193614783	0.01517250225	Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium
754.2569069	1.264658563	0.4337143845	2.915878763	0.003546882969	0.02102794903	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
177.0232909	1.776599012	0.6062650277	2.930399958	0.003385259774	0.02102794903	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
214.5092189	2.099707756	0.5666020505	3.705789194	0.0002107335238	0.001749088248	Ruminococcaceae;D_5__Ruminiclostridium 6;__
149.9534028	3.917624073	1.51816477	2.580499923	0.009865737835	0.04816801414	Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa
38.92808467	8.824512079	1.427806771	6.180466614	0.0000000006391241199	0.000000008841216991	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
2019.466775	9.269818825	2.203252554	4.207333747	0.00002584013765	0.0002383034916	Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium
53.84095289	9.292598686	1.328101098	6.996906108	0	0	Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium
62.8067954	9.514101089	3.293079828	2.889119482	0.003863222531	0.02137649801	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
76.87108532	9.805534228	1.36829318	7.166252356	0	0	Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016
447.5479333	12.34718529	1.245794989	9.911089227	0	0	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

Table S4B. PCB30 Differentially

#Differentially abundant bacteria for PCB30

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
83.46976574	-9.948696447	1.426866799	-6.972407274	0	0.0000000001386455415	Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium
61.1174388	-9.499046883	1.511973717	-6.282547625	0.0000000003330691888	0.000000005928631561	Lachnospiraceae;D_5__A2;__
39.30425587	-8.862241275	2.96685731	-2.987080385	0.002816556532	0.01790525224	Lachnospiraceae;D_5__Acetatifactor;__
307.8175697	-6.935230581	1.27412215	-5.443144191	0.00000005234823872	0.0000006655704638	Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis
334.6713868	-2.313158666	0.3287417297	-7.036401093	0	0.0000000001386455415	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
308.0630698	-1.346206268	0.4204681762	-3.201684084	0.001366267468	0.009353677279	Erysipelotrichaceae;D_5__Turicibacter;__
8798.415146	-0.4334527046	0.1329022528	-3.261439858	0.001108479444	0.008968606407	Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium
532.8390926	0.7735398016	0.2396538735	3.227737529	0.001247734027	0.009254027366	Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium
965.8942038	1.446139973	0.3454244671	4.186559179	0.00002832151155	0.0002800682809	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
332.2258696	2.576372032	0.9118396441	2.825466132	0.004721187874	0.02801238138	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
246.2103261	3.623458987	0.5613278261	6.455156539	0.0000000001081070969	0.000000002405382905	Ruminococcaceae;D_5__uncultured;__
32.70775081	8.350701175	2.012224217	4.149985427	0.00003324964435	0.0002959218347	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
33.11545623	8.369454039	1.915893281	4.36843436	0.00001251404163	0.0001392187131	Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44
107.2867183	10.06452036	1.673272351	6.014872807	0.000000001800279971	0.0000000267041529	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
144.5866908	10.49616302	1.535432272	6.835966137	0	0.0000000002416474138	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

Table S5-a. Correlation between differentially abundant bacteria and metabolties

Biocompartment	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Serum	Serum	Serum	Serum	Serum	Serum
Taxa	3-Hydroxybutyric acid	Acetylcarnitine	Adenylosuccinate	Aminoisobutyric acid	Arginine	Dimethylglycine	Folinic acid	NADP	Shikimic acid	6-Methyl-DL-tryptophan	Asparagine	Proline	Serine	Urocanic acid	Levulinic acid
Lachnospiraceae UCG-001 Ambiguous	0.745869854	-0.1695158759	-0.1525642883	-0.5933055657	-0.2373222263	-0.5424508029	0.288176989	0.01695158759	-0.08475793795	0.1186611131	0.2034190511	0.2034190511	-0.1017095255	0.05085476277	-0.1017095255
Lachnospiraceae UCG-001 uncultured	0.3286335345	0.1825741858	0.1278019301	-0.2921186973	-0.4746928832	-0.3103761159	0.01825741858	0.2008316044	0.2373464416	0.1460593487	0.3834057903	0.4016632088	0.1460593487	0.3651483717	0.1643167673
Lachnospiraceae ASF356 uncultured	0.5659799761	-0.4929503018	-0.3103761159	-0.4016632088	0.1643167673	-0.3286335345	0.2738612788	-0.2921186973	-0.4016632088	0.2008316044	-0.07302967433	-0.1825741858	-0.2373464416	-0.09128709292	-0.07302967433
Clostridium scindens	0.6666666667	-0.65	-0.5833333333	-0.5166666667	0.5833333333	-0.5	0.7	-0.45	-0.4	-0.45	-0.2833333333	-0.4666666667	-0.5166666667	-0.65	-0.7833333333
Ruminococcaceae	0.7166666667	-0.6666666667	-0.1666666667	-0.55	0.05	-0.6	0.1666666667	-0.4	-0.1333333333	0	-0.1166666667	-0.1666666667	-0.4166666667	-0.15	-0.15
Muribaculaceae	0.6833333333	-0.6666666667	0.1	-0.3333333333	-0.03333333333	-0.3666666667	0.03333333333	-0.2333333333	0.05	0.1333333333	-0.08333333333	-0.05	-0.3166666667	-0.1833333333	-0.06666666667
Ruminiclostridium 9 uncultured	-0.6333333333	0.6666666667	0.2	0.4333333333	-0.6	0.45	-0.3833333333	0.3166666667	0.45	0.5833333333	0.4833333333	0.55	0.7833333333	0.6333333333	0.7
Roseburia uncultured	-0.65	0.55	0.55	0.6666666667	-0.7666666667	0.6333333333	-0.4333333333	0.35	0.7333333333	0.6166666667	0.6333333333	0.6	0.8666666667	0.7333333333	0.8333333333
Ruminococcaceae UCG-013 uncultured rumen bacterium	-0.6333333333	0.2833333333	0.7333333333	0.75	-0.35	0.65	-0.6333333333	0.3	0.6166666667	0.4	0.2833333333	0.3333333333	0.4333333333	0.55	0.65
Ruminiclostridium 6	-0.6666666667	0.6	0.6	0.8833333333	-0.1833333333	0.9	-0.1833333333	0.6	0.5166666667	0.2166666667	0.45	0.3833333333	0.6166666667	0.4	0.3
Erysipelatoclostridium Ambiguous	-0.745869854	0.3559833394	-0.08475793795	0.372934927	0.2542738139	0.3051285766	-0.2712254014	0	0.08475793795	-0.2373222263	-0.2373222263	-0.1186611131	0.08475793795	-0.1017095255	-0.05085476277
Family XIII UCG-001 uncultured	-0.8136762043	0.745869854	0.7119666788	0.8814825547	-0.2542738139	0.8136762043	-0.5424508029	0.661111916	0.6780635036	0.3220801642	0.4576928649	0.5424508029	0.6102571533	0.661111916	0.4915960401
Akkermansia muciniphila	-0.5477225575	0.3468909531	-0.1278019301	0.3103761159	0.4199206274	0.3103761159	0.03651483717	0.1095445115	-0.1095445115	-0.4564354646	-0.2556038602	-0.219089023	-0.03651483717	-0.2921186973	-0.3468909531
Enterorhabdus uncultured	-0.6534973784	0.3168472138	0.0990147543	0.6336944275	0.2475368857	0.6336944275	0.0990147543	0.1485221314	0.1188177052	-0.2277339349	0.04950737715	-0.1188177052	0.2574383612	-0.04950737715	-0.1089162297
Oscillibacter uncultured	-0.5744562647	0.6614950926	0.3568591947	0.3568591947	-0.3916747259	0.3916747259	-0.687606741	0.4613057883	0.1914854216	0.4874174367	0.130558242	0.4438980227	0.4177863743	0.5048252023	0.644087327
Clostridiales bacterium CIEAF 016	-0.7525121327	0.4554678698	-0.01980295086	0.5148767223	0.3663545909	0.5148767223	-0.07921180344	0.1683250823	-0.05940885258	-0.2871427875	-0.1485221314	-0.1584236069	0.1188177052	-0.06931032801	-0.1287191806
Clostridium sp. Culture-1	-0.8306277919	0.6272087408	0.2373222263	0.6780635036	-0.2034190511	0.7119666788	-0.2373222263	0.3220801642	0.2542738139	0.1695158759	0.2203706387	0.2034190511	0.5763539781	0.288176989	0.372934927
Anaerotruncus uncultured	0.5659799761	-0.8033264177	-0.8398412548	-0.8580986734	0.5659799761	-0.8580986734	0.4016632088	-0.8580986734	-0.8215838363	-0.5842373947	-0.7850689991	-0.8215838363	-0.8580986734	-0.8215838363	-0.6207522318
Lachnospiraceae A2	0.2872281323	-0.3307475463	-0.3829708431	-0.174077656	0.8964999282	-0.174077656	0.4526019055	-0.1479660076	-0.4351941399	-0.5135290851	-0.3568591947	-0.4526019055	-0.5570484991	-0.4961213195	-0.8007572174
Acetatifactor	0.593366104	-0.6390096504	-0.6390096504	-0.7074749701	0.3195048252	-0.7074749701	0.1825741858	-0.5477225575	-0.3195048252	-0.1597524126	-0.5249007843	-0.3195048252	-0.502079011	-0.7074749701	-0.4792572378
Dubosiella newyorkensis	0.661111916	-0.7628214416	-0.7797730292	-0.7967246168	0.4407412774	-0.7628214416	0.6950150912	-0.7628214416	-0.7119666788	-0.6780635036	-0.5763539781	-0.7628214416	-0.7119666788	-0.8645309671	-0.7289182664
Turicibacter	0.2333333333	-0.3166666667	-0.7666666667	-0.6166666667	0.7666666667	-0.6	0.2	-0.4666666667	-0.8333333333	-0.4833333333	-0.7	-0.6166666667	-0.7333333333	-0.5333333333	-0.5833333333
Muribaculaceae uncultured	-0.1	0.1166666667	-0.6333333333	-0.3333333333	0.65	-0.2666666667	0.2666666667	-0.1666666667	-0.7333333333	-0.65	-0.5833333333	-0.5166666667	-0.4833333333	-0.55	-0.6166666667
Lachnospiraceae GCA-900066575 uncultured	0.3666666667	0.01666666667	0.3333333333	-0.1833333333	-0.75	-0.2	-0.2833333333	0.1833333333	0.4833333333	0.6166666667	0.45	0.6	0.3333333333	0.4666666667	0.5333333333
Ruminococcaceae uncultured	0.1166666667	0.1833333333	0.4	-0.01666666667	-0.4666666667	-0.05	-0.5333333333	0.3166666667	0.35	0.65	0.3333333333	0.5666666667	0.2333333333	0.6333333333	0.5833333333
Clostridium sp. Clone-44	-0.06931032801	0.5049752469	0.5445811486	0.2277339349	-0.8218224607	0.2475368857	-0.4554678698	0.5544826241	0.6039900012	0.8218224607	0.6832018047	0.8416254115	0.6832018047	0.8218224607	0.782216559

	Phase-I Ces2c	Phase-I Cyp1a2	Phase-I Cyp2a5	Phase-I Cyp2b10	Phase-I Cyp2c29	Phase-I Cyp2c54	Phase-I Cyp2j9	Phase-I Cyp3a16	Phase-I Cyp3a41a	Phase-I Cyp17a1	Phase-I Cyp26a1	Phase-I Aldh1a7	Phase-I Ces1b	Phase-I Cyp1a1	Phase-I Cyp2c50	Phase-I Cyp2c55	Phase-I Cyp3a44	Phase-I Cyp4a14	Phase-I Nqo1
Lachnospiraceae UCG-001 Ambiguous	-0.1356127007	-0.06780635036	0.3051285766	-0.01695158759	0	-0.03390317518	0.6272087408	-0.3898865146	-0.5254992153	-0.2712254014	-0.5424508029	0.1525642883	0	0.03390317518	-0.1186611131	0.4576928649	-0.288176989	0.050854762	-0.05085476277
Lachnospiraceae UCG-001 uncultured	0.2921186973	0.4016632088	0.6937819062	0.3834057903	0.4016632088	0.4016632088	0.3468909531	-0.3651483717	-0.1460593487	0.219089023	-0.5477225575	0.4564354646	0.3468909531	0.4016632088	0.3103761159	0.6390096504	-0.1460593487	-0.2738612788	0.3834057903
Lachnospiraceae ASF356 uncultured	-0.4199206274	-0.5477225575	-0.6024948133	-0.3468909531	-0.438178046	-0.4929503018	0.4564354646	0.219089023	-0.3468909531	-0.6390096504	-0.09128709292	-0.4199206274	-0.3651483717	-0.3834057903	-0.5112077203	-0.1278019301	0.1278019301	0.1825741858	-0.4016632088
Clostridium scindens	-0.6666666667	-0.55	-0.3	-0.85	-0.6666666667	-0.7333333333	0.6833333333	0.3166666667	-0.2	-0.7833333333	-0.3666666667	-0.4666666667	-0.7666666667	-0.7333333333	-0.85	-0.4833333333	0.2666666667	0.6333333333	-0.75
Ruminococcaceae	-0.3666666667	-0.4833333333	-0.2833333333	-0.4333333333	-0.4	-0.4833333333	0.5166666667	0.4	0.01666666667	-0.6	-0.1333333333	-0.08333333333	-0.3666666667	-0.35	-0.5	-0.06666666667	0.3833333333	0.06666666667	-0.45
Muribaculaceae	-0.3333333333	-0.5666666667	-0.3833333333	-0.4833333333	-0.3833333333	-0.5166666667	0.1666666667	0.3333333333	0.03333333333	-0.6333333333	0.1	-0.01666666667	-0.2833333333	-0.2666666667	-0.4666666667	-0.03333333333	0.1666666667	0.03333333333	-0.5333333333
Ruminiclostridium 9 uncultured	0.7166666667	0.8166666667	0.5666666667	0.7833333333	0.6833333333	0.8333333333	-0.1333333333	-0.1666666667	0.1	0.7	-0.15	0.06666666667	0.7	0.65	0.75	0.3333333333	-0.1666666667	-0.2333333333	0.85
Roseburia uncultured	0.9333333333	0.8666666667	0.5833333333	0.7833333333	0.7333333333	0.8833333333	-0.4333333333	0.1166666667	0.45	0.6833333333	-0.1333333333	0.15	0.7333333333	0.75	0.8166666667	0.35	0.08333333333	-0.4333333333	0.9
Ruminococcaceae UCG-013 uncultured	0.5833333333	0.3666666667	-0.03333333333	0.4166666667	0.45	0.3666666667	-0.8333333333	0.45	0.8166666667	0.45	0.4166666667	0.3166666667	0.4833333333	0.5	0.45	0.1333333333	0.3833333333	-0.6333333333	0.4
Ruminiclostridium 6	0.5833333333	0.5666666667	0.2333333333	0.4	0.5333333333	0.4666666667	-0.8166666667	-0.03333333333	0.4	0.5	0.01666666667	0.2	0.45	0.5166666667	0.45	0.2	-0.06666666667	-0.35	0.45
Erysipelatoclostridium Ambiguous	0.1017095255	0.288176989	0.1017095255	0.08475793795	0.1356127007	0.1695158759	-0.288176989	0.1356127007	0.4068381022	0.4576928649	0.3390317518	0	0.08475793795	0.01695158759	0.1864674635	-0.3559833394	0.1356127007	0.08475793795	0.1356127007
Family XIII UCG-001 uncultured	0.6780635036	0.7289182664	0.3390317518	0.5933055657	0.7628214416	0.5763539781	-0.8306277919	0.08475793795	0.7289182664	0.745869854	0.1356127007	0.5424508029	0.6780635036	0.7119666788	0.5763539781	0.372934927	0.1525642883	-0.661111916	0.5763539781
Akkermansia muciniphila	-0.05477225575	0.1460593487	0.07302967433	-0.05477225575	0.01825741858	0.03651483717	-0.3103761159	-0.1643167673	0.09128709292	0.3103761159	0.2008316044	-0.01825741858	-0.07302967433	-0.09128709292	0.05477225575	-0.3103761159	-0.1278019301	0.2008316044	-0.01825741858
Enterorhabdus uncultured	0.2376354103	0.3069457383	0.01980295086	0.02970442629	0.1089162297	0.1584236069	-0.4851722961	0.207930984	0.3663545909	0.277241312	0.03960590172	-0.1980295086	-0.01980295086	0.01980295086	0.1188177052	-0.3366501646	0.1881280332	0.06931032801	0.1584236069
Oscillibacter uncultured	0.3829708431	0.3568591947	0.1218543592	0.7137183894	0.5483446163	0.5396407335	-0.5222329679	-0.5222329679	-0.09574271078	0.6614950926	0.4700096711	0.3916747259	0.6963106238	0.600567913	0.6701989754	0.4438980227	-0.5309368507	-0.4438980227	0.5396407335
Clostridiales bacterium CIEAF 016	0.0990147543	0.2475368857	-0.03960590172	0.1089162297	0.1287191806	0.138620656	-0.4653693452	-0.00990147543	0.2475368857	0.4158619681	0.2574383612	-0.05940885258	0.03960590172	0.01980295086	0.1584236069	-0.2970442629	0.02970442629	0.02970442629	0.138620656
Clostridium sp. Culture-1	0.5424508029	0.5763539781	0.2542738139	0.5254992153	0.4407412774	0.5933055657	-0.5594023905	-0.1525642883	0.1525642883	0.6272087408	0.1356127007	-0.05085476277	0.4237896898	0.4068381022	0.5933055657	0	-0.1864674635	-0.1186611131	0.5933055657
Anaerotruncus uncultured	-0.8398412548	-0.8580986734	-0.5659799761	-0.7302967433	-0.9128709292	-0.7485541619	0.7485541619	0.1825741858	-0.438178046	-0.6937819062	0.1825741858	-0.5659799761	-0.8398412548	-0.9128709292	-0.6937819062	-0.6937819062	0.1460593487	0.6755244876	-0.7302967433
Lachnospiraceae A2	-0.7050145066	-0.5396407335	-0.5657523819	-0.7659416862	-0.5135290851	-0.8094611002	0.2175970699	0.3220436635	0.07833494518	-0.5570484991	-0.04351941399	-0.1914854216	-0.6527912098	-0.6266795614	-0.8529805142	-0.4351941399	0.3568591947	0.3046358979	-0.7920533346
Acetatifactor	-0.7302967433	-0.6390096504	-0.2738612788	-0.7302967433	-0.6390096504	-0.6390096504	0.7302967433	0.06846531969	-0.3879701449	-0.6390096504	0.1369306394	-0.3651483717	-0.5249007843	-0.6390096504	-0.6390096504	-0.4564354646	-0.1597524126	0.7302967433	-0.7302967433
Dubosiella newyorkensis	-0.6780635036	-0.6780635036	-0.2542738139	-0.7119666788	-0.8475793795	-0.5933055657	0.7628214416	0.03390317518	-0.5594023905	-0.6950150912	-0.1695158759	-0.6102571533	-0.8475793795	-0.8475793795	-0.6102571533	-0.6102571533	0.01695158759	0.7797730292	-0.6102571533
Turicibacter	-0.8166666667	-0.65	-0.6	-0.5	-0.6	-0.6666666667	0.55	0	-0.35	-0.3833333333	0.25	-0.2833333333	-0.5833333333	-0.6833333333	-0.6166666667	-0.4666666667	0.08333333333	0.4	-0.6166666667
Muribaculaceae uncultured	-0.5333333333	-0.2833333333	-0.1666666667	-0.2166666667	-0.3333333333	-0.2666666667	0.2333333333	-0.5	-0.5333333333	0.01666666667	0.1666666667	-0.1666666667	-0.3666666667	-0.4333333333	-0.2166666667	-0.3333333333	-0.3666666667	0.4333333333	-0.2833333333
Lachnospiraceae GCA-900066575 uncultured	0.35	0.2666666667	0.4666666667	0.3666666667	0.3833333333	0.3666666667	0.2	-0.1833333333	-0.08333333333	0.08333333333	-0.25	0.3666666667	0.4833333333	0.4833333333	0.3333333333	0.6333333333	-0.2166666667	-0.3	0.3333333333
Ruminococcaceae uncultured	0.2333333333	0.1666666667	0.08333333333	0.4166666667	0.4333333333	0.2166666667	-0.05	-0.06666666667	0.1333333333	0.1833333333	0.06666666667	0.5166666667	0.5333333333	0.5	0.25	0.6333333333	-0.03333333333	-0.5833333333	0.25
Clostridium sp. Clone-44	0.6435959029	0.6138914766	0.5445811486	0.7525121327	0.7525121327	0.6832018047	-0.1485221314	-0.34655164	-0.00990147543	0.4653693452	-0.2277339349	0.4950737715	0.8218224607	0.8218224607	0.6435959029	0.8416254115	-0.3267486892	-0.5643840995	0.6832018047

Phase-I	Phase-I	Phase-I	Phase-I	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter
Por	Cyp26b1	Sdr9c7	Cyb5a	Gclc	Gstm2	Gstm3	Sult2a1	Sult2a2	Sult3a1	Gsta2	Gsta4	Gstm1	Gstm4	Gstp1	Atp2a2	Atp2b2	Atp6v0d2	Slc15a2	Slc16a1	Slc25a30	Slc30a10
0.03390317518	-0.08475793795	-0.05085476277	0.1356127007	0.5424508029	-0.1017095255	0.3051285766	-0.1017095255	-0.1525642883	-0.6441603284	0.4068381022	0.4068381022	0.03390317518	0.1525642883	0.4576928649	0.4237896898	0.1525642883	-0.2373222263	0.7967246168	0.06780635036	0.06780635036	0.01695158759
0.4199206274	-0.3103761159	-0.3834057903	0.5477225575	0.07302967433	0.2921186973	0.5477225575	0.3103761159	0.3103761159	-0.1278019301	0.6207522318	0.6207522318	0.3651483717	0.5294651389	0.4564354646	-0.01825741858	-0.2556038602	0.1825741858	0.6207522318	-0.4016632088	-0.03651483717	-0.3834057903
-0.4746928832	-0.01825741858	0.3651483717	-0.5477225575	0.7302967433	-0.5294651389	-0.09128709292	-0.5659799761	-0.6755244876	-0.7120393248	-0.09128709292	-0.09128709292	-0.2738612788	-0.5294651389	0.6024948133	0.657267069	0.4929503018	-0.6755244876	0.4564354646	0.5477225575	0.5477225575	0.4746928832
-0.65	0.45	0.65	-0.6166666667	0.7833333333	-0.7333333333	-0.6	-0.2666666667	-0.3333333333	-0.5333333333	-0.4333333333	-0.4333333333	-0.7333333333	-0.5166666667	-0.15	0.5166666667	0.6166666667	-0.5	0.4833333333	0.55	0.3833333333	0.5833333333
-0.4	-0.1333333333	0.45	-0.45	0.6666666667	-0.4	-0.2	-0.3166666667	-0.4333333333	-0.4166666667	-0.08333333333	-0.08333333333	-0.45	-0.5333333333	0.4333333333	0.5166666667	0.3833333333	-0.3166666667	0.5666666667	0.4833333333	0.8166666667	0.55
-0.4	-0.15	0.4166666667	-0.5666666667	0.5166666667	-0.3	-0.3166666667	-0.4833333333	-0.5833333333	-0.4166666667	-0.1666666667	-0.1666666667	-0.4833333333	-0.6833333333	0.08333333333	0.35	0.2833333333	-0.1166666667	0.2333333333	0.5666666667	0.6666666667	0.6166666667
0.8	-0.25	-0.7	0.6833333333	-0.5666666667	0.45	0.5	0.7166666667	0.7333333333	0.2833333333	0.3833333333	0.3833333333	0.7333333333	0.75	0.4833333333	-0.5	-0.7333333333	0.2333333333	0.15	-0.8166666667	-0.35	-0.8666666667
0.85	-0.4166666667	-0.7	0.5666666667	-0.75	0.5	0.4	0.7166666667	0.7333333333	0.4833333333	0.35	0.35	0.6833333333	0.5833333333	0.3166666667	-0.7666666667	-0.9333333333	0.4833333333	-0.05	-0.8666666667	-0.1666666667	-0.8666666667
0.3	-0.5833333333	-0.35	0.1	-0.6333333333	0.5	0.15	0.1333333333	0.1666666667	0.6833333333	0.1166666667	0.1166666667	0.35	-0.03333333333	0.03333333333	-0.6833333333	-0.5666666667	0.6333333333	-0.6333333333	-0.3666666667	0.2666666667	-0.25
0.3666666667	-0.2333333333	-0.55	0.2666666667	-0.6666666667	0.4666666667	0.2	0.1833333333	0.3	0.4666666667	0.2	0.2	0.4833333333	0.3166666667	-0.3833333333	-0.8166666667	-0.5833333333	0.6	-0.6833333333	-0.5666666667	-0.4666666667	-0.55
0.1356127007	0.1864674635	-0.06780635036	0.2203706387	-0.5085476277	0.2203706387	-0.1864674635	0.4576928649	0.5254992153	0.6780635036	-0.2712254014	-0.2712254014	0.05085476277	0.2373222263	-0.4068381022	-0.4068381022	-0.1864674635	0.3051285766	-0.4746444525	-0.288176989	-0.2542738139	-0.2034190511
0.4576928649	-0.5933055657	-0.6950150912	0.4915960401	-0.7119666788	0.7628214416	0.4407412774	0.3220801642	0.4407412774	0.745869854	0.4237896898	0.4237896898	0.661111916	0.4407412774	-0.03390317518	-0.8984341423	-0.6780635036	0.8475793795	-0.6272087408	-0.7289182664	-0.1525642883	-0.5933055657
-0.01825741858	0.3834057903	-0.01825741858	0.1460593487	-0.4016632088	0.1278019301	-0.2008316044	0.2008316044	0.3103761159	0.4564354646	-0.2556038602	-0.2556038602	-0.01825741858	0.219089023	-0.7302967433	-0.3103761159	0	0.219089023	-0.5842373947	-0.1460593487	-0.5842373947	-0.1278019301
0.06931032801	0.207930984	-0.1089162297	0.00990147543	-0.4950737715	0.04950737715	-0.2178324595	0.2475368857	0.3366501646	0.4950737715	-0.2475368857	-0.2475368857	0.06931032801	0.1188177052	-0.5544826241	-0.5445811486	-0.2376354103	0.2376354103	-0.6039900012	-0.3069457383	-0.3663545909	-0.2871427875
0.4787135539	-0.3307475463	-0.5831601475	0.5483446163	-0.5483446163	0.6614950926	0.5831601475	0.07833494518	0.1392621248	0.2698203667	0.3916747259	0.3916747259	0.6789028582	0.4700096711	0.1914854216	-0.2698203667	-0.3829708431	0.3133397807	-0.4177863743	-0.3568591947	-0.4787135539	-0.4264902571
0.02970442629	0.207930984	-0.1287191806	0.1485221314	-0.4950737715	0.1881280332	-0.07921180344	0.1881280332	0.2970442629	0.5544826241	-0.1881280332	-0.1881280332	0.1485221314	0.2178324595	-0.4950737715	-0.4059604926	-0.0990147543	0.2178324595	-0.6832018047	-0.2475368857	-0.4653693452	-0.2277339349
0.5085476277	0.05085476277	-0.4746444525	0.4068381022	-0.7628214416	0.3559833394	0.1695158759	0.4407412774	0.5254992153	0.4915960401	0.03390317518	0.03390317518	0.4915960401	0.4915960401	-0.2542738139	-0.6102571533	-0.5424508029	0.288176989	-0.5254992153	-0.5763539781	-0.6441603284	-0.6441603284
-0.657267069	0.657267069	0.9128709292	-0.6024948133	0.6390096504	-0.7850689991	-0.6390096504	-0.3103761159	-0.4199206274	-0.4016632088	-0.6755244876	-0.6755244876	-0.8398412548	-0.6024948133	-0.09128709292	0.9128709292	0.8398412548	-0.8215838363	0.3651483717	0.8580986734	0.3468909531	0.8033264177
-0.8442766314	0.1914854216	0.5135290851	-0.5918640302	0.6527912098	-0.4264902571	-0.4090824915	-0.5483446163	-0.5309368507	-0.2175970699	-0.3046358979	-0.3046358979	-0.5396407335	-0.5483446163	-0.2175970699	0.3394514291	0.7050145066	-0.2350048355	-0.08703882798	0.5396407335	0.3829708431	0.6527912098
-0.4336136914	0.502079011	0.6390096504	-0.4564354646	0.6390096504	-0.5477225575	-0.6390096504	-0.1141088661	-0.2282177323	-0.5249007843	-0.5477225575	-0.5477225575	-0.7302967433	-0.4564354646	-0.1369306394	0.6390096504	0.5249007843	-0.4564354646	0.5249007843	0.6390096504	0.2738612788	0.6390096504
-0.4915960401	0.8136762043	0.8136762043	-0.5085476277	0.5424508029	-0.8306277919	-0.661111916	-0.1525642883	-0.2373222263	-0.4746444525	-0.6272087408	-0.6272087408	-0.8136762043	-0.4237896898	-0.3559833394	0.745869854	0.6780635036	-0.7628214416	0.4407412774	0.6780635036	0.03390317518	0.5763539781
-0.6833333333	0.3666666667	0.5833333333	-0.35	0.6166666667	-0.4333333333	-0.2333333333	-0.4166666667	-0.45	-0.2666666667	-0.3333333333	-0.3333333333	-0.45	-0.35	0.15	0.7833333333	0.85	-0.6333333333	0.15	0.65	0.25	0.65
-0.3166666667	0.6166666667	0.2666666667	0.05	0.1	-0.1666666667	-0.1166666667	-0.1333333333	-0.06666666667	-0.03333333333	-0.25	-0.25	-0.1833333333	0.1333333333	-0.4333333333	0.4	0.55	-0.3666666667	-0.2	0.2833333333	-0.5833333333	0.2
0.4666666667	-0.4666666667	-0.3666666667	0.3333333333	0.06666666667	0.2833333333	0.4166666667	0.2	0.1333333333	-0.2666666667	0.5	0.5	0.3166666667	0.25	0.5833333333	-0.03333333333	-0.4	0.2	0.6	-0.2666666667	0.2	-0.2666666667
0.2166666667	-0.75	-0.4	0.2666666667	0.1166666667	0.45	0.6	-0.1166666667	-0.15	-0.1	0.6	0.6	0.45	0.1166666667	0.8166666667	0	-0.2166666667	0.25	0.2666666667	-0.1666666667	0.4333333333	-0.1
0.6832018047	-0.6733003292	-0.7723150835	0.6138914766	-0.2277339349	0.6039900012	0.7723150835	0.2574383612	0.2574383612	-0.07921180344	0.7723150835	0.7723150835	0.7723150835	0.5643840995	0.7030047555	-0.3366501646	-0.6435959029	0.3861575418	0.3168472138	-0.6138914766	-0.07921180344	-0.6336944275

Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Abcc4	Abcg8	Slc10a2	Slc17a2	Slc3a1	Slc46a3	Slc7a2	Slco1a1	Bcl6	Cldn1	Egr1	Lcn2	Nlrp12
0.1695158759	0.1525642883	0.4068381022	0.3051285766	-0.1525642883	-0.3898865146	0.2203706387	-0.2203706387	0.4407412774	0.6102571533	0.4576928649	-0.1864674635	-0.1356127007
0.4016632088	0.3286335345	0.3468909531	-0.1095445115	-0.05477225575	0.09128709292	0.4746928832	-0.4746928832	0.7302967433	0.1095445115	0.3651483717	0.2738612788	-0.3286335345
-0.2373464416	-0.01825741858	0.2921186973	0.4564354646	-0.2556038602	-0.4929503018	-0.3468909531	0.2921186973	-0.3103761159	0.5659799761	-0.01825741858	-0.5842373947	0.05477225575
-0.7	-0.08333333333	-0.25	0.75	-0.6666666667	-0.5333333333	-0.7	0.05	-0.3	0.6	-0.06666666667	-0.15	0.06666666667
-0.35	0	0.2333333333	0.35	-0.6666666667	-0.2833333333	-0.3833333333	0.15	0	0.4833333333	-0.08333333333	-0.1	-0.45
-0.35	-0.1166666667	0.3333333333	0.1833333333	-0.3333333333	-0.35	-0.3333333333	0.2666666667	-0.03333333333	0.4833333333	-0.1	-0.2666666667	-0.4166666667
0.7	0.7	0.3	-0.45	0.5	0.4	0.6666666667	-0.6333333333	0.4166666667	-0.7	0.3	0.1166666667	0.3333333333
0.55	0.6833333333	0.2833333333	-0.7	0.5666666667	0.6833333333	0.5833333333	-0.6	0.6	-0.8833333333	0.01666666667	0.3833333333	0.05
0.15	0.2	0.1833333333	-0.8	0.3333333333	0.6166666667	0.1166666667	-0.05	0.1	-0.7666666667	-0.4833333333	0.3	-0.4
0.1833333333	0.2	-0.01666666667	-0.65	0.7833333333	0.4333333333	0.2333333333	-0.2833333333	0.1666666667	-0.6333333333	-0.2666666667	0.2	0.1
0.01695158759	0.05085476277	-0.4237896898	-0.1864674635	-0.05085476277	0.3051285766	-0.03390317518	-0.1356127007	-0.288176989	-0.6102571533	-0.1356127007	0.3051285766	0.2034190511
0.3559833394	0.3898865146	0.1695158759	-0.8814825547	0.5254992153	0.5763539781	0.3220801642	-0.4407412774	0.2203706387	-0.8475793795	-0.3220801642	0.3559833394	-0.2712254014
-0.09128709292	-0.2373464416	-0.5659799761	-0.03651483717	0.1460593487	0.1278019301	-0.07302967433	0.01825741858	-0.3103761159	-0.2921186973	-0.09128709292	0.2008316044	0.3286335345
-0.1881280332	0.00990147543	-0.4950737715	-0.2178324595	0.3069457383	0.3762560663	-0.1683250823	-0.0990147543	-0.1881280332	-0.5544826241	-0.3663545909	0.3069457383	0.2970442629
0.7485339206	0.04351941399	0.3568591947	-0.5396407335	0.6701989754	0.1479660076	0.687606741	0.008703882798	0.03481553119	-0.3481553119	0.2698203667	-0.2524126011	0.1566698904
-0.02970442629	-0.1287191806	-0.4950737715	-0.1980295086	0.2475368857	0.277241312	-0.06931032801	0.01980295086	-0.3663545909	-0.4950737715	-0.2475368857	0.1881280332	0.3168472138
0.3559833394	0.1695158759	-0.1864674635	-0.4407412774	0.6780635036	0.4576928649	0.372934927	-0.2034190511	0.05085476277	-0.6950150912	-0.01695158759	0.1695158759	0.4576928649
-0.5477225575	-0.5659799761	-0.4564354646	0.8946135106	-0.8580986734	-0.4564354646	-0.5842373947	0.6390096504	-0.5659799761	0.6755244876	0.07302967433	-0.2008316044	0.1643167673
-0.6963106238	-0.2524126011	-0.2872281323	0.4526019055	-0.5396407335	-0.4700096711	-0.8007572174	0.2088931871	-0.6527912098	0.4264902571	-0.3916747259	-0.2088931871	-0.1131504764
-0.3195048252	-0.06846531969	0.02282177323	0.7302967433	-0.6390096504	-0.7302967433	-0.3423265984	0.1141088661	-0.3651483717	0.593366104	0.3879701449	-0.4564354646	0.2282177323
-0.5763539781	-0.5254992153	-0.5763539781	0.9153857299	-0.6441603284	-0.372934927	-0.4915960401	0.4576928649	-0.2542738139	0.6950150912	0.1525642883	-0.01695158759	0.288176989
-0.3166666667	-0.4333333333	-0.3	0.6666666667	-0.7	-0.5166666667	-0.4833333333	0.4833333333	-0.7666666667	0.5333333333	0.01666666667	-0.3666666667	0.1333333333
-0.08333333333	-0.5666666667	-0.5833333333	0.4833333333	-0.15	-0.3	-0.1166666667	0.3666666667	-0.5333333333	0.3333333333	0.2	-0.15	0.4666666667
0.4833333333	0.4833333333	0.7333333333	-0.2333333333	0.1166666667	-0.03333333333	0.5333333333	-0.4166666667	0.6833333333	0.06666666667	0.4166666667	-0.06666666667	-0.3
0.4833333333	0.3833333333	0.8	-0.4	0.06666666667	-0.05	0.3833333333	-0.2166666667	0.2833333333	-0.01666666667	0.1333333333	-0.2333333333	-0.4833333333
0.7723150835	0.6336944275	0.8218224607	-0.5643840995	0.5544826241	0.138620656	0.7723150835	-0.5643840995	0.6832018047	-0.2475368857	0.3663545909	-0.1089162297	-0.1683250823

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Socs2	Cebpb	Hmox1	Icam1	Ifit3	Il6ra	Il1b	Socs3
0.3051285766	-0.8306277919	0.8136762043	0.6272087408	-0.05085476277	-0.2542738139	0.3898865146	0.4068381022
0.3468909531	-0.5294651389	0.6207522318	0.3103761159	0.1643167673	-0.1460593487	0.2738612788	0.6390096504
0.4199206274	-0.4929503018	0.3103761159	0.4929503018	-0.4199206274	-0.4016632088	0.1278019301	-0.05477225575
-0.35	-0.5666666667	0.6666666667	0.8666666667	-0.5333333333	-0.5	0.9	-0.3333333333
0.25	-0.5	0.5166666667	0.6166666667	-0.6166666667	-0.8666666667	0.6	0.1
0.1333333333	-0.2666666667	0.1833333333	0.35	-0.65	-0.6666666667	0.3166666667	-0.01666666667
0.5166666667	0.1833333333	-0.1	-0.5	0.6	0.6166666667	-0.5333333333	0.3166666667
0.4666666667	0.4666666667	-0.3166666667	-0.6166666667	0.3166666667	0.5	-0.5333333333	0.3333333333
0.3	0.75	-0.8333333333	-0.7333333333	-0.06666666667	0.03333333333	-0.55	0.2
-0.05	0.6	-0.7	-0.6166666667	0.25	0.7	-0.5833333333	0.1
-0.3559833394	0.5254992153	-0.4068381022	-0.4576928649	0.3559833394	0.2712254014	-0.1017095255	-0.2542738139
0.2542738139	0.5594023905	-0.7119666788	-0.6950150912	0.3220801642	0.372934927	-0.5254992153	0.4407412774
-0.6390096504	0.4199206274	-0.3651483717	-0.3103761159	0.3651483717	0.4746928832	-0.09128709292	-0.3468909531
-0.4257634435	0.6039900012	-0.5148767223	-0.3663545909	0.1287191806	0.5148767223	-0.1881280332	-0.3168472138
0.3829708431	0.3394514291	-0.5918640302	-0.7920533346	0.6701989754	0.5744562647	-0.9574271078	0.2611164839
-0.4059604926	0.5643840995	-0.5742855749	-0.4653693452	0.3663545909	0.5148767223	-0.3069457383	-0.277241312
-0.08475793795	0.6441603284	-0.5933055657	-0.7119666788	0.5254992153	0.8475793795	-0.6780635036	-0.1186611131
-0.438178046	-0.3103761159	0.4929503018	0.5842373947	-0.3651483717	-0.6024948133	0.6207522318	-0.6207522318
-0.3133397807	-0.3220436635	0.130558242	0.5744562647	-0.4090824915	-0.4613057883	0.600567913	-0.2088931871
-0.2510395055	-0.502079011	0.593366104	0.502079011	-0.2282177323	-0.4336136914	0.593366104	-0.4336136914
-0.661111916	-0.3390317518	0.661111916	0.6950150912	-0.3559833394	-0.3390317518	0.7289182664	-0.6441603284
-0.1666666667	-0.3833333333	0.2666666667	0.4333333333	-0.03333333333	-0.45	0.3666666667	-0.3
-0.6	-0.08333333333	0.06666666667	0.1	0.4166666667	0.2666666667	0.06666666667	-0.4
0.6333333333	-0.4	0.4	0.06666666667	0.01666666667	-0.1666666667	-0.03333333333	0.5666666667
0.8666666667	-0.3	0.01666666667	-0.1	0.05	-0.3166666667	-0.2666666667	0.7
0.8416254115	-0.207930984	0.04950737715	-0.277241312	0.34655164	0.2574383612	-0.4950737715	0.7525121327

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Mt1	Mt2	Bnip3	Nr0b2	Nr1d1	Nr1d2	Gadd45g
0.05085476277	0.2542738139	0.288176989	-0.288176989	0.3220801642	0.4068381022	-0.1525642883
0.4564354646	0.5477225575	0.6390096504	-0.5477225575	0.6207522318	0.6207522318	0.09128709292
-0.5294651389	-0.4564354646	-0.5294651389	0.4016632088	-0.5112077203	-0.3468909531	-0.01825741858
-0.4166666667	-0.35	-0.2	0.3166666667	-0.3166666667	-0.3166666667	-0.4
-0.5166666667	-0.3166666667	-0.2333333333	0.2333333333	-0.35	-0.1833333333	-0.01666666667
-0.6333333333	-0.3166666667	-0.4166666667	0.1666666667	-0.4333333333	-0.2166666667	-0.06666666667
0.8	0.6666666667	0.6333333333	-0.5666666667	0.6333333333	0.5833333333	0.2166666667
0.7666666667	0.7	0.5333333333	-0.65	0.5333333333	0.5333333333	0.3166666667
0.1333333333	0.03333333333	-0.1333333333	-0.1166666667	-0.15	-0.1333333333	0.5833333333
0.5166666667	0.3166666667	0.06666666667	-0.3666666667	0.1833333333	0.05	0.3166666667
0.2542738139	0.01695158759	0.2203706387	0.06780635036	0.1017095255	-0.08475793795	0.05085476277
0.5933055657	0.3051285766	0.2373222263	-0.3898865146	0.2373222263	0.06780635036	0.6780635036
0.2008316044	-0.01825741858	0.09128709292	0.09128709292	0.09128709292	-0.1278019301	-0.1278019301
0.3069457383	0.03960590172	-0.01980295086	0.00990147543	-0.01980295086	-0.1980295086	0.03960590172
0.2785242495	0.2088931871	0.1044465936	-0.1914854216	0.2524126011	0.2437087183	0.3133397807
0.2475368857	-0.07921180344	-0.01980295086	0.1485221314	-0.01980295086	-0.2376354103	0.0990147543
0.5594023905	0.3559833394	0.2203706387	-0.2542738139	0.3051285766	0.1864674635	0.08475793795
-0.7850689991	-0.6207522318	-0.3834057903	0.7302967433	-0.4929503018	-0.3834057903	-0.5842373947
-0.4787135539	-0.6789028582	-0.4961213195	0.5657523819	-0.5918640302	-0.7224222722	0.05222329679
-0.5477225575	-0.2510395055	-0.04564354646	0.2510395055	-0.1597524126	-0.04564354646	-0.593366104
-0.5254992153	-0.3051285766	-0.1695158759	0.4407412774	-0.2203706387	-0.1356127007	-0.7967246168
-0.5833333333	-0.7166666667	-0.3833333333	0.7666666667	-0.4833333333	-0.5333333333	-0.1333333333
-0.1333333333	-0.3	-0.06666666667	0.4333333333	-0.03333333333	-0.2	-0.35
0.2333333333	0.5166666667	0.4333333333	-0.5833333333	0.45	0.6166666667	0.1
0.05	0.1	0.08333333333	-0.2333333333	0.08333333333	0.1833333333	0.55
0.5643840995	0.6336944275	0.4752708206	-0.7030047555	0.5643840995	0.6336944275	0.4059604926

#CV PCB6 & CV PCB30 & GF PCB6 & GF PCB30 COMMON	#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB6 COMMON	#CV PCB6 & GF PCB6 & GF PCB30 COMMOn	#CV PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB30 & CV PCB30 COMMON
Cyp1a2	Cyp17a1	Cyp8b1	Ypel2	Cyp3a16	Igfbp5	Cyp2c29
Arntl	Cyp2a5	Serpina1e	Cldn1	Cyp3a41a		Atp6v0d2
Ces2c	Cyp2j9	Gm24105	Cyp26a1	Cyp3a41b		Cyp2b10
G6pc	Clpx	Gm47283	Sult2a2			Rnf125
Sult2a1	Rab36	AC127342.1				
	Mknk2					
	Lpin1					
	Sdf2l1					
	Creld2					
	Spry4					
	Setbp1					
	Syvn1					
	Loxl4					
	Got1					
	Npas2					
	Acmsd					
	Marco					
	Slc30a10					
	Hspa5					
	Gpcpd1					
	Mthfr					
	Slc34a2					
	Hsph1					
	Atp2b2					
	Mt2					
	Mt1					
	Hyou1					
	Nnmt					
	Manf					
	Slc16a1					
	Hspa13					
	Pim3					
	Pnrc1					
	Gstm2					
	Inhba					
	Rtn4rl1					
	Rbp1					
	Jun					
	Arfgap3					
	Nfil3					
	Ero1lb					
	Dhcr7					
	Tubb2a					
	Rad51b					
	Cyp2c54					
	Ppp1r3c					
	Sult3a1					
	Etnk2					
	Acot1					
	Gm13775					
	Gm15611					
	Gm16348					
	Sult3a2					
	Hspa1b					
	Serpina4-ps1					
	1810053B23Rik					
	Gm21049					

#CV PCB30 & GF PCB6 COMMON	#CV PCB30 & GF PCB6 & CV PCB30 COMMON	#CV PCB30 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only GF PCB6	#only GF PCB30
Socs2	Gstm3	Cyp2c55	Mfsd10	Ckb	Nbr1	Ttyh1
Bcl6	Gadd45g	Nr0b2	Hmox1	Nqo1	Igfbp1	Lars2
Fabp5	Upp2	Cyp3a44	Id3	Por	Per1	Hbb-bt
Slco1a1	Thrsp	Gstp1	Dnajb9	Psmb4	Klc1	Gm13340
Paqr9	Egr1	Hba-a2	Aldoc	Krt23	Lcn2	Gm20594
Gm25687		Hba-a1	Myh11	Abhd8	Ly75	Mir6236
Mup22			Aebp1	Plin5	Smad9	Gm28439
			Map2k6	Lonrf3	Enho	Gm28437
			Id2	Avpr1a	Sult1e1	Gm37194
			Klf11	Nr1d1	H2-Aa	Rmrp
			Hmgcr	Nr1d2	Nmrk1	
			Slc25a30	Cnmd	Ppl	
			Sqle	Sorbs3	Ppp1r3g	
			Slc15a2	Retreg1	Apol9a	
			Noct	Myc	Camk2b	
			Chka	Mpv17l	BC023105	
			Gsn	Slc10a2	H2-Ab1	
			Hdc	Slc3a1	Sult2a3	
			Il6ra	Abcg8	Sult2a5	
			Efna1	Cyb5a	Nlrp12	
			Plk3	Aldh1a7	Gm12390	
			Atp2a2	Spata3	Nbdy	
			Gfpt1	Ngef	Zbed4-ps2	
			Tmem159	Agxt	Mug-ps1	
			Nsdhl	Mpzl1	Gm42796	
			Msmo1	Lrp4	Gm42642	
			Gclc	Knstrn	4833411C07Rik	
			Acta2	Il1b	Gm47789	
			Icam1	Gstm4	Gm34654	
			Vnn1	Pdgfc		
			Gdf15	Hsdl2		
			Lonrf1	Gne		
			Cplane1	Cyp4a14		
			Lrtm1	Per3		
			Phf13	Slc2a5		
			Angptl8	Slc46a3		
			Zfp518a	Gys2		
			Tsku	Scnn1a		
			Tcim	Clec2h		
			Cebpb	Serpina7		
			Fam47e	Slc7a2		
			Fdps	Pllp		
			Defa24	Nectin1		
			mt-Co2	Cyp1a1		
			Rdh11	Gsta4		
			Zbtb16	Trib3		
			Gm5096	Abtb2		
			Osgin1	Abcc4		
			Bhmt	Igf2bp2		
			Ifit3	Dsg1c		
			Igkc	Gnat1		
			Zfp970	Rrp12		
			F830016B08Rik	1810055G02Rik		
			Hmgcs1	Ttc38		
			Mup15	Slc17a2		
			Mup17	Lrfn3		
			Tcf24	Lrg1		
			Ighv1-11	Il22ra1		
			Gm45301	Spon2		
			Eppk1	Inf2		
			Gm31583	Mical2		
				Foxq1		
				Ciart		
				Dsel		

9130409I23Rik
Mreg
Mmd2
Htatip2
Tmem120a
Sdr9c7
Gbp2b
Klhdc8a
Lgalsl
Maff
Pgp
Tafa2
Lsm11
Zfp526
Paxx
Hbb-bs
Pkdrej
Zmat1
Socs3
Smagp
Klf1
Pm20d2
Cyp2c50
Ntrk2
Retsat
Gsta2
Gstm1
Tmed9
Gpc6
Acnat2
H2-Q7
Serpina6
Lsamp
Pclo
Cyp26b1
Gm22220
Mup3
Frat1
Nipal1
Ccnd1
Klhl21
Cib3
Phldb3
Ly6a
Bnip3
Mup20
Ces1b
Gm11340
Gm13771
Rn7s1
Gm6135
Gstm2-ps1
Gm44421
Gm44787
Gm33543
Gm34777
Gm31508
Gm49012
AC138228.1
AC157910.3

#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only CV PCB30
Aminosobutyric acid	G6P	3-Hydroxybutyric acid	Folinic acid	Dopamine
2,3-Dihydroxybenzoic acid	F6P		Shikimic acid	Dextrose
	Raffinose		NADP	Allantoin
			Arginine	Inosine
			Adenylosuccinate	NAD
			Acetylcarnitine	Uridine
				Nicotinamide
				Taurine
				Adenosine
				Adenosyl-L-homocysteine
				UDP-GlcNAc
				3-Methylvaleric acid
				2,3-Dihydroxybenzoic acid
				2-Deoxycytidine

#GF PCB6 & GF PCB30 COMMON	#only CV PCB30	#only CV PCB6	#only CV PCB30
Glucuronic acid	Levulinic acid	Mucic acid	2-Hydroxyphenylacetic acid
	6-Methyl-DL-tryptophan	Mannose	
	Serine	Norvaline	
	Asparagine	Cytosine	
	Proline		
	Urocanic acid		

Genes/metabolites/bacteria	CV_PCB_low_FC	CV_PCB_high_FC	GF_PCB_low_FC	GF_PCB_high_FC
Anaerotruncus	-	-988.225	-	-
Ruminiclostridium 9	1.534	-	-	-
Roseburia	2.403	2.725	-	-
Family XII UCG-001	453.356	326.446	-	-
Arginine	-	-1.99	-	-
Aminoisobutyric acid	2.912	2.597	-	-
Dimethylglycine	2.622	2.327	-	-
D-glucose	-	-	-2.415	-2.527
Glucose 6-phosphate	-	-	2.573	2.503
Fructose 6-phosphate	-	-	2.51	2.469
UDP-GlcNAc	-	-	-	1.62
Cyp1a1	-	52.387	-	-
Cyp1a2	3.053	6.818	1.78	3.08
Cyp2b10	2.009	5.495	-	1.869
Cyp2c50	-	1.756	-	-
Cyp3a16	1.88	-	2.222	2.174
Cyp3a41a	1.733	-	1.732	1.613

Chapter 3.

Neonatal exposure to environmental chemicals BPA, BDE-99, and PCB persistently alters the liver transcriptome in adult mice

ABSTRACT

Exposure to bisphenol A (BPA), polybrominated diphenyl ethers (PBDEs), and polychlorinated biphenyls (PCBs) are linked to many human diseases. Early development is increasingly recognized as a sensitive exposure window for toxic exposures. In this study, we tested our hypothesis that neonatal exposure to these chemicals persistently dysregulates the liver transcriptome. Two-day-old male and female C57BL/6 mice were supralingually exposed to corn oil vehicle (5 ml/kg), BPA (250 µg/kg), BDE-99 (57 mg/kg), or the Fox River PCB Mixture (an environmentally relevant preparation, 30 mg/kg), once daily for three days. RNA-Seq was conducted on mouse livers at postnatal day (PND) 5 (acute response) and 60 (persistent response). Chemical-induced hepatic transcriptomic changes were minimal at PND5, markedly amplified at PND 60, and more pronounced in males. At the given doses, BPA and BDE-99 caused more prominent effects compared to those caused by PCBs. The top persistently altered predicted upstream regulators include genes that control cell cycle (ex. *Trp53*, *Cdkn1a*), sterol biosynthesis (*Scap*), bile acid synthesis (*Fgf15*), and nuclear receptors that regulate lipids (PPARs) and drug metabolism (RORs, CAR, PXR). In accordance, several genes involved with drug/xenobiotic metabolism, oxidative stress, and inflammation were dysregulated by BPA and BDE-99 in young adults (PND 60). The expression of cancer-related long non-coding RNAs (lncRNAs) (i.e. *H19*, *Snhg1*, *Snhg4*) were also persistently dysregulated. Our results demonstrate that neonatal exposure to these environmental chemicals (especially BDE-99 and BPA) leads to persistent hepatic transcriptomic changes in young adulthood, possibly due to cross-talk between epigenetic reprogramming and nuclear receptors, with males being more sensitive than females.

INTRODUCTION

Environmental contaminants, often from anthropogenic sources, such as bisphenol A (BPA), polybrominated diphenyl ethers (PBDEs), and polychlorinated biphenyls (PCBs), are ubiquitously present in the environment and linked to multiple diseases in humans and other animals. BPA is widely used in plastic manufacturing and is found in regular plastic products, personal care products, linings of canned products, and receipts (Brede et al., 2003; Negev et al., 2018). BPA can also be detected in breast milk and previously in bottles for baby formula (Santonicola et al., 2018; Martinez et al., 2019; Sayici et al., 2019). Although BPA detection levels are decreasing, the frequency of exposure still remains high in the U.S. population (Lehmler et al., 2018). BPA can act as a xenoestrogen and has been reported to be associated with the epigenetic regulation of drug-metabolizing enzymes following *in utero* exposure in mice (Bromer et al., 2010; Doherty et al., 2010; Kundakovic et al., 2013), oxidative damage and lipid accumulation in nonalcoholic liver disease in rats (Wei et al., 2014), potential neurodevelopment dysregulation (Cheong et al., 2018), decreased sperm quality in humans (Xiao et al., 2009; Meeker et al., 2010; Li et al., 2011), and increased risk of liver cancer in mice (Weinhouse et al., 2014; Weinhouse et al., 2015; Moscovitz et al., 2016; Weinhouse et al., 2016). Polybrominated diphenyl ethers (PBDEs) were used as flame retardants in construction, plastics, furniture, and upholstery, electronics, and other household products (Vojta et al., 2017; Xu et al., 2019). PBDEs are still persistent in the environment and are found in household dust and, due to their lipophilic and bioaccumulative nature, in meats, fish, dairy, and human milk (Babalola and Adeyi, 2018; Cade et al., 2018; Pietron et al., 2019). PBDEs are linked to thyroid hormone disorders, neurotoxicity, oxidative stress in the liver, and carcinogenesis in both animal models and humans (Blanco et al., 2014; Bruchajzer et al., 2014; Yuan et al., 2017; Albert et al., 2018; Dorman et al., 2018; Dunnick et al., 2018; Gibson et al., 2018; Cowell et al., 2019; de Water et al., 2019; Hurley et al., 2019).

Polychlorinated biphenyls (PCBs) were used as coolants and insulators and are also persistent because of their chemical stability and liphophilicity, resulting in bioaccumulation. PCBs are detected in food, soil, water, and human tissues (Ellsworth et al., 2015; Grimm et al., 2015a; Weber et al., 2018; Boesen et al., 2019; Jahnke and Hornbuckle, 2019; Jin et al., 2019; Ren et al., 2019) and have been associated with dysregulation in neurodevelopment (Schug et al., 2015; He et al., 2018; Ruel et al., 2019), thyroid hormone signaling (Li et al., 2018b), perturbation of the gut microbiome (Cheng et al., 2018; Petriello et al., 2018), type 2 diabetes (Dzierlenga et al., 2019; Meek et al., 2019; Rahman et al., 2019; Tornevi et al., 2019), brain development (Aluru et al., 2017), birth defects (Ju et al., 2017; Romero et al., 2017), and cancer (Leng et al., 2016; He et al., 2017; Ghosh et al., 2018; Georgiadis et al., 2019).

The liver is an essential organ for drug metabolism and nutrient homeostasis (Rui, 2014; Robey et al., 2015). Specifically, the liver serves as a central hub for bile production and excretion, and metabolism of various nutrients such as carbohydrates, lipids (such as fatty acids and cholesterol), amino acids, and nucleotides, as well as hormones, and xenobiotics such as drugs and environmental chemicals (Bechmann et al., 2012). Dysregulated inflammatory, proliferative, and apoptotic signaling are closely linked to disrupted liver function, and can lead to complex diseases, such as metabolic syndrome, obesity, type 2 diabetes, alchoholic and non-alcoholic fatty liver disease (NAFLD), fibrosis (cirrhosis), and cancer (Bechmann et al., 2012; Heindel et al., 2017). The individual steps in liver function are delicately regulated by the interplay of hormones, cellular signaling pathways, and nuclear receptors and other transcription factors (Bechmann et al., 2012). In response to exposures, nuclear receptors and other transcription factors are activated in the liver, which lead to cascades of downstream response elements, such as protein-coding

genes (PCGs) and non-coding RNAs, which can in turn influence the transcription and translation of further responses (Wang and Chang, 2011; Dempsey and Cui, 2017).

It has been increasingly recognized that there is a sensitive developmental time window for toxic exposures that may have a life-long impact on disease risk, such as obesity, metabolic syndrome, heart and kidney diseases as well as Alzheimer's disease, through alterations in the epigenome and developmental reprogramming of vital organs (Almeida et al., 2019; Goyal et al., 2019). Early-life exposures to environmental contaminants increase the risks of obesity and other metabolic diseases, cardiovascular diseases, altered neurodevelopment, and cancer (Weinhouse et al., 2014; Garry et al., 2015; Bellinger et al., 2016; Liu et al., 2017; Park et al., 2017; Wassenaar et al., 2017). Altered bile acid homeostasis was also found after acute exposure to PCBs in mice (Li et al., 2018b). Hepatic tumors were found in the offspring of BPA exposed mice following perinatal exposure (Weinhouse et al., 2014). In addition, transgenerational effects were shown up to the F4 generation in zebrafish exposed to a PCB and PBDE mixture, possibly due to DNA modifications by methyltransferases (Alfonso et al., 2019). Dysregulation of the gut microbiome and altered metabolites related to metabolic syndrome was reported following acute exposure to BDE-99 or BDE-47 in mice (Li and Cui, 2018; Li et al., 2018a; Scoville et al., 2019), and BDE-71 in zebrafish (Chen et al., 2018). Disruption of skeletal development and thyroid hormones were reported following chronic exposure to penta-BDE or hydroxylated PBDE mixtures (Macaulay et al., 2017). It has been shown that perinatal exposure to a mixture of 6 PCB congeners (PCB-28, 52, 101, 138, 153, and 180) resulted in elevated levels of acetylcholinesterase and corticosterone levels in plasma in adulthood (Karkaba et al., 2017).

Although multiple outcomes were reported regarding acute and chronic exposures to PBDEs and PCBs, it is not known to what extent early-life exposure to these two chemicals

persistently modulate the expression of important liver genes involved in xenobiotic and intermediary metabolism pathways and how these two chemicals compare to the effect of early-life exposure to BPA, which is well known to produce delayed-onset liver tumors in rodent models. Therefore, the goal of the present study was to test our hypothesis that similar to BPA, early-life exposure to environmental contaminants PBDEs and PCBs persistently dysregulates the transcriptome of the liver, leading to detrimental effects such as accelerated cell cycle as well as dysregulated drug metabolism pathways.

MATERIALS AND METHODS

Chemicals. BDE-99 (2,2',4,4',5-pentabromodiphenyl-ether, CAS No. 60348-60-9) and BPA (bisphenol A) were purchased from AccuStandard, Inc. (New Haven, CT). Fox River PCB mixture was prepared from technical PCB mixtures and characterized as described previously (Li et al., 2018b). Corn oil was purchased from Sigma-Aldrich (St. Louis, MO).

Animals

All mice were housed according to the Association for Assessment and Accreditation of Laboratory Animal Care International guidelines (https://aaalac.org/resources/theguide.cfm), and studies were approved by the Institutional Animal Care and Use Committee at the University of Washington. Eight-week-old specific pathogen free C57BL/6J mice were purchased from the Jackson Laboratory (Bar Harbor, ME) and were acclimated to the animal facility at the University of Washington for at least 2 breeding generations prior to the experiment. Mice were exposed *ad libitum* to standard laboratory autoclaved rodent diet (LabDiet #5010 after weaning and LabDiet #5021 for breeding; LabDiet, St. Louis, MO) and water (non-acidified autoclaved water), and were housed in standard air-filtered cages using autoclaved bedding (autoclaved Enrich-N'Pure) (Andersons, Maumee, OH). All chemical

solutions were sterilized using the Sterflip Vacuum-Driven Filtration System with a 0.22 µm Millipore Express Plus Membrane (EMD Millipore, Temecula, CA). Litters were randomly allocated to exposures. In biological triplicates per exposure per sex (n=3 per group), pups between 2- to 4-days of age were supralingually exposed to corn oil (vehicle, 5 mL/kg), BPA (250 µg/kg), BDE-99 (57 mg/kg), or the PCB Fox River Mixture (30 mg/kg), once daily for three consecutive days. Mice were euthanized using decapitation (PND 5) or a CO_2 chamber and exsanguination (PNDE 60), and livers were collected at PND 5 (24 hours after the exposure) and 60 (56 days after the last exposure) and immediately frozen in liquid nitrogen.

16S rDNA sequencing

The bacterial contents in different bio-compartments (duodenum, jejunum, ileum, colon, and feces) were respectively thawed overnight at 4°C followed by centrifugation at 10 000 g at 4°C for 1 h. Bacterial DNA was isolated from the LIP using an OMEGA E.Z.N.A. Stool DNA Kit (OMEGA Biotech Inc., Norcross, Georgia). The concentration of DNA was determined using Qubit (Thermo Fisher Scientific, Waltham, Massachusetts). The integrity and quantity of all DNA samples were confirmed using an Agilent 2100 Bioanalyzer (Agilent Technologies Inc., Santa Clara, California). Bacterial 16S rRNA V4 amplicon sequencing was performed using a HiSeq 2500 second-generation sequencer (250 bp paired-end) (Beijing Genome Institute Americans Corporation, Cambridge, Massachusetts) ($n = 5$ per group).

SCFA quantiifcation using GC-MS

Frozen plasma samples were first thawed overnight at 4°C (n = 4 – 8 per group). Afterward, 20 µL of each sample was mixed with 20 µL hexanoic acid-6,6,6-d3 (internal standard), 30 µL

sodium hydroxide solution (NaOH, 0.1 M in water), and 430 µL methanol (MeOH). The pH of the mixture was 9. Upon storage at -20°C for 20 min and centrifugation at 14,000 rpm for 10 min, 450 µL of supernatant were collected and sample pH was adjusted to 10 by adding 30 µL of NaOH:H2O in a 1 to 4 ratio. Samples were then dried, reconstituted in 40 µL of methoxyamine hydrochloride in pyridine (20 mg/mL), and stored at 60°C for 90 min. Afterward, 60 µL of N-Methyl-N-tert-butyldimethylsilyltrifluoroacetamide was added and stored at 60°C for 30 min. Each sample was then vortexed for 30 s and centrifuged at 14,000 rpm for 10 min. Finally, 70 µL of supernatant were collected from each sample for GC-MS analysis.

GC-MS experiments were performed on an Agilent 7820A GC-5977B MSD system (Santa Clara, CA) by injecting 1 µL of prepared samples. Helium was used as the carrier gas with a constant flow rate of 1.2 mL/min. The separation of metabolites was achieved using an Agilent HP-5ms capillary column (30 m x 250 µm x 0.25 µm). The column temperature was maintained at 60°C for 1 min, and then increased at a rate of 10°C/min to 325°C and held at this temperature for 10 min. Mass spectral signals were recorded after a 4.9 min solvent delay.

RNA Isolation

Total RNA was isolated from frozen livers using RNA-Bee reagent (Tel-Test lnc., Friendswood, TX) according to the manufacturer's protocol. RNA concentrations were quantified using a NanoDrop 1000 Spectrophotometer (Thermo Scientific, Waltham, MA) at 260 nm. The integrity of total RNA samples was evaluated by formaldehyde-agarose gel electrophoresis with visualization of 18S and 28S rRNA bands under UV light, and confirmed by an Agilent

2100 Bioanalyzer (Agilent Technologies Inc., Santa Clara, CA). Samples with RNA integrity numbers above 8.0 were used for RNA-Seq.

RNA Sequencing

The cDNA library was constructed using a ribosomal depletion method, and reads were sequenced using a 75 bp paired end sequencing by synthesis strategy per the Illumina manufacturer's protocol. FASTQ files were de-multiplexed and concatenated for each sample. Quality control the FASTQ files was performed using FastQC (http://www.bioinformatics.babraham.ac.uk/projects/fastqc/). Sequenced reads from the FASTQ files were then mapped to the mouse reference genome (National Center for Biotechnology Information [NCBI GRCm38/mm10]) using HISAT2 version 2.1 (Kim et al., 2015). The sequencing alignment/map (SAM) files were converted to binary alignment/map (BAM) format using SAMtools version 1.8 (Li et al., 2009) and were analyzed by Cufflinks version 2.2.1 to estimate the transcript abundance (Trapnell et al., 2010) using Gencode mouse version 19 (vM19) gene transfer format (GTF). Long non-coding RNA (lncRNA) GTF from Gencode (vM19) was used to estimate the lncRNA transcript abundance. The abundance was expressed as fragments per kilobase of transcript per million mapped reads (FPKM) which was then converted to transcripts per million (TPM). Differential expression analysis was performed using Cuffdiff (Trapnell et al., 2010). The differentially expressed genes were defined as false discovery rate Benjamini-Hotchberg adjusted *p* value (FDR-BH) <0.05 in the chemical-exposed groups compared with the vehicle-exposed control group.

Data Analysis

For RNA-seq, samples were categorized by age, sex, and exposure groups. Genes were considered expressed if the average TPM was >1 for at least one group. PCGs were separately categorized based on the Ensembl BioMart gene category. LncRNA data were analyzed separately from PCGs. Differentially expressed PCGs were also categorized and matched with genes in categories of interest (xenobiotic biotransformation, epigenetic modifiers, nuclear receptors, and oxidative stress). These specific gene categories were based on literature searches and extracting gene sets from the Gene Ontology consortium and the Kyoto Encyclopedia of Genes and Genomes (KEGG). Venn diagrams were made for differentially regulated PCGs and lncRNAs for each sex and age group (PND 5 and 60) using the R package VennDiagram (Chen and Boutros, 2011). Hierarchical clustering was generated clustering using R package ComplexHeatmap (Gu et al., 2016). Up- and down-regulations were defined as the absolute value of the fold change greater than 1.5. Lists of differentially up- and down-regulated genes were used as input for gene ontology enrichment using the R package topGO (Alexa and Rahnenfuhrer, 2018) for all groups with the list of genes in the unfiltered expression table was used as the background for gene ontology. Upstream regulators for all differentially regulated genes were determined using IPA. Gene expression values were plotted using bar plots for specific genes of interest using the arithmetic mean TPM in SigmaPlot.

One-way ANOVA followed by Tukey's post-hoc test was performed for each metabolite in base R for the analysis of liver SCFAs.

Liver, serum, and intestinal microbiome paired-end sequence reads, in quintuplicate, were merged, de-multiplexed, quality-checked, and chimera-filtered using QIIME 2 (Vazquez-Baeza et al., 2013; Mandal et al., 2015; Callahan et al., 2016; Vazquez-Baeza et al., 2017; Hall and Beiko, 2018). Community composition and (Bokulich et al., 2013) the Silva 99

version 132 reference (Quast et al., 2013) using QIIME2 (Hall and Beiko, 2018). The OTU table annotated with classified bacteria information was read into R for further analysis (R Core Team, 2019). Differential abundance testing was performed using the ANCOM plugin in QIIME 2 (Mandal et al., 2015). Differentially abundant bacteria (relative abundance of OTU) and differentially regulated hepatic genes were correlated (Spearman correlation) and significant correlation was defined as $|\rho| > 0.8$ and FDR-adjusted p-value < 0.1. Correlation results were plotted using ComplexHeatmap (Gu et al., 2016).

RESULTS

Mapping statistics

The present study utilized RNA-Seq, as well as metabolomics and 16S sequencing, to determine the persistent effect on the liver transcriptome and the interaction between the gut microbiome following neonatal acute exposure to BPA, BDE-99, and PCBs. As shown in Table S1, RNA-Seq yielded approximately 32.6 to 54.5 million reads per sample with 43.5% to 81.5% mapped (median: 75.9%). This is equivalent to 23.7 to 35.4 million uniquely mapped reads with 28.6 million as the median.

Global changes of liver transcriptome following early-life exposure to environmental contaminants BPA, BDE-99, and PCBs

To study the impact of early-life exposures to environmental chemicals in the liver, we compared the transcriptomic changes at PND 5 (acute response to chemical exposure in newborns) and PND 60 (persistent response to early-life chemical exposure in young adults). To visualize the overall expression patterns of the transcriptomic response following neonatal exposure to BPA, BDE-99, or PCBs, one-way hierarchical clustering was performed on the filtered expression table for age, sex, and chemical exposure using filtered gene expression values described in Methods (Fig. 2). A K-means test was used on the expression matrix (k =

3) to cluster the genes. Gene ontology (GO) enrichment was performed on the genes of each cluster to study the biological meaning using the R package topGO. GO terms that had false discovery rate below 0.05 were used (FDR-BH < 0.05). Selected GO biological terms from the top 20 terms are shown in Fig. 2.

A total of three clusters were identified. The biological terms using genes in the first cluster (cluster 1) were generally enriched in neonatal age compared to young adulthood under basal conditions, and were moderately responsive to chemical exposures at both PND 5 and PND 60, indicating that the chromatin architecture around the associated genes is readily accessible by transcription factors at both ages. The top GO terms in cluster 1 include basic cellular and molecular functions, such as autophagy (GO:0006914), golgi vesicle transport (GO:0048194), and mitochondrial translation and organization (GO:007005 and GO:0032543).

The GO biological terms in the second cluster (cluster 2) were adult-specific under basal conditions and were only responsive to chemical exposure in adulthood evidenced by a prominent increase in the expression of genes involved in these terms in all three exposure groups. Conversely, these GO terms remained low following acute chemical exposure in PND 5, which may indicate that the chromatin architecture around these associated genes is not permissive to transcription machinery in either basal or inducible stages or signaling factors, such as from dietary metabolites, that are more abundant in adult age are not as accessible in neonatal age. The top GO terms in cluster 2 contained metabolism related terms, which include fatty acid metabolic process (GO:0006331), cofactor metabolic process (GO:0051186), carboxylic acid metabolic process (GO:0046395), steroid metabolic process (GO:0008202), xenobiotic metabolic process (GO:0006790), and lipid catabolic process (GO:0016042).

The GO terms in the third cluster (cluster 3) were neonatally enriched under basal conditions and were not responsive to any of the three chemical exposures at this age. Although the basal adult levels were low, the associated genes were markedly up-regulated by BPA (both sexes) and BDE-99 (males). The top GO terms in this cluster include cell proliferation and maintenance, such as mRNA processing (GO:0006397), DNA repair (GO:0006281), cell cycle phase transition (GO:0044770), regulation of mitotic cell cycle (GO:0007346), protein-DNA complex subunit organization (GO:0071824), nuclear division (GO:0000280), DNA replication (GO:0006260), and histone modification (GO:0016570).

Comparison of the acute and persistent global changes in the hepatic transcriptome following early-life exposures to environmental chemicals

Principal components analysis (PCA) was performed on the Z-normalized expression matrix and labeled by age and sex (Fig. 3A). Normalized expression levels on the principal component space clustered between age groups supporting the expression changes when comparing livers in neonatal and adult ages. Although the coordinates of adult mice of both ages that had been exposed to PCBs were closer to the adult control groups compared to adult mice that had been exposed neonatally to BPA or BDE-99, there were no clear distinctions among environmental chemical-exposed groups in both ages (Fig. S1A).

Venn diagrams were used to visualize the commonly and differentially regulated PCGs and lncRNAs following neonatal chemical exposures. Overall, for both PND 5 (Fig. S1) and PND 60 (Fig. 3B-3C), early-life exposure to BPA and BDE-99 altered more transcripts (including both PCGs and lncRNAs) than did early-life exposure to PCBs. In addition, males were generally more susceptible than females to chemical induced transcriptomic changes at both ages (Fig. S1 and Fig. 3B-3D). Differentially regulated lncRNAs were relatively exposure-specific at PND 5, in that there was minimal overlap in the commonly regulated

genes among different chemicals (Fig. S1C) compared to PND 60 (Fig. 3C). The majority of PCGs and lncRNAs in livers of male mice, relative to females, were uniquely differentially regulated in PND 5. As shown in Fig. S1B, in PND 5 males, among the three chemicals, acute exposure to BDE-99 had the most prominent effect, having 199 uniquely regulated PCGs. PCBs and BDE-99 shared the highest number of commonly regulated PCGs. In contrast, females at PND 5 had fewer differentially regulated PCGs in response to all three chemicals, with BPA having the most prominent effect.

As shown in Fig. 3C, at PND 60, early-life exposure to the three chemicals commonly regulated 23 PCGs in livers of male mice and 8 in livers of female mice. The majority of differentially regulated PCGs and lncRNAs in liver were shared between BPA and BDE-99 (429 genes and 33 lncRNAs). For females, the number of commonly differentially regulated PCGs comparing two exposed groups (BPA vs. BDE-99; BDE-99 vs. PCBs; and BPA vs. PCBs) were similar. There were two commonly regulated lncRNAs for males and none for females. Neonatal exposure to BDE-99 resulted in the most differentially regulated genes in males, while neonatal exposure to BPA resulted in the most differentially regulated genes in female mice.

The number of differentially regulated PCGs for each contaminant-exposed group and sex were plotted and compared by age (Fig. 3D). Interestingly, compared to vehicle-exposed groups of the same age and sex, early-life exposure to BPA and BDE-99 appeared to change the developmental trajectory of the hepatic transcriptome, resulting in more differentially regulated genes in adult age than in neonatal age for both sexes (Fig. 3D). In comparison, this trend was weaker for PCB exposure. In addition, male pups appeared to be more susceptible to all three of the chemically induced transcriptomic changes at both developmental ages than females (Fig. 3D).

Differentially regulated PCGs and lncRNAs by early-life chemical exposure are shown in Table S2-1-8. The gene expression profiles provide signatures of acute responses as well as the initial metabolism of the exposed toxicants. For males at PND5, the expression of genes that encode drug-metabolizing enzymes were commonly regulated by all three chemicals, including *Cyp1a2*, *Cyp2a4*, *Cyp2c50*, *Cyp2c54*, *Ugt3a2*, and *Slc17a4* (Table S2-1). Chemical-specific responses included fatty acid metabolizing *Cyp4f14* and bile acid metabolizing *Cyp27a1* for BPA-exposed male pups; the cell cycle regulating transcription factor *E2f4*, dual specificity phosphatase in the MAPK pathway (*Dusp1*) for BDE-99 exposed male pups; fatty acid metabolizing genes *Cyp4a14* and *Cyp4a32*; and hepatic bile acid sulfonating *Sult2a8* for PCB-exposed male pups.

In contrast to PND 5 males, which had commonly dysregulated cytochrome P450s by all three chemical exposures, in PND 5 females, the initial toxicant metabolism signature genes were different from those of males (Table S2-3). For example, commonly dysregulated genes by all three chemicals for the acute responses in females did not include any phase-I and -II metabolizers, or transporters, but contained the T cell activation modulator *Cd274*, signal transduction inhibitors *Rgs16*, and *Gbp2*, which are central to GTPase activity. Dysregulated genes in BPA exposed females at PND 5 contained the drug-metabolizing *Cyp2f2* and oxidative stress markers and zinc homeostasis genes metallothionein 1 and 2 (*Mt1* and *Mt2*) (Ruttkay-Nedecky et al., 2013). The orphan nuclear receptor *Rorc* and drug-metabolizing *Cyp1a2*, *Cyp2b10*, *Cyp2b37*, and *Cyp2b50* were dysregulated by BDE-99 in female pups. The signal transducer and activator of transcription (*Stat1*), Jun protooncogene (*Jun*), and the pro-inflammatory gene *Il1b* were dysregulated by PCBs in PND 5 females (Table S2-3).

The number of differentially regulated PCGs and lncRNAs were notably larger in PND 60 than PND 5 (Table S2-4-8). In males, genes persistently dysregulated by all three

chemicals included *Cyp2a4* and insulin-like growth factor binding protein 3 (*Igfbp3*), which can alter the half-life of insulin-like growth factors (IGF) and interactions with their receptors (Wong et al., 1999). In males, *Cyp2b10* and ATPase phospholipid transporting *Atp8a1* were persistently dysregulated by BPA exposure, and drug-metabolizing *Cyp2c39*, *Cyp2c55*, and bile acid metabolizing *Cyp8b1* were persistently dysregulated by BDE-99. DNA methyltransferase 1 (*Dnmt1*), zinc finger protein 334 (*Zfp334*), and the lncRNA *H19*, which is a regulator of cell proliferation and bile acid metabolism, were commonly persistently dysregulated for males that were exposed to BPA or BDE-99. For males that were exposed to PCBs, *Cyp3a41a*, *Nr0b2* (SHP), *Jun*, and Junb protooncogene (*Junb*) were persistently dysregulated.

In comparison to males, females had less persistent responses at PND 60. In females, *Cyp3a16,* a fetal-specific isoform, *Cyp3a44*, and *Igfbp1* were commonly persistently dysregulated by all three contaminants. The tumor suppressor *Brca1*, *Dnmt1*, and aurora kinase 1 (*Aurka1*), which is important in epigenetic modifications were persistently dysregulated in BPA exposed females. Retinoic acid metabolizing *Cyp26b1*, zinc finger protein 970 (*Zfp970*), and *Mt1* and *Mt2*, and lncRNAs related to cell progression (*Snhg1* and *Snhg4*) were persistently dysregulated in BDE-99 exposed females. Sulfotransferases *Sult2a1*, *Sult2a2*, and *Sult3a1* were persistently dysregulated in PCBs exposed females.

Comparison of acute and persistent responses using upstream regulators and overrepresentation analysis

The upstream transcriptional regulators using differentially expressed genes of mouse livers in PND 5 (Table S3) and PND 60 (Fig. 4) were predicted using the Ingenuity knowledgebase. As shown in Table S3, at PND 5, the top upstream regulators of acute response include immune response related genes including the interleukin family *Il1b, Il6,*

Il17a, and *Ikbkg*, and there were predicted inhibitions of interferon function related *Ifng, Irf3* and *Irf7*. Xenobiotic and lipid metabolism-related nuclear receptors *Nr1i2* (PXR) and *Nr1i3* (CAR), fatty acid beta-oxidation enzyme Acyl-CoA oxidase 1 (*Acox*) were also predicted to be inhibited in BPA-exposed male pups. The nuclear receptor mediator *Trim24* and *Il10ra* which are involved in the inhibition of proinflammatory cytokine synthesis were predicted to be activated in BDE-99 male pups. The orphan nuclear receptor RORs and the lipid-sensing nuclear receptor *Pparα* (peroxisome proliferator-activated receptor) were also shown as the top significant upstream regulators following acute chemical exposure.

As shown in Fig. 4A, interestingly, at PND 60, the upstream regulators involved in the persistent chemical-induced transcriptomic changes include the tumor suppressor *Trp53* (p53) in BPA and BDE-99 exposed males as well as BPA-exposed females (with predicted inhibition in this group). Genes that participate in the p53 signaling pathway, such as *Cdkn1a,* which is also a regulator of cell cycle progression, and genes in the E2F family (e.g. *E2f1* and *3*), which also controls cell cycle, as well as *Ccnd1,* which is known to be dysregulated in various cancer types (Burandt et al., 2016; Deane et al., 2001), were predicted to be activated in BPA exposed groups. Overall, the lipid homeostasis regulator *Scap* as well as the endo- and xenobiotic metabolism regulator *Nr1i3* were predicted to be inhibited. *Fgf15,* which is involved in bile acid biosynthesis, the nutrient homeostasis related *Ins, Insr*, and *Ins1*, as well as the nuclear receptors RORs and *Pparα* were also shown as the top upstream regulators.

Overexpression analysis (GO) was performed using the R package topGO to computationally determine the transcriptional change of biological functions using up- and down-regulated genes (absolute fold change greater than 1.5) at $p < 0.01$. In PND 5 (Fig. S2), BPA and BDE-99 resulted in the most up-regulated GO terms and BDE-99 produced the most down-regulated terms in males; whereas PCBs had the most prominent effect in females.

As shown in Fig. 4B, similar to PND 5, BPA and BDE-99 exposure also resulted in the greatest number of up-regulated GO terms, whereas BDE-99 resulted in the most down-regulated GO terms in males. Interestingly, at PND 60 adult age, the effect of early-life exposure for all three chemicals was markedly amplified long after the initial exposure stopped because the number of significant GO terms were generally higher in PND 60 than in PND 5. In general, females were less responsive to the persistent changes than males.

To visualize and compare the overall biological meaning, as well as the chemical, age, and sex-specific differences the GO terms were categorized into 35 categories including chromatin epigenetic modification, cell cycle and DNA synthesis, drug metabolism, and lipid metabolism (Table S4). To investigate liver-specific changes, terms unrelated to liver function were manually removed. Among the top 50 enrichment results, biological gene ontology terms that had at least 5 significant terms ($p < 0.01$) in the same category were summarized in Fig. 4C. At PND 5 (acute exposure), many terms in the following categories were dysregulated, namely blood and immune responses, drug and lipid metabolism, cell cycle and DNA synthesis, as well as chromatin epigenetic modification categories.

At PND 5, exposure to BPA up-regulated the biological processes terms involved in drug and lipid metabolism categories for males, blood and immune response as well as transporter activities for females with relatively lower significance than males (Fig. S3). Down-regulated GO terms in metal response and cell cycle were observed for both sexes. Acute response to BDE-99 (Fig. S3) and, with lower significance levels, PCBs (Fig. S4) both up-regulated biological terms involved in blood and immune response (e.g. response to interferons), drug and lipid metabolism, and down-regulated biological terms related to chromatin epigenetic modification, cell cycle, and blood cell differentiation, such as megakaryocyte (GO:0030219) and myeloid cell differentiation (GO:0030099).

In contrast to the acute response, the persistent response (PND 60) to early-life chemical exposures showed a different trend of dysregulation as compared to the acute response. In general, females were less responsive than males to the persistent changes. Early-life exposure to BPA (Fig. S5) for both sexes and BDE-99 (Fig. S6) for males up-regulated chromatin epigenetic modification (GO:0071103, DNA conformation change) and cell cycle (GO:0000280, Nuclear division), and down-regulated drug (GO:0006790, Sulfur compound metabolic process) and lipid metabolism (GO:0006084, Acetyl-CoA metabolism process). At PND 60, neonatal BDE-99 exposure in females up-regulated histone deacetylation and down-regulated metal response and histone 3 lysine 24 (H3-K24) methylation and -K27 tri-methylation. Persistent response to PCBs (Fig. S7) includes an up-regulation in drug and lipid metabolism, immune response categories (e.g. GO:0016042, lipid catabolic process; GO:0072329, monocarboxylic acid catabolism; and GO:0051923, sulfonation). Carbohydrate metabolism, such as glucose metabolism (GO:0006006) as well as drug metabolism were up-regulated following neonatal exposure to PCBs in females, and down-regulation patterns contained GO terms in drug and lipid metabolism some of which included acetyl-CoA metabolism (GO:0006084), regulation of lipid metabolism (GO:0019216), fatty acid metabolism (GO:0006631), and epoxygenase P450 terms (GO:0019373).

Overall, the biological processes from gene ontology of acute (PND 5) responses for each chemical exposure reflect initial shock from the chemical exposure acutely, up-regulating drug and lipid metabolism, and immune response biological terms, and down-regulating blood cell differentiation, cell-cycle, and metal response biological terms. Surprisingly, compared to the effects in PND 5, the persistent (PND 60) responses due to developmental dysregulation from neonatal exposure had different effects with key biological terms including up-regulation of cell cycle and chromatin epigenetic modification and down-regulation of drug and lipid metabolism and immune response.

In summary, early-life chemical exposure markedly modified the developmental trajectory of the liver transcriptome, and the persistent effect is even greater than the acute effect. Additionally, there are sex specific responses to the chemicals at both ages, indicating the susceptibility to early-life exposure to these chemicals may be dependent on sex. Together, these chemicals may have relatively small effects on the body initially, but the effect may be amplified with age.

Persistently differentially regulated cell proliferation-related lncRNAs following neonatal exposure to environmental contaminants.

To better characterize the persistent changes in the liver transcriptome along with the protein-coding genes, the expression lncRNAs was analyzed as described in Materials and Methods, and examples are shown in Fig. 4D (*Snhg1*, *Snhg4*, and *H19*). Among the differentially regulated lncRNAs in adult age, a few lncRNAs that have been reported to be potential biomarkers for tumor progression (Huang et al., 2018; Pan et al., 2018; Wang et al., 2018; Yoruker et al., 2018) were persistently up-regulated in livers of adult male pups following neonatal exposure to BPA and BDE-99 in males. These lncRNAs include the small nucleolar RNA host gene 1 and 4 (*Snhg1;* persistently up-regulated by BDE-99 and *Snhg4;* persistently up-regulated by BPA or BDE-99, respectively). Interestingly, the lncRNA *H19*, which is up-regulated in various cancers, such as liver and breast, and is also known to regulate bile acid homeostasis (Zhang et al., 2016; Collette et al., 2017; Pope et al., 2017; Song et al., 2017), was persistently up-regulated in adult males, having $\log_2$ fold change greater than 8 (i.e. > 256 fold), following neonatal exposure to BPA or BDE-99; whereas *H19* was minimally altered by early-life exposure to the 3 chemicals in livers of adult females.

The delta-like 1 homolog *Dlk1*, which is an epidermal growth factor, and iodothyronine deiodinase 3 *Dio3*, which is involved in thyroid hormone metabolism, are two PCGs with basic

cell and physiological maintenance roles. Between these two PCGs, a cluster of lncRNAs, Meg3 and Rian, are present and are associated with cell cycle regulation in the liver (Sun et al., 2019; Chen et al., 2020). Meg3 was persistently up-regulated in males neonatally exposed to BPA or BDE-99 and females neonatally exposed to BPA. Rian was persistently up-regulated in males and females neonatally exposed to BPA or BDE-99.

Persistent up-regulation of liver short-chain fatty acids from exposure to BDE-99 in males

As seen in Fig. S10, in the livers of adult males exposed to BDE-99, lactate, the substrate for short-chain fatty acid production (Bolduc et al., 2017), and succinate, which is a necessary component in histone succinylation for active gene expression (Bourriaud et al., 2005), were persistently up-regulated. The level of acetate, which is used for histone acetylation (Smestad et al., 2018), also increased but was not significant in adult males neonatally exposed to BDE-99.

Differential regulation of genes related to xenobiotic metabolism in response to early-life exposure

As one of the major functions of the liver is xenobiotic biotransformation, and the ontogeny of various PCGs encoding drug-metabolizing enzymes and transporters are under tight control of transcriptional and epigenetic regulations, examples of the regulatory patterns of PCG categories involved in xenobiotic biotransformation, epigenetic modification, nuclear receptors, and oxidative stress markers are shown in Fig. S8 (PND 5) and Fig. 5-6 (PND 60). Differentially regulated PCGs for at least one exposure group were categorized based on their known hepatic functions. Two-way hierarchical clustering using Euclidean distance was

performed using the R package ComplexHeatmap as described in MATERIALS AND METHODS.

PCGs that are involved in xenobiotic biotransformation are further classified into three categories, namely phase-I and -II drug-metabolizing enzymes, and transporters. In general, in PND 5 male pups, acute exposure to BPA had the most prominent effect on the expression of xenobiotic biotransformation related genes, followed by BDE-99 and PCBs (Fig. S8 left panel). Notably, livers of BPA and BDE-99 exposed male PND 5 pups had higher expression of genes involved in drug and lipid metabolism, such as *Cyp2b10*, *Cyp1a2*, *Cyp2c50*, and *Cyp2c54*, but lower expression for Acetylcholinesterase (*Ache*), Carboxylesterase 2g (*Ces2g*), and Dehydrogenase/Reductase 11 (*Dhrs11*). Acute BPA exposure in livers of male pups also up-regulated the phase-I enzymes *Cyp4f14*, *Cyp2a4*, *Cyp2b13*, *Cyp7b1*, *Cyp27a1*, *Adh1, Adh4*, *Aldh1a1* and *Aldh1a7*, as well as the phase-II enzymes *Ugt3a2*, *Ugt2a3*, *Gstm2*, and *Gstm3*. For transporters, acute BPA exposure up-regulated the xenobiotic uptake transporters *Slco1a1* (Oatp1a1), *Slco1a4* (Oatp1a4), and *Slco2b1* (Oatp2b1), the amino acid transporter *Slc1a4*, Organic cation transporter (*Slc22a6*), *Slc22a30*, the vacuolar proton pump *Atp6v0d2*, as well as the xenobiotic efflux transporter *Abcc3* (Mrp3). All three chemical exposure groups had up-regulation of sodium/phosphate cotransporter (*Slc17a4*). Exposure to PCBs resulted in up-regulation of *Slc17a3* (Oct3) in PND 5. Lipid transporter (*Abca7*), amino acid transporters *Slc38a5* and *Slc43a3*, organic cation transporter (*Slc22a4*), mitochondrial glycine transporter (*Slc25a38*), glycine transporter (*Slc6a9*), urea transporter (*Slc14a1*), and monocarboxylate transporter 10 (*Slc16a10*) were down-regulated following exposure to BDE-99. Exposure to BDE-99 or PCBs down-regulated the high affinity cation amino acid transporter (*Slc7a1*), sodium potassium transporter (*Atp1b2*), sodium bicarbonate cotransporter (*Slc4a9*) in PND 5 pups. There were no nuclear receptors that were regulated by acute exposure to any of the three chemicals.

In contrast to PND 5 males, livers of PND 5 female pups had fewer differentially regulated drug-processing genes following acute chemical exposure (Fig. S8 right panel). For phase-I genes, acute BDE-99 exposure had the most prominent effect in livers of female pups, including up-regulation in several p450 enzymes (*Cyp1a2*, *Cyp2c50*, *Cyp2c54*, *Cyp2b10*, and *Cyp2c37*). Acute response to BPA down-regulated the expression of *Cyp2f2* in females. No phase-II enzymes and transporter genes were differentially regulated by any of the three chemicals in PND 5 females. *Rorc* was the only nuclear receptor that was differentially regulated in livers of PND 5 females, and its mRNA level was up-regulated in BDE-99 exposed groups.

For epigenetic modifiers, in PND 5 males, the expression of H2A histone family gene (*H2afx*) was down-regulated by acute exposure to all three chemicals, and the SWI/SNF related (*Smarca2*) was up-regulated by acute BDE-99 and PCBs exposures. None of the epigenetic modifiers were altered in PND 5 females by acute chemical exposure (Fig. S8).

For genes involved in oxidative stress and redox cycling, acute BDE-99 exposure down-regulated peroxiredoxin 2 (*Prdx2*), and *Dusp1*. Acute exposure to BPA or BDE-99 down-regulated *Mt2*. Acute exposure to BPA down-regulated *Mt1* and up-regulated eosinophil peroxidase (*Epx*) in livers of PND 5 males (Fig. S8). In livers of female PND 5 pups, the muscle gene *Ttn* was up-regulated by acute BPA or PCB exposure. The *Epx* expression level was up-regulated and *Mt1* and *Mt2* were down-regulated only by acute BPA exposure.

For inflammation and membrane integrity related genes, in PND 5 males (Fig. S9 left panel), acute BDE-99 or PCB exposure down-regulated the mRNAs of claudin 13 (*Cldn13*) and erythropoietin receptor (*Epor*). Acute exposure to BDE-99 also down-regulated sphingosine kinase 1 (*Sphk1*), interleukin 1 receptor like 1 (*Il1rl1*), *Dusp1*, phospholipase A2 group 7 (*Pla2g7*), CXC motif chemokine receptor 4 (*Cxcr4*), tumor necrosis factor receptor

superfamily member 14 (*Tnfrsf14*), and early growth response 1 (*Egr1*). Acute exposure to BPA up-regulated cadherin related family member 5 (*Cdhr5*), and acute exposure to BPA or BDE-99 up-regulated proteoglycan 2 (*Prg2*). Acute exposure to BDE-99 up-regulated colony stimulating factor 1 (*Csf1*), tumor necrosis factor (*Tnfs10*), interferon inducible protein 204 (*Ifi204*), proteasome subunit beta 8 (*Psmb8*), *Stat1*, NOD-like receptor family CARD domain containing 5 (*Nlrc5*), interferon regulatory factor 1 (*Irf1*), and interferon induced protein with tetracopeptide repeats 3 (*Ifit3*) in males. In PND 5 females, acute exposure to PCBs down-regulated *Stat1* and up-regulated *Il1b*. Acute exposure to BPA or BDE-99 up-regulated *Prg2* and acute exposure to BDE-99 up-regulated the ROR gamma/*Rorc* in females.

Surprisingly, in contrast to the acute response in PND 5 males, most phase -I and -II genes were down-regulated and transporter genes were up-regulated for males at PND 60 (Fig. 5 left panel) following neonatal exposure to BPA or BDE-99. Neonatal exposure to PCBs generally had less effect on these genes. The relative expression pattern of phase -I genes had two main clusters. In the first cluster, the expression of the prototypical CAR-target gene *Cyp2b10*, which was up-regulated by BPA in PND 5 male pups, was persistently down-regulated following neonatal exposure to BPA in PND 60. Other genes were persistently up-regulated in this cluster including the drug and steroid metabolizing genes *Cyp2a4* (by all three chemicals, also up-regulated in PND 5 males), *Cyp3a44* and *Cyp2a22* (BPA and BDE-99), the fatty acid metabolizing *Cyp4a31* (BPA and BDE-99), aldo-keto reductase (*Akr1b7*), and spermine oxidase (*Smox*), and lysyl oxidase (*Lox*). *Cyp3a16* was persistently up-regulated in BPA and BDE-99 exposure groups in male adult mice. Neonatal exposure to PCBs up-regulated the expression of the drug and steroid metabolizing *Cyp3a41a.* In the second phase-I heat map cluster for males, the majority of cytochrome P450 genes were down-regulated or had lower expression compared to the vehicle control group following neonatal exposure to BPA and BDE-99 including the *Cyp1a2* (BDE-99, a prototypical target

gene of AhR), *Cyp2c29* (BDE-99, up-regulated in PND 5 BPA and BDE-99 exposed pups), *Cyp2c55*, *Cyp2c39*, *Cyp2f2*, *Cyp2d10*, *Cyp2d34*, *Cyp2d9*, and *Cyp2c38* (BDE-99), *Cyp2c50* (BDE-99, up-regulated in BPA and BDE-99 and down-regulated in PCBs male pups), *Cyp2c40* (BPA and BDE-99), fatty acid oxidizing *Cyp4f13*, *Cyp4a12a*, *Cyp4a12b*, and *Cyp4f14* (BDE-99), the bile acid synthetic enzymes *Cyp7a1* (BDE-99), *Cyp7b1* (up-regulated in BPA exposed pups), *Cyp8b1* (BDE-99), and *Cyp27a1* (BDE-99, up-regulated in BPA exposed pups), as well as the cholesterol metabolizing enzyme *Cyp51* (BDE-99), and *Cyp26b1* (PCBs). Other genes in this cluster which were also down-regulated and had lower expression than the control consisted of the membrane bound oxygenase carrier (*Cyb5b*; BDE-99), retinaldehyde dehydrogenases (*Aldh1a1*), and alcohol dehydrogenases (*Adh1* and *Adh4*; BDE-99, up-regulated in BPA exposed male pups), retinaldehyde dehydrogenase (*Aldh1a7*; BPA and BDE-99, up-regulated in BPA exposed male pups), 10-formyltetrahydrofolate dehydrogenase (*Aldh1l1*) and alcohol dehydrogenase pseudogene 1 (*Adh6-ps1*) (BDE-99), aldehyde oxidase (*Aox1*), carboxylesterase (*Ces1f*; BPA and BDE-99, down-regulated by BPA in male pups), carboxylesterases *Ces1e* and *Ces1g* (BPA and BDE-99), and *Ces1d* (BDE-99), molybdenum cofactor sulfurase (*Mocos*; BPA and BDE-99), sulfite oxidase (*Suox*; BPA), Chymotrypsin like elastase family member 1 (*Cela;* PCBs), and cadherin receptor *Celsr1* (BDE-99) and short chain dehydrogenase/reductase (*Sdr9c7*; BDE-99).

Similar to the regulatory patterns of the phase-I enzymes, most genes in the phase-II metabolism category were down-regulated by BPA or BDE-99 (Fig. 5 left panel). Among the differentially regulated genes in this category, the glutathione *S*-transferase (GST) family, which is known to conjugate many xenobiotics with glutathione (GSH) for detoxification, was the most responsive. *Gsta3*, *Gsta4*, *Gstm1*, *Gstm2*, *Gstm3*, and *Gstt1* were all persistently down-regulated by neonatal BDE-99 exposure, *Gstk1* was persistently down-regulated by

neonatal exposure to BPA, whereas *Gstm4*, *Gstm6*, and *Gstp1* were down-regulated by neonatal exposure to both BPA and BDE-99. In addition to *Gsts*, UDP glucurosyltransferase 2 family polypeptide b38 (*Ugt2b38*), and N-Acetyltransferase 8 (*Nat8*) were persistently down-regulated following neonatal exposure to BDE-99. Conversely, Sulfotransferase (*Sult*) families were up-regulated. The expression of *Sult2a2* was persistently up-regulated by neonatal BPA exposure, *Sult2a1* was persistently up-regulated by neonatal BPA or PCBs exposure, and *Sult1c2* was persistently up-regulated by neonatal BPA or BDE-99 exposure.

Genes in the transporter category contained two main clusters (Fig. 5 left panel). In the first cluster, the zinc transporter in the solute carrier family *Slc39a4*, ATPase copper transporting alpha *Atp7a*, proton-coupled divalent metal ion transporter *Slc40a1*, and vesicular nucleotide transporter *Slc17a9* were down-regulated following neonatal exposure to BDE-99. The small calcium binding *Slc25a25* was down-regulated following neonatal exposure to PCBs, and the oligopeptide transporter *Slc15a2* was down-regulated following neonatal exposure to BPA. Neutral amino acid transporter *Slc1a5*, ATPase phospholipid transporting 8b4 (*Atp8b4*), anion exchangers *Slc4a1* and *Slc7a1* (down-regulated in BDE-99 or PCBs exposed male pups), endoplasmic reticulum calcium pump (*Atp2a3*), *Slc1a4*, sodium/dicarboxylate cotransporter *Slc13a3*, sodium calcium exchanger *Slc8a1*, ATP binding cassette subfamily G member 3 and subfamily D member 2 (*Abcg3* and *Abcd2*, respectively), monocarboxylic acid transporter *Slc16a1*, mitochondrial iron transporter *Slc25a37*, ATPase plasma membrane calcium transporter *Atp2b4*, *Slc14a1* (down-regulated in BDE-99 exposed male pups), and the adenine nucleotide translocator *Slc25a4* (Ant1) were up-regulated following neonatal exposure to BPA or BDE-99. The mitochondrial solute carrier *Slc25a45*, organic anion transporter *Slco2b1* (Oatp2b1, up-regulated in BPA exposed male pups), and mitochondrial proton transporter *Atp5j2* were down-regulated by neonatal exposure to BPA and BDE-99. Neonatal exposure to BDE-99 down-regulated the sodium/potassium

transporting *Atp1a2*, organic anion transporter *Slc22a7* (Oat2), small molecule transporter *Slc46a3*, multidrug resistance-associated protein *3 Abcc3* (Mrp3), glutamate transporting *Slc17a8*, mitochondrial tricarboxylate transporting *Slc25a1*, and mitochondrial solute carrier *Slc25a44*.

Differentially regulated genes in female groups were also further categorized with respect to phase-I, -II, and transporters (Fig. 5 right panel). Females were less responsive to neonatal exposure to the three chemicals, as evidenced by fewer numbers of persistently regulated genes in all categories. In the phase-I category, the *Cyp26b1* was persistently up-regulated and *Cyp4a14* was persistently down-regulated by neonatal exposure to BDE-99. *Cyp3a41a* was up-regulated by BDE-99 or PCBs exposure. *Cyp3a44* and *Cyp3a16* were up-regulated by all three exposure groups. Flavin containing monooxygenase 3 (*Fmo3)* and *Cyp2b13* were down-regulated, whereas aldo-keto reductase family 1 (*Akr1*), *Ache*, as well as *Cyp4a14* and *Cyp4a31* were up-regulated following neonatal exposure to BPA. In females, only early-life exposure to PCBs differentially regulated genes in the phase-II category, and all of these were sulfotransferases, including the bile salt sulfotransferases (*Sult2a1* and *Sult2a2*), as well as the amine sulfotransferase (*Sult3a1*). Genes in the transporter category were differentially regulated by either BDE-99 or BPA. The apical sodium bile salt transporter *Slc10a2* (Asbt) and *Atp1a2* were up-regulated, and *Atp5j2* was persistently down-regulated by neonatal exposure to BDE-99. Early-life exposure to BPA persistently up-regulated *Slc4a1*, *Atp2a3*, *Slc1a4, Slc1a5*, *Slc13a3*, and *Slc25a4*.

In the nuclear receptor category in PND 60 males (Fig. 6 left panel), the orphan nuclear receptor *Nr0b2* (SHP), which is known to down-regulate bile acid synthesis in liver, was persistently up-regulated by PCBs. *Rorc*, which is another orphan nuclear receptor that regulates steroid hormone receptor activity as well as inflammation, was persistently down-regulated following neonatal exposure to BDE-99. Peroxisome proliferator activated receptor

delta (*Ppard),* which regulates lipid metabolism was persistently down-regulated by BDE-99 or PCBs.

Genes important for epigenetic modification in adult males were persistently up-regulated only by neonatal exposure to BPA or BDE-99 (Fig. 6 left panel). Neonatal exposure to BDE-99 up-regulated the expressions of (*Tet1*), which is involved in DNA demethylation and chromatin regulation, histone-lysine N-methyltransferase (*Ezh2*), which dysregulation has been shown in cancer development (Kim and Roberts, 2016), as well as the epigenetic repressor chromobox protein homolog 3 (*Cbx3*). The histone phosphorylation modifier and cell cycle regulator aurora kinase A, (*Aurka*), the histone acetyltransferase establishment of cohesion 1 homolog 2 (*Esco2*), *H2afx*, and *Dnmt1* were all persistently up-regulated by BPA or BDE-99.

Oxidative stress, redox cycling, and inflammation-related genes partitioned into two main clusters (Fig. 6 left panel). The first cluster contains 8 genes: the expression of the tight junction protein 3 (*Tjp3)*, protein kinase C zeta (*Prkcz)*, and NADPH oxidase 4 (*Nox4*) were down-regulated by BDE-99 and *Egr1* was down-regulated by PCB. In the same cluster, cadherin related family member 4 (*Cdhr4)* was persistently down-regulated by BPA or BDE-99 (up-regulated in PND 5 males exposed to BPA), dual specificity phosphatase 1 (*Dusp1)* was down-regulated by BDE-99 or PCB (down-regulated in BDE-99 exposed PND 5 males), titin (*Ttn)* was down-regulated by all three chemicals, and immune and inflammation transcription repressor B-cell lymphoma 6 (*Bcl6*) was down-regulated following neonatal exposure to BPA or PCB. In the second cluster, neonatal exposure to BDE-99 persistently up-regulated the intercellular adhesion molecule 1 (*Icam1)*, integrin beta 2 (*Itgb2)*, toll-like receptor 7 (*Tlr7)*, beta glucan pattern-recognition receptor (*Clec7a)*, Granzyme B (*Gzmb)*, and *Ifi204* (up-regulated by BDE-99 exposed PND 5 males). Neonatal exposure to BPA persistently up-regulated arachidonate 12-lipoxygenase (*Alox12)*, phosphatidylinositol-4,5-bisphosphate 3-

kinase catalytic subunit delta (*Pik3cd*), C-X-C chemokine receptor type 4 (*Cxcr4)*, colony stimulating factor 2 receptor subunit alpha (*Csf2ra)*, and cadherin 11 (*Cdh11)*. Secreted phosphoprotein 1 (*Spp1)* was persistently up-regulated by PCB. In young adults, neonatal exposure to BPA or BDE-99 up-regulated lymphocyte antigen 75 (*Ly75)*, *Pla2g7* (down-regulated in BDE-99 exposed to PND 5 males), interferon gamma receptor 1 (*Ifngr1)*, *Tnfrsf14* (down-regulated in BDE-99 exposed to PND 5 males), proline-serine-threonine phosphatase-interacting protein 1 (*Pstpip1)*, cascular cell adhesion molecule 1 (*Vcam1)*, leptin receptor (Lepr), heme oxygenase 1 (*Hmox1)*, serum amyloid P component (*Apcs)*, lipocalin 2 (*Lcn2)*, phospholipase C gamma 2 (*Plcg2)*, Spleen tyrosine kinase (Syk), *Mt1* (down-regulated in BPA exposed to PND 5 males), *Mt2* (down-regulated in BPA or BDE-99 exposed to PND 5 males), advanced glycosylation end-product specific receptor (*Ager)*, chemokine-like factor (*Cklf)*, interleukin 1 receptor agonist (*Il1rn)*, annexin A1 (*Anxa)*, and neutrophil cytosolic factor 1 (*Ncf1)*.

In livers of adult females, the nuclear receptor genes were not readily regulated in livers by neonatal chemical exposure. In the epigenetics category in adult females, *Aurka*, *Dnmt*, *H2afx*, and aurora kinase B (*Aurkb*) were up-regulated by BPA, and methyl binding domain 1 (*Mbd1*) was up-regulated by BDE-99. In the oxidative stress, redox cycling, and inflammation categories, neonatal exposure to BDE-99 persistently down-regulated *Mt1*, *Mt2*, and cadherin 1 (*Cdh1*), and up-regulated the *Bcl6* in livers of adult females. *Egr1* was persistently up-regulated by BPA and down-regulated by PCB, and *Lcn2* was persistent up-regulated by BPA and PCB. *Vcam1* and the S100 calcium- and zinc-binding protein *S100a9* were also persistently up-regulated by BPA in livers of adult females.

Persistent microbial alterations from exposure to environmental contaminants

Principal coordinates analysis (PCoA) was performed on bacterial abundance to investigate which group explains the major variability in the data (Fig. S11A - D). No clear clusters were present when individual mice were labeled by biocompartment, sex, and exposure. However, when mice were labeled by age, a two distinct clusters were formed, indicating that age is the greatest factor that distinguishes the beta diversity of all groups.

Specific microbiota can colonize and reside in certain biocompartments due to preferences in the different biochemical environment (Tuddenham and Sears, 2015). For instance, *Escherichia coli* is commonly found in the intestine and *Helicobacter pylori* resides in the stomach. The gut and liver are closely connected via the portal vein, biliary tract, as well as through systemic circulation and persistent liver transcriptomic changes were observed. We hypothesized that early-life exposures and the interaction with the liver lead to persistent dysbiosis. To identify the gross change in bacterial composition in adult age, the top 20 microbiota were visualized (Fig. S12). Bacterial abundance of the top 20 microbiota changes were different among different biocompartments and between males and females. Most notably, in males the relative abundance of Lactobacillus casei persistently increased in all biocompartments from neonatal exposure to BPA, BDE-99, or PCBs. However, this trend was attenuated in females. In addition, certain bacteria tended to be present in specific biocomparments. For example, the abundance of Chloroflexi DK4-96 was higher in the colon and feces in both males and females compared to other biocompartments.

The large intestine contains one of the largest microbial ecosystem in the human body with the majority of the composition comprised of obligate anaerobes (Dobbins, 2011). For this reason, the large intestinal microbiome (colon) was used to estimate the relationship between the gut and liver. In males neonatally exposed to BPA, *Ruminococcaceae*,

Ruminococcaceae UCG-005, *Prevotellaceae* UCG-010 uncultured, Family XIII UCG-010 uncultured, and *Oscillibacter* were persistently down-regulated, and *Clostridiales vadin* BB60 group, *Lachnospiraceae* FCS020 group, *Eubacterium ventriosum*, *Lachnospiraceae* bacterium 609, *Mollicutes* RF39 uncultured, *Peptococcaceae* uncultured, Family XIII AD3011 uncultured, *Ruminiclostridium* 9 uncultured, *Ruminiclostridium* 6 uncultured, *Ruminiclostridium* 6, *Firmicutes* bacterium M10-2, *Ruminococcus* 1, and *Anaerotruncus* uncultured were persistently up-regulated (Fig. 7A).

In males neonatally exposed to BDE-99, *Firmicutes* bacterium M10-2, *Ruminococcaceae* UCG-005, *Prevotellaceae* UCG-001 uncultured, *Intestinimonas* ambiguous, and *Lachnospiraceae* uncultured were persistently down-regulated, and *Ruminococcus* 1, Family XIII UCG-001 uncultured, *Ruminococcaceae* UCG-010 uncultured, Anaerotruncus uncultured, *Eubacterium coprostanoligenes*, *Akkermansia muciniphila*, and *Lachnospiraceae* UCG-004 were persistently up-regulated (Fig. 7A).

In males neonatally exposed to PCBs, *Clostridiales vadin* BB60 group, *Ruminiclostridium* 9 uncultured, *Ruminococcaceae* UCG-005, *Anaerotruncus* uncultured, *Oscillibacter* unidentified, *Acetatifactor* ambiguous, *Acetatifactor* uncultured, *Tyzzerella* uncultured, *Oscillibacter*, *Ruminococcaceae* unidentified, *Clostridium sp*. Culture-54, and *Intestinimonas* ambiguous were persistently down-regulated, and *Ruminococcaceae*, *Lachnospiraceae* uncultured species, *Lacknospiraceae* FCS020 group, Family XIII UCG-001 uncultured, *Peptococcaceae* uncultured ambiguous, *Clostdium sp*. Culture-1, *Oscillibacter* uncultured, *Roseburia* uncultured, *Oscillibacter* unidentified, *Ruminiclostridium* 9, and Lacknospiraceae NK4A136 ambiguous were persistently up-regulated (Fig. 7A).

For females neonatally exposed to BPA, muribaculum uncultured, *Ruminiclostridium* 6, *Eubacterium coprostanoligenes*, *Lachnospiraceae* FCS020 group were persistently up-

regulated and *Prevotellaceae* UCG-001 and *Muribaculaceae* uncultured were persistently down-regulated (Fig. 7B).

Ruminococcus 1, *Eubacterium coprostanoligenes*, *Ruminococcaceae* UCG-010, *Anaerotruncus*, Family XIII UCG-001 uncultured, *Akkermansia muciniphila*, and *Lachnospiraceae* UCG-006 were persistently up-regulated, and *Peptococcaceae* uncultured, *Ruminiclostridium* 6, *Firmicutes* bacterium M10-2, *Eubacterium ventriosum*, *Roseburia*, *Lachnospiraceae* UCG-004, and *Clostridium sp*. Culture-27 were persistently down-regulated in females neonatally exposed to BDE-99 (Fig. 7B).

For females neonatally exposed to PCBs, *Anaerotruncus*, *Lachnospiraceae* FCS020 group, *Acetatifactor* ambiguous, *Oscillibacter*, *Tyzzerella* uncultured, *Lachnospiraceae* uncultured, and *Clostridium Sp*. Culture-54 were persistently up-regulated, and *Ruminiclostridium* 6, *Lachnospiraceae* UCG-001, *Ruminiclostridium* 5, *Clostridiales* BB60 uncultured, and *Ruminococcaceae* UCG-005 ambiguous were persistently down-regulated (Fig. 7B).

Predicted altered pathways in colon microbiome from neonatal exposure to BDE-99 in males

Using persistently differentially abundant colon microbiota following early-life exposure to BDE-99,_which led to profound persistent liver transcriptomic alterations. Microbial-derived pathway changes were estimated utilizing the OTU and taxa using PICRUSt2. For males neonatally exposed to BDE-99, glucose and glucose-1-phosphate degradation, 1,4-dihydroxy-2-naphthoate biosynthesis, phylloquinol biosynthesis, menaquinol biosynthesis (demethylmenaquinol-8, menaquinol-13, menaquinol-12, menaquinol-11, menaquinol-8, and menaquinol-7), pyrimidine deoxyribonucleotides de novo biosynthesis IV and from CTP, glycolysis-E-D pathway, N-acetylneuraminate degradation, reductive TCA cycle I, and NAD

biosynthesis II from typtophan were persistently up-regulated in the colon by bacteria. TCA cycle VII (for acetate producers), 2,3-butanediol biosynthesis, succinate fermentation to butanoate, methanogenesis from acetate, hexitol fermentation to lactate, formate, ethanol and acetate, D-glucarate degradation I and II, D-glucarate and D-galactarate degradation, L-lysine biosynthesis, CMP-legionaminate biosynthesis, polyamine biosynthesis II, 4-aminobutanoate degradation V, and pyruvate fermentation to acetone were persistently down-regulated in colons of males neonatally exposed to BDE-99 due to microbial alterations (Fig. 7C).

For females neonatally exposed to BDE-99, L-glutamate degradation, TCA cycle by acetate-producing bacteria, succinate fermentation, R,R- and 2,3-butanediol biosynthesis, 4-aminobutanoate degradation, saturated fatty acid elongation, polyisoprenoid biosynthesis by *E.coli*, inosine 5'-phosphate degradation, pyrimidine deoxyribonucleosides salvage, and glycolysis pathways were persistently up-regulated, and ADP-L-glycero-β-D-manno-heptose biosynthesis, L-alanine biosynthesis, assimilatory sulfate reduction I and cysteine, lactose and galactose degradation I, and mevalonate pathways by eukaryotes and bacteria pathways were persistently down-regulated (Fig. 7D).

Potential relationship between colon microbiome and liver from neonatal exposure to BDE-99

Pearson's correlation was conducted on the differentially abundant colon microbiome and genes in phase-I category to investigate the potential interaction between the microbiome and liver metabolizing enzymes (Fig. 8). The absolute value of Pearson's correlation coefficient greater than 0.8 with FDR-adjusted *p*-value less than 0.1 are highlighted in pink. In males neonatally exposed to BDE-99, *Ruminococcaceae* UCG-005 ambiguous was positively correlated with *Cyp51*. *Eubacterium coprostanoligenes* was negatively correlated with *Ces1d* and *Cyp2c39*. *Akkermansia muciniphila* was negatively correlated with Adh1,

Aldh1a1, *Aldh1a7*, *Aldh1l1*, *Aox1*, *Ces1d*, *Ces1e*, *Ces1f*, *Ces1g*, *Ces2c*, *Cyp2c29*, *Cyp2d10*, *Cyp2d34*, *Cyp2d40*, *Cyp2d9*, *Cyp2f2*, *Cyp2u1*, *Cyp4a12a*, *Cyp4a12b*, *Cyp4f13*, *Cyp4f14*, *Celsr1*, *Cyp27a1*, *Dhrs3*, and *Mocos*, and positively correlated with *Akr1b7*, *Cyp2a22*, *Cyp2b9*, *Cyp3a16*, *Cyp3a44*, *Cyp4a31*, *Lox*, and Smox. *Ruminococcaceae* UCG-010 uncultured was negatively correlated with *Cyp2c39* and *Cyp51*. *Lachnospiraceae* uncultured was negatively correlated with *Akr1b7*, *Cyp2b9*, *Cyp3a16*, *Cyp3a44*, *Cyp4a31*, and *Lox*, and positively correlated with *Adh1*, *Aox1*, *Ces1e*, *Ces1f*, *Ces1g*, *Cyp2c29*, *Cyp2d10*, *Cyp2d40*, *Cyp2f2*, *Cyp4a12a*, *Cyp4a12b*, *Cyp4f14*, *Dhrs3*, and *Mocos*. *Intestinimonas* ambiguous was positively correlated with *Cyp51* and *Cyp7a1*.

For females neonatally exposed to BDE-99, *Ruminiclostridium* 6 was positively correlated wtth *Cyp3a41a* and *Cyp3a44*. Family XIII UCG-001 uncultured was positively correlated with *Cyp3a16*, *Cyp3a41a*, and *Cyp3a44*, and negatively correlated with *Cyp4a14*. *Lachnospiraceae* UCG-006 was negatively correlated with Cyp4a14. *Clostridium sp*. Culture-27 was positively correlated with *Cyp3a16*, *Cyp3a41a*, and *Cyp3a44*, and negatively correlated with *Cyp4a14*.

DISCUSSION

The present study demonstrated that similar to the well-known epigenetic reprogramming chemical BPA, early-life exposure to BDE-99 and PCBs also produced persistent liver transcriptomic responses in young adulthood (Fig. 9). The transcriptomic effect was markedly amplified in PND60 as compared to PND5, indicating that early-life chemical exposure shifted the trajectory of normal liver development and have the potential to aggravate the toxic response in adulthood long after the initial exposure stopped. At the given dose, exposure to BPA and BDE-99 had more prominent persistent effects than those of PCBs, and males were more susceptible than females to persistent hepatic transcriptomc

changes induced by early-life chemical exposures. The expression of crucial upstream regulators involved in maintaining cell cycle (p53, *Cdkn1a*, *E2f1* and *E2f3*), sterol (*Scap*) and bile acid synthesis (*Fgf15*), and nuclear receptors that sense and regulate lipids (PPARs), and drug metabolism (RORs, CAR, PXR) were predicted to be altered. In addition, the expression of cancer-related lncRNAs and genes (i.e. *H19*, *Snhg1* and *Snhg4*, *Gsts*) were persistently dysregulated following neonatal exposure to BPA or BDE-99.

Gene ontology enrichment and hierarchical clustering of persistently differentially regulated genes showed evidence of persistent cell cycle dysfunction, altered epigenetic remodeling, lipid and drug metabolism, as well as oxidative stress and inflammation in the liver. Notably, clear trends of persistent down-regulation of genes that encode phase-I and -II biotransformation enzymes and up-regulation for most transporters and oxidative stress and inflammation-related genes were observed in adults neonatally exposed to BPA and BDE-99 exposed males and BPA exposed females. These results provide strong evidence of altered hepatic metabolism and immune states following exposure to BPA, BDE-99, or PCBs, and have implications for increased risks of chronic diseases throughout the lifetime. To the best of our knowledge, the present study is among the first to show that neonatal exposure to BPA and BDE-99 can cause persistent dysregulation of the liver transcriptome, especially regarding potential for persistent dysregulation of drug processing enzymes and cell proliferation.

BPA and BDE-99 induced changes in cell proliferation gene expression

The altered liver transcriptome including those in the cell cycle disruption and epigenetic modification categories following exposure to the three chemicals have been identified in the present study. The data on BPA are consistent with previous reports, which showed that perinatal exposure to BPA resulted in a 7-fold higher odds of neoplastic and

preneoplastic lesions in mouse litters raised to adults (Weinhouse et al., 2014), accompanied with hypomethylation of DNA of the offspring (Dolinoy et al., 2007). Regarding PBDEs, a study conducted by the National Toxicology Program revealed that chronic exposure to BDE-71, a PBDE mixture that includes BDE-99, induces hepatocellular carcinoma and adenoma in rats and mice (https://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr500580/listedreports/tr589/index.html). Furthermore, exposing mouse and human preadipocytes to BDE-99 resulted in decreased methylation status of the CpG sites at the PPARγ promoter (Wen et al., 2019) and significant decreases were observed in 5-methylcytosine in cytochrome c oxidase Mt-co2 in rats that were perinatally exposed to BDE-47. A single dose of PCB 153, a non-dioxin-like tumor promoter, following N-nitrosodimethylamine (NMDA) exposure was associated with increased liver and lung tumor sizes (Anderson et al., 1986) and perinatal exposure to PCBs (a mixture of PCB 138, 153, and 180) decreased the levels of H3K16Ac and H3K4me3 in the offspring livers (Casati et al., 2012). These PCB congeners are also major constituents of the PCB mixture used in this study (Li et al., 2018b).

The present study is among the first to compare three different persistent environmental pollutants together, and we showed that at the given dose, BPA and BDE-99 had more prominent and similar persistent effects, especially regarding cell cycle and epigenetic modifications, as compared to PCBs. At the upstream, the predicted regulators in adult age of cell cycle included inhibited p53 and *Cdkn1*, activated E2fs, pro-inflammatory *Il6*, and *Ccnd1* (Fig. 4A). Chromatin epigenetic modification and cell cycle related terms had higher enrichment significance and relative proportion for BPA and BDE-99 exposed groups compared to PCBs and other GO categories in adulthood (Fig. 4C and Fig. S2-7). Persistently altered cell cycle regulation was further evidenced by up-regulation of cancer-related lncRNAs, such as *Snhg1, Snhg4*, and *H19, Meg3, and Rian* (Fig. 4D). In addition, succinate and butyrate were persistently up-regulated in males neonatally exposed to BDE-99

(Fig. S10). Combined with the predicted upstream regulators and GO enrichment results, our results suggest that the dysregulation of cell cycle is possibly due to epigenetic reprogramming of the liver transcriptome, followed by persistent inflammation and oxidative stress (Fig. 6 and Fig. S8).

Persistent dysbiosis from early-life exposure to environmental toxicants

In the liver transcriptome, BPA and BDE-99 dysregulated similar genes and the persistent transcriptomic responses from neonatal exposure to PCBs were relatively weak compared to BPA and BDE-99 for males. However, the majority of differentially abundant bacteria from neonatal exposure to PCBs for both males and females were distinct from BPA or BDE-99. For females, early-life exposure to BPA resulted in the most prominent changes, whereas for the colon microbiome, neonatal exposure to BDE-99 produced the most differentially abundant bacteria comapred to the other two environmental contaminants. The mechanism of distinct colon microbial regulation by these environmental contaminatns may differ from that of the host transcriptome. While BPA, BDE-99, and PCBs activate key xenobiotic-sensing transcription factors, such as PXR, CAR, and AhR, to activate xenobiotic metabolizing enzymes (Aleksunes and Klasssen, 2012; Cui and Klaassen, 2016), these environmental contaminants may have different effects on the microbiome, with a different degree of intestinal environment alterations from direct and indirect mechanisms, such as damage from physical and signaling effects. In addition, persistent dysbiosis of certain bacteria, such as *Akkermansia muciniphila*, a SCFA producer and mucin degrader, may indicate that bacteria-bacteria ecosystem relationships have been persistently altered.

The bacteria-derived pathways were also predicted to be altered in the colon by early-life exposure to BDE-99 (Fig. 7C and D). Males had primarily up-regulated sugar metabolism and menaquinol biosynthesis, which is involved in cytoplasmic membrane production and

implicated in nitric oxide reduction (Walther et al., 2013; Cramm and Friedrich, 1999; Attar and Vries, 2015) and down-regulated SCFA degradation and TCA cycle. This suggests that males neonatally exposed to BDE-99 have more active sugar utilization, immune response inhibition, and higher SCFA concentration, which may affect liver activities. Interestingly, in contrast to males, females exposed to BDE-99 early in life had up-regulated TCA cycle and SCFA degradation and down-regulated sugar and amino acid metabolism. This may indicate that females neonatally exposed to BDE-99 have the opposite effect as males, which may partially explain differences in the persistent responses from neonatal exposure to BDE-99. As the gut also serves as a major xenobiotic metabolizing organ, the persistent pathway alterations from the persistent dysbiosis may indicate an altered response to additional chemical exposures throughout the lifetime.

Early-life exposure to contaminants and altered xenobiotic biotransformation and inflammation

Gene expression responses upon exposures to BPA, BDE-99, or PCBs at PND 5 showed that several drug-metabolizing enzymes were more up-regulated in males than those of females (Fig. S8) including *Cyp1a2*, *Cyp2c* families, and *Gstm* genes, which may contribute to the metabolism of these environmental chemicals. These observations are in line with previous studies showing that BPA, PBDEs, and PCBs can be metabolized by certain cytochrome P450 isoforms (Niwa et al., 2001; Stapleton et al., 2009; Grimm et al., 2015b). Interestingly, although the acute exposure resulted in unique target gene expression per chemical exposure at PND 5, the persistent chemical effect showed more similarities in PND 60 (Figs. S1A ,S8, and Fig. 3A), and this is especially true for BPA and BDE-99 exposed groups. In addition, between PND 5 and PND 60, the regulatory patterns of the same genes

are amplified (Fig. 5). Similarly, drug and lipid metabolism-related GO terms were up-regulated in neonatal age, whereas they were down-regulated in adulthood (Fig. 4C, Fig. S2-7). These observations suggest that early-life exposure shifted the developmental trajectory later in life. Inverse regulatory patterns between PND 5 and -60 were also observed for the same gene; for example, *Cyp1a2* and *Cyp2c54* were up-regulated in BPA and BDE-99 exposed males in PND 5 but were down-regulated in PND 60. Transporters, such as *Slco1b1* (Oatp1b1) and *Abcc3* (Mrp4) were up-regulated by BPA exposed PND 5 males, but *Slco1b1* was persistently down-regulated by both BPA and BDE-99; whereas *Abcc3* was down-regulated for BDE-99 exposed adult males.

Moreover, in PND 5, cell cycle and chromatin epigenetic modification-related GO terms, such as nucleosome assembly (GO: 0006334) and DNA conformation change (GO: 0071103) were down-regulated upon exposure; however, terms in these categories were up-regulated in PND 60 (Fig. 4C, Fig. S2-7). Furthermore, evidence of acute and persistent dysregulation was observed including genes in the phase-I, -II, transporters, and inflammation and oxidative stress categories. The perinatal-enriched P450 isoform *Cyp3a16* was persistently up-regulated following neonatal exposure to BPA or BDE-99 for both sexes (Fig. 5). These results suggest that neonatal exposure to BPA or BDE-99 may have greatly altered the normal developmental trajectory and reprogrammed the liver epigenome via inducing overwhelming metabolism of these contaminants and immune responses which led to persistent dysregulation of the liver transcriptome and dedifferentiating the liver.

Bile acid metabolizing genes, such as *Cyp7a1*, *Cyp7b1*, *Cyp8b1*, and *Cyp27a1*, were persistently down-regulated in adult males at PND 60 following BDE-99 exposure, suggesting persistent alteration of bile acid production levels (Fig. 5 left panel). *Mt1* and *Mt2*, which are oxidative stress markers that have important protective roles in exposure to oxidants and electrophiles, were down-regulated in PND 5 upon BPA or BDE-99 exposure but were

persistently up-regulated in BPA or BDE-99 exposed males and down-regulated in BDE-99 exposed females. To note, metallothioneins are also known to bind to heavy metals and endogenous transition metals such as zinc. Interestingly, several zinc finger proteins, such as *Zfp292*, *Zfp334*, *Zfp336*, *Zfp608*, and *Zfp958*, were dysregulated in BPA and BDE-99 exposed males (Table S2-6 and 2-8). Therefore, together these observations suggest that zinc ion homeostasis may be disrupted following early-life exposure to BPA and BDE-99.

Furthermore, in males neonatally exposed to BDE-99, *Akkermansia municiphila* (persistently up-regulated) and an uncultured bacteria in the *Lachnospiraceae* family (persistently down-regulated) were respectively negatively and positively correlated with genes in the *Aldh*, *Ces*, and *Cyp2*, *3*, and *4* families. *Akkermansia muciniphila* has been shown to have beneficial roles in carbohydrate metabolism and immune response and has been implicated in type II diabetes and irritable bowl syndrome (Geerlings et al., 2018). *Lachnospiraceae* is one of the most abundant taxa in the rumen and is a SCFA-producing anaerobe that has been implicated in colorectal cancer (Gao et al., 2017). Certain genus and species in the *Lachnospiraceae* family were found to be involved in key transcription factors important in sensing xenobiotics and lipids, such as AhR, PPARγ through microbial signaling molecules, such as indole and through tryptophan metabolism pathways (Venkatesh et al., 2014). Through similar mechanisms, the decrease in *Lachnospiraceae* may have contributed to the persistently down-regulated gene expression in the phase-I category, which the accompanied oxidative damage and immune responses may have persistently stimulated the gut mucosa, thereby providing a preferable environment for *Akkermansia municiphila*.

For females neonatally exposed to BDE-99, *Ruminiclostridium* 6, Family XIII UCG-001, and *Clostridium sp*. Culture-27 were persistently up-regulated and were positively correlated with genes in the Cyp3a family. Family XIII UCG-001, *Lachnospiraceae* UCG-006, and *Clostridium sp*. Culture-27 were negatively correlated with *Cyp4a14*. Persistent up-regulation

of genes encoding enzymes in the *Cyp3a* family and down-regulation of *Cyp4a14*, a target of PPARα that was predicted to be the top upstream regulator from early-life exposure to BDE-99. The persistent dysregulation of these genes may indicate activation of prolonged xenobiotic metabolism-related cellular machinery and attenuated lipid-sensing from the early-life exposure to BDE-99. While there is not enough evidence to support the interactions between *Ruminiclostridium*, Family XIII, and *Clostridium sp*., these colon gut microbiota may produce metabolites that make the liver transcription more active to transcribe genes in the *Cyp3a* genes and alter the activity of PPARα.

Sex-specific susceptibility in early-life chemical exposure induced transcriptomic changes

Sex differences occur in a wide array of toxicological responses including behavior, anatomy, physiology, biochemistry, and genetics, accounting for male to female differences in response to environmental chemical exposures, diet, and pharmaceuticals (Callan et al., 2016; Boese et al., 2017; Gochfeld, 2017). Interestingly, for all three chemical exposure groups, males were more susceptible and had more evidence of persistent liver disruption than females (Fig. 4-6). In mice, gestational exposure to BPA resulted in a statistically significant increase in DNA methylation of the estrogen receptor alpha gene (*Esr1*) in males only in the cortex and hypothalamus (Kundakovic et al., 2013), whereas perinatal and peripubertal exposure to BPA resulted in higher increases of body weight and adiposity in females compared to males (Rubin et al., 2017). Similarly, exposure to BDE-47 altered the expressions of liver and muscle heat shock proteins in female marine medaka, whereas the exposure induced only apoptosis in males (Deane et al., 2014). In addition, PBDEs have also been shown to have androgen activity disrupting properties (Stoker et al., 2005; Yang et al., 2009). PCBs are known to alter thyroid hormone activities (Berg et al., 2017; Jacobson et al.,

2017). In humans, previous studies have found a higher association between exposures to PCBs and attention deficit hyperactive disorder (ADHD) (Behforooz et al., 2017), as well as enrichment of cancer-related terms in males and immune system-related terms in females at the transcriptome level (Espin-Perez et al., 2019). These sex differences may be due to dissimilarities in the endocrine system, such as the normal average production of androgen and estrogen, and the activities of their receptors.

My study presents novel findings showing persistent dysregulation of genes related to drug processing, cell cycle, epigenetic modification, and immune responses and that the direction of transcriptomic dysregulation can be changed, and responses can be amplified as individuals age. Furthermore, the present study provides evidence for dysregulated SCFA levels and gut-liver axis, and the possibility for the gut microbiome contributing to the persistent liver transcriptomic response. However, the present study includes limitations, such as exposures higher than what the average person is exposed to and small sample sizes ($n < 5$ per exposure group). The dose of BPA was determined by, previous research that studied chronic and developmental effects by *in utero* exposure to BPA in rodent models (Markey et al., 2001; Richter et al., 2007; Betancourt et al., 2010; Jenkins et al., 2011). The doses of BDE-99 and PCBs were based on previous studies that used adult mice (Cheng et al., 2018; Li and Cui, 2018; Li et al., 2018a; Scoville et al., 2019).

To further develop the reported findings and unveil the mechanisms underlying these changes, epigenetic experiments should be conducted, such as studying DNA and histone modifications, dysregulated microRNAs, as well as the roles of the nuclear receptors that were predicted to be activated/inhibited upstream, including *Nr1i2* and *Nr1i3* (CAR and PXR). The gut microbiome is also responsible for numerous metabolism and studies have found that exposures to environmental contaminants can alter the microbial components in the gut (Cheng et al., 2018; Li et al., 2018a). To further study the interaction of gut-liver axis

dysregulation, exposure-specific microbiome functions with more focus on the microbial genes that are regulated should be considered, in addition to disease phenotypes. As mice were used as model organisms for this study, testing species differences should be done using different organisms or cell lines. To truly understand the degree of persistence and altered functions of the liver following early-life exposure to environmental toxicants, trans-generational studies and toxicological responses should also be investigated.

Despite the limitations, the present study provides better comprehension of how early-life exposure to environmental contaminants can alter the normal developmental trajectory of the liver and the degree to which persistent responses occur. Industrial chemicals continue to be manufactured and released. Some are ubiquitous, persistent and bioaccumulative, and they are detectable in multiple media, including water, soil and food. This potentially allows for consistent and repeated exposures. Our results add additional understanding of potential outcomes following such exposures that occur early in life, not only humans, but also other organisms in the natural environment. Furthermore, our study adds knowledge to existing early-life exposure models, which suggest that acute and chronic exposure experiments in adult age may not entirely explain all outcomes that are possible. The findings of the present study show that early-life exposure to toxicants can have a life-long impact on disease risk.

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FOOTNOTES

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FIGURE LEGENDS

Figure 1. A diagram of the experimental design of the study.

From postnatal day (PND) 2 – 4 male and female C57BL/6J mouse pups were supralingually exposed to vehicle (corn oil, 5 mL/kg/day, control), BPA (250 μg/kg/day), BDE-99 (57 mg/kg/day), or the Fox River mixture (PCB) (30 mg/kg/day) once daily for three consecutive days in biological triplicates. The livers were collected at PND 5 (n = 24) and 60 (n = 24). Whole transcriptome RNA-Seq was conducted using the ribosomal deletion method (75 bp paired-end), and data were analyzed using HISAT2, SAMtools, and Cufflinks. Transcript abundance was estimated using Gencode vM19 as the reference genome for both protein-coding genes (PCGs) and long non-coding RNAs (lncRNAs). Differential gene expression was determined using Cuffdiff (FDR-BH < 0.05). For PCGs, gene ontology analysis was performed using the R package topGO. Differentially regulated genes were analyzed using Ingenuity Pathway Analysis (IPA) to identify upstream regulators and enriched networks. The PCGs were selected and relative expression levels were analyzed based on their known hepatic functions including xenobiotic biotransformation (phase -I and -II drug-metabolizing enzymes as well as transporters), epigenetic modification (DNA and histone modifications), nuclear receptors, as well as oxidative stress and inflammation markers.

Figure 2.

One-way hierarchical clustering of the liver transcriptome expression following neonatal exposure to BPA, BDE-99, or PCBs. Age, sex, and exposed groups are labeled on the

columns and legend. Gene (row) clusters were formed by performing k-means clustering (k = 3).

Figure 3.

A. Principal components analysis (PCA) of the liver transcriptome expression following neonatal exposure to environmental contaminants. Values on the principal components are labeled by age and sex. Venn diagrams showing the numbers of uniquely and commonly regulated PCGs (**B**) and lncRNAs (**C**) in livers of mice at PND 60 (young adulthood) following neonatal exposure to BPA (yellow shade), BDE-99 (purple shade), and PCBs (green shade) (FDR-BH < 0.05). The numbers of differentially regulated genes are labeled on the Venn diagrams. Males are displayed on the left and females on the right column. **D.** The number of differentially regulated PCGs in livers of pups at PND 5 and PND 60 following neonatal exposure to BPA, BDE-99, and PCBs (Cuffdiff, FDR-BH < 0.05). Left: males, right: females.

Figure 4.

A. Top 10 upstream regulators predicted by IPA in livers of PND 60 male and female mice following neonatal exposure to BPA, BDE-99, or PCBs. Genes that are predicted to be activated or inhibited are colored in orange and blue, respectively. **B.** Number of differentially regulated gene ontology terms ($p < 0.01$) in livers of PND 60 male and female mice following neonatal chemical exposure. **C.** Summary of gene ontology enrichment results by age, sex, and exposure groups. Up-regulated (left panel, red) and down-regulated (right panel, blue) biological terms related to liver function are included. Categories (row names) that contain at least 5 GO terms among the top 50 per group were included in the figure. The color gradient describes the average significance ($p < 0.01$) in each category per group. The top enriched proportion (size of circles) indicate the proportion of GO terms in each category relative to the top 50 terms ($p < 0.01$). **D.** An example of differential regulated lncRNAs associated with liver tumors. Individual bar graphs with gene symbols show the average transcripts per million

(TPM) ± standard error (SE) of the genes in the cluster. Asterisks represent statistically significant differences compared to vehicle-exposed groups (FDR-BH < 0.05).

Figure 5.

Two-way hierarchical clustering of the mRNAs of differentially regulated genes involved in xenobiotic biotransformation in livers of PND 60 adult mice following neonatal chemical exposure, as generated by the R package ComplexHeatmap. Males are shown on the left and females are displayed in the right column. Gene clustering was performed separately based on distinct gene categories involved in xenobiotic biotransformation (Phase-I, Phase-II, and transporters). All genes were differentially expressed in at least one of the chemical exposure groups (Cuffdiff, FDR-BH < 0.05).

Figure 6.

Two-way hierarchical clustering of the mRNAs of epigenetic modifiers, nuclear receptors, oxidative stress, and inflammation-related genes in livers of PND 60 adult mice following neonatal chemical exposure, as generated by the R package ComplexHeatmap. Males are shown on the left and females are displayed in the right column. Gene clustering was performed separately based on different gene categories listed above (note: nuclear receptors were not differentially regulated in female mice). All genes were differentially expressed in at least one of the chemical exposure groups (Cuffdiff, FDR-BH < 0.05).

Figure 3.7

Persistently regulated colon bacteria from neonatal exposure to BPA, BDE-99, or PCBs in males (A) and females (B). Predicted pathway changes by colon bacteria from neonatal exposure to BDE-99 in males (C) and females (D).

Figure 3.8

Differentially regulated colon bacteria correlated with differentially regulated genes in the phase-I category from neonatal exposure to BDE-99 in males (A) and females (B). Pink

represents significant correlation (absolute Pearson's r > 0.8 and FDR-adjusted p value < 0.1).

Figure 9. Summary of the key findings.

Neonatal oral exposure to human health relevant environmental toxicants BPA, BDE-99, and PCBs (Fox River Mix) was sufficient to acutely and persistently alter the liver transcriptome, and change the ontogenetic trajectory of many key signaling pathways including cell cycle, epigenetic remodeling, drug metabolism, lipid metabolism, and immune response. In general, the effect of neonatal chemical exposure is markedly amplified in adult age: at the doses given, BDE-99 and BPA had more prominent effects on gene regulation than PCBs, and male pups are more susceptible than female pups. The persistent change in the liver transcriptome is possibly due to the developmental reprogramming through cross-talk among nuclear receptors and other transcription factors, as well as epigenetic modifying factors and lncRNAs. In young adults, certain lncRNAs known to be associated with liver cancer were persistently up-regulated by both BPA and BDE-99. This change in expression of these lncRNAs was consistent with the predicted upstream regulation: p53 and up-regulated cell-cycle-related gene ontology terms. Peroxisome proliferator-activated receptors (PPARs) and certain retinoic acid receptor-related orphan receptors (RORs) were also predicted upstream regulators that were in line with global change. The persistent effect due to neonatal exposure may be a point source for altered hepatic biotransformation leading to increased risk for chronic disease.

Figure 1

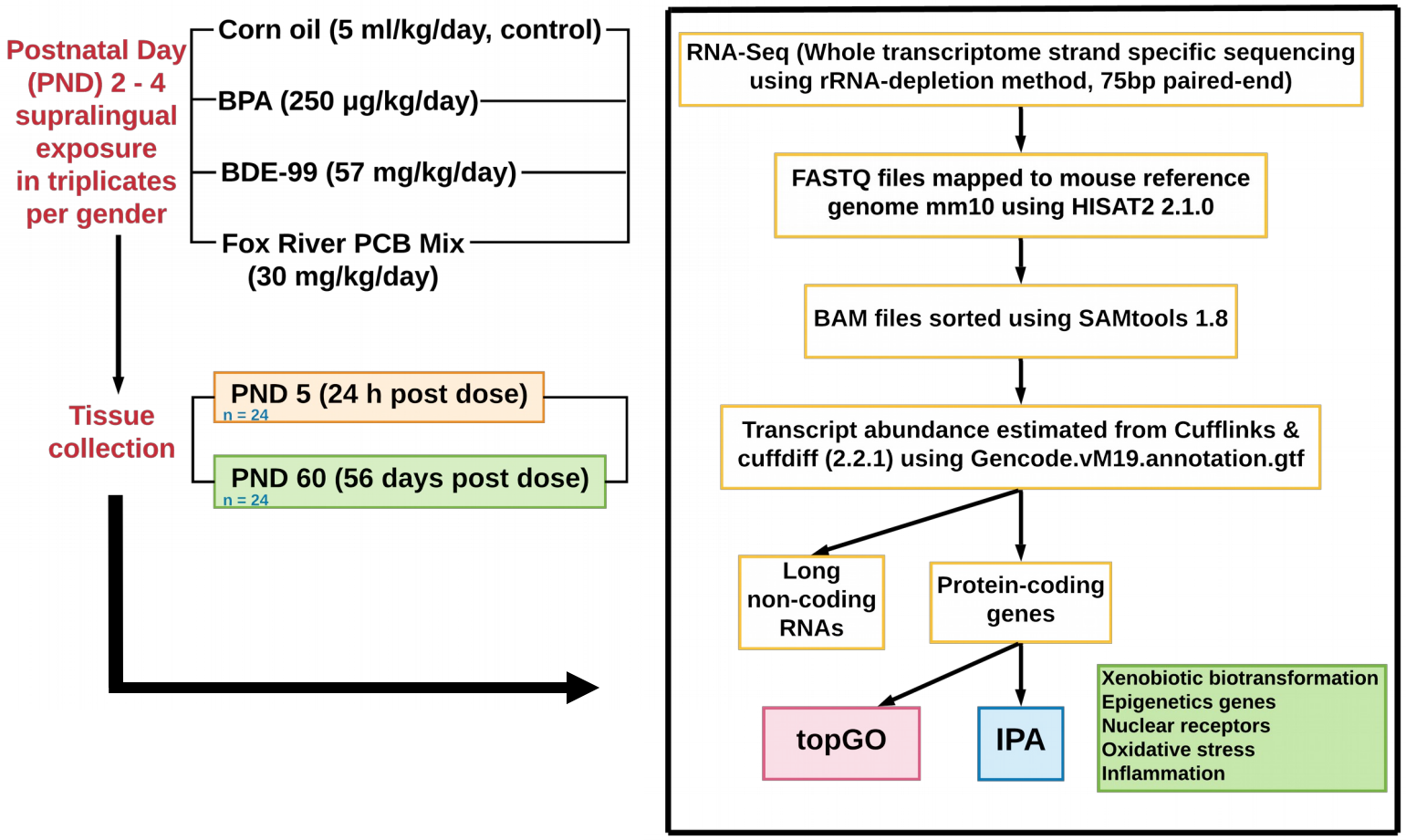
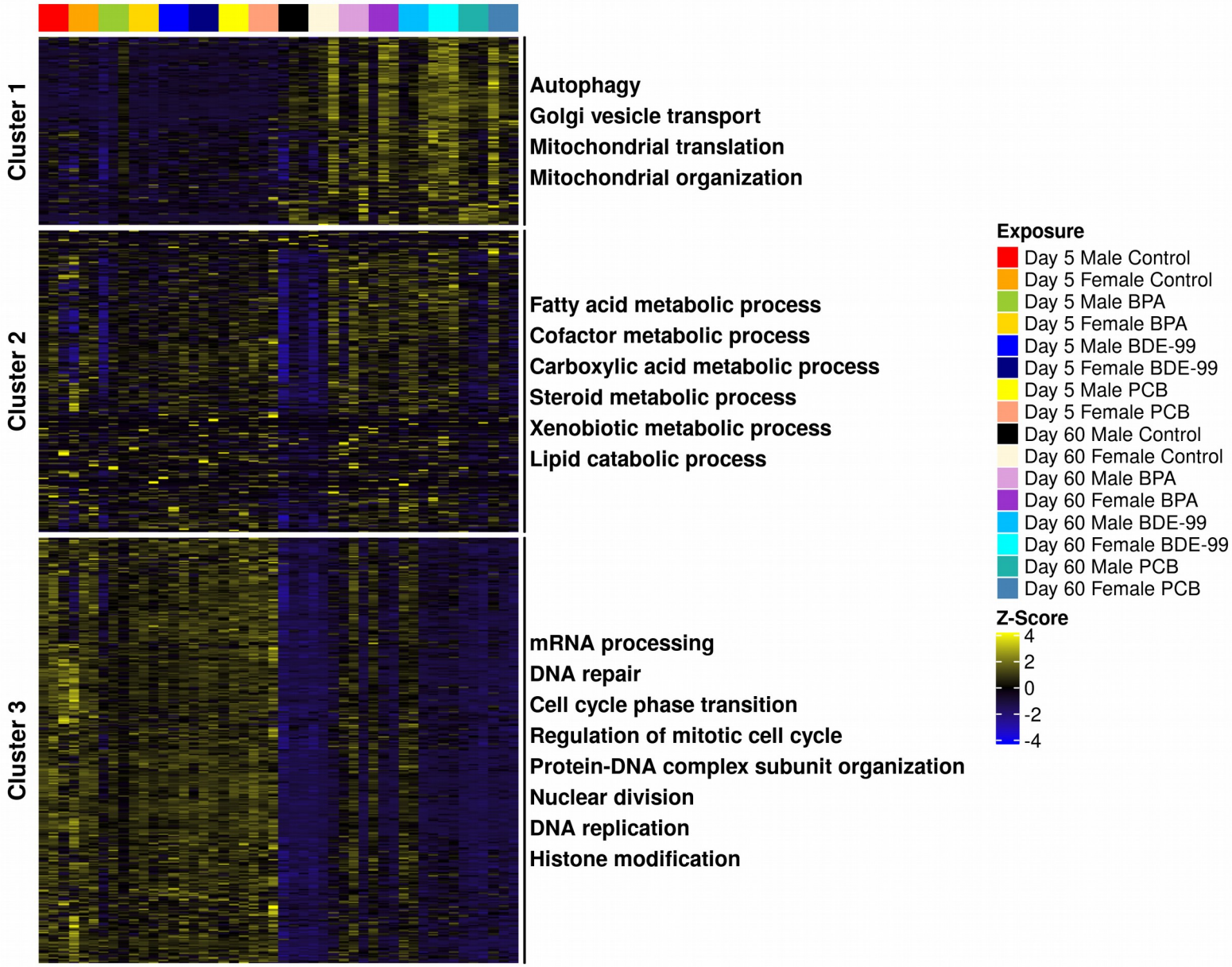

Postnatal Day (PND) 2 - 4 supralingual exposure in triplicates per gender
Corn oil (5 ml/kg/day, control)
BPA (250 µg/kg/day)
BDE-99 (57 mg/kg/day)
Fox River PCB Mix (30 mg/kg/day)
Tissue collection
PND 5 (24 h post dose)
n = 24
PND 60 (56 days post dose)
n = 24
RNA-Seq (Whole transcriptome strand specific sequencing using rRNA-depletion method, 75bp paired-end)
FASTQ files mapped to mouse reference genome mm10 using HISAT2 2.1.0
BAM files sorted using SAMtools 1.8
Transcript abundance estimated from Cufflinks & cuffdiff (2.2.1) using Gencode.vM19.annotation.gtf
Long non-coding RNAs
Protein-coding genes
topGO
IPA
Xenobiotic biotransformation
Epigenetics genes
Nuclear receptors
Oxidative stress
Inflammation

Figure 2


Cluster 1
Autophagy
Golgi vesicle transport
Mitochondrial translation
Mitochondrial organization
Cluster 2
Fatty acid metabolic process
Cofactor metabolic process
Carboxylic acid metabolic process
Steroid metabolic process
Xenobiotic metabolic process
Lipid catabolic process
Cluster 3
mRNA processing
DNA repair
Cell cycle phase transition
Regulation of mitotic cell cycle
Protein-DNA complex subunit organization
Nuclear division
DNA replication
Histone modification
Exposure
Day 5 Male Control
Day 5 Female Control
Day 5 Male BPA
Day 5 Female BPA
Day 5 Male BDE-99
Day 5 Female BDE-99
Day 5 Male PCB
Day 5 Female PCB
Day 60 Male Control
Day 60 Female Control
Day 60 Male BPA
Day 60 Female BPA
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Day 60 Female BDE-99
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Z-Score
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-2
-4

Figure 3

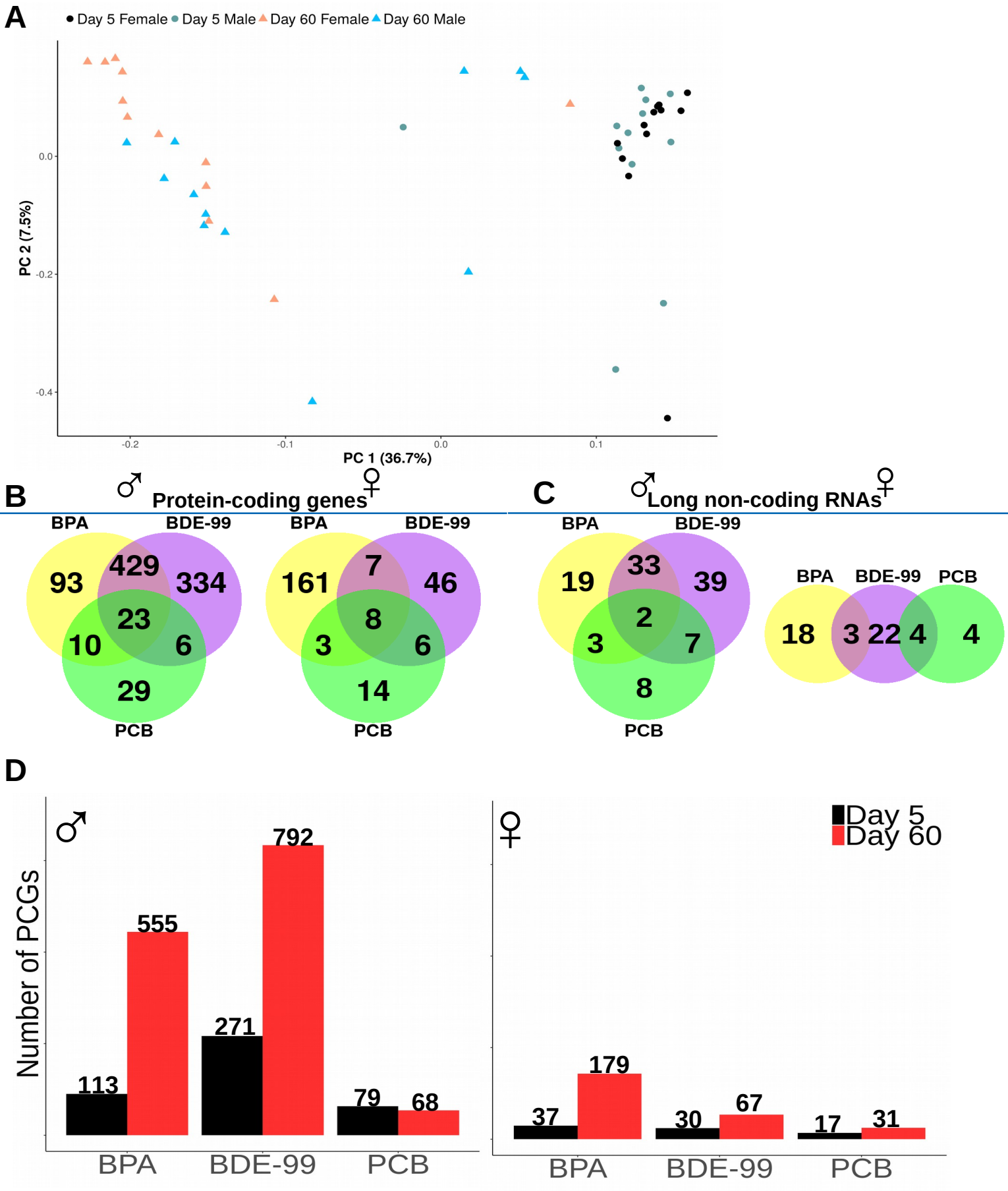

A
Day 5 Female
Day 5 Male
Day 60 Female
Day 60 Male
PC 2 (7.5%)
PC 1 (36.7%)
B
♂
♀
Protein-coding genes
BPA
BDE-99
PCB
93
429
334
23
10
6
29
161
7
46
8
3
6
14
C
Long non-coding RNAs
19
33
39
2
3
7
8
18
3
22
4
4
D
Number of PCGs
Day 5
Day 60
113
555
271
792
79
68
37
179
30
67
17
31

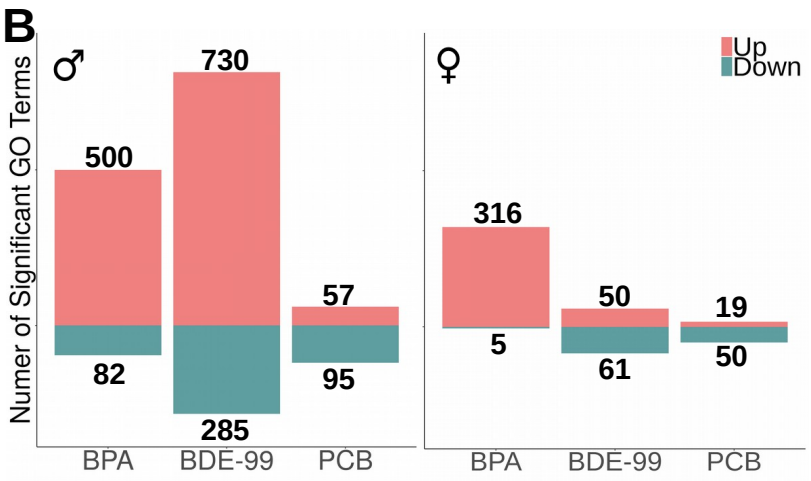
Figure 4

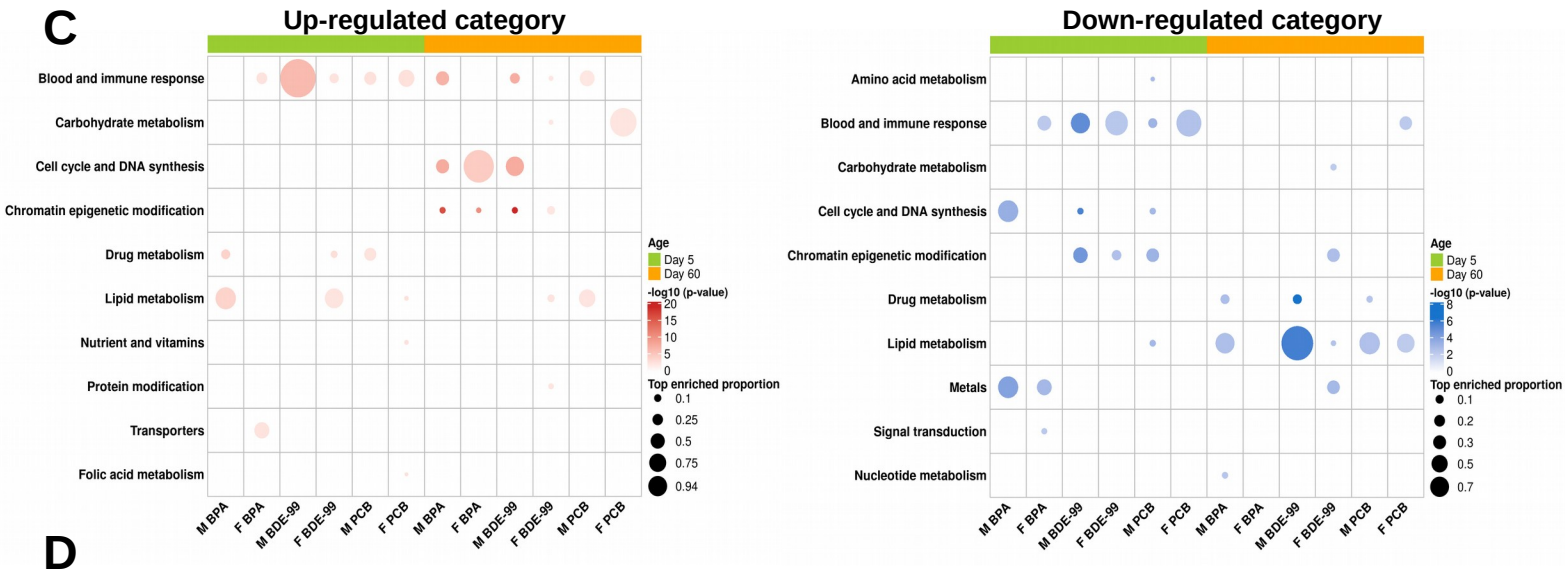
A

	BPA	BDE-99	PCB
Male	Trp53	Ppara	Myod1
	Erbb2	Por	Htt
	Yy1	Trp53	STAT5B
	Csf2	Scap	Scap
	Ccnd1	Erbb2	Rorc
	Ppara	Fgf15	Fgf15
	E2f4	Atp7b	Srebf1
	E2f1	Nr1i3	Nr5a2
	E2f3	Ccnd1	Rora
	Cdkn1a	Il6	Srebf2
Female	Ptger2	Ppara	Rorc
	Cdkn1a	Srebf1	STAT5B
	E2f1	Pparg	Fgf15
	Trp53	Ins1	Rora
	Yy1	Insr	Nr1i2
	E2f4	Ins	Rxra
	Tcf3	Med1	Il1b
	Csf2	Irs1	Cebpa
	Rabl6	Foxa2	Ppara
	Hgf	Fgf15	Irs2

Predicted Activation

Predicted Inhibition





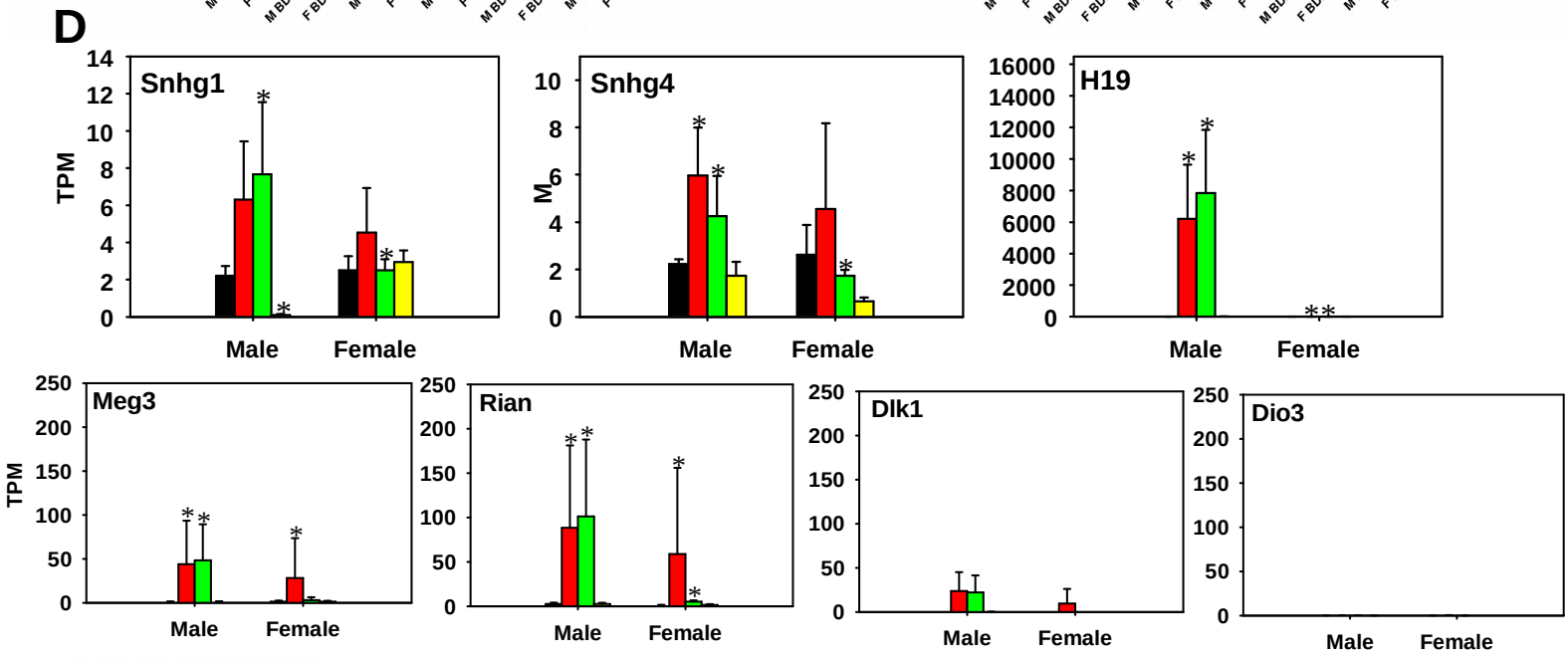


Figure 5

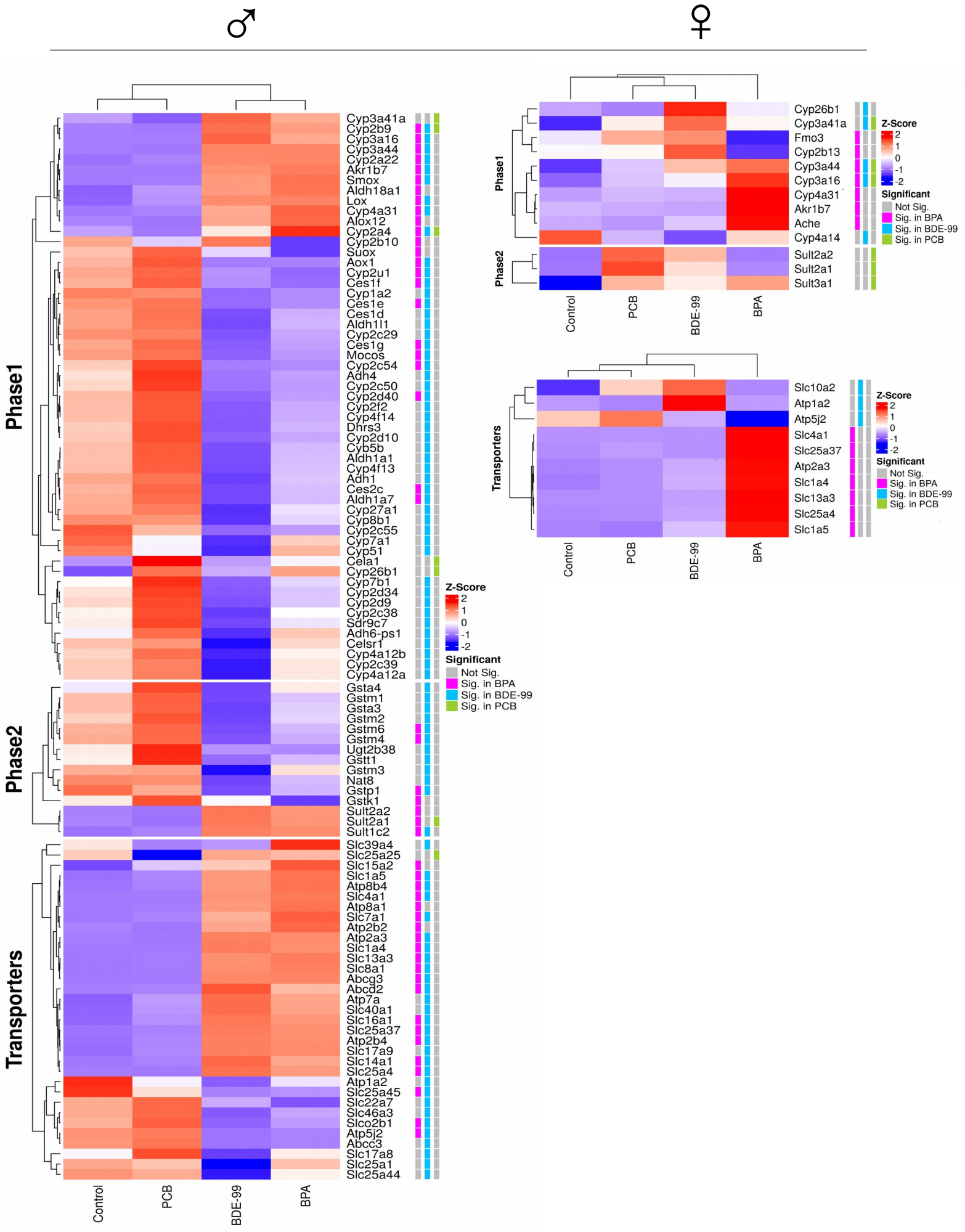

♂
♀
Phase1
Phase2
Transporters
Cyp3a41a
Cyp2b9
Cyp3a16
Cyp3a44
Cyp2a22
Akr1b7
Smox
Aldh18a1
Lox
Cyp4a31
Alox12
Cyp2a4
Cyp2b10
Suox
Aox1
Cyp2u1
Ces1f
Cyp1a2
Ces1e
Ces1d
Aldh1l1
Cyp2c29
Ces1g
Mocos
Cyp2c54
Adh4
Cyp2c50
Cyp2d40
Cyp2f2
Cyp4f14
Dhrs3
Cyp2d10
Cyb5b
Aldh1a1
Cyp4f13
Adh1
Ces2c
Aldh1a7
Cyp27a1
Cyp8b1
Cyp2c55
Cyp7a1
Cyp51
Cela1
Cyp26b1
Cyp7b1
Cyp2d34
Cyp2d9
Cyp2c38
Sdr9c7
Adh6-ps1
Celsr1
Cyp4a12b
Cyp2c39
Cyp4a12a
Gsta4
Gstm1
Gsta3
Gstm2
Gstm6
Gstm4
Ugt2b38
Gstt1
Gstm3
Nat8
Gstp1
Gstk1
Sult2a2
Sult2a1
Sult1c2
Slc39a4
Slc25a25
Slc15a2
Slc1a5
Atp8b4
Slc4a1
Atp8a1
Slc7a1
Atp2b2
Atp2a3
Slc1a4
Slc13a3
Slc8a1
Abcg3
Abcd2
Atp7a
Slc40a1
Slc16a1
Slc25a37
Atp2b4
Slc17a9
Slc14a1
Slc25a4
Atp1a2
Slc25a45
Slc22a7
Slc46a3
Slco2b1
Atp5j2
Abcc3
Slc17a8
Slc25a1
Slc25a44
Control
PCB
BDE-99
BPA
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB
Cyp26b1
Cyp3a41a
Fmo3
Cyp2b13
Cyp3a44
Cyp3a16
Cyp4a31
Akr1b7
Ache
Cyp4a14
Sult2a2
Sult2a1
Sult3a1
Slc10a2
Atp1a2
Atp5j2
Slc4a1
Slc25a37
Atp2a3
Slc1a4
Slc13a3
Slc25a4
Slc1a5

Figure 6

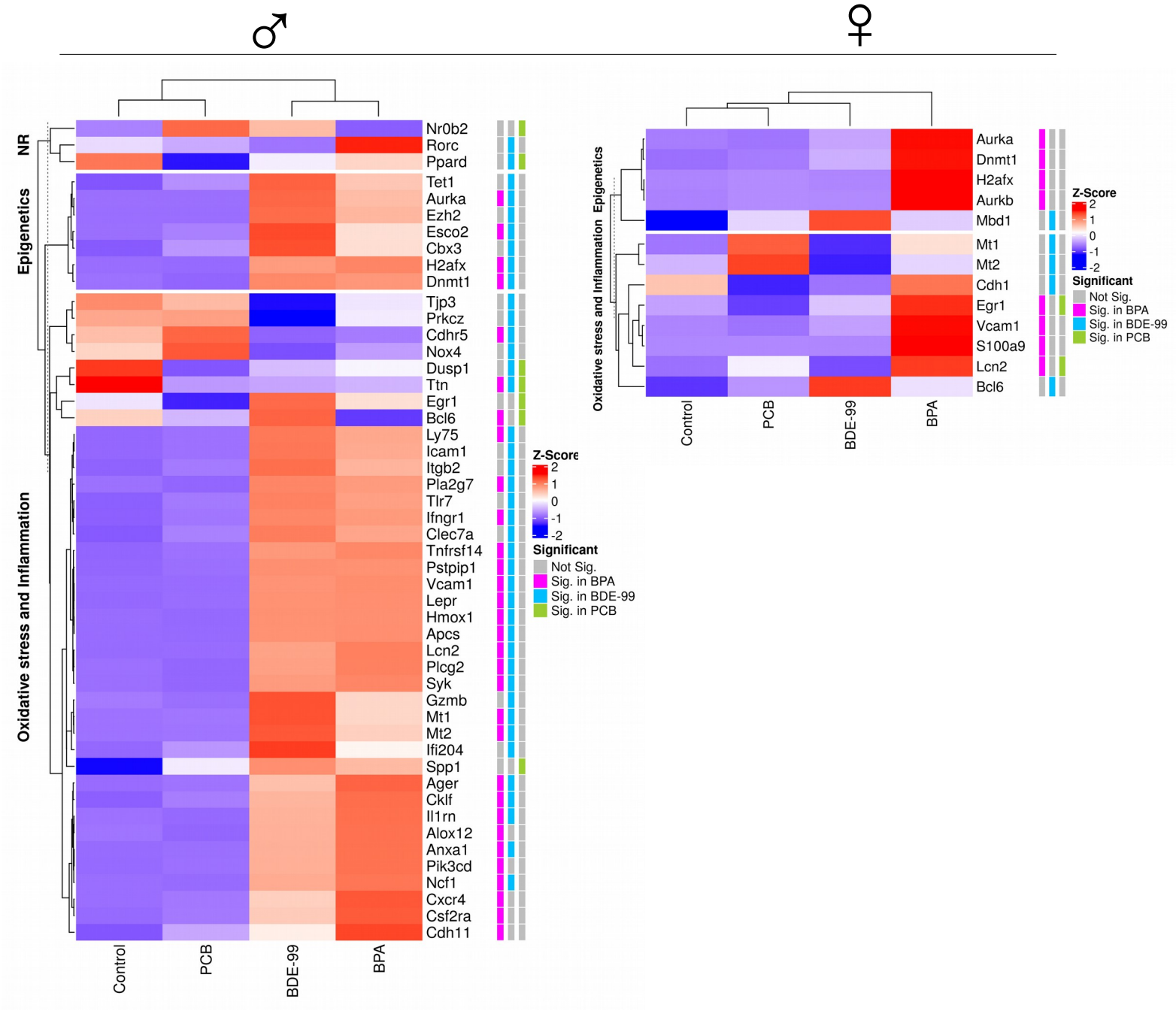

♂
♀
NR
Epigenetics
Oxidative stress and Inflammation
Nr0b2
Rorc
Ppard
Tet1
Aurka
Ezh2
Esco2
Cbx3
H2afx
Dnmt1
Tjp3
Prkcz
Cdhr5
Nox4
Dusp1
Ttn
Egr1
Bcl6
Ly75
Icam1
Itgb2
Pla2g7
Tlr7
Ifngr1
Clec7a
Tnfrsf14
Pstpip1
Vcam1
Lepr
Hmox1
Apcs
Lcn2
Plcg2
Syk
Gzmb
Mt1
Mt2
Ifi204
Spp1
Ager
Cklf
Il1rn
Alox12
Anxa1
Pik3cd
Ncf1
Cxcr4
Csf2ra
Cdh11
Control
PCB
BDE-99
BPA
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB
Epigenetics
Oxidative stress and Inflammation
Aurka
Dnmt1
H2afx
Aurkb
Mbd1
Mt1
Mt2
Cdh1
Egr1
Vcam1
S100a9
Lcn2
Bcl6
Control
PCB
BDE-99
BPA
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB

Figure 7

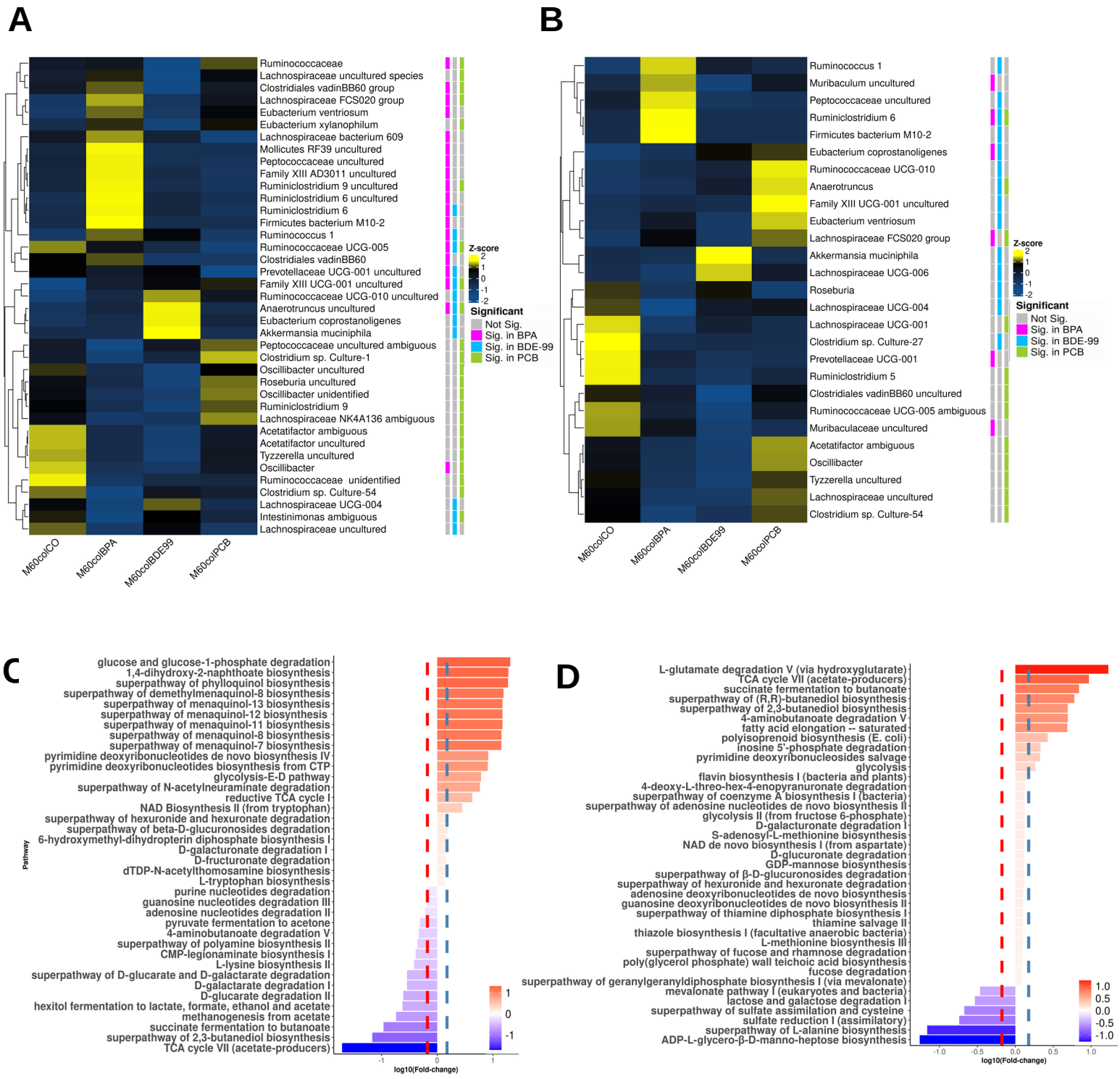
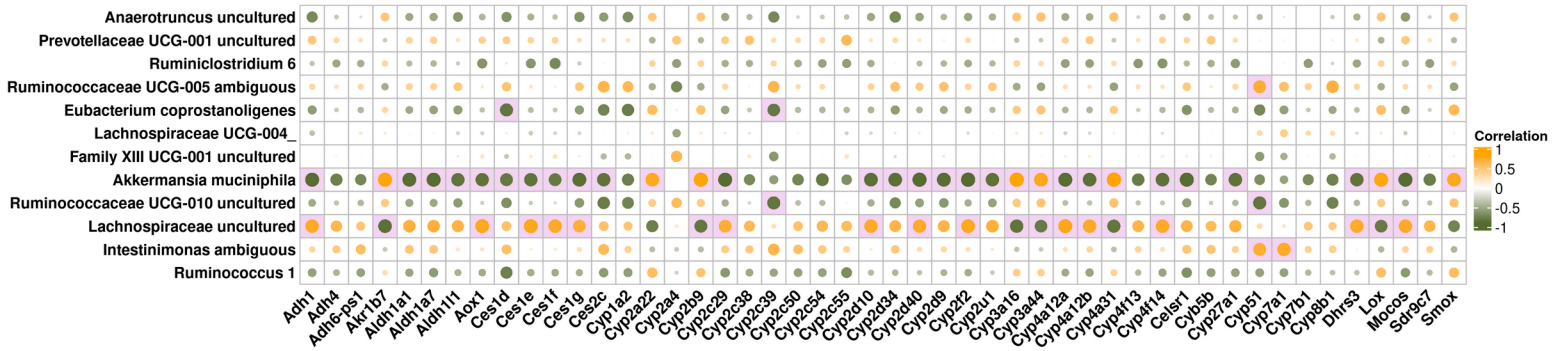

A
Ruminococcaceae
Lachnospiraceae uncultured species
Clostridiales vadinBB60 group
Lachnospiraceae FCS020 group
Eubacterium ventriosum
Eubacterium xylanophilum
Lachnospiraceae bacterium 609
Mollicutes RF39 uncultured
Peptococcaceae uncultured
Family XIII AD3011 uncultured
Ruminiclostridium 9 uncultured
Ruminiclostridium 6 uncultured
Ruminiclostridium 6
Firmicutes bacterium M10-2
Ruminococcus 1
Ruminococcaceae UCG-005
Clostridiales vadinBB60
Prevotellaceae UCG-001 uncultured
Family XIII UCG-001 uncultured
Ruminococcaceae UCG-010 uncultured
Anaerotruncus uncultured
Eubacterium coprostanoligenes
Akkermansia muciniphila
Peptococcaceae uncultured ambiguous
Clostridium sp. Culture-1
Oscillibacter uncultured
Roseburia uncultured
Oscillibacter unidentified
Ruminiclostridium 9
Lachnospiraceae NK4A136 ambiguous
Acetatifactor ambiguous
Acetatifactor uncultured
Tyzzerella uncultured
Oscillibacter
Ruminococcaceae unidentified
Clostridium sp. Culture-54
Lachnospiraceae UCG-004
Intestinimonas ambiguous
Lachnospiraceae uncultured
M60colCO
M60colBPA
M60colBDE99
M60colPCB
Z-score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB
B
Ruminococcus 1
Muribaculum uncultured
Peptococcaceae uncultured
Ruminiclostridium 6
Firmicutes bacterium M10-2
Eubacterium coprostanoligenes
Ruminococcaceae UCG-010
Anaerotruncus
Family XIII UCG-001 uncultured
Eubacterium ventriosum
Lachnospiraceae FCS020 group
Akkermansia muciniphila
Lachnospiraceae UCG-006
Roseburia
Lachnospiraceae UCG-004
Lachnospiraceae UCG-001
Clostridium sp. Culture-27
Prevotellaceae UCG-001
Ruminiclostridium 5
Clostridiales vadinBB60 uncultured
Ruminococcaceae UCG-005 ambiguous
Muribaculaceae uncultured
Acetatifactor ambiguous
Oscillibacter
Tyzzerella uncultured
Lachnospiraceae uncultured
Clostridium sp. Culture-54
M60colCO
M60colBPA
M60colBDE99
M60colPCB
Z-score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB
C
glucose and glucose-1-phosphate degradation
1,4-dihydroxy-2-naphthoate biosynthesis
superpathway of phylloquinol biosynthesis
superpathway of demethylmenaquinol-8 biosynthesis
superpathway of menaquinol-13 biosynthesis
superpathway of menaquinol-12 biosynthesis
superpathway of menaquinol-11 biosynthesis
superpathway of menaquinol-8 biosynthesis
superpathway of menaquinol-7 biosynthesis
pyrimidine deoxyribonucleotides de novo biosynthesis IV
pyrimidine deoxyribonucleotides biosynthesis from CTP
glycolysis-E-D pathway
superpathway of N-acetylneuraminate degradation
reductive TCA cycle I
NAD Biosynthesis II (from tryptophan)
superpathway of hexuronide and hexuronate degradation
superpathway of beta-D-glucuronosides degradation
6-hydroxymethyl-dihydropterin diphosphate biosynthesis I
D-galacturonate degradation I
D-fructuronate degradation
dTDP-N-acetylthomosamine biosynthesis
L-tryptophan biosynthesis
purine nucleotides degradation
guanosine nucleotides degradation III
adenosine nucleotides degradation II
pyruvate fermentation to acetone
4-aminobutanoate degradation V
superpathway of polyamine biosynthesis II
CMP-legionaminate biosynthesis I
L-lysine biosynthesis II
superpathway of D-glucarate and D-galactarate degradation
D-galactarate degradation I
D-glucarate degradation II
hexitol fermentation to lactate, formate, ethanol and acetate
methanogenesis from acetate
succinate fermentation to butanoate
superpathway of 2,3-butanediol biosynthesis
TCA cycle VII (acetate-producers)
Pathway
-1
0
1
log10(Fold-change)
1
0
-1
D
L-glutamate degradation V (via hydroxyglutarate)
TCA cycle VII (acetate-producers)
succinate fermentation to butanoate
superpathway of (R,R)-butanediol biosynthesis
superpathway of 2,3-butanediol biosynthesis
4-aminobutanoate degradation V
fatty acid elongation -- saturated
polyisoprenoid biosynthesis (E. coli)
inosine 5'-phosphate degradation
pyrimidine deoxyribonucleosides salvage
glycolysis
flavin biosynthesis I (bacteria and plants)
4-deoxy-L-threo-hex-4-enopyranuronate degradation
superpathway of coenzyme A biosynthesis I (bacteria)
superpathway of adenosine nucleotides de novo biosynthesis II
glycolysis II (from fructose 6-phosphate)
D-galacturonate degradation I
S-adenosyl-L-methionine biosynthesis
NAD de novo biosynthesis I (from aspartate)
D-glucuronate degradation
GDP-mannose biosynthesis
superpathway of β-D-glucuronosides degradation
superpathway of hexuronide and hexuronate degradation
adenosine deoxyribonucleotides de novo biosynthesis
guanosine deoxyribonucleotides de novo biosynthesis II
superpathway of thiamine diphosphate biosynthesis I
thiamine salvage II
thiazole biosynthesis I (facultative anaerobic bacteria)
L-methionine biosynthesis III
superpathway of fucose and rhamnose degradation
poly(glycerol phosphate) wall teichoic acid biosynthesis
fucose degradation
superpathway of geranylgeranyldiphosphate biosynthesis I (via mevalonate)
mevalonate pathway I (eukaryotes and bacteria)
lactose and galactose degradation I
superpathway of sulfate assimilation and cysteine
sulfate reduction I (assimilatory)
superpathway of L-alanine biosynthesis
ADP-L-glycero-β-D-manno-heptose biosynthesis
-1.0
-0.5
0.0
0.5
1.0
log10(Fold-change)
1.0
0.5
0.0
-0.5
-1.0

Figure 8

A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Prevotellaceae UCG-001 uncultured
Ruminiclostridium 6
Ruminococcaceae UCG-005 ambiguous
Eubacterium coprostanoligenes
Lachnospiraceae UCG-004_
Family XIII UCG-001 uncultured
Akkermansia muciniphila
Ruminococcaceae UCG-010 uncultured
Lachnospiraceae uncultured
Intestinimonas ambiguous
Ruminococcus 1
Adh1
Adh4
Adh6-ps1
Akr1b7
Aldh1a1
Aldh1a7
Aldh1l1
Aox1
Ces1d
Ces1e
Ces1f
Ces1g
Ces2c
Cyp1a2
Cyp2a22
Cyp2a4
Cyp2b9
Cyp2c29
Cyp2c38
Cyp2c39
Cyp2c50
Cyp2c54
Cyp2c55
Cyp2d10
Cyp2d34
Cyp2d40
Cyp2d9
Cyp2f2
Cyp2u1
Cyp3a16
Cyp3a44
Cyp4a12a
Cyp4a12b
Cyp4a31
Cyp4f13
Cyp4f14
Celsr1
Cyp5b
Cyp27a1
Cyp51
Cyp7a1
Cyp7b1
Cyp8b1
Dhrs3
Lox
Mocos
Sdr9c7
Smox
Correlation
1
0.5
0
-0.5
-1

B

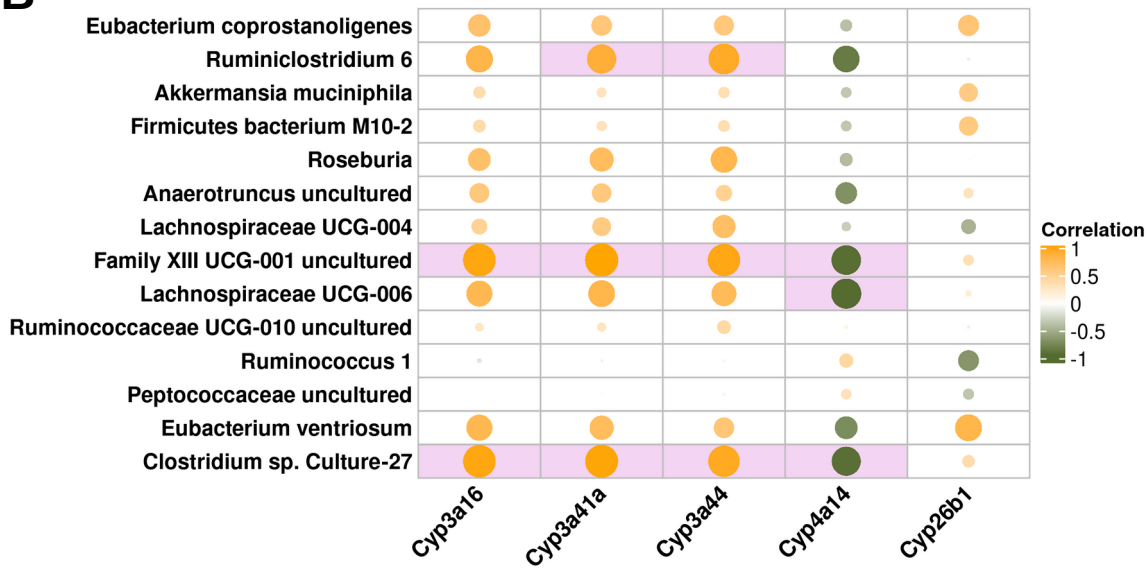
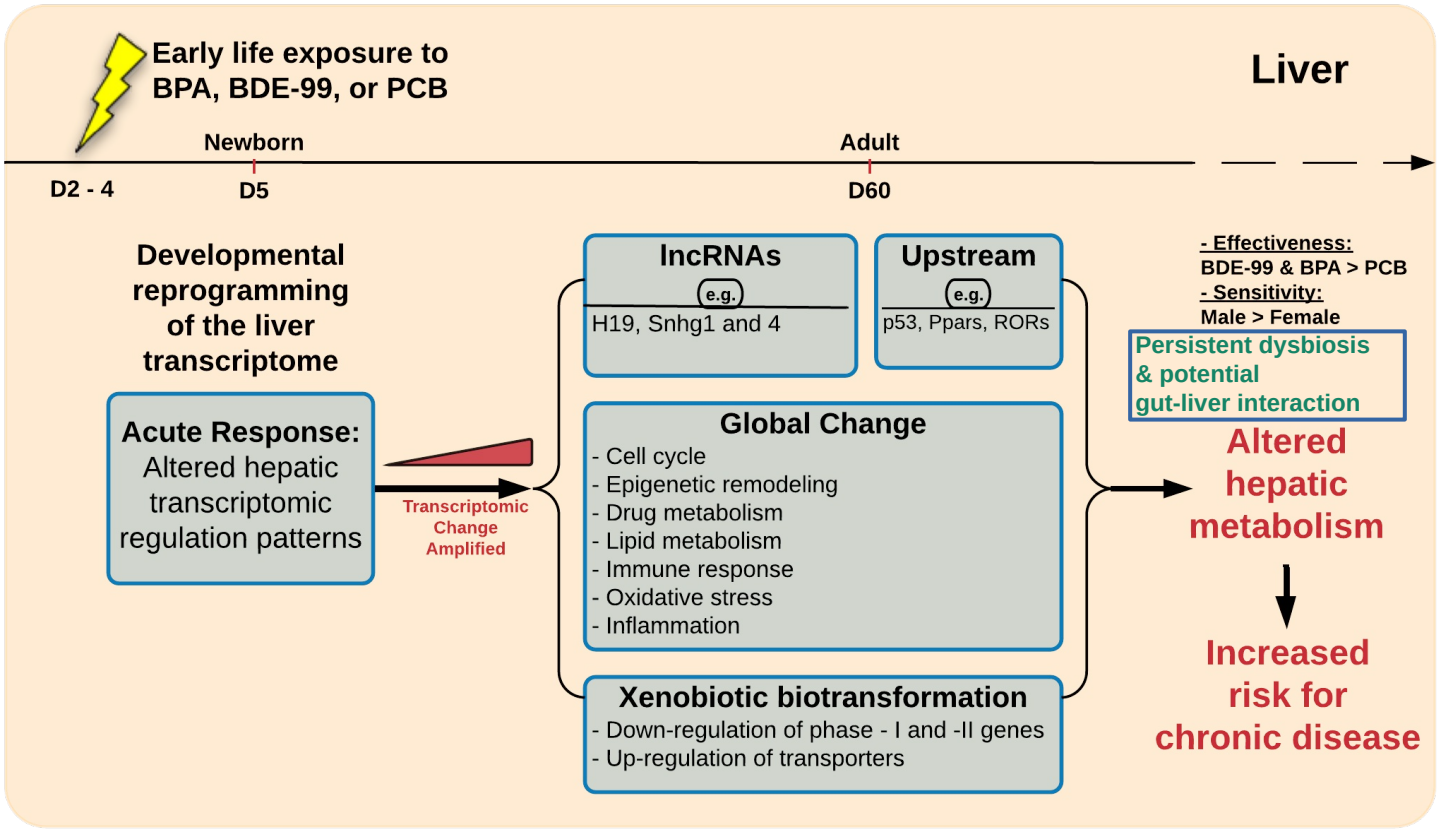

Eubacterium coprostanoligenes
Ruminiclostridium 6
Akkermansia muciniphila
Firmicutes bacterium M10-2
Roseburia
Anaerotruncus uncultured
Lachnospiraceae UCG-004
Family XIII UCG-001 uncultured
Lachnospiraceae UCG-006
Ruminococcaceae UCG-010 uncultured
Ruminococcus 1
Peptococcaceae uncultured
Eubacterium ventriosum
Clostridium sp. Culture-27
Cyp3a16
Cyp3a41a
Cyp3a44
Cyp4a14
Cyp26b1
Correlation
1
0.5
0
-0.5
-1

Figure 9


Early life exposure to
BPA, BDE-99, or PCB
Liver
Newborn
Adult
D2 - 4
D5
D60
Developmental reprogramming of the liver transcriptome
Acute Response:
Altered hepatic transcriptomic regulation patterns
Transcriptomic Change Amplified
lncRNAs
e.g.
H19, Snhg1 and 4
Upstream
e.g.
p53, Ppars, RORs
Global Change
- Cell cycle
- Epigenetic remodeling
- Drug metabolism
- Lipid metabolism
- Immune response
- Oxidative stress
- Inflammation
Xenobiotic biotransformation
- Down-regulation of phase - I and -II genes
- Up-regulation of transporters
- Effectiveness:
BDE-99 & BPA > PCB
- Sensitivity:
Male > Female
Persistent dysbiosis & potential gut-liver interaction
Altered hepatic metabolism
Increased risk for chronic disease

SUPPLEMENTAL FIGURE AND TABLE LEGENDS

Figure S1. **A.** Principal components analysis (PCA) of the liver transcriptome expression following neonatal exposure to environmental contaminants. Values on the principal components are labeled by age, gender, and exposed groups. Venn diagrams showing the numbers of uniquely and commonly regulated PCGs (**B**) and lncRNAs (**C**) in livers of mice at PND 5 newborn age following acute exposure to BPA (yellow shade), BDE-99 (purple shade), and PCB (green shade) (FDR-BH < 0.05). The numbers of differentially regulated genes are labeled on the Venn diagrams. Males are displayed on the left and females on the right column. **D.** Number of differentially regulated gene ontology terms ($p < 0.01$) in livers of PND 5 male and female mice following neonatal chemical exposure.

Figure S2. Up-regulated (top panel) and down-regulated (bottom panel) gene ontology (GO) terms related to liver function at PND 5 following acute exposure to BPA ($p < 0.01$). Top 50 terms are shown if the number of significant terms exceeded 50. Males are shown on the right and females are shown in the left column. GO terms that belong to the same biological terms are colored the same as described in the figure legend. Vertical dashed lines at $x = 2$ represent a statistical threshold ($p = 0.01$) below which GO terms are considered differentially regulated (i.e. $x > 2$).

Figure S3. Up-regulated (top panel) and down-regulated (bottom panel) gene ontology (GO) terms related to liver function at PND 5 following acute exposure to BDE-99 ($p < 0.01$). Top 50 terms are shown if significant terms exceeded 50. Males are shown on the right and females are shown in the left column. GO terms that belong to the same biological terms are colored the same as described in the figure legend. Vertical dashed lines at $x = 2$ represent a statistical threshold ($p = 0.01$) below which GO terms are considered differentially regulated (i.e. $x > 2$).

Figure S4. Up-regulated (top panel) and down-regulated (bottom panel) gene ontology (GO) terms related to liver function at PND 5 following acute exposure to PCB ($p < 0.01$). Top 50 terms are shown if the number of significant terms exceeded 50. Males are shown on the right and females are shown in the left column. GO terms that belong to the same biological terms are colored the same as described in the figure legend. Vertical dashed lines at $x = 2$ represent a statistical threshold ($p = 0.01$) below which GO terms are considered differentially regulated (i.e. $x > 2$).

Figure S5. Up-regulated (top panel) and down-regulated (bottom panel) gene ontology (GO) terms related to liver function at PND 60 upon neonatal exposure to BPA ($p < 0.01$). Top 50 terms are shown if the number of significant terms exceeded 50. Males are shown on the right and females are shown in the left column. GO terms that belong to the same biological terms are colored the same as described in the figure legend. Vertical dashed lines at $x = 2$ represent a statistical threshold ($p = 0.01$) below which GO terms are considered differentially regulated (i.e. $x > 2$).

Figure S6. Up-regulated (top panel) and down-regulated (bottom panel) gene ontology (GO) terms related to liver function at PND 60 following neonatal exposure to BDE-99 ($p < 0.01$). Top 50 terms are shown if the number of significant terms exceeded 50. Males are shown on the right and females are shown in the left column. GO terms that belong to the same biological terms are colored the same as described in the figure legend. Vertical dashed lines at $x = 2$ represent a statistical threshold ($p = 0.01$) below which GO terms are considered differentially regulated (i.e. $x > 2$).

Figure S7. Up-regulated (top panel) and down-regulated (bottom panel) gene ontology (GO) terms related to liver function at PND 60 upon neonatal exposure to PCB ($p < 0.01$). Top 50 terms are shown if the number of significant terms exceeded 50. Males are shown on the right and females are shown in the left column. GO terms that belong to the same biological terms are colored the same as described in the figure legend.

Vertical dashed lines at x = 2 represent a statistical threshold (p = 0.01) below which GO terms are considered differentially regulated (i.e. x > 2).

Figure S8. Two-way hierarchical clustering of the mRNAs of differentially regulated genes involved in xenobiotic biotransformation, epigenetic modification, nuclear receptor, and oxidative stress in livers of PND 5 newborn mice following neonatal chemical exposure, as generated by the R package ComplexHeatmap. Males are shown on the left and females are displayed in the right column. Gene clustering was performed separeately based on different gene categories noted on the left rows of each cluster. Nuclear receptors were note differentially regulated in male mice and phase-II, transporters, and epigenetic modifier genes were not differentially regulated in female mice. All genes were differentially regulated at least one of the chemical exposure groups (Cuffdiff, FDR-BH < 0.05).

Figure S9. Two-way hierarchical clustering of the mRNAs of differentially regulated genes involved in inflammation in livers of PND 5 newborn mice following neonatal chemical exposure, as generated by the R package ComplexHeatmap. Males are shown on the left and females are displayed in the right column. Gene clustering was performed separeately based on different gene categories noted on the left rows of each cluster. Nuclear receptors were note differentially regulated in male mice and phase-II, transporters, and epigenetic modifier genes were not differentially regulated in female mice. All genes were differentially regulated at least one of the chemical exposure groups (Cuffdiff, FDR-BH < 0.05). Genes that are differentially regulated are colored the same as described in the figure legend.

Figure S1

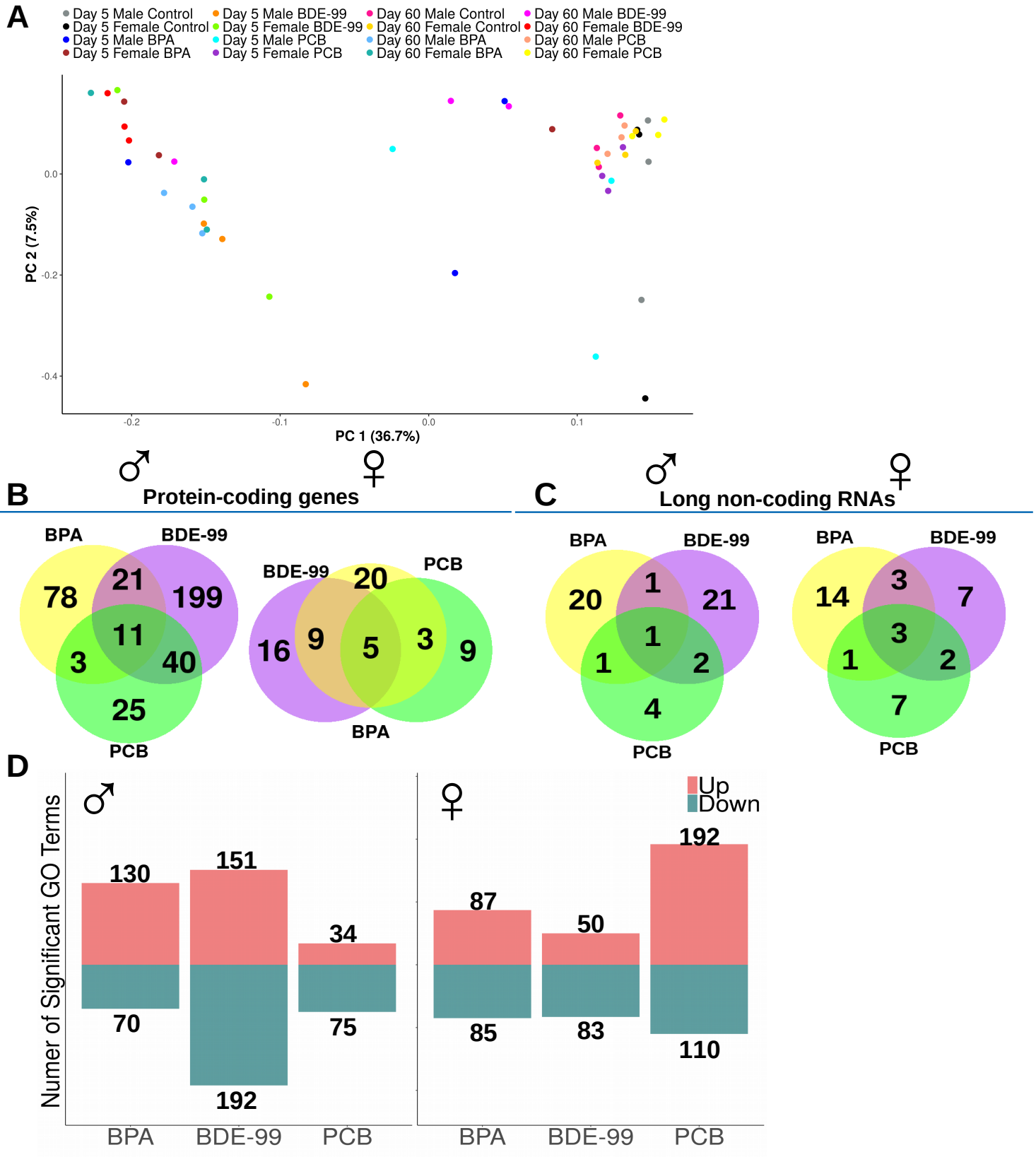

A
Day 5 Male Control
Day 5 Female Control
Day 5 Male BPA
Day 5 Female BPA
Day 5 Male BDE-99
Day 5 Female BDE-99
Day 5 Male PCB
Day 5 Female PCB
Day 60 Male Control
Day 60 Female Control
Day 60 Male BPA
Day 60 Female BPA
Day 60 Male BDE-99
Day 60 Female BDE-99
Day 60 Male PCB
Day 60 Female PCB
PC 2 (7.5%)
PC 1 (36.7%)
♂
♀
B
Protein-coding genes
BPA
BDE-99
PCB
78
21
199
11
3
40
25
BDE-99
PCB
BPA
20
16
9
5
3
9
C
Long non-coding RNAs
BPA
BDE-99
PCB
20
1
21
1
1
2
4
BPA
BDE-99
PCB
14
3
7
3
1
2
7
D
Numer of Significant GO Terms
Up
Down
130
70
151
192
34
75
87
85
50
83
192
110
BPA
BDE-99
PCB

Figure S2

♂
♀
Up-regulated
Epoxygenase p450 pathway
Xenobiotic metabolic process
Exogenous drug catabolic process
Response to xenobiotic stimulus
Cellular response to xenobiotic stimulus
Drug catabolic process
Organic hydroxy compound metabolic process
Benzene-containing compound metabolic process
Purine-containing compound metabolic process
Ethanol metabolic process
Indole-containing compound catabolic process
Indolalkylamine catabolic process
Arachidonic acid metabolic process
Unsaturated fatty acid metabolic process
Long-chain fatty acid metabolic process
Icosanoid metabolic process
Fatty acid metabolic process
Fatty acid derivative metabolic process
Bile acid and bile salt transport
Steroid metabolic process
Terpenoid metabolic process
Monocarboxylic acid biosynthetic process
Isoprenoid metabolic process
Alcohol metabolic process
Retinoid metabolic process
Diterpenoid metabolic process
Retinol metabolic process
Primary alcohol metabolic process
Retinoic acid metabolic process
Organic hydroxy compound transport
Response to stilbenoid
Carboxylic acid biosynthetic process
Organic acid biosynthetic process
Lipid homeostasis
Acetyl-coa metabolic process
9-cis-retinoic acid biosynthetic process
9-cis-retinoic acid metabolic process
Acyl-coa metabolic process
Thioester metabolic process
Cofactor metabolic process
Sodium-independent organic anion transport
Hormone metabolic process
Cellular hormone metabolic process
Tryptophan catabolic process to kynurenine
Tryptophan catabolic process
Alpha-amino acid catabolic process
Phenylpropanoid metabolic process
Coumarin metabolic process
Purine ribonucleotide metabolic process
Ribonucleotide metabolic process
Categories
0
5
10
15
-log10(p-value)
Negative regulation of interleukin-10 production
Positive regulation of interleukin-4 production
Regulation of interleukin-4 production
Interleukin-4 production
Regulation of interleukin-10 production
Interleukin-10 production
Negative regulation of cytokine production
Negative regulation of interleukin-5 production
Regulation of transforming growth factor beta receptor signaling pathway
Regulation of cellular response to transforming growth factor beta stimulus
Regulation of metal ion transport
Regulation of calcium ion import
Regulation of sodium ion transmembrane transporter activity
Negative regulation of calcium ion transport
Regulation of sodium ion transmembrane transport
Regulation of ion transmembrane transporter activity
Regulation of transmembrane transporter activity
Regulation of transporter activity
Regulation of calcium ion transport
Regulation of calcium ion transmembrane transporter activity
Calcium ion import
Regulation of sodium ion transport
Regulation of cation transmembrane transport
Sodium ion transmembrane transport
Regulation of cell adhesion molecule production
Plasma membrane raft assembly
Plasma membrane raft organization
Regulation of caveolin-mediated endocytosis
Plasma membrane repair
Regulation of calcium-transporting atpase activity
Folic acid metabolic process
Response to folic acid
Folate transmembrane transport
Folate import across plasma membrane
Folic acid transport
0
5
10
15
-log10(p-value)
Down-regulated
Detoxification of copper ion
Stress response to copper ion
Stress response to metal ion
Cellular response to zinc ion
Cellular response to copper ion
Cellular response to cadmium ion
Cellular zinc ion homeostasis
Response to copper ion
Zinc ion homeostasis
Response to zinc ion
Response to cadmium ion
Cellular transition metal ion homeostasis
Detoxification of inorganic compound
Detoxification
Nitric oxide mediated signal transduction
Negative regulation of cell cycle phase transition
Cell cycle checkpoint
Negative regulation of cell cycle process
Regulation of mitotic cell cycle phase transition
Regulation of cell cycle phase transition
Negative regulation of cell cycle g2/m phase transition
Mitotic cell cycle phase transition
Regulation of cytokinesis
Cell cycle phase transition
Regulation of g2/m transition of mitotic cell cycle
Regulation of cell cycle g2/m phase transition
Negative regulation of cell cycle
Categories
0
2
4
6
-log10(p-value)
Detoxification of copper ion
Stress response to copper ion
Stress response to metal ion
Cellular response to zinc ion
Cellular response to copper ion
Cellular response to cadmium ion
Cellular zinc ion homeostasis
Response to copper ion
Zinc ion homeostasis
Response to zinc ion
Response to cadmium ion
Cellular transition metal ion homeostasis
Transition metal ion homeostasis
Cellular response to metal ion
Response to metal ion
Detoxification of inorganic compound
Detoxification
Response to toxic substance
Cellular response to inorganic substance
Tolerance induction dependent upon immune response
Positive regulation of interleukin-10 secretion
Negative regulation of cd8-positive alpha-beta t cell activation
Negative regulation of cd4-positive alpha-beta t cell proliferation
Regulation of interleukin-10 secretion
Cd4-positive alpha-beta t cell proliferation
Interleukin-10 secretion
Regulation of cd4-positive alpha-beta t cell proliferation
Negative regulation of activated t cell proliferation
Negative regulation of alpha-beta t cell proliferation
Positive regulation of immune response to tumor cell
Positive regulation of t cell apoptotic process
Cellular response to lipopolysaccharide
Cellular response to molecule of bacterial origin
Insulin metabolic process
Regulation of glucagon secretion
Glucagon secretion
Regulation of asymmetric cell division
Interkinetic nuclear migration
Regulation of timing of cell differentiation
Positive regulation of response to tumor cell
Nitric oxide mediated signal transduction
Negative regulation of rac protein signal transduction
Regulation of ras protein signal transduction
Regulation of small gtpase mediated signal transduction
Regulation of rac protein signal transduction
Regulation of protein kinase c signaling
0
2
4
6
-log10(p-value)
Amino acid metabolism
Blood and immune response
Carbohydrate metabolism
Cell adhesion and motility
Cell cycle and DNA synthesis
Cell membrane
Cell signaling
Cofactors
Dietary factors
Drug metabolism
Folic acid metabolism and transport
Hormone metabolism/ signaling
Lipid metabolism
Metals
Nucleotide metabolism
One carbon metabolism
Signal transduction
Transporters

Figure S3

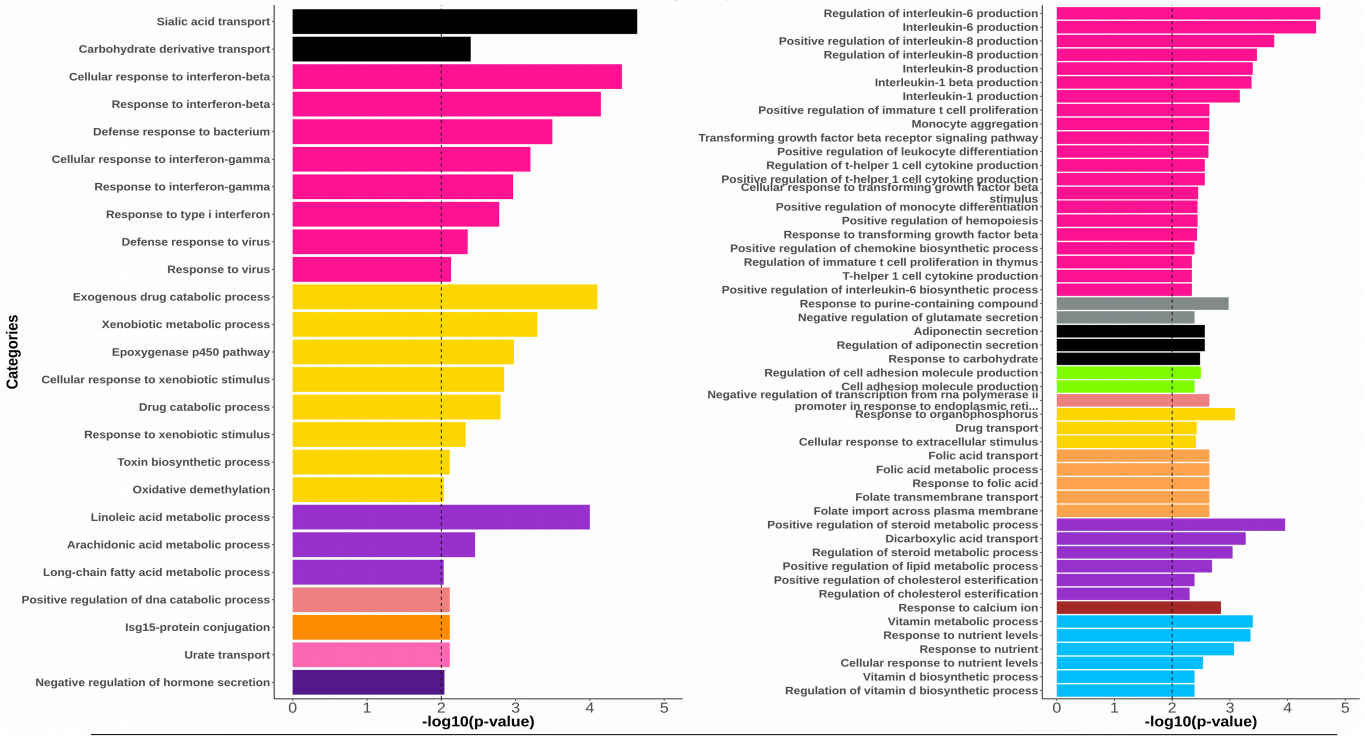
♂ ♀

Up-regulated
Response to interferon-beta
Cellular response to interferon-beta
Response to interferon-gamma
Cellular response to interferon-gamma
Response to virus
Defense response to virus
Defense response to protozoan
Response to protozoan
Response to interferon-alpha
Interferon-gamma-mediated signaling pathway
Antigen processing and presentation of peptide antigen
Antigen processing and presentation
Regulation of innate immune response
Antigen processing and presentation of endogenous peptide antigen
Regulation of leukocyte mediated cytotoxicity
Antigen processing and presentation of endogenous antigen
Response to type i interferon
Positive regulation of cytokine-mediated signaling pathway
Regulation of cell killing
Positive regulation of response to cytokine stimulus
Cellular response to interferon-alpha
Leukocyte mediated cytotoxicity
Negative regulation of innate immune response
Positive regulation of adaptive immune response based on somatic recombination of immune receptors b...
Defense response to bacterium
Antigen processing and presentation of endogenous peptide antigen via mhc class ib
Cytokine-mediated signaling pathway
Positive regulation of adaptive immune response
Antigen processing and presentation of peptide antigen via mhc class ib
Regulation of cytokine-mediated signaling pathway
Type i interferon signaling pathway
Cellular response to type i interferon
Antigen processing and presentation via mhc class ib
Regulation of response to interferon-gamma
Regulation of interferon-gamma-mediated signaling pathway
Regulation of response to cytokine stimulus
Cell killing
T cell mediated cytotoxicity
Regulation of immune effector process
Regulation of lymphocyte mediated immunity
Regulation of adaptive immune response based on somatic recombination of immune receptors built from...
Protection from natural killer cell mediated cytotoxicity
Positive regulation of t cell mediated cytotoxicity
Antigen processing and presentation of peptide antigen via mhc class i
Regulation of adaptive immune response
Positive regulation of response to interferon-gamma
Positive regulation of interferon-gamma-mediated signaling pathway
Exogenous drug catabolic process
Epoxygenase p450 pathway
Xenobiotic metabolic process
Categories
0
10
20
30
-log10(p-value)
Drug catabolic process
Xenobiotic metabolic process
Response to xenobiotic stimulus
Exogenous drug catabolic process
Cellular response to xenobiotic stimulus
Epoxygenase p450 pathway
Reactive oxygen species metabolic process
Toxin biosynthetic process
Oxidative demethylation
Arachidonic acid metabolic process
Long-chain fatty acid metabolic process
Unsaturated fatty acid metabolic process
Icosanoid metabolic process
Fatty acid derivative metabolic process
Hydrogen peroxide metabolic process
Fatty acid metabolic process
Linoleic acid metabolic process
Steroid metabolic process
Hydrogen peroxide catabolic process
Regulation of steroid metabolic process
Regulation of intestinal cholesterol absorption
Very-low-density lipoprotein particle remodeling
Positive regulation of cholesterol esterification
Triglyceride-rich lipoprotein particle remodeling
Regulation of intestinal lipid absorption
Positive regulation of triglyceride catabolic process
High-density lipoprotein particle assembly
Hydrogen peroxide biosynthetic process
Positive regulation of lipoprotein lipase activity
Cellular ketone metabolic process
Regulation of cholesterol esterification
Phospholipid efflux
Positive regulation of triglyceride lipase activity
Positive regulation of interleukin-4 production
Regulation of interleukin-4 production
Interleukin-4 production
Regulation of interleukin-10 production
Negative regulation of cytokine production
Interleukin-10 production
Negative regulation of interleukin-5 production
Interleukin-17 secretion
Regulation of gamma-delta t cell differentiation
Regulation of gamma-delta t cell activation
Negative regulation of thymocyte apoptotic process
Gamma-delta t cell differentiation
Regulation of cell adhesion molecule production
Cell adhesion molecule production
Cofactor catabolic process
Cofactor metabolic process
0
10
20
30
-log10(p-value)
Down-regulated
Nucleosome assembly
Chromatin assembly or disassembly
Nucleosome organization
Chromatin assembly
Dna packaging
Protein-dna complex assembly
Protein-dna complex subunit organization
Regulation of gene silencing
Nucleosome positioning
Negative regulation of chromatin silencing
Regulation of chromatin organization
Gene silencing
Positive regulation of histone h3-k9 methylation
Negative regulation of chromatin organization
Regulation of chromatin silencing
Positive regulation of gene expression
Dna conformation change
Dna replication-dependent nucleosome assembly
Dna replication-dependent nucleosome organization
Dna replication-independent nucleosome assembly
Dna replication-independent nucleosome organization
Homeostasis of number of cells
Negative regulation of dna recombination
Protein heterotetramerization
Protein tetramerization
Protein heterooligomerization
Negative regulation of megakaryocyte differentiation
Myeloid cell differentiation
Megakaryocyte differentiation
Regulation of megakaryocyte differentiation
Regulation of myeloid cell differentiation
Negative regulation of myeloid cell differentiation
Negative regulation of hemopoiesis
Negative regulation of immune system process
Porphyrin-containing compound biosynthetic process
Tetrapyrrole biosynthetic process
Porphyrin-containing compound metabolic process
Erythrocyte homeostasis
Tetrapyrrole metabolic process
Erythrocyte differentiation
Myeloid cell homeostasis
Erythrocyte development
Heme biosynthetic process
Myeloid cell development
Heme metabolic process
Positive regulation of myeloid cell differentiation
Regulation of hemopoiesis
One-carbon compound transport
Glycine transport
Homotypic cell-cell adhesion
Categories
0
10
20
30
-log10(p-value)
Negative regulation of immune system process
Defense response to gram-positive bacterium
Tolerance induction dependent upon immune response
Positive regulation of interleukin-10 secretion
Negative regulation of cd8-positive alpha-beta t cell activation
Negative regulation of complement activation
Regulation of interleukin-10 secretion
Stem cell differentiation
Interleukin-10 secretion
Regulation of cd4-positive alpha-beta t cell proliferation
Complement activation lectin pathway
Negative regulation of activated t cell proliferation
Regulation of complement activation
Negative regulation of alpha-beta t cell proliferation
Cellular response to molecule of bacterial origin
Positive regulation of response to tumor cell
Positive regulation of immune response to tumor cell
Positive regulation of t cell apoptotic process
Negative regulation of megakaryocyte differentiation
Nucleosome assembly
Chromatin assembly
Nucleosome organization
Chromatin assembly or disassembly
Dna packaging
Protein-dna complex assembly
Dna conformation change
Protein-dna complex subunit organization
Regulation of asymmetric cell division
Interkinetic nuclear migration
Regulation of timing of cell differentiation
Insulin metabolic process
Regulation of glucagon secretion
Glucagon secretion
Negative regulation of humoral immune response
Cellular response to lipopolysaccharide
Protein heterooligomerization
Negative regulation of protein activation cascade
Regulation of protein activation cascade
0
10
20
30
-log10(p-value)
Amino acid metabolism
Blood and immune response
Carbohydrate metabolism
Cell adhesion and motility
Cell cycle and DNA synthesis
Chromatin epigenetic modification
Cofactors
Drug metabolism
Hormone metabolism/ signaling
Lipid metabolism
One carbon metabolism
Protein modification

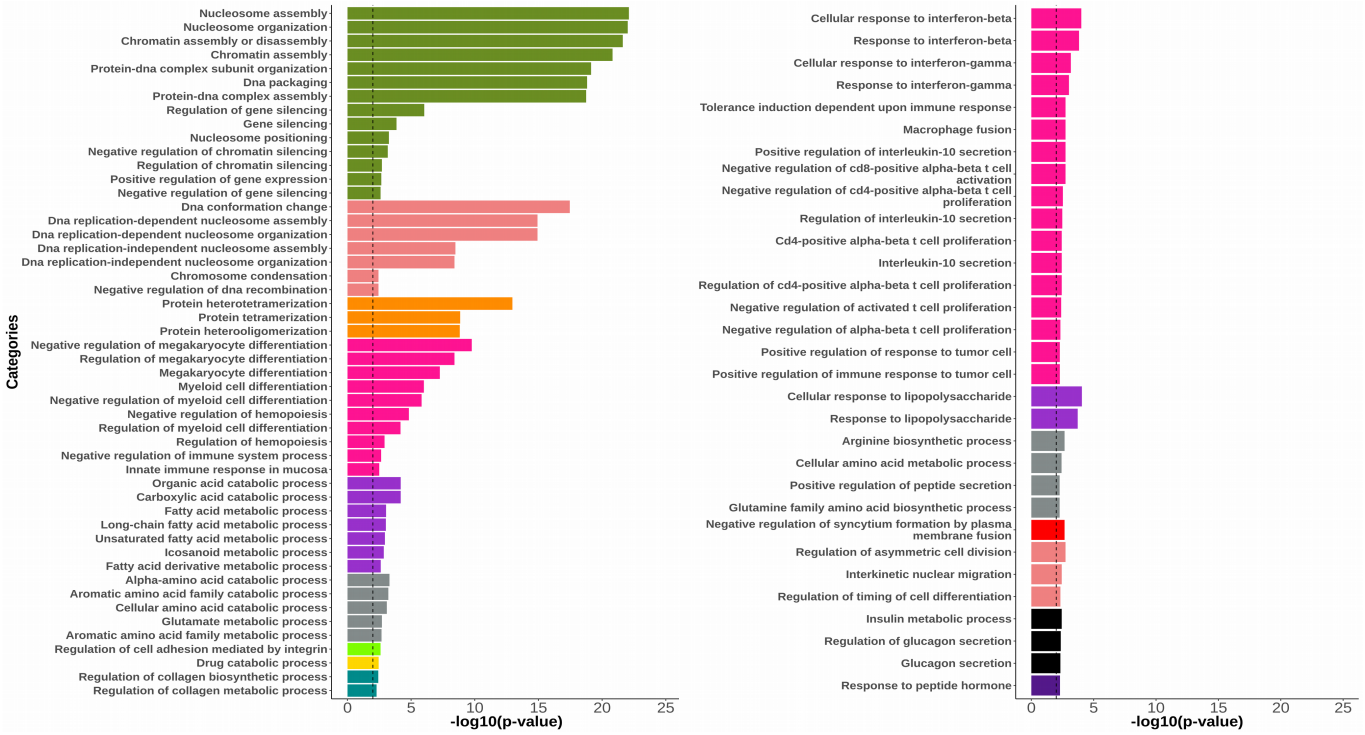
Figure S4

♂ ♀

Up-regulated



Down-regulated



- Amino acid metabolism
- Blood and immune response
- Carbohydrate metabolism
- Cell adhesion and motility
- Cell cycle and DNA synthesis
- Cell membrane
- Chromatin epigenetic modification
- Collagen synthesis
- Drug metabolism
- Folic acid metabolism
- Hormone metabolism/ signaling
- Lipid metabolism
- Metals
- Nutrient and vitamins
- Protein modification
- Transporters

Figure S5

♂ ♀

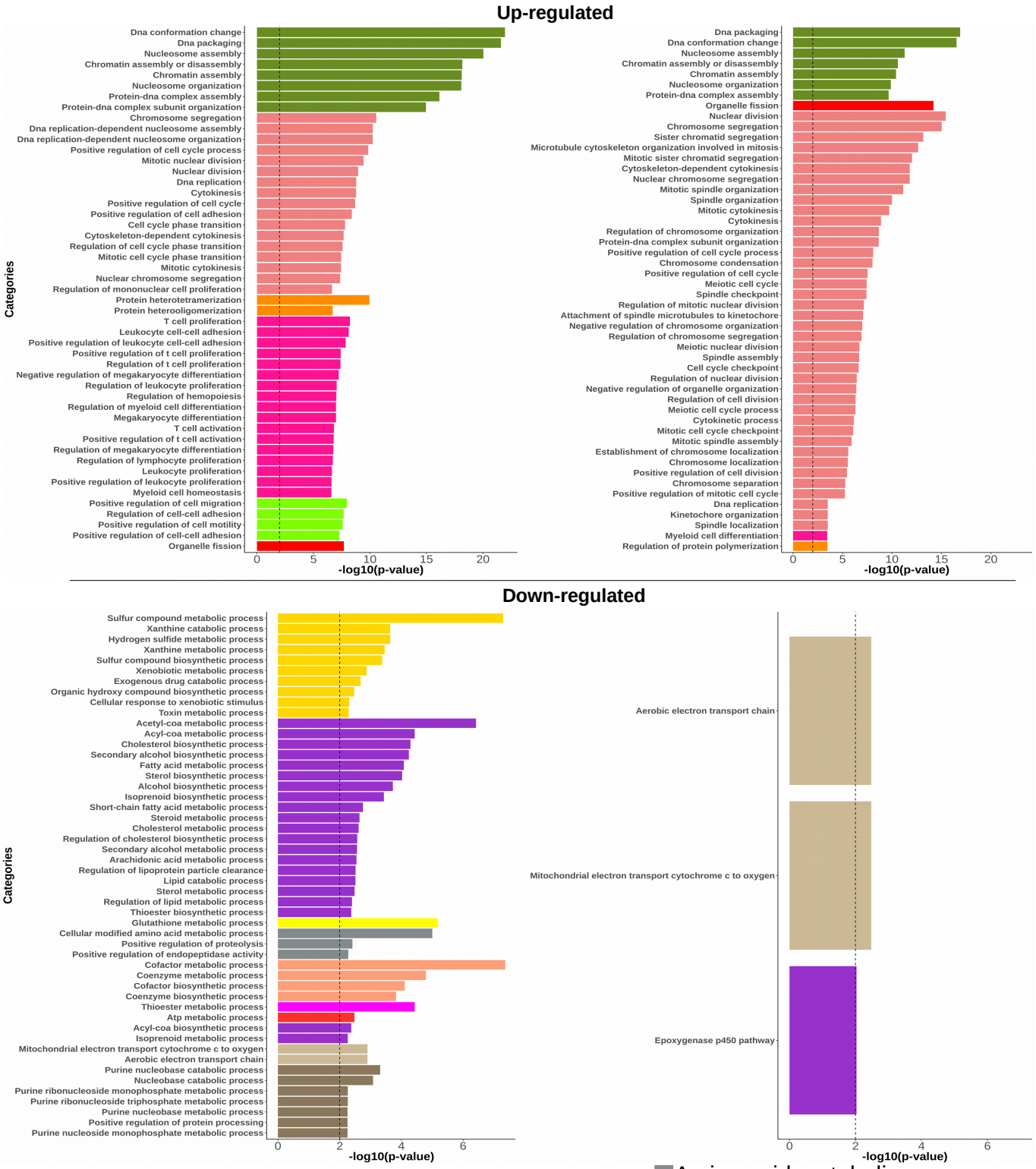

Up-regulated
Dna conformation change
Dna packaging
Nucleosome assembly
Chromatin assembly or disassembly
Chromatin assembly
Nucleosome organization
Protein-dna complex assembly
Protein-dna complex subunit organization
Chromosome segregation
Dna replication-dependent nucleosome assembly
Dna replication-dependent nucleosome organization
Positive regulation of cell cycle process
Mitotic nuclear division
Nuclear division
Dna replication
Cytokinesis
Positive regulation of cell cycle
Positive regulation of cell adhesion
Cell cycle phase transition
Cytoskeleton-dependent cytokinesis
Regulation of cell cycle phase transition
Mitotic cell cycle phase transition
Mitotic cytokinesis
Nuclear chromosome segregation
Regulation of mononuclear cell proliferation
Protein heterotetramerization
Protein heterooligomerization
T cell proliferation
Leukocyte cell-cell adhesion
Positive regulation of leukocyte cell-cell adhesion
Positive regulation of t cell proliferation
Regulation of t cell proliferation
Negative regulation of megakaryocyte differentiation
Regulation of leukocyte proliferation
Regulation of hemopoiesis
Regulation of myeloid cell differentiation
Megakaryocyte differentiation
T cell activation
Positive regulation of t cell activation
Regulation of megakaryocyte differentiation
Regulation of lymphocyte proliferation
Leukocyte proliferation
Positive regulation of leukocyte proliferation
Myeloid cell homeostasis
Positive regulation of cell migration
Regulation of cell-cell adhesion
Positive regulation of cell motility
Positive regulation of cell-cell adhesion
Organelle fission
Categories
0 5 10 15 20
-log10(p-value)
Dna packaging
Dna conformation change
Nucleosome assembly
Chromatin assembly or disassembly
Chromatin assembly
Nucleosome organization
Protein-dna complex assembly
Organelle fission
Nuclear division
Chromosome segregation
Sister chromatid segregation
Microtubule cytoskeleton organization involved in mitosis
Mitotic sister chromatid segregation
Cytoskeleton-dependent cytokinesis
Nuclear chromosome segregation
Mitotic spindle organization
Spindle organization
Mitotic cytokinesis
Cytokinesis
Regulation of chromosome organization
Protein-dna complex subunit organization
Positive regulation of cell cycle process
Chromosome condensation
Positive regulation of cell cycle
Meiotic cell cycle
Spindle checkpoint
Regulation of mitotic nuclear division
Attachment of spindle microtubules to kinetochore
Negative regulation of chromosome organization
Regulation of chromosome segregation
Meiotic nuclear division
Spindle assembly
Cell cycle checkpoint
Regulation of nuclear division
Negative regulation of organelle organization
Regulation of cell division
Meiotic cell cycle process
Cytokinetic process
Mitotic cell cycle checkpoint
Mitotic spindle assembly
Establishment of chromosome localization
Chromosome localization
Positive regulation of cell division
Chromosome separation
Positive regulation of mitotic cell cycle
Dna replication
Kinetochore organization
Spindle localization
Myeloid cell differentiation
Regulation of protein polymerization
0 5 10 15 20
-log10(p-value)
Down-regulated
Sulfur compound metabolic process
Xanthine catabolic process
Hydrogen sulfide metabolic process
Xanthine metabolic process
Sulfur compound biosynthetic process
Xenobiotic metabolic process
Exogenous drug catabolic process
Organic hydroxy compound biosynthetic process
Cellular response to xenobiotic stimulus
Toxin metabolic process
Acetyl-coa metabolic process
Acyl-coa metabolic process
Cholesterol biosynthetic process
Secondary alcohol biosynthetic process
Fatty acid metabolic process
Sterol biosynthetic process
Alcohol biosynthetic process
Isoprenoid biosynthetic process
Short-chain fatty acid metabolic process
Steroid metabolic process
Cholesterol metabolic process
Regulation of cholesterol biosynthetic process
Secondary alcohol metabolic process
Arachidonic acid metabolic process
Regulation of lipoprotein particle clearance
Lipid catabolic process
Sterol metabolic process
Regulation of lipid metabolic process
Thioester biosynthetic process
Glutathione metabolic process
Cellular modified amino acid metabolic process
Positive regulation of proteolysis
Positive regulation of endopeptidase activity
Cofactor metabolic process
Coenzyme metabolic process
Cofactor biosynthetic process
Coenzyme biosynthetic process
Thioester metabolic process
Atp metabolic process
Acyl-coa biosynthetic process
Isoprenoid metabolic process
Mitochondrial electron transport cytochrome c to oxygen
Aerobic electron transport chain
Purine nucleobase catabolic process
Nucleobase catabolic process
Purine ribonucleoside monophosphate metabolic process
Purine ribonucleoside triphosphate metabolic process
Purine nucleobase metabolic process
Positive regulation of protein processing
Purine nucleoside monophosphate metabolic process
Categories
0 2 4 6
-log10(p-value)
Aerobic electron transport chain
Mitochondrial electron transport cytochrome c to oxygen
Epoxygenase p450 pathway
0 2 4 6
-log10(p-value)
Amino acid metabolism
Blood and immune response
Cell adhesion and motility
Cell cycle and DNA synthesis
Chromatin epigenetic modification
Cofactors
Drug metabolism
Energy metabolism
Glutathione metabolism
Lipid metabolism
Mitochondrial energy metabolism
Nucleotide metabolism
Organelle fission
Protein modification
Thioester metabolism

Figure S6

♂
♀
Up-regulated
Dna conformation change
Dna packaging
Nucleosome assembly
Protein-dna complex assembly
Chromatin assembly
Chromatin assembly or disassembly
Nucleosome organization
Protein-dna complex subunit organization
Cell cycle phase transition
Chromosome segregation
Mitotic cell cycle phase transition
Mitotic nuclear division
Nuclear division
Dna replication
Regulation of cell cycle phase transition
Positive regulation of cell cycle process
Dna replication-dependent nucleosome assembly
Dna replication-dependent nucleosome organization
Nuclear chromosome segregation
Regulation of mitotic cell cycle phase transition
Positive regulation of cell cycle
Negative regulation of cell cycle phase transition
Sister chromatid segregation
Mitotic sister chromatid segregation
Dna-dependent dna replication
Cytoskeleton-dependent cytokinesis
Mitotic cytokinesis
Negative regulation of mitotic cell cycle phase transition
Mitotic cell cycle checkpoint
Dna repair
Spindle organization
Dna recombination
Leukocyte cell-cell adhesion
T cell activation
Positive regulation of leukocyte cell-cell adhesion
Regulation of leukocyte cell-cell adhesion
Myeloid cell differentiation
Positive regulation of t cell activation
T cell proliferation
Regulation of hemopoiesis
Regulation of t cell activation
Positive regulation of t cell proliferation
Regulation of t cell proliferation
Leukocyte proliferation
Lymphocyte differentiation
Organelle fission
Positive regulation of cell-cell adhesion
Positive regulation of cell adhesion
Regulation of cell-cell adhesion
Positive regulation of cell migration
Categories
0 5 10 15 20 25
-log10(p-value)
Establishment of lymphocyte polarity
Establishment of t cell polarity
Immunological memory formation process
Immunological memory process
Memory t cell differentiation
Negative regulation of lipoprotein lipase activity
Fructose 2 6-bisphosphate metabolic process
Glucose metabolic process
Hexose metabolic process
Carbohydrate homeostasis
Glucose homeostasis
Monosaccharide metabolic process
Proton transmembrane transport
Monovalent inorganic cation transport
Organic hydroxy compound transport
Response to leptin
Atp metabolic process
Regulation of cell-substrate adhesion
Positive regulation of histone deacetylation
Regulation of histone deacetylation
Histone deacetylation
Covalent chromatin modification
Purine ribonucleoside monophosphate metabolic process
Purine ribonucleoside triphosphate metabolic process
Purine nucleoside monophosphate metabolic process
Ribonucleoside monophosphate metabolic process
Ribonucleoside triphosphate metabolic process
Purine nucleoside triphosphate metabolic process
Negative regulation of ras protein signal transduction
Negative regulation of small gtpase mediated signal transduction
Retinoic acid metabolic process
Lipid homeostasis
Cellular response to fatty acid
Response to fatty acid
Retinoid metabolic process
Diterpenoid metabolic process
Terpenoid metabolic process
Regulation of lipase activity
Isoprenoid metabolic process
Nucleoside monophosphate metabolic process
Positive regulation of protein processing
Positive regulation of protein maturation
Positive regulation of protein deacetylation
Regulation of protein deacetylation
Regulation of protein processing
Regulation of protein maturation
Protein deacetylation
0 5 10 15 20 25
-log10(p-value)
Down-regulated
Fatty acid metabolic process
Sterol metabolic process
Cholesterol metabolic process
Sterol biosynthetic process
Secondary alcohol metabolic process
Alcohol metabolic process
Cholesterol biosynthetic process
Secondary alcohol biosynthetic process
Steroid metabolic process
Isoprenoid metabolic process
Steroid biosynthetic process
Arachidonic acid metabolic process
Terpenoid metabolic process
Alcohol biosynthetic process
Icosanoid metabolic process
Long-chain fatty acid metabolic process
Unsaturated fatty acid metabolic process
Fatty acid derivative metabolic process
Isoprenoid biosynthetic process
Acyl-coa metabolic process
Acetyl-coa metabolic process
Diterpenoid metabolic process
Lipid catabolic process
Regulation of lipid metabolic process
Carboxylic acid biosynthetic process
Organic acid biosynthetic process
Small molecule catabolic process
Regulation of lipid biosynthetic process
Monocarboxylic acid biosynthetic process
Organic acid catabolic process
Carboxylic acid catabolic process
Acylglycerol metabolic process
Neutral lipid metabolic process
Regulation of triglyceride metabolic process
Fatty acid catabolic process
Cofactor metabolic process
Coenzyme metabolic process
Xenobiotic metabolic process
Organic hydroxy compound metabolic process
Sulfur compound metabolic process
Exogenous drug catabolic process
Cellular response to xenobiotic stimulus
Response to xenobiotic stimulus
Organic hydroxy compound biosynthetic process
Drug catabolic process
Epoxygenase p450 pathway
Toxin metabolic process
Cellular modified amino acid metabolic process
Glutathione metabolic process
Thioester metabolic process
Categories
0 5 10 15
-log10(p-value)
Detoxification of copper ion
Stress response to copper ion
Stress response to metal ion
Cellular response to zinc ion
Cellular response to copper ion
Cellular response to cadmium ion
Response to copper ion
Cellular zinc ion homeostasis
Zinc ion homeostasis
Cellular response to metal ion
Transition metal ion homeostasis
Response to zinc ion
Response to cadmium ion
Response to metal ion
Nucleosome positioning
Histone h3-k27 trimethylation
Histone h3-k4 trimethylation
Histone h3-k27 methylation
Nucleosome assembly
Chromatin assembly
Nucleosome organization
Chromatin assembly or disassembly
Peptidyl-lysine trimethylation
Dna packaging
Protein-dna complex assembly
Histone h3-k4 methylation
Dna conformation change
Protein-dna complex subunit organization
Detoxification of inorganic compound
Detoxification
Cellular response to inorganic substance
Response to inorganic substance
Isoprenoid metabolic process
Acetyl-coa metabolic process
Retinoid metabolic process
Diterpenoid metabolic process
Terpenoid metabolic process
Acyl-coa metabolic process
Nitric oxide mediated signal transduction
Glucose metabolic process
Hexose metabolic process
Cellular glucan metabolic process
Glucan metabolic process
Glycogen metabolic process
Monosaccharide metabolic process
Hexose phosphate transport
Propionate metabolic process
Quinolinate biosynthetic process
Energy derivation by oxidation of organic compounds
Thioester metabolic process
0 5 10 15
-log10(p-value)
Amino acid metabolism
Blood and immune response
Carbohydrate metabolism
Cell adhesion and motility
Cell cycle and DNA synthesis
Chromatin epigenetic modification
Cofactors
Drug metabolism
Energy metabolism
Glutathione metabolism
Lipid metabolism
Metals
Nucleotide metabolism
Organelle fission
Protein modification
Signal transduction
Thioester metabolism
Transporters

Figure S7

♂ ♀

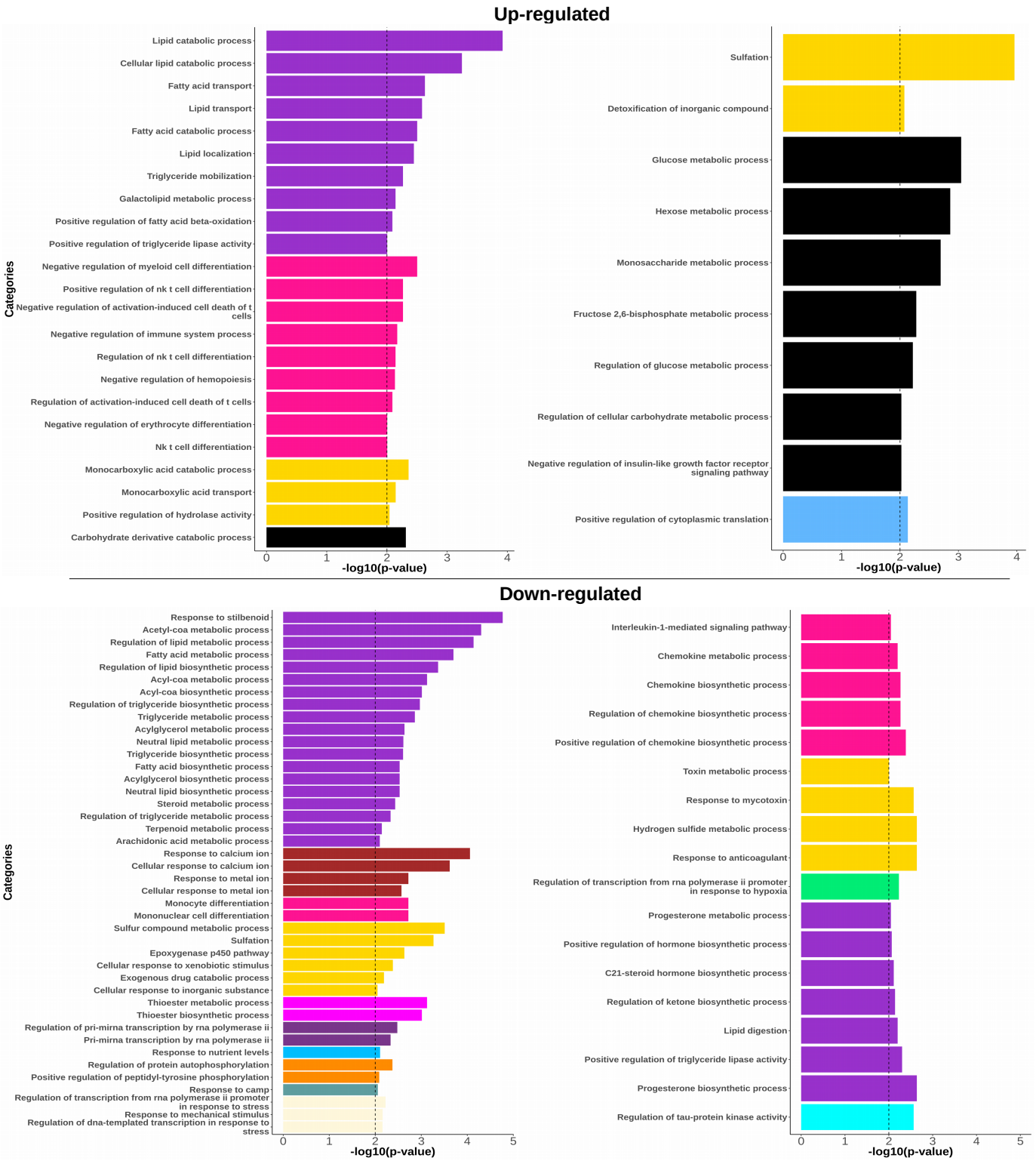

Up-regulated
Lipid catabolic process
Cellular lipid catabolic process
Fatty acid transport
Lipid transport
Fatty acid catabolic process
Lipid localization
Triglyceride mobilization
Galactolipid metabolic process
Positive regulation of fatty acid beta-oxidation
Positive regulation of triglyceride lipase activity
Negative regulation of myeloid cell differentiation
Positive regulation of nk t cell differentiation
Negative regulation of activation-induced cell death of t cells
Negative regulation of immune system process
Regulation of nk t cell differentiation
Negative regulation of hemopoiesis
Regulation of activation-induced cell death of t cells
Negative regulation of erythrocyte differentiation
Nk t cell differentiation
Monocarboxylic acid catabolic process
Monocarboxylic acid transport
Positive regulation of hydrolase activity
Carbohydrate derivative catabolic process
Categories
0 1 2 3 4
-log10(p-value)
Sulfation
Detoxification of inorganic compound
Glucose metabolic process
Hexose metabolic process
Monosaccharide metabolic process
Fructose 2,6-bisphosphate metabolic process
Regulation of glucose metabolic process
Regulation of cellular carbohydrate metabolic process
Negative regulation of insulin-like growth factor receptor signaling pathway
Positive regulation of cytoplasmic translation
0 1 2 3 4
-log10(p-value)
Down-regulated
Response to stilbenoid
Acetyl-coa metabolic process
Regulation of lipid metabolic process
Fatty acid metabolic process
Regulation of lipid biosynthetic process
Acyl-coa metabolic process
Acyl-coa biosynthetic process
Regulation of triglyceride biosynthetic process
Triglyceride metabolic process
Acylglycerol metabolic process
Neutral lipid metabolic process
Triglyceride biosynthetic process
Fatty acid biosynthetic process
Acylglycerol biosynthetic process
Neutral lipid biosynthetic process
Steroid metabolic process
Regulation of triglyceride metabolic process
Terpenoid metabolic process
Arachidonic acid metabolic process
Response to calcium ion
Cellular response to calcium ion
Response to metal ion
Cellular response to metal ion
Monocyte differentiation
Mononuclear cell differentiation
Sulfur compound metabolic process
Sulfation
Epoxygenase p450 pathway
Cellular response to xenobiotic stimulus
Exogenous drug catabolic process
Cellular response to inorganic substance
Thioester metabolic process
Thioester biosynthetic process
Regulation of pri-mirna transcription by rna polymerase ii
Pri-mirna transcription by rna polymerase ii
Response to nutrient levels
Regulation of protein autophosphorylation
Positive regulation of peptidyl-tyrosine phosphorylation
Response to camp
Regulation of transcription from rna polymerase ii promoter in response to stress
Response to mechanical stimulus
Regulation of dna-templated transcription in response to stress
Categories
0 1 2 3 4 5
-log10(p-value)
Interleukin-1-mediated signaling pathway
Chemokine metabolic process
Chemokine biosynthetic process
Regulation of chemokine biosynthetic process
Positive regulation of chemokine biosynthetic process
Toxin metabolic process
Response to mycotoxin
Hydrogen sulfide metabolic process
Response to anticoagulant
Regulation of transcription from rna polymerase ii promoter in response to hypoxia
Progesterone metabolic process
Positive regulation of hormone biosynthetic process
C21-steroid hormone biosynthetic process
Regulation of ketone biosynthetic process
Lipid digestion
Positive regulation of triglyceride lipase activity
Progesterone biosynthetic process
Regulation of tau-protein kinase activity
0 1 2 3 4 5
-log10(p-value)
Blood and immune response
Carbohydrate metabolism
Cytoplasmic translation
Drug metabolism
Hypoxia
Lipid metabolism
Metals
miRNA transcription
Nutrient & vitamins
Protein modification
Secondary messenger
Stress response
Tau protein
Thioester metabolism

Figure S8

♂ ♀

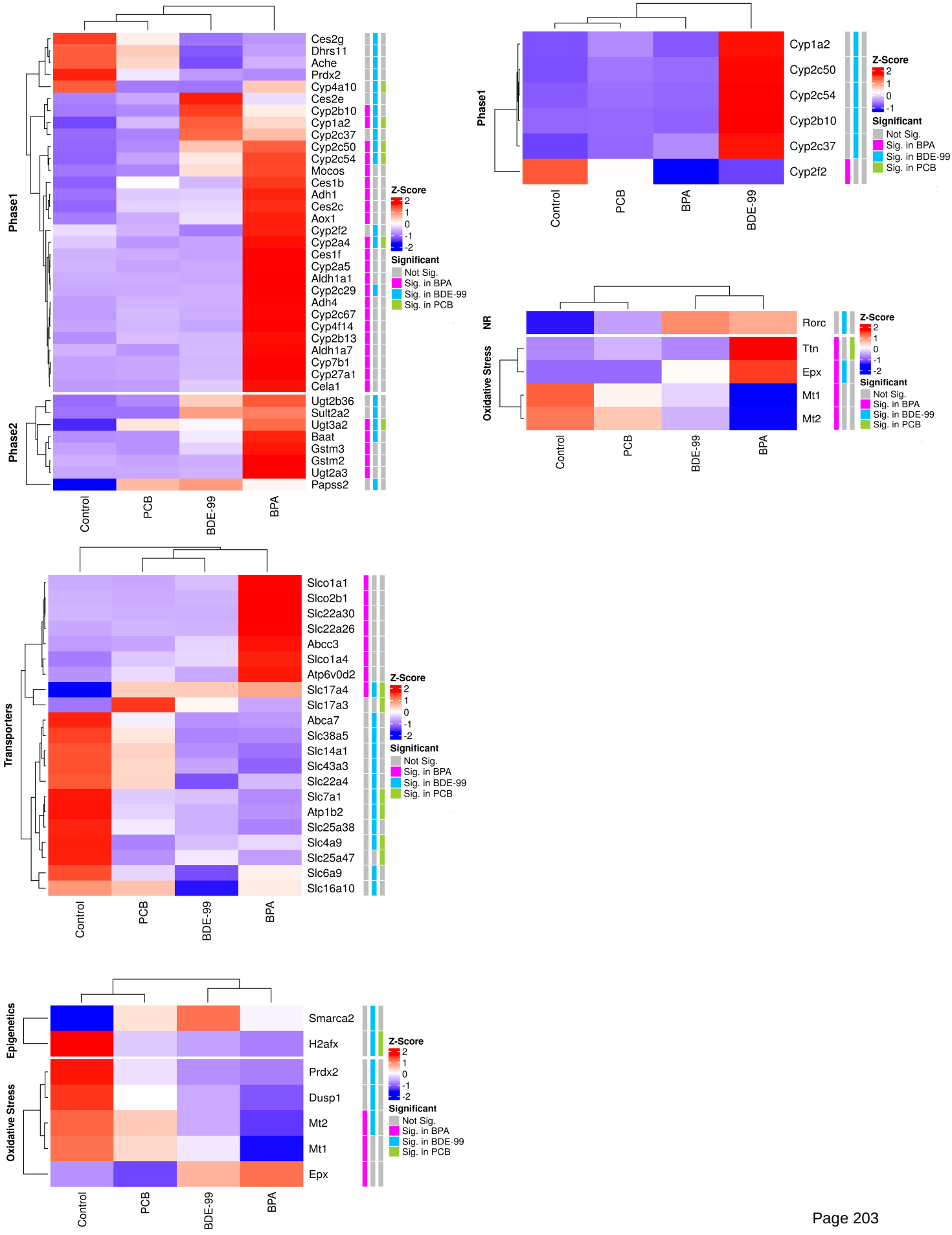

Phase1
Phase2
Ces2g
Dhrs11
Ache
Prdx2
Cyp4a10
Ces2e
Cyp2b10
Cyp1a2
Cyp2c37
Cyp2c50
Cyp2c54
Mocos
Ces1b
Adh1
Ces2c
Aox1
Cyp2f2
Cyp2a4
Ces1f
Cyp2a5
Aldh1a1
Cyp2c29
Adh4
Cyp2c67
Cyp4f14
Cyp2b13
Aldh1a7
Cyp7b1
Cyp27a1
Cela1
Ugt2b36
Sult2a2
Ugt3a2
Baat
Gstm3
Gstm2
Ugt2a3
Papss2
Control
PCB
BDE-99
BPA
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB
Phase1
Cyp1a2
Cyp2c50
Cyp2c54
Cyp2b10
Cyp2c37
Cyp2f2
Control
PCB
BPA
BDE-99
NR
Oxidative Stress
Rorc
Ttn
Epx
Mt1
Mt2
Control
PCB
BDE-99
BPA
Transporters
Slco1a1
Slco2b1
Slc22a30
Slc22a26
Abcc3
Slco1a4
Atp6v0d2
Slc17a4
Slc17a3
Abca7
Slc38a5
Slc14a1
Slc43a3
Slc22a4
Slc7a1
Atp1b2
Slc25a38
Slc4a9
Slc25a47
Slc6a9
Slc16a10
Control
PCB
BDE-99
BPA
Epigenetics
Oxidative Stress
Smarca2
H2afx
Prdx2
Dusp1
Mt2
Mt1
Epx
Control
PCB
BDE-99
BPA

Figure S9

♂ ♀

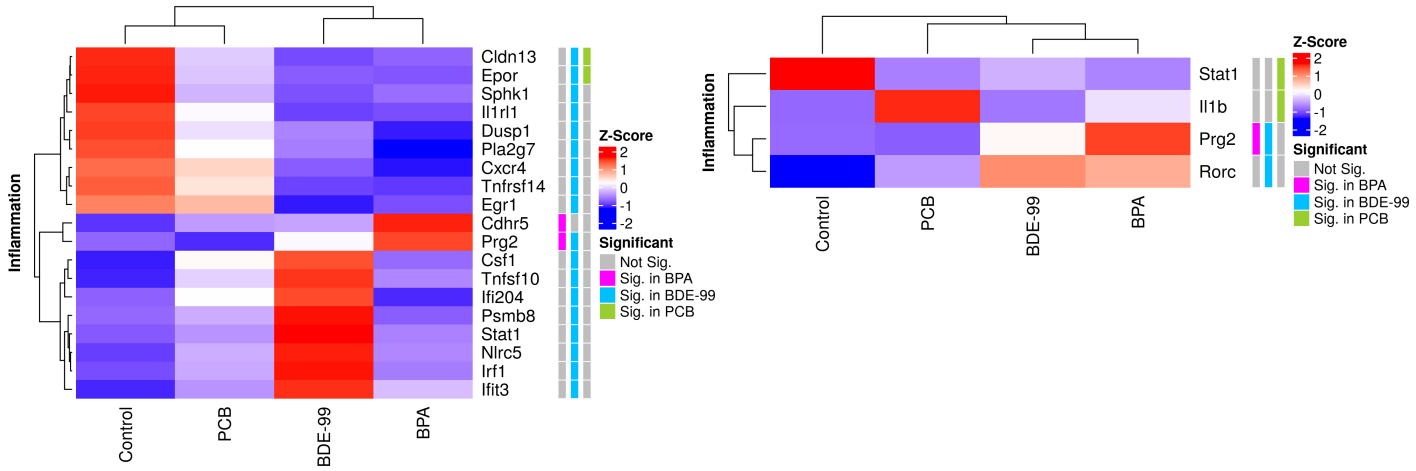

Inflammation
Cldn13
Epor
Sphk1
Il1rl1
Dusp1
Pla2g7
Cxcr4
Tnfrsf14
Egr1
Cdhr5
Prg2
Csf1
Tnfsf10
Ifi204
Psmb8
Stat1
Nlrc5
Irf1
Ifit3
Control
PCB
BDE-99
BPA
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB
Inflammation
Stat1
Il1b
Prg2
Rorc
Control
PCB
BDE-99
BPA
Z-Score
2
1
0
-1
-2
Significant
Not Sig.
Sig. in BPA
Sig. in BDE-99
Sig. in PCB

Figure S10

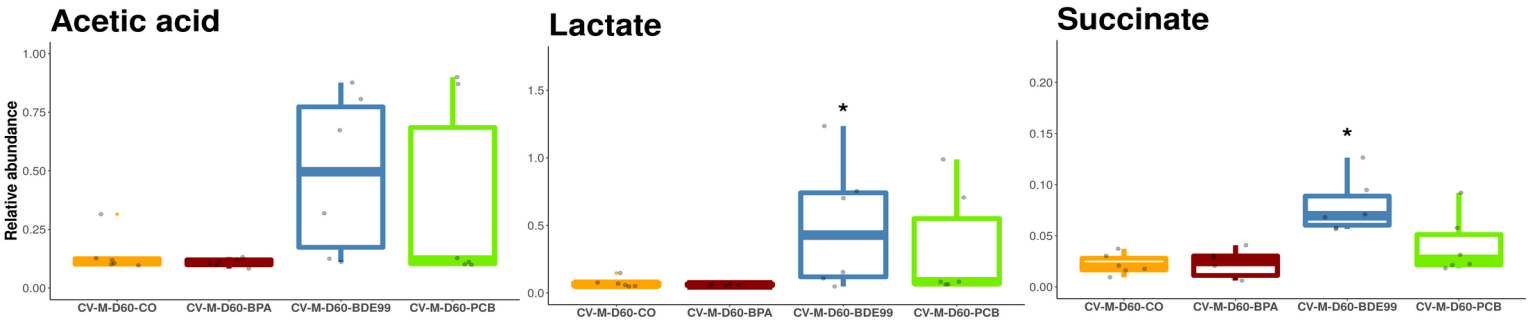
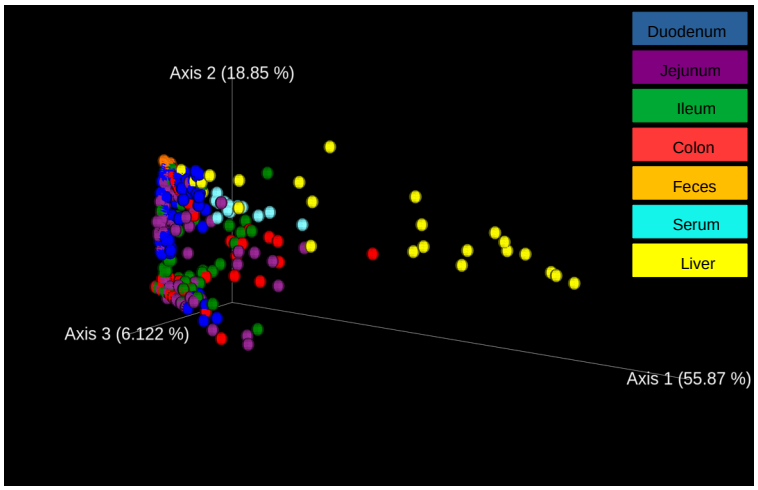
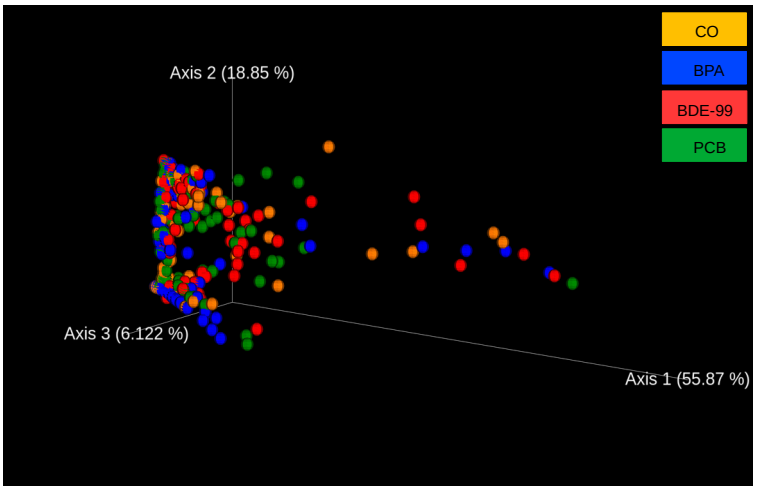

Acetic acid
Lactate
Succinate
Relative abundance
1.00
0.75
0.50
0.25
0.00
1.5
1.0
0.5
0.0
0.20
0.15
0.10
0.05
0.00
*
*
CV-M-D60-CO
CV-M-D60-BPA
CV-M-D60-BDE99
CV-M-D60-PCB

Figure S11

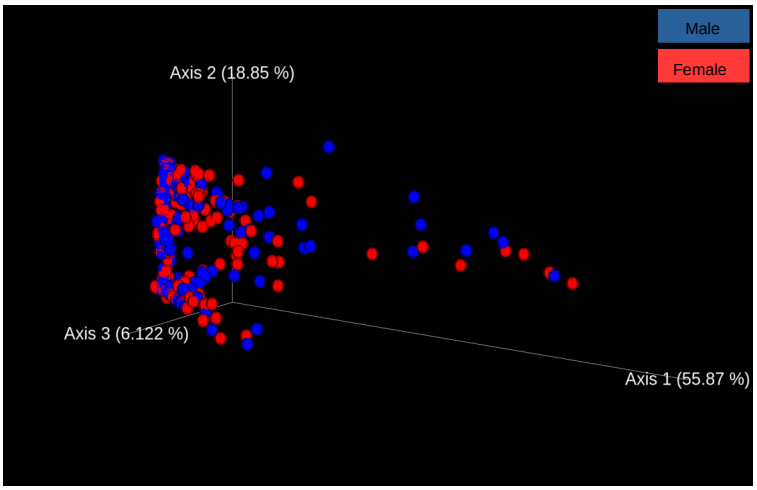
A



B



C



D

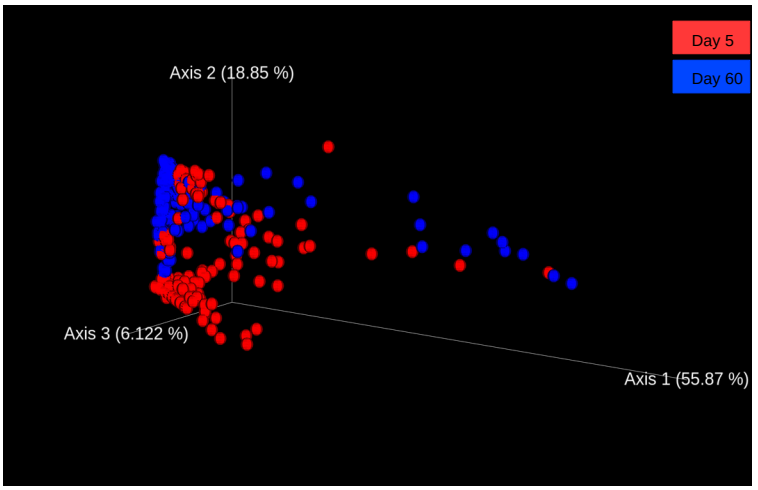
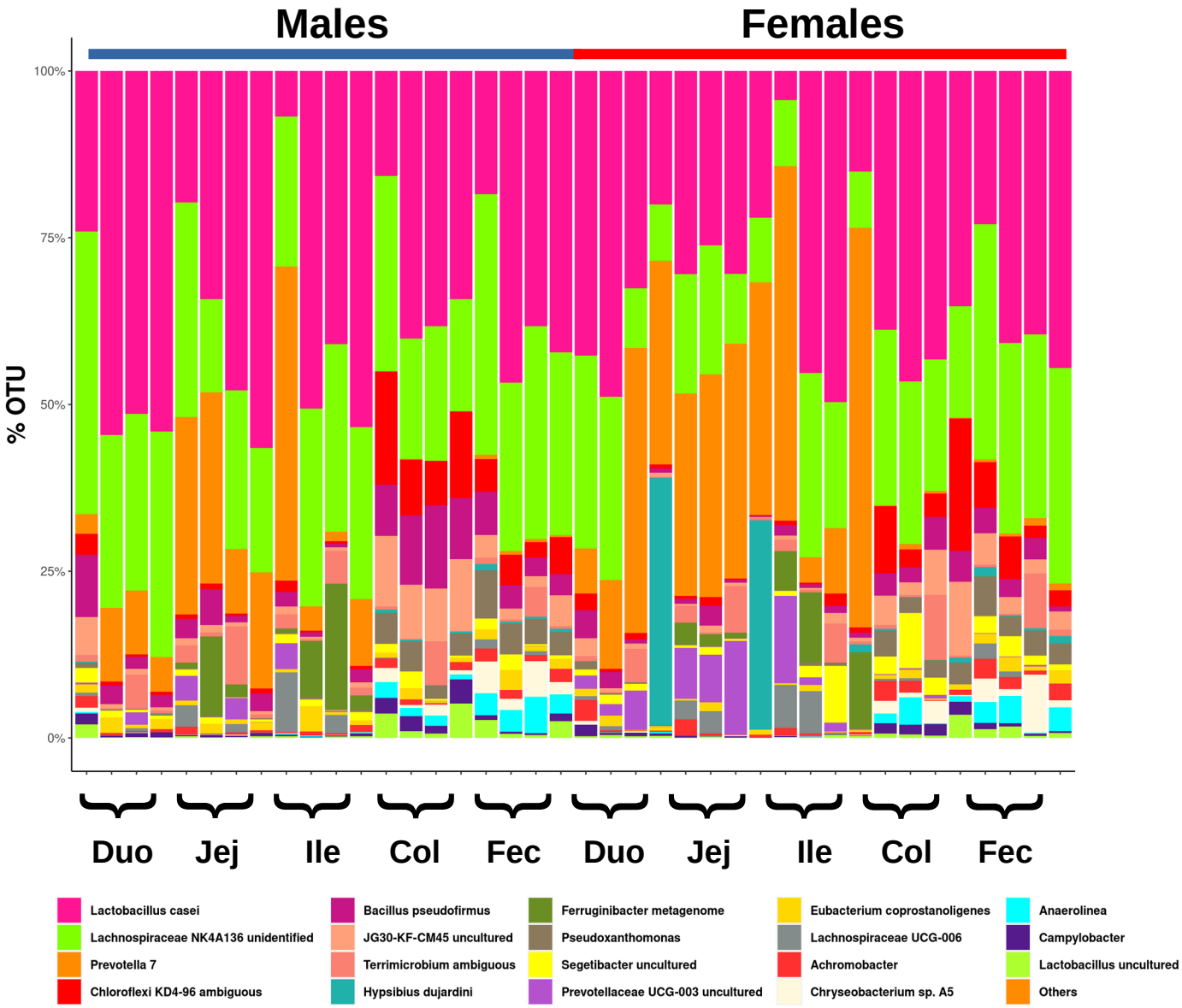


Figure S12


Males
Females
100%
75%
50%
25%
0%
% OTU
Duo
Jej
Ile
Col
Fec
Duo
Jej
Ile
Col
Fec
Lactobacillus casei
Lachnospiraceae NK4A136 unidentified
Prevotella 7
Chloroflexi KD4-96 ambiguous
Bacillus pseudofirmus
JG30-KF-CM45 uncultured
Terrimicrobium ambiguous
Hypsibius dujardini
Ferruginibacter metagenome
Pseudoxanthomonas
Segetibacter uncultured
Prevotellaceae UCG-003 uncultured
Eubacterium coprostanoligenes
Lachnospiraceae UCG-006
Achromobacter
Chryseobacterium sp. A5
Anaerolinea
Campylobacter
Lactobacillus uncultured
Others

ADDENDUM

Chapter 2.

Table S1. Lists of differentially expressed genes for CV PCB 6 (A), CV PCB 30 (B), GF PCB 6 (C), and GF PCB 30 (D).

Table S2. Normalized metabolites detected in liver (A) and serum (B).

Table S3. Operational taxonomic units (OTUs) for 16s rDNA sequencing data.

Table S4. Differentially abundant bacteria for CV PCB 6 (A) and CV PCB 30 (B).

Table S5. Spearman's correlation results for bacteria and liver and serum metabolites (A) and bacteria and FDR-adjusted p-values (B), and differentially regulated genes (C) and FDR-adjusted p-values (D).

Table S6. Commonly and differentially regulated genes by PCBs (A), commonly and differentially regulated liver metabolites by PCBs (B), and commonly and differentially regulated serum metabolites by PCBs (C).

Chapter 3.

Table S1. Mapping statistics of RNA-Seq reads.

Table S2. List of genes in Venn diagrams in each age (day 5 and 60), chemical-treated (BPA, BDE-99), and PCB), and sex groups. Genes that are commonly and uniquely regulated by each chemical are listed.

Table S3. Summary of Ingenuity Pathway Analysis (IPA) results using differentially regulated genes (Cuffdiff, FDR-BH < 0.05). Names of networks, significant canonical pathways and tox functions ($p < 0.01$), top 100 predicted upstream regulators, predicted increased and decreased functions, and top 10 predicted upstream regulators are included.

Table S4. List of gene ontology (GO) categories used to visualize and cluster GO terms.

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001082.12	Mfsd10	6.27489	1.7969	-1.80408	-1.666	0.00005	0.00761968
ENSMUSG00000003053.17	Cyp2c29	505.17	834.73	0.72454	2.77488	0.00005	0.00761968
ENSMUSG00000003555.8	Cyp17a1	30.7127	66.9781	1.12485	3.97657	0.00005	0.00761968
ENSMUSG00000004038.9	Gstm3	20.5927	33.851	0.717065	2.92459	0.00005	0.00761968
ENSMUSG00000005413.8	Hmox1	10.8956	7.33838	-0.570219	-2.05123	0.00035	0.037983
ENSMUSG00000005547.14	Cyp2a5	430.556	721.13	0.744058	2.24398	0.00015	0.0193581
ENSMUSG00000007872.3	Id3	27.5332	13.3798	-1.04111	-3.69018	0.00005	0.00761968
ENSMUSG00000014905.4	Dnajb9	24.6827	16.6976	-0.563856	-2.44755	0.00005	0.00761968
ENSMUSG00000015224.10	Cyp2j9	8.84831	4.99311	-0.825464	-2.92044	0.00005	0.00761968
ENSMUSG00000015357.10	Clpx	78.2269	50.077	-0.643518	-2.64475	0.00005	0.00761968
ENSMUSG00000017390.15	Aldoc	3.30235	6.26799	0.924508	1.8897	0.00045	0.0460446
ENSMUSG00000018427.7	Ypel2	9.95094	5.96948	-0.737227	-3.14699	0.00005	0.00761968
ENSMUSG00000018830.10	Myh11	0.856366	1.92082	1.16542	2.76044	0.00005	0.00761968
ENSMUSG00000020175.15	Rab36	7.24259	4.05831	-0.835627	-2.23857	0.00005	0.00761968
ENSMUSG00000020190.13	Mknk2	16.502	34.2124	1.05188	2.706	0.00005	0.00761968
ENSMUSG00000020473.13	Aebp1	0.537474	1.24369	1.21036	1.91027	0.00015	0.0193581
ENSMUSG00000020593.15	Lpin1	23.3481	63.294	1.43876	4.53512	0.00005	0.00761968
ENSMUSG00000020623.11	Map2k6	2.79563	4.8047	0.781271	2.25429	0.00015	0.0193581
ENSMUSG00000020644.9	Id2	65.4148	42.2437	-0.630882	-2.77822	0.00005	0.00761968
ENSMUSG00000020653.12	Klf11	4.00267	1.83482	-1.12533	-2.16824	0.00005	0.00761968
ENSMUSG00000021453.2	Gadd45g	4.23384	9.3219	1.13866	3.01194	0.00005	0.00761968
ENSMUSG00000021670.14	Hmgcr	42.2238	98.0346	1.21523	3.29717	0.00005	0.00761968
ENSMUSG00000022003.7	Slc25a30	21.1229	8.85161	-1.2548	-2.70092	0.00005	0.00761968
ENSMUSG00000022351.14	Sqle	14.4701	22.8969	0.662076	2.85745	0.00005	0.00761968
ENSMUSG00000022512.3	Cldn1	25.5877	18.7521	-0.448393	-2.02615	0.00035	0.037983
ENSMUSG00000022769.9	Sdf2l1	44.9273	25.0223	-0.844377	-3.54758	0.00005	0.00761968
ENSMUSG00000022899.9	Slc15a2	3.0659	0.37101	-3.04678	-1.38684	0.00005	0.00761968
ENSMUSG00000023087.15	Noct	3.11413	6.68196	1.10144	2.47459	0.00005	0.00761968
ENSMUSG00000023272.4	Creld2	42.1392	14.3552	-1.55359	-6.28154	0.00005	0.00761968
ENSMUSG00000024427.7	Spry4	3.84589	5.82326	0.598512	2.37281	0.00005	0.00761968
ENSMUSG00000024548.11	Setbp1	0.571063	0.898115	0.65325	2.01298	0.0004	0.0421324
ENSMUSG00000024807.18	Syvn1	26.659	12.2223	-1.12511	-3.46232	0.00005	0.00761968
ENSMUSG00000024843.15	Chka	45.983	21.79	-1.07743	-2.35525	0.00025	0.028881
ENSMUSG00000024987.6	Cyp26a1	11.1487	24.2118	1.11883	3.82575	0.00005	0.00761968
ENSMUSG00000025185.14	Loxl4	3.94432	2.11188	-0.90125	-2.33915	0.00005	0.00761968
ENSMUSG00000025190.13	Got1	73.9132	114.605	0.632762	2.52771	0.00005	0.00761968
ENSMUSG00000026077.15	Npas2	8.47762	1.95208	-2.11865	-2.21209	0.0001	0.0140441
ENSMUSG00000026185.8	Igfbp5	5.37805	8.0981	0.590499	2.46113	0.00005	0.00761968
ENSMUSG00000026348.7	Acmsd	7.9453	11.3608	0.515893	2.05887	0.00025	0.028881
ENSMUSG00000026390.7	Marco	4.51252	2.20537	-1.03291	-2.38186	0.00005	0.00761968
ENSMUSG00000026614.7	Slc30a10	12.8976	7.77189	-0.730768	-3.05461	0.00005	0.00761968
ENSMUSG00000026839.17	Upp2	61.1429	142.443	1.22013	4.83935	0.00005	0.00761968
ENSMUSG00000026864.13	Hspa5	838.917	453.702	-0.886781	-2.47163	0.00005	0.00761968
ENSMUSG00000026879.14	Gsn	5.39704	11.4131	1.08046	3.81852	0.00005	0.00761968
ENSMUSG00000027346.15	Gpcpd1	23.3608	40.7371	0.802254	2.42579	0.0001	0.0140441
ENSMUSG00000027360.5	Hdc	3.45119	1.89382	-0.865796	-1.76936	0.00045	0.0460446
ENSMUSG00000027947.11	Il6ra	12.7959	19.116	0.579098	2.29486	0.00025	0.028881
ENSMUSG00000027954.9	Efna1	27.2749	14.7794	-0.883989	-3.61654	0.00005	0.00761968
ENSMUSG00000028238.6	Atp6v0d2	5.28464	8.4326	0.674173	2.16648	0.0001	0.0140441
ENSMUSG00000028680.14	Plk3	10.5138	6.01814	-0.804897	-3.05136	0.00005	0.00761968
ENSMUSG00000029009.17	Mthfr	7.1591	3.44294	-1.05613	-2.20818	0.00035	0.037983

ENSMUSG00000029188.14	Slc34a2	1.56037	0.365782	-2.09283	-2.78098	0.00005	0.00761968
ENSMUSG00000029467.15	Atp2a2	86.4356	60.473	-0.515334	-1.97184	0.00035	0.037983
ENSMUSG00000029657.15	Hsph1	47.3595	28.792	-0.717988	-2.07578	0.00015	0.0193581
ENSMUSG00000029992.14	Gfpt1	13.4599	9.01933	-0.577579	-1.84116	0.00045	0.0460446
ENSMUSG00000030302.16	Atp2b2	4.38644	2.77593	-0.66008	-2.11664	0.0002	0.0244872
ENSMUSG00000030483.14	Cyp2b10	17.3823	34.9186	1.00638	4.20068	0.00005	0.00761968
ENSMUSG00000030917.13	Tmem159	0.899211	4.33785	2.27025	1.53715	0.0004	0.0421324
ENSMUSG00000031349.4	Nsdhl	10.9891	18.7202	0.768519	3.05432	0.00005	0.00761968
ENSMUSG00000031604.10	Msmo1	88.8162	141.341	0.67029	2.3651	0.0002	0.0244872
ENSMUSG00000031762.7	Mt2	14.6712	30.7685	1.06847	2.79551	0.00005	0.00761968
ENSMUSG00000031765.8	Mt1	41.5758	103.19	1.31148	4.86124	0.00005	0.00761968
ENSMUSG00000032115.14	Hyou1	67.4029	46.7624	-0.527462	-2.28962	0.00005	0.00761968
ENSMUSG00000032271.13	Nnmt	56.8868	84.4939	0.570754	2.3728	0.00005	0.00761968
ENSMUSG00000032310.4	Cyp1a2	347.498	1061.1	1.61048	5.9896	0.00005	0.00761968
ENSMUSG00000032350.9	Gclc	79.3815	50.4684	-0.653422	-2.42429	0.00005	0.00761968
ENSMUSG00000032575.16	Manf	239.221	135.412	-0.820986	-2.2734	0.0001	0.0140441
ENSMUSG00000032902.1	Slc16a1	19.0525	12.3003	-0.631283	-2.79129	0.00005	0.00761968
ENSMUSG00000032932.15	Hspa13	14.3906	9.10349	-0.660639	-2.73434	0.00005	0.00761968
ENSMUSG00000033107.6	Rnf125	123.021	61.7043	-0.995457	-4.47951	0.00005	0.00761968
ENSMUSG00000035686.8	Thrsp	108.608	275.462	1.34273	5.6328	0.00005	0.00761968
ENSMUSG00000035783.9	Acta2	1.51116	4.87177	1.68878	2.67871	0.00005	0.00761968
ENSMUSG00000035828.11	Pim3	5.49715	9.06074	0.720943	2.54131	0.00005	0.00761968
ENSMUSG00000037405.8	Icam1	7.588	5.10752	-0.571098	-2.12615	0.0004	0.0421324
ENSMUSG00000037440.8	Vnn1	26.6312	18.1146	-0.555968	-2.3665	0.0001	0.0140441
ENSMUSG00000038418.7	Egr1	8.5935	4.36381	-0.977659	-3.36242	0.00005	0.00761968
ENSMUSG00000038508.7	Gdf15	2.87642	1.396	-1.04298	-2.33349	0.00035	0.037983
ENSMUSG00000038656.5	Cyp3a16	15.6662	29.4555	0.910887	3.44256	0.00005	0.00761968
ENSMUSG00000039633.6	Lonrf1	1.73883	1.02745	-0.759046	-2.12834	0.0004	0.0421324
ENSMUSG00000039801.7	Cplane1	1.57608	11.8302	2.90806	2.79653	0.00015	0.0193581
ENSMUSG00000040128.9	Pnrc1	65.8791	42.2407	-0.641185	-2.71807	0.00005	0.00761968
ENSMUSG00000040562.12	Gstm2	44.5903	65.892	0.563373	2.4444	0.00005	0.00761968
ENSMUSG00000041324.14	Inhba	9.92684	4.22896	-1.23103	-2.8545	0.00005	0.00761968
ENSMUSG00000045287.6	Rtn4rl1	6.73191	4.46	-0.593973	-2.31529	0.00015	0.0193581
ENSMUSG00000045776.3	Lrtm1	4.59023	7.84042	0.772364	2.57822	0.00005	0.00761968
ENSMUSG00000046402.10	Rbp1	2.24938	3.8182	0.763363	2.38685	0.00005	0.00761968
ENSMUSG00000047777.9	Phf13	2.44905	1.25344	-0.966331	-2.7493	0.00005	0.00761968
ENSMUSG00000047822.8	Angptl8	82.3516	37.7627	-1.12484	-2.15144	0.00045	0.0460446
ENSMUSG00000049164.7	Zfp518a	3.42441	2.24797	-0.607233	-2.21996	0.00005	0.00761968
ENSMUSG00000049580.12	Tsku	7.78541	17.2903	1.15112	2.39263	0.0002	0.0244872
ENSMUSG00000052684.4	Jun	8.02239	3.56567	-1.16986	-4.3468	0.00005	0.00761968
ENSMUSG00000054277.8	Arfgap3	4.98675	2.38411	-1.06465	-2.77345	0.00005	0.00761968
ENSMUSG00000055116.8	Arntl	9.47854	4.66962	-1.02136	-3.41105	0.00005	0.00761968
ENSMUSG00000056313.5	Tcim	6.3628	10.6007	0.736431	2.63227	0.00005	0.00761968
ENSMUSG00000056501.3	Cebpb	33.2417	49.8658	0.585055	2.15225	0.0002	0.0244872
ENSMUSG00000056749.7	Nfil3	11.4209	6.76087	-0.756389	-2.86792	0.00005	0.00761968
ENSMUSG00000057068.15	Fam47e	6.37728	11.3884	0.836547	2.00781	0.00025	0.028881
ENSMUSG00000057069.7	Ero1lb	12.8374	8.73738	-0.555077	-2.29919	0.0001	0.0140441
ENSMUSG00000058454.15	Dhcr7	16.3576	28.6402	0.808075	2.67257	0.00005	0.00761968
ENSMUSG00000058672.7	Tubb2a	60.3828	42.6623	-0.501177	-2.22162	0.0002	0.0244872
ENSMUSG00000059060.15	Rad51b	2.98263	1.00564	-1.56846	-2.7696	0.00005	0.00761968
ENSMUSG00000059743.12	Fdps	68.1418	100.306	0.557798	2.3204	0.00005	0.00761968

ENSMUSG00000061825.10	Ces2c	4.32809	7.73435	0.837552	2.81141	0.00005	0.00761968
ENSMUSG00000064213.5	Defa24	1.36432	0	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000064354.1	mt-Co2	6.53406	11.5824	0.825885	2.28304	0.00015	0.0193581
ENSMUSG00000066441.14	Rdh11	16.5169	23.867	0.531074	2.24242	0.00005	0.00761968
ENSMUSG00000066687.5	Zbtb16	17.6103	35.1446	0.996886	3.99134	0.00005	0.00761968
ENSMUSG00000067225.2	Cyp2c54	162.272	224.41	0.467721	2.06478	0.00025	0.028881
ENSMUSG00000067279.3	Ppp1r3c	27.6268	14.325	-0.947532	-4.13342	0.00005	0.00761968
ENSMUSG00000069324.6	Gm5096	15.1526	23.2798	0.619511	2.53681	0.00005	0.00761968
ENSMUSG00000069668.4	Sult3a1	97.163	160.62	0.725176	3.28788	0.00005	0.00761968
ENSMUSG00000070644.13	Etnk2	62.5601	96.255	0.621618	2.63482	0.00005	0.00761968
ENSMUSG00000070811.6	Sult2a2	47.5462	75.7986	0.672841	2.07079	0.0003	0.03438
ENSMUSG00000072949.6	Acot1	33.817	19.1723	-0.818729	-2.60084	0.00005	0.00761968
ENSMUSG00000074063.10	Osgin1	93.9424	49.382	-0.927792	-4.03213	0.00005	0.00761968
ENSMUSG00000074768.6	Bhmt	276.248	458.526	0.731038	2.73971	0.00005	0.00761968
ENSMUSG00000074896.3	Ifit3	4.81246	7.59939	0.659108	2.2256	0.00025	0.028881
ENSMUSG00000075551.4	Cyp3a41a	33.4333	57.9428	0.793345	3.43636	0.00005	0.00761968
ENSMUSG00000075552.4	Cyp3a41b	4.55117	8.51163	0.903198	3.06479	0.00005	0.00761968
ENSMUSG00000076609.2	Igkc	9.38561	17.1417	0.868984	2.35993	0.00005	0.00761968
ENSMUSG00000078650.2	G6pc	118.654	70.8163	-0.744612	-3.34005	0.00005	0.00761968
ENSMUSG00000078798.4	Sult2a1	56.4787	97.1215	0.782085	3.19123	0.00005	0.00761968
ENSMUSG00000078866.10	Zfp970	11.5288	17.8725	0.632507	2.15652	0.00015	0.0193581
ENSMUSG00000081207.4	Gm13775	12.4872	21.3006	0.770447	2.48423	0.00005	0.00761968
ENSMUSG00000084923.1	Gm15611	21.2021	5.05847	-2.06744	-4.28501	0.00005	0.00761968
ENSMUSG00000085445.1	Gm16348	0.998651	2.12188	1.08729	2.36459	0.00005	0.00761968
ENSMUSG00000090298.2	Sult3a2	3.39104	7.38886	1.12362	2.81264	0.00005	0.00761968
ENSMUSG00000090877.3	Hspa1b	1.21104	0.49013	-1.305	-2.62497	0.0002	0.0244872
ENSMUSG00000090942.1	F830016B	18.3992	13.1678	-0.482627	-2.08238	0.00035	0.037983
ENSMUSG00000092075.1	Serpina4-	21.4399	5.39866	-1.98962	-6.65923	0.00005	0.00761968
ENSMUSG00000093930.2	Hmgcs1	79.4702	111.752	0.491821	1.79112	0.00015	0.0193581
ENSMUSG00000096674.1	Mup15	16.0544	25.2402	0.652756	2.36601	0.00005	0.00761968
ENSMUSG00000096688.1	Mup17	35.5827	61.429	0.787745	3.16456	0.00005	0.00761968
ENSMUSG00000099032.2	Tcf24	4.46246	2.40791	-0.890059	-2.74594	0.00005	0.00761968
ENSMUSG00000100277.8	1810053B	0.732602	2.66094	1.86084	1.18658	0.0001	0.0140441
ENSMUSG00000102888.1	Ighv1-11	0	6.24986	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000106397.1	Gm21049	4.52985	7.62193	0.750694	2.11318	0.00035	0.037983
ENSMUSG00000110384.1	Gm45301	1.01899	2.77951	1.44769	2.41211	0.00025	0.028881
ENSMUSG00000115388.2	Eppk1	5.00691	7.2053	0.525136	2.22729	0.0001	0.0140441
ENSMUSG00000115919.1	Gm31583	2.90438	5.0658	0.802558	2.71184	0.00005	0.00761968

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001270.9	Ckb	4.9592	2.82251	-0.813128	-1.925	0.00055	0.0404152
ENSMUSG00000003053.17	Cyp2c29	502.057	1871.49	1.89827	4.7931	0.00005	0.00618632
ENSMUSG00000003555.8	Cyp17a1	30.523	69.3286	1.18355	3.76365	0.00005	0.00618632
ENSMUSG00000003849.8	Nqo1	4.13848	8.59917	1.05509	3.10818	0.00005	0.00618632
ENSMUSG00000004038.9	Gstm3	20.4693	75.9074	1.89078	6.88927	0.00005	0.00618632
ENSMUSG00000005514.14	Por	143.718	286.806	0.996833	2.93999	0.00005	0.00618632
ENSMUSG00000005547.14	Cyp2a5	427.875	1202.66	1.49096	3.44719	0.00005	0.00618632
ENSMUSG00000005779.12	Psmb4	57.871	84.627	0.548278	1.92037	0.00065	0.0456767
ENSMUSG00000006777.7	Krt23	1.02612	5.09059	2.31064	4.50613	0.00005	0.00618632
ENSMUSG00000007950.9	Abhd8	1.46653	0.490162	-1.58107	-2.25758	0.0002	0.0194309
ENSMUSG00000011305.11	Plin5	16.8478	11.2536	-0.582169	-2.14557	0.00015	0.0159662
ENSMUSG00000015224.10	Cyp2j9	8.79124	5.13102	-0.776822	-2.50401	0.00005	0.00618632
ENSMUSG00000015357.10	Clpx	77.7399	44.4332	-0.807017	-2.76713	0.00005	0.00618632
ENSMUSG00000016239.11	Lonrf3	2.78045	1.06184	-1.38874	-2.97987	0.00005	0.00618632
ENSMUSG00000020027.18	Socs2	8.61402	16.6749	0.952916	2.06	0.00005	0.00618632
ENSMUSG00000020123.6	Avpr1a	24.1839	14.3293	-0.755076	-2.41315	0.00005	0.00618632
ENSMUSG00000020175.15	Rab36	7.19819	4.01968	-0.840554	-2.06135	0.00035	0.029457
ENSMUSG00000020190.13	Mknk2	16.398	38.746	1.24053	2.84633	0.00005	0.00618632
ENSMUSG00000020593.15	Lpin1	23.2003	40.0422	0.78738	2.19992	0.00055	0.0404152
ENSMUSG00000020889.11	Nr1d1	17.095	37.493	1.13305	2.42106	0.0005	0.0385
ENSMUSG00000021453.2	Gadd45g	4.2085	13.5086	1.6825	4.46078	0.00005	0.00618632
ENSMUSG00000021775.11	Nr1d2	18.5393	32.2923	0.800601	2.14163	0.0001	0.0113094
ENSMUSG00000022025.13	Cnmd	2.94353	7.12175	1.27469	2.30779	0.0001	0.0113094
ENSMUSG00000022091.6	Sorbs3	8.7422	15.3301	0.810301	2.61385	0.00005	0.00618632
ENSMUSG00000022270.16	Retreg1	33.766	64.9642	0.944073	2.71635	0.00005	0.00618632
ENSMUSG00000022346.15	Myc	1.47519	5.7052	1.95138	3.05112	0.00005	0.00618632
ENSMUSG00000022508.5	Bcl6	3.5485	6.1976	0.804501	2.72117	0.00005	0.00618632
ENSMUSG00000022679.13	Mpv17l	3.4023	7.38539	1.11816	2.33264	0.00005	0.00618632
ENSMUSG00000022769.9	Sdf2l1	44.6531	24.9449	-0.840016	-3.10498	0.00005	0.00618632
ENSMUSG00000023073.2	Slc10a2	3.87084	6.00992	0.634701	2.23853	0.0002	0.0194309
ENSMUSG00000023272.4	Creld2	41.8868	10.7104	-1.96748	-6.82395	0.00005	0.00618632
ENSMUSG00000024131.8	Slc3a1	16.845	27.1766	0.690046	1.95102	0.00055	0.0404152
ENSMUSG00000024254.15	Abcg8	23.9899	44.5496	0.892986	2.2514	0.00005	0.00618632
ENSMUSG00000024427.7	Spry4	3.8216	7.52294	0.977118	3.54048	0.00005	0.00618632
ENSMUSG00000024548.11	Setbp1	0.567395	0.943684	0.733949	2.09591	0.00035	0.029457
ENSMUSG00000024646.14	Cyb5a	1372.68	2262.27	0.720771	2.28567	0.00005	0.00618632
ENSMUSG00000024747.3	Aldh1a7	74.5145	106.783	0.519085	1.98059	0.0006	0.043428
ENSMUSG00000024807.18	Syvn1	26.4973	12.6676	-1.0647	-2.99172	0.00005	0.00618632
ENSMUSG00000025002.5	Cyp2c55	5.11	22.678	2.1499	7.12158	0.00005	0.00618632
ENSMUSG00000025185.14	Loxl4	3.92033	1.51462	-1.37202	-2.71184	0.00005	0.00618632
ENSMUSG00000025190.13	Got1	73.4621	143.402	0.964996	3.33157	0.00005	0.00618632
ENSMUSG00000026077.15	Npas2	8.42746	1.66594	-2.33876	-3.01011	0.0001	0.0113094
ENSMUSG00000026226.16	Spata3	2.63728	0.875213	-1.59135	-1.67117	0.0001	0.0113094
ENSMUSG00000026259.14	Ngef	11.0126	17.9847	0.707619	2.38152	0.00005	0.00618632
ENSMUSG00000026272.6	Agxt	102.981	151.74	0.559222	2.16773	0.00005	0.00618632
ENSMUSG00000026348.7	Acmsd	7.89756	21.2665	1.42911	4.87646	0.00005	0.00618632
ENSMUSG00000026390.7	Marco	4.48507	2.16164	-1.05301	-2.28692	0.00005	0.00618632
ENSMUSG00000026566.15	Mpzl1	6.70294	2.77735	-1.27108	-2.14427	0.00025	0.0235
ENSMUSG00000026614.7	Slc30a10	12.8176	6.44774	-0.991257	-3.4987	0.00005	0.00618632
ENSMUSG00000026839.17	Upp2	60.7617	218.9	1.84904	6.12168	0.00005	0.00618632
ENSMUSG00000026864.13	Hspa5	833.809	437.932	-0.929011	-2.08676	0.00015	0.0159662

ENSMUSG00000027253.15	Lrp4	4.77798	7.06684	0.564666	2.03091	0.0002	0.0194309
ENSMUSG00000027331.15	Knstrn	0.217572	1.42377	2.71015	1.00013	0.00015	0.0159662
ENSMUSG00000027346.15	Gpcpd1	23.2178	53.4558	1.20312	3.25032	0.00005	0.00618632
ENSMUSG00000027398.13	Il1b	3.56328	1.05211	-1.75992	-2.14464	0.0001	0.0113094
ENSMUSG00000027533.10	Fabp5	26.5272	16.0182	-0.727761	-2.43622	0.00005	0.00618632
ENSMUSG00000027890.17	Gstm4	22.8624	40.384	0.820811	3.1403	0.00005	0.00618632
ENSMUSG00000028019.9	Pdgfc	2.88046	1.70807	-0.753934	-1.99822	0.0006	0.043428
ENSMUSG00000028238.6	Atp6v0d2	5.25254	9.46139	0.849037	2.4918	0.00005	0.00618632
ENSMUSG00000028383.17	Hsdl2	27.8303	19.1411	-0.539983	-2.08801	0.0003	0.0264805
ENSMUSG00000028479.18	Gne	79.8364	128.18	0.683054	2.04104	0.00065	0.0456767
ENSMUSG00000028715.2	Cyp4a14	391.915	237.782	-0.720899	-2.27606	0.00015	0.0159662
ENSMUSG00000028957.12	Per3	1.72562	11.0867	2.68365	4.12698	0.00005	0.00618632
ENSMUSG00000028976.10	Slc2a5	0.440546	1.76822	2.00493	1.65217	0.00065	0.0456767
ENSMUSG00000029009.17	Mthfr	7.11418	2.70437	-1.3954	-2.97286	0.00005	0.00618632
ENSMUSG00000029188.14	Slc34a2	1.55125	0.246171	-2.65571	-2.62671	0.00005	0.00618632
ENSMUSG00000029650.10	Slc46a3	31.8414	52.3096	0.71617	2.06244	0.0003	0.0264805
ENSMUSG00000029657.15	Hsph1	47.0702	27.7613	-0.761739	-2.01922	0.00025	0.0235
ENSMUSG00000030244.7	Gys2	36.9491	64.0714	0.794143	2.09027	0.00055	0.0404152
ENSMUSG00000030302.16	Atp2b2	4.35972	2.18107	-0.999203	-2.83779	0.00005	0.00618632
ENSMUSG00000030340.16	Scnn1a	6.11295	9.11203	0.575904	2.05878	0.00065	0.0456767
ENSMUSG00000030364.6	Clec2h	1.55662	4.31177	1.46986	2.18053	0.00005	0.00618632
ENSMUSG00000030483.14	Cyp2b10	17.2776	94.9368	2.45806	8.74658	0.00005	0.00618632
ENSMUSG00000031271.14	Serpina7	9.22525	4.97408	-0.891158	-2.09026	0.0004	0.033088
ENSMUSG00000031596.15	Slc7a2	85.9182	171.302	0.995503	2.42586	0.00005	0.00618632
ENSMUSG00000031762.7	Mt2	14.5776	52.8041	1.8569	4.62578	0.00005	0.00618632
ENSMUSG00000031765.8	Mt1	41.3184	148.541	1.84601	6.05154	0.00005	0.00618632
ENSMUSG00000031775.5	Pllp	6.14127	2.78882	-1.13888	-2.14469	0.00045	0.0359901
ENSMUSG00000032012.8	Nectin1	24.696	17.389	-0.506108	-1.94543	0.00055	0.0404152
ENSMUSG00000032115.14	Hyou1	66.9891	43.0138	-0.639125	-2.34774	0.00005	0.00618632
ENSMUSG00000032271.13	Nnmt	56.5371	127.246	1.17034	4.24758	0.00005	0.00618632
ENSMUSG00000032310.4	Cyp1a2	345.376	2354.78	2.76935	6.42721	0.00005	0.00618632
ENSMUSG00000032315.6	Cyp1a1	0.408235	21.3863	5.71114	10.8865	0.00005	0.00618632
ENSMUSG00000032348.6	Gsta4	52.469	81.8235	0.641049	2.47242	0.00005	0.00618632
ENSMUSG00000032575.16	Manf	237.772	126.916	-0.905701	-2.11863	0.0003	0.0264805
ENSMUSG00000032715.9	Trib3	3.62747	8.68618	1.25976	2.03279	0.00035	0.029457
ENSMUSG00000032724.5	Abtb2	5.87529	3.77695	-0.637439	-2.04753	0.0004	0.033088
ENSMUSG00000032849.14	Abcc4	1.71548	3.77068	1.13622	2.61385	0.00005	0.00618632
ENSMUSG00000032902.1	Slc16a1	18.9328	10.1797	-0.8952	-3.40735	0.00005	0.00618632
ENSMUSG00000032932.15	Hspa13	14.303	9.86525	-0.535886	-1.97593	0.00025	0.0235
ENSMUSG00000033107.6	Rnf125	122.257	74.8678	-0.707494	-2.81318	0.00005	0.00618632
ENSMUSG00000033581.17	Igf2bp2	1.66105	0.509047	-1.70623	-1.12591	0.0003	0.0264805
ENSMUSG00000034774.6	Dsg1c	1.07675	2.19221	1.0257	2.76946	0.0001	0.0113094
ENSMUSG00000034837.12	Gnat1	12.5088	21.0651	0.751915	2.1181	0.00035	0.029457
ENSMUSG00000035049.4	Rrp12	2.74802	1.48642	-0.886549	-2.6113	0.00005	0.00618632
ENSMUSG00000035372.2	1810055G	6.32408	10.8725	0.781761	1.96938	0.00035	0.029457
ENSMUSG00000035686.8	Thrsp	107.955	205.081	0.925768	3.34836	0.00005	0.00618632
ENSMUSG00000035828.11	Pim3	5.46211	9.62427	0.81722	2.71331	0.00005	0.00618632
ENSMUSG00000035944.17	Ttc38	14.0742	20.1391	0.516941	1.96377	0.00055	0.0404152
ENSMUSG00000036110.14	Slc17a2	47.9669	31.78	-0.59392	-2.07519	0.00015	0.0159662
ENSMUSG00000036957.8	Lrfn3	2.96637	1.17429	-1.33691	-3.36685	0.00005	0.00618632
ENSMUSG00000037095.8	Lrg1	67.2168	47.361	-0.505121	-1.98627	0.00065	0.0456767

ENSMUSG00000037157.8	Il22ra1	3.93685	2.30756	-0.770677	-2.21827	0.0002	0.0194309
ENSMUSG00000037379.7	Spon2	4.43994	1.82471	-1.28287	-2.45754	0.00005	0.00618632
ENSMUSG00000037583.2	Nr0b2	25.807	16.3589	-0.657683	-2.30236	0.0002	0.0194309
ENSMUSG00000037679.9	Inf2	14.5959	21.2562	0.542318	1.95943	0.0005	0.0385
ENSMUSG00000038244.14	Mical2	7.57323	4.32506	-0.808189	-2.30005	0.00005	0.00618632
ENSMUSG00000038415.10	Foxq1	3.1372	4.80063	0.613744	2.07957	0.00045	0.0359901
ENSMUSG00000038418.7	Egr1	8.53806	14.7592	0.789639	2.33622	0.00015	0.0159662
ENSMUSG00000038550.10	Ciart	0.635327	4.26202	2.74597	2.5058	0.00005	0.00618632
ENSMUSG00000038702.6	Dsel	0.318647	1.1368	1.83495	1.59147	0.0005	0.0385
ENSMUSG00000038768.8	9130409I	1.69012	3.3601	0.991375	2.38357	0.0002	0.0194309
ENSMUSG00000039395.8	Mreg	31.446	22.0227	-0.513883	-2.00407	0.0005	0.0385
ENSMUSG00000039533.8	Mmd2	1.90734	4.59768	1.26934	2.91012	0.00005	0.00618632
ENSMUSG00000039745.8	Htatip2	13.6124	21.7983	0.679289	2.28578	0.0001	0.0113094
ENSMUSG00000039886.8	Tmem12(	16.7696	27.8392	0.731267	2.68188	0.00005	0.00618632
ENSMUSG00000040127.13	Sdr9c7	19.4072	11.0266	-0.815607	-2.73366	0.00005	0.00618632
ENSMUSG00000040128.9	Pnrc1	65.4718	42.3024	-0.630135	-2.33326	0.00005	0.00618632
ENSMUSG00000040264.10	Gbp2b	2.41906	1.40646	-0.782373	-1.95544	0.0007	0.0487173
ENSMUSG00000040562.12	Gstm2	44.3194	85.0048	0.939604	3.60356	0.00005	0.00618632
ENSMUSG00000041324.14	Inhba	9.86411	3.40919	-1.53276	-3.38139	0.00005	0.00618632
ENSMUSG00000041698.11	Slco1a1	51.4801	33.2839	-0.62919	-2.3143	0.00005	0.00618632
ENSMUSG00000042115.4	Klhdc8a	0.80677	0.334395	-1.2706	-2.44981	0.00025	0.0235
ENSMUSG00000042363.14	Lgalsl	8.00763	4.41853	-0.857811	-2.18413	0.00005	0.00618632
ENSMUSG00000042622.14	Maff	1.85114	4.3513	1.23303	2.48105	0.00005	0.00618632
ENSMUSG00000043445.7	Pgp	4.53206	2.65663	-0.770568	-2.30203	0.00005	0.00618632
ENSMUSG00000044071.8	Tafa2	0.48376	1.16023	1.26205	2.303	0.0003	0.0264805
ENSMUSG00000044847.13	Lsm11	0.880467	0.334164	-1.39771	-2.60413	0.00005	0.00618632
ENSMUSG00000045287.6	Rtn4rl1	6.68976	3.11675	-1.10191	-3.68259	0.00005	0.00618632
ENSMUSG00000046402.10	Rbp1	2.23594	3.74793	0.745215	2.09243	0.0003	0.0264805
ENSMUSG00000046541.9	Zfp526	1.73728	3.00717	0.791579	2.28551	0.0001	0.0113094
ENSMUSG00000047617.11	Paxx	39.0765	17.0249	-1.19866	-2.96755	0.00005	0.00618632
ENSMUSG00000052305.6	Hbb-bs	63.8974	36.6592	-0.80158	-2.85373	0.00005	0.00618632
ENSMUSG00000052496.5	Pkdrej	0.475661	1.0218	1.10311	2.72703	0.00005	0.00618632
ENSMUSG00000052676.16	Zmat1	4.08129	6.4258	0.654851	2.13824	0.00025	0.0235
ENSMUSG00000052684.4	Jun	7.97305	4.26725	-0.901823	-3.1051	0.00005	0.00618632
ENSMUSG00000053113.3	Socs3	2.49474	5.38121	1.10904	2.11745	0.0003	0.0264805
ENSMUSG00000053559.13	Smagp	31.1285	19.9458	-0.642154	-2.13389	0.00035	0.029457
ENSMUSG00000054191.8	Klf1	1.62248	3.2131	0.985766	2.18554	0.00045	0.0359901
ENSMUSG00000054277.8	Arfgap3	4.95607	2.07293	-1.25753	-2.8446	0.00005	0.00618632
ENSMUSG00000054417.5	Cyp3a44	25.8573	17.1078	-0.595916	-2.16753	0.0002	0.0194309
ENSMUSG00000054659.13	Pm20d2	3.10156	1.32451	-1.22753	-2.48902	0.0002	0.0194309
ENSMUSG00000054827.12	Cyp2c50	357.009	627.067	0.812659	2.57099	0.00005	0.00618632
ENSMUSG00000055116.8	Arntl	9.41997	3.72741	-1.33755	-3.70408	0.00005	0.00618632
ENSMUSG00000055254.15	Ntrk2	1.32876	2.94734	1.14933	1.80865	0.0003	0.0264805
ENSMUSG00000056666.13	Retsat	163.179	84.9098	-0.942452	-2.9787	0.00005	0.00618632
ENSMUSG00000056749.7	Nfil3	11.3496	6.37484	-0.832181	-2.80945	0.00005	0.00618632
ENSMUSG00000057069.7	Ero1lb	12.7588	7.57204	-0.752743	-2.69188	0.00005	0.00618632
ENSMUSG00000057933.10	Gsta2	14.8876	36.6186	1.29846	4.13678	0.00005	0.00618632
ENSMUSG00000058135.12	Gstm1	591.115	1077.86	0.866655	2.73107	0.00005	0.00618632
ENSMUSG00000058454.15	Dhcr7	16.2573	24.4437	0.588377	1.73799	0.00045	0.0359901
ENSMUSG00000058569.8	Tmed9	27.8989	18.8487	-0.565745	-2.03359	0.00055	0.0404152
ENSMUSG00000058571.11	Gpc6	0.925695	2.30111	1.31372	2.76731	0.00005	0.00618632

ENSMUSG00000058672.7	Tubb2a	60.0095	29.3901	-1.02986	-3.68327	0.00005	0.00618632
ENSMUSG00000059060.15	Rad51b	2.96318	0.790659	-1.90602	-2.70012	0.00005	0.00618632
ENSMUSG00000060317.9	Acnat2	62.994	36.0946	-0.803432	-3.04246	0.00005	0.00618632
ENSMUSG00000060550.16	H2-Q7	26.9214	17.4807	-0.622989	-2.11728	0.0002	0.0194309
ENSMUSG00000060803.6	Gstp1	52.2482	94.5054	0.855015	3.20267	0.00005	0.00618632
ENSMUSG00000060807.7	Serpina6	169.985	262.86	0.628886	2.32333	0.00005	0.00618632
ENSMUSG00000061080.11	Lsamp	1.22575	0.291018	-2.07448	-1.14479	0.0001	0.0113094
ENSMUSG00000061601.15	Pclo	0.57566	0.977399	0.763729	2.10847	0.00035	0.029457
ENSMUSG00000061825.10	Ces2c	4.3022	11.1216	1.37022	4.14522	0.00005	0.00618632
ENSMUSG00000063415.12	Cyp26b1	6.19951	2.65142	-1.22539	-4.09556	0.00005	0.00618632
ENSMUSG00000064225.6	Paqr9	57.3054	30.826	-0.894525	-3.17638	0.00005	0.00618632
ENSMUSG00000064605.3	Gm22220	0	7.00551	#NUM!	#NUM!	0.00005	0.00618632
ENSMUSG00000066154.11	Mup3	2026.5	1252.6	-0.694063	-2.02644	0.00045	0.0359901
ENSMUSG00000067199.4	Frat1	3.39578	1.93858	-0.808739	-2.24788	0.0002	0.0194309
ENSMUSG00000067219.9	Nipal1	4.44909	8.25715	0.892133	2.59416	0.00005	0.00618632
ENSMUSG00000067225.2	Cyp2c54	161.282	296.593	0.878904	3.09255	0.00005	0.00618632
ENSMUSG00000067279.3	Ppp1r3c	27.4578	14.4551	-0.925639	-3.55848	0.00005	0.00618632
ENSMUSG00000069668.4	Sult3a1	96.5726	152.327	0.657483	2.4394	0.00005	0.00618632
ENSMUSG00000069917.7	Hba-a2	15.9522	7.92925	-1.0085	-2.53543	0.00005	0.00618632
ENSMUSG00000069919.7	Hba-a1	123.857	80.1852	-0.627271	-2.30735	0.0002	0.0194309
ENSMUSG00000070348.5	Ccnd1	28.8011	18.0061	-0.677632	-2.00581	0.00015	0.0159662
ENSMUSG00000070644.13	Etnk2	62.1735	97.5737	0.650192	2.3878	0.00005	0.00618632
ENSMUSG00000072949.6	Acot1	33.5979	19.9522	-0.751821	-2.2701	0.0002	0.0194309
ENSMUSG00000073700.3	Klhl21	4.84991	8.7584	0.85271	3.05752	0.00005	0.00618632
ENSMUSG00000074240.4	Cib3	0.143641	2.40529	4.06566	2.29099	0.00035	0.029457
ENSMUSG00000074277.4	Phldb3	4.05555	2.40923	-0.751325	-1.90668	0.00045	0.0359901
ENSMUSG00000075602.10	Ly6a	9.16001	4.67716	-0.969716	-2.31759	0.00005	0.00618632
ENSMUSG00000078566.8	Bnip3	89.9067	133.144	0.566486	1.97231	0.00055	0.0404152
ENSMUSG00000078650.2	G6pc	117.921	34.0649	-1.79147	-6.18411	0.00005	0.00618632
ENSMUSG00000078672.2	Mup20	28.4851	45.4009	0.672516	2.49254	0.00005	0.00618632
ENSMUSG00000078798.4	Sult2a1	56.1121	88.0628	0.650222	2.29294	0.0002	0.0194309
ENSMUSG00000078964.2	Ces1b	38.6623	59.9889	0.633769	2.50962	0.00005	0.00618632
ENSMUSG00000081207.4	Gm13775	12.4095	21.5678	0.797432	2.15377	0.00005	0.00618632
ENSMUSG00000083409.1	Gm11340	7.21515	2.24671	-1.68321	-2.46551	0.00055	0.0404152
ENSMUSG00000083832.1	Gm13771	1.8277	0	#NUM!	#NUM!	0.0005	0.0385
ENSMUSG00000084923.1	Gm15611	21.0683	6.28033	-1.74616	-3.69593	0.00005	0.00618632
ENSMUSG00000085445.1	Gm16348	0.992266	3.40219	1.77767	3.9325	0.00005	0.00618632
ENSMUSG00000090298.2	Sult3a2	3.37105	7.75229	1.20143	2.72803	0.00005	0.00618632
ENSMUSG00000090877.3	Hspa1b	1.20366	0.247192	-2.28373	-3.46215	0.00005	0.00618632
ENSMUSG00000092075.1	Serpina4-	21.3086	5.73997	-1.89232	-5.72874	0.00005	0.00618632
ENSMUSG00000093183.2	Gm25687	30.7806	63.7545	1.0505	2.67769	0.00005	0.00618632
ENSMUSG00000099021.1	Rn7s1	700.234	447.929	-0.644568	-2.2057	0.0003	0.0264805
ENSMUSG00000100277.8	1810053E	0.727864	4.99681	2.77927	2.15033	0.00005	0.00618632
ENSMUSG00000106069.1	Gm6135	34.0333	18.6619	-0.866848	-2.29436	0.00015	0.0159662
ENSMUSG00000106397.1	Gm21049	4.50211	8.69691	0.949903	2.48844	0.0001	0.0113094
ENSMUSG00000107369.1	Gstm2-ps	5.28283	9.53136	0.851371	2.01229	0.0007	0.0487173
ENSMUSG00000107451.1	Gm44421	1.80148	3.62615	1.00925	2.14888	0.0006	0.043428
ENSMUSG00000108822.1	Gm44787	1.69451	5.98364	1.82015	2.27612	0.00005	0.00618632
ENSMUSG00000110353.1	Gm33543	7.64038	13.1396	0.782206	2.39977	0.00005	0.00618632
ENSMUSG00000110439.1	Mup22	99.9007	68.6497	-0.541243	-2.05099	0.00065	0.0456767
ENSMUSG00000111923.1	Gm34777	2.67348	4.37875	0.711799	2.03435	0.0005	0.0385

ENSMUSG00000113387.1	Gm31508	1.24582	0.612387	-1.02458	-2.20024	0.0004	0.033088
ENSMUSG00000115509.1	Gm49012	1.8745	0.444212	-2.07719	-3.09822	0.0001	0.0113094
ENSMUSG00000117879.1	AC138228	8.67119	4.72504	-0.875903	-2.12505	0.0003	0.0264805
ENSMUSG00000118017.1	AC15791(	211.714	108.509	-0.964301	-1.99521	0.0005	0.0385

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000004038.9	Gstm3	38.0431	58.9022	0.630687	2.46013	0.00005	0.0145745
ENSMUSG00000017119.19	Nbr1	76	156.094	1.03834	3.08994	0.00005	0.0145745
ENSMUSG00000018427.7	Ypel2	5.3982	3.31232	-0.704637	-2.41028	0.00005	0.0145745
ENSMUSG00000020027.18	Socs2	13.2242	6.3375	-1.0612	-2.2998	0.00005	0.0145745
ENSMUSG00000020429.7	Igfbp1	53.6002	26.8102	-0.999456	-3.89039	0.00005	0.0145745
ENSMUSG00000020893.17	Per1	3.68334	6.25289	0.76351	2.15347	0.00005	0.0145745
ENSMUSG00000021288.18	Klc1	12.9409	6.37187	-1.02214	-2.07132	0.00015	0.0387736
ENSMUSG00000021453.2	Gadd45g	4.11008	1.45737	-1.4958	-2.59523	0.00005	0.0145745
ENSMUSG00000022508.5	Bcl6	2.65652	4.42275	0.735406	2.26063	0.0002	0.0472414
ENSMUSG00000022512.3	Cldn1	26.1421	15.2533	-0.777248	-3.02367	0.00005	0.0145745
ENSMUSG00000024987.6	Cyp26a1	7.22284	16.3768	1.18101	3.76685	0.00005	0.0145745
ENSMUSG00000026822.14	Lcn2	3.61183	6.99576	0.953752	2.06076	0.0002	0.0472414
ENSMUSG00000026839.17	Upp2	141.068	212.088	0.588275	2.19764	0.0002	0.0472414
ENSMUSG00000026980.15	Ly75	1.02455	1.86615	0.865078	2.35758	0.0001	0.0268627
ENSMUSG00000027533.10	Fabp5	20.9053	11.7917	-0.826097	-2.64221	0.00005	0.0145745
ENSMUSG00000027796.2	Smad9	3.96217	1.89784	-1.06193	-3.47194	0.00005	0.0145745
ENSMUSG00000028445.7	Enho	5.8256	2.52464	-1.20633	-2.74623	0.00005	0.0145745
ENSMUSG00000029272.8	Sult1e1	3.01955	12.0294	1.99416	4.46773	0.00005	0.0145745
ENSMUSG00000032310.4	Cyp1a2	580.244	1032.94	0.832029	2.805	0.00005	0.0145745
ENSMUSG00000035686.8	Thrsp	75.4226	108.929	0.530321	2.11579	0.00015	0.0387736
ENSMUSG00000036594.15	H2-Aa	12.3664	24.7286	0.999753	3.13856	0.00005	0.0145745
ENSMUSG00000037847.14	Nmrk1	8.65751	16.9132	0.966125	2.32446	0.00005	0.0145745
ENSMUSG00000038418.7	Egr1	13.1471	6.28833	-1.064	-3.7676	0.00005	0.0145745
ENSMUSG00000038656.5	Cyp3a16	7.12851	15.836	1.15154	3.67862	0.00005	0.0145745
ENSMUSG00000039457.4	Ppl	4.08077	7.12185	0.803411	2.80195	0.00005	0.0145745
ENSMUSG00000041698.11	Slco1a1	21.356	5.97873	-1.83673	-5.94679	0.00005	0.0145745
ENSMUSG00000050423.11	Ppp1r3g	2.1755	0.629848	-1.78827	-2.64187	0.00005	0.0145745
ENSMUSG00000050445.4	Cyp8b1	29.9766	12.9283	-1.2133	-3.83764	0.00005	0.0145745
ENSMUSG00000055116.8	Arntl	4.50112	1.45834	-1.62596	-3.46099	0.00005	0.0145745
ENSMUSG00000057346.12	Apol9a	19.3931	32.688	0.753217	2.48492	0.00005	0.0145745
ENSMUSG00000057897.14	Camk2b	0.84208	2.11891	1.33129	1.48241	0.0002	0.0472414
ENSMUSG00000061825.10	Ces2c	4.35545	8.60041	0.981582	2.97034	0.00005	0.0145745
ENSMUSG00000063388.5	BC023105	3.59428	6.85076	0.930563	2.34984	0.0001	0.0268627
ENSMUSG00000064225.6	Paqr9	35.9574	23.9919	-0.583741	-2.37141	0.00005	0.0145745
ENSMUSG00000070811.6	Sult2a2	45.0135	98.3588	1.12769	3.25888	0.00005	0.0145745
ENSMUSG00000072849.10	Serpina1e	78.1579	34.9136	-1.1626	-4.35291	0.00005	0.0145745
ENSMUSG00000073421.6	H2-Ab1	23.9638	51.1132	1.09284	2.55741	0.00005	0.0145745
ENSMUSG00000074375.3	Sult2a3	0.913931	5.76955	2.6583	3.99495	0.0001	0.0268627
ENSMUSG00000075551.4	Cyp3a41a	26.1917	45.374	0.79276	3.08305	0.00005	0.0145745
ENSMUSG00000075552.4	Cyp3a41b	2.76118	6.39617	1.21192	3.37149	0.00005	0.0145745
ENSMUSG00000078650.2	G6pc	83.6587	38.114	-1.1342	-4.05012	0.00005	0.0145745
ENSMUSG00000078798.4	Sult2a1	36.972	91.5233	1.30771	4.24884	0.00005	0.0145745
ENSMUSG00000078799.5	Sult2a5	2.28821	5.90122	1.36679	2.19044	0.0002	0.0472414
ENSMUSG00000078817.4	Nlrp12	6.13793	3.48939	-0.814775	-2.95155	0.00005	0.0145745
ENSMUSG00000082008.1	Gm12390	0	2.18739	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000086316.8	Nbdy	0.965126	9.08573	3.23481	2.3883	0.00005	0.0145745
ENSMUSG00000092674.2	Gm24105	94.9427	153.292	0.691157	2.26807	0.00005	0.0145745
ENSMUSG00000093183.2	Gm25687	16.9584	55.347	1.7065	3.05133	0.00005	0.0145745
ENSMUSG00000096768.8	Gm47283	21.0555	8.4086	-1.32426	-3.46356	0.00005	0.0145745
ENSMUSG00000099901.1	Zbed4-ps2	3.94207	10.8342	1.45857	2.99773	0.00005	0.0145745
ENSMUSG00000101397.6	Mug-ps1	34.2915	22.1456	-0.630835	-2.52439	0.00005	0.0145745

ENSMUSG00000105192.1	Gm42796	9.81164	3.82683	-1.35835	-2.85412	0.00005	0.0145745
ENSMUSG00000107185.1	Gm42642	1.32544	0	#NUM!	#NUM!	0.0001	0.0268627
ENSMUSG00000109089.1	4833411C	13.8725	7.63832	-0.860895	-2.57638	0.00005	0.0145745
ENSMUSG00000110439.1	Mup22	64.7271	39.1905	-0.723867	-2.61227	0.00005	0.0145745
ENSMUSG00000110838.1	Gm47789	1.24793	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000111253.1	Gm34654	1.07187	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000117780.1	AC127342	13.9016	5.9063	-1.23493	-4.21178	0.00005	0.0145745

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000003053.17	Cyp2c29	673.766	1232.86	0.871696	2.7636	0.00005	0.0237172
ENSMUSG00000025002.5	Cyp2c55	5.10794	9.57033	0.905826	2.8894	0.00005	0.0237172
ENSMUSG00000026185.8	Igfbp5	4.14362	7.52489	0.860778	3.06263	0.00005	0.0237172
ENSMUSG00000028238.6	Atp6v0d2	14.2949	8.46584	-0.755773	-2.57671	0.0001	0.0404588
ENSMUSG00000030428.16	Ttyh1	7.83723	20.5459	1.39044	3.46049	0.00005	0.0237172
ENSMUSG00000030483.14	Cyp2b10	18.4894	34.553	0.902114	3.34575	0.00005	0.0237172
ENSMUSG00000032310.4	Cyp1a2	573.897	1767.5	1.62285	4.7819	0.00005	0.0237172
ENSMUSG00000033107.6	Rnf125	119.634	73.9456	-0.694086	-2.68283	0.00005	0.0237172
ENSMUSG00000035202.8	Lars2	37.9931	16.2798	-1.22265	-3.96694	0.00005	0.0237172
ENSMUSG00000037583.2	Nr0b2	19.8513	11.5096	-0.786389	-2.59725	0.0001	0.0404588
ENSMUSG00000038656.5	Cyp3a16	7.05363	15.3354	1.12043	3.49577	0.00005	0.0237172
ENSMUSG00000050445.4	Cyp8b1	29.6178	11.0736	-1.41934	-4.51314	0.00005	0.0237172
ENSMUSG00000054417.5	Cyp3a44	19.7219	34.2151	0.794836	3.04706	0.00005	0.0237172
ENSMUSG00000055116.8	Arntl	4.44971	1.11565	-1.99583	-4.29871	0.00005	0.0237172
ENSMUSG00000060803.6	Gstp1	38.6763	66.8057	0.788521	2.91206	0.00005	0.0237172
ENSMUSG00000061825.10	Ces2c	4.30826	10.0339	1.21971	3.75254	0.00005	0.0237172
ENSMUSG00000069917.7	Hba-a2	12.5054	28.9749	1.21225	3.16461	0.00005	0.0237172
ENSMUSG00000069919.7	Hba-a1	161.435	257.664	0.674535	2.60695	0.00005	0.0237172
ENSMUSG00000072849.10	Serpina1e	77.2634	33.2336	-1.21714	-4.58994	0.00005	0.0237172
ENSMUSG00000073940.3	Hbb-bt	11.4866	32.257	1.48966	4.17862	0.00005	0.0237172
ENSMUSG00000075551.4	Cyp3a41a	25.9157	41.7969	0.689571	2.51749	0.0001	0.0404588
ENSMUSG00000075552.4	Cyp3a41b	2.73222	5.71036	1.06351	2.88173	0.00005	0.0237172
ENSMUSG00000078650.2	G6pc	82.715	52.4814	-0.656343	-2.57516	0.0001	0.0404588
ENSMUSG00000078798.4	Sult2a1	36.5984	71.0306	0.95666	3.13829	0.00005	0.0237172
ENSMUSG00000083563.1	Gm13340	22.2303	36.8976	0.731	2.47186	0.0001	0.0404588
ENSMUSG00000092674.2	Gm24105	93.8984	264.708	1.49523	4.56281	0.00005	0.0237172
ENSMUSG00000096768.8	Gm47283	20.8212	9.60095	-1.1168	-3.03589	0.00005	0.0237172
ENSMUSG00000096887.2	Gm20594	84.8472	147.632	0.799063	2.84097	0.00005	0.0237172
ENSMUSG00000098973.1	Mir6236	2424.83	1036.7	-1.22589	-4.1389	0.00005	0.0237172
ENSMUSG00000100131.1	Gm28439	7.92885	17.6712	1.15622	2.9385	0.00005	0.0237172
ENSMUSG00000101111.1	Gm28437	27.3548	48.503	0.826281	2.816	0.00005	0.0237172
ENSMUSG00000102189.1	Gm37194	1.33501	3.28318	1.29824	3.26943	0.00005	0.0237172
ENSMUSG00000115420.1	Rmrp	783.954	1427.45	0.864595	2.95006	0.00005	0.0237172
ENSMUSG00000117780.1	AC127342	13.7433	7.49599	-0.874538	-3.05459	0.00005	0.0237172

Table S2A. Liver metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	0.6417779	0.7530381	0.8854124	1.3165750	1.0407458	0.7608884	0.9882787	0.7862970	1.0625771	1.1283548	1.2155264	1.1977029	1.1177079	1.0111845	0.9166488	1.1527351	0.5878772	1.3592881	0.8895624	1.4278042	0.6871709	0.9504117	0.5052311	0.9326832
Indole-3-acetic.acid	0.7860392	1.9509565	0.5580886	1.5278171	1.0873190	0.7463817	0.1771168	0.3526087	0.4630552	0.5291279	0.7148218	0.4862421	0.5835993	0.4962891	0.7906378	1.5020283	0.6540461	1.0075090	1.0404164	0.8920219	0.2602962	0.5700573	0.5769496	0.6458184
Indole-3-pyruvic.acid	0.06424609	1.10713323	0.19021050	0.33843027	0.11897162	0.46282540	0.37132059	0.22765562	0.18087326	0.38830899	0.02884164	0.26659506	0.14896618	0.51208752	0.16279090	0.28747783	0.37848709	0.37283283	0.00000000	0.14392771	0.29731054	1.18302681	0.16473559	0.51285387
Kynurenine	1.5130420	1.8160458	1.1177367	3.3235912	1.4236657	1.8332443	0.4968082	0.4627796	1.0845344	1.1908755	0.8681831	1.3064311	1.4310919	1.0449380	0.7998276	2.0758060	0.9268621	1.9954938	1.5519350	2.5454728	1.1179864	2.3883236	0.7527254	1.1935632
2-Deoxycytidine	0.1456107	0.2046070	0.1144417	0.2018454	0.2570833	0.1523639	0.1548636	0.2199208	0.2156768	0.4964199	0.3365320	0.2922682	0.4379804	0.2772534	0.1278656	0.3985392	0.1284519	0.4021005	0.3026561	0.2529262	0.1450090	0.1766973	0.2007113	0.5602648
2-aminoadipic.acid	0.4075929	1.8351217	0.9447126	1.2758676	0.8124402	0.8410186	0.4128866	0.5227665	1.3971905	0.9069514	1.2938552	0.6817271	0.8004980	0.8948402	0.7905779	1.0971095	1.0229457	1.4079170	1.8391106	1.8948830	5.3693974	5.3069206	0.8495688	1.1904178
2-deoxyguanosine	0.58479568	0.00000000	0.00000000	0.44162009	0.58363951	0.00000000	1.63457253	0.37970606	0.00000000	0.38769672	0.06838577	0.19997020	0.80554615	0.29129296	0.00000000	0.23430805	0.06706320	1.46333000	0.00000000	0.15525769	0.00000000	0.00000000	0.00000000	0.52384648
3-Aminoisobutyric.acid	0.3103612	0.2316226	0.2791112	0.3631104	0.2398946	0.2452838	0.2880905	0.1962715	0.3782312	0.3797402	0.3751967	0.2140135	0.2781475	0.3356190	0.1825315	0.3856304	0.1752509	0.4551243	0.3276935	0.3667051	0.3028023	0.3385240	0.2649583	0.2924743
3-Hydroxybutyric.acid	1.7156741	0.6825009	1.6340875	0.7728069	0.6845594	3.0031276	1.4763494	1.4043569	1.8066952	0.5647619	0.8475344	1.0578820	1.6273289	2.9045689	1.5403997	1.5944642	0.5934880	0.8834803	0.6819804	0.8640724	0.8097863	0.9743788	1.3148739	1.5162630
4-Aminobutyric.acid	0.5156079	0.9141045	1.1005954	2.3476444	1.3140889	0.7357734	0.6096718	0.4719302	1.4989862	1.1886618	1.0745111	1.6027557	1.1806124	1.5513006	1.0620008	0.9948536	1.2875127	1.3189201	2.1056291	2.6841771	1.0229754	1.3207144	0.4810400	1.0543936
5-Aminolevulinic.acid	0.2867715	0.8398926	0.2810464	0.2019449	0.1020569	0.1164548	0.2761496	0.1963395	0.2273984	0.1812200	0.3716822	0.2694858	0.2225276	0.2574289	0.3098547	0.4189624	0.1705895	0.4910491	0.4734825	0.3410167	0.8565262	0.8064531	0.3156030	0.4568366
5-Methylcytidine	2.6366484	2.3470198	0.7913250	3.1443083	4.0459524	1.9228826	0.8837537	2.5323469	0.7833072	1.5051036	2.2849148	2.9870170	2.6811237	2.1907469	1.9084163	3.1802859	1.1070842	2.1720066	2.3003041	2.3661019	1.8300040	3.8581447	1.5396344	1.0123362
7-ketocholesterol	1.2891896	1.0073455	0.8360030	0.4664388	1.2795914	1.3383909	1.0546935	1.9164554	0.4051727	0.6767182	0.4498655	0.7065973	0.6043564	1.3701550	1.0951610	1.3300680	1.3873236	1.1263964	0.3944428	0.9683976	0.9645003	0.7742208	0.6170155	2.0484274
Acetyl-L-glutamine	0.4553014	0.4776746	0.4556176	1.1360893	0.4899839	0.4115659	0.4724127	0.3995740	0.7519312	0.7612600	0.5757849	0.8012261	0.9084725	0.7581108	0.5658879	0.6871090	0.4090363	0.6004718	0.4349892	0.7548255	0.3635997	0.5794367	0.3717956	0.6783111
Acetylcarnitine	0.02915257	0.05742605	0.04085568	0.04646320	0.01610918	0.02863787	0.02092485	0.04034642	0.02849962	0.03521710	0.03001347	0.03903095	0.06032182	0.06379381	0.03554116	0.08904216	0.13924858	0.08820948	0.25276956	0.11555283	0.15110799	0.11136802	0.18095977	0.19759626
Acetylglucosamine	1.3115664	1.2280059	1.0550751	1.8277008	1.5382448	0.8317039	0.9006399	0.7437013	0.8639561	1.1169542	1.2680750	1.4683521	0.8830023	1.0020359	1.2230501	1.0899670	0.6023287	1.6330727	1.0205687	1.5326382	0.7522740	0.9907671	0.6387737	1.1292635
Acetylglycine	0.2617616	1.5929109	1.2342161	2.1902251	2.0066785	1.0029190	1.9138947	0.8145704	1.6919136	2.5442625	2.4643134	1.7957466	0.2814305	0.3470204	1.2344673	0.8244505	0.2272679	2.3645095	0.3638673	0.9529061	1.4823383	0.8343840	1.0978394	0.7816405
Acetylornithine	0.23480651	0.10218698	0.15858941	0.19771777	0.62851733	0.05134179	0.18836825	0.08521779	0.11193669	0.26567215	0.32023260	0.26012605	0.47490123	1.12893094	0.14985087	0.74458555	0.45819030	1.06512125	0.75622866	0.72796858	0.76879026	0.70500716	0.82648159	0.71440786
Adenosine	0.3581978	0.5481528	0.5538759	0.5637655	0.7135748	0.7417769	0.9125724	0.7036831	1.2996513	1.2692738	1.3658697	0.8970467	0.9973923	1.5460150	0.6196735	1.0165961	0.6620103	2.0082194	1.1925067	0.4137528	1.0192838	1.0090414	1.8101009	1.6507011
Adenosyl-L-homocysteine	0.3163094	0.6499900	0.5642770	0.6660210	0.7347727	0.6880711	0.7655124	0.5100250	1.0084109	1.0896944	1.0674588	0.8004986	0.6242744	1.0607179	0.5468198	0.8729612	0.5892073	1.5979238	1.2145764	1.4491398	0.8496154	1.1124521	0.8608683	1.2268764
Adenylosuccinate	0.03907467	0.10987980	0.07196339	0.18365262	0.02049657	0.18750397	0.10259660	0.10153863	0.17733045	0.22357127	0.13469431	0.08656620	0.13093812	0.10786607	0.06330485	0.11795322	0.09404531	0.17072564	0.16554603	0.07081627	0.25297802	0.31067335	0.16538933	0.14309574
Alanine	0.8571079	0.8937346	1.2829469	1.2536040	1.3312153	1.0258898	0.9927881	0.8043505	1.3840192	1.2575998	1.3394220	1.3339071	1.3476500	1.2322631	0.9589156	1.1416117	0.9940162	1.2597832	1.1339764	1.4759244	1.1721014	1.4205798	0.6686826	0.9158186
Aminoisobutyric.acid	0.4493258	0.5828958	0.6461483	0.8794325	0.4539889	0.6068997	0.5862818	0.4553500	0.4213689	1.0816655	0.7381336	1.2356525	0.4183226	0.2992163	0.3076177	0.5605960	0.5548940	1.4832715	1.2783811	1.3008123	1.1644110	1.2625703	1.0386166	0.6530749
Arginine	0.5230813	0.8326213	0.3829666	0.3855671	0.2697902	0.3039470	0.3348270	0.2517091	0.3584439	0.5363771	0.4821799	0.4340597	0.5603556	0.3996499	0.4430393	0.4462321	0.3594968	0.3102111	0.5864398	0.2758807	0.1643636	0.2102865	0.2007999	0.3539812
Asparagine	0.8842260	0.8152583	0.9024042	1.3833165	1.2449474	0.9768765	1.1941756	0.9351111	0.9971121	1.3182055	1.2117728	1.3431893	1.1858922	0.9978230	1.2058328	1.2294066	0.6536824	1.4452643	1.2063691	1.3491411	0.8293748	1.0875278	0.7053539	0.9158058
Aspartic.acid	0.3762233	0.4292970	0.2857379	0.5451212	0.4423451	0.3255798	0.4889660	0.4377361	0.4992604	0.6124258	0.6449889	0.4799587	0.5048493	0.4952580	0.4067786	0.5631700	0.2476733	0.7353890	0.5144635	0.4634559	0.2357814	0.3112372	0.4857510	0.4860391
Betaine	0.7509563	0.7301263	0.6645387	0.8280204	0.7483555	0.7586245	0.6799378	0.7332552	0.5995388	1.1140138	0.9279227	1.0862676	0.7167985	0.4884979	0.8491893	1.0252541	0.6586413	1.5355912	0.9498598	1.0125740	0.7907893	0.8387790	1.0066512	1.0111870
Carnitine	0.4638704	0.6540949	0.5326691	1.0417368	0.7563746	0.5297869	0.5900569	0.5139531	0.7313478	0.9329322	0.8872217	0.9785690	1.1477622	0.8874642	0.6541203	1.1244702	0.7064974	1.6744503	1.3159400	1.4626136	0.9617662	1.2497777	0.6554014	1.3367312
Carnosine	0.1379304	0.1837529	0.1527487	0.3168994	0.2416656	0.1920351	0.2827001	0.2258543	0.2003689	0.5326479	0.2786935	0.3996725	0.3411534	0.1948664	0.1848126	0.3064725	0.2054774	0.4477849	0.3000470	0.4893805	0.2089623	0.2489793	0.1568765	0.2635589
Choline	0.7764507	0.8191480	0.6335699	0.6340663	0.8203244	0.6701257	0.8159180	0.6395891	0.6805273	0.9335008	0.9493801	1.0877272	0.6584530	0.8890556	0.3250131	0.9338085	0.6925649	1.0695122	1.0062782	1.0230024	0.8411477	0.9132406	0.4218052	1.0180560
Citrulline	0.4214526	1.4571427	0.4513969	0.6357133	0.5489945	0.4507589	0.3650552	0.3008129	0.3946912	0.7066947	0.6170127	0.5663506	0.3569724	0.5146847	0.4069223	0.6087197	0.3548486	0.4907301	0.6420626	0.6432533	1.0133808	0.8909440	0.3728396	0.6870457
Creatine	0.4086522	1.8336104	0.4751913	0.5582335	0.5536743	0.4931385	0.5850576	0.4867122	0.5313360	0.7563221	0.6526906	0.7692563	0.5293707	0.6098790	0.4726509	0.7157762	0.6398291	0.8875395	0.8520455	0.9165180	0.5239349	0.6135616	0.4791432	0.8448273
Creatinine	0.5057162	0.8707744	0.4629378	0.6562094	0.6613873	0.5594884	0.5854751	0.4851771	0.5782317	0.7563661	0.8161167	0.8193643	0.8426159	1.0442179	0.6368156	0.9255601	0.6743669	0.9832099	1.0984917	1.1851292	1.0670715	1.4789607	0.5438834	1.0728971
Cystathionine	0.2459859	0.3683612	0.3431268	0.4048110	0.2935433	0.4965935	0.3682411	0.2695575	0.3493903	0.4215621	0.3267381	0.3072462	0.2838443	0.2927669	0.2830256	0.3648586	0.1816999	0.2010483	0.2689415	0.2830604	0.4150128	0.3916642	0.1232459	0.2743187
Cytidine	1.0704769	1.1045405	0.5452250	1.1143852	2.2242367	0.8437256	0.8379310	0.7302953	0.8250596	1.2351377	1.2415660	1.4356379	1.0721686	1.3694450	1.1486803	1.3431894	0.5011534	1.7333319	1.2794172	1.8635491	0.4951477	0.7534005	0.9403074	1.1735831
D2-phosphoglyceric.acid	0.3310944	0.5996730	0.5421477	0.5783187	0.4516969	0.6160839	0.5869482	0.8026354	0.5160980	1.7919010	1.3227615	0.7696889	0.8412157	0.9673621	0.5756555	0.7466133	0.4928834	0.5637712	1.2022054	1.3578467	0.5968598	0.8221555	0.7988284	1.3712116
Dimethylarginine	0.9740189	1.0761789	0.9286955	1.7805238	1.3582373	0.9595825	0.9619014	0.7611321	0.8233580	1.2680150	1.1986943	1.4689141	1.1321591	0.7743156	1.1449154	1.2622517	0.5733991	1.5776915	1.3679222	1.4523821	0.6839601	1.0027647	0.7136403	0.9098727
Dimethylglycine	0.4607362	0.6099623	0.5798673	0.8415445	0.4800336	0.5956410	0.6211296	0.4700505	0.4793892	0.9944620	0.7717746	1.1394720	0.4232337	0.3249359	0.3335234	0.5717760	0.5680419	1.2948865	1.2641046	1.2082976	0.9839331	1.1826156	0.9984687	0.6824968
Dopamine	0.6221969	0.9233208	1.7799437	2.9220513	0.8243819	1.2029912	1.5160785	1.6078648	2.8711232	2.7599863	3.4069383	2.7410775	2.4948055	1.5058086	1.1234065	1.5403673	1.5234156	1.8589505	2.4006292	2.3461096	1.2409628	0.7001368	0.6745019	1.0942887
Folic.acid	0.2239471	0.7487736	1.0598652	1.7528520	0.5643385	0.1206645	2.1591450	1.4651981	1.3696177	1.7913465	0.6001736	1.0758190	1.3699781	2.3413983	1.4799907	1.6345688	1.0877975	3.9654829	0.6068767	2.1335282	1.1901542	1.7785697	2.3565170	0.7551478
Folinic.acid	0.7674852	1.6268925	1.0852252	0.7893310	1.2473922	0.7184188	1.4028261	0.6030513	0.9306193	0.9450751	1.3213389	0.8735870	3.0728728	1.7100075	1.2098770	2.9880290	0.8017804	1.8047687	1.0751854	0.9404757	0.2533398	0.4022695	1.6236487	1.0310206
GDP	0.2824551	0.4104324	0.6581356	0.6326138	0.5607096	0.6279206	0.9077773	0.7229344	0.7825835	1.1341158	0.8687443	0.7987579	0.8721362	0.8370757	0.5121924	0.7037107	0.6499428	0.7694018	0.9147735	1.0046965	0.7964523	0.8625709	0.5791299	0.8675360
Glucosamine	2.0459784	1.8586589	0.9763065	2.3173203	2.7368014	1.2832705	1.5635184	1.1995193	0.8349244	1.1213999	1.3293286	1.9080310	0.7805758	1.1948329	2.3484920	1.5326383	0.5317680	2.6586547	0.9757728	1.2297610	0.5173460	1.3240417	0.6768534	1.0608675
Glutamic.acid	0.3867288	0.6585914	0.2594397	0.6983488	0.4513374	0.4237792	0.2899086	0.2583647	0.4606375	0.4076183	0.4274454	0.4655869	0.5175806	0.6526626	0.7723591	0.7010507	0.4853293	1.0569855	0.8696258	0.9357680	0.3399974	0.5327368	0.6822027	0.9084132
Glutathione.oxidized	0.8428468	0.9934283	0.8284747	1.2904800	1.1288540	0.9433971	0.9309067	0.8341607	0.7050951	1.7922744	1.5380908	1.2666532	1.1660800	1.1961860	0.7966210	1.7078418	1.1142226	1.7799967	1.4630840	1.4101672	0.9523861	1.1156960	0.7591486	2.1125401
Glutathione.reduced	0.8328146	0.9973012	0.9263039	1.1861743	1.0307202	0.9995192	0.8701441	0.8078348	0.7663752	1.5181023	1.4216837	1.1157582	1.0358050	1.2074976	0.8834492	1.4707737	1.1736260	1.5332945	1.3728646	1.2931630	0.9865631	0.9085870	0.8146667	1.6901167
Glycerol.3-phosphate	0.4728707	0.9220561	0.5403641	0.4929494	1.1101013	0.6136874	0.5507888	0.5474192	0.5800091	0.8919979	0.6383870	0.8603690	0.9634107	1.0130460	1.1563273	0.9250990	1.3260552	2.9327821	1.8083472	1.8427419	0.4780161	0.5059864	2.0318877	0.9390341
Glycine	0.8730863	1.3705099	0.9158263	1.2231668	1.3027717	0.9159551	1.0228547	0.7828555	1.2443312	1.3262574	1.2728658	1.2074510	0.8440967	0.9126339	0.8707803	0.9282927	0.6426631	1.1847707	0.9643004	1.1552033	1.0063595	1.2029528	0.7578952	0.9970674
Glycocyamine	0.4700012	1.6812018	0.8093291	0.8862727	0.6447139	0.6131750	0.7258364	0.4538833	1.4261794	0.9214418	0.9556441	0.9071715	0.5539589	0.7430127	0.6726305	0.7824019	0.6505485	0.9903394	0.9944325	1.4137428	1.1282637	1.3375366	0.6221903	0.5836888
Glycylproline	1.8354316	2.4923578	2.6578428	3.1714119	2.4727788	1.9152073	1.8255724	1.7998914	1.5739886	2.8731885	2.3700045	2.6665893	2.2624526	1.4006515	1.9016969	1.9771679	0.8534983	2.6499820	2.2516603	2.3700619	1.9364397	2.2477298	0.8725860	1.5342976
Guanine	0.17621558	0.02278745	0.15415498	0.29704774	0.21663483	0.08342667	0.18120350	0.32614899	0.24036579	0.20259922	0.38402340	0.28300992	0.43238992	0.27333795	0.16728693	0.38415723	0.22893049	0.42081721	0.22346236	0.41695774	0.20548302	0.27833217	0.47305873	0.55053296
Guanosine	0.3246598	0.7685011	0.5047241	0.6499907	0.5206282	0.6397830	0.6747621	0.6381834	0.8289680	0.7105909	1.0300515	0.7829405	0.9793604	1.3265568	0.7543370	1.1106217	0.7258154	1.5540844	0.7140582	1.4509617	0.4875484	0.7297572	0.8773832	1.3040662
HIAA	2.4412992	2.6983910	0.8340145	3.2664718	1.4622671	0.6602276	0.6127725	0.4979979	1.9400444	0.9404046	0.9567780	2.4501998	1.1286798	0.4954157	1.8092108	1.3313670	0.6916914	2.1301379	0.9272512	2.2856990	1.5603747	3.5012040	0.4755159	1.8120372
Homoserine	0.8509122	0.8893932	0.7896290	1.2645999	1.2080315	0.8902052	1.0056840	0.7481959	0.9495331	1.1548321	1.1279660	1.1857805	0.9891440	0.8623097	0.9327528	1.0666565	0.5662173	1.0695083	0.9945852	1.1881665	0.8156957	1.0217079	0.5884026	0.8560951
Hydroxyproline	0.2787770	0.4799966	0.2375902	0.3059802	0.3431303	0.2190838	0.2147382	0.1216726	0.2352834	0.1174432	0.3323629	0.3495331	0.2464465	0.3174669	0.3419158	0.4244054	0.3477392	0.3852723	0.4589917	0.6555311	0.6199176	0.9536136	0.2041111	0.4815902
Hypoxanthine	0.9974282	1.0928235	0.8876036	1.2570637	1.4171350	0.9833092	0.8904424	0.8622482	0.9724418	1.0087576	1.1682902	1.2436913	1.1114261	1.1937916	1.1325733	1.3134446	0.7104519	1.3286557	1.0959749	1.3218071	0.8378953	1.0824028	0.8661801	1.1903877
Inosine	0.7073993	0.8391119	0.7140293	1.0391484	1.2535338	0.8420802	1.1015346	0.8319424	1.1457617	1.2143153	1.3476063	1.2969553	1.2625817	1.5320379	1.1991691	1.5026616	0.9335940	1.9186397	1.4259257	1.8834052	0.7778325	1.0904168	1.1187931	1.5236756
Isoleucine	0.8528558	0.9125115	1.0217673	1.5496715	1.2388609	1.0109370	1.1912526	0.9214470	1.1406629	1.2647698	1.2625838	1.3054733	1.2786902	1.0450159	1.0627395	1.1645459	0.6330773	1.4210589	1.0894039	1.3649646	0.9157909	1.1766452	0.7847429	0.9943086
L-Alloisoleucine	0.8517790	0.9111445	1.0125399	1.5249889	1.2311331	1.0197709	1.1902293	0.9271793	1.1383725	1.2737694	1.2513103	1.3068848	1.2579197	1.0529558	1.0765331	1.1544872	0.6385982	1.4168104	1.0940247	1.3688610	0.9093086	1.1719494	0.7768059	0.9903981
Leucine	0.8476465	0.8962709	1.0266517	1.5385229	1.2401560	1.0079082	1.2035426	0.9227276	1.1359438	1.2795848	1.2575548	1.3011260	1.2710841	1.0653769	1.0637925	1.1611670	0.6377768	1.4253318	1.0888724	1.3837039	0.9196804	1.1688058	0.7811297	1.0016315
Lysine	1.4482072	1.0568177	1.1645744	1.8665608	1.4198726	1.0589478	1.4302917	1.0602397	1.1560245	1.7148566	1.6197058	1.6151634	1.4481528	1.2386714	1.1956266	1.5964858	0.7940763	1.7900829	1.5315174	1.4456983	1.2263541	1.3774511	0.9487037	1.6550266
Methionine	0.8972607	0.9251098	0.9370634	1.6825585	1.3009507	0.9540860	1.2933955	0.9654324	1.0819269	1.3994877	1.3717682	1.5317663	1.4078088	1.1686087	1.2161785	1.3539391	0.7224215	1.6457019	1.4097348	1.6598803	1.0329937	1.4074516	0.8338763	1.0874213
N-Acetylneuraminic.acid	0.6206421	0.8199069	0.5600818	1.0237435	0.6379889	0.5087411	0.5873233	0.5743446	0.6651696	0.9633031	0.8905661	0.8053625	0.4815686	0.4091472	0.4826958	0.6580611	0.4163223	0.8383301	0.9182577	0.9383752	0.5135255	0.5525025	0.4070563	0.6223561
NAD	0.5189115	0.7432001	0.7848089	0.9723333	1.0264845	0.8151934	0.9443994	0.8430001	1.0739810	1.7751225	1.4312229	1.1960606	1.1191554	1.5435374	0.8247645	1.0287660	0.7932043	1.3737844	1.6242790	1.4497317	1.2129971	1.2927545	1.2158123	1.1611846
NADP	0.4645545	1.0033445	0.9597302	1.0300501	0.5523697	0.9305444	0.8770339	0.8463191	1.1799497	1.6125850	1.5100842	0.8503701	0.8669583	0.9652894	0.4649232	0.7248484	0.8139846	0.9654545	1.3477053	0.9537815	1.0817424	1.1563229	1.1929342	1.3127996
Nicotinamide	0.7178230	0.8810389	0.8387394	1.1619439	1.0747429	0.8485019	0.9581953	0.8306311	1.1420243	1.1893909	1.1554375	1.2419390	1.2246746	1.2373342	0.9347814	1.1588332	0.7229536	1.2618774	1.0789894	1.4088462	0.8409249	1.1128264	0.9288390	0.9164444
Norleucine	0.8518739	0.9031989	1.0352939	1.5405561	1.2409032	1.0051005	1.2031724	0.9123117	1.1186044	1.2682845	1.2530081	1.3082198	1.2709141	1.0547923	1.0632294	1.1498179	0.6271827	1.4302944	1.0885495	1.3559512	0.9163913	1.1671295	0.7881985	0.9965756
Norvaline	0.9124836	0.9298527	1.0368697	1.6448278	1.1552369	1.0535945	1.1661068	0.8477787	1.1226926	1.1524275	1.1425004	1.2132199	1.2447680	1.0239704	1.0882174	1.2925641	0.6011751	1.3398496	1.0437265	1.2117027	1.0259126	1.1945400	0.9568618	0.9967921
Ornithine	1.0332296	0.8179956	0.7856410	1.3515693	0.9279344	0.7778656	0.9067942	0.6364167	0.7778348	1.0385131	1.0756493	0.9922528	1.2363026	0.9490234	0.9931245	1.3358021	0.6026925	1.4751211	1.2747343	1.1052278	1.2221460	1.3833450	0.8267835	1.4047324
Pantothenic.acid	0.5843001	0.7413393	0.6365224	0.9997849	0.8483685	0.7045172	0.6561683	0.6052149	0.7990996	0.8561870	0.8310670	0.8831817	0.8910804	0.7766499	0.7562383	0.9005148	0.4408332	1.1369992	0.7531680	0.8794983	0.4826726	0.7702197	0.6456869	0.7288907
Phenylalanine	0.8266777	0.9186807	1.0043263	1.5735330	1.3371442	0.9285578	1.2423992	0.9631628	1.1908843	1.3133446	1.3050369	1.4669236	1.4456966	1.1005134	1.1502301	1.2907528	0.7015021	1.6027515	1.1682306	1.6519843	0.9048820	1.2502029	0.7999375	1.0173964
Pipecolinic.acid	0.3294063	1.0094060	0.3818550	0.5711961	0.4551660	0.3332365	0.4550962	0.3707791	0.4427522	0.6345462	0.4652044	0.5736943	0.5446118	0.6177807	0.4724979	0.6498503	0.4190516	0.8724576	0.6294419	0.8597367	0.5914717	0.7777559	0.5766327	0.5802869
Proline	0.5141562	0.6178646	0.5822266	1.3063838	0.7457581	0.5776894	0.7298739	0.5105093	0.6245210	0.8541810	0.6404874	0.9124592	0.7089632	0.6439353	0.6385716	0.7810780	0.3922450	0.9376606	0.7503399	1.0259594	0.7327704	0.9253374	0.5640057	0.5703749
Pyroglutamic.acid	0.3082117	0.8843707	0.4362193	0.5921241	0.4758751	0.4111866	0.4229338	0.3914758	0.4400848	0.5739163	0.4679617	0.5115939	0.5537708	0.6806015	0.4737140	0.5919037	0.4162531	0.8276363	0.6802242	0.8473929	0.4889404	0.6901764	0.5664578	0.5789078
Sarcosine	1.0084766	1.0659462	1.4043571	1.3180316	1.3173108	0.9578035	1.0446095	0.8087390	1.2527798	1.4248970	1.4078169	1.4296566	1.4621763	1.4146250	1.1970317	1.2222388	0.9605841	1.4551496	1.1998666	1.4855036	1.1753213	1.1102789	0.7256942	0.9738131
Serine	0.9631746	0.7482507	0.8027561	1.4342633	1.2503764	0.9510122	1.1738940	0.8230972	0.9846277	1.2222407	1.2662427	1.2908321	1.1188887	0.8060649	1.1238529	1.1654594	0.5992233	1.2091939	1.1286308	1.2184897	0.7885404	1.0498191	0.6902211	0.8701550
TMAO	0.09437101	0.43303428	0.27471777	0.11216410	0.77217358	0.46438820	0.18648344	0.22312431	0.83269885	0.48161575	0.14550246	0.22655480	2.34051394	0.79755627	7.29396053	7.28121795	0.61150801	0.84295022	2.54722104	1.89654121	2.66298055	2.24567385	0.86779300	1.35080682
Taurine	0.7178835	0.8336343	0.8542148	1.1605061	1.0823282	0.8895874	1.1038355	0.9200192	1.0612253	1.3159387	1.2440577	1.2424510	0.5820055	1.3399539	0.6293543	0.8610343	0.6677345	1.4970880	1.0986328	1.0589133	0.8018202	1.0684514	1.1126616	1.4430778
Threonine	0.8232457	0.8706377	0.7730140	1.2312086	1.2037216	0.8912114	0.9660505	0.7585548	0.9620484	1.1447777	1.0785856	1.1441714	0.9735837	0.8573386	0.9307297	1.0386725	0.5642106	1.0126094	1.0241260	1.2153759	0.7968829	1.0072283	0.6001133	0.8525195
Tyrosine	0.9150162	1.0841190	1.0359367	2.4642402	1.2867226	0.9170167	1.3293614	1.0450251	1.2348882	1.6267038	1.1748098	1.7505491	1.3043186	1.1454333	1.0372301	1.3440036	0.6115674	1.8582848	1.1087729	1.8802615	0.6253943	1.0400158	0.8149456	0.8355209
UDP-GlcNAc	0.2934447	0.5004356	0.4652797	0.5732223	0.7177815	0.5265830	0.5310480	0.5149530	0.6552245	0.8666439	0.7747757	0.6714735	0.5809566	0.6796868	0.6131760	0.7155939	0.5540551	1.0615481	1.0151025	0.9471085	0.4996689	0.6153224	0.8202686	0.8398630
Uracil	0.8606104	1.1405109	0.9367328	1.1936004	1.0690069	0.8014622	0.9855269	1.0904810	0.9049300	1.1703200	0.9967556	1.3101537	0.6560391	0.7866817	0.8377139	0.9379920	0.6340143	1.5360757	0.7688687	1.2509321	0.8756824	1.2854795	0.7315423	1.0174820
Uridine	0.8463357	0.9289961	0.7456293	0.9695010	1.0747293	0.7520132	0.8439773	0.7566538	1.0583116	1.0561338	1.1516558	1.1443289	1.3153369	1.4348080	1.2522523	1.4124399	1.1748731	1.0449634	1.4928727	1.7468186	0.7417218	1.0299351	0.6787251	1.1677144
Urocanic.acid	0.8638117	0.3212854	0.2892404	1.7392963	1.1278006	1.1803694	4.6323495	0.8480094	0.1972440	1.0285895	0.5361097	1.2196895	0.9425947	0.2852366	0.4181020	0.3113765	0.3851985	0.4109156	0.4547907	0.4721768	0.2222827	0.3274246	0.3922131	0.4958654
Valine	0.9146230	0.9386614	1.0100753	1.5698269	1.1371203	1.0416494	1.1706341	0.8330754	1.1107848	1.1486198	1.1281245	1.1790151	1.2029580	0.9875298	1.0709863	1.2544596	0.6194352	1.3227468	1.0324728	1.1931394	1.0201331	1.1820476	0.9588230	0.9909290
Xanthosine	1.1578918	1.0963044	1.8140309	2.5780088	1.6815118	0.7748606	1.4037110	1.4535702	1.6892207	2.5296336	1.9151461	2.4928248	1.8328610	1.4805901	1.0967489	1.4175627	1.0784961	1.4506998	1.4556784	2.4213394	0.9455076	1.1696542	0.6661710	0.9053000
3-Indoxylsulfate	0.0014066653	0.0004189127	0.0010537000	0.0083676171	0.0142302571	0.0009821833	0.0053553740	0.0037918780	0.0099701690	0.0018319320	0.0000000000	0.0032034815	1.6957355303	1.7628992518	1.6905300705	2.6690102670	2.6662227663	1.2041302524	2.8159077618	3.9225468829	1.4879194492	1.2193387223	0.5481725665	0.6420550854
4-Methoxyphenylacetic.acid	0.6466108	0.8747982	0.6853639	0.4635535	0.6923135	0.9081214	0.3864574	0.5932554	0.8592044	0.7749379	0.6144890	1.6048136	1.3247088	1.9877733	0.5777823	0.4745502	0.6657401	0.7476548	1.1156824	0.3347995	0.4634213	0.4693551	0.7580660	0.8725201
2,3-Dihydroxybenzoic.acid	0.2284087	0.0000000	0.1073506	0.1197521	0.3433866	0.2394200	0.2957455	0.1572915	0.2597474	0.4494817	0.2776771	0.5415174	1.1314134	2.0412582	1.3909532	2.0095700	1.0359663	1.9621842	1.1671127	1.7748041	1.5807294	1.5394085	2.0435920	1.5376939
2-Hydroxybenzoic.acid	0.9912718	1.0984016	0.8859903	2.9777668	1.2496739	0.8263873	0.4437614	0.6297594	0.7991838	1.2558908	0.4339783	1.1235803	1.7674413	2.4987940	1.7318874	3.3508043	2.1025498	1.1283852	1.9534964	2.6782763	3.6617174	2.3740483	1.5164736	2.3913293
2-Methylbutyric.acid	0.7510326	0.0000000	0.5933317	0.4652210	0.8170571	0.6277748	0.5667496	1.2758309	0.4076446	0.6058693	0.5857997	0.7638084	0.5694005	0.5361239	5.5609744	0.6463784	0.8742257	0.6882732	0.5173637	0.7346524	1.1216587	0.9157327	0.5570880	1.4616018

Table S2A. Liver metabolites

4-Hydroxybenzoic.acid	0.9001782	1.0560988	0.5165869	1.6783153	0.5699435	0.8027474	0.7099929	0.9605478	0.4151053	0.8681392	0.5752243	1.0260255	1.6784020	2.1886534	2.2593682	3.0059774	1.4193347	1.8491539	1.9264320	2.0369756	2.6518981	1.4725679	0.8501041	2.2330271
4-Methoxyphenylacetic.acid.1	1.9877733	2.0373450	0.8337383	1.6048136	2.0658340	1.2979754	1.1156824	1.9172275	0.7001501	1.3116874	0.6853639	0.7476548	0.9081214	0.7218465	1.3247088	0.6144890	1.4894123	0.3347995	0.6466108	0.9913256	2.3431603	1.4964245	0.8747982	0.5932554
4-Methylvaleric.acid	0.2696367	0.2186943	0.2389721	0.2746247	0.3590760	0.3322700	0.3165805	0.2152099	1.1698982	0.4311654	0.7466173	0.7422495	0.6337153	0.3439619	0.5406916	0.2775697	0.2417917	0.6953245	0.8615943	0.9623980	0.8432549	0.8873891	0.8374581	0.2084494
Acetoacetate	0.9898180	0.8188094	0.9803567	0.9251530	0.9654123	0.9608998	0.9271387	1.0024227	0.8747964	0.9635099	0.9376343	1.0259165	0.9012016	0.9546399	1.0628470	1.0269441	0.9713463	0.9222361	0.9781181	0.8887658	0.9629445	0.9882867	0.9223725	1.0056272
Allantoin	0.9081038	1.1675675	1.0835233	1.4973499	1.3482714	1.1630004	1.2846565	1.3128294	1.4097008	1.5623482	1.4565717	1.4920634	1.3007490	1.1960430	0.9304598	1.1245904	0.8584241	1.5205353	1.0506660	1.2419266	1.0761671	1.2260110	1.3543364	0.9334865
Benzoic.acid	1.5878079	1.6902164	0.4250484	0.9203602	1.8134949	0.8459258	0.8249963	1.2637116	0.2394484	1.2308995	0.5166132	0.3333922	1.2684222	0.5741011	1.0986724	0.5265405	1.6702033	0.4627586	1.1916263	1.1436699	3.5990895	2.2423102	1.1203569	0.9979186
Citraconic.acid	1.3647653	2.2112889	0.8797576	1.4538588	1.7578296	1.5525089	0.7205279	1.0104727	0.5281336	2.3166094	0.4419381	0.6244150	0.9155004	0.7162225	0.9572177	0.5355094	1.0329688	0.2687801	0.5441814	1.9064968	2.0203813	0.9108907	0.8113292	0.5437640
Dextrose	1.7685669	4.6572716	2.3556058	1.7827129	1.1974816	1.1544892	1.2490300	0.7734221	0.9285326	0.8872297	1.2075044	1.1579873	1.2059183	0.9654718	1.2255272	1.3560641	0.5118914	1.3100008	0.6316051	1.1003823	0.6802550	1.0078298	0.6595299	1.2910940
Ethylmalonic.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
F6P	0.6739597	0.2447394	0.1826924	0.5818162	0.6716709	0.9746235	1.6123935	1.0723225	1.1070088	1.1154111	1.1312938	0.8015774	0.8302518	1.1814138	1.0512689	1.3252791	0.9051761	1.2707456	1.0729524	0.9041556	0.5528828	0.8035899	1.1194059	1.3061925
Fumarate	1.4192990	0.9868137	0.8213347	1.4978703	1.0743669	0.7292620	1.0526249	0.6276190	1.0221781	1.3314953	1.0614763	0.9885643	1.1486085	1.1050599	1.0235470	1.4572782	0.8988348	1.4704258	1.0546681	1.0817807	0.7715662	0.9892307	1.4595397	1.6709555
G1P	0.6752635	0.8029834	0.7627249	0.6158372	0.6249657	1.1037194	1.7901152	1.1289605	1.1985437	1.2173511	1.2187953	0.7115492	0.8453992	1.3293391	0.9983102	1.4457266	1.0017281	1.3487788	1.1853711	1.0712144	0.5663022	0.8982037	1.1802936	1.3657570
G6P	0.6688839	0.2380527	0.1925240	0.6659184	0.6797407	0.9710578	1.7391819	1.0406175	1.1499232	1.1649878	1.2167404	0.8868503	0.9159730	1.2787757	1.0400833	1.4203444	0.9207098	1.4076844	1.1534235	1.0067520	0.5166500	0.8859144	1.1368587	1.3662755
Galactose	1.5341257	5.2179303	2.3947257	1.5528834	1.3580207	1.1063219	1.1401609	0.8658799	0.9155313	0.9234025	1.1114644	1.1004973	1.1229601	1.0896220	1.1545220	1.3138040	0.6990620	1.1046280	0.7290189	1.1359700	0.7966584	1.1953606	0.7623118	1.0896942
Gentisic.acid	0.3546276	0.0000000	0.4713781	0.7467572	0.3560114	0.5168665	0.7327730	0.4047499	0.3646098	0.3597696	0.4111592	0.9474256	1.0461493	2.6593919	1.7835470	2.1266823	0.8074980	2.2794278	1.0550036	1.2916958	1.2224337	1.0283997	1.5228155	1.2681876
Glucuronic.acid	0.8618951	1.2635837	0.3914980	0.5864809	0.7149729	0.8905112	0.6466698	0.4523792	0.8934652	0.5236532	0.5877000	0.5639786	1.8837233	1.5606799	1.5985878	1.6699945	1.0047435	1.2180814	1.2296122	1.6472588	2.2245028	3.2449828	1.3460268	1.4921735
Glutaric.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
Glyceric.acid	1.1496164	2.5195502	1.1739954	1.3951672	1.4599438	0.8746264	0.9923443	1.2507857	0.8864898	1.5545627	0.9987718	0.9439196	0.7221400	1.4318077	0.8648158	1.2905391	1.3513554	0.8347342	0.9936521	0.7147244	0.7321524	0.8865097	0.8960178	1.4822709
Isobutyric.acid	0.00000000	0.05244963	0.50898333	0.82647449	0.00000000	0.65901154	0.56581734	0.71041992	1.32707167	0.56170639	1.01099565	1.18177968	0.84196243	1.21985165	0.69521063	1.08410990	1.63819382	0.52221008	2.05200836	1.27874196	1.92633325	1.10015048	1.10209239	1.01358025
Isovaleric.acid	0.7155741	0.0000000	1.0151671	0.4655771	0.9275040	0.4950023	0.7486756	1.0320418	0.8385003	0.7539450	0.5534565	0.6301668	0.4893295	0.5065836	5.2080493	0.7206219	0.7182304	0.4833982	0.6210143	0.8176440	1.0377181	1.1049437	0.3567986	1.2920695
Lactose	1.7278542	12.3361306	3.5970124	1.6204874	1.3170386	1.1452639	0.9148891	0.7427353	0.8165284	0.7769225	0.9731502	1.0814995	1.1334146	0.9947503	1.0370356	1.3653067	0.6670843	1.2811463	0.6614136	1.0377394	0.5529015	1.0834332	0.5707073	1.3489137
Levulinic.acid	1.5570665	1.2926634	0.7031304	0.6362157	0.7702267	0.6458151	0.4586144	0.6789458	1.2085580	0.9497924	0.8597124	0.6798147	0.8956509	0.6319326	0.9339435	0.5457088	0.9271357	0.9459671	1.2397537	1.8196988	0.9844683	0.8069519	0.7865500	0.4809240
Mannose	1.4952340	1.0294612	1.1193161	2.1812875	1.5518865	1.0888375	1.4574358	1.2740713	1.5870256	1.4937340	1.4813516	1.7636578	2.0195185	1.3265372	1.5246655	1.5385679	1.2863063	1.3664471	1.2684240	1.7166670	0.8845929	1.3531122	0.9221497	1.3065198
Methyl.alpha-D-glucopyranoside	0.7022848	1.3289890	0.7121133	0.9536818	1.1250414	0.6308415	1.1896947	0.8454161	1.2042655	0.9617926	0.8191024	1.0102836	0.9483462	1.1641299	0.6849502	1.0440661	0.6582924	1.3262151	0.9590109	0.8453300	0.8214475	1.1854478	1.1363926	1.0440430
Myoinositol	0.8694791	1.1178407	1.3772587	1.7509144	1.7419164	1.1912207	0.7806327	1.1023066	1.0258326	1.0494177	1.3554179	0.9649657	1.4025886	1.1070176	0.9472456	0.8104337	1.1539989	0.8418495	0.9136361	1.4517492	0.8450081	1.6781317	0.7083603	1.0566861
Nonadecanoic.acid	0.8291083	0.4843062	0.7006170	0.6379930	0.6590255	0.7834945	0.6717061	0.6468235	0.6136272	0.6344273	0.5468030	0.7088714	0.5691938	0.8135633	0.7518102	0.7726551	0.7042177	0.6471807	0.5237051	0.3273494	0.4570268	0.4718718	0.5502521	0.7504966
OAA	0.4706844	1.4768433	0.9478751	0.9480796	0.7043471	1.0231675	0.7729994	0.5138535	0.8686459	0.6839295	0.7601366	0.4938531	0.7716700	0.7003961	0.7052642	0.7108140	0.7430833	1.2272501	0.7375726	0.8898757	2.6271150	2.4659336	0.8769646	0.6642809
Palmitic.acid	0.6576104	2.4876173	1.1086988	0.9933969	0.6654050	0.5312395	0.7647661	0.7191476	0.6994420	0.7180929	0.5547641	0.8033647	0.6966770	0.8559372	0.7094591	0.7680809	0.5930325	0.8984361	0.5270847	0.9339967	0.4984569	0.6610013	0.5752758	0.5048961
Pentadecanoic.acid	1.1427298	0.5870484	0.6274741	0.6752754	0.6227439	0.7262631	0.5656418	0.5217017	0.6089249	0.4430046	0.4323494	0.7093060	0.4577233	0.5140927	0.6343803	0.6179902	0.4894114	0.5277205	0.3626343	0.3959666	0.4648136	0.3559489	0.5488784	0.4773791
Phthalic.acid	2.2467277	2.8811973	0.9590323	1.4759390	2.5516393	1.2665585	1.1557750	3.2708233	0.9187764	1.8053250	1.1865923	1.0920811	1.5253343	1.5010486	1.5789988	1.0036075	1.6275219	0.6693168	1.1291957	0.9520331	4.1384040	1.7908762	1.4875792	0.9633425
Raffinose	4.2406534	2.6381289	2.8986832	2.2229446	1.4063470	1.9821988	1.7797267	0.5603099	1.5427157	1.3383924	1.8955090	1.5934417	1.6822064	2.1903529	1.6188200	1.7642422	1.2483946	2.6886577	1.1058582	1.3579173	0.4961662	0.9152473	1.6370885	1.6808395
Shikimic.acid	0.4566439	1.6953687	0.4436559	0.5014321	0.9789059	0.6421197	0.8611503	0.8154816	0.4553175	0.8477968	0.7800669	0.6293811	0.6921569	0.9635854	0.7885012	0.8913415	0.7719212	1.1031032	1.0271294	1.0289196	1.1278543	1.0499156	1.0467217	1.3644345
Sorbitol	1.585376	2.068789	2.017347	2.935154	2.439898	1.695450	1.235273	0.948883	1.877812	1.083459	1.648626	2.228505	2.471795	1.821555	3.012169	1.975258	2.174246	2.263342	2.427025	4.434080	1.370861	1.535353	1.067649	1.186329
Stearic.acid	0.7809648	2.2287310	1.2442121	1.0303458	0.9092352	0.7524102	0.7931729	0.8663392	0.7608388	0.7868036	0.6238720	0.8245983	0.8188588	0.8765730	0.8958090	0.8963560	0.7338885	0.8893772	0.7047385	0.9714868	0.8025889	0.8111246	0.7017546	0.7680203
Trehalose	2.1142004	13.2894395	3.9071349	2.2777436	1.5761671	1.0666695	1.5014004	0.6787332	0.8279424	0.7812906	1.2507457	1.4231432	1.3643417	0.9935851	1.1759800	1.3869828	0.5431801	1.0142042	0.8030972	0.9663495	0.5082489	1.0376458	0.7117123	1.6965194
Urate	1.3406364	1.5250610	0.8473836	1.1140390	2.4907067	1.2353838	1.7609205	1.1875856	1.5123852	1.3022075	1.4339406	1.0269305	0.6765105	1.0893236	0.6584594	0.7040288	0.7428215	1.9296033	0.8196379	1.6574426	0.8632615	0.8101919	1.2833077	2.1605345
Valeric.acid	0.70749133	0.09470111	0.98921146	0.46459669	0.91370278	0.47580163	0.74021893	1.03119080	0.81706168	0.75332329	0.55229107	0.62304875	0.48829916	0.49363134	5.14922195	0.71910449	0.69037095	0.47793804	0.60513635	0.78592837	1.03686237	1.08850223	0.34767608	1.28934875
X5P	1.201143	1.276757	1.413303	1.653952	1.267569	1.278849	1.780746	1.354567	1.779299	1.577205	1.707360	1.920431	1.580249	1.517633	1.585497	2.195201	1.459374	1.733696	1.705658	2.215318	1.187748	1.478072	1.491918	1.627948
Xanthine	1.479659	1.481760	1.402484	1.887153	1.778127	1.252138	1.518562	1.382384	1.521875	1.459015	1.538795	1.813552	1.511328	1.476498	1.470618	1.495125	1.065810	1.728239	1.406754	1.589197	1.155761	1.426024	1.365320	1.292267
alpha-Hydroxyisovaleric.acid	0.22652691	0.06324408	0.24138572	0.38533503	0.40858595	0.08999759	0.13680320	0.24739137	0.67448423	0.27068110	0.05595278	0.38246377	1.40021748	0.40581075	0.59413534	0.16162409	0.14820324	0.80589746	0.45462266	0.50294160	0.51224833	0.62746522	0.94315331	0.27787725
alpha-ketoisovaleric.acid	1.6450600	1.9676816	0.9101139	0.7138070	0.8190894	0.5382239	0.4271922	0.7849076	1.1082485	0.9436748	0.6605273	0.5106391	1.2123041	0.5905675	0.8120547	0.5422817	0.3049550	1.0403584	1.1329032	1.8615979	0.9017435	0.8825711	0.9590286	0.7871725

Table S2B. Serum metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	1.0317667	1.0303621	0.9847637	0.9921081	0.9160872	1.0764221	1.0336387	1.4405943	0.7765993	0.9986675	1.0874466	1.0637402	0.6305017	0.5213879	0.7407689	0.8465473	0.6182256	0.6951432	1.0381927	0.6869308	1.1003884	0.7616520	0.7266176	0.6292298
3-Indolepropionic.acid	0.01904275	0.00000000	0.00000000	0.01174865	0.00000000	0.03955007	0.06561667	0.03874387	0.00000000	0.00000000	0.00000000	0.00000000	0.55859613	0.47659752	0.71442760	0.27750775	0.61415979	1.10075666	0.37694018	1.13900959	0.22864990	0.44264462	0.75318881	2.27604977
6-Methyl-DL-tryptophan	0.41570933	0.55659384	0.67931578	0.49104472	0.80584709	1.93103976	0.63320850	0.66146933	1.08739075	0.65511807	0.75366381	0.74293619	0.09812646	0.17093453	0.45117283	0.25733516	0.22503132	0.36726015	0.26036736	0.33192057	0.59247137	0.78618775	0.94471496	0.45148486
Indole-3-acetic.acid	0.5580839	0.5380495	0.5656663	0.5636264	0.4919839	0.4800485	0.4241354	0.6233548	0.3343458	0.5122234	0.6933088	0.4484751	0.7917882	0.9824133	1.0578317	1.1315136	0.6962389	1.0884141	1.7883287	1.4874967	1.2532215	1.2294161	2.2210241	1.7300960
Indole-3-lactic.acid	1.1092210	0.8554817	0.8354971	1.1621817	0.7877591	1.0869508	0.8945694	1.5749362	0.6616183	1.0120818	1.0766544	0.9578828	0.6190572	0.4244500	0.7577282	0.8598728	0.5966954	0.7057665	1.0638820	0.6138955	1.0639085	0.6896377	0.6855773	0.5902174
Kynurenine	1.0909688	0.8734492	0.3294966	0.7872656	0.2680286	0.8604749	1.0273913	0.9765153	0.8797466	0.7120567	0.7678117	0.9076418	0.3653122	0.6868505	0.6065237	0.7695144	0.5623107	0.3753020	0.5503452	0.4305640	0.3471962	0.5665617	0.6669201	0.4597565
Serotonin	0.8442799	0.9014375	0.7353003	0.7508531	0.8737883	1.3184758	0.8002665	0.7634158	0.7392552	0.8125640	0.8092775	0.8531453	0.4321848	0.5080711	0.4937651	0.5775824	0.5864579	0.5811751	0.6443621	0.5838568	0.7712975	0.5235457	0.8569040	0.5515420
2-Deoxycytidine	0.3174848	0.2913996	0.2822617	0.3026962	0.2133915	0.3491761	0.2773496	0.3324238	0.2194807	0.2744738	0.2549853	0.2950616	0.2459364	0.2298095	0.3028967	0.3110092	0.2116033	0.3872227	0.2877459	0.3042525	0.2941973	0.2165142	0.3662207	0.3591027
213C-Glutamic.acid	0.9844852	0.9950125	0.9327800	1.0003609	0.9661615	0.9508437	0.9988592	0.9277253	1.0146637	0.9506263	1.0051244	1.0134514	1.0141268	1.0258431	1.0099926	1.0166979	0.9702272	1.0188772	0.9572153	0.9783577	0.9923269	0.9244512	0.9319085	1.0222706
5-Aminolevulinic.acid	0.7795518	0.7610577	0.6979264	0.6854502	0.9618818	1.2366398	0.7757380	0.8759584	0.7565268	0.8750895	0.6972154	0.5884368	0.5317662	0.4935351	0.5312805	0.6134248	0.6264979	0.4866220	0.6992055	0.7625584	0.7390534	0.5473003	0.6652192	0.5197771
6-Hydroxynicotinic.acid	0.028878300	0.053021903	0.055377422	0.067188470	0.069876473	0.033207796	0.050327910	0.064691863	0.057382380	0.066923263	0.050205179	0.020650789	0.023744369	0.012478698	0.008996055	0.025685372	0.020600780	0.016676094	0.009066213	0.020656543	0.027477553	0.000000000	0.038251691	0.035514356
7-ketocholesterol	0.2924918	0.2284840	0.4863401	0.3812536	0.5532410	0.2924774	0.4050716	0.6754374	0.3572131	0.5246027	0.4581334	0.5209997	1.3684958	2.2957026	0.9383200	10.2231564	0.3468779	0.7566915	5.0969810	0.5870745	0.6553080	0.5284319	0.9099085	2.8210692
Acetylcarnitine	0.9441641	0.9762040	0.8584805	0.8966743	0.8083222	1.2599501	0.9270292	1.1218529	0.6377153	0.9340284	0.9575799	1.0547174	0.8179229	0.7078616	1.3668700	1.1744102	0.8729917	1.4676838	1.0122209	1.3667082	0.8370880	0.5816249	0.8944781	1.2286137
Acetylglucosamine	0.40392903	0.20460270	0.40498773	0.42430252	0.40644811	0.73773239	0.37272404	0.36942373	0.34369816	0.43376192	0.32548500	0.30721539	0.31563018	0.10564735	0.17228083	0.24874233	0.24854459	0.28460983	0.31103168	0.36955219	0.19195022	0.09980531	0.34108868	0.20726354
Acetylglycine	1.4991894	1.2571867	1.4613053	1.3676502	0.8618283	0.8963021	1.3151055	1.5117083	1.2874666	1.2558855	2.0225116	2.1556291	0.3764896	0.1361418	0.9900842	0.7101797	0.3881535	0.8370687	0.1611271	0.3595276	0.5242699	0.2188906	0.2776544	1.1418755
Adenosine	0.2140969	0.2102831	0.2204731	0.2183226	0.1923837	0.1817932	0.2516306	0.3133118	0.3362446	0.5335153	0.2711058	0.2710070	0.1909757	0.1598037	0.3264152	0.1133139	0.9777930	0.2111847	0.2169560	1.1616375	0.2937814	0.2245176	0.2665889	0.2164441
Adenosyl-L-homocysteine	0.6714422	0.4308204	1.5075238	1.2276340	1.5873233	1.2629599	1.1093691	2.1367804	1.2361365	2.0044919	0.7645900	0.3509771	0.7865940	0.3838238	0.4334325	0.8561266	0.8834433	0.3909437	0.7933884	1.1344111	1.2445698	0.8234503	0.2881118	0.3432706
Alanine	0.8039607	0.7589530	1.5213952	0.7050528	2.4600018	1.6993623	0.7328026	0.5635759	0.9061994	1.0124162	0.8918277	1.1135432	0.6239487	1.1980224	0.4809799	0.8274591	1.5761646	1.5665982	1.4870625	0.8288178	2.1276307	0.8214103	1.1012487	0.6655912
Allopurinol	0.03371837	0.03982831	0.07967565	0.09631134	0.29066584	0.43212536	0.10127359	0.13557639	0.15064015	0.43628029	0.07268631	0.04541401	0.18894061	0.15836448	0.86294382	0.35844435	0.26588665	0.01586960	0.21502325	0.77772557	0.23225748	0.19562593	0.24672431	0.21442101
Asparagine	0.4449370	0.4373391	0.4302286	0.4423950	0.4736336	0.8986803	0.4141668	0.4037197	0.4344819	0.4441081	0.4378873	0.4320793	0.3776924	0.3610497	0.3550619	0.3946823	0.3544344	0.7584599	0.4232461	0.4070500	0.6391954	0.5276892	0.8365307	0.6913280
Aspartic.acid	0.4152065	0.4430707	0.5818116	0.5320270	0.7732795	0.5713789	0.3907554	0.5394307	0.3698395	0.6125440	0.4739644	0.9147199	0.6267113	0.6123835	0.5933458	1.0165807	0.6299843	0.7023535	0.7167973	0.5597980	0.7913604	0.5099731	0.8173880	0.5713535
Betaine	0.7234086	0.7048656	0.6882660	0.7301375	1.0328520	1.0547873	0.8330171	0.7567204	0.8401010	1.0007066	0.7405565	0.6415822	0.4648153	0.6546769	0.6748845	0.7449814	0.5910158	0.7913117	0.6501385	0.9196811	0.5226326	0.4670694	0.8190514	1.0041040
Carnitine	1.0364532	0.9510847	0.6900549	0.7823069	0.8722678	1.4882140	1.0155252	1.0430504	0.7671293	1.1915917	0.9239250	0.6549932	1.2215885	1.1295841	1.0461135	1.1959042	1.1850933	1.0845366	1.4431300	1.6938279	1.3330664	1.1024471	1.5497510	1.0555476
Creatinine	2.0182532	3.1826911	0.6806979	1.3364505	1.0357324	1.0650838	0.9285776	1.0191995	2.2516750	1.1956444	1.5971185	0.8120371	1.4682139	1.1740891	1.8848313	1.5277349	0.4602601	1.4305611	1.3358876	1.8145411	1.3705444	1.2221740	1.0911130	1.7973037
Cystathionine	0.28309420	0.22951454	0.19001737	0.36697649	0.24784214	0.79328559	0.51016562	0.33012475	0.19901532	0.36555136	0.24005707	0.43611053	0.11324349	0.25762183	0.16868932	0.20845813	0.14641402	0.22658746	0.15482380	0.16571156	0.18506241	0.09193353	0.33018113	0.17725964
Cystine	0.2811702	0.2796157	0.2622289	0.4158454	0.2951822	0.4626571	0.2329457	0.4313985	0.3481685	0.7131780	0.1786220	0.1504858	0.4354672	0.3925378	0.7481704	1.2502132	0.5341248	0.2328273	0.3078212	1.0104342	0.6121067	0.7567378	1.1014113	0.2250691
Cytidine	0.5210576	0.5032761	0.5765483	0.5981420	0.6814616	0.8751241	0.6748009	0.6019237	0.5428900	0.7095091	0.5425272	0.7119897	0.4274866	0.2924270	0.6648767	0.5449437	0.3117971	0.5249493	0.3719328	0.5661403	0.4281487	0.2193708	0.5383064	0.6722130
Cytosine	0.5724007	0.5687503	0.6540320	0.6572037	0.7955865	0.9571722	0.7971547	0.6449386	0.5586945	0.6774215	0.6049335	0.7243051	0.4699204	0.2732985	0.7717965	0.5282462	0.3810730	0.6414866	0.4522232	0.6106754	0.4545835	0.1679954	0.4922570	0.7779320
Decanoylcarnitine	1.03977434	0.99283216	0.43905377	1.23286038	0.21996057	1.66219197	1.14613326	1.16848327	0.86426812	0.72083633	1.21367682	0.93209662	0.40954643	0.77981803	2.03456776	0.62146441	1.09213349	2.43900461	0.36883592	1.46662126	0.38505780	0.09040753	0.38388122	1.57232054
Glutamic.acid	0.5190196	0.5011747	0.4923732	0.4956872	0.6323800	0.5782931	0.3782653	0.4835876	0.3689661	0.6442815	0.4484648	0.6992172	0.6507610	0.4443386	0.6106565	0.6727734	0.4415760	0.6311273	0.4996465	0.5072568	0.5993526	0.4951351	0.6628929	0.6303698
Glutathione.oxidized	0.05294285	0.07759938	0.29613676	0.37270704	1.55391661	0.73383892	0.28143294	0.37137794	0.38844261	0.74461270	0.14097362	0.19893314	0.53946391	0.77446884	0.80577163	2.06643648	0.20456022	0.49325699	1.32663578	0.77536742	0.29639357	0.38259976	0.67550784	0.48181953
Glutathione.reduced	1.1026759	0.8923498	1.1151582	0.5953181	1.6980991	0.6901809	0.7222110	1.1313823	0.7949924	1.5343012	0.7254251	0.4263253	0.1457852	0.1639876	0.3207433	0.3435307	0.5711687	0.6251995	0.2651110	0.2859727	0.5322789	0.5886255	0.2908863	0.3738287
Glycine	0.7725024	0.9251390	0.8940421	0.7024416	0.9043963	1.0035431	0.8484915	0.9572646	0.8936362	0.7776883	1.1724503	0.9329527	0.3696696	0.4106501	0.5924033	0.5879735	0.5078564	0.7956602	0.4571842	0.5517679	0.7122945	0.4886854	0.6821170	0.7807791
Glycocyamine	0.8074463	0.3146842	0.4313919	0.7983406	0.7402149	0.9057195	0.2322731	0.3787078	0.4721578	0.9536144	0.6623463	0.1779486	0.3463183	0.2636901	0.4921304	0.4061054	0.6702330	1.0676197	0.2848171	0.6642394	0.7265750	0.6081363	0.6230967	1.7139250
Guanine	0.02532942	0.05454220	0.44570051	0.44655817	0.75594909	0.43156865	0.31297704	0.65911714	0.11930541	0.99610076	0.14866761	0.15196284	0.03857490	0.02812718	0.64312146	0.13858959	0.30982399	0.00000000	0.08996413	0.61969980	0.04445479	0.10089361	0.11101912	0.10465782
Guanosine	0.041368434	0.027223213	0.439538214	0.393871216	0.755126475	0.359767631	0.387946879	0.525422776	0.131452859	0.908707699	0.114507263	0.107079476	0.038413887	0.043984439	0.470480486	0.110833692	0.298855593	0.005636157	0.076048250	0.663438323	0.119137456	0.048801513	0.090631906	0.058864363
HIAA	0.4614215	0.4563886	0.5361250	0.6674289	0.5526476	0.7528907	0.6618530	0.8154046	0.3770931	0.5050472	0.8687341	1.0162924	0.5355136	0.4474822	0.5572884	0.7506275	0.2775017	0.3348267	0.5920746	0.4323071	0.8289809	0.4134172	0.6647502	0.4651709
Homoserine	0.6983023	0.7018378	0.7149072	0.7242009	0.6649812	0.8189758	0.7640266	0.6782549	0.5256616	0.7163832	0.6410018	0.4788504	0.4438158	0.5528304	0.3849193	0.6326310	0.6478078	0.3654759	0.5773910	0.6299180	0.7322205	0.5901563	0.8331537	0.3790520
Hydroxyproline	0.7868130	0.7673889	0.6748305	0.6843264	0.9174251	1.2313570	0.7636354	0.8520473	0.7546107	0.9010612	0.7151542	0.6026010	0.5303085	0.4746016	0.5074172	0.6101571	0.6367897	0.4844010	0.6824918	0.7603418	0.7412404	0.5531942	0.6457549	0.5127148
Hypoxanthine	0.03108008	0.03295078	0.07230745	0.10605112	0.24210361	0.46310881	0.10167784	0.14625749	0.16616489	0.51041860	0.06533173	0.04225448	0.24245563	0.13432216	0.87837180	0.36355552	0.25734567	0.01519113	0.21277908	0.74516568	0.21031964	0.20654750	0.27581957	0.22056332
Inosine	0.02600116	0.02615317	0.07605084	0.07720853	0.24970896	0.38404333	0.09108355	0.12666396	0.13240581	0.36308907	0.06973492	0.04524077	0.16349696	0.16517816	0.90361214	0.37945644	0.29174887	0.01648628	0.22917311	0.71077105	0.24821758	0.17251436	0.22439895	0.20742862
Isoleucine	0.7734905	0.7720793	0.6809624	0.7169639	0.9427465	1.2809432	0.7698176	0.8840363	0.7578946	0.9174449	0.6951529	0.5988584	0.5521642	0.4869889	0.5300929	0.6111975	0.6246363	0.4812083	0.6819774	0.7716538	0.7384486	0.5738182	0.6861106	0.5234358
L-Alloisoleucine	0.7816351	0.7675873	0.6931879	0.7254023	0.9586529	1.2948073	0.7777563	0.8893020	0.7541538	0.9230311	0.6862217	0.5978543	0.5540295	0.4943954	0.5348676	0.6202152	0.6324164	0.4872354	0.6973422	0.7748112	0.7349445	0.5754398	0.6966434	0.5213951
Leucine	0.7762630	0.7700904	0.6859590	0.7049883	0.9531758	1.2854569	0.7691488	0.8836390	0.7621739	0.9174278	0.7043351	0.6034554	0.5525940	0.4889069	0.5287984	0.6207396	0.6323462	0.4784675	0.6888833	0.7697485	0.7440186	0.5678910	0.6857679	0.5269246
Methionine	0.4595065	0.4579772	0.4746533	0.4885255	0.4920350	0.6604720	0.4462489	0.4727000	0.4003232	0.4848580	0.4535979	0.4214641	0.3289654	0.4052902	0.3049758	0.4320432	0.4224938	0.3929081	0.5814995	0.4638038	0.7436927	0.5635675	0.7926240	0.3739858
Methylguanidine	0.6083126	0.5991099	0.7510126	0.7478605	0.6616402	0.7147471	0.7355709	0.7186135	0.5271701	0.7047024	0.6328199	0.3575302	0.4456060	0.4159211	0.3919142	0.5690907	0.6021682	0.2794409	0.6075165	0.5859735	0.8534668	0.5224783	0.8782036	0.3948659
N,N'-Dicyclohexylurea	0.4491116	0.7786632	1.0568974	0.8605733	0.3151338	0.2683889	0.8111300	0.8860459	0.9300668	0.6072164	0.7132078	0.7497717	0.5024905	0.3967395	0.3895438	0.4417970	0.4784667	0.7943685	0.4818193	0.5755309	0.3671177	0.5808789	0.8349089	1.5812582
N-Acetylethanolamine	0.1837007	0.3351524	0.1712734	0.1999842	0.1839945	0.3390010	0.3605331	0.4625985	0.1857110	0.2160144	0.1688903	0.1901620	0.1246755	0.1620703	0.3036458	0.2729194	0.3908199	0.4101847	0.3189875	0.2665719	0.3897250	0.1503872	0.4816167	0.3320829
N-Acetylneuraminic.acid	0.06720457	0.11616575	0.06952991	0.06068203	0.14038777	0.16392413	0.06753194	0.15396054	0.07783408	0.20979568	0.16580744	0.18465772	0.09179428	0.11928544	0.17453190	0.10237460	0.08390267	0.17293004	0.09089243	0.13104024	0.08846533	0.08536574	0.14463525	0.10738479
Nicotinamide	1.1086306	1.0155569	0.9927073	1.0139620	1.7020512	2.0952281	1.2648053	1.1001351	1.0931990	2.0225090	1.1455333	1.2253957	0.8691954	0.8242333	1.0545029	1.3757596	0.9047593	0.6271669	1.1229611	1.3799018	0.8479625	0.6773855	1.0690791	0.7598487
Norleucine	0.7688610	0.7655194	0.6721997	0.7120115	0.9469902	1.2760697	0.7667306	0.8749643	0.7609668	0.9137877	0.6953367	0.5920285	0.5545982	0.4870829	0.5265577	0.6099556	0.6318839	0.4853943	0.6818889	0.7537906	0.7431439	0.5691091	0.6839599	0.5239574
Normetanephrine	0.4602634	0.7922858	1.0278972	1.1844420	1.1925011	1.0998287	1.4460477	1.2505234	0.8085146	0.8390345	0.7908881	0.6272976	0.7473370	0.6527553	0.9018705	0.9717988	1.1085613	0.6866956	1.8133871	0.7053081	1.5459995	0.7414323	0.8043796	0.5152777
Norvaline	0.7456426	0.7479910	0.6948016	0.6796876	0.8187685	1.0167348	0.7761884	0.8805773	0.7022088	0.7862304	0.7152055	0.6146859	0.4932867	0.5133007	0.4637410	0.6137076	0.6419375	0.4975852	0.6883464	0.7023230	0.8132069	0.6068848	0.6269995	0.4917820
Phenylalanine	0.6926250	0.7008467	0.6459153	0.6778132	0.8648654	1.2378989	0.6956844	0.8330104	0.7424098	0.8759900	0.6224442	0.5904636	0.5133810	0.4601704	0.5379103	0.5883836	0.5392128	0.6769541	0.6840378	0.7221243	0.7056662	0.5232141	0.7153008	0.6231087
Proline	0.2536354	0.2665351	0.2729979	0.2910349	0.3455349	0.5739777	0.2744232	0.3060478	0.2541320	0.3370148	0.2492915	0.2561445	0.1759309	0.2077588	0.2071730	0.2544563	0.2057017	0.2743556	0.2967707	0.3282657	0.4057957	0.2971243	0.5417059	0.3029315
Sarcosine	0.7972464	0.6285018	1.1937639	0.6966922	2.1649467	1.8733796	0.6445680	0.5183578	0.7599217	0.8395287	0.5969229	1.3593589	0.5837919	1.1513682	0.4793732	0.7341413	1.3038976	1.6908640	1.6649814	0.7639477	2.0942908	0.5273449	0.8220729	0.6044479
Serine	0.5353581	0.5267698	0.4793458	0.4622670	0.5259625	0.7771565	0.5041540	0.4785595	0.4262779	0.5054402	0.5073924	0.4689129	0.3561538	0.3706829	0.4047429	0.4597577	0.4136697	0.5811335	0.4466357	0.4885491	0.5757121	0.4545363	0.7522944	0.5896785
TMAO	0.85451078	0.65696505	1.21903340	0.39266798	1.48554668	0.47086960	0.40870485	0.92978038	0.64500025	1.40691014	0.49913503	0.04325557	0.00000000	0.33761085	0.18429464	0.25384521	0.63396713	0.61949213	0.26769308	0.25273734	0.31276815	0.33318616	0.14893635	0.28665877
Threonine	0.7150959	0.7015677	0.7629955	0.7761223	0.6462053	0.8520302	0.7351514	0.6963445	0.5208669	0.7185048	0.6479620	0.4750623	0.4655190	0.5523690	0.3989872	0.6481275	0.5915996	0.3782476	0.5667950	0.6336898	0.7189485	0.6165406	0.9114231	0.3670283
Tyrosine	0.6030869	0.6125875	0.7887788	0.8232557	1.0062731	1.2490204	0.6071225	0.8777774	0.6561377	0.8893080	0.6613815	0.6228148	0.3730047	0.3463561	0.4792403	0.4594995	0.3938609	0.5973173	0.5438654	0.5633916	0.6423756	0.4651992	0.6423144	0.4970374
UDP-GlcNAc	0.000000000	0.000000000	0.000000000	0.004592017	0.193086076	0.040915595	0.004539314	0.145934213	0.178034558	0.116639623	0.000000000	0.070587210	0.149759237	0.000000000	0.055340246	0.339265912	0.000000000	0.018765855	0.038192797	0.065482356	0.000000000	0.000000000	0.070706147	0.000000000
Uracil	0.8457426	0.8495759	1.0951227	1.2036762	2.6855035	3.3864430	1.5948670	1.2708232	1.4810583	2.7345165	0.0000000	0.5702306	1.3042441	0.5982922	1.2443398	0.8348638	0.7037339	0.5697256	0.7155200	1.7113136	0.5957357	0.4716715	0.6942587	0.6309362
Uridine	0.8880025	0.8636672	0.9870649	1.0857023	2.5189912	3.0324660	1.5176027	1.2631859	1.6074507	2.5373434	1.0135393	0.6157471	1.2844979	0.6318885	1.2363457	0.8629738	0.7619592	0.5965804	0.7071004	1.7040465	0.6145321	0.4385381	0.6160858	0.6436844
Urocanic.acid	0.03376918	0.04254745	0.05724673	0.04831958	0.04635670	0.04936237	0.03685679	0.04165554	0.04238366	0.03293443	0.03548771	0.04557768	0.01823145	0.01534968	0.01744506	0.01649835	0.01764671	0.02310776	0.02532258	0.01928040	0.04746682	0.02773702	0.03005870	0.02772801
Valine	0.7459956	0.7503615	0.7026255	0.7024037	0.8202731	1.0275209	0.7588466	0.8909467	0.7097040	0.7982574	0.7008425	0.6146873	0.5054868	0.5030490	0.4737987	0.6111390	0.6462739	0.5020537	0.6864407	0.6854861	0.8229823	0.6217540	0.6254272	0.4997380
Xanthosine	0.4577110	0.4849641	0.6241970	0.6766769	4.2558855	7.7630219	1.5764167	1.0264283	4.2477904	7.8442639	1.0624214	0.1908877	0.8124879	0.1524969	1.8590245	0.6193012	0.4041642	0.1813820	0.2700349	2.3332162	0.1061311	0.1309162	0.1285644	0.3067931
methyl-a-D-galactopyranoside	1.3477293	0.9038175	0.7205699	0.5291660	1.0640751	1.5175823	0.9536713	0.7824787	1.0652578	0.6404905	1.0459692	1.1463473	0.6403432	0.7595554	1.0700229	0.9111508	0.7905356	0.9514611	0.9061882	1.0269884	1.2904433	0.9006732	1.4165315	0.9374045
3-Indoxylsulfate	0.0039742006	0.0023391308	0.0353740607	0.0016464954	0.0022620914	0.0031716151	0.0032944106	0.0030293134	0.0014770960	0.0010762186	0.0009190207	0.0016898664	1.6172315346	2.2955004825	3.8331504617	1.8889801044	2.9435636983	1.0289100428	1.5241429637	4.5331715267	1.5340171634	1.4178092065	2.0482161824	0.6584347506
2,3-Dihydroxybenzoic.acid	0.48998087	0.45925943	0.20171275	0.11165078	0.40996557	0.48016548	0.38672610	0.54687554	0.11396917	0.11675343	0.11986621	0.07671945	1.24635923	1.42578176	1.18469069	2.02295701	1.50349511	2.05013084	1.32332791	1.94655749	1.59277083	1.10832205	1.72193673	1.59378286
2-Hydroxybenzoic.acid	0.7965871	0.7728044	0.3218101	0.2447120	0.6136844	0.3744148	0.4319101	0.7563006	0.3510303	0.2609883	0.2320656	0.3058933	2.2558602	2.5915402	1.5055872	4.0838144	2.3711602	1.4305851	2.8694710	3.5659023	3.3476204	3.0332858	3.9963234	1.7222825
2-Hydroxyphenylacetic.acid	0.8336771	0.7515347	0.6511527	0.4969051	0.6434132	0.9558337	0.8266350	0.8324308	0.3614684	0.4623572	0.5138190	0.3820153	1.1250300	0.9010148	1.0660509	0.6361450	0.8173596	0.5060616	0.6922646	1.0914150	0.6260436	0.7397448	1.0785493	0.3409159
2-Methylbutyric.acid	0.9162436	0.7647800	0.8114202	0.6791095	0.5724590	0.7517002	0.3763115	1.2930302	0.9617106	0.9124321	0.8012958	0.5613845	0.4573325	0.4679710	0.4829717	0.7781003	0.8911581	0.3806420	0.3924137	0.6863296	0.4486746	0.7857104	0.3367745	0.6051235
3-Hydroxyphenylacetic.acid	0.6300611	0.8019803	0.4395543	0.3531513	0.5712445	0.7262196	0.5517035	0.7293511	0.4730190	0.6674977	0.4150897	0.2773652	0.9234166	0.9577731	1.4031874	0.7612582	0.9709512	0.7315022	1.3207369	1.7982472	1.0991215	0.8245665	1.2208213	0.7844164
3-Indoleacrylic.acid	0.06863647	0.07993838	0.29599954	0.01919182	0.00000000	0.13184064	0.03164545	0.14464441	0.09467593	0.11117823	0.01868143	0.01239224	0.92060183	0.61627943	0.93140097	0.66541385	0.56434471	1.32301774	1.42618439	1.99700779	0.37785536	0.20324056	0.60686634	1.64759696
3-Methyl-2-oxovaleric.acid	0.7284818	0.7998605	0.8214719	0.7937070	0.4602629	0.6143488	0.5652290	0.8385703	0.5941437	0.4562508	0.6723339	0.7837716	0.3804015	0.3810327	0.5773716	0.7591478	0.7364682	0.4953530	0.4704629	0.6691918	0.4352169	0.4875276	0.4163757	0.3738398
3-Phenyllactic.acid	0.1588272	0.1628897	0.1481714	0.2012786	0.1907786	0.3345011	0.1358782	0.2337874	0.1476731	0.1240542	0.1009023	0.1153669	0.3804044	0.5534323	0.1483201	0.6223141	0.3725672	0.1412559	0.6140716	0.9084644	0.3132405	0.3880331	0.2251292	0.3031758
4-Hydroxybenzaldehyde	0.2899898	0.4539353	0.2719443	0.1845166	0.4342202	0.1635672	0.3338587	0.3637891	0.3575433	0.3653502	0.3196463	0.1567934	0.1617343	0.6138772	0.2441290	0.4573647	0.5656350	0.4557670	0.6785351	0.7462931	1.9606845	1.3874968	0.6191694	0.2239879
4-Hydroxybenzoic.acid	0.7415720	0.6427323	0.3418409	0.2771368	0.5039981	0.4729974	0.4056269	0.8144809	0.2511309	0.2701269	0.2969636	0.2283418	2.4564177	2.5600532	1.7188250	3.7086417	2.5128617	1.5046030	3.0486985	3.3705885	3.2851761	3.2291628	4.4785681	1.5404096
4-Hydroxyphenylacetic.acid	1.0741901	0.9484975	0.6531368	0.4162101	0.6926568	0.7114619	0.7534805	0.7216074	0.8789581	0.6506508	0.8736327	0.2907721	1.0987438	0.8528024	0.9308913	1.0528581	0.7804062	0.4420478	0.9035063	1.3928209	0.8826471	0.8112688	1.0836423	0.7085074
4-Hydroxyphenylpyruvic.acid	1.14921842	0.98845607	1.98099909	1.72171599	1.23177289	1.72876545	0.83944057	2.56334937	1.38221909	0.52593743	1.12397307	1.22757429	0.24319700	0.39547674	0.44914055	0.12458038	0.68509201	0.18949878	0.47693233	0.48118769	2.00381191	1.66541921	0.79929192	0.08403531
4-Methyl-2-oxopentanoic.acid	0.5350964	0.7260103	0.8990688	0.8404178	0.5670097	0.4391739	0.5110427	0.6475787	0.4532219	0.3383676	0.7675285	0.6123645	0.4158343	0.4958764	0.5988977	0.8790783	0.7914478	0.4360865	0.6702444	0.6582298	0.4875331	0.4562112	0.4409016	0.5753140
4-Methylvaleric.acid	1.2193120	1.1373415	1.2803601	1.2649514	0.7155701	1.2545237	1.0279050	1.3477962	1.2666246	0.6921735	1.1916585	0.9646052	0.5288983	0.4787545	0.5958022	0.8224816	0.8099802	0.6323150	0.5876209	0.7061165	0.6493778	0.6388923	0.6152713	0.6383928
Acetyl-L-tyrosine	1.3823909	1.5654071	2.4631201	1.8466601	2.5207747	1.8986028	1.1913219	2.1991471	1.1217505	1.2484589	1.8941245	1.1053379	0.7384137	0.6968520	1.0445795	0.9093524	0.7819208	3.3148925	1.3974540	0.6655445	2.4891795	1.5615589	1.2013689	1.0886114
Allantoin	0.4179758	0.3920830	0.4618506	0.5288154	0.4099781	0.9940990	0.5244163	0.5888625	0.3894575	0.4465263	0.4335474	0.5277082	0.3798188	0.4607883	0.4766550	0.5942443	0.5207472	0.4367983	0.6263660	0.3932992	0.6471256	0.5786775	0.7884335	0.3839070

Table S2B. Serum metabolites

Benzoic.acid	0.5137459	0.8011919	0.8700612	0.7071747	0.7833871	0.5132784	0.9021533	1.0397754	0.6048753	0.4560824	0.7378836	0.9754978	1.1409319	1.1780068	0.7153125	1.3047273	0.8824771	0.6084236	1.1787358	0.6067928	1.2885574	0.9537052	0.9203954	0.6804284
Citraconic.acid	1.1832005	0.8655313	0.8829787	0.9384341	0.7149742	0.9088399	0.8197862	0.9260997	0.7828447	0.6176995	0.8662048	1.0564296	0.6012591	0.5014137	0.6816109	0.8420866	0.9668129	0.6730451	0.7962384	1.0701069	0.6463906	0.4847092	0.6272626	0.4146637
F6P	0.6148911	0.6397381	0.4180315	0.4791333	0.8018948	1.0489481	0.5600311	0.4700166	0.5596413	0.7723185	0.5416507	0.8945571	1.3691818	0.9980324	0.7388595	2.4056484	0.4272504	1.0292442	1.8827413	1.0846360	1.0310069	0.7883688	1.5219983	1.0737757
G6P	0.5960554	0.6725720	0.5424209	0.4639696	0.7149186	1.0277904	0.6028397	0.4610059	0.5065798	0.6587487	0.6167404	0.6808418	1.2350843	1.1748242	0.8482595	2.0001126	0.6219998	1.0504048	1.8062061	1.1607852	0.8258928	0.6993957	1.1175112	1.3118745
Gentisic.acid	0.5139415	0.4151858	0.1699240	0.1634507	0.4950193	0.5381677	0.4975664	0.4815131	0.1646657	0.1868625	0.1272859	0.1044369	1.2590846	1.5629216	1.2770249	2.0023922	1.5103748	1.8111364	1.2449566	2.1445328	1.5509669	1.2755833	1.7910363	1.3444712
Glucuronic.acid	0.2943072	0.3285132	0.3076357	0.3028917	0.4062023	0.3879114	0.3706921	0.4386659	0.3901433	0.3952716	0.3387479	0.4035722	0.3447072	0.3041804	0.3525938	0.3387238	0.4254461	0.2811051	0.3409680	0.3958022	0.2665106	0.3763200	0.4654544	0.4758465
Glutaconic.acid	0.8936806	0.7301086	0.9696221	0.8526519	0.5442453	0.5880147	0.5992676	0.9477549	0.6377112	0.4061179	0.7163246	0.8437270	0.5472146	0.4245548	0.7144656	0.9034756	0.8900980	0.5316449	0.6503364	0.7681063	0.4747078	0.4802786	0.3834784	0.3985794
Isobutyric.acid	1.2611450	1.0617315	1.2009763	1.0144702	1.6725007	1.3712387	0.9813562	1.1676435	1.0259964	1.1891182	1.1904247	1.0942924	1.5989614	1.4913369	1.5619882	2.1045380	1.2262023	2.0379971	1.5637909	1.3742913	1.7912535	2.4635205	2.4077597	0.8333862
Isocitrate	0.9363562	0.9694145	1.8275446	1.6172730	1.9900427	5.4531547	0.8358172	2.2995017	0.9928619	1.4021071	1.0910185	1.6178133	0.6324479	0.5417913	1.1534480	1.0034652	0.4038732	1.0685027	0.8624940	1.8233722	0.7640728	0.5662017	1.4586538	1.0827235
Isovaleric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
Ketoisoleucine	0.6320128	0.6428483	0.8286818	0.8677048	0.5299760	0.6119989	0.6528786	0.9677705	0.5359146	0.4973663	0.6318207	0.7465316	0.4568074	0.5057830	0.6968982	0.8765001	0.8146209	0.5613216	0.6569281	0.7444931	0.5323563	0.4600245	0.4162702	0.4342382
Ketoleucine	0.7407093	0.6770491	0.8666374	0.8526344	0.4862419	0.6715415	0.6274490	0.9300686	0.5821689	0.4755816	0.6434545	0.7973945	0.4390582	0.4554591	0.6420511	0.8235266	0.8422553	0.5404413	0.5446198	0.7969653	0.5417458	0.5267113	0.3870948	0.4680990
Leucic.acid	0.07332520	0.05691064	0.16240462	0.13844880	0.00000000	0.13192383	0.18425088	0.09091516	0.09485068	0.09601863	0.12344032	0.07552676	0.07950051	0.18992066	0.18504689	0.23065715	0.09115326	0.08444802	0.03149924	0.39720394	0.12766977	0.17789873	0.05538901	0.09050159
Levulinic.acid	0.8733528	0.7773803	1.1885660	0.9115188	0.7639572	0.6718761	0.8896795	1.1401628	0.7158665	0.5367945	0.7854932	1.2883168	0.3414807	0.3001495	0.3850537	0.3747144	0.5945561	0.5645422	0.3800352	0.4273772	0.8644449	0.6055051	0.5948493	0.3990532
Mannose	0.6683804	0.7490577	0.9983012	0.8180795	1.3001285	1.6448997	1.1464313	1.2114073	0.8301304	1.2382297	0.8439367	0.8125773	0.6266621	0.8626987	0.8407750	0.8446483	0.6687708	0.4966768	0.7226429	1.1309506	1.0346696	0.5709434	0.9154449	0.4778395
Mucic.acid	1.4449558	1.5175796	1.7136174	1.7628124	2.9718829	3.5026565	2.1747000	2.7953622	1.7672312	2.1885316	1.4510821	1.0805201	0.9881322	0.4407361	0.5894630	0.4070065	1.0587811	0.3780752	1.0418203	0.6686453	1.6099692	1.3606473	1.4986516	0.2406813
Myoinositol	0.9158956	1.0903492	1.0132274	0.7188772	1.0656828	1.1381421	1.0394161	1.4046805	0.7925365	1.0714162	0.8230511	1.0257722	0.9557425	0.9178068	1.1749202	0.9482438	0.8227359	0.9848646	0.8354734	1.0013812	1.1290946	0.6984916	0.7774978	0.6192854
Nonadecanoic.acid	0.7597794	1.0984831	1.0566841	0.6869035	0.7567158	0.6152611	1.1422799	0.7788149	0.9910287	0.5742253	0.6355600	0.7711078	0.6560131	0.6744979	0.6686692	0.4608864	0.5979236	0.7173817	0.5101773	0.4252656	0.8019144	0.5360187	0.6069391	0.7542067
Palmitic.acid	1.1697404	1.1289978	1.0746644	1.0579965	1.0081349	1.0744314	1.1476871	1.1941974	0.8681928	1.2085481	0.9326418	1.0318683	0.8677152	0.6149741	1.0140553	0.7505703	0.9214058	0.8712176	0.6402457	0.9742409	0.8439879	0.7187422	0.7523927	0.6433307
Pentadecanoic.acid	1.0416191	1.0968575	1.2484225	1.3574081	1.1434541	1.0799144	1.1658474	1.1948132	1.3305186	1.2054729	1.2713009	1.5459406	0.8983497	0.5198255	0.6073550	0.4853418	0.5751780	1.0182041	0.5896763	0.4666398	0.7345063	0.5951775	0.7111444	1.3217963
Phenylglyoxylic.acid	0.6505425	0.7622024	0.4309066	0.4541979	0.2762495	0.7508618	0.5632261	0.6586299	0.5866884	0.5445800	0.4662587	0.1722703	0.7744946	0.6864339	0.7886320	1.3051016	0.5019615	0.4552686	0.6690830	1.0880316	0.3913430	0.4653460	0.7296399	0.4115943
Phenylpyruvic.acid	1.6837193	1.1946551	1.2117800	1.4134552	1.2954706	2.1709991	1.1442532	2.6172624	1.0717084	1.3957800	1.0979073	1.1359335	1.1605814	1.1434987	1.1531757	0.9821010	1.4858917	0.9080724	1.9169820	1.1176169	2.5614484	2.4989341	1.3980044	0.5780909
Phthalic.acid	0.8312283	1.6718001	1.6295232	0.6950160	0.9813302	0.7106078	1.0632694	0.8647620	0.8410628	0.7436008	0.7956362	1.1354350	0.8725004	0.8293501	1.0938052	0.5822359	1.4563201	0.5690216	0.9613559	0.6940954	1.4272887	0.7233408	0.5024063	0.4871232
Pregnenolone.sulfate	0.15109681	0.06450606	0.07824688	0.11139556	0.16581628	0.10776864	0.25053390	0.01274011	0.18073139	0.11896680	0.04564024	0.04885158	0.01195747	0.02402525	0.01011219	0.17572145	0.13117700	0.39292133	0.39154295	0.10137071	0.05705211	0.00000000	0.16982081	0.79087325
Sorbitol	0.5263006	1.1125334	0.8735987	1.0204774	1.8649705	2.9610703	1.1785228	1.5158011	2.0153651	1.8722321	1.1390051	0.8823096	1.0456780	0.9890519	1.3129599	1.0471344	0.9181730	0.6389121	0.9514893	1.4349702	0.5031007	0.5956122	1.2551092	1.2870245
Stearic.acid	1.0184713	1.0750990	1.2224773	1.0051354	0.9065094	0.7811735	1.1789520	0.8386794	0.7374513	0.8942426	0.7940715	1.0533583	0.9066691	0.8976884	0.9911621	0.7727796	1.1123866	0.8484215	0.7059182	0.8682556	1.0533575	0.7744590	0.7948777	0.6558604
Suberic.acid	0.6717550	0.7711379	1.0687371	1.0001316	1.0048246	0.9080725	0.9082036	1.1276302	0.8134137	0.8582683	0.7563850	0.8792998	0.7326972	0.6036770	0.8775342	0.9730880	0.7433058	0.9116463	0.9155839	0.7838742	0.8153078	0.6814005	0.7289064	0.8155878
Valeric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
X5P	0.5027232	0.5146277	0.3386513	0.4047086	0.8736686	0.7205287	0.3494380	0.3850901	0.2681374	1.0155902	0.3328307	0.5785047	2.9203121	2.3234867	2.2986260	4.6446462	1.7533107	2.0129461	3.7469756	2.2407628	2.3747651	1.7961056	2.2261729	2.3189625
alpha-Hydroxyisovaleric.acid	0.2371994	0.2527587	0.3991637	0.3119418	0.2179633	0.4664979	0.3021191	0.2406591	0.1822040	0.2528320	0.4813419	0.2408560	0.1477089	0.1300373	0.2515798	0.1820547	0.2035981	0.1894338	0.3520112	0.1956317	0.1405861	0.1275436	0.3147498	0.1255165
alpha-ketoisovaleric.acid	1.1483537	0.9211920	1.0424223	1.1143107	0.6507956	0.7640291	0.9224072	1.3979542	0.8386406	0.5159111	1.0674584	1.1048148	0.5318858	0.4081003	0.6895266	0.8388138	0.6593168	0.4917263	0.4880581	0.7309270	0.7401869	0.6986751	0.6619629	0.5088614
p-Coumaric.acid	0.8884362	2.5429656	0.8671267	0.3814133	0.4828513	0.4830849	0.3138755	1.1793190	1.9050500	0.2601965	1.4171255	0.5975559	0.5928540	0.5256743	0.5782154	0.6462564	0.6272135	0.2994134	0.7650979	0.6735591	1.3843546	0.5536971	4.3952783	2.8617781

Constructed from biom file

#OTU ID	CO.1	CO.2	CO.3	PCB6.1	PCB6.2	PCB6.3	PCB30.1	PCB30.2	PCB30.3
D_0__Bacteria;D_1__Actinobacteria;D_2__Actinobacteria;D_3__Bifidobacteriales;D_4__Bifidobacteriaceae;D_5__Bifidobacterium;__	0	0	18	0	0	0	0	0	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;Ambiguous_taxa	19	26	15	43	0	0	0	37	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium	0	0	0	74	122	109	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Barnesiellaceae;D_5__uncultured;D_6__Bacteroides sp. Tilapia9	0	12	0	0	16	0	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	9296	10607	8015	13871	7845	10279	6933	7367	10551
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;__;__	8115	8838	9280	5390	6298	5799	7923	10196	7843
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Rikenellaceae;D_5__Alistipes;__	2588	2712	2528	1387	2374	1818	3313	2397	2808
D_0__Bacteria;D_1__Cyanobacteria;D_2__Oxyphotobacteria;D_3__Chloroplast;__;__;__	8	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Bacillales;D_4__Bacillaceae;D_5__Bacillus;__	0	0	0	0	0	0	61	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Lactobacillaceae;D_5__Lactobacillus;D_6__Lactobacillus gasseri	329	316	457	795	190	685	1548	189	1114
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Streptococcaceae;D_5__Lactococcus;__	39	0	30	35	59	37	0	0	40
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiaceae 1;D_5__Clostridium sensu stricto 1;D_6__uncultured bacterium	62	58	55	18	0	0	0	0	254
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;Ambiguous_taxa;Ambiguous_taxa	0	57	0	0	103	0	109	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;D_5__uncultured bacterium;D_6__uncultured bacterium	46	228	28	41	198	39	178	80	188
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;__;__	94	120	0	127	141	161	65	180	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Defluviitaleaceae;D_5__Defluviitaleaceae UCG-011;Ambiguous_taxa	131	154	92	70	0	188	0	0	159
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium	0	0	0	55	60	105	106	57	41
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] brachy group;D_6__uncultured bacterium	0	0	0	0	0	7	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured bacterium	0	16	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured organism	0	3	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;__	67	62	63	0	185	0	94	208	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;D_6__uncultured bacterium	1455	1296	1162	1122	1580	431	1767	1383	1644
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;__	121	91	123	0	17	1803	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium	109	0	162	0	0	0	0	37	64
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;Ambiguous_taxa	303	293	302	0	287	0	278	0	279
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;D_6__uncultured bacterium	0	362	472	585	226	498	237	393	324
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;__	0	106	114	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetitomaculum;D_6__Firmicutes bacterium CAG_194_44_15	262	245	321	454	304	0	319	241	294
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;D_6__Lachnospiraceae bacterium 609	203	0	320	0	1693	0	0	0	128
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;__	257	183	319	222	0	250	83	117	206
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium	331	388	366	244	287	206	757	591	869
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens	486	530	520	91	214	151	130	84	161
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__uncultured bacterium	244	0	512	0	0	572	0	631	636
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;__	905	727	990	1994	843	1142	628	1336	656
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae FCS020 group;__	143	117	105	173	98	92	183	212	147
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;D_6__uncultured bacterium	4489	4932	2051	4199	4272	3122	2789	1700	3057
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;__	8765	8865	8624	6923	9399	7884	12717	12190	11786
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa	718	738	571	0	0	0	668	406	1198
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium	466	499	0	0	0	0	858	0	897
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;__	1120	848	1065	0	313	0	0	878	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;D_6__uncultured bacterium	112	142	0	1124	150	150	218	226	821
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;__	0	0	70	0	0	193	0	287	154
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;Ambiguous_taxa	0	0	0	0	0	36	51	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;D_6__uncultured bacterium	297	293	243	425	252	0	106	231	208
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44	0	0	0	0	0	0	74	43	109
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium	474	445	507	945	1516	529	2001	861	1832
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;__	0	0	129	0	0	0	27	126	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella 3;D_6__uncultured bacterium	183	31	283	415	0	5	37	703	431
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella;D_6__uncultured bacterium	57	67	0	72	58	72	84	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;D_6__uncultured bacterium	226	227	201	0	825	0	912	291	295
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;__	0	0	0	0	0	0	181	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016	0	0	0	159	97	171	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Clone-47	234	331	135	0	112	195	68	73	541

D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture Jar-19	0	0	0	93	0	0	0	0	94
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-27	0	0	164	0	118	0	125	0	72
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-54	0	0	0	0	0	71	50	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__uncultured bacterium	3274	2630	2983	2961	2110	2254	3683	2587	3054
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;__	350	385	616	511	297	410	584	497	381
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;__;__	6804	5724	7057	7593	6563	4562	6732	5530	11105
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptococcaceae;D_5__uncultured;Ambiguous_taxa	89	70	66	64	43	104	88	128	132
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptostreptococcaceae;D_5__Romboutsia;__	0	0	0	0	0	0	0	62	84
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium	149	111	197	98	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;__	76	0	54	127	88	175	51	0	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__GCA-900066225;__	64	0	95	0	104	0	0	84	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Harryflintia;D_6__uncultured bacterium	0	0	0	0	0	0	0	30	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	258	141	349	112	119	391	0	129	155
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	227	254	153	0	320	0	0	265	432
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;D_6__uncultured bacterium	101	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium	0	0	0	270	0	58	51	440	164
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__unidentified	1602	1557	1495	1500	1279	920	524	1258	1403
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;__	436	440	421	340	213	176	800	266	354
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;Ambiguous_taxa	501	564	356	762	366	492	415	540	394
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;D_6__uncultured bacterium	387	58	461	124	290	213	335	405	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 6;__	91	104	64	190	562	242	118	235	218
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium	232	220	248	325	308	299	351	238	463
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;__	1161	1127	873	1270	1378	1155	1290	1131	1291
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium;D_6__uncultured bacterium	2409	2239	2033	1913	1367	1784	2656	2134	2415
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae NK4A214 group;D_6__uncultured bacterium	0	0	0	0	0	25	0	81	34
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-005;Ambiguous_taxa	0	95	0	164	116	212	35	180	114
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-009;Ambiguous_taxa	454	473	388	283	552	265	684	622	611
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-010;D_6__uncultured organism	77	53	70	79	59	134	59	54	112
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium	94	48	118	158	437	187	502	1052	104
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;__	0	0	0	0	0	70	0	0	60
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;D_6__uncultured bacterium	0	32	0	72	183	75	0	72	264
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;__	277	280	352	51	163	136	95	57	731
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcus 1;__	1370	1132	1457	263	1098	139	1583	2721	1531
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__[Eubacterium] coprostanoligenes group;__	401	231	489	14	315	34	134	85	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1	0	0	0	980	816	685	110	176	785
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__unidentified	120	139	147	108	144	110	421	134	140
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;__	37	22	42	21	0	24	653	394	406
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;__;__	1109	1025	1157	441	580	499	1166	1030	902
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis	556	613	516	135	106	0	0	0	20
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa	0	23	37	200	63	530	55	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Turicibacter;__	471	277	460	329	133	421	191	149	237
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	0	0	0	39	31	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured;D_6__uncultured bacterium	0	55	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Anaeroplasmatales;D_4__Anaeroplasmataceae;D_5__Anaeroplasma;Ambiguous_taxa	275	338	0	562	1369	786	922	665	625
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;Ambiguous_taxa;Ambiguous_taxa;Ambiguous_taxa	0	0	16	0	0	0	0	0	50
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;D_4__uncultured bacterium;D_5__uncultured bacterium;D_6__uncultured bacterium	138	137	0	100	147	87	44	87	66
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;__;__;__	245	479	91	42	203	0	417	216	279
D_0__Bacteria;D_1__Verrucomicrobia;D_2__Verrucomicrobiae;D_3__Verrucomicrobiales;D_4__Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium	0	20	0	2363	1475	7608	0	0	0

#Differentially abundant for PCB6

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
316.7182704	-11.65082862	1.236665352	-9.421165231	0	0	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa
153.3172368	-10.60410763	3.148390595	-3.368104215	0.0007568698067	0.005710926723	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium
41.03072715	-8.702464375	3.274032281	-2.658026442	0.007859972585	0.04077360779	Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium
319.3213166	-1.580215074	0.3616598924	-4.369340109	0.00001246225466	0.0001292958921	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
781.7386176	-0.9207800117	0.1196190574	-7.69760297	0	0	Ruminococcaceae;__;__
7200.677116	-0.3902585448	0.08636488756	-4.518717685	0.000006221528614	0.00007376955357	Muribaculaceae;__;__
275.8941433	0.6171854875	0.2015178394	3.062684124	0.002193614783	0.01517250225	Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium
754.2569069	1.264658563	0.4337143845	2.915878763	0.003546882969	0.02102794903	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
177.0232909	1.776599012	0.6062650277	2.930399958	0.003385259774	0.02102794903	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
214.5092189	2.099707756	0.5666020505	3.705789194	0.0002107335238	0.001749088248	Ruminococcaceae;D_5__Ruminiclostridium 6;__
149.9534028	3.917624073	1.51816477	2.580499923	0.009865737835	0.04816801414	Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa
38.92808467	8.824512079	1.427806771	6.180466614	0.0000000006391241199	0.000000008841216991	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
2019.466775	9.269818825	2.203252554	4.207333747	0.00002584013765	0.0002383034916	Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium
53.84095289	9.292598686	1.328101098	6.996906108	0	0	Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium
62.8067954	9.514101089	3.293079828	2.889119482	0.003863222531	0.02137649801	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
76.87108532	9.805534228	1.36829318	7.166252356	0	0	Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016
447.5479333	12.34718529	1.245794989	9.911089227	0	0	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

#Differentially abundant bacteria for PCB30

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
83.46976574	-9.948696447	1.426866799	-6.972407274	0	0.0000000001386455415	Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium
61.1174388	-9.499046883	1.511973717	-6.282547625	0.0000000003330691888	0.000000005928631561	Lachnospiraceae;D_5__A2;__
39.30425587	-8.862241275	2.96685731	-2.987080385	0.002816556532	0.01790525224	Lachnospiraceae;D_5__Acetatifactor;__
307.8175697	-6.935230581	1.27412215	-5.443144191	0.00000005234823872	0.0000006655704638	Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis
334.6713868	-2.313158666	0.3287417297	-7.036401093	0	0.0000000001386455415	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
308.0630698	-1.346206268	0.4204681762	-3.201684084	0.001366267468	0.009353677279	Erysipelotrichaceae;D_5__Turicibacter;__
8798.415146	-0.4334527046	0.1329022528	-3.261439858	0.001108479444	0.008968606407	Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium
532.8390926	0.7735398016	0.2396538735	3.227737529	0.001247734027	0.009254027366	Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium
965.8942038	1.446139973	0.3454244671	4.186559179	0.00002832151155	0.0002800682809	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
332.2258696	2.576372032	0.9118396441	2.825466132	0.004721187874	0.02801238138	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
246.2103261	3.623458987	0.5613278261	6.455156539	0.0000000001081070969	0.000000002405382905	Ruminococcaceae;D_5__uncultured;__
32.70775081	8.350701175	2.012224217	4.149985427	0.00003324964435	0.0002959218347	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
33.11545623	8.369454039	1.915893281	4.36843436	0.00001251404163	0.0001392187131	Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44
107.2867183	10.06452036	1.673272351	6.014872807	0.000000001800279971	0.0000000267041529	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
144.5866908	10.49616302	1.535432272	6.835966137	0	0.0000000002416474138	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

Table S5-a. Correlation between differentially abundant bacteria and metabolties

Biocompartment	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Serum	Serum	Serum	Serum	Serum	Serum
Taxa	3-Hydroxybutyric acid	Acetylcarnitine	Adenylosuccinate	Aminoisobutyric acid	Arginine	Dimethylglycine	Folinic acid	NADP	Shikimic acid	6-Methyl-DL-tryptophan	Asparagine	Proline	Serine	Urocanic acid	Levulinic acid
Lachnospiraceae UCG-001 Ambiguous	0.745869854	-0.1695158759	-0.1525642883	-0.5933055657	-0.2373222263	-0.5424508029	0.288176989	0.01695158759	-0.08475793795	0.1186611131	0.2034190511	0.2034190511	-0.1017095255	0.05085476277	-0.1017095255
Lachnospiraceae UCG-001 uncultured	0.3286335345	0.1825741858	0.1278019301	-0.2921186973	-0.4746928832	-0.3103761159	0.01825741858	0.2008316044	0.2373464416	0.1460593487	0.3834057903	0.4016632088	0.1460593487	0.3651483717	0.1643167673
Lachnospiraceae ASF356 uncultured	0.5659799761	-0.4929503018	-0.3103761159	-0.4016632088	0.1643167673	-0.3286335345	0.2738612788	-0.2921186973	-0.4016632088	0.2008316044	-0.07302967433	-0.1825741858	-0.2373464416	-0.09128709292	-0.07302967433
Clostridium scindens	0.6666666667	-0.65	-0.5833333333	-0.5166666667	0.5833333333	-0.5	0.7	-0.45	-0.4	-0.45	-0.2833333333	-0.4666666667	-0.5166666667	-0.65	-0.7833333333
Ruminococcaceae	0.7166666667	-0.6666666667	-0.1666666667	-0.55	0.05	-0.6	0.1666666667	-0.4	-0.1333333333	0	-0.1166666667	-0.1666666667	-0.4166666667	-0.15	-0.15
Muribaculaceae	0.6833333333	-0.6666666667	0.1	-0.3333333333	-0.03333333333	-0.3666666667	0.03333333333	-0.2333333333	0.05	0.1333333333	-0.08333333333	-0.05	-0.3166666667	-0.1833333333	-0.06666666667
Ruminiclostridium 9 uncultured	-0.6333333333	0.6666666667	0.2	0.4333333333	-0.6	0.45	-0.3833333333	0.3166666667	0.45	0.5833333333	0.4833333333	0.55	0.7833333333	0.6333333333	0.7
Roseburia uncultured	-0.65	0.55	0.55	0.6666666667	-0.7666666667	0.6333333333	-0.4333333333	0.35	0.7333333333	0.6166666667	0.6333333333	0.6	0.8666666667	0.7333333333	0.8333333333
Ruminococcaceae UCG-013 uncultured rumen bacterium	-0.6333333333	0.2833333333	0.7333333333	0.75	-0.35	0.65	-0.6333333333	0.3	0.6166666667	0.4	0.2833333333	0.3333333333	0.4333333333	0.55	0.65
Ruminiclostridium 6	-0.6666666667	0.6	0.6	0.8833333333	-0.1833333333	0.9	-0.1833333333	0.6	0.5166666667	0.2166666667	0.45	0.3833333333	0.6166666667	0.4	0.3
Erysipelatoclostridium Ambiguous	-0.745869854	0.3559833394	-0.08475793795	0.372934927	0.2542738139	0.3051285766	-0.2712254014	0	0.08475793795	-0.2373222263	-0.2373222263	-0.1186611131	0.08475793795	-0.1017095255	-0.05085476277
Family XIII UCG-001 uncultured	-0.8136762043	0.745869854	0.7119666788	0.8814825547	-0.2542738139	0.8136762043	-0.5424508029	0.661111916	0.6780635036	0.3220801642	0.4576928649	0.5424508029	0.6102571533	0.661111916	0.4915960401
Akkermansia muciniphila	-0.5477225575	0.3468909531	-0.1278019301	0.3103761159	0.4199206274	0.3103761159	0.03651483717	0.1095445115	-0.1095445115	-0.4564354646	-0.2556038602	-0.219089023	-0.03651483717	-0.2921186973	-0.3468909531
Enterorhabdus uncultured	-0.6534973784	0.3168472138	0.0990147543	0.6336944275	0.2475368857	0.6336944275	0.0990147543	0.1485221314	0.1188177052	-0.2277339349	0.04950737715	-0.1188177052	0.2574383612	-0.04950737715	-0.1089162297
Oscillibacter uncultured	-0.5744562647	0.6614950926	0.3568591947	0.3568591947	-0.3916747259	0.3916747259	-0.687606741	0.4613057883	0.1914854216	0.4874174367	0.130558242	0.4438980227	0.4177863743	0.5048252023	0.644087327
Clostridiales bacterium CIEAF 016	-0.7525121327	0.4554678698	-0.01980295086	0.5148767223	0.3663545909	0.5148767223	-0.07921180344	0.1683250823	-0.05940885258	-0.2871427875	-0.1485221314	-0.1584236069	0.1188177052	-0.06931032801	-0.1287191806
Clostridium sp. Culture-1	-0.8306277919	0.6272087408	0.2373222263	0.6780635036	-0.2034190511	0.7119666788	-0.2373222263	0.3220801642	0.2542738139	0.1695158759	0.2203706387	0.2034190511	0.5763539781	0.288176989	0.372934927
Anaerotruncus uncultured	0.5659799761	-0.8033264177	-0.8398412548	-0.8580986734	0.5659799761	-0.8580986734	0.4016632088	-0.8580986734	-0.8215838363	-0.5842373947	-0.7850689991	-0.8215838363	-0.8580986734	-0.8215838363	-0.6207522318
Lachnospiraceae A2	0.2872281323	-0.3307475463	-0.3829708431	-0.174077656	0.8964999282	-0.174077656	0.4526019055	-0.1479660076	-0.4351941399	-0.5135290851	-0.3568591947	-0.4526019055	-0.5570484991	-0.4961213195	-0.8007572174
Acetatifactor	0.593366104	-0.6390096504	-0.6390096504	-0.7074749701	0.3195048252	-0.7074749701	0.1825741858	-0.5477225575	-0.3195048252	-0.1597524126	-0.5249007843	-0.3195048252	-0.502079011	-0.7074749701	-0.4792572378
Dubosiella newyorkensis	0.661111916	-0.7628214416	-0.7797730292	-0.7967246168	0.4407412774	-0.7628214416	0.6950150912	-0.7628214416	-0.7119666788	-0.6780635036	-0.5763539781	-0.7628214416	-0.7119666788	-0.8645309671	-0.7289182664
Turicibacter	0.2333333333	-0.3166666667	-0.7666666667	-0.6166666667	0.7666666667	-0.6	0.2	-0.4666666667	-0.8333333333	-0.4833333333	-0.7	-0.6166666667	-0.7333333333	-0.5333333333	-0.5833333333
Muribaculaceae uncultured	-0.1	0.1166666667	-0.6333333333	-0.3333333333	0.65	-0.2666666667	0.2666666667	-0.1666666667	-0.7333333333	-0.65	-0.5833333333	-0.5166666667	-0.4833333333	-0.55	-0.6166666667
Lachnospiraceae GCA-900066575 uncultured	0.3666666667	0.01666666667	0.3333333333	-0.1833333333	-0.75	-0.2	-0.2833333333	0.1833333333	0.4833333333	0.6166666667	0.45	0.6	0.3333333333	0.4666666667	0.5333333333
Ruminococcaceae uncultured	0.1166666667	0.1833333333	0.4	-0.01666666667	-0.4666666667	-0.05	-0.5333333333	0.3166666667	0.35	0.65	0.3333333333	0.5666666667	0.2333333333	0.6333333333	0.5833333333
Clostridium sp. Clone-44	-0.06931032801	0.5049752469	0.5445811486	0.2277339349	-0.8218224607	0.2475368857	-0.4554678698	0.5544826241	0.6039900012	0.8218224607	0.6832018047	0.8416254115	0.6832018047	0.8218224607	0.782216559

Table S5-a. Correlation between differentially abundant bacteria and metabolties

Biocompartment	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Serum	Serum	Serum	Serum	Serum	Serum
Taxa	3-Hydroxybutyric acid	Acetylcarnitine	Adenylosuccinate	Aminoisobutyric acid	Arginine	Dimethylglycine	Folinic acid	NADP	Shikimic acid	6-Methyl-DL-tryptophan	Asparagine	Proline	Serine	Urocanic acid	Levulinic acid
Lachnospiraceae UCG-001 Ambiguous	0.189	0.894	0.894	0.394	0.894	0.394	0.894	0.965	0.932	0.897	0.897	0.897	0.897	0.897	0.897
Lachnospiraceae UCG-001 uncultured	0.821	0.821	0.836	0.821	0.821	0.821	0.963	0.821	0.821	0.708	0.668	0.668	0.708	0.668	0.708
Lachnospiraceae ASF356 uncultured	0.535	0.535	0.535	0.535	0.673	0.535	0.535	0.535	0.535	0.852	0.852	0.852	0.852	0.852	0.852
Clostridium scindens	0.194	0.194	0.194	0.228	0.194	0.228	0.194	0.259	0.291	0.276	0.463	0.276	0.276	0.2	0.103
Ruminococcaceae	0.265	0.265	0.836	0.299	0.912	0.29	0.836	0.524	0.836	1	0.931	0.931	0.931	0.931	0.931
Muribaculaceae	0.265	0.265	0.948	0.867	0.948	0.867	0.948	0.948	0.948	0.912	0.912	0.912	0.912	0.912	0.912
Ruminiclostridium 9 uncultured	0.29	0.29	0.613	0.375	0.29	0.375	0.402	0.461	0.375	0.159	0.194	0.159	0.103	0.152	0.13
Roseburia uncultured	0.137	0.171	0.171	0.137	0.137	0.137	0.281	0.359	0.137	0.097	0.097	0.097	0.025	0.062	0.025
Ruminococcaceae UCG-013 uncultured rumen bacterium	0.129	0.463	0.129	0.129	0.461	0.129	0.129	0.463	0.129	0.437	0.463	0.462	0.437	0.398	0.398
Ruminiclostridium 6	0.145	0.145	0.145	0.014	0.644	0.014	0.644	0.145	0.208	0.581	0.469	0.469	0.469	0.469	0.524
Erysipelatoclostridium Ambiguous	0.189	0.764	0.932	0.764	0.764	0.764	0.764	1	0.932	0.897	0.897	0.897	0.897	0.897	0.897
Family XIII UCG-001 uncultured	0.023	0.047	0.057	0.015	0.509	0.023	0.148	0.068	0.067	0.398	0.258	0.258	0.243	0.243	0.258
Akkermansia muciniphila	0.749	0.749	0.876	0.749	0.749	0.749	0.926	0.876	0.876	0.685	0.685	0.685	0.926	0.685	0.685
Enterorhabdus uncultured	0.201	0.8	0.8	0.201	0.8	0.201	0.8	0.8	0.8	0.899	0.899	0.899	0.899	0.899	0.899
Oscillibacter uncultured	0.317	0.235	0.389	0.389	0.389	0.389	0.235	0.389	0.622	0.316	0.738	0.316	0.316	0.316	0.316
Clostridiales bacterium CIEAF 016	0.174	0.49	0.96	0.468	0.598	0.468	0.96	0.96	0.96	0.859	0.859	0.859	0.859	0.859	0.859
Clostridium sp. Culture-1	0.05	0.159	0.6	0.134	0.6	0.134	0.6	0.6	0.6	0.663	0.663	0.663	0.626	0.663	0.663
Anaerotruncus uncultured	0.126	0.014	0.01	0.009	0.126	0.009	0.284	0.009	0.012	0.099	0.018	0.013	0.013	0.013	0.089
Lachnospiraceae A2	0.68	0.68	0.68	0.704	0.01	0.704	0.68	0.704	0.68	0.262	0.346	0.265	0.262	0.262	0.057
Acetatifactor	0.166	0.144	0.144	0.144	0.452	0.144	0.638	0.19	0.452	0.681	0.288	0.482	0.288	0.198	0.288
Dubosiella newyorkensis	0.059	0.03	0.03	0.03	0.235	0.03	0.048	0.03	0.047	0.054	0.104	0.047	0.047	0.016	0.047
Turicibacter	0.613	0.527	0.064	0.174	0.064	0.174	0.613	0.319	0.064	0.194	0.13	0.162	0.13	0.177	0.162
Muribaculaceae uncultured	0.81	0.81	0.228	0.74	0.228	0.74	0.74	0.81	0.228	0.194	0.194	0.194	0.194	0.194	0.194
Lachnospiraceae GCA-900066575 uncultured	0.724	0.982	0.724	0.724	0.229	0.724	0.724	0.724	0.724	0.276	0.276	0.276	0.385	0.276	0.276
Ruminococcaceae uncultured	0.982	0.965	0.738	0.982	0.738	0.982	0.738	0.738	0.738	0.181	0.462	0.181	0.552	0.181	0.181
Clostridium sp. Clone-44	0.859	0.298	0.291	0.625	0.059	0.625	0.327	0.291	0.291	0.013	0.042	0.013	0.042	0.013	0.019

	Phase-I Ces2c	Phase-I Cyp1a2	Phase-I Cyp2a5	Phase-I Cyp2b10	Phase-I Cyp2c29	Phase-I Cyp2c54	Phase-I Cyp2j9	Phase-I Cyp3a16	Phase-I Cyp3a41a	Phase-I Cyp17a1	Phase-I Cyp26a1	Phase-I Aldh1a7	Phase-I Ces1b	Phase-I Cyp1a1	Phase-I Cyp2c50	Phase-I Cyp2c55	Phase-I Cyp3a44	Phase-I Cyp4a14	Phase-I Nqo1
Lachnospiraceae UCG-001 Ambiguous	-0.1356127007	-0.06780635036	0.3051285766	-0.01695158759	0	-0.03390317518	0.6272087408	-0.3898865146	-0.5254992153	-0.2712254014	-0.5424508029	0.1525642883	0	0.03390317518	-0.1186611131	0.4576928649	-0.288176989	0.050854762	-0.05085476277
Lachnospiraceae UCG-001 uncultured	0.2921186973	0.4016632088	0.6937819062	0.3834057903	0.4016632088	0.4016632088	0.3468909531	-0.3651483717	-0.1460593487	0.219089023	-0.5477225575	0.4564354646	0.3468909531	0.4016632088	0.3103761159	0.6390096504	-0.1460593487	-0.2738612788	0.3834057903
Lachnospiraceae ASF356 uncultured	-0.4199206274	-0.5477225575	-0.6024948133	-0.3468909531	-0.438178046	-0.4929503018	0.4564354646	0.219089023	-0.3468909531	-0.6390096504	-0.09128709292	-0.4199206274	-0.3651483717	-0.3834057903	-0.5112077203	-0.1278019301	0.1278019301	0.1825741858	-0.4016632088
Clostridium scindens	-0.6666666667	-0.55	-0.3	-0.85	-0.6666666667	-0.7333333333	0.6833333333	0.3166666667	-0.2	-0.7833333333	-0.3666666667	-0.4666666667	-0.7666666667	-0.7333333333	-0.85	-0.4833333333	0.2666666667	0.6333333333	-0.75
Ruminococcaceae	-0.3666666667	-0.4833333333	-0.2833333333	-0.4333333333	-0.4	-0.4833333333	0.5166666667	0.4	0.01666666667	-0.6	-0.1333333333	-0.08333333333	-0.3666666667	-0.35	-0.5	-0.06666666667	0.3833333333	0.06666666667	-0.45
Muribaculaceae	-0.3333333333	-0.5666666667	-0.3833333333	-0.4833333333	-0.3833333333	-0.5166666667	0.1666666667	0.3333333333	0.03333333333	-0.6333333333	0.1	-0.01666666667	-0.2833333333	-0.2666666667	-0.4666666667	-0.03333333333	0.1666666667	0.03333333333	-0.5333333333
Ruminiclostridium 9 uncultured	0.7166666667	0.8166666667	0.5666666667	0.7833333333	0.6833333333	0.8333333333	-0.1333333333	-0.1666666667	0.1	0.7	-0.15	0.06666666667	0.7	0.65	0.75	0.3333333333	-0.1666666667	-0.2333333333	0.85
Roseburia uncultured	0.9333333333	0.8666666667	0.5833333333	0.7833333333	0.7333333333	0.8833333333	-0.4333333333	0.1166666667	0.45	0.6833333333	-0.1333333333	0.15	0.7333333333	0.75	0.8166666667	0.35	0.08333333333	-0.4333333333	0.9
Ruminococcaceae UCG-013 uncultured	0.5833333333	0.3666666667	-0.03333333333	0.4166666667	0.45	0.3666666667	-0.8333333333	0.45	0.8166666667	0.45	0.4166666667	0.3166666667	0.4833333333	0.5	0.45	0.1333333333	0.3833333333	-0.6333333333	0.4
Ruminiclostridium 6	0.5833333333	0.5666666667	0.2333333333	0.4	0.5333333333	0.4666666667	-0.8166666667	-0.03333333333	0.4	0.5	0.01666666667	0.2	0.45	0.5166666667	0.45	0.2	-0.06666666667	-0.35	0.45
Erysipelatoclostridium Ambiguous	0.1017095255	0.288176989	0.1017095255	0.08475793795	0.1356127007	0.1695158759	-0.288176989	0.1356127007	0.4068381022	0.4576928649	0.3390317518	0	0.08475793795	0.01695158759	0.1864674635	-0.3559833394	0.1356127007	0.08475793795	0.1356127007
Family XIII UCG-001 uncultured	0.6780635036	0.7289182664	0.3390317518	0.5933055657	0.7628214416	0.5763539781	-0.8306277919	0.08475793795	0.7289182664	0.745869854	0.1356127007	0.5424508029	0.6780635036	0.7119666788	0.5763539781	0.372934927	0.1525642883	-0.661111916	0.5763539781
Akkermansia muciniphila	-0.05477225575	0.1460593487	0.07302967433	-0.05477225575	0.01825741858	0.03651483717	-0.3103761159	-0.1643167673	0.09128709292	0.3103761159	0.2008316044	-0.01825741858	-0.07302967433	-0.09128709292	0.05477225575	-0.3103761159	-0.1278019301	0.2008316044	-0.01825741858
Enterorhabdus uncultured	0.2376354103	0.3069457383	0.01980295086	0.02970442629	0.1089162297	0.1584236069	-0.4851722961	0.207930984	0.3663545909	0.277241312	0.03960590172	-0.1980295086	-0.01980295086	0.01980295086	0.1188177052	-0.3366501646	0.1881280332	0.06931032801	0.1584236069
Oscillibacter uncultured	0.3829708431	0.3568591947	0.1218543592	0.7137183894	0.5483446163	0.5396407335	-0.5222329679	-0.5222329679	-0.09574271078	0.6614950926	0.4700096711	0.3916747259	0.6963106238	0.600567913	0.6701989754	0.4438980227	-0.5309368507	-0.4438980227	0.5396407335
Clostridiales bacterium CIEAF 016	0.0990147543	0.2475368857	-0.03960590172	0.1089162297	0.1287191806	0.138620656	-0.4653693452	-0.00990147543	0.2475368857	0.4158619681	0.2574383612	-0.05940885258	0.03960590172	0.01980295086	0.1584236069	-0.2970442629	0.02970442629	0.02970442629	0.138620656
Clostridium sp. Culture-1	0.5424508029	0.5763539781	0.2542738139	0.5254992153	0.4407412774	0.5933055657	-0.5594023905	-0.1525642883	0.1525642883	0.6272087408	0.1356127007	-0.05085476277	0.4237896898	0.4068381022	0.5933055657	0	-0.1864674635	-0.1186611131	0.5933055657
Anaerotruncus uncultured	-0.8398412548	-0.8580986734	-0.5659799761	-0.7302967433	-0.9128709292	-0.7485541619	0.7485541619	0.1825741858	-0.438178046	-0.6937819062	0.1825741858	-0.5659799761	-0.8398412548	-0.9128709292	-0.6937819062	-0.6937819062	0.1460593487	0.6755244876	-0.7302967433
Lachnospiraceae A2	-0.7050145066	-0.5396407335	-0.5657523819	-0.7659416862	-0.5135290851	-0.8094611002	0.2175970699	0.3220436635	0.07833494518	-0.5570484991	-0.04351941399	-0.1914854216	-0.6527912098	-0.6266795614	-0.8529805142	-0.4351941399	0.3568591947	0.3046358979	-0.7920533346
Acetatifactor	-0.7302967433	-0.6390096504	-0.2738612788	-0.7302967433	-0.6390096504	-0.6390096504	0.7302967433	0.06846531969	-0.3879701449	-0.6390096504	0.1369306394	-0.3651483717	-0.5249007843	-0.6390096504	-0.6390096504	-0.4564354646	-0.1597524126	0.7302967433	-0.7302967433
Dubosiella newyorkensis	-0.6780635036	-0.6780635036	-0.2542738139	-0.7119666788	-0.8475793795	-0.5933055657	0.7628214416	0.03390317518	-0.5594023905	-0.6950150912	-0.1695158759	-0.6102571533	-0.8475793795	-0.8475793795	-0.6102571533	-0.6102571533	0.01695158759	0.7797730292	-0.6102571533
Turicibacter	-0.8166666667	-0.65	-0.6	-0.5	-0.6	-0.6666666667	0.55	0	-0.35	-0.3833333333	0.25	-0.2833333333	-0.5833333333	-0.6833333333	-0.6166666667	-0.4666666667	0.08333333333	0.4	-0.6166666667
Muribaculaceae uncultured	-0.5333333333	-0.2833333333	-0.1666666667	-0.2166666667	-0.3333333333	-0.2666666667	0.2333333333	-0.5	-0.5333333333	0.01666666667	0.1666666667	-0.1666666667	-0.3666666667	-0.4333333333	-0.2166666667	-0.3333333333	-0.3666666667	0.4333333333	-0.2833333333
Lachnospiraceae GCA-900066575 uncultured	0.35	0.2666666667	0.4666666667	0.3666666667	0.3833333333	0.3666666667	0.2	-0.1833333333	-0.08333333333	0.08333333333	-0.25	0.3666666667	0.4833333333	0.4833333333	0.3333333333	0.6333333333	-0.2166666667	-0.3	0.3333333333
Ruminococcaceae uncultured	0.2333333333	0.1666666667	0.08333333333	0.4166666667	0.4333333333	0.2166666667	-0.05	-0.06666666667	0.1333333333	0.1833333333	0.06666666667	0.5166666667	0.5333333333	0.5	0.25	0.6333333333	-0.03333333333	-0.5833333333	0.25
Clostridium sp. Clone-44	0.6435959029	0.6138914766	0.5445811486	0.7525121327	0.7525121327	0.6832018047	-0.1485221314	-0.34655164	-0.00990147543	0.4653693452	-0.2277339349	0.4950737715	0.8218224607	0.8218224607	0.6435959029	0.8416254115	-0.3267486892	-0.5643840995	0.6832018047

Phase-I	Phase-I	Phase-I	Phase-I	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter
Por	Cyp26b1	Sdr9c7	Cyb5a	Gclc	Gstm2	Gstm3	Sult2a1	Sult2a2	Sult3a1	Gsta2	Gsta4	Gstm1	Gstm4	Gstp1	Atp2a2	Atp2b2	Atp6v0d2	Slc15a2	Slc16a1	Slc25a30	Slc30a10
0.03390317518	-0.08475793795	-0.05085476277	0.1356127007	0.5424508029	-0.1017095255	0.3051285766	-0.1017095255	-0.1525642883	-0.6441603284	0.4068381022	0.4068381022	0.03390317518	0.1525642883	0.4576928649	0.4237896898	0.1525642883	-0.2373222263	0.7967246168	0.06780635036	0.06780635036	0.01695158759
0.4199206274	-0.3103761159	-0.3834057903	0.5477225575	0.07302967433	0.2921186973	0.5477225575	0.3103761159	0.3103761159	-0.1278019301	0.6207522318	0.6207522318	0.3651483717	0.5294651389	0.4564354646	-0.01825741858	-0.2556038602	0.1825741858	0.6207522318	-0.4016632088	-0.03651483717	-0.3834057903
-0.4746928832	-0.01825741858	0.3651483717	-0.5477225575	0.7302967433	-0.5294651389	-0.09128709292	-0.5659799761	-0.6755244876	-0.7120393248	-0.09128709292	-0.09128709292	-0.2738612788	-0.5294651389	0.6024948133	0.657267069	0.4929503018	-0.6755244876	0.4564354646	0.5477225575	0.5477225575	0.4746928832
-0.65	0.45	0.65	-0.6166666667	0.7833333333	-0.7333333333	-0.6	-0.2666666667	-0.3333333333	-0.5333333333	-0.4333333333	-0.4333333333	-0.7333333333	-0.5166666667	-0.15	0.5166666667	0.6166666667	-0.5	0.4833333333	0.55	0.3833333333	0.5833333333
-0.4	-0.1333333333	0.45	-0.45	0.6666666667	-0.4	-0.2	-0.3166666667	-0.4333333333	-0.4166666667	-0.08333333333	-0.08333333333	-0.45	-0.5333333333	0.4333333333	0.5166666667	0.3833333333	-0.3166666667	0.5666666667	0.4833333333	0.8166666667	0.55
-0.4	-0.15	0.4166666667	-0.5666666667	0.5166666667	-0.3	-0.3166666667	-0.4833333333	-0.5833333333	-0.4166666667	-0.1666666667	-0.1666666667	-0.4833333333	-0.6833333333	0.08333333333	0.35	0.2833333333	-0.1166666667	0.2333333333	0.5666666667	0.6666666667	0.6166666667
0.8	-0.25	-0.7	0.6833333333	-0.5666666667	0.45	0.5	0.7166666667	0.7333333333	0.2833333333	0.3833333333	0.3833333333	0.7333333333	0.75	0.4833333333	-0.5	-0.7333333333	0.2333333333	0.15	-0.8166666667	-0.35	-0.8666666667
0.85	-0.4166666667	-0.7	0.5666666667	-0.75	0.5	0.4	0.7166666667	0.7333333333	0.4833333333	0.35	0.35	0.6833333333	0.5833333333	0.3166666667	-0.7666666667	-0.9333333333	0.4833333333	-0.05	-0.8666666667	-0.1666666667	-0.8666666667
0.3	-0.5833333333	-0.35	0.1	-0.6333333333	0.5	0.15	0.1333333333	0.1666666667	0.6833333333	0.1166666667	0.1166666667	0.35	-0.03333333333	0.03333333333	-0.6833333333	-0.5666666667	0.6333333333	-0.6333333333	-0.3666666667	0.2666666667	-0.25
0.3666666667	-0.2333333333	-0.55	0.2666666667	-0.6666666667	0.4666666667	0.2	0.1833333333	0.3	0.4666666667	0.2	0.2	0.4833333333	0.3166666667	-0.3833333333	-0.8166666667	-0.5833333333	0.6	-0.6833333333	-0.5666666667	-0.4666666667	-0.55
0.1356127007	0.1864674635	-0.06780635036	0.2203706387	-0.5085476277	0.2203706387	-0.1864674635	0.4576928649	0.5254992153	0.6780635036	-0.2712254014	-0.2712254014	0.05085476277	0.2373222263	-0.4068381022	-0.4068381022	-0.1864674635	0.3051285766	-0.4746444525	-0.288176989	-0.2542738139	-0.2034190511
0.4576928649	-0.5933055657	-0.6950150912	0.4915960401	-0.7119666788	0.7628214416	0.4407412774	0.3220801642	0.4407412774	0.745869854	0.4237896898	0.4237896898	0.661111916	0.4407412774	-0.03390317518	-0.8984341423	-0.6780635036	0.8475793795	-0.6272087408	-0.7289182664	-0.1525642883	-0.5933055657
-0.01825741858	0.3834057903	-0.01825741858	0.1460593487	-0.4016632088	0.1278019301	-0.2008316044	0.2008316044	0.3103761159	0.4564354646	-0.2556038602	-0.2556038602	-0.01825741858	0.219089023	-0.7302967433	-0.3103761159	0	0.219089023	-0.5842373947	-0.1460593487	-0.5842373947	-0.1278019301
0.06931032801	0.207930984	-0.1089162297	0.00990147543	-0.4950737715	0.04950737715	-0.2178324595	0.2475368857	0.3366501646	0.4950737715	-0.2475368857	-0.2475368857	0.06931032801	0.1188177052	-0.5544826241	-0.5445811486	-0.2376354103	0.2376354103	-0.6039900012	-0.3069457383	-0.3663545909	-0.2871427875
0.4787135539	-0.3307475463	-0.5831601475	0.5483446163	-0.5483446163	0.6614950926	0.5831601475	0.07833494518	0.1392621248	0.2698203667	0.3916747259	0.3916747259	0.6789028582	0.4700096711	0.1914854216	-0.2698203667	-0.3829708431	0.3133397807	-0.4177863743	-0.3568591947	-0.4787135539	-0.4264902571
0.02970442629	0.207930984	-0.1287191806	0.1485221314	-0.4950737715	0.1881280332	-0.07921180344	0.1881280332	0.2970442629	0.5544826241	-0.1881280332	-0.1881280332	0.1485221314	0.2178324595	-0.4950737715	-0.4059604926	-0.0990147543	0.2178324595	-0.6832018047	-0.2475368857	-0.4653693452	-0.2277339349
0.5085476277	0.05085476277	-0.4746444525	0.4068381022	-0.7628214416	0.3559833394	0.1695158759	0.4407412774	0.5254992153	0.4915960401	0.03390317518	0.03390317518	0.4915960401	0.4915960401	-0.2542738139	-0.6102571533	-0.5424508029	0.288176989	-0.5254992153	-0.5763539781	-0.6441603284	-0.6441603284
-0.657267069	0.657267069	0.9128709292	-0.6024948133	0.6390096504	-0.7850689991	-0.6390096504	-0.3103761159	-0.4199206274	-0.4016632088	-0.6755244876	-0.6755244876	-0.8398412548	-0.6024948133	-0.09128709292	0.9128709292	0.8398412548	-0.8215838363	0.3651483717	0.8580986734	0.3468909531	0.8033264177
-0.8442766314	0.1914854216	0.5135290851	-0.5918640302	0.6527912098	-0.4264902571	-0.4090824915	-0.5483446163	-0.5309368507	-0.2175970699	-0.3046358979	-0.3046358979	-0.5396407335	-0.5483446163	-0.2175970699	0.3394514291	0.7050145066	-0.2350048355	-0.08703882798	0.5396407335	0.3829708431	0.6527912098
-0.4336136914	0.502079011	0.6390096504	-0.4564354646	0.6390096504	-0.5477225575	-0.6390096504	-0.1141088661	-0.2282177323	-0.5249007843	-0.5477225575	-0.5477225575	-0.7302967433	-0.4564354646	-0.1369306394	0.6390096504	0.5249007843	-0.4564354646	0.5249007843	0.6390096504	0.2738612788	0.6390096504
-0.4915960401	0.8136762043	0.8136762043	-0.5085476277	0.5424508029	-0.8306277919	-0.661111916	-0.1525642883	-0.2373222263	-0.4746444525	-0.6272087408	-0.6272087408	-0.8136762043	-0.4237896898	-0.3559833394	0.745869854	0.6780635036	-0.7628214416	0.4407412774	0.6780635036	0.03390317518	0.5763539781
-0.6833333333	0.3666666667	0.5833333333	-0.35	0.6166666667	-0.4333333333	-0.2333333333	-0.4166666667	-0.45	-0.2666666667	-0.3333333333	-0.3333333333	-0.45	-0.35	0.15	0.7833333333	0.85	-0.6333333333	0.15	0.65	0.25	0.65
-0.3166666667	0.6166666667	0.2666666667	0.05	0.1	-0.1666666667	-0.1166666667	-0.1333333333	-0.06666666667	-0.03333333333	-0.25	-0.25	-0.1833333333	0.1333333333	-0.4333333333	0.4	0.55	-0.3666666667	-0.2	0.2833333333	-0.5833333333	0.2
0.4666666667	-0.4666666667	-0.3666666667	0.3333333333	0.06666666667	0.2833333333	0.4166666667	0.2	0.1333333333	-0.2666666667	0.5	0.5	0.3166666667	0.25	0.5833333333	-0.03333333333	-0.4	0.2	0.6	-0.2666666667	0.2	-0.2666666667
0.2166666667	-0.75	-0.4	0.2666666667	0.1166666667	0.45	0.6	-0.1166666667	-0.15	-0.1	0.6	0.6	0.45	0.1166666667	0.8166666667	0	-0.2166666667	0.25	0.2666666667	-0.1666666667	0.4333333333	-0.1
0.6832018047	-0.6733003292	-0.7723150835	0.6138914766	-0.2277339349	0.6039900012	0.7723150835	0.2574383612	0.2574383612	-0.07921180344	0.7723150835	0.7723150835	0.7723150835	0.5643840995	0.7030047555	-0.3366501646	-0.6435959029	0.3861575418	0.3168472138	-0.6138914766	-0.07921180344	-0.6336944275

Table S5D. Bacteria-gene significance

	Phase-I Ces2c	Phase-I Cyp1a2	Phase-I Cyp2a5	Phase-I Cyp2b10	Phase-I Cyp2c29	Phase-I Cyp2c54	Phase-I Cyp2j9	Phase-I Cyp3a16	Phase-I Cyp3a41a	Phase-I Cyp17a1	Phase-I Cyp26a1	Phase-I Aldh1a7	Phase-I Ces1b	Phase-I Cyp1a1	Phase-I Cyp2c50	Phase-I Cyp2c55	Phase-I Cyp3a44	Phase-I Cyp4a14	Phase-I Nqo1	Phase-I Por	Phase-I Cyp26b1	Phase-I Sdr9c7	Phase-I Cyb5a	Phase-II Gclc	Phase-II Gstm2	Phase-II Gstm3	Phase-II Sult2a1	Phase-II Sult2a2	Phase-II Sult3a1	Phase-II Gsta2	Phase-II Gsta4	Phase-II Gstm1
Lachnospiraceae UCG-001 Ambiguous	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.61	0.874	0.778	0.874	0.874	0.61	0.61	0.61	0.931
Lachnospiraceae UCG-001 uncultured	0.539	0.518	0.518	0.518	0.518	0.518	0.518	0.518	0.708	0.626	0.518	0.518	0.518	0.518	0.532	0.518	0.708	0.547	0.518	0.518	0.532	0.518	0.518	0.852	0.545	0.392	0.545	0.545	0.817	0.392	0.392	0.545
Lachnospiraceae ASF356 uncultured	0.488	0.488	0.488	0.488	0.488	0.488	0.488	0.73	0.488	0.488	0.852	0.488	0.488	0.488	0.488	0.814	0.814	0.773	0.488	0.488	0.963	0.488	0.488	0.168	0.224	0.815	0.224	0.168	0.168	0.815	0.815	0.654
Clostridium scindens	0.128	0.204	0.478	0.07	0.128	0.102	0.128	0.472	0.613	0.102	0.407	0.288	0.102	0.102	0.07	0.279	0.516	0.135	0.102	0.128	0.294	0.128	0.141	0.114	0.114	0.266	0.543	0.471	0.297	0.344	0.344	0.114
Ruminococcaceae	0.515	0.515	0.626	0.515	0.515	0.515	0.515	0.515	0.982	0.515	0.9	0.92	0.515	0.515	0.515	0.92	0.515	0.92	0.515	0.515	0.9	0.515	0.515	0.458	0.458	0.75	0.564	0.458	0.458	0.843	0.843	0.458
Muribaculaceae	0.682	0.653	0.653	0.653	0.653	0.653	0.905	0.682	0.982	0.653	0.981	0.982	0.756	0.756	0.653	0.982	0.905	0.982	0.653	0.653	0.905	0.653	0.653	0.426	0.6	0.6	0.426	0.426	0.494	0.746	0.746	0.426
Ruminiclostridium 9 uncultured	0.096	0.079	0.198	0.079	0.096	0.079	0.814	0.814	0.847	0.096	0.814	0.88	0.096	0.118	0.096	0.591	0.814	0.746	0.079	0.079	0.746	0.096	0.096	0.265	0.316	0.305	0.101	0.101	0.463	0.344	0.344	0.101
Roseburia uncultured	0.017	0.026	0.191	0.057	0.072	0.024	0.338	0.811	0.338	0.096	0.811	0.811	0.072	0.072	0.041	0.434	0.843	0.338	0.023	0.028	0.344	0.09	0.198	0.135	0.305	0.394	0.135	0.135	0.305	0.394	0.394	0.138
Ruminococcaceae UCG-013 uncultured	0.455	0.455	0.948	0.455	0.455	0.455	0.124	0.455	0.124	0.455	0.455	0.496	0.455	0.455	0.455	0.814	0.455	0.455	0.455	0.502	0.455	0.458	0.847	0.418	0.651	0.948	0.948	0.948	0.418	0.948	0.948	0.948
Ruminiclostridium 6	0.481	0.481	0.705	0.515	0.481	0.481	0.248	0.982	0.515	0.481	0.982	0.705	0.481	0.481	0.481	0.705	0.964	0.55	0.481	0.55	0.705	0.481	0.705	0.584	0.584	0.644	0.644	0.644	0.584	0.644	0.644	0.584
Erysipelatoclostridium Ambiguous	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	1	0.945	1	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.945	0.592	0.694	0.694	0.592	0.592	0.492	0.694	0.694	0.897
Family XIII UCG-001 uncultured	0.114	0.114	0.428	0.16	0.114	0.16	0.114	0.828	0.114	0.114	0.761	0.189	0.114	0.114	0.16	0.391	0.761	0.121	0.16	0.275	0.16	0.114	0.242	0.115	0.115	0.312	0.438	0.312	0.115	0.312	0.312	0.144
Akkermansia muciniphila	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.963	0.739	0.817	0.739	0.739	0.739	0.739	0.739	0.739	0.963
Enterorhabdus uncultured	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.643	0.899	0.788	0.788	0.788	0.643	0.788	0.788	0.899
Oscillibacter uncultured	0.374	0.398	0.789	0.264	0.264	0.264	0.264	0.264	0.806	0.264	0.309	0.374	0.264	0.264	0.264	0.313	0.264	0.313	0.264	0.309	0.421	0.264	0.264	0.347	0.288	0.347	0.841	0.793	0.664	0.467	0.467	0.288
Clostridiales bacterium CIEAF 016	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.98	0.643	0.767	0.839	0.767	0.767	0.643	0.767	0.767	0.773
Clostridium sp. Culture-1	0.414	0.414	0.781	0.414	0.455	0.414	0.414	0.875	0.875	0.414	0.875	0.937	0.455	0.455	0.414	1	0.875	0.875	0.414	0.414	0.937	0.452	0.455	0.185	0.545	0.81	0.431	0.394	0.394	0.931	0.931	0.394
Anaerotruncus uncultured	0.018	0.018	0.136	0.059	0.005	0.058	0.058	0.667	0.274	0.068	0.667	0.136	0.018	0.005	0.068	0.068	0.708	0.075	0.059	0.078	0.078	0.005	0.116	0.117	0.067	0.117	0.458	0.347	0.347	0.117	0.117	0.051
Lachnospiraceae A2	0.13	0.256	0.249	0.074	0.258	0.063	0.681	0.539	0.879	0.249	0.911	0.681	0.186	0.204	0.048	0.371	0.497	0.544	0.063	0.048	0.681	0.258	0.238	0.311	0.431	0.431	0.311	0.311	0.574	0.52	0.52	0.311
Acetatifactor	0.117	0.123	0.547	0.117	0.123	0.123	0.117	0.861	0.386	0.123	0.758	0.404	0.26	0.123	0.123	0.312	0.746	0.117	0.117	0.33	0.277	0.123	0.312	0.231	0.231	0.231	0.77	0.678	0.231	0.231	0.231	0.231
Dubosiella newyorkensis	0.093	0.093	0.585	0.09	0.03	0.132	0.055	0.965	0.159	0.093	0.726	0.124	0.03	0.03	0.124	0.124	0.965	0.051	0.124	0.217	0.035	0.035	0.207	0.241	0.042	0.155	0.695	0.593	0.309	0.155	0.155	0.042
Turicibacter	0.226	0.226	0.226	0.314	0.226	0.226	0.254	1	0.434	0.434	0.57	0.532	0.226	0.226	0.226	0.349	0.882	0.434	0.226	0.226	0.434	0.226	0.434	0.53	0.53	0.607	0.53	0.53	0.603	0.53	0.53	0.53
Muribaculaceae uncultured	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.982	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.742	0.953	0.948	0.948	0.948	0.948	0.948	0.948	0.948	0.948	0.948
Lachnospiraceae GCA-900066575 uncultured	0.591	0.665	0.591	0.591	0.591	0.591	0.705	0.705	0.843	0.843	0.665	0.591	0.591	0.591	0.591	0.591	0.703	0.628	0.591	0.591	0.591	0.591	0.591	0.88	0.716	0.716	0.75	0.818	0.716	0.651	0.651	0.716
Ruminococcaceae uncultured	0.891	0.917	0.948	0.744	0.744	0.891	0.948	0.948	0.948	0.917	0.948	0.681	0.681	0.681	0.891	0.681	0.948	0.681	0.891	0.891	0.586	0.744	0.891	0.81	0.421	0.266	0.81	0.81	0.81	0.266	0.266	0.421
Clostridium sp. Clone-44	0.118	0.129	0.186	0.074	0.074	0.108	0.735	0.437	0.98	0.264	0.609	0.237	0.05	0.05	0.118	0.05	0.449	0.174	0.108	0.108	0.108	0.074	0.129	0.611	0.156	0.04	0.611	0.611	0.839	0.04	0.04	0.04

Table S5D. Bacteria-gene significance

Phase-II Gstm4	Phase-II Gstp1	Transporter Atp2a2	Transporter Atp2b2	Transporter Atp6v0d2	Transporter Slc15a2	Transporter Slc16a1	Transporter Slc25a30	Transporter Slc30a10	Transporter Abcc4	Transporter Abcg8	Transporter Slc10a2	Transporter Slc17a2	Transporter Slc3a1	Transporter Slc46a3	Transporter Slc7a2	Transporter Slco1a1	NR, immune response and oxidative stress, epi Bcl6	NR, immune response and oxidative stress, epi Cldn1
0.874	0.61	0.869	0.869	0.869	0.152	0.924	0.924	0.965	0.869	0.869	0.869	0.869	0.869	0.869	0.869	0.869	0.666	0.405
0.392	0.477	0.963	0.845	0.957	0.727	0.727	0.963	0.727	0.727	0.727	0.727	0.963	0.963	0.963	0.727	0.727	0.248	0.815
0.224	0.224	0.361	0.361	0.361	0.361	0.361	0.361	0.361	0.577	0.963	0.557	0.361	0.577	0.361	0.541	0.557	0.555	0.473
0.297	0.708	0.264	0.257	0.264	0.264	0.264	0.391	0.264	0.216	0.903	0.601	0.216	0.221	0.264	0.216	0.912	0.546	0.482
0.458	0.458	0.484	0.538	0.559	0.484	0.484	0.162	0.484	0.538	1	0.637	0.538	0.442	0.579	0.538	0.759	1	0.484
0.426	0.843	0.642	0.673	0.776	0.69	0.603	0.603	0.603	0.642	0.776	0.642	0.743	0.642	0.642	0.642	0.673	0.982	0.77
0.101	0.305	0.296	0.13	0.591	0.708	0.081	0.448	0.068	0.13	0.13	0.504	0.345	0.296	0.397	0.147	0.163	0.415	0.268
0.238	0.41	0.08	0.011	0.242	0.912	0.023	0.726	0.023	0.181	0.108	0.534	0.108	0.181	0.108	0.18	0.18	0.295	0.062
0.948	0.948	0.257	0.301	0.257	0.257	0.721	0.781	0.781	0.817	0.805	0.805	0.207	0.722	0.257	0.831	0.912	0.948	0.156
0.644	0.644	0.129	0.249	0.249	0.249	0.249	0.354	0.249	0.69	0.69	0.982	0.249	0.129	0.375	0.69	0.631	0.904	0.36
0.694	0.61	0.946	0.946	0.946	0.946	0.946	0.946	0.946	0.965	0.965	0.946	0.946	0.965	0.946	0.965	0.965	0.922	0.922
0.312	0.931	0.013	0.134	0.02	0.177	0.097	0.695	0.196	0.434	0.409	0.695	0.013	0.244	0.196	0.459	0.353	0.599	0.078
0.739	0.28	1	1	1	0.561	1	0.561	1	1	1	0.561	1	1	1	1	1	0.858	0.858
0.899	0.643	0.767	0.767	0.767	0.767	0.767	0.767	0.767	0.767	0.98	0.767	0.767	0.767	0.767	0.767	0.857	0.897	0.78
0.444	0.76	0.603	0.519	0.561	0.519	0.519	0.519	0.519	0.241	0.977	0.519	0.501	0.241	0.812	0.241	0.982	0.929	0.703
0.767	0.643	0.914	0.96	0.914	0.637	0.914	0.914	0.914	0.96	0.96	0.914	0.914	0.914	0.914	0.96	0.96	0.769	0.769
0.394	0.7	0.304	0.313	0.565	0.313	0.313	0.304	0.304	0.473	0.663	0.663	0.392	0.304	0.392	0.473	0.663	0.944	0.224
0.135	0.815	0.008	0.014	0.017	0.358	0.012	0.36	0.02	0.173	0.168	0.25	0.008	0.012	0.25	0.164	0.12	0.224	0.219
0.311	0.574	0.557	0.186	0.626	0.824	0.334	0.515	0.212	0.186	0.626	0.619	0.415	0.334	0.415	0.143	0.632	0.321	0.457
0.298	0.77	0.16	0.275	0.361	0.275	0.16	0.595	0.16	0.548	0.923	0.954	0.16	0.16	0.16	0.548	0.889	0.556	0.461
0.352	0.424	0.105	0.134	0.105	0.271	0.134	0.931	0.174	0.174	0.219	0.174	0.008	0.153	0.346	0.244	0.269	0.679	0.175
0.53	0.708	0.129	0.091	0.163	0.708	0.163	0.558	0.163	0.504	0.341	0.504	0.163	0.163	0.291	0.291	0.291	0.214	0.492
0.948	0.948	0.63	0.498	0.63	0.767	0.694	0.498	0.767	0.843	0.498	0.498	0.581	0.817	0.694	0.831	0.63	0.926	0.926
0.716	0.651	0.948	0.624	0.767	0.581	0.767	0.767	0.767	0.581	0.581	0.467	0.767	0.895	0.948	0.581	0.624	0.482	0.978
0.81	0.118	1	0.871	0.871	0.871	0.924	0.781	0.977	0.781	0.781	0.207	0.781	0.977	0.977	0.781	0.871	0.982	0.982
0.178	0.076	0.469	0.167	0.415	0.469	0.169	0.839	0.167	0.074	0.167	0.074	0.182	0.182	0.774	0.074	0.182	0.212	0.651

Table S5D. Bacteria-gene significance

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Egr1	Lcn2	Nlrp12	Socs2	Cebpb	Hmox1	Icam1
0.666	0.789	0.809	0.679	0.076	0.076	0.405
0.595	0.595	0.595	0.595	0.317	0.248	0.595
0.963	0.473	0.963	0.473	0.473	0.555	0.473
0.88	0.787	0.88	0.546	0.482	0.393	0.045
0.937	0.937	0.511	0.788	0.484	0.484	0.484
0.953	0.822	0.77	0.929	0.822	0.904	0.82
0.546	0.81	0.546	0.294	0.715	0.81	0.296
0.982	0.446	0.96	0.327	0.327	0.456	0.295
0.554	0.873	0.728	0.873	0.156	0.156	0.156
0.868	0.904	0.912	0.912	0.36	0.36	0.36
0.944	0.922	0.922	0.922	0.922	0.922	0.922
0.599	0.599	0.599	0.599	0.391	0.224	0.224
0.858	0.858	0.858	0.858	0.858	0.858	0.858
0.796	0.796	0.796	0.796	0.78	0.78	0.796
0.703	0.703	0.764	0.703	0.703	0.423	0.109
0.769	0.837	0.769	0.769	0.769	0.769	0.769
0.965	0.884	0.479	0.92	0.245	0.307	0.224
0.852	0.672	0.708	0.366	0.49	0.296	0.219
0.457	0.694	0.813	0.549	0.549	0.813	0.321
0.549	0.487	0.653	0.653	0.481	0.461	0.481
0.766	0.965	0.646	0.175	0.62	0.175	0.175
0.982	0.517	0.826	0.826	0.517	0.658	0.517
0.926	0.926	0.926	0.926	0.926	0.926	0.926
0.529	0.978	0.728	0.482	0.529	0.529	0.978
0.982	0.982	0.969	0.09	0.982	0.982	0.982
0.554	0.821	0.739	0.089	0.696	0.899	0.651

Table S5D. Bacteria-gene significance

NR, immune response and oxidative stress, epi Ifit3	NR, immune response and oxidative stress, epi Il6ra	NR, immune response and oxidative stress, epi Il1b	NR, immune response and oxidative stress, epi Socs3	NR, immune response and oxidative stress, epi Mt1	NR, immune response and oxidative stress, epi Mt2	NR, immune response and oxidative stress, epi Bnip3
0.897	0.679	0.666	0.666	0.897	0.679	0.679
0.786	0.786	0.595	0.248	0.434	0.317	0.248
0.473	0.473	0.929	0.963	0.473	0.473	0.473
0.492	0.508	0.041	0.546	0.546	0.546	0.722
0.484	0.09	0.484	0.937	0.484	0.746	0.788
0.507	0.507	0.82	0.982	0.507	0.82	0.77
0.268	0.268	0.294	0.546	0.268	0.268	0.268
0.456	0.323	0.295	0.456	0.214	0.288	0.295
0.948	0.948	0.443	0.948	0.948	0.948	0.948
0.868	0.36	0.36	0.912	0.462	0.82	0.912
0.922	0.922	0.944	0.922	0.922	0.965	0.922
0.599	0.599	0.418	0.588	0.369	0.599	0.599
0.858	0.858	0.858	0.858	0.858	0.963	0.858
0.98	0.78	0.897	0.796	0.796	0.98	0.98
0.322	0.423	0.001	0.703	0.703	0.731	0.831
0.769	0.769	0.769	0.769	0.769	0.933	0.96
0.366	0.078	0.224	0.92	0.335	0.694	0.875
0.417	0.219	0.219	0.219	0.219	0.219	0.411
0.457	0.423	0.321	0.694	0.423	0.321	0.423
0.653	0.487	0.461	0.487	0.481	0.653	0.907
0.62	0.62	0.175	0.175	0.366	0.646	0.766
0.982	0.517	0.517	0.624	0.492	0.246	0.517
0.926	0.926	0.926	0.926	0.926	0.926	0.926
0.982	0.968	0.982	0.482	0.849	0.529	0.529
0.982	0.982	0.982	0.433	0.982	0.982	0.982
0.555	0.651	0.39	0.193	0.284	0.223	0.392

Table S5D. Bacteria-gene significance

NR, immune response and oxidative stress, epi Nr0b2	NR, immune response and oxidative stress, epi Nr1d1	NR, immune response and oxidative stress, epi Nr1d2	NR, immune response and oxidative stress, epi Gadd45g
0.679	0.679	0.666	0.809
0.317	0.248	0.248	0.815
0.473	0.473	0.554	0.963
0.546	0.546	0.546	0.546
0.788	0.717	0.858	1
0.904	0.77	0.894	0.978
0.268	0.268	0.268	0.683
0.295	0.295	0.295	0.456
0.948	0.948	0.948	0.432
0.82	0.904	0.912	0.82
0.944	0.944	0.944	0.944
0.599	0.599	0.862	0.224
0.858	0.858	0.858	0.858
0.98	0.98	0.897	0.98
0.731	0.703	0.703	0.703
0.879	0.96	0.769	0.933
0.849	0.772	0.884	0.92
0.219	0.296	0.411	0.219
0.321	0.321	0.321	0.894
0.653	0.757	0.907	0.461
0.522	0.711	0.766	0.175
0.214	0.517	0.492	0.826
0.926	0.948	0.926	0.926
0.482	0.529	0.482	0.978
0.982	0.982	0.982	0.885
0.212	0.284	0.223	0.506

Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Abcc4	Abcg8	Slc10a2	Slc17a2	Slc3a1	Slc46a3	Slc7a2	Slco1a1	Bcl6	Cldn1	Egr1	Lcn2	Nlrp12
0.1695158759	0.1525642883	0.4068381022	0.3051285766	-0.1525642883	-0.3898865146	0.2203706387	-0.2203706387	0.4407412774	0.6102571533	0.4576928649	-0.1864674635	-0.1356127007
0.4016632088	0.3286335345	0.3468909531	-0.1095445115	-0.05477225575	0.09128709292	0.4746928832	-0.4746928832	0.7302967433	0.1095445115	0.3651483717	0.2738612788	-0.3286335345
-0.2373464416	-0.01825741858	0.2921186973	0.4564354646	-0.2556038602	-0.4929503018	-0.3468909531	0.2921186973	-0.3103761159	0.5659799761	-0.01825741858	-0.5842373947	0.05477225575
-0.7	-0.08333333333	-0.25	0.75	-0.6666666667	-0.5333333333	-0.7	0.05	-0.3	0.6	-0.06666666667	-0.15	0.06666666667
-0.35	0	0.2333333333	0.35	-0.6666666667	-0.2833333333	-0.3833333333	0.15	0	0.4833333333	-0.08333333333	-0.1	-0.45
-0.35	-0.1166666667	0.3333333333	0.1833333333	-0.3333333333	-0.35	-0.3333333333	0.2666666667	-0.03333333333	0.4833333333	-0.1	-0.2666666667	-0.4166666667
0.7	0.7	0.3	-0.45	0.5	0.4	0.6666666667	-0.6333333333	0.4166666667	-0.7	0.3	0.1166666667	0.3333333333
0.55	0.6833333333	0.2833333333	-0.7	0.5666666667	0.6833333333	0.5833333333	-0.6	0.6	-0.8833333333	0.01666666667	0.3833333333	0.05
0.15	0.2	0.1833333333	-0.8	0.3333333333	0.6166666667	0.1166666667	-0.05	0.1	-0.7666666667	-0.4833333333	0.3	-0.4
0.1833333333	0.2	-0.01666666667	-0.65	0.7833333333	0.4333333333	0.2333333333	-0.2833333333	0.1666666667	-0.6333333333	-0.2666666667	0.2	0.1
0.01695158759	0.05085476277	-0.4237896898	-0.1864674635	-0.05085476277	0.3051285766	-0.03390317518	-0.1356127007	-0.288176989	-0.6102571533	-0.1356127007	0.3051285766	0.2034190511
0.3559833394	0.3898865146	0.1695158759	-0.8814825547	0.5254992153	0.5763539781	0.3220801642	-0.4407412774	0.2203706387	-0.8475793795	-0.3220801642	0.3559833394	-0.2712254014
-0.09128709292	-0.2373464416	-0.5659799761	-0.03651483717	0.1460593487	0.1278019301	-0.07302967433	0.01825741858	-0.3103761159	-0.2921186973	-0.09128709292	0.2008316044	0.3286335345
-0.1881280332	0.00990147543	-0.4950737715	-0.2178324595	0.3069457383	0.3762560663	-0.1683250823	-0.0990147543	-0.1881280332	-0.5544826241	-0.3663545909	0.3069457383	0.2970442629
0.7485339206	0.04351941399	0.3568591947	-0.5396407335	0.6701989754	0.1479660076	0.687606741	0.008703882798	0.03481553119	-0.3481553119	0.2698203667	-0.2524126011	0.1566698904
-0.02970442629	-0.1287191806	-0.4950737715	-0.1980295086	0.2475368857	0.277241312	-0.06931032801	0.01980295086	-0.3663545909	-0.4950737715	-0.2475368857	0.1881280332	0.3168472138
0.3559833394	0.1695158759	-0.1864674635	-0.4407412774	0.6780635036	0.4576928649	0.372934927	-0.2034190511	0.05085476277	-0.6950150912	-0.01695158759	0.1695158759	0.4576928649
-0.5477225575	-0.5659799761	-0.4564354646	0.8946135106	-0.8580986734	-0.4564354646	-0.5842373947	0.6390096504	-0.5659799761	0.6755244876	0.07302967433	-0.2008316044	0.1643167673
-0.6963106238	-0.2524126011	-0.2872281323	0.4526019055	-0.5396407335	-0.4700096711	-0.8007572174	0.2088931871	-0.6527912098	0.4264902571	-0.3916747259	-0.2088931871	-0.1131504764
-0.3195048252	-0.06846531969	0.02282177323	0.7302967433	-0.6390096504	-0.7302967433	-0.3423265984	0.1141088661	-0.3651483717	0.593366104	0.3879701449	-0.4564354646	0.2282177323
-0.5763539781	-0.5254992153	-0.5763539781	0.9153857299	-0.6441603284	-0.372934927	-0.4915960401	0.4576928649	-0.2542738139	0.6950150912	0.1525642883	-0.01695158759	0.288176989
-0.3166666667	-0.4333333333	-0.3	0.6666666667	-0.7	-0.5166666667	-0.4833333333	0.4833333333	-0.7666666667	0.5333333333	0.01666666667	-0.3666666667	0.1333333333
-0.08333333333	-0.5666666667	-0.5833333333	0.4833333333	-0.15	-0.3	-0.1166666667	0.3666666667	-0.5333333333	0.3333333333	0.2	-0.15	0.4666666667
0.4833333333	0.4833333333	0.7333333333	-0.2333333333	0.1166666667	-0.03333333333	0.5333333333	-0.4166666667	0.6833333333	0.06666666667	0.4166666667	-0.06666666667	-0.3
0.4833333333	0.3833333333	0.8	-0.4	0.06666666667	-0.05	0.3833333333	-0.2166666667	0.2833333333	-0.01666666667	0.1333333333	-0.2333333333	-0.4833333333
0.7723150835	0.6336944275	0.8218224607	-0.5643840995	0.5544826241	0.138620656	0.7723150835	-0.5643840995	0.6832018047	-0.2475368857	0.3663545909	-0.1089162297	-0.1683250823

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Socs2	Cebpb	Hmox1	Icam1	Ifit3	Il6ra	Il1b	Socs3
0.3051285766	-0.8306277919	0.8136762043	0.6272087408	-0.05085476277	-0.2542738139	0.3898865146	0.4068381022
0.3468909531	-0.5294651389	0.6207522318	0.3103761159	0.1643167673	-0.1460593487	0.2738612788	0.6390096504
0.4199206274	-0.4929503018	0.3103761159	0.4929503018	-0.4199206274	-0.4016632088	0.1278019301	-0.05477225575
-0.35	-0.5666666667	0.6666666667	0.8666666667	-0.5333333333	-0.5	0.9	-0.3333333333
0.25	-0.5	0.5166666667	0.6166666667	-0.6166666667	-0.8666666667	0.6	0.1
0.1333333333	-0.2666666667	0.1833333333	0.35	-0.65	-0.6666666667	0.3166666667	-0.01666666667
0.5166666667	0.1833333333	-0.1	-0.5	0.6	0.6166666667	-0.5333333333	0.3166666667
0.4666666667	0.4666666667	-0.3166666667	-0.6166666667	0.3166666667	0.5	-0.5333333333	0.3333333333
0.3	0.75	-0.8333333333	-0.7333333333	-0.06666666667	0.03333333333	-0.55	0.2
-0.05	0.6	-0.7	-0.6166666667	0.25	0.7	-0.5833333333	0.1
-0.3559833394	0.5254992153	-0.4068381022	-0.4576928649	0.3559833394	0.2712254014	-0.1017095255	-0.2542738139
0.2542738139	0.5594023905	-0.7119666788	-0.6950150912	0.3220801642	0.372934927	-0.5254992153	0.4407412774
-0.6390096504	0.4199206274	-0.3651483717	-0.3103761159	0.3651483717	0.4746928832	-0.09128709292	-0.3468909531
-0.4257634435	0.6039900012	-0.5148767223	-0.3663545909	0.1287191806	0.5148767223	-0.1881280332	-0.3168472138
0.3829708431	0.3394514291	-0.5918640302	-0.7920533346	0.6701989754	0.5744562647	-0.9574271078	0.2611164839
-0.4059604926	0.5643840995	-0.5742855749	-0.4653693452	0.3663545909	0.5148767223	-0.3069457383	-0.277241312
-0.08475793795	0.6441603284	-0.5933055657	-0.7119666788	0.5254992153	0.8475793795	-0.6780635036	-0.1186611131
-0.438178046	-0.3103761159	0.4929503018	0.5842373947	-0.3651483717	-0.6024948133	0.6207522318	-0.6207522318
-0.3133397807	-0.3220436635	0.130558242	0.5744562647	-0.4090824915	-0.4613057883	0.600567913	-0.2088931871
-0.2510395055	-0.502079011	0.593366104	0.502079011	-0.2282177323	-0.4336136914	0.593366104	-0.4336136914
-0.661111916	-0.3390317518	0.661111916	0.6950150912	-0.3559833394	-0.3390317518	0.7289182664	-0.6441603284
-0.1666666667	-0.3833333333	0.2666666667	0.4333333333	-0.03333333333	-0.45	0.3666666667	-0.3
-0.6	-0.08333333333	0.06666666667	0.1	0.4166666667	0.2666666667	0.06666666667	-0.4
0.6333333333	-0.4	0.4	0.06666666667	0.01666666667	-0.1666666667	-0.03333333333	0.5666666667
0.8666666667	-0.3	0.01666666667	-0.1	0.05	-0.3166666667	-0.2666666667	0.7
0.8416254115	-0.207930984	0.04950737715	-0.277241312	0.34655164	0.2574383612	-0.4950737715	0.7525121327

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Mt1	Mt2	Bnip3	Nr0b2	Nr1d1	Nr1d2	Gadd45g
0.05085476277	0.2542738139	0.288176989	-0.288176989	0.3220801642	0.4068381022	-0.1525642883
0.4564354646	0.5477225575	0.6390096504	-0.5477225575	0.6207522318	0.6207522318	0.09128709292
-0.5294651389	-0.4564354646	-0.5294651389	0.4016632088	-0.5112077203	-0.3468909531	-0.01825741858
-0.4166666667	-0.35	-0.2	0.3166666667	-0.3166666667	-0.3166666667	-0.4
-0.5166666667	-0.3166666667	-0.2333333333	0.2333333333	-0.35	-0.1833333333	-0.01666666667
-0.6333333333	-0.3166666667	-0.4166666667	0.1666666667	-0.4333333333	-0.2166666667	-0.06666666667
0.8	0.6666666667	0.6333333333	-0.5666666667	0.6333333333	0.5833333333	0.2166666667
0.7666666667	0.7	0.5333333333	-0.65	0.5333333333	0.5333333333	0.3166666667
0.1333333333	0.03333333333	-0.1333333333	-0.1166666667	-0.15	-0.1333333333	0.5833333333
0.5166666667	0.3166666667	0.06666666667	-0.3666666667	0.1833333333	0.05	0.3166666667
0.2542738139	0.01695158759	0.2203706387	0.06780635036	0.1017095255	-0.08475793795	0.05085476277
0.5933055657	0.3051285766	0.2373222263	-0.3898865146	0.2373222263	0.06780635036	0.6780635036
0.2008316044	-0.01825741858	0.09128709292	0.09128709292	0.09128709292	-0.1278019301	-0.1278019301
0.3069457383	0.03960590172	-0.01980295086	0.00990147543	-0.01980295086	-0.1980295086	0.03960590172
0.2785242495	0.2088931871	0.1044465936	-0.1914854216	0.2524126011	0.2437087183	0.3133397807
0.2475368857	-0.07921180344	-0.01980295086	0.1485221314	-0.01980295086	-0.2376354103	0.0990147543
0.5594023905	0.3559833394	0.2203706387	-0.2542738139	0.3051285766	0.1864674635	0.08475793795
-0.7850689991	-0.6207522318	-0.3834057903	0.7302967433	-0.4929503018	-0.3834057903	-0.5842373947
-0.4787135539	-0.6789028582	-0.4961213195	0.5657523819	-0.5918640302	-0.7224222722	0.05222329679
-0.5477225575	-0.2510395055	-0.04564354646	0.2510395055	-0.1597524126	-0.04564354646	-0.593366104
-0.5254992153	-0.3051285766	-0.1695158759	0.4407412774	-0.2203706387	-0.1356127007	-0.7967246168
-0.5833333333	-0.7166666667	-0.3833333333	0.7666666667	-0.4833333333	-0.5333333333	-0.1333333333
-0.1333333333	-0.3	-0.06666666667	0.4333333333	-0.03333333333	-0.2	-0.35
0.2333333333	0.5166666667	0.4333333333	-0.5833333333	0.45	0.6166666667	0.1
0.05	0.1	0.08333333333	-0.2333333333	0.08333333333	0.1833333333	0.55
0.5643840995	0.6336944275	0.4752708206	-0.7030047555	0.5643840995	0.6336944275	0.4059604926

#CV PCB6 & CV PCB30 & GF PCB6 & GF PCB30 COMMON	#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB6 COMMON	#CV PCB6 & GF PCB6 & GF PCB30 COMMOn	#CV PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB30 & CV PCB30 COMMON
Cyp1a2	Cyp17a1	Cyp8b1	Ypel2	Cyp3a16	Igfbp5	Cyp2c29
Arntl	Cyp2a5	Serpina1e	Cldn1	Cyp3a41a		Atp6v0d2
Ces2c	Cyp2j9	Gm24105	Cyp26a1	Cyp3a41b		Cyp2b10
G6pc	Clpx	Gm47283	Sult2a2			Rnf125
Sult2a1	Rab36	AC127342.1				
	Mknk2					
	Lpin1					
	Sdf2l1					
	Creld2					
	Spry4					
	Setbp1					
	Syvn1					
	Loxl4					
	Got1					
	Npas2					
	Acmsd					
	Marco					
	Slc30a10					
	Hspa5					
	Gpcpd1					
	Mthfr					
	Slc34a2					
	Hsph1					
	Atp2b2					
	Mt2					
	Mt1					
	Hyou1					
	Nnmt					
	Manf					
	Slc16a1					
	Hspa13					
	Pim3					
	Pnrc1					
	Gstm2					
	Inhba					
	Rtn4rl1					
	Rbp1					
	Jun					
	Arfgap3					
	Nfil3					
	Ero1lb					
	Dhcr7					
	Tubb2a					
	Rad51b					
	Cyp2c54					
	Ppp1r3c					
	Sult3a1					
	Etnk2					
	Acot1					
	Gm13775					
	Gm15611					
	Gm16348					
	Sult3a2					
	Hspa1b					
	Serpina4-ps1					
	1810053B23Rik					
	Gm21049					

#CV PCB30 & GF PCB6 COMMON	#CV PCB30 & GF PCB6 & CV PCB30 COMMON	#CV PCB30 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only GF PCB6	#only GF PCB30
Socs2	Gstm3	Cyp2c55	Mfsd10	Ckb	Nbr1	Ttyh1
Bcl6	Gadd45g	Nr0b2	Hmox1	Nqo1	Igfbp1	Lars2
Fabp5	Upp2	Cyp3a44	Id3	Por	Per1	Hbb-bt
Slco1a1	Thrsp	Gstp1	Dnajb9	Psmb4	Klc1	Gm13340
Paqr9	Egr1	Hba-a2	Aldoc	Krt23	Lcn2	Gm20594
Gm25687		Hba-a1	Myh11	Abhd8	Ly75	Mir6236
Mup22			Aebp1	Plin5	Smad9	Gm28439
			Map2k6	Lonrf3	Enho	Gm28437
			Id2	Avpr1a	Sult1e1	Gm37194
			Klf11	Nr1d1	H2-Aa	Rmrp
			Hmgcr	Nr1d2	Nmrk1	
			Slc25a30	Cnmd	Ppl	
			Sqle	Sorbs3	Ppp1r3g	
			Slc15a2	Retreg1	Apol9a	
			Noct	Myc	Camk2b	
			Chka	Mpv17l	BC023105	
			Gsn	Slc10a2	H2-Ab1	
			Hdc	Slc3a1	Sult2a3	
			Il6ra	Abcg8	Sult2a5	
			Efna1	Cyb5a	Nlrp12	
			Plk3	Aldh1a7	Gm12390	
			Atp2a2	Spata3	Nbdy	
			Gfpt1	Ngef	Zbed4-ps2	
			Tmem159	Agxt	Mug-ps1	
			Nsdhl	Mpzl1	Gm42796	
			Msmo1	Lrp4	Gm42642	
			Gclc	Knstrn	4833411C07Rik	
			Acta2	Il1b	Gm47789	
			Icam1	Gstm4	Gm34654	
			Vnn1	Pdgfc		
			Gdf15	Hsdl2		
			Lonrf1	Gne		
			Cplane1	Cyp4a14		
			Lrtm1	Per3		
			Phf13	Slc2a5		
			Angptl8	Slc46a3		
			Zfp518a	Gys2		
			Tsku	Scnn1a		
			Tcim	Clec2h		
			Cebpb	Serpina7		
			Fam47e	Slc7a2		
			Fdps	Pllp		
			Defa24	Nectin1		
			mt-Co2	Cyp1a1		
			Rdh11	Gsta4		
			Zbtb16	Trib3		
			Gm5096	Abtb2		
			Osgin1	Abcc4		
			Bhmt	Igf2bp2		
			Ifit3	Dsg1c		
			Igkc	Gnat1		
			Zfp970	Rrp12		
			F830016B08Rik	1810055G02Rik		
			Hmgcs1	Ttc38		
			Mup15	Slc17a2		
			Mup17	Lrfn3		
			Tcf24	Lrg1		
			Ighv1-11	Il22ra1		
			Gm45301	Spon2		
			Eppk1	Inf2		
			Gm31583	Mical2		
				Foxq1		
				Ciart		
				Dsel		

9130409I23Rik
Mreg
Mmd2
Htatip2
Tmem120a
Sdr9c7
Gbp2b
Klhdc8a
Lgalsl
Maff
Pgp
Tafa2
Lsm11
Zfp526
Paxx
Hbb-bs
Pkdrej
Zmat1
Socs3
Smagp
Klf1
Pm20d2
Cyp2c50
Ntrk2
Retsat
Gsta2
Gstm1
Tmed9
Gpc6
Acnat2
H2-Q7
Serpina6
Lsamp
Pclo
Cyp26b1
Gm22220
Mup3
Frat1
Nipal1
Ccnd1
Klhl21
Cib3
Phldb3
Ly6a
Bnip3
Mup20
Ces1b
Gm11340
Gm13771
Rn7s1
Gm6135
Gstm2-ps1
Gm44421
Gm44787
Gm33543
Gm34777
Gm31508
Gm49012
AC138228.1
AC157910.3

#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only CV PCB30
Aminosobutyric acid	G6P	3-Hydroxybutyric acid	Folinic acid	Dopamine
2,3-Dihydroxybenzoic acid	F6P		Shikimic acid	Dextrose
	Raffinose		NADP	Allantoin
			Arginine	Inosine
			Adenylosuccinate	NAD
			Acetylcarnitine	Uridine
				Nicotinamide
				Taurine
				Adenosine
				Adenosyl-L-homocysteine
				UDP-GlcNAc
				3-Methylvaleric acid
				2,3-Dihydroxybenzoic acid
				2-Deoxycytidine

#GF PCB6 & GF PCB30 COMMON	#only CV PCB30	#only CV PCB6	#only CV PCB30
Glucuronic acid	Levulinic acid	Mucic acid	2-Hydroxyphenylacetic acid
	6-Methyl-DL-tryptophan	Mannose	
	Serine	Norvaline	
	Asparagine	Cytosine	
	Proline		
	Urocanic acid		

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001082.12	Mfsd10	6.27489	1.7969	-1.80408	-1.666	0.00005	0.00761968
ENSMUSG00000003053.17	Cyp2c29	505.17	834.73	0.72454	2.77488	0.00005	0.00761968
ENSMUSG00000003555.8	Cyp17a1	30.7127	66.9781	1.12485	3.97657	0.00005	0.00761968
ENSMUSG00000004038.9	Gstm3	20.5927	33.851	0.717065	2.92459	0.00005	0.00761968
ENSMUSG00000005413.8	Hmox1	10.8956	7.33838	-0.570219	-2.05123	0.00035	0.037983
ENSMUSG00000005547.14	Cyp2a5	430.556	721.13	0.744058	2.24398	0.00015	0.0193581
ENSMUSG00000007872.3	Id3	27.5332	13.3798	-1.04111	-3.69018	0.00005	0.00761968
ENSMUSG00000014905.4	Dnajb9	24.6827	16.6976	-0.563856	-2.44755	0.00005	0.00761968
ENSMUSG00000015224.10	Cyp2j9	8.84831	4.99311	-0.825464	-2.92044	0.00005	0.00761968
ENSMUSG00000015357.10	Clpx	78.2269	50.077	-0.643518	-2.64475	0.00005	0.00761968
ENSMUSG00000017390.15	Aldoc	3.30235	6.26799	0.924508	1.8897	0.00045	0.0460446
ENSMUSG00000018427.7	Ypel2	9.95094	5.96948	-0.737227	-3.14699	0.00005	0.00761968
ENSMUSG00000018830.10	Myh11	0.856366	1.92082	1.16542	2.76044	0.00005	0.00761968
ENSMUSG00000020175.15	Rab36	7.24259	4.05831	-0.835627	-2.23857	0.00005	0.00761968
ENSMUSG00000020190.13	Mknk2	16.502	34.2124	1.05188	2.706	0.00005	0.00761968
ENSMUSG00000020473.13	Aebp1	0.537474	1.24369	1.21036	1.91027	0.00015	0.0193581
ENSMUSG00000020593.15	Lpin1	23.3481	63.294	1.43876	4.53512	0.00005	0.00761968
ENSMUSG00000020623.11	Map2k6	2.79563	4.8047	0.781271	2.25429	0.00015	0.0193581
ENSMUSG00000020644.9	Id2	65.4148	42.2437	-0.630882	-2.77822	0.00005	0.00761968
ENSMUSG00000020653.12	Klf11	4.00267	1.83482	-1.12533	-2.16824	0.00005	0.00761968
ENSMUSG00000021453.2	Gadd45g	4.23384	9.3219	1.13866	3.01194	0.00005	0.00761968
ENSMUSG00000021670.14	Hmgcr	42.2238	98.0346	1.21523	3.29717	0.00005	0.00761968
ENSMUSG00000022003.7	Slc25a30	21.1229	8.85161	-1.2548	-2.70092	0.00005	0.00761968
ENSMUSG00000022351.14	Sqle	14.4701	22.8969	0.662076	2.85745	0.00005	0.00761968
ENSMUSG00000022512.3	Cldn1	25.5877	18.7521	-0.448393	-2.02615	0.00035	0.037983
ENSMUSG00000022769.9	Sdf2l1	44.9273	25.0223	-0.844377	-3.54758	0.00005	0.00761968
ENSMUSG00000022899.9	Slc15a2	3.0659	0.37101	-3.04678	-1.38684	0.00005	0.00761968
ENSMUSG00000023087.15	Noct	3.11413	6.68196	1.10144	2.47459	0.00005	0.00761968
ENSMUSG00000023272.4	Creld2	42.1392	14.3552	-1.55359	-6.28154	0.00005	0.00761968
ENSMUSG00000024427.7	Spry4	3.84589	5.82326	0.598512	2.37281	0.00005	0.00761968
ENSMUSG00000024548.11	Setbp1	0.571063	0.898115	0.65325	2.01298	0.0004	0.0421324
ENSMUSG00000024807.18	Syvn1	26.659	12.2223	-1.12511	-3.46232	0.00005	0.00761968
ENSMUSG00000024843.15	Chka	45.983	21.79	-1.07743	-2.35525	0.00025	0.028881
ENSMUSG00000024987.6	Cyp26a1	11.1487	24.2118	1.11883	3.82575	0.00005	0.00761968
ENSMUSG00000025185.14	Loxl4	3.94432	2.11188	-0.90125	-2.33915	0.00005	0.00761968
ENSMUSG00000025190.13	Got1	73.9132	114.605	0.632762	2.52771	0.00005	0.00761968
ENSMUSG00000026077.15	Npas2	8.47762	1.95208	-2.11865	-2.21209	0.0001	0.0140441
ENSMUSG00000026185.8	Igfbp5	5.37805	8.0981	0.590499	2.46113	0.00005	0.00761968
ENSMUSG00000026348.7	Acmsd	7.9453	11.3608	0.515893	2.05887	0.00025	0.028881
ENSMUSG00000026390.7	Marco	4.51252	2.20537	-1.03291	-2.38186	0.00005	0.00761968
ENSMUSG00000026614.7	Slc30a10	12.8976	7.77189	-0.730768	-3.05461	0.00005	0.00761968
ENSMUSG00000026839.17	Upp2	61.1429	142.443	1.22013	4.83935	0.00005	0.00761968
ENSMUSG00000026864.13	Hspa5	838.917	453.702	-0.886781	-2.47163	0.00005	0.00761968
ENSMUSG00000026879.14	Gsn	5.39704	11.4131	1.08046	3.81852	0.00005	0.00761968
ENSMUSG00000027346.15	Gpcpd1	23.3608	40.7371	0.802254	2.42579	0.0001	0.0140441
ENSMUSG00000027360.5	Hdc	3.45119	1.89382	-0.865796	-1.76936	0.00045	0.0460446
ENSMUSG00000027947.11	Il6ra	12.7959	19.116	0.579098	2.29486	0.00025	0.028881
ENSMUSG00000027954.9	Efna1	27.2749	14.7794	-0.883989	-3.61654	0.00005	0.00761968
ENSMUSG00000028238.6	Atp6v0d2	5.28464	8.4326	0.674173	2.16648	0.0001	0.0140441
ENSMUSG00000028680.14	Plk3	10.5138	6.01814	-0.804897	-3.05136	0.00005	0.00761968
ENSMUSG00000029009.17	Mthfr	7.1591	3.44294	-1.05613	-2.20818	0.00035	0.037983

ENSMUSG00000029188.14	Slc34a2	1.56037	0.365782	-2.09283	-2.78098	0.00005	0.00761968
ENSMUSG00000029467.15	Atp2a2	86.4356	60.473	-0.515334	-1.97184	0.00035	0.037983
ENSMUSG00000029657.15	Hsph1	47.3595	28.792	-0.717988	-2.07578	0.00015	0.0193581
ENSMUSG00000029992.14	Gfpt1	13.4599	9.01933	-0.577579	-1.84116	0.00045	0.0460446
ENSMUSG00000030302.16	Atp2b2	4.38644	2.77593	-0.66008	-2.11664	0.0002	0.0244872
ENSMUSG00000030483.14	Cyp2b10	17.3823	34.9186	1.00638	4.20068	0.00005	0.00761968
ENSMUSG00000030917.13	Tmem159	0.899211	4.33785	2.27025	1.53715	0.0004	0.0421324
ENSMUSG00000031349.4	Nsdhl	10.9891	18.7202	0.768519	3.05432	0.00005	0.00761968
ENSMUSG00000031604.10	Msmo1	88.8162	141.341	0.67029	2.3651	0.0002	0.0244872
ENSMUSG00000031762.7	Mt2	14.6712	30.7685	1.06847	2.79551	0.00005	0.00761968
ENSMUSG00000031765.8	Mt1	41.5758	103.19	1.31148	4.86124	0.00005	0.00761968
ENSMUSG00000032115.14	Hyou1	67.4029	46.7624	-0.527462	-2.28962	0.00005	0.00761968
ENSMUSG00000032271.13	Nnmt	56.8868	84.4939	0.570754	2.3728	0.00005	0.00761968
ENSMUSG00000032310.4	Cyp1a2	347.498	1061.1	1.61048	5.9896	0.00005	0.00761968
ENSMUSG00000032350.9	Gclc	79.3815	50.4684	-0.653422	-2.42429	0.00005	0.00761968
ENSMUSG00000032575.16	Manf	239.221	135.412	-0.820986	-2.2734	0.0001	0.0140441
ENSMUSG00000032902.1	Slc16a1	19.0525	12.3003	-0.631283	-2.79129	0.00005	0.00761968
ENSMUSG00000032932.15	Hspa13	14.3906	9.10349	-0.660639	-2.73434	0.00005	0.00761968
ENSMUSG00000033107.6	Rnf125	123.021	61.7043	-0.995457	-4.47951	0.00005	0.00761968
ENSMUSG00000035686.8	Thrsp	108.608	275.462	1.34273	5.6328	0.00005	0.00761968
ENSMUSG00000035783.9	Acta2	1.51116	4.87177	1.68878	2.67871	0.00005	0.00761968
ENSMUSG00000035828.11	Pim3	5.49715	9.06074	0.720943	2.54131	0.00005	0.00761968
ENSMUSG00000037405.8	Icam1	7.588	5.10752	-0.571098	-2.12615	0.0004	0.0421324
ENSMUSG00000037440.8	Vnn1	26.6312	18.1146	-0.555968	-2.3665	0.0001	0.0140441
ENSMUSG00000038418.7	Egr1	8.5935	4.36381	-0.977659	-3.36242	0.00005	0.00761968
ENSMUSG00000038508.7	Gdf15	2.87642	1.396	-1.04298	-2.33349	0.00035	0.037983
ENSMUSG00000038656.5	Cyp3a16	15.6662	29.4555	0.910887	3.44256	0.00005	0.00761968
ENSMUSG00000039633.6	Lonrf1	1.73883	1.02745	-0.759046	-2.12834	0.0004	0.0421324
ENSMUSG00000039801.7	Cplane1	1.57608	11.8302	2.90806	2.79653	0.00015	0.0193581
ENSMUSG00000040128.9	Pnrc1	65.8791	42.2407	-0.641185	-2.71807	0.00005	0.00761968
ENSMUSG00000040562.12	Gstm2	44.5903	65.892	0.563373	2.4444	0.00005	0.00761968
ENSMUSG00000041324.14	Inhba	9.92684	4.22896	-1.23103	-2.8545	0.00005	0.00761968
ENSMUSG00000045287.6	Rtn4rl1	6.73191	4.46	-0.593973	-2.31529	0.00015	0.0193581
ENSMUSG00000045776.3	Lrtm1	4.59023	7.84042	0.772364	2.57822	0.00005	0.00761968
ENSMUSG00000046402.10	Rbp1	2.24938	3.8182	0.763363	2.38685	0.00005	0.00761968
ENSMUSG00000047777.9	Phf13	2.44905	1.25344	-0.966331	-2.7493	0.00005	0.00761968
ENSMUSG00000047822.8	Angptl8	82.3516	37.7627	-1.12484	-2.15144	0.00045	0.0460446
ENSMUSG00000049164.7	Zfp518a	3.42441	2.24797	-0.607233	-2.21996	0.00005	0.00761968
ENSMUSG00000049580.12	Tsku	7.78541	17.2903	1.15112	2.39263	0.0002	0.0244872
ENSMUSG00000052684.4	Jun	8.02239	3.56567	-1.16986	-4.3468	0.00005	0.00761968
ENSMUSG00000054277.8	Arfgap3	4.98675	2.38411	-1.06465	-2.77345	0.00005	0.00761968
ENSMUSG00000055116.8	Arntl	9.47854	4.66962	-1.02136	-3.41105	0.00005	0.00761968
ENSMUSG00000056313.5	Tcim	6.3628	10.6007	0.736431	2.63227	0.00005	0.00761968
ENSMUSG00000056501.3	Cebpb	33.2417	49.8658	0.585055	2.15225	0.0002	0.0244872
ENSMUSG00000056749.7	Nfil3	11.4209	6.76087	-0.756389	-2.86792	0.00005	0.00761968
ENSMUSG00000057068.15	Fam47e	6.37728	11.3884	0.836547	2.00781	0.00025	0.028881
ENSMUSG00000057069.7	Ero1lb	12.8374	8.73738	-0.555077	-2.29919	0.0001	0.0140441
ENSMUSG00000058454.15	Dhcr7	16.3576	28.6402	0.808075	2.67257	0.00005	0.00761968
ENSMUSG00000058672.7	Tubb2a	60.3828	42.6623	-0.501177	-2.22162	0.0002	0.0244872
ENSMUSG00000059060.15	Rad51b	2.98263	1.00564	-1.56846	-2.7696	0.00005	0.00761968
ENSMUSG00000059743.12	Fdps	68.1418	100.306	0.557798	2.3204	0.00005	0.00761968

ENSMUSG00000061825.10	Ces2c	4.32809	7.73435	0.837552	2.81141	0.00005	0.00761968
ENSMUSG00000064213.5	Defa24	1.36432	0	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000064354.1	mt-Co2	6.53406	11.5824	0.825885	2.28304	0.00015	0.0193581
ENSMUSG00000066441.14	Rdh11	16.5169	23.867	0.531074	2.24242	0.00005	0.00761968
ENSMUSG00000066687.5	Zbtb16	17.6103	35.1446	0.996886	3.99134	0.00005	0.00761968
ENSMUSG00000067225.2	Cyp2c54	162.272	224.41	0.467721	2.06478	0.00025	0.028881
ENSMUSG00000067279.3	Ppp1r3c	27.6268	14.325	-0.947532	-4.13342	0.00005	0.00761968
ENSMUSG00000069324.6	Gm5096	15.1526	23.2798	0.619511	2.53681	0.00005	0.00761968
ENSMUSG00000069668.4	Sult3a1	97.163	160.62	0.725176	3.28788	0.00005	0.00761968
ENSMUSG00000070644.13	Etnk2	62.5601	96.255	0.621618	2.63482	0.00005	0.00761968
ENSMUSG00000070811.6	Sult2a2	47.5462	75.7986	0.672841	2.07079	0.0003	0.03438
ENSMUSG00000072949.6	Acot1	33.817	19.1723	-0.818729	-2.60084	0.00005	0.00761968
ENSMUSG00000074063.10	Osgin1	93.9424	49.382	-0.927792	-4.03213	0.00005	0.00761968
ENSMUSG00000074768.6	Bhmt	276.248	458.526	0.731038	2.73971	0.00005	0.00761968
ENSMUSG00000074896.3	Ifit3	4.81246	7.59939	0.659108	2.2256	0.00025	0.028881
ENSMUSG00000075551.4	Cyp3a41a	33.4333	57.9428	0.793345	3.43636	0.00005	0.00761968
ENSMUSG00000075552.4	Cyp3a41b	4.55117	8.51163	0.903198	3.06479	0.00005	0.00761968
ENSMUSG00000076609.2	Igkc	9.38561	17.1417	0.868984	2.35993	0.00005	0.00761968
ENSMUSG00000078650.2	G6pc	118.654	70.8163	-0.744612	-3.34005	0.00005	0.00761968
ENSMUSG00000078798.4	Sult2a1	56.4787	97.1215	0.782085	3.19123	0.00005	0.00761968
ENSMUSG00000078866.10	Zfp970	11.5288	17.8725	0.632507	2.15652	0.00015	0.0193581
ENSMUSG00000081207.4	Gm13775	12.4872	21.3006	0.770447	2.48423	0.00005	0.00761968
ENSMUSG00000084923.1	Gm15611	21.2021	5.05847	-2.06744	-4.28501	0.00005	0.00761968
ENSMUSG00000085445.1	Gm16348	0.998651	2.12188	1.08729	2.36459	0.00005	0.00761968
ENSMUSG00000090298.2	Sult3a2	3.39104	7.38886	1.12362	2.81264	0.00005	0.00761968
ENSMUSG00000090877.3	Hspa1b	1.21104	0.49013	-1.305	-2.62497	0.0002	0.0244872
ENSMUSG00000090942.1	F830016B	18.3992	13.1678	-0.482627	-2.08238	0.00035	0.037983
ENSMUSG00000092075.1	Serpina4-	21.4399	5.39866	-1.98962	-6.65923	0.00005	0.00761968
ENSMUSG00000093930.2	Hmgcs1	79.4702	111.752	0.491821	1.79112	0.00015	0.0193581
ENSMUSG00000096674.1	Mup15	16.0544	25.2402	0.652756	2.36601	0.00005	0.00761968
ENSMUSG00000096688.1	Mup17	35.5827	61.429	0.787745	3.16456	0.00005	0.00761968
ENSMUSG00000099032.2	Tcf24	4.46246	2.40791	-0.890059	-2.74594	0.00005	0.00761968
ENSMUSG00000100277.8	1810053B	0.732602	2.66094	1.86084	1.18658	0.0001	0.0140441
ENSMUSG00000102888.1	Ighv1-11	0	6.24986	#NUM!	#NUM!	0.00005	0.00761968
ENSMUSG00000106397.1	Gm21049	4.52985	7.62193	0.750694	2.11318	0.00035	0.037983
ENSMUSG00000110384.1	Gm45301	1.01899	2.77951	1.44769	2.41211	0.00025	0.028881
ENSMUSG00000115388.2	Eppk1	5.00691	7.2053	0.525136	2.22729	0.0001	0.0140441
ENSMUSG00000115919.1	Gm31583	2.90438	5.0658	0.802558	2.71184	0.00005	0.00761968

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000001270.9	Ckb	4.9592	2.82251	-0.813128	-1.925	0.00055	0.0404152
ENSMUSG00000003053.17	Cyp2c29	502.057	1871.49	1.89827	4.7931	0.00005	0.00618632
ENSMUSG00000003555.8	Cyp17a1	30.523	69.3286	1.18355	3.76365	0.00005	0.00618632
ENSMUSG00000003849.8	Nqo1	4.13848	8.59917	1.05509	3.10818	0.00005	0.00618632
ENSMUSG00000004038.9	Gstm3	20.4693	75.9074	1.89078	6.88927	0.00005	0.00618632
ENSMUSG00000005514.14	Por	143.718	286.806	0.996833	2.93999	0.00005	0.00618632
ENSMUSG00000005547.14	Cyp2a5	427.875	1202.66	1.49096	3.44719	0.00005	0.00618632
ENSMUSG00000005779.12	Psmb4	57.871	84.627	0.548278	1.92037	0.00065	0.0456767
ENSMUSG00000006777.7	Krt23	1.02612	5.09059	2.31064	4.50613	0.00005	0.00618632
ENSMUSG00000007950.9	Abhd8	1.46653	0.490162	-1.58107	-2.25758	0.0002	0.0194309
ENSMUSG00000011305.11	Plin5	16.8478	11.2536	-0.582169	-2.14557	0.00015	0.0159662
ENSMUSG00000015224.10	Cyp2j9	8.79124	5.13102	-0.776822	-2.50401	0.00005	0.00618632
ENSMUSG00000015357.10	Clpx	77.7399	44.4332	-0.807017	-2.76713	0.00005	0.00618632
ENSMUSG00000016239.11	Lonrf3	2.78045	1.06184	-1.38874	-2.97987	0.00005	0.00618632
ENSMUSG00000020027.18	Socs2	8.61402	16.6749	0.952916	2.06	0.00005	0.00618632
ENSMUSG00000020123.6	Avpr1a	24.1839	14.3293	-0.755076	-2.41315	0.00005	0.00618632
ENSMUSG00000020175.15	Rab36	7.19819	4.01968	-0.840554	-2.06135	0.00035	0.029457
ENSMUSG00000020190.13	Mknk2	16.398	38.746	1.24053	2.84633	0.00005	0.00618632
ENSMUSG00000020593.15	Lpin1	23.2003	40.0422	0.78738	2.19992	0.00055	0.0404152
ENSMUSG00000020889.11	Nr1d1	17.095	37.493	1.13305	2.42106	0.0005	0.0385
ENSMUSG00000021453.2	Gadd45g	4.2085	13.5086	1.6825	4.46078	0.00005	0.00618632
ENSMUSG00000021775.11	Nr1d2	18.5393	32.2923	0.800601	2.14163	0.0001	0.0113094
ENSMUSG00000022025.13	Cnmd	2.94353	7.12175	1.27469	2.30779	0.0001	0.0113094
ENSMUSG00000022091.6	Sorbs3	8.7422	15.3301	0.810301	2.61385	0.00005	0.00618632
ENSMUSG00000022270.16	Retreg1	33.766	64.9642	0.944073	2.71635	0.00005	0.00618632
ENSMUSG00000022346.15	Myc	1.47519	5.7052	1.95138	3.05112	0.00005	0.00618632
ENSMUSG00000022508.5	Bcl6	3.5485	6.1976	0.804501	2.72117	0.00005	0.00618632
ENSMUSG00000022679.13	Mpv17l	3.4023	7.38539	1.11816	2.33264	0.00005	0.00618632
ENSMUSG00000022769.9	Sdf2l1	44.6531	24.9449	-0.840016	-3.10498	0.00005	0.00618632
ENSMUSG00000023073.2	Slc10a2	3.87084	6.00992	0.634701	2.23853	0.0002	0.0194309
ENSMUSG00000023272.4	Creld2	41.8868	10.7104	-1.96748	-6.82395	0.00005	0.00618632
ENSMUSG00000024131.8	Slc3a1	16.845	27.1766	0.690046	1.95102	0.00055	0.0404152
ENSMUSG00000024254.15	Abcg8	23.9899	44.5496	0.892986	2.2514	0.00005	0.00618632
ENSMUSG00000024427.7	Spry4	3.8216	7.52294	0.977118	3.54048	0.00005	0.00618632
ENSMUSG00000024548.11	Setbp1	0.567395	0.943684	0.733949	2.09591	0.00035	0.029457
ENSMUSG00000024646.14	Cyb5a	1372.68	2262.27	0.720771	2.28567	0.00005	0.00618632
ENSMUSG00000024747.3	Aldh1a7	74.5145	106.783	0.519085	1.98059	0.0006	0.043428
ENSMUSG00000024807.18	Syvn1	26.4973	12.6676	-1.0647	-2.99172	0.00005	0.00618632
ENSMUSG00000025002.5	Cyp2c55	5.11	22.678	2.1499	7.12158	0.00005	0.00618632
ENSMUSG00000025185.14	Loxl4	3.92033	1.51462	-1.37202	-2.71184	0.00005	0.00618632
ENSMUSG00000025190.13	Got1	73.4621	143.402	0.964996	3.33157	0.00005	0.00618632
ENSMUSG00000026077.15	Npas2	8.42746	1.66594	-2.33876	-3.01011	0.0001	0.0113094
ENSMUSG00000026226.16	Spata3	2.63728	0.875213	-1.59135	-1.67117	0.0001	0.0113094
ENSMUSG00000026259.14	Ngef	11.0126	17.9847	0.707619	2.38152	0.00005	0.00618632
ENSMUSG00000026272.6	Agxt	102.981	151.74	0.559222	2.16773	0.00005	0.00618632
ENSMUSG00000026348.7	Acmsd	7.89756	21.2665	1.42911	4.87646	0.00005	0.00618632
ENSMUSG00000026390.7	Marco	4.48507	2.16164	-1.05301	-2.28692	0.00005	0.00618632
ENSMUSG00000026566.15	Mpzl1	6.70294	2.77735	-1.27108	-2.14427	0.00025	0.0235
ENSMUSG00000026614.7	Slc30a10	12.8176	6.44774	-0.991257	-3.4987	0.00005	0.00618632
ENSMUSG00000026839.17	Upp2	60.7617	218.9	1.84904	6.12168	0.00005	0.00618632
ENSMUSG00000026864.13	Hspa5	833.809	437.932	-0.929011	-2.08676	0.00015	0.0159662

ENSMUSG00000027253.15	Lrp4	4.77798	7.06684	0.564666	2.03091	0.0002	0.0194309
ENSMUSG00000027331.15	Knstrn	0.217572	1.42377	2.71015	1.00013	0.00015	0.0159662
ENSMUSG00000027346.15	Gpcpd1	23.2178	53.4558	1.20312	3.25032	0.00005	0.00618632
ENSMUSG00000027398.13	Il1b	3.56328	1.05211	-1.75992	-2.14464	0.0001	0.0113094
ENSMUSG00000027533.10	Fabp5	26.5272	16.0182	-0.727761	-2.43622	0.00005	0.00618632
ENSMUSG00000027890.17	Gstm4	22.8624	40.384	0.820811	3.1403	0.00005	0.00618632
ENSMUSG00000028019.9	Pdgfc	2.88046	1.70807	-0.753934	-1.99822	0.0006	0.043428
ENSMUSG00000028238.6	Atp6v0d2	5.25254	9.46139	0.849037	2.4918	0.00005	0.00618632
ENSMUSG00000028383.17	Hsdl2	27.8303	19.1411	-0.539983	-2.08801	0.0003	0.0264805
ENSMUSG00000028479.18	Gne	79.8364	128.18	0.683054	2.04104	0.00065	0.0456767
ENSMUSG00000028715.2	Cyp4a14	391.915	237.782	-0.720899	-2.27606	0.00015	0.0159662
ENSMUSG00000028957.12	Per3	1.72562	11.0867	2.68365	4.12698	0.00005	0.00618632
ENSMUSG00000028976.10	Slc2a5	0.440546	1.76822	2.00493	1.65217	0.00065	0.0456767
ENSMUSG00000029009.17	Mthfr	7.11418	2.70437	-1.3954	-2.97286	0.00005	0.00618632
ENSMUSG00000029188.14	Slc34a2	1.55125	0.246171	-2.65571	-2.62671	0.00005	0.00618632
ENSMUSG00000029650.10	Slc46a3	31.8414	52.3096	0.71617	2.06244	0.0003	0.0264805
ENSMUSG00000029657.15	Hsph1	47.0702	27.7613	-0.761739	-2.01922	0.00025	0.0235
ENSMUSG00000030244.7	Gys2	36.9491	64.0714	0.794143	2.09027	0.00055	0.0404152
ENSMUSG00000030302.16	Atp2b2	4.35972	2.18107	-0.999203	-2.83779	0.00005	0.00618632
ENSMUSG00000030340.16	Scnn1a	6.11295	9.11203	0.575904	2.05878	0.00065	0.0456767
ENSMUSG00000030364.6	Clec2h	1.55662	4.31177	1.46986	2.18053	0.00005	0.00618632
ENSMUSG00000030483.14	Cyp2b10	17.2776	94.9368	2.45806	8.74658	0.00005	0.00618632
ENSMUSG00000031271.14	Serpina7	9.22525	4.97408	-0.891158	-2.09026	0.0004	0.033088
ENSMUSG00000031596.15	Slc7a2	85.9182	171.302	0.995503	2.42586	0.00005	0.00618632
ENSMUSG00000031762.7	Mt2	14.5776	52.8041	1.8569	4.62578	0.00005	0.00618632
ENSMUSG00000031765.8	Mt1	41.3184	148.541	1.84601	6.05154	0.00005	0.00618632
ENSMUSG00000031775.5	Pllp	6.14127	2.78882	-1.13888	-2.14469	0.00045	0.0359901
ENSMUSG00000032012.8	Nectin1	24.696	17.389	-0.506108	-1.94543	0.00055	0.0404152
ENSMUSG00000032115.14	Hyou1	66.9891	43.0138	-0.639125	-2.34774	0.00005	0.00618632
ENSMUSG00000032271.13	Nnmt	56.5371	127.246	1.17034	4.24758	0.00005	0.00618632
ENSMUSG00000032310.4	Cyp1a2	345.376	2354.78	2.76935	6.42721	0.00005	0.00618632
ENSMUSG00000032315.6	Cyp1a1	0.408235	21.3863	5.71114	10.8865	0.00005	0.00618632
ENSMUSG00000032348.6	Gsta4	52.469	81.8235	0.641049	2.47242	0.00005	0.00618632
ENSMUSG00000032575.16	Manf	237.772	126.916	-0.905701	-2.11863	0.0003	0.0264805
ENSMUSG00000032715.9	Trib3	3.62747	8.68618	1.25976	2.03279	0.00035	0.029457
ENSMUSG00000032724.5	Abtb2	5.87529	3.77695	-0.637439	-2.04753	0.0004	0.033088
ENSMUSG00000032849.14	Abcc4	1.71548	3.77068	1.13622	2.61385	0.00005	0.00618632
ENSMUSG00000032902.1	Slc16a1	18.9328	10.1797	-0.8952	-3.40735	0.00005	0.00618632
ENSMUSG00000032932.15	Hspa13	14.303	9.86525	-0.535886	-1.97593	0.00025	0.0235
ENSMUSG00000033107.6	Rnf125	122.257	74.8678	-0.707494	-2.81318	0.00005	0.00618632
ENSMUSG00000033581.17	Igf2bp2	1.66105	0.509047	-1.70623	-1.12591	0.0003	0.0264805
ENSMUSG00000034774.6	Dsg1c	1.07675	2.19221	1.0257	2.76946	0.0001	0.0113094
ENSMUSG00000034837.12	Gnat1	12.5088	21.0651	0.751915	2.1181	0.00035	0.029457
ENSMUSG00000035049.4	Rrp12	2.74802	1.48642	-0.886549	-2.6113	0.00005	0.00618632
ENSMUSG00000035372.2	1810055G	6.32408	10.8725	0.781761	1.96938	0.00035	0.029457
ENSMUSG00000035686.8	Thrsp	107.955	205.081	0.925768	3.34836	0.00005	0.00618632
ENSMUSG00000035828.11	Pim3	5.46211	9.62427	0.81722	2.71331	0.00005	0.00618632
ENSMUSG00000035944.17	Ttc38	14.0742	20.1391	0.516941	1.96377	0.00055	0.0404152
ENSMUSG00000036110.14	Slc17a2	47.9669	31.78	-0.59392	-2.07519	0.00015	0.0159662
ENSMUSG00000036957.8	Lrfn3	2.96637	1.17429	-1.33691	-3.36685	0.00005	0.00618632
ENSMUSG00000037095.8	Lrg1	67.2168	47.361	-0.505121	-1.98627	0.00065	0.0456767

ENSMUSG00000037157.8	Il22ra1	3.93685	2.30756	-0.770677	-2.21827	0.0002	0.0194309
ENSMUSG00000037379.7	Spon2	4.43994	1.82471	-1.28287	-2.45754	0.00005	0.00618632
ENSMUSG00000037583.2	Nr0b2	25.807	16.3589	-0.657683	-2.30236	0.0002	0.0194309
ENSMUSG00000037679.9	Inf2	14.5959	21.2562	0.542318	1.95943	0.0005	0.0385
ENSMUSG00000038244.14	Mical2	7.57323	4.32506	-0.808189	-2.30005	0.00005	0.00618632
ENSMUSG00000038415.10	Foxq1	3.1372	4.80063	0.613744	2.07957	0.00045	0.0359901
ENSMUSG00000038418.7	Egr1	8.53806	14.7592	0.789639	2.33622	0.00015	0.0159662
ENSMUSG00000038550.10	Ciart	0.635327	4.26202	2.74597	2.5058	0.00005	0.00618632
ENSMUSG00000038702.6	Dsel	0.318647	1.1368	1.83495	1.59147	0.0005	0.0385
ENSMUSG00000038768.8	9130409I	1.69012	3.3601	0.991375	2.38357	0.0002	0.0194309
ENSMUSG00000039395.8	Mreg	31.446	22.0227	-0.513883	-2.00407	0.0005	0.0385
ENSMUSG00000039533.8	Mmd2	1.90734	4.59768	1.26934	2.91012	0.00005	0.00618632
ENSMUSG00000039745.8	Htatip2	13.6124	21.7983	0.679289	2.28578	0.0001	0.0113094
ENSMUSG00000039886.8	Tmem12(	16.7696	27.8392	0.731267	2.68188	0.00005	0.00618632
ENSMUSG00000040127.13	Sdr9c7	19.4072	11.0266	-0.815607	-2.73366	0.00005	0.00618632
ENSMUSG00000040128.9	Pnrc1	65.4718	42.3024	-0.630135	-2.33326	0.00005	0.00618632
ENSMUSG00000040264.10	Gbp2b	2.41906	1.40646	-0.782373	-1.95544	0.0007	0.0487173
ENSMUSG00000040562.12	Gstm2	44.3194	85.0048	0.939604	3.60356	0.00005	0.00618632
ENSMUSG00000041324.14	Inhba	9.86411	3.40919	-1.53276	-3.38139	0.00005	0.00618632
ENSMUSG00000041698.11	Slco1a1	51.4801	33.2839	-0.62919	-2.3143	0.00005	0.00618632
ENSMUSG00000042115.4	Klhdc8a	0.80677	0.334395	-1.2706	-2.44981	0.00025	0.0235
ENSMUSG00000042363.14	Lgalsl	8.00763	4.41853	-0.857811	-2.18413	0.00005	0.00618632
ENSMUSG00000042622.14	Maff	1.85114	4.3513	1.23303	2.48105	0.00005	0.00618632
ENSMUSG00000043445.7	Pgp	4.53206	2.65663	-0.770568	-2.30203	0.00005	0.00618632
ENSMUSG00000044071.8	Tafa2	0.48376	1.16023	1.26205	2.303	0.0003	0.0264805
ENSMUSG00000044847.13	Lsm11	0.880467	0.334164	-1.39771	-2.60413	0.00005	0.00618632
ENSMUSG00000045287.6	Rtn4rl1	6.68976	3.11675	-1.10191	-3.68259	0.00005	0.00618632
ENSMUSG00000046402.10	Rbp1	2.23594	3.74793	0.745215	2.09243	0.0003	0.0264805
ENSMUSG00000046541.9	Zfp526	1.73728	3.00717	0.791579	2.28551	0.0001	0.0113094
ENSMUSG00000047617.11	Paxx	39.0765	17.0249	-1.19866	-2.96755	0.00005	0.00618632
ENSMUSG00000052305.6	Hbb-bs	63.8974	36.6592	-0.80158	-2.85373	0.00005	0.00618632
ENSMUSG00000052496.5	Pkdrej	0.475661	1.0218	1.10311	2.72703	0.00005	0.00618632
ENSMUSG00000052676.16	Zmat1	4.08129	6.4258	0.654851	2.13824	0.00025	0.0235
ENSMUSG00000052684.4	Jun	7.97305	4.26725	-0.901823	-3.1051	0.00005	0.00618632
ENSMUSG00000053113.3	Socs3	2.49474	5.38121	1.10904	2.11745	0.0003	0.0264805
ENSMUSG00000053559.13	Smagp	31.1285	19.9458	-0.642154	-2.13389	0.00035	0.029457
ENSMUSG00000054191.8	Klf1	1.62248	3.2131	0.985766	2.18554	0.00045	0.0359901
ENSMUSG00000054277.8	Arfgap3	4.95607	2.07293	-1.25753	-2.8446	0.00005	0.00618632
ENSMUSG00000054417.5	Cyp3a44	25.8573	17.1078	-0.595916	-2.16753	0.0002	0.0194309
ENSMUSG00000054659.13	Pm20d2	3.10156	1.32451	-1.22753	-2.48902	0.0002	0.0194309
ENSMUSG00000054827.12	Cyp2c50	357.009	627.067	0.812659	2.57099	0.00005	0.00618632
ENSMUSG00000055116.8	Arntl	9.41997	3.72741	-1.33755	-3.70408	0.00005	0.00618632
ENSMUSG00000055254.15	Ntrk2	1.32876	2.94734	1.14933	1.80865	0.0003	0.0264805
ENSMUSG00000056666.13	Retsat	163.179	84.9098	-0.942452	-2.9787	0.00005	0.00618632
ENSMUSG00000056749.7	Nfil3	11.3496	6.37484	-0.832181	-2.80945	0.00005	0.00618632
ENSMUSG00000057069.7	Ero1lb	12.7588	7.57204	-0.752743	-2.69188	0.00005	0.00618632
ENSMUSG00000057933.10	Gsta2	14.8876	36.6186	1.29846	4.13678	0.00005	0.00618632
ENSMUSG00000058135.12	Gstm1	591.115	1077.86	0.866655	2.73107	0.00005	0.00618632
ENSMUSG00000058454.15	Dhcr7	16.2573	24.4437	0.588377	1.73799	0.00045	0.0359901
ENSMUSG00000058569.8	Tmed9	27.8989	18.8487	-0.565745	-2.03359	0.00055	0.0404152
ENSMUSG00000058571.11	Gpc6	0.925695	2.30111	1.31372	2.76731	0.00005	0.00618632

ENSMUSG00000058672.7	Tubb2a	60.0095	29.3901	-1.02986	-3.68327	0.00005	0.00618632
ENSMUSG00000059060.15	Rad51b	2.96318	0.790659	-1.90602	-2.70012	0.00005	0.00618632
ENSMUSG00000060317.9	Acnat2	62.994	36.0946	-0.803432	-3.04246	0.00005	0.00618632
ENSMUSG00000060550.16	H2-Q7	26.9214	17.4807	-0.622989	-2.11728	0.0002	0.0194309
ENSMUSG00000060803.6	Gstp1	52.2482	94.5054	0.855015	3.20267	0.00005	0.00618632
ENSMUSG00000060807.7	Serpina6	169.985	262.86	0.628886	2.32333	0.00005	0.00618632
ENSMUSG00000061080.11	Lsamp	1.22575	0.291018	-2.07448	-1.14479	0.0001	0.0113094
ENSMUSG00000061601.15	Pclo	0.57566	0.977399	0.763729	2.10847	0.00035	0.029457
ENSMUSG00000061825.10	Ces2c	4.3022	11.1216	1.37022	4.14522	0.00005	0.00618632
ENSMUSG00000063415.12	Cyp26b1	6.19951	2.65142	-1.22539	-4.09556	0.00005	0.00618632
ENSMUSG00000064225.6	Paqr9	57.3054	30.826	-0.894525	-3.17638	0.00005	0.00618632
ENSMUSG00000064605.3	Gm22220	0	7.00551	#NUM!	#NUM!	0.00005	0.00618632
ENSMUSG00000066154.11	Mup3	2026.5	1252.6	-0.694063	-2.02644	0.00045	0.0359901
ENSMUSG00000067199.4	Frat1	3.39578	1.93858	-0.808739	-2.24788	0.0002	0.0194309
ENSMUSG00000067219.9	Nipal1	4.44909	8.25715	0.892133	2.59416	0.00005	0.00618632
ENSMUSG00000067225.2	Cyp2c54	161.282	296.593	0.878904	3.09255	0.00005	0.00618632
ENSMUSG00000067279.3	Ppp1r3c	27.4578	14.4551	-0.925639	-3.55848	0.00005	0.00618632
ENSMUSG00000069668.4	Sult3a1	96.5726	152.327	0.657483	2.4394	0.00005	0.00618632
ENSMUSG00000069917.7	Hba-a2	15.9522	7.92925	-1.0085	-2.53543	0.00005	0.00618632
ENSMUSG00000069919.7	Hba-a1	123.857	80.1852	-0.627271	-2.30735	0.0002	0.0194309
ENSMUSG00000070348.5	Ccnd1	28.8011	18.0061	-0.677632	-2.00581	0.00015	0.0159662
ENSMUSG00000070644.13	Etnk2	62.1735	97.5737	0.650192	2.3878	0.00005	0.00618632
ENSMUSG00000072949.6	Acot1	33.5979	19.9522	-0.751821	-2.2701	0.0002	0.0194309
ENSMUSG00000073700.3	Klhl21	4.84991	8.7584	0.85271	3.05752	0.00005	0.00618632
ENSMUSG00000074240.4	Cib3	0.143641	2.40529	4.06566	2.29099	0.00035	0.029457
ENSMUSG00000074277.4	Phldb3	4.05555	2.40923	-0.751325	-1.90668	0.00045	0.0359901
ENSMUSG00000075602.10	Ly6a	9.16001	4.67716	-0.969716	-2.31759	0.00005	0.00618632
ENSMUSG00000078566.8	Bnip3	89.9067	133.144	0.566486	1.97231	0.00055	0.0404152
ENSMUSG00000078650.2	G6pc	117.921	34.0649	-1.79147	-6.18411	0.00005	0.00618632
ENSMUSG00000078672.2	Mup20	28.4851	45.4009	0.672516	2.49254	0.00005	0.00618632
ENSMUSG00000078798.4	Sult2a1	56.1121	88.0628	0.650222	2.29294	0.0002	0.0194309
ENSMUSG00000078964.2	Ces1b	38.6623	59.9889	0.633769	2.50962	0.00005	0.00618632
ENSMUSG00000081207.4	Gm13775	12.4095	21.5678	0.797432	2.15377	0.00005	0.00618632
ENSMUSG00000083409.1	Gm11340	7.21515	2.24671	-1.68321	-2.46551	0.00055	0.0404152
ENSMUSG00000083832.1	Gm13771	1.8277	0	#NUM!	#NUM!	0.0005	0.0385
ENSMUSG00000084923.1	Gm15611	21.0683	6.28033	-1.74616	-3.69593	0.00005	0.00618632
ENSMUSG00000085445.1	Gm16348	0.992266	3.40219	1.77767	3.9325	0.00005	0.00618632
ENSMUSG00000090298.2	Sult3a2	3.37105	7.75229	1.20143	2.72803	0.00005	0.00618632
ENSMUSG00000090877.3	Hspa1b	1.20366	0.247192	-2.28373	-3.46215	0.00005	0.00618632
ENSMUSG00000092075.1	Serpina4-	21.3086	5.73997	-1.89232	-5.72874	0.00005	0.00618632
ENSMUSG00000093183.2	Gm25687	30.7806	63.7545	1.0505	2.67769	0.00005	0.00618632
ENSMUSG00000099021.1	Rn7s1	700.234	447.929	-0.644568	-2.2057	0.0003	0.0264805
ENSMUSG00000100277.8	1810053B	0.727864	4.99681	2.77927	2.15033	0.00005	0.00618632
ENSMUSG00000106069.1	Gm6135	34.0333	18.6619	-0.866848	-2.29436	0.00015	0.0159662
ENSMUSG00000106397.1	Gm21049	4.50211	8.69691	0.949903	2.48844	0.0001	0.0113094
ENSMUSG00000107369.1	Gstm2-ps	5.28283	9.53136	0.851371	2.01229	0.0007	0.0487173
ENSMUSG00000107451.1	Gm44421	1.80148	3.62615	1.00925	2.14888	0.0006	0.043428
ENSMUSG00000108822.1	Gm44787	1.69451	5.98364	1.82015	2.27612	0.00005	0.00618632
ENSMUSG00000110353.1	Gm33543	7.64038	13.1396	0.782206	2.39977	0.00005	0.00618632
ENSMUSG00000110439.1	Mup22	99.9007	68.6497	-0.541243	-2.05099	0.00065	0.0456767
ENSMUSG00000111923.1	Gm34777	2.67348	4.37875	0.711799	2.03435	0.0005	0.0385

ENSMUSG00000113387.1	Gm31508	1.24582	0.612387	-1.02458	-2.20024	0.0004	0.033088
ENSMUSG00000115509.1	Gm49012	1.8745	0.444212	-2.07719	-3.09822	0.0001	0.0113094
ENSMUSG00000117879.1	AC138228	8.67119	4.72504	-0.875903	-2.12505	0.0003	0.0264805
ENSMUSG00000118017.1	AC15791(	211.714	108.509	-0.964301	-1.99521	0.0005	0.0385

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000004038.9	Gstm3	38.0431	58.9022	0.630687	2.46013	0.00005	0.0145745
ENSMUSG00000017119.19	Nbr1	76	156.094	1.03834	3.08994	0.00005	0.0145745
ENSMUSG00000018427.7	Ypel2	5.3982	3.31232	-0.704637	-2.41028	0.00005	0.0145745
ENSMUSG00000020027.18	Socs2	13.2242	6.3375	-1.0612	-2.2998	0.00005	0.0145745
ENSMUSG00000020429.7	Igfbp1	53.6002	26.8102	-0.999456	-3.89039	0.00005	0.0145745
ENSMUSG00000020893.17	Per1	3.68334	6.25289	0.76351	2.15347	0.00005	0.0145745
ENSMUSG00000021288.18	Klc1	12.9409	6.37187	-1.02214	-2.07132	0.00015	0.0387736
ENSMUSG00000021453.2	Gadd45g	4.11008	1.45737	-1.4958	-2.59523	0.00005	0.0145745
ENSMUSG00000022508.5	Bcl6	2.65652	4.42275	0.735406	2.26063	0.0002	0.0472414
ENSMUSG00000022512.3	Cldn1	26.1421	15.2533	-0.777248	-3.02367	0.00005	0.0145745
ENSMUSG00000024987.6	Cyp26a1	7.22284	16.3768	1.18101	3.76685	0.00005	0.0145745
ENSMUSG00000026822.14	Lcn2	3.61183	6.99576	0.953752	2.06076	0.0002	0.0472414
ENSMUSG00000026839.17	Upp2	141.068	212.088	0.588275	2.19764	0.0002	0.0472414
ENSMUSG00000026980.15	Ly75	1.02455	1.86615	0.865078	2.35758	0.0001	0.0268627
ENSMUSG00000027533.10	Fabp5	20.9053	11.7917	-0.826097	-2.64221	0.00005	0.0145745
ENSMUSG00000027796.2	Smad9	3.96217	1.89784	-1.06193	-3.47194	0.00005	0.0145745
ENSMUSG00000028445.7	Enho	5.8256	2.52464	-1.20633	-2.74623	0.00005	0.0145745
ENSMUSG00000029272.8	Sult1e1	3.01955	12.0294	1.99416	4.46773	0.00005	0.0145745
ENSMUSG00000032310.4	Cyp1a2	580.244	1032.94	0.832029	2.805	0.00005	0.0145745
ENSMUSG00000035686.8	Thrsp	75.4226	108.929	0.530321	2.11579	0.00015	0.0387736
ENSMUSG00000036594.15	H2-Aa	12.3664	24.7286	0.999753	3.13856	0.00005	0.0145745
ENSMUSG00000037847.14	Nmrk1	8.65751	16.9132	0.966125	2.32446	0.00005	0.0145745
ENSMUSG00000038418.7	Egr1	13.1471	6.28833	-1.064	-3.7676	0.00005	0.0145745
ENSMUSG00000038656.5	Cyp3a16	7.12851	15.836	1.15154	3.67862	0.00005	0.0145745
ENSMUSG00000039457.4	Ppl	4.08077	7.12185	0.803411	2.80195	0.00005	0.0145745
ENSMUSG00000041698.11	Slco1a1	21.356	5.97873	-1.83673	-5.94679	0.00005	0.0145745
ENSMUSG00000050423.11	Ppp1r3g	2.1755	0.629848	-1.78827	-2.64187	0.00005	0.0145745
ENSMUSG00000050445.4	Cyp8b1	29.9766	12.9283	-1.2133	-3.83764	0.00005	0.0145745
ENSMUSG00000055116.8	Arntl	4.50112	1.45834	-1.62596	-3.46099	0.00005	0.0145745
ENSMUSG00000057346.12	Apol9a	19.3931	32.688	0.753217	2.48492	0.00005	0.0145745
ENSMUSG00000057897.14	Camk2b	0.84208	2.11891	1.33129	1.48241	0.0002	0.0472414
ENSMUSG00000061825.10	Ces2c	4.35545	8.60041	0.981582	2.97034	0.00005	0.0145745
ENSMUSG00000063388.5	BC023105	3.59428	6.85076	0.930563	2.34984	0.0001	0.0268627
ENSMUSG00000064225.6	Paqr9	35.9574	23.9919	-0.583741	-2.37141	0.00005	0.0145745
ENSMUSG00000070811.6	Sult2a2	45.0135	98.3588	1.12769	3.25888	0.00005	0.0145745
ENSMUSG00000072849.10	Serpina1e	78.1579	34.9136	-1.1626	-4.35291	0.00005	0.0145745
ENSMUSG00000073421.6	H2-Ab1	23.9638	51.1132	1.09284	2.55741	0.00005	0.0145745
ENSMUSG00000074375.3	Sult2a3	0.913931	5.76955	2.6583	3.99495	0.0001	0.0268627
ENSMUSG00000075551.4	Cyp3a41a	26.1917	45.374	0.79276	3.08305	0.00005	0.0145745
ENSMUSG00000075552.4	Cyp3a41b	2.76118	6.39617	1.21192	3.37149	0.00005	0.0145745
ENSMUSG00000078650.2	G6pc	83.6587	38.114	-1.1342	-4.05012	0.00005	0.0145745
ENSMUSG00000078798.4	Sult2a1	36.972	91.5233	1.30771	4.24884	0.00005	0.0145745
ENSMUSG00000078799.5	Sult2a5	2.28821	5.90122	1.36679	2.19044	0.0002	0.0472414
ENSMUSG00000078817.4	Nlrp12	6.13793	3.48939	-0.814775	-2.95155	0.00005	0.0145745
ENSMUSG00000082008.1	Gm12390	0	2.18739	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000086316.8	Nbdy	0.965126	9.08573	3.23481	2.3883	0.00005	0.0145745
ENSMUSG00000092674.2	Gm24105	94.9427	153.292	0.691157	2.26807	0.00005	0.0145745
ENSMUSG00000093183.2	Gm25687	16.9584	55.347	1.7065	3.05133	0.00005	0.0145745
ENSMUSG00000096768.8	Gm47283	21.0555	8.4086	-1.32426	-3.46356	0.00005	0.0145745
ENSMUSG00000099901.1	Zbed4-ps2	3.94207	10.8342	1.45857	2.99773	0.00005	0.0145745
ENSMUSG00000101397.6	Mug-ps1	34.2915	22.1456	-0.630835	-2.52439	0.00005	0.0145745

ENSMUSG00000105192.1	Gm42796	9.81164	3.82683	-1.35835	-2.85412	0.00005	0.0145745
ENSMUSG00000107185.1	Gm42642	1.32544	0	#NUM!	#NUM!	0.0001	0.0268627
ENSMUSG00000109089.1	4833411C	13.8725	7.63832	-0.860895	-2.57638	0.00005	0.0145745
ENSMUSG00000110439.1	Mup22	64.7271	39.1905	-0.723867	-2.61227	0.00005	0.0145745
ENSMUSG00000110838.1	Gm47789	1.24793	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000111253.1	Gm34654	1.07187	0	#NUM!	#NUM!	0.00005	0.0145745
ENSMUSG00000117780.1	AC127342	13.9016	5.9063	-1.23493	-4.21178	0.00005	0.0145745

gene_id	gene	value_2	value_1	log2(fold_change)	test_stat	p_value	q_value
ENSMUSG00000003053.17	Cyp2c29	673.766	1232.86	0.871696	2.7636	0.00005	0.0237172
ENSMUSG00000025002.5	Cyp2c55	5.10794	9.57033	0.905826	2.8894	0.00005	0.0237172
ENSMUSG00000026185.8	Igfbp5	4.14362	7.52489	0.860778	3.06263	0.00005	0.0237172
ENSMUSG00000028238.6	Atp6v0d2	14.2949	8.46584	-0.755773	-2.57671	0.0001	0.0404588
ENSMUSG00000030428.16	Ttyh1	7.83723	20.5459	1.39044	3.46049	0.00005	0.0237172
ENSMUSG00000030483.14	Cyp2b10	18.4894	34.553	0.902114	3.34575	0.00005	0.0237172
ENSMUSG00000032310.4	Cyp1a2	573.897	1767.5	1.62285	4.7819	0.00005	0.0237172
ENSMUSG00000033107.6	Rnf125	119.634	73.9456	-0.694086	-2.68283	0.00005	0.0237172
ENSMUSG00000035202.8	Lars2	37.9931	16.2798	-1.22265	-3.96694	0.00005	0.0237172
ENSMUSG00000037583.2	Nr0b2	19.8513	11.5096	-0.786389	-2.59725	0.0001	0.0404588
ENSMUSG00000038656.5	Cyp3a16	7.05363	15.3354	1.12043	3.49577	0.00005	0.0237172
ENSMUSG00000050445.4	Cyp8b1	29.6178	11.0736	-1.41934	-4.51314	0.00005	0.0237172
ENSMUSG00000054417.5	Cyp3a44	19.7219	34.2151	0.794836	3.04706	0.00005	0.0237172
ENSMUSG00000055116.8	Arntl	4.44971	1.11565	-1.99583	-4.29871	0.00005	0.0237172
ENSMUSG00000060803.6	Gstp1	38.6763	66.8057	0.788521	2.91206	0.00005	0.0237172
ENSMUSG00000061825.10	Ces2c	4.30826	10.0339	1.21971	3.75254	0.00005	0.0237172
ENSMUSG00000069917.7	Hba-a2	12.5054	28.9749	1.21225	3.16461	0.00005	0.0237172
ENSMUSG00000069919.7	Hba-a1	161.435	257.664	0.674535	2.60695	0.00005	0.0237172
ENSMUSG00000072849.10	Serpina1e	77.2634	33.2336	-1.21714	-4.58994	0.00005	0.0237172
ENSMUSG00000073940.3	Hbb-bt	11.4866	32.257	1.48966	4.17862	0.00005	0.0237172
ENSMUSG00000075551.4	Cyp3a41a	25.9157	41.7969	0.689571	2.51749	0.0001	0.0404588
ENSMUSG00000075552.4	Cyp3a41b	2.73222	5.71036	1.06351	2.88173	0.00005	0.0237172
ENSMUSG00000078650.2	G6pc	82.715	52.4814	-0.656343	-2.57516	0.0001	0.0404588
ENSMUSG00000078798.4	Sult2a1	36.5984	71.0306	0.95666	3.13829	0.00005	0.0237172
ENSMUSG00000083563.1	Gm13340	22.2303	36.8976	0.731	2.47186	0.0001	0.0404588
ENSMUSG00000092674.2	Gm24105	93.8984	264.708	1.49523	4.56281	0.00005	0.0237172
ENSMUSG00000096768.8	Gm47283	20.8212	9.60095	-1.1168	-3.03589	0.00005	0.0237172
ENSMUSG00000096887.2	Gm20594	84.8472	147.632	0.799063	2.84097	0.00005	0.0237172
ENSMUSG00000098973.1	Mir6236	2424.83	1036.7	-1.22589	-4.1389	0.00005	0.0237172
ENSMUSG00000100131.1	Gm28439	7.92885	17.6712	1.15622	2.9385	0.00005	0.0237172
ENSMUSG00000101111.1	Gm28437	27.3548	48.503	0.826281	2.816	0.00005	0.0237172
ENSMUSG00000102189.1	Gm37194	1.33501	3.28318	1.29824	3.26943	0.00005	0.0237172
ENSMUSG00000115420.1	Rmrp	783.954	1427.45	0.864595	2.95006	0.00005	0.0237172
ENSMUSG00000117780.1	AC127342	13.7433	7.49599	-0.874538	-3.05459	0.00005	0.0237172

Table S2A. Liver metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	0.6417779	0.7530381	0.8854124	1.3165750	1.0407458	0.7608884	0.9882787	0.7862970	1.0625771	1.1283548	1.2155264	1.1977029	1.1177079	1.0111845	0.9166488	1.1527351	0.5878772	1.3592881	0.8895624	1.4278042	0.6871709	0.9504117	0.5052311	0.9326832
Indole-3-acetic.acid	0.7860392	1.9509565	0.5580886	1.5278171	1.0873190	0.7463817	0.1771168	0.3526087	0.4630552	0.5291279	0.7148218	0.4862421	0.5835993	0.4962891	0.7906378	1.5020283	0.6540461	1.0075090	1.0404164	0.8920219	0.2602962	0.5700573	0.5769496	0.6458184
Indole-3-pyruvic.acid	0.06424609	1.10713323	0.19021050	0.33843027	0.11897162	0.46282540	0.37132059	0.22765562	0.18087326	0.38830899	0.02884164	0.26659506	0.14896618	0.51208752	0.16279090	0.28747783	0.37848709	0.37283283	0.00000000	0.14392771	0.29731054	1.18302681	0.16473559	0.51285387
Kynurenine	1.5130420	1.8160458	1.1177367	3.3235912	1.4236657	1.8332443	0.4968082	0.4627796	1.0845344	1.1908755	0.8681831	1.3064311	1.4310919	1.0449380	0.7998276	2.0758060	0.9268621	1.9954938	1.5519350	2.5454728	1.1179864	2.3883236	0.7527254	1.1935632
2-Deoxycytidine	0.1456107	0.2046070	0.1144417	0.2018454	0.2570833	0.1523639	0.1548636	0.2199208	0.2156768	0.4964199	0.3365320	0.2922682	0.4379804	0.2772534	0.1278656	0.3985392	0.1284519	0.4021005	0.3026561	0.2529262	0.1450090	0.1766973	0.2007113	0.5602648
2-aminoadipic.acid	0.4075929	1.8351217	0.9447126	1.2758676	0.8124402	0.8410186	0.4128866	0.5227665	1.3971905	0.9069514	1.2938552	0.6817271	0.8004980	0.8948402	0.7905779	1.0971095	1.0229457	1.4079170	1.8391106	1.8948830	5.3693974	5.3069206	0.8495688	1.1904178
2-deoxyguanosine	0.58479568	0.00000000	0.00000000	0.44162009	0.58363951	0.00000000	1.63457253	0.37970606	0.00000000	0.38769672	0.06838577	0.19997020	0.80554615	0.29129296	0.00000000	0.23430805	0.06706320	1.46333000	0.00000000	0.15525769	0.00000000	0.00000000	0.00000000	0.52384648
3-Aminoisobutyric.acid	0.3103612	0.2316226	0.2791112	0.3631104	0.2398946	0.2452838	0.2880905	0.1962715	0.3782312	0.3797402	0.3751967	0.2140135	0.2781475	0.3356190	0.1825315	0.3856304	0.1752509	0.4551243	0.3276935	0.3667051	0.3028023	0.3385240	0.2649583	0.2924743
3-Hydroxybutyric.acid	1.7156741	0.6825009	1.6340875	0.7728069	0.6845594	3.0031276	1.4763494	1.4043569	1.8066952	0.5647619	0.8475344	1.0578820	1.6273289	2.9045689	1.5403997	1.5944642	0.5934880	0.8834803	0.6819804	0.8640724	0.8097863	0.9743788	1.3148739	1.5162630
4-Aminobutyric.acid	0.5156079	0.9141045	1.1005954	2.3476444	1.3140889	0.7357734	0.6096718	0.4719302	1.4989862	1.1886618	1.0745111	1.6027557	1.1806124	1.5513006	1.0620008	0.9948536	1.2875127	1.3189201	2.1056291	2.6841771	1.0229754	1.3207144	0.4810400	1.0543936
5-Aminolevulinic.acid	0.2867715	0.8398926	0.2810464	0.2019449	0.1020569	0.1164548	0.2761496	0.1963395	0.2273984	0.1812200	0.3716822	0.2694858	0.2225276	0.2574289	0.3098547	0.4189624	0.1705895	0.4910491	0.4734825	0.3410167	0.8565262	0.8064531	0.3156030	0.4568366
5-Methylcytidine	2.6366484	2.3470198	0.7913250	3.1443083	4.0459524	1.9228826	0.8837537	2.5323469	0.7833072	1.5051036	2.2849148	2.9870170	2.6811237	2.1907469	1.9084163	3.1802859	1.1070842	2.1720066	2.3003041	2.3661019	1.8300040	3.8581447	1.5396344	1.0123362
7-ketocholesterol	1.2891896	1.0073455	0.8360030	0.4664388	1.2795914	1.3383909	1.0546935	1.9164554	0.4051727	0.6767182	0.4498655	0.7065973	0.6043564	1.3701550	1.0951610	1.3300680	1.3873236	1.1263964	0.3944428	0.9683976	0.9645003	0.7742208	0.6170155	2.0484274
Acetyl-L-glutamine	0.4553014	0.4776746	0.4556176	1.1360893	0.4899839	0.4115659	0.4724127	0.3995740	0.7519312	0.7612600	0.5757849	0.8012261	0.9084725	0.7581108	0.5658879	0.6871090	0.4090363	0.6004718	0.4349892	0.7548255	0.3635997	0.5794367	0.3717956	0.6783111
Acetylcarnitine	0.02915257	0.05742605	0.04085568	0.04646320	0.01610918	0.02863787	0.02092485	0.04034642	0.02849962	0.03521710	0.03001347	0.03903095	0.06032182	0.06379381	0.03554116	0.08904216	0.13924858	0.08820948	0.25276956	0.11555283	0.15110799	0.11136802	0.18095977	0.19759626
Acetylglucosamine	1.3115664	1.2280059	1.0550751	1.8277008	1.5382448	0.8317039	0.9006399	0.7437013	0.8639561	1.1169542	1.2680750	1.4683521	0.8830023	1.0020359	1.2230501	1.0899670	0.6023287	1.6330727	1.0205687	1.5326382	0.7522740	0.9907671	0.6387737	1.1292635
Acetylglycine	0.2617616	1.5929109	1.2342161	2.1902251	2.0066785	1.0029190	1.9138947	0.8145704	1.6919136	2.5442625	2.4643134	1.7957466	0.2814305	0.3470204	1.2344673	0.8244505	0.2272679	2.3645095	0.3638673	0.9529061	1.4823383	0.8343840	1.0978394	0.7816405
Acetylornithine	0.23480651	0.10218698	0.15858941	0.19771777	0.62851733	0.05134179	0.18836825	0.08521779	0.11193669	0.26567215	0.32023260	0.26012605	0.47490123	1.12893094	0.14985087	0.74458555	0.45819030	1.06512125	0.75622866	0.72796858	0.76879026	0.70500716	0.82648159	0.71440786
Adenosine	0.3581978	0.5481528	0.5538759	0.5637655	0.7135748	0.7417769	0.9125724	0.7036831	1.2996513	1.2692738	1.3658697	0.8970467	0.9973923	1.5460150	0.6196735	1.0165961	0.6620103	2.0082194	1.1925067	0.4137528	1.0192838	1.0090414	1.8101009	1.6507011
Adenosyl-L-homocysteine	0.3163094	0.6499900	0.5642770	0.6660210	0.7347727	0.6880711	0.7655124	0.5100250	1.0084109	1.0896944	1.0674588	0.8004986	0.6242744	1.0607179	0.5468198	0.8729612	0.5892073	1.5979238	1.2145764	1.4491398	0.8496154	1.1124521	0.8608683	1.2268764
Adenylosuccinate	0.03907467	0.10987980	0.07196339	0.18365262	0.02049657	0.18750397	0.10259660	0.10153863	0.17733045	0.22357127	0.13469431	0.08656620	0.13093812	0.10786607	0.06330485	0.11795322	0.09404531	0.17072564	0.16554603	0.07081627	0.25297802	0.31067335	0.16538933	0.14309574
Alanine	0.8571079	0.8937346	1.2829469	1.2536040	1.3312153	1.0258898	0.9927881	0.8043505	1.3840192	1.2575998	1.3394220	1.3339071	1.3476500	1.2322631	0.9589156	1.1416117	0.9940162	1.2597832	1.1339764	1.4759244	1.1721014	1.4205798	0.6686826	0.9158186
Aminoisobutyric.acid	0.4493258	0.5828958	0.6461483	0.8794325	0.4539889	0.6068997	0.5862818	0.4553500	0.4213689	1.0816655	0.7381336	1.2356525	0.4183226	0.2992163	0.3076177	0.5605960	0.5548940	1.4832715	1.2783811	1.3008123	1.1644110	1.2625703	1.0386166	0.6530749
Arginine	0.5230813	0.8326213	0.3829666	0.3855671	0.2697902	0.3039470	0.3348270	0.2517091	0.3584439	0.5363771	0.4821799	0.4340597	0.5603556	0.3996499	0.4430393	0.4462321	0.3594968	0.3102111	0.5864398	0.2758807	0.1643636	0.2102865	0.2007999	0.3539812
Asparagine	0.8842260	0.8152583	0.9024042	1.3833165	1.2449474	0.9768765	1.1941756	0.9351111	0.9971121	1.3182055	1.2117728	1.3431893	1.1858922	0.9978230	1.2058328	1.2294066	0.6536824	1.4452643	1.2063691	1.3491411	0.8293748	1.0875278	0.7053539	0.9158058
Aspartic.acid	0.3762233	0.4292970	0.2857379	0.5451212	0.4423451	0.3255798	0.4889660	0.4377361	0.4992604	0.6124258	0.6449889	0.4799587	0.5048493	0.4952580	0.4067786	0.5631700	0.2476733	0.7353890	0.5144635	0.4634559	0.2357814	0.3112372	0.4857510	0.4860391
Betaine	0.7509563	0.7301263	0.6645387	0.8280204	0.7483555	0.7586245	0.6799378	0.7332552	0.5995388	1.1140138	0.9279227	1.0862676	0.7167985	0.4884979	0.8491893	1.0252541	0.6586413	1.5355912	0.9498598	1.0125740	0.7907893	0.8387790	1.0066512	1.0111870
Carnitine	0.4638704	0.6540949	0.5326691	1.0417368	0.7563746	0.5297869	0.5900569	0.5139531	0.7313478	0.9329322	0.8872217	0.9785690	1.1477622	0.8874642	0.6541203	1.1244702	0.7064974	1.6744503	1.3159400	1.4626136	0.9617662	1.2497777	0.6554014	1.3367312
Carnosine	0.1379304	0.1837529	0.1527487	0.3168994	0.2416656	0.1920351	0.2827001	0.2258543	0.2003689	0.5326479	0.2786935	0.3996725	0.3411534	0.1948664	0.1848126	0.3064725	0.2054774	0.4477849	0.3000470	0.4893805	0.2089623	0.2489793	0.1568765	0.2635589
Choline	0.7764507	0.8191480	0.6335699	0.6340663	0.8203244	0.6701257	0.8159180	0.6395891	0.6805273	0.9335008	0.9493801	1.0877272	0.6584530	0.8890556	0.3250131	0.9338085	0.6925649	1.0695122	1.0062782	1.0230024	0.8411477	0.9132406	0.4218052	1.0180560
Citrulline	0.4214526	1.4571427	0.4513969	0.6357133	0.5489945	0.4507589	0.3650552	0.3008129	0.3946912	0.7066947	0.6170127	0.5663506	0.3569724	0.5146847	0.4069223	0.6087197	0.3548486	0.4907301	0.6420626	0.6432533	1.0133808	0.8909440	0.3728396	0.6870457
Creatine	0.4086522	1.8336104	0.4751913	0.5582335	0.5536743	0.4931385	0.5850576	0.4867122	0.5313360	0.7563221	0.6526906	0.7692563	0.5293707	0.6098790	0.4726509	0.7157762	0.6398291	0.8875395	0.8520455	0.9165180	0.5239349	0.6135616	0.4791432	0.8448273
Creatinine	0.5057162	0.8707744	0.4629378	0.6562094	0.6613873	0.5594884	0.5854751	0.4851771	0.5782317	0.7563661	0.8161167	0.8193643	0.8426159	1.0442179	0.6368156	0.9255601	0.6743669	0.9832099	1.0984917	1.1851292	1.0670715	1.4789607	0.5438834	1.0728971
Cystathionine	0.2459859	0.3683612	0.3431268	0.4048110	0.2935433	0.4965935	0.3682411	0.2695575	0.3493903	0.4215621	0.3267381	0.3072462	0.2838443	0.2927669	0.2830256	0.3648586	0.1816999	0.2010483	0.2689415	0.2830604	0.4150128	0.3916642	0.1232459	0.2743187
Cytidine	1.0704769	1.1045405	0.5452250	1.1143852	2.2242367	0.8437256	0.8379310	0.7302953	0.8250596	1.2351377	1.2415660	1.4356379	1.0721686	1.3694450	1.1486803	1.3431894	0.5011534	1.7333319	1.2794172	1.8635491	0.4951477	0.7534005	0.9403074	1.1735831
D2-phosphoglyceric.acid	0.3310944	0.5996730	0.5421477	0.5783187	0.4516969	0.6160839	0.5869482	0.8026354	0.5160980	1.7919010	1.3227615	0.7696889	0.8412157	0.9673621	0.5756555	0.7466133	0.4928834	0.5637712	1.2022054	1.3578467	0.5968598	0.8221555	0.7988284	1.3712116
Dimethylarginine	0.9740189	1.0761789	0.9286955	1.7805238	1.3582373	0.9595825	0.9619014	0.7611321	0.8233580	1.2680150	1.1986943	1.4689141	1.1321591	0.7743156	1.1449154	1.2622517	0.5733991	1.5776915	1.3679222	1.4523821	0.6839601	1.0027647	0.7136403	0.9098727
Dimethylglycine	0.4607362	0.6099623	0.5798673	0.8415445	0.4800336	0.5956410	0.6211296	0.4700505	0.4793892	0.9944620	0.7717746	1.1394720	0.4232337	0.3249359	0.3335234	0.5717760	0.5680419	1.2948865	1.2641046	1.2082976	0.9839331	1.1826156	0.9984687	0.6824968
Dopamine	0.6221969	0.9233208	1.7799437	2.9220513	0.8243819	1.2029912	1.5160785	1.6078648	2.8711232	2.7599863	3.4069383	2.7410775	2.4948055	1.5058086	1.1234065	1.5403673	1.5234156	1.8589505	2.4006292	2.3461096	1.2409628	0.7001368	0.6745019	1.0942887
Folic.acid	0.2239471	0.7487736	1.0598652	1.7528520	0.5643385	0.1206645	2.1591450	1.4651981	1.3696177	1.7913465	0.6001736	1.0758190	1.3699781	2.3413983	1.4799907	1.6345688	1.0877975	3.9654829	0.6068767	2.1335282	1.1901542	1.7785697	2.3565170	0.7551478
Folinic.acid	0.7674852	1.6268925	1.0852252	0.7893310	1.2473922	0.7184188	1.4028261	0.6030513	0.9306193	0.9450751	1.3213389	0.8735870	3.0728728	1.7100075	1.2098770	2.9880290	0.8017804	1.8047687	1.0751854	0.9404757	0.2533398	0.4022695	1.6236487	1.0310206
GDP	0.2824551	0.4104324	0.6581356	0.6326138	0.5607096	0.6279206	0.9077773	0.7229344	0.7825835	1.1341158	0.8687443	0.7987579	0.8721362	0.8370757	0.5121924	0.7037107	0.6499428	0.7694018	0.9147735	1.0046965	0.7964523	0.8625709	0.5791299	0.8675360
Glucosamine	2.0459784	1.8586589	0.9763065	2.3173203	2.7368014	1.2832705	1.5635184	1.1995193	0.8349244	1.1213999	1.3293286	1.9080310	0.7805758	1.1948329	2.3484920	1.5326383	0.5317680	2.6586547	0.9757728	1.2297610	0.5173460	1.3240417	0.6768534	1.0608675
Glutamic.acid	0.3867288	0.6585914	0.2594397	0.6983488	0.4513374	0.4237792	0.2899086	0.2583647	0.4606375	0.4076183	0.4274454	0.4655869	0.5175806	0.6526626	0.7723591	0.7010507	0.4853293	1.0569855	0.8696258	0.9357680	0.3399974	0.5327368	0.6822027	0.9084132
Glutathione.oxidized	0.8428468	0.9934283	0.8284747	1.2904800	1.1288540	0.9433971	0.9309067	0.8341607	0.7050951	1.7922744	1.5380908	1.2666532	1.1660800	1.1961860	0.7966210	1.7078418	1.1142226	1.7799967	1.4630840	1.4101672	0.9523861	1.1156960	0.7591486	2.1125401
Glutathione.reduced	0.8328146	0.9973012	0.9263039	1.1861743	1.0307202	0.9995192	0.8701441	0.8078348	0.7663752	1.5181023	1.4216837	1.1157582	1.0358050	1.2074976	0.8834492	1.4707737	1.1736260	1.5332945	1.3728646	1.2931630	0.9865631	0.9085870	0.8146667	1.6901167
Glycerol.3-phosphate	0.4728707	0.9220561	0.5403641	0.4929494	1.1101013	0.6136874	0.5507888	0.5474192	0.5800091	0.8919979	0.6383870	0.8603690	0.9634107	1.0130460	1.1563273	0.9250990	1.3260552	2.9327821	1.8083472	1.8427419	0.4780161	0.5059864	2.0318877	0.9390341
Glycine	0.8730863	1.3705099	0.9158263	1.2231668	1.3027717	0.9159551	1.0228547	0.7828555	1.2443312	1.3262574	1.2728658	1.2074510	0.8440967	0.9126339	0.8707803	0.9282927	0.6426631	1.1847707	0.9643004	1.1552033	1.0063595	1.2029528	0.7578952	0.9970674
Glycocyamine	0.4700012	1.6812018	0.8093291	0.8862727	0.6447139	0.6131750	0.7258364	0.4538833	1.4261794	0.9214418	0.9556441	0.9071715	0.5539589	0.7430127	0.6726305	0.7824019	0.6505485	0.9903394	0.9944325	1.4137428	1.1282637	1.3375366	0.6221903	0.5836888
Glycylproline	1.8354316	2.4923578	2.6578428	3.1714119	2.4727788	1.9152073	1.8255724	1.7998914	1.5739886	2.8731885	2.3700045	2.6665893	2.2624526	1.4006515	1.9016969	1.9771679	0.8534983	2.6499820	2.2516603	2.3700619	1.9364397	2.2477298	0.8725860	1.5342976
Guanine	0.17621558	0.02278745	0.15415498	0.29704774	0.21663483	0.08342667	0.18120350	0.32614899	0.24036579	0.20259922	0.38402340	0.28300992	0.43238992	0.27333795	0.16728693	0.38415723	0.22893049	0.42081721	0.22346236	0.41695774	0.20548302	0.27833217	0.47305873	0.55053296
Guanosine	0.3246598	0.7685011	0.5047241	0.6499907	0.5206282	0.6397830	0.6747621	0.6381834	0.8289680	0.7105909	1.0300515	0.7829405	0.9793604	1.3265568	0.7543370	1.1106217	0.7258154	1.5540844	0.7140582	1.4509617	0.4875484	0.7297572	0.8773832	1.3040662
HIAA	2.4412992	2.6983910	0.8340145	3.2664718	1.4622671	0.6602276	0.6127725	0.4979979	1.9400444	0.9404046	0.9567780	2.4501998	1.1286798	0.4954157	1.8092108	1.3313670	0.6916914	2.1301379	0.9272512	2.2856990	1.5603747	3.5012040	0.4755159	1.8120372
Homoserine	0.8509122	0.8893932	0.7896290	1.2645999	1.2080315	0.8902052	1.0056840	0.7481959	0.9495331	1.1548321	1.1279660	1.1857805	0.9891440	0.8623097	0.9327528	1.0666565	0.5662173	1.0695083	0.9945852	1.1881665	0.8156957	1.0217079	0.5884026	0.8560951
Hydroxyproline	0.2787770	0.4799966	0.2375902	0.3059802	0.3431303	0.2190838	0.2147382	0.1216726	0.2352834	0.1174432	0.3323629	0.3495331	0.2464465	0.3174669	0.3419158	0.4244054	0.3477392	0.3852723	0.4589917	0.6555311	0.6199176	0.9536136	0.2041111	0.4815902
Hypoxanthine	0.9974282	1.0928235	0.8876036	1.2570637	1.4171350	0.9833092	0.8904424	0.8622482	0.9724418	1.0087576	1.1682902	1.2436913	1.1114261	1.1937916	1.1325733	1.3134446	0.7104519	1.3286557	1.0959749	1.3218071	0.8378953	1.0824028	0.8661801	1.1903877
Inosine	0.7073993	0.8391119	0.7140293	1.0391484	1.2535338	0.8420802	1.1015346	0.8319424	1.1457617	1.2143153	1.3476063	1.2969553	1.2625817	1.5320379	1.1991691	1.5026616	0.9335940	1.9186397	1.4259257	1.8834052	0.7778325	1.0904168	1.1187931	1.5236756
Isoleucine	0.8528558	0.9125115	1.0217673	1.5496715	1.2388609	1.0109370	1.1912526	0.9214470	1.1406629	1.2647698	1.2625838	1.3054733	1.2786902	1.0450159	1.0627395	1.1645459	0.6330773	1.4210589	1.0894039	1.3649646	0.9157909	1.1766452	0.7847429	0.9943086
L-Alloisoleucine	0.8517790	0.9111445	1.0125399	1.5249889	1.2311331	1.0197709	1.1902293	0.9271793	1.1383725	1.2737694	1.2513103	1.3068848	1.2579197	1.0529558	1.0765331	1.1544872	0.6385982	1.4168104	1.0940247	1.3688610	0.9093086	1.1719494	0.7768059	0.9903981
Leucine	0.8476465	0.8962709	1.0266517	1.5385229	1.2401560	1.0079082	1.2035426	0.9227276	1.1359438	1.2795848	1.2575548	1.3011260	1.2710841	1.0653769	1.0637925	1.1611670	0.6377768	1.4253318	1.0888724	1.3837039	0.9196804	1.1688058	0.7811297	1.0016315
Lysine	1.4482072	1.0568177	1.1645744	1.8665608	1.4198726	1.0589478	1.4302917	1.0602397	1.1560245	1.7148566	1.6197058	1.6151634	1.4481528	1.2386714	1.1956266	1.5964858	0.7940763	1.7900829	1.5315174	1.4456983	1.2263541	1.3774511	0.9487037	1.6550266
Methionine	0.8972607	0.9251098	0.9370634	1.6825585	1.3009507	0.9540860	1.2933955	0.9654324	1.0819269	1.3994877	1.3717682	1.5317663	1.4078088	1.1686087	1.2161785	1.3539391	0.7224215	1.6457019	1.4097348	1.6598803	1.0329937	1.4074516	0.8338763	1.0874213
N-Acetylneuraminic.acid	0.6206421	0.8199069	0.5600818	1.0237435	0.6379889	0.5087411	0.5873233	0.5743446	0.6651696	0.9633031	0.8905661	0.8053625	0.4815686	0.4091472	0.4826958	0.6580611	0.4163223	0.8383301	0.9182577	0.9383752	0.5135255	0.5525025	0.4070563	0.6223561
NAD	0.5189115	0.7432001	0.7848089	0.9723333	1.0264845	0.8151934	0.9443994	0.8430001	1.0739810	1.7751225	1.4312229	1.1960606	1.1191554	1.5435374	0.8247645	1.0287660	0.7932043	1.3737844	1.6242790	1.4497317	1.2129971	1.2927545	1.2158123	1.1611846
NADP	0.4645545	1.0033445	0.9597302	1.0300501	0.5523697	0.9305444	0.8770339	0.8463191	1.1799497	1.6125850	1.5100842	0.8503701	0.8669583	0.9652894	0.4649232	0.7248484	0.8139846	0.9654545	1.3477053	0.9537815	1.0817424	1.1563229	1.1929342	1.3127996
Nicotinamide	0.7178230	0.8810389	0.8387394	1.1619439	1.0747429	0.8485019	0.9581953	0.8306311	1.1420243	1.1893909	1.1554375	1.2419390	1.2246746	1.2373342	0.9347814	1.1588332	0.7229536	1.2618774	1.0789894	1.4088462	0.8409249	1.1128264	0.9288390	0.9164444
Norleucine	0.8518739	0.9031989	1.0352939	1.5405561	1.2409032	1.0051005	1.2031724	0.9123117	1.1186044	1.2682845	1.2530081	1.3082198	1.2709141	1.0547923	1.0632294	1.1498179	0.6271827	1.4302944	1.0885495	1.3559512	0.9163913	1.1671295	0.7881985	0.9965756
Norvaline	0.9124836	0.9298527	1.0368697	1.6448278	1.1552369	1.0535945	1.1661068	0.8477787	1.1226926	1.1524275	1.1425004	1.2132199	1.2447680	1.0239704	1.0882174	1.2925641	0.6011751	1.3398496	1.0437265	1.2117027	1.0259126	1.1945400	0.9568618	0.9967921
Ornithine	1.0332296	0.8179956	0.7856410	1.3515693	0.9279344	0.7778656	0.9067942	0.6364167	0.7778348	1.0385131	1.0756493	0.9922528	1.2363026	0.9490234	0.9931245	1.3358021	0.6026925	1.4751211	1.2747343	1.1052278	1.2221460	1.3833450	0.8267835	1.4047324
Pantothenic.acid	0.5843001	0.7413393	0.6365224	0.9997849	0.8483685	0.7045172	0.6561683	0.6052149	0.7990996	0.8561870	0.8310670	0.8831817	0.8910804	0.7766499	0.7562383	0.9005148	0.4408332	1.1369992	0.7531680	0.8794983	0.4826726	0.7702197	0.6456869	0.7288907
Phenylalanine	0.8266777	0.9186807	1.0043263	1.5735330	1.3371442	0.9285578	1.2423992	0.9631628	1.1908843	1.3133446	1.3050369	1.4669236	1.4456966	1.1005134	1.1502301	1.2907528	0.7015021	1.6027515	1.1682306	1.6519843	0.9048820	1.2502029	0.7999375	1.0173964
Pipecolinic.acid	0.3294063	1.0094060	0.3818550	0.5711961	0.4551660	0.3332365	0.4550962	0.3707791	0.4427522	0.6345462	0.4652044	0.5736943	0.5446118	0.6177807	0.4724979	0.6498503	0.4190516	0.8724576	0.6294419	0.8597367	0.5914717	0.7777559	0.5766327	0.5802869
Proline	0.5141562	0.6178646	0.5822266	1.3063838	0.7457581	0.5776894	0.7298739	0.5105093	0.6245210	0.8541810	0.6404874	0.9124592	0.7089632	0.6439353	0.6385716	0.7810780	0.3922450	0.9376606	0.7503399	1.0259594	0.7327704	0.9253374	0.5640057	0.5703749
Pyroglutamic.acid	0.3082117	0.8843707	0.4362193	0.5921241	0.4758751	0.4111866	0.4229338	0.3914758	0.4400848	0.5739163	0.4679617	0.5115939	0.5537708	0.6806015	0.4737140	0.5919037	0.4162531	0.8276363	0.6802242	0.8473929	0.4889404	0.6901764	0.5664578	0.5789078
Sarcosine	1.0084766	1.0659462	1.4043571	1.3180316	1.3173108	0.9578035	1.0446095	0.8087390	1.2527798	1.4248970	1.4078169	1.4296566	1.4621763	1.4146250	1.1970317	1.2222388	0.9605841	1.4551496	1.1998666	1.4855036	1.1753213	1.1102789	0.7256942	0.9738131
Serine	0.9631746	0.7482507	0.8027561	1.4342633	1.2503764	0.9510122	1.1738940	0.8230972	0.9846277	1.2222407	1.2662427	1.2908321	1.1188887	0.8060649	1.1238529	1.1654594	0.5992233	1.2091939	1.1286308	1.2184897	0.7885404	1.0498191	0.6902211	0.8701550
TMAO	0.09437101	0.43303428	0.27471777	0.11216410	0.77217358	0.46438820	0.18648344	0.22312431	0.83269885	0.48161575	0.14550246	0.22655480	2.34051394	0.79755627	7.29396053	7.28121795	0.61150801	0.84295022	2.54722104	1.89654121	2.66298055	2.24567385	0.86779300	1.35080682
Taurine	0.7178835	0.8336343	0.8542148	1.1605061	1.0823282	0.8895874	1.1038355	0.9200192	1.0612253	1.3159387	1.2440577	1.2424510	0.5820055	1.3399539	0.6293543	0.8610343	0.6677345	1.4970880	1.0986328	1.0589133	0.8018202	1.0684514	1.1126616	1.4430778
Threonine	0.8232457	0.8706377	0.7730140	1.2312086	1.2037216	0.8912114	0.9660505	0.7585548	0.9620484	1.1447777	1.0785856	1.1441714	0.9735837	0.8573386	0.9307297	1.0386725	0.5642106	1.0126094	1.0241260	1.2153759	0.7968829	1.0072283	0.6001133	0.8525195
Tyrosine	0.9150162	1.0841190	1.0359367	2.4642402	1.2867226	0.9170167	1.3293614	1.0450251	1.2348882	1.6267038	1.1748098	1.7505491	1.3043186	1.1454333	1.0372301	1.3440036	0.6115674	1.8582848	1.1087729	1.8802615	0.6253943	1.0400158	0.8149456	0.8355209
UDP-GlcNAc	0.2934447	0.5004356	0.4652797	0.5732223	0.7177815	0.5265830	0.5310480	0.5149530	0.6552245	0.8666439	0.7747757	0.6714735	0.5809566	0.6796868	0.6131760	0.7155939	0.5540551	1.0615481	1.0151025	0.9471085	0.4996689	0.6153224	0.8202686	0.8398630
Uracil	0.8606104	1.1405109	0.9367328	1.1936004	1.0690069	0.8014622	0.9855269	1.0904810	0.9049300	1.1703200	0.9967556	1.3101537	0.6560391	0.7866817	0.8377139	0.9379920	0.6340143	1.5360757	0.7688687	1.2509321	0.8756824	1.2854795	0.7315423	1.0174820
Uridine	0.8463357	0.9289961	0.7456293	0.9695010	1.0747293	0.7520132	0.8439773	0.7566538	1.0583116	1.0561338	1.1516558	1.1443289	1.3153369	1.4348080	1.2522523	1.4124399	1.1748731	1.0449634	1.4928727	1.7468186	0.7417218	1.0299351	0.6787251	1.1677144
Urocanic.acid	0.8638117	0.3212854	0.2892404	1.7392963	1.1278006	1.1803694	4.6323495	0.8480094	0.1972440	1.0285895	0.5361097	1.2196895	0.9425947	0.2852366	0.4181020	0.3113765	0.3851985	0.4109156	0.4547907	0.4721768	0.2222827	0.3274246	0.3922131	0.4958654
Valine	0.9146230	0.9386614	1.0100753	1.5698269	1.1371203	1.0416494	1.1706341	0.8330754	1.1107848	1.1486198	1.1281245	1.1790151	1.2029580	0.9875298	1.0709863	1.2544596	0.6194352	1.3227468	1.0324728	1.1931394	1.0201331	1.1820476	0.9588230	0.9909290
Xanthosine	1.1578918	1.0963044	1.8140309	2.5780088	1.6815118	0.7748606	1.4037110	1.4535702	1.6892207	2.5296336	1.9151461	2.4928248	1.8328610	1.4805901	1.0967489	1.4175627	1.0784961	1.4506998	1.4556784	2.4213394	0.9455076	1.1696542	0.6661710	0.9053000
3-Indoxylsulfate	0.0014066653	0.0004189127	0.0010537000	0.0083676171	0.0142302571	0.0009821833	0.0053553740	0.0037918780	0.0099701690	0.0018319320	0.0000000000	0.0032034815	1.6957355303	1.7628992518	1.6905300705	2.6690102670	2.6662227663	1.2041302524	2.8159077618	3.9225468829	1.4879194492	1.2193387223	0.5481725665	0.6420550854
4-Methoxyphenylacetic.acid	0.6466108	0.8747982	0.6853639	0.4635535	0.6923135	0.9081214	0.3864574	0.5932554	0.8592044	0.7749379	0.6144890	1.6048136	1.3247088	1.9877733	0.5777823	0.4745502	0.6657401	0.7476548	1.1156824	0.3347995	0.4634213	0.4693551	0.7580660	0.8725201
2,3-Dihydroxybenzoic.acid	0.2284087	0.0000000	0.1073506	0.1197521	0.3433866	0.2394200	0.2957455	0.1572915	0.2597474	0.4494817	0.2776771	0.5415174	1.1314134	2.0412582	1.3909532	2.0095700	1.0359663	1.9621842	1.1671127	1.7748041	1.5807294	1.5394085	2.0435920	1.5376939
2-Hydroxybenzoic.acid	0.9912718	1.0984016	0.8859903	2.9777668	1.2496739	0.8263873	0.4437614	0.6297594	0.7991838	1.2558908	0.4339783	1.1235803	1.7674413	2.4987940	1.7318874	3.3508043	2.1025498	1.1283852	1.9534964	2.6782763	3.6617174	2.3740483	1.5164736	2.3913293
2-Methylbutyric.acid	0.7510326	0.0000000	0.5933317	0.4652210	0.8170571	0.6277748	0.5667496	1.2758309	0.4076446	0.6058693	0.5857997	0.7638084	0.5694005	0.5361239	5.5609744	0.6463784	0.8742257	0.6882732	0.5173637	0.7346524	1.1216587	0.9157327	0.5570880	1.4616018

Table S2A. Liver metabolites

4-Hydroxybenzoic.acid	0.9001782	1.0560988	0.5165869	1.6783153	0.5699435	0.8027474	0.7099929	0.9605478	0.4151053	0.8681392	0.5752243	1.0260255	1.6784020	2.1886534	2.2593682	3.0059774	1.4193347	1.8491539	1.9264320	2.0369756	2.6518981	1.4725679	0.8501041	2.2330271
4-Methoxyphenylacetic.acid.1	1.9877733	2.0373450	0.8337383	1.6048136	2.0658340	1.2979754	1.1156824	1.9172275	0.7001501	1.3116874	0.6853639	0.7476548	0.9081214	0.7218465	1.3247088	0.6144890	1.4894123	0.3347995	0.6466108	0.9913256	2.3431603	1.4964245	0.8747982	0.5932554
4-Methylvaleric.acid	0.2696367	0.2186943	0.2389721	0.2746247	0.3590760	0.3322700	0.3165805	0.2152099	1.1698982	0.4311654	0.7466173	0.7422495	0.6337153	0.3439619	0.5406916	0.2775697	0.2417917	0.6953245	0.8615943	0.9623980	0.8432549	0.8873891	0.8374581	0.2084494
Acetoacetate	0.9898180	0.8188094	0.9803567	0.9251530	0.9654123	0.9608998	0.9271387	1.0024227	0.8747964	0.9635099	0.9376343	1.0259165	0.9012016	0.9546399	1.0628470	1.0269441	0.9713463	0.9222361	0.9781181	0.8887658	0.9629445	0.9882867	0.9223725	1.0056272
Allantoin	0.9081038	1.1675675	1.0835233	1.4973499	1.3482714	1.1630004	1.2846565	1.3128294	1.4097008	1.5623482	1.4565717	1.4920634	1.3007490	1.1960430	0.9304598	1.1245904	0.8584241	1.5205353	1.0506660	1.2419266	1.0761671	1.2260110	1.3543364	0.9334865
Benzoic.acid	1.5878079	1.6902164	0.4250484	0.9203602	1.8134949	0.8459258	0.8249963	1.2637116	0.2394484	1.2308995	0.5166132	0.3333922	1.2684222	0.5741011	1.0986724	0.5265405	1.6702033	0.4627586	1.1916263	1.1436699	3.5990895	2.2423102	1.1203569	0.9979186
Citraconic.acid	1.3647653	2.2112889	0.8797576	1.4538588	1.7578296	1.5525089	0.7205279	1.0104727	0.5281336	2.3166094	0.4419381	0.6244150	0.9155004	0.7162225	0.9572177	0.5355094	1.0329688	0.2687801	0.5441814	1.9064968	2.0203813	0.9108907	0.8113292	0.5437640
Dextrose	1.7685669	4.6572716	2.3556058	1.7827129	1.1974816	1.1544892	1.2490300	0.7734221	0.9285326	0.8872297	1.2075044	1.1579873	1.2059183	0.9654718	1.2255272	1.3560641	0.5118914	1.3100008	0.6316051	1.1003823	0.6802550	1.0078298	0.6595299	1.2910940
Ethylmalonic.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
F6P	0.6739597	0.2447394	0.1826924	0.5818162	0.6716709	0.9746235	1.6123935	1.0723225	1.1070088	1.1154111	1.1312938	0.8015774	0.8302518	1.1814138	1.0512689	1.3252791	0.9051761	1.2707456	1.0729524	0.9041556	0.5528828	0.8035899	1.1194059	1.3061925
Fumarate	1.4192990	0.9868137	0.8213347	1.4978703	1.0743669	0.7292620	1.0526249	0.6276190	1.0221781	1.3314953	1.0614763	0.9885643	1.1486085	1.1050599	1.0235470	1.4572782	0.8988348	1.4704258	1.0546681	1.0817807	0.7715662	0.9892307	1.4595397	1.6709555
G1P	0.6752635	0.8029834	0.7627249	0.6158372	0.6249657	1.1037194	1.7901152	1.1289605	1.1985437	1.2173511	1.2187953	0.7115492	0.8453992	1.3293391	0.9983102	1.4457266	1.0017281	1.3487788	1.1853711	1.0712144	0.5663022	0.8982037	1.1802936	1.3657570
G6P	0.6688839	0.2380527	0.1925240	0.6659184	0.6797407	0.9710578	1.7391819	1.0406175	1.1499232	1.1649878	1.2167404	0.8868503	0.9159730	1.2787757	1.0400833	1.4203444	0.9207098	1.4076844	1.1534235	1.0067520	0.5166500	0.8859144	1.1368587	1.3662755
Galactose	1.5341257	5.2179303	2.3947257	1.5528834	1.3580207	1.1063219	1.1401609	0.8658799	0.9155313	0.9234025	1.1114644	1.1004973	1.1229601	1.0896220	1.1545220	1.3138040	0.6990620	1.1046280	0.7290189	1.1359700	0.7966584	1.1953606	0.7623118	1.0896942
Gentisic.acid	0.3546276	0.0000000	0.4713781	0.7467572	0.3560114	0.5168665	0.7327730	0.4047499	0.3646098	0.3597696	0.4111592	0.9474256	1.0461493	2.6593919	1.7835470	2.1266823	0.8074980	2.2794278	1.0550036	1.2916958	1.2224337	1.0283997	1.5228155	1.2681876
Glucuronic.acid	0.8618951	1.2635837	0.3914980	0.5864809	0.7149729	0.8905112	0.6466698	0.4523792	0.8934652	0.5236532	0.5877000	0.5639786	1.8837233	1.5606799	1.5985878	1.6699945	1.0047435	1.2180814	1.2296122	1.6472588	2.2245028	3.2449828	1.3460268	1.4921735
Glutaric.acid	0.6255251	1.5050742	0.8120027	0.8111482	0.7230183	1.1111658	0.7304700	0.4656906	0.9388864	0.5379055	0.8971992	0.5454438	0.6180019	0.7336748	0.7200757	0.6911322	0.7825310	1.2197160	0.6192276	1.0192715	2.1257195	2.6211511	1.0164347	0.7943975
Glyceric.acid	1.1496164	2.5195502	1.1739954	1.3951672	1.4599438	0.8746264	0.9923443	1.2507857	0.8864898	1.5545627	0.9987718	0.9439196	0.7221400	1.4318077	0.8648158	1.2905391	1.3513554	0.8347342	0.9936521	0.7147244	0.7321524	0.8865097	0.8960178	1.4822709
Isobutyric.acid	0.00000000	0.05244963	0.50898333	0.82647449	0.00000000	0.65901154	0.56581734	0.71041992	1.32707167	0.56170639	1.01099565	1.18177968	0.84196243	1.21985165	0.69521063	1.08410990	1.63819382	0.52221008	2.05200836	1.27874196	1.92633325	1.10015048	1.10209239	1.01358025
Isovaleric.acid	0.7155741	0.0000000	1.0151671	0.4655771	0.9275040	0.4950023	0.7486756	1.0320418	0.8385003	0.7539450	0.5534565	0.6301668	0.4893295	0.5065836	5.2080493	0.7206219	0.7182304	0.4833982	0.6210143	0.8176440	1.0377181	1.1049437	0.3567986	1.2920695
Lactose	1.7278542	12.3361306	3.5970124	1.6204874	1.3170386	1.1452639	0.9148891	0.7427353	0.8165284	0.7769225	0.9731502	1.0814995	1.1334146	0.9947503	1.0370356	1.3653067	0.6670843	1.2811463	0.6614136	1.0377394	0.5529015	1.0834332	0.5707073	1.3489137
Levulinic.acid	1.5570665	1.2926634	0.7031304	0.6362157	0.7702267	0.6458151	0.4586144	0.6789458	1.2085580	0.9497924	0.8597124	0.6798147	0.8956509	0.6319326	0.9339435	0.5457088	0.9271357	0.9459671	1.2397537	1.8196988	0.9844683	0.8069519	0.7865500	0.4809240
Mannose	1.4952340	1.0294612	1.1193161	2.1812875	1.5518865	1.0888375	1.4574358	1.2740713	1.5870256	1.4937340	1.4813516	1.7636578	2.0195185	1.3265372	1.5246655	1.5385679	1.2863063	1.3664471	1.2684240	1.7166670	0.8845929	1.3531122	0.9221497	1.3065198
Methyl.alpha-D-glucopyranoside	0.7022848	1.3289890	0.7121133	0.9536818	1.1250414	0.6308415	1.1896947	0.8454161	1.2042655	0.9617926	0.8191024	1.0102836	0.9483462	1.1641299	0.6849502	1.0440661	0.6582924	1.3262151	0.9590109	0.8453300	0.8214475	1.1854478	1.1363926	1.0440430
Myoinositol	0.8694791	1.1178407	1.3772587	1.7509144	1.7419164	1.1912207	0.7806327	1.1023066	1.0258326	1.0494177	1.3554179	0.9649657	1.4025886	1.1070176	0.9472456	0.8104337	1.1539989	0.8418495	0.9136361	1.4517492	0.8450081	1.6781317	0.7083603	1.0566861
Nonadecanoic.acid	0.8291083	0.4843062	0.7006170	0.6379930	0.6590255	0.7834945	0.6717061	0.6468235	0.6136272	0.6344273	0.5468030	0.7088714	0.5691938	0.8135633	0.7518102	0.7726551	0.7042177	0.6471807	0.5237051	0.3273494	0.4570268	0.4718718	0.5502521	0.7504966
OAA	0.4706844	1.4768433	0.9478751	0.9480796	0.7043471	1.0231675	0.7729994	0.5138535	0.8686459	0.6839295	0.7601366	0.4938531	0.7716700	0.7003961	0.7052642	0.7108140	0.7430833	1.2272501	0.7375726	0.8898757	2.6271150	2.4659336	0.8769646	0.6642809
Palmitic.acid	0.6576104	2.4876173	1.1086988	0.9933969	0.6654050	0.5312395	0.7647661	0.7191476	0.6994420	0.7180929	0.5547641	0.8033647	0.6966770	0.8559372	0.7094591	0.7680809	0.5930325	0.8984361	0.5270847	0.9339967	0.4984569	0.6610013	0.5752758	0.5048961
Pentadecanoic.acid	1.1427298	0.5870484	0.6274741	0.6752754	0.6227439	0.7262631	0.5656418	0.5217017	0.6089249	0.4430046	0.4323494	0.7093060	0.4577233	0.5140927	0.6343803	0.6179902	0.4894114	0.5277205	0.3626343	0.3959666	0.4648136	0.3559489	0.5488784	0.4773791
Phthalic.acid	2.2467277	2.8811973	0.9590323	1.4759390	2.5516393	1.2665585	1.1557750	3.2708233	0.9187764	1.8053250	1.1865923	1.0920811	1.5253343	1.5010486	1.5789988	1.0036075	1.6275219	0.6693168	1.1291957	0.9520331	4.1384040	1.7908762	1.4875792	0.9633425
Raffinose	4.2406534	2.6381289	2.8986832	2.2229446	1.4063470	1.9821988	1.7797267	0.5603099	1.5427157	1.3383924	1.8955090	1.5934417	1.6822064	2.1903529	1.6188200	1.7642422	1.2483946	2.6886577	1.1058582	1.3579173	0.4961662	0.9152473	1.6370885	1.6808395
Shikimic.acid	0.4566439	1.6953687	0.4436559	0.5014321	0.9789059	0.6421197	0.8611503	0.8154816	0.4553175	0.8477968	0.7800669	0.6293811	0.6921569	0.9635854	0.7885012	0.8913415	0.7719212	1.1031032	1.0271294	1.0289196	1.1278543	1.0499156	1.0467217	1.3644345
Sorbitol	1.585376	2.068789	2.017347	2.935154	2.439898	1.695450	1.235273	0.948883	1.877812	1.083459	1.648626	2.228505	2.471795	1.821555	3.012169	1.975258	2.174246	2.263342	2.427025	4.434080	1.370861	1.535353	1.067649	1.186329
Stearic.acid	0.7809648	2.2287310	1.2442121	1.0303458	0.9092352	0.7524102	0.7931729	0.8663392	0.7608388	0.7868036	0.6238720	0.8245983	0.8188588	0.8765730	0.8958090	0.8963560	0.7338885	0.8893772	0.7047385	0.9714868	0.8025889	0.8111246	0.7017546	0.7680203
Trehalose	2.1142004	13.2894395	3.9071349	2.2777436	1.5761671	1.0666695	1.5014004	0.6787332	0.8279424	0.7812906	1.2507457	1.4231432	1.3643417	0.9935851	1.1759800	1.3869828	0.5431801	1.0142042	0.8030972	0.9663495	0.5082489	1.0376458	0.7117123	1.6965194
Urate	1.3406364	1.5250610	0.8473836	1.1140390	2.4907067	1.2353838	1.7609205	1.1875856	1.5123852	1.3022075	1.4339406	1.0269305	0.6765105	1.0893236	0.6584594	0.7040288	0.7428215	1.9296033	0.8196379	1.6574426	0.8632615	0.8101919	1.2833077	2.1605345
Valeric.acid	0.70749133	0.09470111	0.98921146	0.46459669	0.91370278	0.47580163	0.74021893	1.03119080	0.81706168	0.75332329	0.55229107	0.62304875	0.48829916	0.49363134	5.14922195	0.71910449	0.69037095	0.47793804	0.60513635	0.78592837	1.03686237	1.08850223	0.34767608	1.28934875
X5P	1.201143	1.276757	1.413303	1.653952	1.267569	1.278849	1.780746	1.354567	1.779299	1.577205	1.707360	1.920431	1.580249	1.517633	1.585497	2.195201	1.459374	1.733696	1.705658	2.215318	1.187748	1.478072	1.491918	1.627948
Xanthine	1.479659	1.481760	1.402484	1.887153	1.778127	1.252138	1.518562	1.382384	1.521875	1.459015	1.538795	1.813552	1.511328	1.476498	1.470618	1.495125	1.065810	1.728239	1.406754	1.589197	1.155761	1.426024	1.365320	1.292267
alpha-Hydroxyisovaleric.acid	0.22652691	0.06324408	0.24138572	0.38533503	0.40858595	0.08999759	0.13680320	0.24739137	0.67448423	0.27068110	0.05595278	0.38246377	1.40021748	0.40581075	0.59413534	0.16162409	0.14820324	0.80589746	0.45462266	0.50294160	0.51224833	0.62746522	0.94315331	0.27787725
alpha-ketoisovaleric.acid	1.6450600	1.9676816	0.9101139	0.7138070	0.8190894	0.5382239	0.4271922	0.7849076	1.1082485	0.9436748	0.6605273	0.5106391	1.2123041	0.5905675	0.8120547	0.5422817	0.3049550	1.0403584	1.1329032	1.8615979	0.9017435	0.8825711	0.9590286	0.7871725

Table S2B. Serum metabolites

	GF_VEH	GF_VEH	GF_VEH	GF_VEH	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB6	GF_PCB30	GF_PCB30	GF_PCB30	GF_PCB30	CV_VEH	CV_VEH	CV_VEH	CV_VEH	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB6	CV_PCB30	CV_PCB30	CV_PCB30	CV_PCB30
Tryptophan	1.0317667	1.0303621	0.9847637	0.9921081	0.9160872	1.0764221	1.0336387	1.4405943	0.7765993	0.9986675	1.0874466	1.0637402	0.6305017	0.5213879	0.7407689	0.8465473	0.6182256	0.6951432	1.0381927	0.6869308	1.1003884	0.7616520	0.7266176	0.6292298
3-Indolepropionic.acid	0.01904275	0.00000000	0.00000000	0.01174865	0.00000000	0.03955007	0.06561667	0.03874387	0.00000000	0.00000000	0.00000000	0.00000000	0.55859613	0.47659752	0.71442760	0.27750775	0.61415979	1.10075666	0.37694018	1.13900959	0.22864990	0.44264462	0.75318881	2.27604977
6-Methyl-DL-tryptophan	0.41570933	0.55659384	0.67931578	0.49104472	0.80584709	1.93103976	0.63320850	0.66146933	1.08739075	0.65511807	0.75366381	0.74293619	0.09812646	0.17093453	0.45117283	0.25733516	0.22503132	0.36726015	0.26036736	0.33192057	0.59247137	0.78618775	0.94471496	0.45148486
Indole-3-acetic.acid	0.5580839	0.5380495	0.5656663	0.5636264	0.4919839	0.4800485	0.4241354	0.6233548	0.3343458	0.5122234	0.6933088	0.4484751	0.7917882	0.9824133	1.0578317	1.1315136	0.6962389	1.0884141	1.7883287	1.4874967	1.2532215	1.2294161	2.2210241	1.7300960
Indole-3-lactic.acid	1.1092210	0.8554817	0.8354971	1.1621817	0.7877591	1.0869508	0.8945694	1.5749362	0.6616183	1.0120818	1.0766544	0.9578828	0.6190572	0.4244500	0.7577282	0.8598728	0.5966954	0.7057665	1.0638820	0.6138955	1.0639085	0.6896377	0.6855773	0.5902174
Kynurenine	1.0909688	0.8734492	0.3294966	0.7872656	0.2680286	0.8604749	1.0273913	0.9765153	0.8797466	0.7120567	0.7678117	0.9076418	0.3653122	0.6868505	0.6065237	0.7695144	0.5623107	0.3753020	0.5503452	0.4305640	0.3471962	0.5665617	0.6669201	0.4597565
Serotonin	0.8442799	0.9014375	0.7353003	0.7508531	0.8737883	1.3184758	0.8002665	0.7634158	0.7392552	0.8125640	0.8092775	0.8531453	0.4321848	0.5080711	0.4937651	0.5775824	0.5864579	0.5811751	0.6443621	0.5838568	0.7712975	0.5235457	0.8569040	0.5515420
2-Deoxycytidine	0.3174848	0.2913996	0.2822617	0.3026962	0.2133915	0.3491761	0.2773496	0.3324238	0.2194807	0.2744738	0.2549853	0.2950616	0.2459364	0.2298095	0.3028967	0.3110092	0.2116033	0.3872227	0.2877459	0.3042525	0.2941973	0.2165142	0.3662207	0.3591027
213C-Glutamic.acid	0.9844852	0.9950125	0.9327800	1.0003609	0.9661615	0.9508437	0.9988592	0.9277253	1.0146637	0.9506263	1.0051244	1.0134514	1.0141268	1.0258431	1.0099926	1.0166979	0.9702272	1.0188772	0.9572153	0.9783577	0.9923269	0.9244512	0.9319085	1.0222706
5-Aminolevulinic.acid	0.7795518	0.7610577	0.6979264	0.6854502	0.9618818	1.2366398	0.7757380	0.8759584	0.7565268	0.8750895	0.6972154	0.5884368	0.5317662	0.4935351	0.5312805	0.6134248	0.6264979	0.4866220	0.6992055	0.7625584	0.7390534	0.5473003	0.6652192	0.5197771
6-Hydroxynicotinic.acid	0.028878300	0.053021903	0.055377422	0.067188470	0.069876473	0.033207796	0.050327910	0.064691863	0.057382380	0.066923263	0.050205179	0.020650789	0.023744369	0.012478698	0.008996055	0.025685372	0.020600780	0.016676094	0.009066213	0.020656543	0.027477553	0.000000000	0.038251691	0.035514356
7-ketocholesterol	0.2924918	0.2284840	0.4863401	0.3812536	0.5532410	0.2924774	0.4050716	0.6754374	0.3572131	0.5246027	0.4581334	0.5209997	1.3684958	2.2957026	0.9383200	10.2231564	0.3468779	0.7566915	5.0969810	0.5870745	0.6553080	0.5284319	0.9099085	2.8210692
Acetylcarnitine	0.9441641	0.9762040	0.8584805	0.8966743	0.8083222	1.2599501	0.9270292	1.1218529	0.6377153	0.9340284	0.9575799	1.0547174	0.8179229	0.7078616	1.3668700	1.1744102	0.8729917	1.4676838	1.0122209	1.3667082	0.8370880	0.5816249	0.8944781	1.2286137
Acetylglucosamine	0.40392903	0.20460270	0.40498773	0.42430252	0.40644811	0.73773239	0.37272404	0.36942373	0.34369816	0.43376192	0.32548500	0.30721539	0.31563018	0.10564735	0.17228083	0.24874233	0.24854459	0.28460983	0.31103168	0.36955219	0.19195022	0.09980531	0.34108868	0.20726354
Acetylglycine	1.4991894	1.2571867	1.4613053	1.3676502	0.8618283	0.8963021	1.3151055	1.5117083	1.2874666	1.2558855	2.0225116	2.1556291	0.3764896	0.1361418	0.9900842	0.7101797	0.3881535	0.8370687	0.1611271	0.3595276	0.5242699	0.2188906	0.2776544	1.1418755
Adenosine	0.2140969	0.2102831	0.2204731	0.2183226	0.1923837	0.1817932	0.2516306	0.3133118	0.3362446	0.5335153	0.2711058	0.2710070	0.1909757	0.1598037	0.3264152	0.1133139	0.9777930	0.2111847	0.2169560	1.1616375	0.2937814	0.2245176	0.2665889	0.2164441
Adenosyl-L-homocysteine	0.6714422	0.4308204	1.5075238	1.2276340	1.5873233	1.2629599	1.1093691	2.1367804	1.2361365	2.0044919	0.7645900	0.3509771	0.7865940	0.3838238	0.4334325	0.8561266	0.8834433	0.3909437	0.7933884	1.1344111	1.2445698	0.8234503	0.2881118	0.3432706
Alanine	0.8039607	0.7589530	1.5213952	0.7050528	2.4600018	1.6993623	0.7328026	0.5635759	0.9061994	1.0124162	0.8918277	1.1135432	0.6239487	1.1980224	0.4809799	0.8274591	1.5761646	1.5665982	1.4870625	0.8288178	2.1276307	0.8214103	1.1012487	0.6655912
Allopurinol	0.03371837	0.03982831	0.07967565	0.09631134	0.29066584	0.43212536	0.10127359	0.13557639	0.15064015	0.43628029	0.07268631	0.04541401	0.18894061	0.15836448	0.86294382	0.35844435	0.26588665	0.01586960	0.21502325	0.77772557	0.23225748	0.19562593	0.24672431	0.21442101
Asparagine	0.4449370	0.4373391	0.4302286	0.4423950	0.4736336	0.8986803	0.4141668	0.4037197	0.4344819	0.4441081	0.4378873	0.4320793	0.3776924	0.3610497	0.3550619	0.3946823	0.3544344	0.7584599	0.4232461	0.4070500	0.6391954	0.5276892	0.8365307	0.6913280
Aspartic.acid	0.4152065	0.4430707	0.5818116	0.5320270	0.7732795	0.5713789	0.3907554	0.5394307	0.3698395	0.6125440	0.4739644	0.9147199	0.6267113	0.6123835	0.5933458	1.0165807	0.6299843	0.7023535	0.7167973	0.5597980	0.7913604	0.5099731	0.8173880	0.5713535
Betaine	0.7234086	0.7048656	0.6882660	0.7301375	1.0328520	1.0547873	0.8330171	0.7567204	0.8401010	1.0007066	0.7405565	0.6415822	0.4648153	0.6546769	0.6748845	0.7449814	0.5910158	0.7913117	0.6501385	0.9196811	0.5226326	0.4670694	0.8190514	1.0041040
Carnitine	1.0364532	0.9510847	0.6900549	0.7823069	0.8722678	1.4882140	1.0155252	1.0430504	0.7671293	1.1915917	0.9239250	0.6549932	1.2215885	1.1295841	1.0461135	1.1959042	1.1850933	1.0845366	1.4431300	1.6938279	1.3330664	1.1024471	1.5497510	1.0555476
Creatinine	2.0182532	3.1826911	0.6806979	1.3364505	1.0357324	1.0650838	0.9285776	1.0191995	2.2516750	1.1956444	1.5971185	0.8120371	1.4682139	1.1740891	1.8848313	1.5277349	0.4602601	1.4305611	1.3358876	1.8145411	1.3705444	1.2221740	1.0911130	1.7973037
Cystathionine	0.28309420	0.22951454	0.19001737	0.36697649	0.24784214	0.79328559	0.51016562	0.33012475	0.19901532	0.36555136	0.24005707	0.43611053	0.11324349	0.25762183	0.16868932	0.20845813	0.14641402	0.22658746	0.15482380	0.16571156	0.18506241	0.09193353	0.33018113	0.17725964
Cystine	0.2811702	0.2796157	0.2622289	0.4158454	0.2951822	0.4626571	0.2329457	0.4313985	0.3481685	0.7131780	0.1786220	0.1504858	0.4354672	0.3925378	0.7481704	1.2502132	0.5341248	0.2328273	0.3078212	1.0104342	0.6121067	0.7567378	1.1014113	0.2250691
Cytidine	0.5210576	0.5032761	0.5765483	0.5981420	0.6814616	0.8751241	0.6748009	0.6019237	0.5428900	0.7095091	0.5425272	0.7119897	0.4274866	0.2924270	0.6648767	0.5449437	0.3117971	0.5249493	0.3719328	0.5661403	0.4281487	0.2193708	0.5383064	0.6722130
Cytosine	0.5724007	0.5687503	0.6540320	0.6572037	0.7955865	0.9571722	0.7971547	0.6449386	0.5586945	0.6774215	0.6049335	0.7243051	0.4699204	0.2732985	0.7717965	0.5282462	0.3810730	0.6414866	0.4522232	0.6106754	0.4545835	0.1679954	0.4922570	0.7779320
Decanoylcarnitine	1.03977434	0.99283216	0.43905377	1.23286038	0.21996057	1.66219197	1.14613326	1.16848327	0.86426812	0.72083633	1.21367682	0.93209662	0.40954643	0.77981803	2.03456776	0.62146441	1.09213349	2.43900461	0.36883592	1.46662126	0.38505780	0.09040753	0.38388122	1.57232054
Glutamic.acid	0.5190196	0.5011747	0.4923732	0.4956872	0.6323800	0.5782931	0.3782653	0.4835876	0.3689661	0.6442815	0.4484648	0.6992172	0.6507610	0.4443386	0.6106565	0.6727734	0.4415760	0.6311273	0.4996465	0.5072568	0.5993526	0.4951351	0.6628929	0.6303698
Glutathione.oxidized	0.05294285	0.07759938	0.29613676	0.37270704	1.55391661	0.73383892	0.28143294	0.37137794	0.38844261	0.74461270	0.14097362	0.19893314	0.53946391	0.77446884	0.80577163	2.06643648	0.20456022	0.49325699	1.32663578	0.77536742	0.29639357	0.38259976	0.67550784	0.48181953
Glutathione.reduced	1.1026759	0.8923498	1.1151582	0.5953181	1.6980991	0.6901809	0.7222110	1.1313823	0.7949924	1.5343012	0.7254251	0.4263253	0.1457852	0.1639876	0.3207433	0.3435307	0.5711687	0.6251995	0.2651110	0.2859727	0.5322789	0.5886255	0.2908863	0.3738287
Glycine	0.7725024	0.9251390	0.8940421	0.7024416	0.9043963	1.0035431	0.8484915	0.9572646	0.8936362	0.7776883	1.1724503	0.9329527	0.3696696	0.4106501	0.5924033	0.5879735	0.5078564	0.7956602	0.4571842	0.5517679	0.7122945	0.4886854	0.6821170	0.7807791
Glycocyamine	0.8074463	0.3146842	0.4313919	0.7983406	0.7402149	0.9057195	0.2322731	0.3787078	0.4721578	0.9536144	0.6623463	0.1779486	0.3463183	0.2636901	0.4921304	0.4061054	0.6702330	1.0676197	0.2848171	0.6642394	0.7265750	0.6081363	0.6230967	1.7139250
Guanine	0.02532942	0.05454220	0.44570051	0.44655817	0.75594909	0.43156865	0.31297704	0.65911714	0.11930541	0.99610076	0.14866761	0.15196284	0.03857490	0.02812718	0.64312146	0.13858959	0.30982399	0.00000000	0.08996413	0.61969980	0.04445479	0.10089361	0.11101912	0.10465782
Guanosine	0.041368434	0.027223213	0.439538214	0.393871216	0.755126475	0.359767631	0.387946879	0.525422776	0.131452859	0.908707699	0.114507263	0.107079476	0.038413887	0.043984439	0.470480486	0.110833692	0.298855593	0.005636157	0.076048250	0.663438323	0.119137456	0.048801513	0.090631906	0.058864363
HIAA	0.4614215	0.4563886	0.5361250	0.6674289	0.5526476	0.7528907	0.6618530	0.8154046	0.3770931	0.5050472	0.8687341	1.0162924	0.5355136	0.4474822	0.5572884	0.7506275	0.2775017	0.3348267	0.5920746	0.4323071	0.8289809	0.4134172	0.6647502	0.4651709
Homoserine	0.6983023	0.7018378	0.7149072	0.7242009	0.6649812	0.8189758	0.7640266	0.6782549	0.5256616	0.7163832	0.6410018	0.4788504	0.4438158	0.5528304	0.3849193	0.6326310	0.6478078	0.3654759	0.5773910	0.6299180	0.7322205	0.5901563	0.8331537	0.3790520
Hydroxyproline	0.7868130	0.7673889	0.6748305	0.6843264	0.9174251	1.2313570	0.7636354	0.8520473	0.7546107	0.9010612	0.7151542	0.6026010	0.5303085	0.4746016	0.5074172	0.6101571	0.6367897	0.4844010	0.6824918	0.7603418	0.7412404	0.5531942	0.6457549	0.5127148
Hypoxanthine	0.03108008	0.03295078	0.07230745	0.10605112	0.24210361	0.46310881	0.10167784	0.14625749	0.16616489	0.51041860	0.06533173	0.04225448	0.24245563	0.13432216	0.87837180	0.36355552	0.25734567	0.01519113	0.21277908	0.74516568	0.21031964	0.20654750	0.27581957	0.22056332
Inosine	0.02600116	0.02615317	0.07605084	0.07720853	0.24970896	0.38404333	0.09108355	0.12666396	0.13240581	0.36308907	0.06973492	0.04524077	0.16349696	0.16517816	0.90361214	0.37945644	0.29174887	0.01648628	0.22917311	0.71077105	0.24821758	0.17251436	0.22439895	0.20742862
Isoleucine	0.7734905	0.7720793	0.6809624	0.7169639	0.9427465	1.2809432	0.7698176	0.8840363	0.7578946	0.9174449	0.6951529	0.5988584	0.5521642	0.4869889	0.5300929	0.6111975	0.6246363	0.4812083	0.6819774	0.7716538	0.7384486	0.5738182	0.6861106	0.5234358
L-Alloisoleucine	0.7816351	0.7675873	0.6931879	0.7254023	0.9586529	1.2948073	0.7777563	0.8893020	0.7541538	0.9230311	0.6862217	0.5978543	0.5540295	0.4943954	0.5348676	0.6202152	0.6324164	0.4872354	0.6973422	0.7748112	0.7349445	0.5754398	0.6966434	0.5213951
Leucine	0.7762630	0.7700904	0.6859590	0.7049883	0.9531758	1.2854569	0.7691488	0.8836390	0.7621739	0.9174278	0.7043351	0.6034554	0.5525940	0.4889069	0.5287984	0.6207396	0.6323462	0.4784675	0.6888833	0.7697485	0.7440186	0.5678910	0.6857679	0.5269246
Methionine	0.4595065	0.4579772	0.4746533	0.4885255	0.4920350	0.6604720	0.4462489	0.4727000	0.4003232	0.4848580	0.4535979	0.4214641	0.3289654	0.4052902	0.3049758	0.4320432	0.4224938	0.3929081	0.5814995	0.4638038	0.7436927	0.5635675	0.7926240	0.3739858
Methylguanidine	0.6083126	0.5991099	0.7510126	0.7478605	0.6616402	0.7147471	0.7355709	0.7186135	0.5271701	0.7047024	0.6328199	0.3575302	0.4456060	0.4159211	0.3919142	0.5690907	0.6021682	0.2794409	0.6075165	0.5859735	0.8534668	0.5224783	0.8782036	0.3948659
N,N'-Dicyclohexylurea	0.4491116	0.7786632	1.0568974	0.8605733	0.3151338	0.2683889	0.8111300	0.8860459	0.9300668	0.6072164	0.7132078	0.7497717	0.5024905	0.3967395	0.3895438	0.4417970	0.4784667	0.7943685	0.4818193	0.5755309	0.3671177	0.5808789	0.8349089	1.5812582
N-Acetylethanolamine	0.1837007	0.3351524	0.1712734	0.1999842	0.1839945	0.3390010	0.3605331	0.4625985	0.1857110	0.2160144	0.1688903	0.1901620	0.1246755	0.1620703	0.3036458	0.2729194	0.3908199	0.4101847	0.3189875	0.2665719	0.3897250	0.1503872	0.4816167	0.3320829
N-Acetylneuraminic.acid	0.06720457	0.11616575	0.06952991	0.06068203	0.14038777	0.16392413	0.06753194	0.15396054	0.07783408	0.20979568	0.16580744	0.18465772	0.09179428	0.11928544	0.17453190	0.10237460	0.08390267	0.17293004	0.09089243	0.13104024	0.08846533	0.08536574	0.14463525	0.10738479
Nicotinamide	1.1086306	1.0155569	0.9927073	1.0139620	1.7020512	2.0952281	1.2648053	1.1001351	1.0931990	2.0225090	1.1455333	1.2253957	0.8691954	0.8242333	1.0545029	1.3757596	0.9047593	0.6271669	1.1229611	1.3799018	0.8479625	0.6773855	1.0690791	0.7598487
Norleucine	0.7688610	0.7655194	0.6721997	0.7120115	0.9469902	1.2760697	0.7667306	0.8749643	0.7609668	0.9137877	0.6953367	0.5920285	0.5545982	0.4870829	0.5265577	0.6099556	0.6318839	0.4853943	0.6818889	0.7537906	0.7431439	0.5691091	0.6839599	0.5239574
Normetanephrine	0.4602634	0.7922858	1.0278972	1.1844420	1.1925011	1.0998287	1.4460477	1.2505234	0.8085146	0.8390345	0.7908881	0.6272976	0.7473370	0.6527553	0.9018705	0.9717988	1.1085613	0.6866956	1.8133871	0.7053081	1.5459995	0.7414323	0.8043796	0.5152777
Norvaline	0.7456426	0.7479910	0.6948016	0.6796876	0.8187685	1.0167348	0.7761884	0.8805773	0.7022088	0.7862304	0.7152055	0.6146859	0.4932867	0.5133007	0.4637410	0.6137076	0.6419375	0.4975852	0.6883464	0.7023230	0.8132069	0.6068848	0.6269995	0.4917820
Phenylalanine	0.6926250	0.7008467	0.6459153	0.6778132	0.8648654	1.2378989	0.6956844	0.8330104	0.7424098	0.8759900	0.6224442	0.5904636	0.5133810	0.4601704	0.5379103	0.5883836	0.5392128	0.6769541	0.6840378	0.7221243	0.7056662	0.5232141	0.7153008	0.6231087
Proline	0.2536354	0.2665351	0.2729979	0.2910349	0.3455349	0.5739777	0.2744232	0.3060478	0.2541320	0.3370148	0.2492915	0.2561445	0.1759309	0.2077588	0.2071730	0.2544563	0.2057017	0.2743556	0.2967707	0.3282657	0.4057957	0.2971243	0.5417059	0.3029315
Sarcosine	0.7972464	0.6285018	1.1937639	0.6966922	2.1649467	1.8733796	0.6445680	0.5183578	0.7599217	0.8395287	0.5969229	1.3593589	0.5837919	1.1513682	0.4793732	0.7341413	1.3038976	1.6908640	1.6649814	0.7639477	2.0942908	0.5273449	0.8220729	0.6044479
Serine	0.5353581	0.5267698	0.4793458	0.4622670	0.5259625	0.7771565	0.5041540	0.4785595	0.4262779	0.5054402	0.5073924	0.4689129	0.3561538	0.3706829	0.4047429	0.4597577	0.4136697	0.5811335	0.4466357	0.4885491	0.5757121	0.4545363	0.7522944	0.5896785
TMAO	0.85451078	0.65696505	1.21903340	0.39266798	1.48554668	0.47086960	0.40870485	0.92978038	0.64500025	1.40691014	0.49913503	0.04325557	0.00000000	0.33761085	0.18429464	0.25384521	0.63396713	0.61949213	0.26769308	0.25273734	0.31276815	0.33318616	0.14893635	0.28665877
Threonine	0.7150959	0.7015677	0.7629955	0.7761223	0.6462053	0.8520302	0.7351514	0.6963445	0.5208669	0.7185048	0.6479620	0.4750623	0.4655190	0.5523690	0.3989872	0.6481275	0.5915996	0.3782476	0.5667950	0.6336898	0.7189485	0.6165406	0.9114231	0.3670283
Tyrosine	0.6030869	0.6125875	0.7887788	0.8232557	1.0062731	1.2490204	0.6071225	0.8777774	0.6561377	0.8893080	0.6613815	0.6228148	0.3730047	0.3463561	0.4792403	0.4594995	0.3938609	0.5973173	0.5438654	0.5633916	0.6423756	0.4651992	0.6423144	0.4970374
UDP-GlcNAc	0.000000000	0.000000000	0.000000000	0.004592017	0.193086076	0.040915595	0.004539314	0.145934213	0.178034558	0.116639623	0.000000000	0.070587210	0.149759237	0.000000000	0.055340246	0.339265912	0.000000000	0.018765855	0.038192797	0.065482356	0.000000000	0.000000000	0.070706147	0.000000000
Uracil	0.8457426	0.8495759	1.0951227	1.2036762	2.6855035	3.3864430	1.5948670	1.2708232	1.4810583	2.7345165	0.0000000	0.5702306	1.3042441	0.5982922	1.2443398	0.8348638	0.7037339	0.5697256	0.7155200	1.7113136	0.5957357	0.4716715	0.6942587	0.6309362
Uridine	0.8880025	0.8636672	0.9870649	1.0857023	2.5189912	3.0324660	1.5176027	1.2631859	1.6074507	2.5373434	1.0135393	0.6157471	1.2844979	0.6318885	1.2363457	0.8629738	0.7619592	0.5965804	0.7071004	1.7040465	0.6145321	0.4385381	0.6160858	0.6436844
Urocanic.acid	0.03376918	0.04254745	0.05724673	0.04831958	0.04635670	0.04936237	0.03685679	0.04165554	0.04238366	0.03293443	0.03548771	0.04557768	0.01823145	0.01534968	0.01744506	0.01649835	0.01764671	0.02310776	0.02532258	0.01928040	0.04746682	0.02773702	0.03005870	0.02772801
Valine	0.7459956	0.7503615	0.7026255	0.7024037	0.8202731	1.0275209	0.7588466	0.8909467	0.7097040	0.7982574	0.7008425	0.6146873	0.5054868	0.5030490	0.4737987	0.6111390	0.6462739	0.5020537	0.6864407	0.6854861	0.8229823	0.6217540	0.6254272	0.4997380
Xanthosine	0.4577110	0.4849641	0.6241970	0.6766769	4.2558855	7.7630219	1.5764167	1.0264283	4.2477904	7.8442639	1.0624214	0.1908877	0.8124879	0.1524969	1.8590245	0.6193012	0.4041642	0.1813820	0.2700349	2.3332162	0.1061311	0.1309162	0.1285644	0.3067931
methyl-a-D-galactopyranoside	1.3477293	0.9038175	0.7205699	0.5291660	1.0640751	1.5175823	0.9536713	0.7824787	1.0652578	0.6404905	1.0459692	1.1463473	0.6403432	0.7595554	1.0700229	0.9111508	0.7905356	0.9514611	0.9061882	1.0269884	1.2904433	0.9006732	1.4165315	0.9374045
3-Indoxylsulfate	0.0039742006	0.0023391308	0.0353740607	0.0016464954	0.0022620914	0.0031716151	0.0032944106	0.0030293134	0.0014770960	0.0010762186	0.0009190207	0.0016898664	1.6172315346	2.2955004825	3.8331504617	1.8889801044	2.9435636983	1.0289100428	1.5241429637	4.5331715267	1.5340171634	1.4178092065	2.0482161824	0.6584347506
2,3-Dihydroxybenzoic.acid	0.48998087	0.45925943	0.20171275	0.11165078	0.40996557	0.48016548	0.38672610	0.54687554	0.11396917	0.11675343	0.11986621	0.07671945	1.24635923	1.42578176	1.18469069	2.02295701	1.50349511	2.05013084	1.32332791	1.94655749	1.59277083	1.10832205	1.72193673	1.59378286
2-Hydroxybenzoic.acid	0.7965871	0.7728044	0.3218101	0.2447120	0.6136844	0.3744148	0.4319101	0.7563006	0.3510303	0.2609883	0.2320656	0.3058933	2.2558602	2.5915402	1.5055872	4.0838144	2.3711602	1.4305851	2.8694710	3.5659023	3.3476204	3.0332858	3.9963234	1.7222825
2-Hydroxyphenylacetic.acid	0.8336771	0.7515347	0.6511527	0.4969051	0.6434132	0.9558337	0.8266350	0.8324308	0.3614684	0.4623572	0.5138190	0.3820153	1.1250300	0.9010148	1.0660509	0.6361450	0.8173596	0.5060616	0.6922646	1.0914150	0.6260436	0.7397448	1.0785493	0.3409159
2-Methylbutyric.acid	0.9162436	0.7647800	0.8114202	0.6791095	0.5724590	0.7517002	0.3763115	1.2930302	0.9617106	0.9124321	0.8012958	0.5613845	0.4573325	0.4679710	0.4829717	0.7781003	0.8911581	0.3806420	0.3924137	0.6863296	0.4486746	0.7857104	0.3367745	0.6051235
3-Hydroxyphenylacetic.acid	0.6300611	0.8019803	0.4395543	0.3531513	0.5712445	0.7262196	0.5517035	0.7293511	0.4730190	0.6674977	0.4150897	0.2773652	0.9234166	0.9577731	1.4031874	0.7612582	0.9709512	0.7315022	1.3207369	1.7982472	1.0991215	0.8245665	1.2208213	0.7844164
3-Indoleacrylic.acid	0.06863647	0.07993838	0.29599954	0.01919182	0.00000000	0.13184064	0.03164545	0.14464441	0.09467593	0.11117823	0.01868143	0.01239224	0.92060183	0.61627943	0.93140097	0.66541385	0.56434471	1.32301774	1.42618439	1.99700779	0.37785536	0.20324056	0.60686634	1.64759696
3-Methyl-2-oxovaleric.acid	0.7284818	0.7998605	0.8214719	0.7937070	0.4602629	0.6143488	0.5652290	0.8385703	0.5941437	0.4562508	0.6723339	0.7837716	0.3804015	0.3810327	0.5773716	0.7591478	0.7364682	0.4953530	0.4704629	0.6691918	0.4352169	0.4875276	0.4163757	0.3738398
3-Phenyllactic.acid	0.1588272	0.1628897	0.1481714	0.2012786	0.1907786	0.3345011	0.1358782	0.2337874	0.1476731	0.1240542	0.1009023	0.1153669	0.3804044	0.5534323	0.1483201	0.6223141	0.3725672	0.1412559	0.6140716	0.9084644	0.3132405	0.3880331	0.2251292	0.3031758
4-Hydroxybenzaldehyde	0.2899898	0.4539353	0.2719443	0.1845166	0.4342202	0.1635672	0.3338587	0.3637891	0.3575433	0.3653502	0.3196463	0.1567934	0.1617343	0.6138772	0.2441290	0.4573647	0.5656350	0.4557670	0.6785351	0.7462931	1.9606845	1.3874968	0.6191694	0.2239879
4-Hydroxybenzoic.acid	0.7415720	0.6427323	0.3418409	0.2771368	0.5039981	0.4729974	0.4056269	0.8144809	0.2511309	0.2701269	0.2969636	0.2283418	2.4564177	2.5600532	1.7188250	3.7086417	2.5128617	1.5046030	3.0486985	3.3705885	3.2851761	3.2291628	4.4785681	1.5404096
4-Hydroxyphenylacetic.acid	1.0741901	0.9484975	0.6531368	0.4162101	0.6926568	0.7114619	0.7534805	0.7216074	0.8789581	0.6506508	0.8736327	0.2907721	1.0987438	0.8528024	0.9308913	1.0528581	0.7804062	0.4420478	0.9035063	1.3928209	0.8826471	0.8112688	1.0836423	0.7085074
4-Hydroxyphenylpyruvic.acid	1.14921842	0.98845607	1.98099909	1.72171599	1.23177289	1.72876545	0.83944057	2.56334937	1.38221909	0.52593743	1.12397307	1.22757429	0.24319700	0.39547674	0.44914055	0.12458038	0.68509201	0.18949878	0.47693233	0.48118769	2.00381191	1.66541921	0.79929192	0.08403531
4-Methyl-2-oxopentanoic.acid	0.5350964	0.7260103	0.8990688	0.8404178	0.5670097	0.4391739	0.5110427	0.6475787	0.4532219	0.3383676	0.7675285	0.6123645	0.4158343	0.4958764	0.5988977	0.8790783	0.7914478	0.4360865	0.6702444	0.6582298	0.4875331	0.4562112	0.4409016	0.5753140
4-Methylvaleric.acid	1.2193120	1.1373415	1.2803601	1.2649514	0.7155701	1.2545237	1.0279050	1.3477962	1.2666246	0.6921735	1.1916585	0.9646052	0.5288983	0.4787545	0.5958022	0.8224816	0.8099802	0.6323150	0.5876209	0.7061165	0.6493778	0.6388923	0.6152713	0.6383928
Acetyl-L-tyrosine	1.3823909	1.5654071	2.4631201	1.8466601	2.5207747	1.8986028	1.1913219	2.1991471	1.1217505	1.2484589	1.8941245	1.1053379	0.7384137	0.6968520	1.0445795	0.9093524	0.7819208	3.3148925	1.3974540	0.6655445	2.4891795	1.5615589	1.2013689	1.0886114
Allantoin	0.4179758	0.3920830	0.4618506	0.5288154	0.4099781	0.9940990	0.5244163	0.5888625	0.3894575	0.4465263	0.4335474	0.5277082	0.3798188	0.4607883	0.4766550	0.5942443	0.5207472	0.4367983	0.6263660	0.3932992	0.6471256	0.5786775	0.7884335	0.3839070

Table S2B. Serum metabolites

Benzoic.acid	0.5137459	0.8011919	0.8700612	0.7071747	0.7833871	0.5132784	0.9021533	1.0397754	0.6048753	0.4560824	0.7378836	0.9754978	1.1409319	1.1780068	0.7153125	1.3047273	0.8824771	0.6084236	1.1787358	0.6067928	1.2885574	0.9537052	0.9203954	0.6804284
Citraconic.acid	1.1832005	0.8655313	0.8829787	0.9384341	0.7149742	0.9088399	0.8197862	0.9260997	0.7828447	0.6176995	0.8662048	1.0564296	0.6012591	0.5014137	0.6816109	0.8420866	0.9668129	0.6730451	0.7962384	1.0701069	0.6463906	0.4847092	0.6272626	0.4146637
F6P	0.6148911	0.6397381	0.4180315	0.4791333	0.8018948	1.0489481	0.5600311	0.4700166	0.5596413	0.7723185	0.5416507	0.8945571	1.3691818	0.9980324	0.7388595	2.4056484	0.4272504	1.0292442	1.8827413	1.0846360	1.0310069	0.7883688	1.5219983	1.0737757
G6P	0.5960554	0.6725720	0.5424209	0.4639696	0.7149186	1.0277904	0.6028397	0.4610059	0.5065798	0.6587487	0.6167404	0.6808418	1.2350843	1.1748242	0.8482595	2.0001126	0.6219998	1.0504048	1.8062061	1.1607852	0.8258928	0.6993957	1.1175112	1.3118745
Gentisic.acid	0.5139415	0.4151858	0.1699240	0.1634507	0.4950193	0.5381677	0.4975664	0.4815131	0.1646657	0.1868625	0.1272859	0.1044369	1.2590846	1.5629216	1.2770249	2.0023922	1.5103748	1.8111364	1.2449566	2.1445328	1.5509669	1.2755833	1.7910363	1.3444712
Glucuronic.acid	0.2943072	0.3285132	0.3076357	0.3028917	0.4062023	0.3879114	0.3706921	0.4386659	0.3901433	0.3952716	0.3387479	0.4035722	0.3447072	0.3041804	0.3525938	0.3387238	0.4254461	0.2811051	0.3409680	0.3958022	0.2665106	0.3763200	0.4654544	0.4758465
Glutaconic.acid	0.8936806	0.7301086	0.9696221	0.8526519	0.5442453	0.5880147	0.5992676	0.9477549	0.6377112	0.4061179	0.7163246	0.8437270	0.5472146	0.4245548	0.7144656	0.9034756	0.8900980	0.5316449	0.6503364	0.7681063	0.4747078	0.4802786	0.3834784	0.3985794
Isobutyric.acid	1.2611450	1.0617315	1.2009763	1.0144702	1.6725007	1.3712387	0.9813562	1.1676435	1.0259964	1.1891182	1.1904247	1.0942924	1.5989614	1.4913369	1.5619882	2.1045380	1.2262023	2.0379971	1.5637909	1.3742913	1.7912535	2.4635205	2.4077597	0.8333862
Isocitrate	0.9363562	0.9694145	1.8275446	1.6172730	1.9900427	5.4531547	0.8358172	2.2995017	0.9928619	1.4021071	1.0910185	1.6178133	0.6324479	0.5417913	1.1534480	1.0034652	0.4038732	1.0685027	0.8624940	1.8233722	0.7640728	0.5662017	1.4586538	1.0827235
Isovaleric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
Ketoisoleucine	0.6320128	0.6428483	0.8286818	0.8677048	0.5299760	0.6119989	0.6528786	0.9677705	0.5359146	0.4973663	0.6318207	0.7465316	0.4568074	0.5057830	0.6968982	0.8765001	0.8146209	0.5613216	0.6569281	0.7444931	0.5323563	0.4600245	0.4162702	0.4342382
Ketoleucine	0.7407093	0.6770491	0.8666374	0.8526344	0.4862419	0.6715415	0.6274490	0.9300686	0.5821689	0.4755816	0.6434545	0.7973945	0.4390582	0.4554591	0.6420511	0.8235266	0.8422553	0.5404413	0.5446198	0.7969653	0.5417458	0.5267113	0.3870948	0.4680990
Leucic.acid	0.07332520	0.05691064	0.16240462	0.13844880	0.00000000	0.13192383	0.18425088	0.09091516	0.09485068	0.09601863	0.12344032	0.07552676	0.07950051	0.18992066	0.18504689	0.23065715	0.09115326	0.08444802	0.03149924	0.39720394	0.12766977	0.17789873	0.05538901	0.09050159
Levulinic.acid	0.8733528	0.7773803	1.1885660	0.9115188	0.7639572	0.6718761	0.8896795	1.1401628	0.7158665	0.5367945	0.7854932	1.2883168	0.3414807	0.3001495	0.3850537	0.3747144	0.5945561	0.5645422	0.3800352	0.4273772	0.8644449	0.6055051	0.5948493	0.3990532
Mannose	0.6683804	0.7490577	0.9983012	0.8180795	1.3001285	1.6448997	1.1464313	1.2114073	0.8301304	1.2382297	0.8439367	0.8125773	0.6266621	0.8626987	0.8407750	0.8446483	0.6687708	0.4966768	0.7226429	1.1309506	1.0346696	0.5709434	0.9154449	0.4778395
Mucic.acid	1.4449558	1.5175796	1.7136174	1.7628124	2.9718829	3.5026565	2.1747000	2.7953622	1.7672312	2.1885316	1.4510821	1.0805201	0.9881322	0.4407361	0.5894630	0.4070065	1.0587811	0.3780752	1.0418203	0.6686453	1.6099692	1.3606473	1.4986516	0.2406813
Myoinositol	0.9158956	1.0903492	1.0132274	0.7188772	1.0656828	1.1381421	1.0394161	1.4046805	0.7925365	1.0714162	0.8230511	1.0257722	0.9557425	0.9178068	1.1749202	0.9482438	0.8227359	0.9848646	0.8354734	1.0013812	1.1290946	0.6984916	0.7774978	0.6192854
Nonadecanoic.acid	0.7597794	1.0984831	1.0566841	0.6869035	0.7567158	0.6152611	1.1422799	0.7788149	0.9910287	0.5742253	0.6355600	0.7711078	0.6560131	0.6744979	0.6686692	0.4608864	0.5979236	0.7173817	0.5101773	0.4252656	0.8019144	0.5360187	0.6069391	0.7542067
Palmitic.acid	1.1697404	1.1289978	1.0746644	1.0579965	1.0081349	1.0744314	1.1476871	1.1941974	0.8681928	1.2085481	0.9326418	1.0318683	0.8677152	0.6149741	1.0140553	0.7505703	0.9214058	0.8712176	0.6402457	0.9742409	0.8439879	0.7187422	0.7523927	0.6433307
Pentadecanoic.acid	1.0416191	1.0968575	1.2484225	1.3574081	1.1434541	1.0799144	1.1658474	1.1948132	1.3305186	1.2054729	1.2713009	1.5459406	0.8983497	0.5198255	0.6073550	0.4853418	0.5751780	1.0182041	0.5896763	0.4666398	0.7345063	0.5951775	0.7111444	1.3217963
Phenylglyoxylic.acid	0.6505425	0.7622024	0.4309066	0.4541979	0.2762495	0.7508618	0.5632261	0.6586299	0.5866884	0.5445800	0.4662587	0.1722703	0.7744946	0.6864339	0.7886320	1.3051016	0.5019615	0.4552686	0.6690830	1.0880316	0.3913430	0.4653460	0.7296399	0.4115943
Phenylpyruvic.acid	1.6837193	1.1946551	1.2117800	1.4134552	1.2954706	2.1709991	1.1442532	2.6172624	1.0717084	1.3957800	1.0979073	1.1359335	1.1605814	1.1434987	1.1531757	0.9821010	1.4858917	0.9080724	1.9169820	1.1176169	2.5614484	2.4989341	1.3980044	0.5780909
Phthalic.acid	0.8312283	1.6718001	1.6295232	0.6950160	0.9813302	0.7106078	1.0632694	0.8647620	0.8410628	0.7436008	0.7956362	1.1354350	0.8725004	0.8293501	1.0938052	0.5822359	1.4563201	0.5690216	0.9613559	0.6940954	1.4272887	0.7233408	0.5024063	0.4871232
Pregnenolone.sulfate	0.15109681	0.06450606	0.07824688	0.11139556	0.16581628	0.10776864	0.25053390	0.01274011	0.18073139	0.11896680	0.04564024	0.04885158	0.01195747	0.02402525	0.01011219	0.17572145	0.13117700	0.39292133	0.39154295	0.10137071	0.05705211	0.00000000	0.16982081	0.79087325
Sorbitol	0.5263006	1.1125334	0.8735987	1.0204774	1.8649705	2.9610703	1.1785228	1.5158011	2.0153651	1.8722321	1.1390051	0.8823096	1.0456780	0.9890519	1.3129599	1.0471344	0.9181730	0.6389121	0.9514893	1.4349702	0.5031007	0.5956122	1.2551092	1.2870245
Stearic.acid	1.0184713	1.0750990	1.2224773	1.0051354	0.9065094	0.7811735	1.1789520	0.8386794	0.7374513	0.8942426	0.7940715	1.0533583	0.9066691	0.8976884	0.9911621	0.7727796	1.1123866	0.8484215	0.7059182	0.8682556	1.0533575	0.7744590	0.7948777	0.6558604
Suberic.acid	0.6717550	0.7711379	1.0687371	1.0001316	1.0048246	0.9080725	0.9082036	1.1276302	0.8134137	0.8582683	0.7563850	0.8792998	0.7326972	0.6036770	0.8775342	0.9730880	0.7433058	0.9116463	0.9155839	0.7838742	0.8153078	0.6814005	0.7289064	0.8155878
Valeric.acid	0.8703589	0.9404384	0.7334958	0.6955710	0.3452065	0.6477333	0.2803587	0.8845414	0.4816621	0.5179478	0.7071104	0.5326932	0.5218911	0.4431907	0.5254116	0.8564636	1.0983867	0.3690062	0.4726979	0.5599881	0.4818807	0.6349104	0.4954288	0.4364075
X5P	0.5027232	0.5146277	0.3386513	0.4047086	0.8736686	0.7205287	0.3494380	0.3850901	0.2681374	1.0155902	0.3328307	0.5785047	2.9203121	2.3234867	2.2986260	4.6446462	1.7533107	2.0129461	3.7469756	2.2407628	2.3747651	1.7961056	2.2261729	2.3189625
alpha-Hydroxyisovaleric.acid	0.2371994	0.2527587	0.3991637	0.3119418	0.2179633	0.4664979	0.3021191	0.2406591	0.1822040	0.2528320	0.4813419	0.2408560	0.1477089	0.1300373	0.2515798	0.1820547	0.2035981	0.1894338	0.3520112	0.1956317	0.1405861	0.1275436	0.3147498	0.1255165
alpha-ketoisovaleric.acid	1.1483537	0.9211920	1.0424223	1.1143107	0.6507956	0.7640291	0.9224072	1.3979542	0.8386406	0.5159111	1.0674584	1.1048148	0.5318858	0.4081003	0.6895266	0.8388138	0.6593168	0.4917263	0.4880581	0.7309270	0.7401869	0.6986751	0.6619629	0.5088614
p-Coumaric.acid	0.8884362	2.5429656	0.8671267	0.3814133	0.4828513	0.4830849	0.3138755	1.1793190	1.9050500	0.2601965	1.4171255	0.5975559	0.5928540	0.5256743	0.5782154	0.6462564	0.6272135	0.2994134	0.7650979	0.6735591	1.3843546	0.5536971	4.3952783	2.8617781

Constructed from biom file

#OTU ID	CO.1	CO.2	CO.3	PCB6.1	PCB6.2	PCB6.3	PCB30.1	PCB30.2	PCB30.3
D_0__Bacteria;D_1__Actinobacteria;D_2__Actinobacteria;D_3__Bifidobacteriales;D_4__Bifidobacteriaceae;D_5__Bifidobacterium;__	0	0	18	0	0	0	0	0	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;Ambiguous_taxa	19	26	15	43	0	0	0	37	0
D_0__Bacteria;D_1__Actinobacteria;D_2__Coriobacteriia;D_3__Coriobacteriales;D_4__Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium	0	0	0	74	122	109	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Barnesiellaceae;D_5__uncultured;D_6__Bacteroides sp. Tilapia9	0	12	0	0	16	0	0	0	0
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	9296	10607	8015	13871	7845	10279	6933	7367	10551
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Muribaculaceae;__;__	8115	8838	9280	5390	6298	5799	7923	10196	7843
D_0__Bacteria;D_1__Bacteroidetes;D_2__Bacteroidia;D_3__Bacteroidales;D_4__Rikenellaceae;D_5__Alistipes;__	2588	2712	2528	1387	2374	1818	3313	2397	2808
D_0__Bacteria;D_1__Cyanobacteria;D_2__Oxyphotobacteria;D_3__Chloroplast;__;__;__	8	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Bacillales;D_4__Bacillaceae;D_5__Bacillus;__	0	0	0	0	0	0	61	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Lactobacillaceae;D_5__Lactobacillus;D_6__Lactobacillus gasseri	329	316	457	795	190	685	1548	189	1114
D_0__Bacteria;D_1__Firmicutes;D_2__Bacilli;D_3__Lactobacillales;D_4__Streptococcaceae;D_5__Lactococcus;__	39	0	30	35	59	37	0	0	40
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiaceae 1;D_5__Clostridium sensu stricto 1;D_6__uncultured bacterium	62	58	55	18	0	0	0	0	254
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;Ambiguous_taxa;Ambiguous_taxa	0	57	0	0	103	0	109	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;D_5__uncultured bacterium;D_6__uncultured bacterium	46	228	28	41	198	39	178	80	188
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Clostridiales vadinBB60 group;__;__	94	120	0	127	141	161	65	180	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Defluviitaleaceae;D_5__Defluviitaleaceae UCG-011;Ambiguous_taxa	131	154	92	70	0	188	0	0	159
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium	0	0	0	55	60	105	106	57	41
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] brachy group;D_6__uncultured bacterium	0	0	0	0	0	7	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured bacterium	0	16	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;D_6__uncultured organism	0	3	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Family XIII;D_5__[Eubacterium] nodatum group;__	67	62	63	0	185	0	94	208	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;D_6__uncultured bacterium	1455	1296	1162	1122	1580	431	1767	1383	1644
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__A2;__	121	91	123	0	17	1803	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium	109	0	162	0	0	0	0	37	64
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;Ambiguous_taxa	303	293	302	0	287	0	278	0	279
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;D_6__uncultured bacterium	0	362	472	585	226	498	237	393	324
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetatifactor;__	0	106	114	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Acetitomaculum;D_6__Firmicutes bacterium CAG_194_44_15	262	245	321	454	304	0	319	241	294
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;D_6__Lachnospiraceae bacterium 609	203	0	320	0	1693	0	0	0	128
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Blautia;__	257	183	319	222	0	250	83	117	206
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium	331	388	366	244	287	206	757	591	869
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens	486	530	520	91	214	151	130	84	161
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;D_6__uncultured bacterium	244	0	512	0	0	572	0	631	636
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnoclostridium;__	905	727	990	1994	843	1142	628	1336	656
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae FCS020 group;__	143	117	105	173	98	92	183	212	147
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;D_6__uncultured bacterium	4489	4932	2051	4199	4272	3122	2789	1700	3057
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae NK4A136 group;__	8765	8865	8624	6923	9399	7884	12717	12190	11786
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa	718	738	571	0	0	0	668	406	1198
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium	466	499	0	0	0	0	858	0	897
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-001;__	1120	848	1065	0	313	0	0	878	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;D_6__uncultured bacterium	112	142	0	1124	150	150	218	226	821
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Lachnospiraceae UCG-006;__	0	0	70	0	0	193	0	287	154
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;Ambiguous_taxa	0	0	0	0	0	36	51	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Marvinbryantia;D_6__uncultured bacterium	297	293	243	425	252	0	106	231	208
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44	0	0	0	0	0	0	74	43	109
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium	474	445	507	945	1516	529	2001	861	1832
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Roseburia;__	0	0	129	0	0	0	27	126	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella 3;D_6__uncultured bacterium	183	31	283	415	0	5	37	703	431
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__Tyzzerella;D_6__uncultured bacterium	57	67	0	72	58	72	84	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;D_6__uncultured bacterium	226	227	201	0	825	0	912	291	295
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__[Eubacterium] xylanophilum group;__	0	0	0	0	0	0	181	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016	0	0	0	159	97	171	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Clone-47	234	331	135	0	112	195	68	73	541

D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture Jar-19	0	0	0	93	0	0	0	0	94
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-27	0	0	164	0	118	0	125	0	72
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__Clostridium sp. Culture-54	0	0	0	0	0	71	50	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;D_6__uncultured bacterium	3274	2630	2983	2961	2110	2254	3683	2587	3054
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;D_5__uncultured;__	350	385	616	511	297	410	584	497	381
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Lachnospiraceae;__;__	6804	5724	7057	7593	6563	4562	6732	5530	11105
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptococcaceae;D_5__uncultured;Ambiguous_taxa	89	70	66	64	43	104	88	128	132
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Peptostreptococcaceae;D_5__Romboutsia;__	0	0	0	0	0	0	0	62	84
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium	149	111	197	98	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Anaerotruncus;__	76	0	54	127	88	175	51	0	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__GCA-900066225;__	64	0	95	0	104	0	0	84	81
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Harryflintia;D_6__uncultured bacterium	0	0	0	0	0	0	0	30	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	258	141	349	112	119	391	0	129	155
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;Ambiguous_taxa	227	254	153	0	320	0	0	265	432
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Intestinimonas;D_6__uncultured bacterium	101	0	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium	0	0	0	270	0	58	51	440	164
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;D_6__unidentified	1602	1557	1495	1500	1279	920	524	1258	1403
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Oscillibacter;__	436	440	421	340	213	176	800	266	354
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;Ambiguous_taxa	501	564	356	762	366	492	415	540	394
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 5;D_6__uncultured bacterium	387	58	461	124	290	213	335	405	163
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 6;__	91	104	64	190	562	242	118	235	218
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium	232	220	248	325	308	299	351	238	463
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium 9;__	1161	1127	873	1270	1378	1155	1290	1131	1291
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminiclostridium;D_6__uncultured bacterium	2409	2239	2033	1913	1367	1784	2656	2134	2415
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae NK4A214 group;D_6__uncultured bacterium	0	0	0	0	0	25	0	81	34
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-005;Ambiguous_taxa	0	95	0	164	116	212	35	180	114
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-009;Ambiguous_taxa	454	473	388	283	552	265	684	622	611
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-010;D_6__uncultured organism	77	53	70	79	59	134	59	54	112
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium	94	48	118	158	437	187	502	1052	104
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-013;__	0	0	0	0	0	70	0	0	60
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;D_6__uncultured bacterium	0	32	0	72	183	75	0	72	264
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcaceae UCG-014;__	277	280	352	51	163	136	95	57	731
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__Ruminococcus 1;__	1370	1132	1457	263	1098	139	1583	2721	1531
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__[Eubacterium] coprostanoligenes group;__	401	231	489	14	315	34	134	85	1116
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1	0	0	0	980	816	685	110	176	785
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;D_6__unidentified	120	139	147	108	144	110	421	134	140
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;D_5__uncultured;__	37	22	42	21	0	24	653	394	406
D_0__Bacteria;D_1__Firmicutes;D_2__Clostridia;D_3__Clostridiales;D_4__Ruminococcaceae;__;__	1109	1025	1157	441	580	499	1166	1030	902
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis	556	613	516	135	106	0	0	0	20
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa	0	23	37	200	63	530	55	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__Turicibacter;__	471	277	460	329	133	421	191	149	237
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured bacterium;D_6__uncultured bacterium	0	0	0	39	31	0	0	0	0
D_0__Bacteria;D_1__Firmicutes;D_2__Erysipelotrichia;D_3__Erysipelotrichales;D_4__Erysipelotrichaceae;D_5__uncultured;D_6__uncultured bacterium	0	55	0	0	0	0	0	0	0
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Anaeroplasmatales;D_4__Anaeroplasmataceae;D_5__Anaeroplasma;Ambiguous_taxa	275	338	0	562	1369	786	922	665	625
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;Ambiguous_taxa;Ambiguous_taxa;Ambiguous_taxa	0	0	16	0	0	0	0	0	50
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;D_4__uncultured bacterium;D_5__uncultured bacterium;D_6__uncultured bacterium	138	137	0	100	147	87	44	87	66
D_0__Bacteria;D_1__Tenericutes;D_2__Mollicutes;D_3__Mollicutes RF39;__;__;__	245	479	91	42	203	0	417	216	279
D_0__Bacteria;D_1__Verrucomicrobia;D_2__Verrucomicrobiae;D_3__Verrucomicrobiales;D_4__Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium	0	20	0	2363	1475	7608	0	0	0

#Differentially abundant for PCB6

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
316.7182704	-11.65082862	1.236665352	-9.421165231	0	0	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;Ambiguous_taxa
153.3172368	-10.60410763	3.148390595	-3.368104215	0.0007568698067	0.005710926723	Lachnospiraceae;D_5__Lachnospiraceae UCG-001;D_6__uncultured bacterium
41.03072715	-8.702464375	3.274032281	-2.658026442	0.007859972585	0.04077360779	Lachnospiraceae;D_5__ASF356;D_6__uncultured bacterium
319.3213166	-1.580215074	0.3616598924	-4.369340109	0.00001246225466	0.0001292958921	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
781.7386176	-0.9207800117	0.1196190574	-7.69760297	0	0	Ruminococcaceae;__;__
7200.677116	-0.3902585448	0.08636488756	-4.518717685	0.000006221528614	0.00007376955357	Muribaculaceae;__;__
275.8941433	0.6171854875	0.2015178394	3.062684124	0.002193614783	0.01517250225	Ruminococcaceae;D_5__Ruminiclostridium 9;D_6__uncultured bacterium
754.2569069	1.264658563	0.4337143845	2.915878763	0.003546882969	0.02102794903	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
177.0232909	1.776599012	0.6062650277	2.930399958	0.003385259774	0.02102794903	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
214.5092189	2.099707756	0.5666020505	3.705789194	0.0002107335238	0.001749088248	Ruminococcaceae;D_5__Ruminiclostridium 6;__
149.9534028	3.917624073	1.51816477	2.580499923	0.009865737835	0.04816801414	Erysipelotrichaceae;D_5__Erysipelatoclostridium;Ambiguous_taxa
38.92808467	8.824512079	1.427806771	6.180466614	0.0000000006391241199	0.000000008841216991	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
2019.466775	9.269818825	2.203252554	4.207333747	0.00002584013765	0.0002383034916	Akkermansiaceae;D_5__Akkermansia;D_6__uncultured bacterium
53.84095289	9.292598686	1.328101098	6.996906108	0	0	Eggerthellaceae;D_5__Enterorhabdus;D_6__uncultured bacterium
62.8067954	9.514101089	3.293079828	2.889119482	0.003863222531	0.02137649801	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
76.87108532	9.805534228	1.36829318	7.166252356	0	0	Lachnospiraceae;D_5__uncultured;D_6__Clostridiales bacterium CIEAF 016
447.5479333	12.34718529	1.245794989	9.911089227	0	0	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

#Differentially abundant bacteria for PCB30

baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	taxon
83.46976574	-9.948696447	1.426866799	-6.972407274	0	0.0000000001386455415	Ruminococcaceae;D_5__Anaerotruncus;D_6__uncultured bacterium
61.1174388	-9.499046883	1.511973717	-6.282547625	0.0000000003330691888	0.000000005928631561	Lachnospiraceae;D_5__A2;__
39.30425587	-8.862241275	2.96685731	-2.987080385	0.002816556532	0.01790525224	Lachnospiraceae;D_5__Acetatifactor;__
307.8175697	-6.935230581	1.27412215	-5.443144191	0.00000005234823872	0.0000006655704638	Erysipelotrichaceae;D_5__Dubosiella;D_6__Dubosiella newyorkensis
334.6713868	-2.313158666	0.3287417297	-7.036401093	0	0.0000000001386455415	Lachnospiraceae;D_5__Lachnoclostridium;D_6__[Clostridium] scindens
308.0630698	-1.346206268	0.4204681762	-3.201684084	0.001366267468	0.009353677279	Erysipelotrichaceae;D_5__Turicibacter;__
8798.415146	-0.4334527046	0.1329022528	-3.261439858	0.001108479444	0.008968606407	Muribaculaceae;D_5__uncultured bacterium;D_6__uncultured bacterium
532.8390926	0.7735398016	0.2396538735	3.227737529	0.001247734027	0.009254027366	Lachnospiraceae;D_5__GCA-900066575;D_6__uncultured bacterium
965.8942038	1.446139973	0.3454244671	4.186559179	0.00002832151155	0.0002800682809	Lachnospiraceae;D_5__Roseburia;D_6__uncultured bacterium
332.2258696	2.576372032	0.9118396441	2.825466132	0.004721187874	0.02801238138	Ruminococcaceae;D_5__Ruminococcaceae UCG-013;D_6__uncultured rumen bacterium
246.2103261	3.623458987	0.5613278261	6.455156539	0.0000000001081070969	0.000000002405382905	Ruminococcaceae;D_5__uncultured;__
32.70775081	8.350701175	2.012224217	4.149985427	0.00003324964435	0.0002959218347	Family XIII;D_5__Family XIII UCG-001;D_6__uncultured bacterium
33.11545623	8.369454039	1.915893281	4.36843436	0.00001251404163	0.0001392187131	Lachnospiraceae;D_5__Roseburia;D_6__Clostridium sp. Clone-44
107.2867183	10.06452036	1.673272351	6.014872807	0.000000001800279971	0.0000000267041529	Ruminococcaceae;D_5__Oscillibacter;D_6__uncultured bacterium
144.5866908	10.49616302	1.535432272	6.835966137	0	0.0000000002416474138	Ruminococcaceae;D_5__uncultured;D_6__Clostridium sp. Culture-1

Table S5-a. Correlation between differentially abundant bacteria and metabolties

Biocompartment	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Liver	Serum	Serum	Serum	Serum	Serum	Serum
Taxa	3-Hydroxybutyric acid	Acetylcarnitine	Adenylosuccinate	Aminoisobutyric acid	Arginine	Dimethylglycine	Folinic acid	NADP	Shikimic acid	6-Methyl-DL-tryptophan	Asparagine	Proline	Serine	Urocanic acid	Levulinic acid
Lachnospiraceae UCG-001 Ambiguous	0.745869854	-0.1695158759	-0.1525642883	-0.5933055657	-0.2373222263	-0.5424508029	0.288176989	0.01695158759	-0.08475793795	0.1186611131	0.2034190511	0.2034190511	-0.1017095255	0.05085476277	-0.1017095255
Lachnospiraceae UCG-001 uncultured	0.3286335345	0.1825741858	0.1278019301	-0.2921186973	-0.4746928832	-0.3103761159	0.01825741858	0.2008316044	0.2373464416	0.1460593487	0.3834057903	0.4016632088	0.1460593487	0.3651483717	0.1643167673
Lachnospiraceae ASF356 uncultured	0.5659799761	-0.4929503018	-0.3103761159	-0.4016632088	0.1643167673	-0.3286335345	0.2738612788	-0.2921186973	-0.4016632088	0.2008316044	-0.07302967433	-0.1825741858	-0.2373464416	-0.09128709292	-0.07302967433
Clostridium scindens	0.6666666667	-0.65	-0.5833333333	-0.5166666667	0.5833333333	-0.5	0.7	-0.45	-0.4	-0.45	-0.2833333333	-0.4666666667	-0.5166666667	-0.65	-0.7833333333
Ruminococcaceae	0.7166666667	-0.6666666667	-0.1666666667	-0.55	0.05	-0.6	0.1666666667	-0.4	-0.1333333333	0	-0.1166666667	-0.1666666667	-0.4166666667	-0.15	-0.15
Muribaculaceae	0.6833333333	-0.6666666667	0.1	-0.3333333333	-0.03333333333	-0.3666666667	0.03333333333	-0.2333333333	0.05	0.1333333333	-0.08333333333	-0.05	-0.3166666667	-0.1833333333	-0.06666666667
Ruminiclostridium 9 uncultured	-0.6333333333	0.6666666667	0.2	0.4333333333	-0.6	0.45	-0.3833333333	0.3166666667	0.45	0.5833333333	0.4833333333	0.55	0.7833333333	0.6333333333	0.7
Roseburia uncultured	-0.65	0.55	0.55	0.6666666667	-0.7666666667	0.6333333333	-0.4333333333	0.35	0.7333333333	0.6166666667	0.6333333333	0.6	0.8666666667	0.7333333333	0.8333333333
Ruminococcaceae UCG-013 uncultured rumen bacterium	-0.6333333333	0.2833333333	0.7333333333	0.75	-0.35	0.65	-0.6333333333	0.3	0.6166666667	0.4	0.2833333333	0.3333333333	0.4333333333	0.55	0.65
Ruminiclostridium 6	-0.6666666667	0.6	0.6	0.8833333333	-0.1833333333	0.9	-0.1833333333	0.6	0.5166666667	0.2166666667	0.45	0.3833333333	0.6166666667	0.4	0.3
Erysipelatoclostridium Ambiguous	-0.745869854	0.3559833394	-0.08475793795	0.372934927	0.2542738139	0.3051285766	-0.2712254014	0	0.08475793795	-0.2373222263	-0.2373222263	-0.1186611131	0.08475793795	-0.1017095255	-0.05085476277
Family XIII UCG-001 uncultured	-0.8136762043	0.745869854	0.7119666788	0.8814825547	-0.2542738139	0.8136762043	-0.5424508029	0.661111916	0.6780635036	0.3220801642	0.4576928649	0.5424508029	0.6102571533	0.661111916	0.4915960401
Akkermansia muciniphila	-0.5477225575	0.3468909531	-0.1278019301	0.3103761159	0.4199206274	0.3103761159	0.03651483717	0.1095445115	-0.1095445115	-0.4564354646	-0.2556038602	-0.219089023	-0.03651483717	-0.2921186973	-0.3468909531
Enterorhabdus uncultured	-0.6534973784	0.3168472138	0.0990147543	0.6336944275	0.2475368857	0.6336944275	0.0990147543	0.1485221314	0.1188177052	-0.2277339349	0.04950737715	-0.1188177052	0.2574383612	-0.04950737715	-0.1089162297
Oscillibacter uncultured	-0.5744562647	0.6614950926	0.3568591947	0.3568591947	-0.3916747259	0.3916747259	-0.687606741	0.4613057883	0.1914854216	0.4874174367	0.130558242	0.4438980227	0.4177863743	0.5048252023	0.644087327
Clostridiales bacterium CIEAF 016	-0.7525121327	0.4554678698	-0.01980295086	0.5148767223	0.3663545909	0.5148767223	-0.07921180344	0.1683250823	-0.05940885258	-0.2871427875	-0.1485221314	-0.1584236069	0.1188177052	-0.06931032801	-0.1287191806
Clostridium sp. Culture-1	-0.8306277919	0.6272087408	0.2373222263	0.6780635036	-0.2034190511	0.7119666788	-0.2373222263	0.3220801642	0.2542738139	0.1695158759	0.2203706387	0.2034190511	0.5763539781	0.288176989	0.372934927
Anaerotruncus uncultured	0.5659799761	-0.8033264177	-0.8398412548	-0.8580986734	0.5659799761	-0.8580986734	0.4016632088	-0.8580986734	-0.8215838363	-0.5842373947	-0.7850689991	-0.8215838363	-0.8580986734	-0.8215838363	-0.6207522318
Lachnospiraceae A2	0.2872281323	-0.3307475463	-0.3829708431	-0.174077656	0.8964999282	-0.174077656	0.4526019055	-0.1479660076	-0.4351941399	-0.5135290851	-0.3568591947	-0.4526019055	-0.5570484991	-0.4961213195	-0.8007572174
Acetatifactor	0.593366104	-0.6390096504	-0.6390096504	-0.7074749701	0.3195048252	-0.7074749701	0.1825741858	-0.5477225575	-0.3195048252	-0.1597524126	-0.5249007843	-0.3195048252	-0.502079011	-0.7074749701	-0.4792572378
Dubosiella newyorkensis	0.661111916	-0.7628214416	-0.7797730292	-0.7967246168	0.4407412774	-0.7628214416	0.6950150912	-0.7628214416	-0.7119666788	-0.6780635036	-0.5763539781	-0.7628214416	-0.7119666788	-0.8645309671	-0.7289182664
Turicibacter	0.2333333333	-0.3166666667	-0.7666666667	-0.6166666667	0.7666666667	-0.6	0.2	-0.4666666667	-0.8333333333	-0.4833333333	-0.7	-0.6166666667	-0.7333333333	-0.5333333333	-0.5833333333
Muribaculaceae uncultured	-0.1	0.1166666667	-0.6333333333	-0.3333333333	0.65	-0.2666666667	0.2666666667	-0.1666666667	-0.7333333333	-0.65	-0.5833333333	-0.5166666667	-0.4833333333	-0.55	-0.6166666667
Lachnospiraceae GCA-900066575 uncultured	0.3666666667	0.01666666667	0.3333333333	-0.1833333333	-0.75	-0.2	-0.2833333333	0.1833333333	0.4833333333	0.6166666667	0.45	0.6	0.3333333333	0.4666666667	0.5333333333
Ruminococcaceae uncultured	0.1166666667	0.1833333333	0.4	-0.01666666667	-0.4666666667	-0.05	-0.5333333333	0.3166666667	0.35	0.65	0.3333333333	0.5666666667	0.2333333333	0.6333333333	0.5833333333
Clostridium sp. Clone-44	-0.06931032801	0.5049752469	0.5445811486	0.2277339349	-0.8218224607	0.2475368857	-0.4554678698	0.5544826241	0.6039900012	0.8218224607	0.6832018047	0.8416254115	0.6832018047	0.8218224607	0.782216559

	Phase-I Ces2c	Phase-I Cyp1a2	Phase-I Cyp2a5	Phase-I Cyp2b10	Phase-I Cyp2c29	Phase-I Cyp2c54	Phase-I Cyp2j9	Phase-I Cyp3a16	Phase-I Cyp3a41a	Phase-I Cyp17a1	Phase-I Cyp26a1	Phase-I Aldh1a7	Phase-I Ces1b	Phase-I Cyp1a1	Phase-I Cyp2c50	Phase-I Cyp2c55	Phase-I Cyp3a44	Phase-I Cyp4a14	Phase-I Nqo1
Lachnospiraceae UCG-001 Ambiguous	-0.1356127007	-0.06780635036	0.3051285766	-0.01695158759	0	-0.03390317518	0.6272087408	-0.3898865146	-0.5254992153	-0.2712254014	-0.5424508029	0.1525642883	0	0.03390317518	-0.1186611131	0.4576928649	-0.288176989	0.050854762	-0.05085476277
Lachnospiraceae UCG-001 uncultured	0.2921186973	0.4016632088	0.6937819062	0.3834057903	0.4016632088	0.4016632088	0.3468909531	-0.3651483717	-0.1460593487	0.219089023	-0.5477225575	0.4564354646	0.3468909531	0.4016632088	0.3103761159	0.6390096504	-0.1460593487	-0.2738612788	0.3834057903
Lachnospiraceae ASF356 uncultured	-0.4199206274	-0.5477225575	-0.6024948133	-0.3468909531	-0.438178046	-0.4929503018	0.4564354646	0.219089023	-0.3468909531	-0.6390096504	-0.09128709292	-0.4199206274	-0.3651483717	-0.3834057903	-0.5112077203	-0.1278019301	0.1278019301	0.1825741858	-0.4016632088
Clostridium scindens	-0.6666666667	-0.55	-0.3	-0.85	-0.6666666667	-0.7333333333	0.6833333333	0.3166666667	-0.2	-0.7833333333	-0.3666666667	-0.4666666667	-0.7666666667	-0.7333333333	-0.85	-0.4833333333	0.2666666667	0.6333333333	-0.75
Ruminococcaceae	-0.3666666667	-0.4833333333	-0.2833333333	-0.4333333333	-0.4	-0.4833333333	0.5166666667	0.4	0.01666666667	-0.6	-0.1333333333	-0.08333333333	-0.3666666667	-0.35	-0.5	-0.06666666667	0.3833333333	0.06666666667	-0.45
Muribaculaceae	-0.3333333333	-0.5666666667	-0.3833333333	-0.4833333333	-0.3833333333	-0.5166666667	0.1666666667	0.3333333333	0.03333333333	-0.6333333333	0.1	-0.01666666667	-0.2833333333	-0.2666666667	-0.4666666667	-0.03333333333	0.1666666667	0.03333333333	-0.5333333333
Ruminiclostridium 9 uncultured	0.7166666667	0.8166666667	0.5666666667	0.7833333333	0.6833333333	0.8333333333	-0.1333333333	-0.1666666667	0.1	0.7	-0.15	0.06666666667	0.7	0.65	0.75	0.3333333333	-0.1666666667	-0.2333333333	0.85
Roseburia uncultured	0.9333333333	0.8666666667	0.5833333333	0.7833333333	0.7333333333	0.8833333333	-0.4333333333	0.1166666667	0.45	0.6833333333	-0.1333333333	0.15	0.7333333333	0.75	0.8166666667	0.35	0.08333333333	-0.4333333333	0.9
Ruminococcaceae UCG-013 uncultured	0.5833333333	0.3666666667	-0.03333333333	0.4166666667	0.45	0.3666666667	-0.8333333333	0.45	0.8166666667	0.45	0.4166666667	0.3166666667	0.4833333333	0.5	0.45	0.1333333333	0.3833333333	-0.6333333333	0.4
Ruminiclostridium 6	0.5833333333	0.5666666667	0.2333333333	0.4	0.5333333333	0.4666666667	-0.8166666667	-0.03333333333	0.4	0.5	0.01666666667	0.2	0.45	0.5166666667	0.45	0.2	-0.06666666667	-0.35	0.45
Erysipelatoclostridium Ambiguous	0.1017095255	0.288176989	0.1017095255	0.08475793795	0.1356127007	0.1695158759	-0.288176989	0.1356127007	0.4068381022	0.4576928649	0.3390317518	0	0.08475793795	0.01695158759	0.1864674635	-0.3559833394	0.1356127007	0.08475793795	0.1356127007
Family XIII UCG-001 uncultured	0.6780635036	0.7289182664	0.3390317518	0.5933055657	0.7628214416	0.5763539781	-0.8306277919	0.08475793795	0.7289182664	0.745869854	0.1356127007	0.5424508029	0.6780635036	0.7119666788	0.5763539781	0.372934927	0.1525642883	-0.661111916	0.5763539781
Akkermansia muciniphila	-0.05477225575	0.1460593487	0.07302967433	-0.05477225575	0.01825741858	0.03651483717	-0.3103761159	-0.1643167673	0.09128709292	0.3103761159	0.2008316044	-0.01825741858	-0.07302967433	-0.09128709292	0.05477225575	-0.3103761159	-0.1278019301	0.2008316044	-0.01825741858
Enterorhabdus uncultured	0.2376354103	0.3069457383	0.01980295086	0.02970442629	0.1089162297	0.1584236069	-0.4851722961	0.207930984	0.3663545909	0.277241312	0.03960590172	-0.1980295086	-0.01980295086	0.01980295086	0.1188177052	-0.3366501646	0.1881280332	0.06931032801	0.1584236069
Oscillibacter uncultured	0.3829708431	0.3568591947	0.1218543592	0.7137183894	0.5483446163	0.5396407335	-0.5222329679	-0.5222329679	-0.09574271078	0.6614950926	0.4700096711	0.3916747259	0.6963106238	0.600567913	0.6701989754	0.4438980227	-0.5309368507	-0.4438980227	0.5396407335
Clostridiales bacterium CIEAF 016	0.0990147543	0.2475368857	-0.03960590172	0.1089162297	0.1287191806	0.138620656	-0.4653693452	-0.00990147543	0.2475368857	0.4158619681	0.2574383612	-0.05940885258	0.03960590172	0.01980295086	0.1584236069	-0.2970442629	0.02970442629	0.02970442629	0.138620656
Clostridium sp. Culture-1	0.5424508029	0.5763539781	0.2542738139	0.5254992153	0.4407412774	0.5933055657	-0.5594023905	-0.1525642883	0.1525642883	0.6272087408	0.1356127007	-0.05085476277	0.4237896898	0.4068381022	0.5933055657	0	-0.1864674635	-0.1186611131	0.5933055657
Anaerotruncus uncultured	-0.8398412548	-0.8580986734	-0.5659799761	-0.7302967433	-0.9128709292	-0.7485541619	0.7485541619	0.1825741858	-0.438178046	-0.6937819062	0.1825741858	-0.5659799761	-0.8398412548	-0.9128709292	-0.6937819062	-0.6937819062	0.1460593487	0.6755244876	-0.7302967433
Lachnospiraceae A2	-0.7050145066	-0.5396407335	-0.5657523819	-0.7659416862	-0.5135290851	-0.8094611002	0.2175970699	0.3220436635	0.07833494518	-0.5570484991	-0.04351941399	-0.1914854216	-0.6527912098	-0.6266795614	-0.8529805142	-0.4351941399	0.3568591947	0.3046358979	-0.7920533346
Acetatifactor	-0.7302967433	-0.6390096504	-0.2738612788	-0.7302967433	-0.6390096504	-0.6390096504	0.7302967433	0.06846531969	-0.3879701449	-0.6390096504	0.1369306394	-0.3651483717	-0.5249007843	-0.6390096504	-0.6390096504	-0.4564354646	-0.1597524126	0.7302967433	-0.7302967433
Dubosiella newyorkensis	-0.6780635036	-0.6780635036	-0.2542738139	-0.7119666788	-0.8475793795	-0.5933055657	0.7628214416	0.03390317518	-0.5594023905	-0.6950150912	-0.1695158759	-0.6102571533	-0.8475793795	-0.8475793795	-0.6102571533	-0.6102571533	0.01695158759	0.7797730292	-0.6102571533
Turicibacter	-0.8166666667	-0.65	-0.6	-0.5	-0.6	-0.6666666667	0.55	0	-0.35	-0.3833333333	0.25	-0.2833333333	-0.5833333333	-0.6833333333	-0.6166666667	-0.4666666667	0.08333333333	0.4	-0.6166666667
Muribaculaceae uncultured	-0.5333333333	-0.2833333333	-0.1666666667	-0.2166666667	-0.3333333333	-0.2666666667	0.2333333333	-0.5	-0.5333333333	0.01666666667	0.1666666667	-0.1666666667	-0.3666666667	-0.4333333333	-0.2166666667	-0.3333333333	-0.3666666667	0.4333333333	-0.2833333333
Lachnospiraceae GCA-900066575 uncultured	0.35	0.2666666667	0.4666666667	0.3666666667	0.3833333333	0.3666666667	0.2	-0.1833333333	-0.08333333333	0.08333333333	-0.25	0.3666666667	0.4833333333	0.4833333333	0.3333333333	0.6333333333	-0.2166666667	-0.3	0.3333333333
Ruminococcaceae uncultured	0.2333333333	0.1666666667	0.08333333333	0.4166666667	0.4333333333	0.2166666667	-0.05	-0.06666666667	0.1333333333	0.1833333333	0.06666666667	0.5166666667	0.5333333333	0.5	0.25	0.6333333333	-0.03333333333	-0.5833333333	0.25
Clostridium sp. Clone-44	0.6435959029	0.6138914766	0.5445811486	0.7525121327	0.7525121327	0.6832018047	-0.1485221314	-0.34655164	-0.00990147543	0.4653693452	-0.2277339349	0.4950737715	0.8218224607	0.8218224607	0.6435959029	0.8416254115	-0.3267486892	-0.5643840995	0.6832018047

Phase-I	Phase-I	Phase-I	Phase-I	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Phase-II	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter	Transporter
Por	Cyp26b1	Sdr9c7	Cyb5a	Gclc	Gstm2	Gstm3	Sult2a1	Sult2a2	Sult3a1	Gsta2	Gsta4	Gstm1	Gstm4	Gstp1	Atp2a2	Atp2b2	Atp6v0d2	Slc15a2	Slc16a1	Slc25a30	Slc30a10
0.03390317518	-0.08475793795	-0.05085476277	0.1356127007	0.5424508029	-0.1017095255	0.3051285766	-0.1017095255	-0.1525642883	-0.6441603284	0.4068381022	0.4068381022	0.03390317518	0.1525642883	0.4576928649	0.4237896898	0.1525642883	-0.2373222263	0.7967246168	0.06780635036	0.06780635036	0.01695158759
0.4199206274	-0.3103761159	-0.3834057903	0.5477225575	0.07302967433	0.2921186973	0.5477225575	0.3103761159	0.3103761159	-0.1278019301	0.6207522318	0.6207522318	0.3651483717	0.5294651389	0.4564354646	-0.01825741858	-0.2556038602	0.1825741858	0.6207522318	-0.4016632088	-0.03651483717	-0.3834057903
-0.4746928832	-0.01825741858	0.3651483717	-0.5477225575	0.7302967433	-0.5294651389	-0.09128709292	-0.5659799761	-0.6755244876	-0.7120393248	-0.09128709292	-0.09128709292	-0.2738612788	-0.5294651389	0.6024948133	0.657267069	0.4929503018	-0.6755244876	0.4564354646	0.5477225575	0.5477225575	0.4746928832
-0.65	0.45	0.65	-0.6166666667	0.7833333333	-0.7333333333	-0.6	-0.2666666667	-0.3333333333	-0.5333333333	-0.4333333333	-0.4333333333	-0.7333333333	-0.5166666667	-0.15	0.5166666667	0.6166666667	-0.5	0.4833333333	0.55	0.3833333333	0.5833333333
-0.4	-0.1333333333	0.45	-0.45	0.6666666667	-0.4	-0.2	-0.3166666667	-0.4333333333	-0.4166666667	-0.08333333333	-0.08333333333	-0.45	-0.5333333333	0.4333333333	0.5166666667	0.3833333333	-0.3166666667	0.5666666667	0.4833333333	0.8166666667	0.55
-0.4	-0.15	0.4166666667	-0.5666666667	0.5166666667	-0.3	-0.3166666667	-0.4833333333	-0.5833333333	-0.4166666667	-0.1666666667	-0.1666666667	-0.4833333333	-0.6833333333	0.08333333333	0.35	0.2833333333	-0.1166666667	0.2333333333	0.5666666667	0.6666666667	0.6166666667
0.8	-0.25	-0.7	0.6833333333	-0.5666666667	0.45	0.5	0.7166666667	0.7333333333	0.2833333333	0.3833333333	0.3833333333	0.7333333333	0.75	0.4833333333	-0.5	-0.7333333333	0.2333333333	0.15	-0.8166666667	-0.35	-0.8666666667
0.85	-0.4166666667	-0.7	0.5666666667	-0.75	0.5	0.4	0.7166666667	0.7333333333	0.4833333333	0.35	0.35	0.6833333333	0.5833333333	0.3166666667	-0.7666666667	-0.9333333333	0.4833333333	-0.05	-0.8666666667	-0.1666666667	-0.8666666667
0.3	-0.5833333333	-0.35	0.1	-0.6333333333	0.5	0.15	0.1333333333	0.1666666667	0.6833333333	0.1166666667	0.1166666667	0.35	-0.03333333333	0.03333333333	-0.6833333333	-0.5666666667	0.6333333333	-0.6333333333	-0.3666666667	0.2666666667	-0.25
0.3666666667	-0.2333333333	-0.55	0.2666666667	-0.6666666667	0.4666666667	0.2	0.1833333333	0.3	0.4666666667	0.2	0.2	0.4833333333	0.3166666667	-0.3833333333	-0.8166666667	-0.5833333333	0.6	-0.6833333333	-0.5666666667	-0.4666666667	-0.55
0.1356127007	0.1864674635	-0.06780635036	0.2203706387	-0.5085476277	0.2203706387	-0.1864674635	0.4576928649	0.5254992153	0.6780635036	-0.2712254014	-0.2712254014	0.05085476277	0.2373222263	-0.4068381022	-0.4068381022	-0.1864674635	0.3051285766	-0.4746444525	-0.288176989	-0.2542738139	-0.2034190511
0.4576928649	-0.5933055657	-0.6950150912	0.4915960401	-0.7119666788	0.7628214416	0.4407412774	0.3220801642	0.4407412774	0.745869854	0.4237896898	0.4237896898	0.661111916	0.4407412774	-0.03390317518	-0.8984341423	-0.6780635036	0.8475793795	-0.6272087408	-0.7289182664	-0.1525642883	-0.5933055657
-0.01825741858	0.3834057903	-0.01825741858	0.1460593487	-0.4016632088	0.1278019301	-0.2008316044	0.2008316044	0.3103761159	0.4564354646	-0.2556038602	-0.2556038602	-0.01825741858	0.219089023	-0.7302967433	-0.3103761159	0	0.219089023	-0.5842373947	-0.1460593487	-0.5842373947	-0.1278019301
0.06931032801	0.207930984	-0.1089162297	0.00990147543	-0.4950737715	0.04950737715	-0.2178324595	0.2475368857	0.3366501646	0.4950737715	-0.2475368857	-0.2475368857	0.06931032801	0.1188177052	-0.5544826241	-0.5445811486	-0.2376354103	0.2376354103	-0.6039900012	-0.3069457383	-0.3663545909	-0.2871427875
0.4787135539	-0.3307475463	-0.5831601475	0.5483446163	-0.5483446163	0.6614950926	0.5831601475	0.07833494518	0.1392621248	0.2698203667	0.3916747259	0.3916747259	0.6789028582	0.4700096711	0.1914854216	-0.2698203667	-0.3829708431	0.3133397807	-0.4177863743	-0.3568591947	-0.4787135539	-0.4264902571
0.02970442629	0.207930984	-0.1287191806	0.1485221314	-0.4950737715	0.1881280332	-0.07921180344	0.1881280332	0.2970442629	0.5544826241	-0.1881280332	-0.1881280332	0.1485221314	0.2178324595	-0.4950737715	-0.4059604926	-0.0990147543	0.2178324595	-0.6832018047	-0.2475368857	-0.4653693452	-0.2277339349
0.5085476277	0.05085476277	-0.4746444525	0.4068381022	-0.7628214416	0.3559833394	0.1695158759	0.4407412774	0.5254992153	0.4915960401	0.03390317518	0.03390317518	0.4915960401	0.4915960401	-0.2542738139	-0.6102571533	-0.5424508029	0.288176989	-0.5254992153	-0.5763539781	-0.6441603284	-0.6441603284
-0.657267069	0.657267069	0.9128709292	-0.6024948133	0.6390096504	-0.7850689991	-0.6390096504	-0.3103761159	-0.4199206274	-0.4016632088	-0.6755244876	-0.6755244876	-0.8398412548	-0.6024948133	-0.09128709292	0.9128709292	0.8398412548	-0.8215838363	0.3651483717	0.8580986734	0.3468909531	0.8033264177
-0.8442766314	0.1914854216	0.5135290851	-0.5918640302	0.6527912098	-0.4264902571	-0.4090824915	-0.5483446163	-0.5309368507	-0.2175970699	-0.3046358979	-0.3046358979	-0.5396407335	-0.5483446163	-0.2175970699	0.3394514291	0.7050145066	-0.2350048355	-0.08703882798	0.5396407335	0.3829708431	0.6527912098
-0.4336136914	0.502079011	0.6390096504	-0.4564354646	0.6390096504	-0.5477225575	-0.6390096504	-0.1141088661	-0.2282177323	-0.5249007843	-0.5477225575	-0.5477225575	-0.7302967433	-0.4564354646	-0.1369306394	0.6390096504	0.5249007843	-0.4564354646	0.5249007843	0.6390096504	0.2738612788	0.6390096504
-0.4915960401	0.8136762043	0.8136762043	-0.5085476277	0.5424508029	-0.8306277919	-0.661111916	-0.1525642883	-0.2373222263	-0.4746444525	-0.6272087408	-0.6272087408	-0.8136762043	-0.4237896898	-0.3559833394	0.745869854	0.6780635036	-0.7628214416	0.4407412774	0.6780635036	0.03390317518	0.5763539781
-0.6833333333	0.3666666667	0.5833333333	-0.35	0.6166666667	-0.4333333333	-0.2333333333	-0.4166666667	-0.45	-0.2666666667	-0.3333333333	-0.3333333333	-0.45	-0.35	0.15	0.7833333333	0.85	-0.6333333333	0.15	0.65	0.25	0.65
-0.3166666667	0.6166666667	0.2666666667	0.05	0.1	-0.1666666667	-0.1166666667	-0.1333333333	-0.06666666667	-0.03333333333	-0.25	-0.25	-0.1833333333	0.1333333333	-0.4333333333	0.4	0.55	-0.3666666667	-0.2	0.2833333333	-0.5833333333	0.2
0.4666666667	-0.4666666667	-0.3666666667	0.3333333333	0.06666666667	0.2833333333	0.4166666667	0.2	0.1333333333	-0.2666666667	0.5	0.5	0.3166666667	0.25	0.5833333333	-0.03333333333	-0.4	0.2	0.6	-0.2666666667	0.2	-0.2666666667
0.2166666667	-0.75	-0.4	0.2666666667	0.1166666667	0.45	0.6	-0.1166666667	-0.15	-0.1	0.6	0.6	0.45	0.1166666667	0.8166666667	0	-0.2166666667	0.25	0.2666666667	-0.1666666667	0.4333333333	-0.1
0.6832018047	-0.6733003292	-0.7723150835	0.6138914766	-0.2277339349	0.6039900012	0.7723150835	0.2574383612	0.2574383612	-0.07921180344	0.7723150835	0.7723150835	0.7723150835	0.5643840995	0.7030047555	-0.3366501646	-0.6435959029	0.3861575418	0.3168472138	-0.6138914766	-0.07921180344	-0.6336944275

Transporter Abcc4	Transporter Abcg8	Transporter Slc10a2	Transporter Slc17a2	Transporter Slc3a1	Transporter Slc46a3	Transporter Slc7a2	Transporter Slco1a1	NR, immune response and oxidative stress, epi Bcl6	NR, immune response and oxidative stress, epi Cldn1	NR, immune response and oxidative stress, epi Egr1	NR, immune response and oxidative stress, epi Lcn2	NR, immune response and oxidative stress, epi Nlrp12
0.1695158759	0.1525642883	0.4068381022	0.3051285766	-0.1525642883	-0.3898865146	0.2203706387	-0.2203706387	0.4407412774	0.6102571533	0.4576928649	-0.1864674635	-0.1356127007
0.4016632088	0.3286335345	0.3468909531	-0.1095445115	-0.05477225575	0.09128709292	0.4746928832	-0.4746928832	0.7302967433	0.1095445115	0.3651483717	0.2738612788	-0.3286335345
-0.2373464416	-0.01825741858	0.2921186973	0.4564354646	-0.2556038602	-0.4929503018	-0.3468909531	0.2921186973	-0.3103761159	0.5659799761	-0.01825741858	-0.5842373947	0.05477225575
-0.7	-0.08333333333	-0.25	0.75	-0.6666666667	-0.5333333333	-0.7	0.05	-0.3	0.6	-0.06666666667	-0.15	0.06666666667
-0.35	0	0.2333333333	0.35	-0.6666666667	-0.2833333333	-0.3833333333	0.15	0	0.4833333333	-0.08333333333	-0.1	-0.45
-0.35	-0.1166666667	0.3333333333	0.1833333333	-0.3333333333	-0.35	-0.3333333333	0.2666666667	-0.03333333333	0.4833333333	-0.1	-0.2666666667	-0.4166666667
0.7	0.7	0.3	-0.45	0.5	0.4	0.6666666667	-0.6333333333	0.4166666667	-0.7	0.3	0.1166666667	0.3333333333
0.55	0.6833333333	0.2833333333	-0.7	0.5666666667	0.6833333333	0.5833333333	-0.6	0.6	-0.8833333333	0.01666666667	0.3833333333	0.05
0.15	0.2	0.1833333333	-0.8	0.3333333333	0.6166666667	0.1166666667	-0.05	0.1	-0.7666666667	-0.4833333333	0.3	-0.4
0.1833333333	0.2	-0.01666666667	-0.65	0.7833333333	0.4333333333	0.2333333333	-0.2833333333	0.1666666667	-0.6333333333	-0.2666666667	0.2	0.1
0.01695158759	0.05085476277	-0.4237896898	-0.1864674635	-0.05085476277	0.3051285766	-0.03390317518	-0.1356127007	-0.288176989	-0.6102571533	-0.1356127007	0.3051285766	0.2034190511
0.3559833394	0.3898865146	0.1695158759	-0.8814825547	0.5254992153	0.5763539781	0.3220801642	-0.4407412774	0.2203706387	-0.8475793795	-0.3220801642	0.3559833394	-0.2712254014
-0.09128709292	-0.2373464416	-0.5659799761	-0.03651483717	0.1460593487	0.1278019301	-0.07302967433	0.01825741858	-0.3103761159	-0.2921186973	-0.09128709292	0.2008316044	0.3286335345
-0.1881280332	0.00990147543	-0.4950737715	-0.2178324595	0.3069457383	0.3762560663	-0.1683250823	-0.0990147543	-0.1881280332	-0.5544826241	-0.3663545909	0.3069457383	0.2970442629
0.7485339206	0.04351941399	0.3568591947	-0.5396407335	0.6701989754	0.1479660076	0.687606741	0.008703882798	0.03481553119	-0.3481553119	0.2698203667	-0.2524126011	0.1566698904
-0.02970442629	-0.1287191806	-0.4950737715	-0.1980295086	0.2475368857	0.277241312	-0.06931032801	0.01980295086	-0.3663545909	-0.4950737715	-0.2475368857	0.1881280332	0.3168472138
0.3559833394	0.1695158759	-0.1864674635	-0.4407412774	0.6780635036	0.4576928649	0.372934927	-0.2034190511	0.05085476277	-0.6950150912	-0.01695158759	0.1695158759	0.4576928649
-0.5477225575	-0.5659799761	-0.4564354646	0.8946135106	-0.8580986734	-0.4564354646	-0.5842373947	0.6390096504	-0.5659799761	0.6755244876	0.07302967433	-0.2008316044	0.1643167673
-0.6963106238	-0.2524126011	-0.2872281323	0.4526019055	-0.5396407335	-0.4700096711	-0.8007572174	0.2088931871	-0.6527912098	0.4264902571	-0.3916747259	-0.2088931871	-0.1131504764
-0.3195048252	-0.06846531969	0.02282177323	0.7302967433	-0.6390096504	-0.7302967433	-0.3423265984	0.1141088661	-0.3651483717	0.593366104	0.3879701449	-0.4564354646	0.2282177323
-0.5763539781	-0.5254992153	-0.5763539781	0.9153857299	-0.6441603284	-0.372934927	-0.4915960401	0.4576928649	-0.2542738139	0.6950150912	0.1525642883	-0.01695158759	0.288176989
-0.3166666667	-0.4333333333	-0.3	0.6666666667	-0.7	-0.5166666667	-0.4833333333	0.4833333333	-0.7666666667	0.5333333333	0.01666666667	-0.3666666667	0.1333333333
-0.08333333333	-0.5666666667	-0.5833333333	0.4833333333	-0.15	-0.3	-0.1166666667	0.3666666667	-0.5333333333	0.3333333333	0.2	-0.15	0.4666666667
0.4833333333	0.4833333333	0.7333333333	-0.2333333333	0.1166666667	-0.03333333333	0.5333333333	-0.4166666667	0.6833333333	0.06666666667	0.4166666667	-0.06666666667	-0.3
0.4833333333	0.3833333333	0.8	-0.4	0.06666666667	-0.05	0.3833333333	-0.2166666667	0.2833333333	-0.01666666667	0.1333333333	-0.2333333333	-0.4833333333
0.7723150835	0.6336944275	0.8218224607	-0.5643840995	0.5544826241	0.138620656	0.7723150835	-0.5643840995	0.6832018047	-0.2475368857	0.3663545909	-0.1089162297	-0.1683250823

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Socs2	Cebpb	Hmox1	Icam1	Ifit3	Il6ra	Il1b	Socs3
0.3051285766	-0.8306277919	0.8136762043	0.6272087408	-0.05085476277	-0.2542738139	0.3898865146	0.4068381022
0.3468909531	-0.5294651389	0.6207522318	0.3103761159	0.1643167673	-0.1460593487	0.2738612788	0.6390096504
0.4199206274	-0.4929503018	0.3103761159	0.4929503018	-0.4199206274	-0.4016632088	0.1278019301	-0.05477225575
-0.35	-0.5666666667	0.6666666667	0.8666666667	-0.5333333333	-0.5	0.9	-0.3333333333
0.25	-0.5	0.5166666667	0.6166666667	-0.6166666667	-0.8666666667	0.6	0.1
0.1333333333	-0.2666666667	0.1833333333	0.35	-0.65	-0.6666666667	0.3166666667	-0.01666666667
0.5166666667	0.1833333333	-0.1	-0.5	0.6	0.6166666667	-0.5333333333	0.3166666667
0.4666666667	0.4666666667	-0.3166666667	-0.6166666667	0.3166666667	0.5	-0.5333333333	0.3333333333
0.3	0.75	-0.8333333333	-0.7333333333	-0.06666666667	0.03333333333	-0.55	0.2
-0.05	0.6	-0.7	-0.6166666667	0.25	0.7	-0.5833333333	0.1
-0.3559833394	0.5254992153	-0.4068381022	-0.4576928649	0.3559833394	0.2712254014	-0.1017095255	-0.2542738139
0.2542738139	0.5594023905	-0.7119666788	-0.6950150912	0.3220801642	0.372934927	-0.5254992153	0.4407412774
-0.6390096504	0.4199206274	-0.3651483717	-0.3103761159	0.3651483717	0.4746928832	-0.09128709292	-0.3468909531
-0.4257634435	0.6039900012	-0.5148767223	-0.3663545909	0.1287191806	0.5148767223	-0.1881280332	-0.3168472138
0.3829708431	0.3394514291	-0.5918640302	-0.7920533346	0.6701989754	0.5744562647	-0.9574271078	0.2611164839
-0.4059604926	0.5643840995	-0.5742855749	-0.4653693452	0.3663545909	0.5148767223	-0.3069457383	-0.277241312
-0.08475793795	0.6441603284	-0.5933055657	-0.7119666788	0.5254992153	0.8475793795	-0.6780635036	-0.1186611131
-0.438178046	-0.3103761159	0.4929503018	0.5842373947	-0.3651483717	-0.6024948133	0.6207522318	-0.6207522318
-0.3133397807	-0.3220436635	0.130558242	0.5744562647	-0.4090824915	-0.4613057883	0.600567913	-0.2088931871
-0.2510395055	-0.502079011	0.593366104	0.502079011	-0.2282177323	-0.4336136914	0.593366104	-0.4336136914
-0.661111916	-0.3390317518	0.661111916	0.6950150912	-0.3559833394	-0.3390317518	0.7289182664	-0.6441603284
-0.1666666667	-0.3833333333	0.2666666667	0.4333333333	-0.03333333333	-0.45	0.3666666667	-0.3
-0.6	-0.08333333333	0.06666666667	0.1	0.4166666667	0.2666666667	0.06666666667	-0.4
0.6333333333	-0.4	0.4	0.06666666667	0.01666666667	-0.1666666667	-0.03333333333	0.5666666667
0.8666666667	-0.3	0.01666666667	-0.1	0.05	-0.3166666667	-0.2666666667	0.7
0.8416254115	-0.207930984	0.04950737715	-0.277241312	0.34655164	0.2574383612	-0.4950737715	0.7525121327

NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi	NR, immune response and oxidative stress, epi
Mt1	Mt2	Bnip3	Nr0b2	Nr1d1	Nr1d2	Gadd45g
0.05085476277	0.2542738139	0.288176989	-0.288176989	0.3220801642	0.4068381022	-0.1525642883
0.4564354646	0.5477225575	0.6390096504	-0.5477225575	0.6207522318	0.6207522318	0.09128709292
-0.5294651389	-0.4564354646	-0.5294651389	0.4016632088	-0.5112077203	-0.3468909531	-0.01825741858
-0.4166666667	-0.35	-0.2	0.3166666667	-0.3166666667	-0.3166666667	-0.4
-0.5166666667	-0.3166666667	-0.2333333333	0.2333333333	-0.35	-0.1833333333	-0.01666666667
-0.6333333333	-0.3166666667	-0.4166666667	0.1666666667	-0.4333333333	-0.2166666667	-0.06666666667
0.8	0.6666666667	0.6333333333	-0.5666666667	0.6333333333	0.5833333333	0.2166666667
0.7666666667	0.7	0.5333333333	-0.65	0.5333333333	0.5333333333	0.3166666667
0.1333333333	0.03333333333	-0.1333333333	-0.1166666667	-0.15	-0.1333333333	0.5833333333
0.5166666667	0.3166666667	0.06666666667	-0.3666666667	0.1833333333	0.05	0.3166666667
0.2542738139	0.01695158759	0.2203706387	0.06780635036	0.1017095255	-0.08475793795	0.05085476277
0.5933055657	0.3051285766	0.2373222263	-0.3898865146	0.2373222263	0.06780635036	0.6780635036
0.2008316044	-0.01825741858	0.09128709292	0.09128709292	0.09128709292	-0.1278019301	-0.1278019301
0.3069457383	0.03960590172	-0.01980295086	0.00990147543	-0.01980295086	-0.1980295086	0.03960590172
0.2785242495	0.2088931871	0.1044465936	-0.1914854216	0.2524126011	0.2437087183	0.3133397807
0.2475368857	-0.07921180344	-0.01980295086	0.1485221314	-0.01980295086	-0.2376354103	0.0990147543
0.5594023905	0.3559833394	0.2203706387	-0.2542738139	0.3051285766	0.1864674635	0.08475793795
-0.7850689991	-0.6207522318	-0.3834057903	0.7302967433	-0.4929503018	-0.3834057903	-0.5842373947
-0.4787135539	-0.6789028582	-0.4961213195	0.5657523819	-0.5918640302	-0.7224222722	0.05222329679
-0.5477225575	-0.2510395055	-0.04564354646	0.2510395055	-0.1597524126	-0.04564354646	-0.593366104
-0.5254992153	-0.3051285766	-0.1695158759	0.4407412774	-0.2203706387	-0.1356127007	-0.7967246168
-0.5833333333	-0.7166666667	-0.3833333333	0.7666666667	-0.4833333333	-0.5333333333	-0.1333333333
-0.1333333333	-0.3	-0.06666666667	0.4333333333	-0.03333333333	-0.2	-0.35
0.2333333333	0.5166666667	0.4333333333	-0.5833333333	0.45	0.6166666667	0.1
0.05	0.1	0.08333333333	-0.2333333333	0.08333333333	0.1833333333	0.55
0.5643840995	0.6336944275	0.4752708206	-0.7030047555	0.5643840995	0.6336944275	0.4059604926

#CV PCB6 & CV PCB30 & GF PCB6 & GF PCB30 COMMON	#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB6 COMMON	#CV PCB6 & GF PCB6 & GF PCB30 COMMOn	#CV PCB6 & GF PCB30 COMMON	#CV PCB6 & GF PCB30 & CV PCB30 COMMON
Cyp1a2	Cyp17a1	Cyp8b1	Ypel2	Cyp3a16	Igfbp5	Cyp2c29
Arntl	Cyp2a5	Serpina1e	Cldn1	Cyp3a41a		Atp6v0d2
Ces2c	Cyp2j9	Gm24105	Cyp26a1	Cyp3a41b		Cyp2b10
G6pc	Clpx	Gm47283	Sult2a2			Rnf125
Sult2a1	Rab36	AC127342.1				
	Mknk2					
	Lpin1					
	Sdf2l1					
	Creld2					
	Spry4					
	Setbp1					
	Syvn1					
	Loxl4					
	Got1					
	Npas2					
	Acmsd					
	Marco					
	Slc30a10					
	Hspa5					
	Gpcpd1					
	Mthfr					
	Slc34a2					
	Hsph1					
	Atp2b2					
	Mt2					
	Mt1					
	Hyou1					
	Nnmt					
	Manf					
	Slc16a1					
	Hspa13					
	Pim3					
	Pnrc1					
	Gstm2					
	Inhba					
	Rtn4rl1					
	Rbp1					
	Jun					
	Arfgap3					
	Nfil3					
	Ero1lb					
	Dhcr7					
	Tubb2a					
	Rad51b					
	Cyp2c54					
	Ppp1r3c					
	Sult3a1					
	Etnk2					
	Acot1					
	Gm13775					
	Gm15611					
	Gm16348					
	Sult3a2					
	Hspa1b					
	Serpina4-ps1					
	1810053B23Rik					
	Gm21049					

#CV PCB30 & GF PCB6 COMMON	#CV PCB30 & GF PCB6 & CV PCB30 COMMON	#CV PCB30 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only GF PCB6	#only GF PCB30
Socs2	Gstm3	Cyp2c55	Mfsd10	Ckb	Nbr1	Ttyh1
Bcl6	Gadd45g	Nr0b2	Hmox1	Nqo1	Igfbp1	Lars2
Fabp5	Upp2	Cyp3a44	Id3	Por	Per1	Hbb-bt
Slco1a1	Thrsp	Gstp1	Dnajb9	Psmb4	Klc1	Gm13340
Paqr9	Egr1	Hba-a2	Aldoc	Krt23	Lcn2	Gm20594
Gm25687		Hba-a1	Myh11	Abhd8	Ly75	Mir6236
Mup22			Aebp1	Plin5	Smad9	Gm28439
			Map2k6	Lonrf3	Enho	Gm28437
			Id2	Avpr1a	Sult1e1	Gm37194
			Klf11	Nr1d1	H2-Aa	Rmrp
			Hmgcr	Nr1d2	Nmrk1	
			Slc25a30	Cnmd	Ppl	
			Sqle	Sorbs3	Ppp1r3g	
			Slc15a2	Retreg1	Apol9a	
			Noct	Myc	Camk2b	
			Chka	Mpv17l	BC023105	
			Gsn	Slc10a2	H2-Ab1	
			Hdc	Slc3a1	Sult2a3	
			Il6ra	Abcg8	Sult2a5	
			Efna1	Cyb5a	Nlrp12	
			Plk3	Aldh1a7	Gm12390	
			Atp2a2	Spata3	Nbdy	
			Gfpt1	Ngef	Zbed4-ps2	
			Tmem159	Agxt	Mug-ps1	
			Nsdhl	Mpzl1	Gm42796	
			Msmo1	Lrp4	Gm42642	
			Gclc	Knstrn	4833411C07Rik	
			Acta2	Il1b	Gm47789	
			Icam1	Gstm4	Gm34654	
			Vnn1	Pdgfc		
			Gdf15	Hsdl2		
			Lonrf1	Gne		
			Cplane1	Cyp4a14		
			Lrtm1	Per3		
			Phf13	Slc2a5		
			Angptl8	Slc46a3		
			Zfp518a	Gys2		
			Tsku	Scnn1a		
			Tcim	Clec2h		
			Cebpb	Serpina7		
			Fam47e	Slc7a2		
			Fdps	Pllp		
			Defa24	Nectin1		
			mt-Co2	Cyp1a1		
			Rdh11	Gsta4		
			Zbtb16	Trib3		
			Gm5096	Abtb2		
			Osgin1	Abcc4		
			Bhmt	Igf2bp2		
			Ifit3	Dsg1c		
			Igkc	Gnat1		
			Zfp970	Rrp12		
			F830016B08Rik	1810055G02Rik		
			Hmgcs1	Ttc38		
			Mup15	Slc17a2		
			Mup17	Lrfn3		
			Tcf24	Lrg1		
			Ighv1-11	Il22ra1		
			Gm45301	Spon2		
			Eppk1	Inf2		
			Gm31583	Mical2		
				Foxq1		
				Ciart		
				Dsel		

9130409I23Rik
Mreg
Mmd2
Htatip2
Tmem120a
Sdr9c7
Gbp2b
Klhdc8a
Lgalsl
Maff
Pgp
Tafa2
Lsm11
Zfp526
Paxx
Hbb-bs
Pkdrej
Zmat1
Socs3
Smagp
Klf1
Pm20d2
Cyp2c50
Ntrk2
Retsat
Gsta2
Gstm1
Tmed9
Gpc6
Acnat2
H2-Q7
Serpina6
Lsamp
Pclo
Cyp26b1
Gm22220
Mup3
Frat1
Nipal1
Ccnd1
Klhl21
Cib3
Phldb3
Ly6a
Bnip3
Mup20
Ces1b
Gm11340
Gm13771
Rn7s1
Gm6135
Gstm2-ps1
Gm44421
Gm44787
Gm33543
Gm34777
Gm31508
Gm49012
AC138228.1
AC157910.3

#CV PCB6 & CV PCB30 COMMON	#GF PCB6 & GF PCB30 COMMON	#only CV PCB6	#only CV PCB30	#only CV PCB30
Aminosobutyric acid	G6P	3-Hydroxybutyric acid	Folinic acid	Dopamine
2,3-Dihydroxybenzoic acid	F6P		Shikimic acid	Dextrose
	Raffinose		NADP	Allantoin
			Arginine	Inosine
			Adenylosuccinate	NAD
			Acetylcarnitine	Uridine
				Nicotinamide
				Taurine
				Adenosine
				Adenosyl-L-homocysteine
				UDP-GlcNAc
				3-Methylvaleric acid
				2,3-Dihydroxybenzoic acid
				2-Deoxycytidine

#GF PCB6 & GF PCB30 COMMON	#only CV PCB30	#only CV PCB6	#only CV PCB30
Glucuronic acid	Levulinic acid	Mucic acid	2-Hydroxyphenylacetic acid
	6-Methyl-DL-tryptophan	Mannose	
	Serine	Norvaline	
	Asparagine	Cytosine	
	Proline		
	Urocanic acid		

Table S1. mapping statistics

Sample_ID	Age	Gender	Exposure	Total_reads	Reads_mapped	%_Mapped
205643	Day 5	Male	Control	38249766	28515200.55	74.55
205644	Day 5	Male	Control	40437684	32519985.47	80.42
205645	Day 5	Male	Control	42781100	33630222.71	78.61
205646	Day 5	Female	Control	43095252	28024842.38	65.03
205647	Day 5	Female	Control	42781100	33630222.71	78.61
205648	Day 5	Female	Control	37444955	28349575.43	75.71
205649	Day 5	Male	PCB	36294351	27779696.26	76.54
205650	Day 5	Male	PCB	41526448	32228676.29	77.61
205651	Day 5	Male	PCB	35701747	27211871.56	76.22
205652	Day 5	Female	PCB	39408816	30431487.72	77.22
205653	Day 5	Female	PCB	37268098	28361022.58	76.1
205654	Day 5	Female	PCB	42781100	33630222.71	78.61
205655	Day 60	Male	Control	54493152	23709970.44	43.51
205656	Day 60	Male	Control	41920601	27864623.48	66.47
205657	Day 60	Male	Control	46925798	29793189.15	63.49
205658	Day 60	Female	Control	46019544	28140951.16	61.15
205659	Day 60	Female	Control	41903784	27086605.98	64.64
205660	Day 60	Female	Control	37451474	30185888.04	80.6
205661	Day 60	Male	PCB	42711825	25383637.6	59.43
205662	Day 60	Male	PCB	51083060	28667813.27	56.12
205663	Day 60	Male	PCB	52924362	31617013.86	59.74
205664	Day 60	Female	PCB	34204550	27866446.89	81.47
205665	Day 60	Female	PCB	38012061	25076556.64	65.97
205666	Day 60	Female	PCB	46466576	23990693.19	51.63
205667	Day 5	Male	PBDE	37702982	29864532.04	79.21
205668	Day 5	Male	PBDE	36710976	28480375.18	77.58
205669	Day 5	Male	PBDE	40668682	32201462.41	79.18
205670	Day 5	Female	PBDE	38812848	30266258.87	77.98
205671	Day 5	Female	PBDE	44334680	34820457.67	78.54
205672	Day 5	Female	PBDE	37399137	28991811	77.52
205673	Day 5	Male	BPA	42838839	28008032.94	65.38
205674	Day 5	Male	BPA	37229752	28086124.91	75.44
205675	Day 5	Male	BPA	37048908	27897827.72	75.3
205676	Day 5	Female	BPA	37754168	27975838.49	74.1
205677	Day 5	Female	BPA	45358368	33456332.24	73.76
205678	Day 5	Female	BPA	47203966	35426576.48	75.05
205679	Day 60	Male	PBDE	43320532	34067266.36	78.64
205680	Day 60	Male	PBDE	37666661	29692628.87	78.83
205681	Day 60	Male	PBDE	33847431	24475077.36	72.31
205682	Day 60	Female	PBDE	37212705	28895665.43	77.65
205683	Day 60	Female	PBDE	39478024	30524408.16	77.32
205684	Day 60	Female	PBDE	38719254	28965873.92	74.81
205685	Day 60	Male	BPA	39244849	28303385.1	72.12
205686	Day 60	Male	BPA	39734472	30841897.17	77.62
205687	Day 60	Male	BPA	44871197	27860526.22	62.09
205688	Day 60	Female	BPA	35534684	27038341.06	76.09
205689	Day 60	Female	BPA	32575317	25294733.65	77.65
205690	Day 60	Female	BPA	42208643	28617459.95	67.8

Table S2-1. Day 5 Male PCGs

Common				Different		
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**	**Only BPA**	**Only BDE-99**	**Only PCB**
Slc17a4	Cyp2c29	Epor	Nat8f2	Prodh	Tspan32	Tat
Plk3	Phyhip	Cldn13	Ppp1r3g	Gstm3	Bcl11a	Hif3a
Cyp1a2	Inmt	Lpin1	Ddo	Cyp2a5	Tspan33	Igfbp3
Ifit1	Cdc6	Tmem14c		Pls3	Cd79a	Per1
Lars2	Prg2	Tff3		Pyy	Eno2	Ttc8
Isg15	A2m	Aqp4		Abcc3	Ctse	Rida
Pnliprp1	Clec2d	Slc4a9		C9	Aqp1	Acy3
Ugt3a2	Cyp2b10	Marco		Gpt	Prdx2	Got1
Cyp2c50	Mt2	Zbp1		Cela1	Spib	Cfh
Cyp2c54	Mt1	Car1		Slc10a2	Pabpc4	Hdc
Cyp2a4	Dclk3	Smad9		Cela3b	Csf1	Efna1
	Dtl	Gbp3		Tff2	E2f4	Cyp4a14
	Baat	Inhbb		Cyp4f14	Xk	Sult2a8
	Prss2	Gbp7		Aldh1a7	Cd5l	Adamtsl2
	Apol9a	Slc7a1		Pnliprp2	Tubb1	Slc17a3
	Serpina6	Atp1b2		Fasn	Cd274	Serpine1
	Apol9b	Hist1h1a		Cdhr5	Irf1	Saa4
	Rdh16	H2afx		Cyp27a1	Iyd	Rps2
	Prss3	Junb		Pigr	Slc16a10	Slc25a47
	Try10	Iigp1		Car3	Myb	Catsperg1
	Ccdc162	Klf1		Tdo2	Slc22a4	D630039A03Rik
		Hist1h1b		Atp6v0d2	Btg2	Cyp4a32
		Hist1h4c		Orm3	Btnl10	Cyp2d9
		Hist1h2bk		Prkaa2	Rrm2	Prok1
		Hist1h4k		Dck	Itgb3	Rtl1
		Cyp4a10		Mug2	Sptb	
		Ppp1r3c		Slco1a4	Rdh12	
		Hist1h3a		Csrp3	Lect2	
		Hist1h3b		Slco2b1	Lpcat1	
		Hist1h2bf		Chic1	Rgcc	
		Hist1h3e		Ido2	Fabp2	
		Hist1h4f		Ucp1	Ache	
		Hist1h2bj		Ces1f	Pla2g7	
		Hist1h4m		Nudt7	Rhag	
		Hist1h3c		Ctrl	Ift140	
		Cited4		Tmed6	Dusp1	
		Hist3h2a		Apoc3	Rfx2	
		Hist1h2ao		Cyp2c38	Psmb8	
		Hist1h2bn		Serpini2	Spire1	
		Hist4h4		Dio1	Rab3il1	
				Thrsp	Pacs1	
				Ugt2a3	Papss2	
				Scd1	Smarca2	
				Lrg1	Ehbp1l1	
				Adh4	Fermt3	
				Cyp7b1	Fn3k	
				Mocos	Mettl7b	
				Rgl3	Hsd17b6	
				Gstm2	Ifitm3	
				Cyp2b13	6030468B19Rik	
				Ildr2	Il1rl1	
				Myh6	Stat1	
				Slco1a1	Tnnt2	
				Gck	Pycr2	
				Adamts16	Spta1	
				Apon	Rgs5	
				Epx	Gfi1b	
				Slc22a30	Slc43a3	
				Aldh1a1	Rbm38	
				Slc22a26	Car2	
				Lipg	Samhd1	
				Mug1	Gbp2	
				Tnnt3	Hemgn	

Table S2-2. Day 5 Male lncRNAs

Common			
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**
Gm15564	A730089K16Rik	Pip5k1bos	Gm45724
		Egfros	

Different		
Only BPA	**Only BDE-99**	**Only PCB**
Notumos	Gm12000	Gm4117
9630013D21Rik	AW112010	Gm26881
Gm13775	Gm11131	A430010J10Rik
Gm15611	Mir142hg	Gm47320
Gm12909	Gm15816	
Xist	Gm20406	
Hectd2os	Gm20456	
4732419C18Rik	Redrum	
C730036E19Rik	9330175E14Rik	
Gm37273	Gm26762	
Gm43525	1700120K04Rik	
Gm43605	Gm28967	
Gm6135	Gm28177	
Gm44662	Gm10766	
Gm47077	Gm42884	
1810028F09Rik	Gm42867	
4930402D18Rik	Gm43051	
Gm49431	Gm44005	
4930478M13Rik	Gm45193	
AC113006.1	Gm34095	
	Gm49512	

Table S2-3. Day 5 Female PCGs

Common			
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**
Cd274	Cpb1		Folr1
Aqp4	Prg2		Lars2
Rgs16	2210010C04Rik		Ttn
Pax6	Pnliprp1		
Gbp2	Epx		
	Gm5771		
	Ear6		
	Gm10334		
	Gm8113		

Different		
Only BPA	**Only BDE-99**	**Only PCB**
Sez6	Hbq1a	Afap1l2
Kcnq2	Rorc	Stat1
Eef1a2	A2m	Il1b
Hsd17b6	Cyp2b10	Kap
Neb	Ctrl	Scd1
Stmn3	Apoa4	Syngr4
Tnni2	Cyp1a2	Serpina3g
Mt2	Cyp2c37	Jun
Mt1	Cyp2c50	Gm21320
Hrc	Prss2	
Sln	Hist1h2bg	
Tubb2b	Cyp2c54	
Gprin3	Hist1h2ae	
Cmya5	Hist1h2bj	
Cyp2f2	Hist4h4	
Arhgef33	Hist1h2bm	
Fxyd2		
Obscn		
Cav3		
Ear2		

Table S2-4. Day 5 Female PCGs

Common				Different		
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**	**Only BPA**	**Only BDE-99**	**Only PCB**
Gm13267	Gm15883	Gm12602	Gm28177	Gm15632	Gm16161	Gm16283
Gm13523	Mir124a-1hg	Gm17210		Gm15564	Gm17111	1700122E12Rik
Gm44787	Gm45081			Gm14225	Gm28644	4930518C09Rik
				Gm12238	Gm34655	Gm37899
				Gm20069	Gm48757	Gm37336
				Gm28513	Gm48495	Gm17590
				Gm28535	1810028F09Rik	Gm42884
				Gm38225		
				Gm37008		
				Gm43189		
				Gm44292		
				Gm44877		
				Gm48311		
				A630019I02Rik		

Table S2-5. Day 60 Male PCGs

Common				Different		
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**	**Only BPA**	**Only BDE-99**	**Only PCB**
Igfbp1	Tspan32	Ppard	Bcl6	Alox12	Itgb2	Tnnc2
Ckmt2	Bcl11a	Dusp1	Pnliprp2	Tubb5	Mx1	Lpin1
Fasn	Mmp14	Pcsk9	Efna1	Spag5	Gm2a	Cela1
Cox8b	Uhrf1	Reg1	Ctrl	Inmt	Haao	Sik1
Rgs16	Col1a1	Mup19	Rnase1	Sst	Cyp51	Slc25a25
Acss2	Tspan33	Mup18	Zg16	Mthfd2	Gstt1	Mfsd2a
Pmvk	Slc1a5		Try4	Cdc6	Smo	Spp1
Tpm2	Unc119		Myh1	Baiap2l2	Ltbp2	Ckm
Ccdc88a	Peg3		Hba-a2	Ikzf1	Snrpd1	Hmgn5
Myh2	Rgs19		Sult2a1	Vnn3	Mcm2	Tsc22d3
Thrsp	Tgfb1			Ube2o	Cyp2c29	Rrp12
Cyp2b9	Prkar2b			Ccdc88c	Slc25a1	Lars2
Acacb	Hmgn2			Rgcc	Gstm3	Nr0b2
Ttn	Dnmt1			Spry2	Asf1b	Hrc
Hbb-bs	Ctse			Rogdi	Fbln1	Egr1
Hist1h1d	Sgce			Slc15a2	Atp1a2	Pnlip
Myh4	Hspb1			Kcnk5	Stx1a	Zmat1
Fdps	Cd44			Epb41l3	Pou2f2	Jun
Tnnt3	Spc25			Myo1f	Acaa1b	Junb
Hba-a1	Nid1			Psat1	Plin5	Fabp1
Hbb-bt	Mcm5			Ms4a6d	Tppp3	Obscn
Cyp2a4	Hmox1			Aldh18a1	Actn1	Cyp26b1
Gm21320	Igf1r			Arhgap19	Cd83	Tnnt1
	Mmp8			Meig1	Gzmb	Zbtb16
	Slc4a1			Frmd4a	Cd5l	Myoz1
	Pola1			Ccdc3	Celsr1	Sult3a1
	Krt23			Elf5	Cd274	3425401B19Rik
	Pole			Mknk1	Kpna2	Mafb
	Dennd2c			Extl1	Sparc	Cyp3a41a
	Ubc			Kcnab2	Slc17a8	
	Cldn13			Cgref1	Myb	
	Apol7a			Ppbp	Rfx4	
	Psen2			Gstk1	Ndufs7	
	Gltp			Atp2b2	Ddc	
	Kif11			Cyp2b10	E2f7	
	Cybb			Sema4b	Rsad2	
	Ager			Coro1a	Cep112	
	Lpl			Pak1	Itgb4	
	Qdpr			Gata1	Abcc3	
	Ncf1			Slc38a5	Acly	
	Tubb1			Renbp	Adam11	
	Brca1			Gins3	Fut8	
	Atad5			Cdh11	Vrk1	
	Zfp334			Hmbs	Trip13	
	Birc5			Nnmt	Hmgcr	
	Slc13a3			Cdc25a	Emb	
	E2f2			Dclk3	Fst	
	Arid3a			Igdcc4	Dnajc9	
	Plagl1			Prr5l	Gpr65	
	Cdk1			Pygb	Epsti1	
	Ifngr1			Serpini2	Scara5	
	Plek			Neu3	Bora	
	Slc1a4			Ins1	Npr3	
	Dock2			Palm	Sqle	
	Grb10			Hk1	Oplah	
	Hmmr			Atp8a1	Gbe1	
	Cyfip2			Dusp8	Sdf2l1	
	Btg2			Higd1a	Ccdc14	
	Tspan13			Pik3cd	Adipoq	
	Rrm2			Plcb2	Adamts1	
	Itgb3			Rcsd1	Enah	
	Atp2a3			Hspb8	Fmnl3	
	Rflnb			Gck	Racgap1	

Table S2-5. D60 Male PCGs

	Top2a		
	Efcab11		
	Syk		
	Lpcat1		
	4930452B06Rik		
	Diaph3		
	Esco2		
	Dmtn		
	Cmbl		
	Sybu		
	Atad2		
	Sla		
	Parvb		
	Gpt		
	Mcm4		
	Tfrc		
	Fstl1		
	Samsn1		
	Stfa2		
	Sult1c2		
	Cdca3		
	Thbs2		
	Pla2g7		
	Tnfrsf21		
	Ndc80		
	Qpct		
	Spink1		
	Lox		
	Me2		
	Lmnb1		
	Fbn2		
	Anxa1		
	Incenp		
	Fam111a		
	Fen1		
	Aldh1a7		
	Stambpl1		
	Kif20b		
	Slc25a45		
	Ehbp1l1		
	Fermt3		
	Cd63		
	Adam8		
	Cdhr5		
	Plk4		
	Clec3b		
	Sema4c		
	Ptpn18		
	Bard1		
	Obsl1		
	Inpp5d		
	Spp2		
	Mcm6		
	Marco		
	Atp2b4		
	Lamc1		
	Spta1		
	Apcs		
	Cenpf		
	Nuf2		
	Apbb1ip		
	Lcn2		
	Col5a1		
	Gsn		
	Ly75		
	Il1rn		

Cxcr4	Slc17a9	
Sh3tc2	Acat2	
Selplg	Smoc2	
Tmprss11f	Cyp4f13	
Tsku	Fkbp5	
Suox	Cyp4f14	
Arhgef39	Aqp4	
Kcnt2	Ttc39c	
Lipg	Cabyr	
Sytl5	Spire1	
Mia3	Ppic	
Adap1	Cep192	
Fxyd3	Tm7sf2	
Gm5771	Yif1a	
Nfe2	Gpam	
Csf2ra	Hhex	
H2-Q7	Hells	
Serpina6	Cyp2c55	
Ppp1r3c	Cyp2c39	
Hist1h4m	Afap1l2	
Hist1h2an	Loxl4	
Tmem200b	Scd2	
Sult2a6	Pitx3	
Sult2a2	Prim1	
Gm10334	Shmt2	
Try10	Tyms	
Amy2a5	Hk3	
Zfp808	Snca	
Gm8113	Sgk3	
Hist2h4	Gsta3	
	Slc40a1	
	Npas2	
	Gls	
	Cyp27a1	
	Ptprc	
	Glul	
	Kif18a	
	Ccdc34	
	Sema6d	
	Rad51	
	Knstrn	
	Spred1	
	Zbp1	
	Ahcy	
	Map1lc3a	
	Postn	
	Mme	
	Hsd3b1	
	Ifi44	
	Cks1b	
	Rorc	
	Cyp7a1	
	Gbp3	
	Casp8ap2	
	Anp32b	
	Aco1	
	Npr2	
	Prkaa2	
	Ttc39a	
	Usp1	
	Plk3	
	Nasp	
	Rhd	
	Cdca8	
	Rpa2	
	Per3	

Table S2-5. D60 Male PCGs

	Itga4		
	Cers6		
	Prg2		
	Nusap1		
	Knl1		
	Smox		
	Pcna		
	Cd93		
	Tpx2		
	E2f1		
	Aurka		
	Rbm38		
	Fabp5		
	Car2		
	Rbl1		
	Fam83d		
	Ocstamp		
	Ect2		
	Nbea		
	Gstm4		
	S100a11		
	Vcam1		
	Cyp2u1		
	Iqgap3		
	Cyr61		
	Gbp2		
	Smc2		
	Zfp618		
	Tnc		
	Cyp4a31		
	Tal1		
	Stmn1		
	Cdk14		
	Fam126a		
	Mfn2		
	Khk		
	Cenpa		
	Abcg3		
	Aacs		
	Dtx1		
	Eln		
	Asns		
	A2m		
	Art4		
	Arhgdib		
	Kcnj8		
	Rad18		
	Mfge8		
	Plekhb1		
	Slco2b1		
	Far1		
	Lyve1		
	Tead2		
	Cdr2		
	Rrm1		
	Mki67		
	Dock11		
	Rbm3		
	Itm2a		
	Serpina7		
	Flna		
	Gpm6b		
	Dusp9		
	Morc4		
	Ptpn7		
	Slc25a4		

	Prkcz	
	Cenpc1	
	Cdc7	
	Plac8	
	Dck	
	Cit	
	Mmab	
	Slc46a3	
	Ezh2	
	Cbx3	
	Mad2l1	
	Nat8	
	Bmp10	
	Aldh1l1	
	Olr1	
	Csrp3	
	Plin1	
	Nox4	
	Tyrobp	
	Aqp8	
	Trim30a	
	Ebp	
	Cenpi	
	Adgrg2	
	Nsdhl	
	Gas6	
	Ank1	
	Ido2	
	Fgl1	
	Msmo1	
	Snx20	
	Gpt2	
	Tecr	
	Mmp15	
	Cyb5b	
	Nectin1	
	Apoc3	
	Cyp1a2	
	Mb21d1	
	Gsta4	
	Me1	
	Cyp2c38	
	Npat	
	Rnf125	
	Armcx1	
	Arhgap39	
	Sfxn5	
	Atp7a	
	Brip1	
	Exph5	
	Chst11	
	BC030867	
	Dio1	
	Tespa1	
	Tjp3	
	Arl4d	
	G2e3	
	Melk	
	Fam110c	
	Leap2	
	Kif15	
	C1qc	
	C1qb	
	Lrg1	
	Icam1	
	Cdkn1c	

Table S2-5. D60 Male PCGs

	Mylk3		
	Ces1f		
	Mt2		
	Mt1		
	Cotl1		
	Bco1		
	Apoa4		
	Kif23		
	Pkm		
	Pstpip1		
	Ngp		
	Chsy1		
	Slc16a1		
	Adamts15		
	Asprv1		
	Aspm		
	Jcad		
	Fancd2		
	Ypel4		
	Vav1		
	Ccnd3		
	Loxl2		
	Polq		
	Slc25a37		
	Flvcr2		
	Trim59		
	Plcg2		
	Ppp1r18		
	Dusp5		
	Grip1		
	Ncaph		
	Ncapd3		
	Pdk3		
	1810055G02Rik		
	Fignl1		
	Pcdh17		
	Cerk		
	Ints6l		
	Hist1h1c		
	Anln		
	Rab8b		
	Inhbb		
	Trim58		
	Mfsd2b		
	Rims2		
	Dtl		
	Dlgap5		
	Adgrl3		
	Ckap2		
	Sirpa		
	Tlcd2		
	Camp		
	Cyp3a16		
	Atp5j2		
	Pkhd1l1		
	Gcnt1		
	Fam117a		
	Prc1		
	Ppp1r9b		
	Akna		
	Orm1		
	Abhd2		
	Isg20		
	Fndc3b		
	Igfbp2		
	Neil3		

	Themis2	
	Mbl1	
	Vopp1	
	Adh4	
	Ninj1	
	Cntln	
	Plekhg6	
	Fam198a	
	Ncapd2	
	Rgs4	
	Susd4	
	Colec10	
	Dock10	
	Elovl3	
	Sema6c	
	Stx11	
	Mreg	
	Ppl	
	Cyp7b1	
	Sdr9c7	
	Gbp7	
	Gstm2	
	Ildr2	
	St8sia4	
	Ppp1r13l	
	Tmem205	
	Lrit1	
	Adgrf1	
	B4galnt3	
	Serpina3g	
	Serpina12	
	Amot	
	Oasl1	
	Mvk	
	Zfand4	
	Reln	
	Ifi209	
	Filip1l	
	Mdga1	
	S100a1	
	Tlr7	
	Zfp36	
	Insig1	
	Mms22l	
	Cavin2	
	Ankle1	
	AI464131	
	Bdh1	
	Bst2	
	Fam83h	
	Ppp1r3b	
	Tet1	
	Paxx	
	Bex4	
	Rarres1	
	Bex1	
	Slc25a44	
	Synpo2	
	Cyp8b1	
	Adra1b	
	Vstm4	
	Olfml1	
	Vtcn1	
	Nup160	
	Tceal8	
	Apon	

Table S2-5. D60 Male PCGs

	Mmd2		
	Myo9a		
	Mocos		
	Mrap		
	Thbs1		
	Ggt6		
	Pck2		
	Ccdc8		
	Arhgap11a		
	Slc7a1		
	Cox6a1		
	Trem3		
	Enc1		
	Lad1		
	Fhdc1		
	Mcm3		
	S100a10		
	Ncapg2		
	Tmcc2		
	Klhl23		
	Ammecr1		
	Cilp		
	Specc1		
	Tnfrsf14		
	Grap2		
	Clspn		
	Cux2		
	Tceal9		
	Id1		
	Bex2		
	Nrep		
	Greb1l		
	Klhl6		
	Palb2		
	Defb1		
	4930503L19Rik		
	Cenpe		
	Adrb2		
	Ifit2		
	Rbp1		
	Bex3		
	Ar		
	Ticrr		
	Ckap4		
	Cd24a		
	Samd14		
	Cd300lf		
	Ccdc88b		
	Cdca4		
	Marcksl1		
	Gm4737		
	Ckap2l		
	Igf2		
	Arhgap30		
	Cdca2		
	Sorl1		
	Hist1h1a		
	Tmsb4x		
	Armcx4		
	H2afx		
	Tcf19		
	Gen1		
	Zgrf1		
	Spn		
	Usp29		
	Hist1h1e		

	Ccdc171	
	Robo2	
	Zfp608	
	Map1b	
	Cyp2f2	
	Aldh1a1	
	9130230L23Rik	
	Cyp2c50	
	Fbxo6	
	Lig1	
	Retsat	
	Nfil3	
	Ces1d	
	AB124611	
	Nsd2	
	Prtn3	
	Gstm1	
	Idi1	
	Tubb2a	
	Zfp958	
	Samd5	
	H2-K1	
	Ppp1r1b	
	Cfd	
	Ugt2b38	
	Slc39a4	
	Tnfrsf11b	
	Dpp3	
	Ifi27	
	Dhrs3	
	Cyp4a12a	
	Rdh11	
	Slc22a7	
	Cyp2d9	
	Cep152	
	Selenbp2	
	Gm5096	
	Rdh16	
	Tmem19	
	Fcho1	
	Sp110	
	Ccnd1	
	Lrrc8b	
	Treml2	
	Acot1	
	Bhlhb9	
	Ifi204	
	Ifi207	
	Mup11	
	Adh1	
	Mex3a	
	Cyp4a12b	
	Mup16	
	Mup1	
	Mup9	
	Mup6	
	Ccdc82	
	Haus3	
	Gm5483	
	Rtl1	
	Mup13	
	Col6a5	
	Hmgcs1	
	Cyp2d34	
	Mup12	
	Cyp2d10	

Table S2-5. D60 Male PCGs

	Wfdc21		
	Sox12		
	Gypa		
	Mest		
	Akr1b7		
	Nrros		
	Hunk		
	Klf1		
	Cklf		
	Cyp3a44		
	Atpif1		
	Slc8a1		
	Hmgb2		
	Stfa3		
	Afp		
	Gpc3		
	Abcd2		
	Clca3a1		
	B4galt6		
	Fry		
	Ces1g		
	Ebf1		
	Chst3		
	Apol9a		
	Lepr		
	Gstp3		
	Espl1		
	Hist1h2bg		
	Dhcr7		
	Gpc6		
	Hist1h1b		
	Slc14a1		
	Fcgr3		
	Stfa2l1		
	Adamts14		
	Hist1h4a		
	Atp8b4		
	Gstp1		
	Nol4l		
	Cep128		
	Ces2c		
	Ces1e		
	Hist1h2af		
	Nsl1		
	Prss1		
	Hist1h2ak		
	Aox1		
	Ethe1		
	Hist1h4k		
	Rnasel		
	Hes6		
	Nipal1		
	Cyp2c54		
	Capn6		
	Hist1h4j		
	Cyp2d40		
	Apol9b		
	Gstm6		
	Hist2h2ac		
	Selenbp1		
	Hist1h3a		
	Hist1h3b		
	Hist1h3e		
	Hist1h4f		
	Hist1h2bj		
	Hist1h3c		

	Mup15	
	Mup17	
	Kctd12	
	Gbp6	
	Gbp5	
	Gm4756	
	A630089N07Rik	

Table S2-5. D60 Male PCGs

	Marcks		
	Slfn9		
	Prok1		
	Tlnrd1		
	Mpst		
	Ccnf		
	Fam84b		
	Ear2		
	Slfn2		
	Zcchc3		
	Hist1h2bb		
	Sox4		
	Acsf2		
	Hist3h2a		
	C7		
	Nat8f5		
	Ulbp1		
	Spaca6		
	Slfn14		
	Apold1		
	Ccdc71l		
	Eid1		
	Cyp2a22		
	Peg10		
	Hist1h2bl		
	Itpripl2		
	Hist1h2bn		
	Hist4h4		
	Cdkn2d		
	Tcf24		
	Hist1h3f		
	Hist1h3i		
	Hist2h2bb		
	Hist1h2bm		
	Hist1h2bh		
	Eppk1		

Table S2-6. Day 60 Male lncRNAs

	Common				Different	
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**	**Only BPA**	**Only BDE-99**	**Only PCB**
Myhas	H19	Gm13938	Gm37804	5830444B04Rik	Gm9869	Xist
Gm28872	Meg3	Gm28967	Gm31172	C230037L18Rik	Gm830	1700023H06Rik
	3930402G23Rik	Gm38204	1810028F09Rik	Gm12847	Egfros	Gm38070
	Gm10143	Gm43314		Gm15736	Gm14493	Gm44036
	F630028O10Rik	Snhg1		Gm13558	Gm12905	Gm44549
	Gm15611	Gm48342		Gm15345	1700054M17Rik	Gm32872
	Gm11505	Gm49540		Gm11773	Gm15998	4930544F09Rik
	Gm15816			Gm13381	Nudt12os	AC154912.3
	Gm13431			Gm16549	Gm15883	
	Gm17300			D630002J18Rik	AI662270	
	Gm20628			Gm26971	Gm11586	
	Redrum			Lockd	Gm15845	
	Rian			F830112A20Rik	Gm16568	
	4930534D22Rik			Gm42777	Gm20507	
	Snhg4			Gm44901	Gm26778	
	Gm28857			Gm38416	Gm10605	
	Gm37233			Gm47465	Gm28505	
	Gm38346			Gm48199	Gm38377	
	Gm37527			CT009718.2	Gm37905	
	Gm43581				Gm37159	
	Gm42993				A730089K16Rik	
	AI506816				Gm43323	
	Gm42992				Gm8239	
	Gm43188				Gm45053	
	Gm44371				2610306O10Rik	
	Gm44089				Gm44623	
	Gm43864				Gm44732	
	Gm39041				Gm32540	
	Gm44639				Gm44913	
	Gm44862				Gm42047	
	Gm45240				BC049987	
	Gm39929				Gm32468	
	AC160637.1				Gm48478	
					Gm47737	
					D430020J02Rik	
					Gm31508	
					Ndufb1-ps	
					Gm10865	
					5730414N17Rik	

Table S2-7. Day 60 Female PCGs

Common				Different		
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**	**Only BPA**	**Only BDE-99**	**Only PCB**
Igfbp1	Hsd17b6	Igfbp5	Lcn2	Tspan32	Cdh1	Mfsd10
Rgs16	Fabp5	Gck	Plxna3	Mxd1	Atp1a2	A1bg
Lars2	1810055G02Rik	Onecut1	Egr1	Uhrf1	Id3	Foxp2
Cyp3a16	Cox6a1	5430402E10Rik		Slc1a5	Rps15a	Saa4
Cyp3a44	Hbb-bs	Pnlip		Unc119	Rpl19	Tmed9
Hist2h2ac	Hist1h1d	Cyp3a41a		Peg3	Phlda1	Capn11
Cyp3a41b	Hba-a1			Dbf4	Lpin1	Hist1h2bk
Gm14744				Prkar2b	Bcl6	Ethe1
				Dnmt1	Slc10a2	Sult3a1
				Spc25	Spry4	Sult2a2
				Mcm5	Mbd1	Mup14
				Slc4a1	Cox8b	Mup7
				Pole	Acmsd	Mup10
				Cldn13	Pfkfb3	Sult2a1
				Tnfrsf13b	Gsn	
				Kif11	Acss2	
				Lpl	Hao2	
				Brca1	Pmvk	
				Birc5	Cyp4a14	
				Slc13a3	Bhlhe40	
				Ikzf1	Ucp1	
				E2f2	Mt2	
				Arid3a	Mt1	
				Cdk1	Tspoap1	
				Slc1a4	Arl4d	
				Grb10	Pim3	
				Hmmr	Klf10	
				Rrm2	Foxq1	
				Atp2a3	Atp5j2	
				Ube2o	Irs2	
				Aurkb	Hist1h1e	
				Top2a	Rdh9	
				Efcab11	Retsat	
				Diaph3	Spock2	
				Dmtn	Dhcr7	
				Atad2	Rex1bd	
				Tfrc	Fabp4	
				Stfa2	Cyp26b1	
				Racgap1	Rdh11	
				Ache	Gm10226	
				Thbs2	Ccnd1	
				Ndc80	Mafb	
				Aqp4	G6pc	
				Spire1	Zfp970	
				Ppic	Rps13	
				Psat1	Mup17	
				Incenp		
				Fen1		
				Kif20b		
				Fermt3		
				Plk4		
				Snca		
				Mcm6		
				Marco		
				Spta1		
				Cenpf		
				Nuf2		
				Fmo3		
				Prg2		
				Nusap1		
				Knl1		

Table S2-7. D60 Female PCGs

Tpx2
Aurka
Car2
Dsn1
Hsd3b1
Vcam1
Iqgap3
Kif2c
Cyp4a31
Tal1
Stmn1
Kcnab2
Eln
Add2
Gp9
Klrc1
Plk1
Cdr2
Mki67
Serpina7
Morc4
Ank1
Slit2
Slc25a4
Abcg4
Ccnb2
Kif23
Zwilch
Ngp
Troap
Igdcc4
Aspm
Ypel4
Slc25a37
Smc4
Ncaph
Fignl1
C530008M17Rik
Inhbb
Mfsd2b
Dlgap5
Wdhd1
Isg20
Neil3
Bub1b
Thbs1
Cyp2b13
Arhgap11a
Ccnb1
Mcm3
Ncapg2
Tmcc2
Specc1
Tceal9
Bex2
Fam129c
Sowaha
Cenpe
Bex3
Cd24a
Samd14
Mis18bp1
Tenm4
Ckap2l
Igf2

Table S2-7. D60 Female PCGs

Hist1h1a
H2afx
Spn
Akr1b7
Kcnn4
Stfa3
Afp
Gpc3
S100a9
Hist1h1b
Stfa2l1
Hist1h2af
Hist1h2ak
Jakmip1
Hist1h4k
Capn6
Hist1h4j
Hist1h4f
Hist1h2bj
Hist1h3c
Slfn9
Hba-a2
Prok1
Treml2
Hbb-bt
Hist1h2bb
Mup20
Mup19
Peg10
Hist1h2bn
Samd11
Hist1h3d
Hist1h3f
Hist2h2bb
Hist1h2bm

Table S2-7. Day 60 Female PCGs

Common			
All three chemicals	**BPA and BDE-99**	**BDE-99 and PCB**	**BPA and PCB**
	H19	Gm11670	
	Gm15564	Gm28086	
	Rian	Gm49076	
		AC154912.3	

Different		
Only BPA	**Only BDE-99**	**Only PCB**
Meg3	4930506C21Rik	1700054M17Rik
Gm10143	Gm11773	Gm20686
Gm15611	Gm17041	B930025P03Rik
Gm13388	Gm17300	Gm47921
Gm11505	Gm20649	
Gm15816	Snhg4	
Recql5os1	Gm28872	
Gm20628	Gm28592	
Redrum	Gm37159	
Gm29093	Gm38357	
Gm37899	Gm36638	
Gm37527	Gm37174	
Gm44366	Gm43314	
Gm43864	Gm43702	
Gm44732	Gm6135	
Gm39929	Gm43195	
1700022H01Rik	Snhg1	
Gm49189	Gm44646	
	Gm45424	
	Gm42047	
	Gm32017	
	AL732506.1	

Table S3-1. IPA Network
IPA Network

Network	Molecules in Network	Score	Focus Molecules
Day 5 Male BPA	Molecules in Network	Score	Focus Molecules
Drug Metabolism, Lipid Metabolism, Small Molecule Biochemistry	[illegible]	4.80E+01	23
Endocrine System Disorders, Gastrointestinal Disease, Immunological Disease	[illegible]	4.00E+01	20
Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	[illegible]	2.70E+01	15
Amino Acid Metabolism, Small Molecule Biochemistry, Drug Metabolism	[illegible]	2.50E+01	14
Amino Acid Metabolism, Small Molecule Biochemistry, Cellular Movement	[illegible]	2.50E+01	14
Lipid Metabolism, Small Molecule Biochemistry, Molecular Transport	[illegible]	1.80E+01	11
Tissue Morphology, Organ Morphology, Reproductive System Development and Function	[illegible]	1.60E+01	10
Day 60 Male BPA	Molecules in Network	Score	Focus Molecules
Cellular Assembly and Organization, Cell Cycle, DNA Replication, Recombination, and Repair	[illegible]	46	30
Cell Cycle, DNA Replication, Recombination, and Repair, Cellular Assembly and Organization	[illegible]	42	29
Cell Morphology, Hematological System Development and Function, Hematopoiesis	[illegible]	42	28
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Cell Cycle	[illegible]	42	28
Organ Morphology, Organismal Development, Reproductive System Development and Function	[illegible]	39	27
DNA Replication, Recombination, and Repair, Cell Cycle, Cellular Assembly and Organization	[illegible]	39	27
Post-Translational Modification, Cellular Movement, Nervous System Development and Function	[illegible]	33	24
Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	[illegible]	31	23
Cell Cycle, Cell Morphology, Cellular Function and Maintenance	[illegible]	29	22
Drug Metabolism, Small Molecule Biochemistry, Lipid Metabolism	[illegible]	23	19
Cell Cycle, Connective Tissue Development and Function, Embryonic Development	[illegible]	23	19
Cell Death and Survival, Connective Tissue Development and Function, Tissue Morphology	[illegible]	23	19
Auditory Disease, Hereditary Disorder, Neurological Disease	[illegible]	22	18
Cellular Assembly and Organization, Cellular Function and Maintenance, Tissue Development	[illegible]	22	18
Cancer, Hematological Disease, Immunological Disease	[illegible]	22	18
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Cell Cycle	[illegible]	20	17
Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	[illegible]	18	16
Small Molecule Biochemistry, Post-Translational Modification, Cell-To-Cell Signaling and Interaction	[illegible]	18	16
Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Dermatological Diseases and Conditions	[illegible]	16	15
Hereditary Disorder, Organismal Injury and Abnormalities, Skeletal and Muscular Disorders	[illegible]	16	15
Endocrine System Disorders, Gastrointestinal Disease, Hereditary Disorder	[illegible]	15	14
Lipid Metabolism, Small Molecule Biochemistry, Carbohydrate Metabolism	[illegible]	15	14
Carbohydrate Metabolism, Hereditary Disorder, Ophthalmic Disease	[illegible]	15	14
Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	[illegible]	15	14
Cancer, Dermatological Diseases and Conditions, Organismal Injury and Abnormalities	[illegible]	13	13
Day 5 Male BDE-99	Molecules in Network	Score	Focus Molecules
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Post-Translational Modification	[illegible]	4.90E+01	27
Drug Metabolism, Hematological Disease, Hereditary Disorder	[illegible]	4.40E+01	26
Cell Morphology, Molecular Transport, Connective Tissue Disorders	[illegible]	4.40E+01	25
Infectious Diseases, Antimicrobial Response, Inflammatory Response	[illegible]	3.40E+01	21
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Cellular Development	[illegible]	3.00E+01	19
Ophthalmic Disease, Organismal Injury and Abnormalities, Skeletal and Muscular Disorders	[illegible]	2.80E+01	18
Cell Death and Survival, Lipid Metabolism, Molecular Transport	[illegible]	2.10E+01	15
Cell-To-Cell Signaling and Interaction, Nervous System Development and Function, Cell Death and Survival	[illegible]	2.00E+01	14
Cell Morphology, Nervous System Development and Function, Neurological Disease	[illegible]	2.00E+01	14
Free Radical Scavenging, Small Molecule Biochemistry, Cell Morphology	[illegible]	1.80E+01	13
Cell Morphology, Hematological System Development and Function, Cell-To-Cell Signaling and Interaction	[illegible]	1.60E+01	12
Organismal Injury and Abnormalities, Renal Damage, Renal Tubule Injury	[illegible]	1.60E+01	12
Cellular Assembly and Organization, Cellular Compromise, Cell Cycle	[illegible]	1.60E+01	12
Cellular Compromise, Neurological Disease, Organismal Injury and Abnormalities	[illegible]	1.20E+01	10
Cardiovascular System Development and Function, Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance	[illegible]	1.10E+01	9
Inflammatory Response, Hematological System Development and Function, Tissue Morphology	[illegible]	1.10E+01	9
Auditory Disease, Auditory and Vestibular System Development and Function, Cardiovascular System Development and Function	[illegible]	2.00E+00	1
Cancer, Gastrointestinal Disease, Organismal Injury and Abnormalities	[illegible]	2.00E+00	1
Day 60 Male BDE-99	Molecules in Network	Score	Focus Molecules
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Post-Translational Modification	[illegible]	49	33
Cellular Assembly and Organization, Cell Morphology, Cellular Movement	[illegible]	44	31
Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	[illegible]	40	29
Cell Morphology, Immunological Disease, Amino Acid Metabolism	[illegible]	40	29
Cell Cycle, Cell Morphology, Cellular Assembly and Organization	[illegible]	40	29
Cell Cycle, Cellular Assembly and Organization, DNA Replication, Recombination, and Repair	[illegible]	37	28
Hematological Disease, Hereditary Disorder, Organismal Injury and Abnormalities	[illegible]	37	28
Cellular Assembly and Organization, Cellular Development, Neurological Disease	[illegible]	37	28
Connective Tissue Disorders, Hematological Disease, Organismal Injury and Abnormalities	[illegible]	33	26
DNA Replication, Recombination, and Repair, Cell Cycle, Cell Morphology	[illegible]	33	26
Cell Cycle, Cancer, Endocrine System Disorders	[illegible]	33	26
Cellular Development, Cellular Growth and Proliferation, Organ Development	[illegible]	31	25
Drug Metabolism, Energy Production, Lipid Metabolism	[illegible]	27	23
Cellular Assembly and Organization, Tissue Development, Cell-To-Cell Signaling and Interaction	[illegible]	26	22
Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	[illegible]	26	22
DNA Replication, Recombination, and Repair, Cancer, Cardiovascular Disease	[illegible]	26	22
Lipid Metabolism, Small Molecule Biochemistry, Hematological Disease	[illegible]	26	22
Drug Metabolism, Glutathione Depletion In Liver, Protein Synthesis	[illegible]	24	21
Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	[illegible]	24	21
Carbohydrate Metabolism, Connective Tissue Disorders, Organismal Injury and Abnormalities	[illegible]	22	20
Cardiovascular Disease, Tissue Development, Organismal Injury and Abnormalities	[illegible]	20	19
Cell Death and Survival, Cellular Assembly and Organization, Cellular Compromise	[illegible]	19	18
Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	[illegible]	19	18
Cellular Function and Maintenance, Hematological System Development and Function, Inflammatory Response	[illegible]	19	18
Drug Metabolism, Protein Synthesis, Neurological Disease	[illegible]	19	18
Day 5 Male PCB	Molecules in Network	Score	Focus Molecules
Lipid Metabolism, Small Molecule Biochemistry, Cardiovascular System Development and Function	[illegible]	5.40E+01	24
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Post-Translational Modification	[illegible]	3.20E+01	16
Cell Cycle, Embryonic Development, Developmental Disorder	[illegible]	2.90E+01	15
Small Molecule Biochemistry, Lipid Metabolism, Cardiovascular System Development and Function	[illegible]	2.40E+01	13
Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Cell Cycle	[illegible]	2.40E+01	13
Lipid Metabolism, Small Molecule Biochemistry, Carbohydrate Metabolism	[illegible]	9.00E+00	6
Cardiac Arrythmia, Cardiovascular Disease, Cardiovascular System Development and Function	[illegible]	2.00E+00	1
Auditory Disease, Auditory and Vestibular System Development and Function, Cardiovascular System Development and Function	[illegible]	2.00E+00	1
Cancer, Carbohydrate Metabolism, Cardiovascular Disease	[illegible]	2.00E+00	1
Day 60 Male PCB	Molecules in Network	Score	Focus Molecules
Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	[illegible]	41	19
Organ Development, Skeletal and Muscular System Development and Function, Organ Morphology	[illegible]	30	15
Cancer, Organismal Injury and Abnormalities, Reproductive System Disease	[illegible]	21	11
Cell-To-Cell Signaling and Interaction, Cellular Movement, Hematological System Development and Function	[illegible]	18	10
Carbohydrate Metabolism, Lipid Metabolism, Small Molecule Biochemistry	[illegible]	16	9
Cellular Movement, Skeletal and Muscular System Development and Function, Organismal Injury and Abnormalities	[illegible]	10	6
	Amy2b,amylase	2	1
Inflammatory Disease, Organismal Injury and Abnormalities	RNU12,snRNP	2	1
Cell-To-Cell Signaling and Interaction, Inflammatory Response, DNA Replication, Recombination, and Repair	Rpph1,TLR3,TLR9	2	1
Post-Translational Modification, Cell Cycle, Cellular Development	C10orf71,DCAF7,DYRK1A,DYRK1B,FNTA,FNTB	2	1

Table S3-2. Canonical Pathways p < 0.01

Day 5 Male BPA

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
Nicotine Degradation II	1.09E+01	-3	1.38E-01	CYP2B6,CYP1A2,UGT2A3,Cyp2c40 (includes others),CYP2C8,AOX1,UGT3A1,INMT,CYP2A6 (includes others)
PXR/RXR Activation	1.09E+01	NaN	1.38E-01	CYP2B6,GSTM1,CYP1A2,ALDH1A1,Aldh1a7,SCD,CYP2C8,ABCC3,CYP2A6 (includes others)
Nicotine Degradation III	9.83E+00	-2.828427125	1.43E-01	CYP2B6,CYP1A2,UGT2A3,Cyp2c40 (includes others),CYP2C8,AOX1,UGT3A1,CYP2A6 (includes others)
Melatonin Degradation I	7.78E+00	-2.645751311	1.08E-01	CYP2B6,CYP1A2,UGT2A3,Cyp2c40 (includes others),CYP2C8,UGT3A1,CYP2A6 (includes others)
Superpathway of Melatonin Degradation	7.55E+00	-2.645751311	1.00E-01	CYP2B6,CYP1A2,UGT2A3,Cyp2c40 (includes others),CYP2C8,UGT3A1,CYP2A6 (includes others)
Bupropion Degradation	7.09E+00	-2.236067977	2.00E-01	CYP2B6,CYP1A2,Cyp2c40 (includes others),CYP2C8,CYP2A6 (includes others)
Acetone Degradation I (to Methylglyoxal)	6.67E+00	-2.236067977	1.67E-01	CYP2B6,CYP1A2,Cyp2c40 (includes others),CYP2C8,CYP2A6 (includes others)
SPINK1 Pancreatic Cancer Pathway	6.54E+00	2.449489743	1.00E-01	PRSS1,CTRL,Prss1 (includes others),PRSS2,CELA3B,CELA1
Estrogen Biosynthesis	5.97E+00	-2.236067977	1.22E-01	CYP2B6,CYP1A2,Cyp2c40 (includes others),CYP2C8,CYP2A6 (includes others)
Retinoate Biosynthesis I	4.80E+00	-2	1.18E-01	RDH16,ADH1C,ALDH1A1,ADH4
Serotonin Degradation	4.60E+00	-2.236067977	6.49E-02	ADH1C,ALDH1A1,UGT2A3,UGT3A1,ADH4
SPINK1 General Cancer Pathway	4.55E+00	0.447213595	6.33E-02	PRSS1,Mt1,Mt2,Prss1 (includes others),PRSS2
LPS/IL-1 Mediated Inhibition of RXR Function	4.18E+00	NaN	3.14E-02	CYP2B6,GSTM1,ALDH1A1,Gstm3,CYP2C8,ABCC3,CYP2A6 (includes others)
Triacylglycerol Degradation	3.99E+00	-2	7.41E-02	PNLIPRP2,PNLIPRP1,Ces1b/Ces1c,LIPG
FXR/RXR Activation	3.58E+00	NaN	3.97E-02	BAAT,FASN,C9,SLC10A2,CYP27A1
Xenobiotic Metabolism Signaling	3.41E+00	NaN	2.36E-02	CYP2B6,GSTM1,CYP1A2,ALDH1A1,Gstm3,CYP2C8,ABCC3
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	3.26E+00	NaN	2.50E-01	IDO2,TDO2
Ethanol Degradation II	3.22E+00	NaN	8.11E-02	ADH1C,ALDH1A1,ADH4
Noradrenaline and Adrenaline Degradation	3.11E+00	NaN	7.50E-02	ADH1C,ALDH1A1,ADH4
Retinol Biosynthesis	3.05E+00	NaN	7.14E-02	PNLIPRP2,PNLIPRP1,LIPG
Thyroid Hormone Metabolism II (via Conjugation and/or Degradation)	3.02E+00	NaN	6.98E-02	UGT2A3,UGT3A1,DIO1
TR/RXR Activation	3.00E+00	NaN	4.08E-02	THRSP,UCP1,FASN,DIO1
PPARα/RXRα Activation	2.82E+00	-2.236067977	2.69E-02	Cyp2c54 (includes others),Cyp2c40 (includes others),CYP2C8,PRKAA2,FASN
Bile Acid Biosynthesis, Neutral Pathway	2.82E+00	NaN	1.54E-01	BAAT,CYP27A1
RAR Activation	2.78E+00	NaN	2.63E-02	RDH16,ADH1C,ALDH1A1,Aldh1a7,ADH4
NAD biosynthesis II (from tryptophan)	2.70E+00	NaN	1.33E-01	IDO2,TDO2
Aryl Hydrocarbon Receptor Signaling	2.41E+00	NaN	2.82E-02	GSTM1,CYP1A2,ALDH1A1,Gstm3
Thio-molybdenum Cofactor Biosynthesis	2.35E+00	NaN	1.00E+00	MOCOS,
Apelin Adipocyte Signaling Pathway	2.25E+00	NaN	3.75E-02	GSTM1,UCP1,PRKAA2
Tryptophan Degradation III (Eukaryotic)	2.25E+00	NaN	8.00E-02	IDO2,TDO2
Hepatic Cholestasis	2.23E+00	NaN	2.50E-02	CYP7B1,SLC10A2,ABCC3,CYP27A1
Alanine Biosynthesis II	2.05E+00	NaN	5.00E-01	GPT,
Alanine Degradation III	2.05E+00	NaN	5.00E-01	GPT,
Fatty Acid Biosynthesis Initiation II	2.05E+00	NaN	5.00E-01	FASN,
Palmitate Biosynthesis I (Animals)	2.05E+00	NaN	5.00E-01	FASN,
Glutathione-mediated Detoxification	2.04E+00	NaN	6.25E-02	GSTM1,Gstm3

Day 5 Female BPA

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
SPINK1 Pancreatic Cancer Pathway	3.84E+00	NaN	5.00E-02	Prss1 (includes others),CPB1,2210010C04Rik
SPINK1 General Cancer Pathway	3.49E+00	NaN	3.80E-02	Mt1,Mt2,Prss1 (includes others)

Day 60 Male BPA

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
Cell Cycle Control of Chromosomal Replication	7.05E+00	NaN	1.96E-01	TOP2A,POLA1,CDK14,POLE,MCM3,MCM4,MCM6,CDC6,PCNA,MCM5,CDK1
DNA Methylation and Transcriptional Repression Signaling	5.91E+00	NaN	2.35E-01	HIST1H4D,HIST1H4K,DNMT1,HIST1H4C,HIST1H4H,HIST2H4B,HIST1H4B,HIST1H4J
PXR/RXR Activation	4.57E+00	NaN	1.38E-01	Ins1,PCK2,IGFBP1,CYP2B6,PRKAR2B,Aldh1a7,CYP3A5,SULT2A1,CYP2A6 (includes others)
NER Pathway	4.37E+00	-1.666666667	1.07E-01	TOP2A,HIST1H4D,POLA1,HIST1H4K,HIST1H4C,POLE,HIST1H4H,HIST2H4B,PCNA,HIST1H4B,HIST1H4J
Retinol Biosynthesis	4.20E+00	0.377964473	1.67E-01	PNLIPRP2,Ces1e,RBP1,LPL,Ces1g,BCO1,LIPG
Atherosclerosis Signaling	4.15E+00	NaN	9.38E-02	TNFRSF14,CXCR4,APOA4,ALOX12,IL1RN,TGFB1,SELPLG,LPL,ITGA4,COL1A1,PLA2G7,VCAM1
Mitotic Roles of Polo-Like Kinase	3.71E+00	1.133893419	1.21E-01	KIF23,TGFB1,ESPL1,CDC25A,PRC1,PLK4,KIF11,CDK1
Leukocyte Extravasation Signaling	3.61E+00	3.31662479	7.04E-02	SPN,NCF1,Cldn13,CD44,VAV1,VCAM1,PLCG2,CXCR4,PIK3CD,SELPLG,MMP8,ITGA4,ITGB3,CYBB,MMP14
Transcriptional Regulatory Network in Embryonic Stem Cells	3.49E+00	NaN	1.30E-01	HIST1H4D,HIST1H4K,HIST1H4C,HIST1H4H,HIST2H4B,HIST1H4B,HIST1H4J
Estrogen-mediated S-phase Entry	3.44E+00	1.341640786	1.92E-01	E2F2,CDC25A,E2F1,RBL1,CDK1
LPS/IL-1 Mediated Inhibition of RXR Function	3.40E+00	NaN	6.73E-02	CHST3,SMOX,CYP4A11,ALDH18A1,GSTK1,SULT1C2,IL1RN,CYP2B6,CYP3A5,GSTM4,FABP5,SULT2A1,GSTP1,Cyp2a12/Cyp2a22,CYP2A6 (includes others)
Role of CHK Proteins in Cell Cycle Checkpoint Control	3.34E+00	-1	1.23E-01	BRCA1,E2F2,CDC25A,E2F1,CLSPN,PCNA,CDK1
Actin Cytoskeleton Signaling	3.24E+00	0.632455532	6.49E-02	MYH1,MYH2,FLNA,PAK1,MYLK3,VAV1,Ins1,IQGAP3,PIK3CD,MYH4,GSN,ITGA4,CYFIP2,DIAPH3,TTN
Hepatic Fibrosis / Hepatic Stellate Cell Activation	3.17E+00	NaN	6.99E-02	MYH1,MYH2,TGFB1,COL1A1,LEPR,COL5A1,VCAM1,IGF2,A2M,IGF1R,IFNGR1,PROK1,MYH4
Acetone Degradation I (to Methylglyoxal)	3.14E+00	0.447213595	1.67E-01	CYP2B6,CYP2U1,CYP4A11,CYP3A5,CYP2A6 (includes others)
Protein Kinase A Signaling	3.06E+00	0.942809042	5.26E-02	DUSP8,MYH2,TGFB1,FLNA,PRKAR2B,PLCB2,CDC25A,Hist1h1e,MYLK3,PLCG2,PTPN18,HIST1H1C,HIST1H1D,PYGB,DUSP5,PPP1R3C,MYH4,DUSP9,SIRPA,TTN,PTPN7
Agranulocyte Adhesion and Diapedesis	3.05E+00	NaN	6.77E-02	MYH1,MYH2,Cldn13,VCAM1,Ppbp,CXCR4,CKLF,IL1RN,MYH4,SELPLG,MMP8,ITGA4,MMP14
GADD45 Signaling	3.00E+00	NaN	2.11E-01	CCND3,BRCA1,PCNA,CDK1
Cell Cycle: G1/S Checkpoint Regulation	2.92E+00	-0.816496581	1.04E-01	CCND3,TGFB1,CDKN2D,E2F2,CDC25A,E2F1,RBL1
Granzyme A Signaling	2.91E+00	NaN	2.00E-01	HIST1H1C,HIST1H1D,HMGB2,Hist1h1e
Calcium Transport I	2.82E+00	NaN	3.00E-01	ATP2A3,ATP2B2,ATP2B4
Superpathway of Melatonin Degradation	2.81E+00	1.133893419	1.00E-01	CYP2B6,SMOX,CYP2U1,CYP3A5,SULT2A1,CYP2A6 (includes others),SULT1C2
Granulocyte Adhesion and Diapedesis	2.80E+00	NaN	6.67E-02	HSPB1,CXCR4,CKLF,IL1RN,SELPLG,MMP8,Cldn13,ITGA4,ITGB3,VCAM1,Ppbp,MMP14
Aryl Hydrocarbon Receptor Signaling	2.59E+00	0.447213595	7.04E-02	CCND3,HSPB1,POLA1,TGFB1,E2F1,GSTM4,ALDH18A1,RBL1,GSTP1,GSTK1
BER pathway	2.57E+00	NaN	2.50E-01	FEN1,POLE,PCNA
Bupropion Degradation	2.53E+00	0	1.60E-01	CYP2B6,CYP2U1,CYP3A5,CYP2A6 (includes others)
Estrogen Biosynthesis	2.51E+00	0.447213595	1.22E-01	CYP2B6,CYP2U1,Akr1b7,CYP3A5,CYP2A6 (includes others)
SPINK1 Pancreatic Cancer Pathway	2.47E+00	-1.632993162	1.00E-01	PRSS1,TGFB1,CTRL,PRSS3,Prss1 (includes others),SPINK1
Cyclins and Cell Cycle Regulation	2.44E+00	1.133893419	8.64E-02	CCND3,TGFB1,CDKN2D,E2F2,CDC25A,E2F1,CDK1
SPINK1 General Cancer Pathway	2.41E+00	-1.133893419	8.54E-02	PRSS1,PIK3CD,Mt1,PRSS3,Prss1 (includes others),Mt2,SPINK1
DNA Double-Strand Break Repair by Homologous Recombination	2.37E+00	NaN	2.14E-01	BRCA1,POLA1,GEN1
Melatonin Degradation I	2.30E+00	0.816496581	9.23E-02	CYP2B6,CYP2U1,CYP3A5,SULT2A1,CYP2A6 (includes others),SULT1C2
Nicotine Degradation II	2.30E+00	-0.816496581	9.23E-02	CYP2B6,CYP2U1,CYP3A5,AOX1,INMT,CYP2A6 (includes others)
Trehalose Degradation II (Trehalase)	2.25E+00	NaN	4.00E-01	GCK,HK1
GP6 Signaling Pathway	2.23E+00	2.828427125	6.67E-02	GRAP2,SYK,PIK3CD,LAMC1,APBB1IP,ITGB3,COL1A1,COL5A1,PLCG2
Xenobiotic Metabolism Signaling	2.16E+00	NaN	5.02E-02	CHST3,SMOX,ALDH18A1,Ces1g,GSTK1,HMOX1,SULT1C2,PIK3CD,CYP2B6,Ces1e,CYP3A5,GSTM4,GRIP1,SULT2A1,GSTP1
Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes	2.14E+00	2.645751311	7.61E-02	SYK,INPP5D,PAK1,NCF1,VAV1,HMOX1,FCGR2A
Molecular Mechanisms of Cancer	2.07E+00	NaN	4.57E-02	BRCA1,TGFB1,PRKAR2B,AURKA,PLCB2,CDK14,PAK1,CDC25A,E2F1,CCND3,PIK3CD,FANCD2,PSEN2,CDKN2D,E2F2,ITGA4,RBL1,CDK1
ATM Signaling	2.02E+00	0.816496581	7.22E-02	BRCA1,FANCD2,CDC25A,SMC2,H2AFX,CDK1,HIST1H4J

Day 60 Female BPA

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	6.96E+00	-1.889822365	1.43E-01	TOP2A,BRCA1,AURKA,CCNB2,CDK1,PLK1,CCNB1
Cell Cycle Control of Chromosomal Replication	6.55E+00	NaN	1.25E-01	TOP2A,POLE,MCM3,MCM6,DBF4,MCM5,CDK1
Mitotic Roles of Polo-Like Kinase	6.05E+00	2.645751311	1.06E-01	KIF23,PLK4,CCNB2,KIF11,CDK1,PLK1,CCNB1
DNA damage-induced 14-3-3σ Signaling	4.88E+00	NaN	2.11E-01	BRCA1,CCNB2,CDK1,CCNB1
ATM Signaling	3.92E+00	-0.447213595	6.19E-02	BRCA1,CCNB2,H2AFX,CDK1,CCNB1,HIST1H4J
DNA Methylation and Transcriptional Repression Signaling	3.84E+00	NaN	1.18E-01	HIST1H4K,DNMT1,HIST1H4H,HIST1H4J
GADD45 Signaling	3.37E+00	NaN	1.58E-01	BRCA1,CDK1,CCNB1
Role of CHK Proteins in Cell Cycle Checkpoint Control	2.97E+00	-1	7.02E-02	BRCA1,E2F2,CDK1,PLK1
NER Pathway	2.87E+00	-1	4.85E-02	TOP2A,HIST1H4K,POLE,HIST1H4H,HIST1H4J
Sonic Hedgehog Signaling	2.77E+00	NaN	1.00E-01	PRKAR2B,CDK1,CCNB1
Cyclins and Cell Cycle Regulation	2.41E+00	2	4.94E-02	E2F2,CCNB2,CDK1,CCNB1
BER pathway	2.41E+00	NaN	1.67E-01	FEN1,POLE
Transcriptional Regulatory Network in Embryonic Stem Cells	2.05E+00	NaN	5.56E-02	HIST1H4K,HIST1H4H,HIST1H4J
Methylglyoxal Degradation III	2.01E+00	NaN	1.05E-01	Akr1b7,CYP4A11

Day 5 Male BDE-99

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
DNA Methylation and Transcriptional Repression Signaling	1.14E+01	NaN	2.94E-01	HIST1H4D,HIST1H4K,HIST1H4F,HIST1H4C,HIST1H4A,HIST1H4H,HIST2H4A,HIST1H4I,HIST1H4B,HIST1H4J
Transcriptional Regulatory Network in Embryonic Stem Cells	9.25E+00	NaN	1.85E-01	HIST1H4D,HIST1H4K,HIST1H4F,HIST1H4C,HIST1H4A,HIST1H4H,HIST2H4A,HIST1H4I,HIST1H4B,HIST1H4J
Acetone Degradation I (to Methylglyoxal)	7.38E+00	0.377964473	2.33E-01	CYP2B6,CYP1A2,CYP4A11,CYP2C8,CYP2F1,DHRS11,CYP2A6 (includes others)
Interferon Signaling	6.79E+00	-2.645751311	1.94E-01	IRF1,STAT1,IFIT3,ISG15,IFITM3,TAP1,PSMB8
NER Pathway	6.48E+00	-3.16227766	9.71E-02	HIST1H4D,HIST1H4K,HIST1H4F,HIST1H4C,HIST1H4A,HIST1H4H,HIST2H4A,HIST1H4I,HIST1H4B,HIST1H4J
Nicotine Degradation II	6.08E+00	-1.414213562	1.23E-01	CYP2B6,CYP1A2,UGT2B7,CYP2C8,CYP2F1,UGT3A1,INMT,CYP2A6 (includes others)
Nicotine Degradation III	5.43E+00	-1.133893419	1.25E-01	CYP2B6,CYP1A2,UGT2B7,CYP2C8,CYP2F1,UGT3A1,CYP2A6 (includes others)
Estrogen Biosynthesis	5.14E+00	0	1.46E-01	CYP2B6,CYP1A2,CYP2C8,CYP2F1,DHRS11,CYP2A6 (includes others)
Bupropion Degradation	5.05E+00	-0.447213595	2.00E-01	CYP2B6,CYP1A2,CYP2C8,CYP2F1,CYP2A6 (includes others)
Melatonin Degradation I	4.99E+00	-1.133893419	1.08E-01	CYP2B6,CYP1A2,UGT2B7,CYP2C8,CYP2F1,UGT3A1,CYP2A6 (includes others)
Superpathway of Melatonin Degradation	4.78E+00	-1.133893419	1.00E-01	CYP2B6,CYP1A2,UGT2B7,CYP2C8,CYP2F1,UGT3A1,CYP2A6 (includes others)
Antigen Presentation Pathway	4.13E+00	NaN	1.32E-01	HLA-A,HLA-DQB1,NLRC5,TAP1,PSMB8
Heme Biosynthesis II	3.91E+00	NaN	3.33E-01	UROD,HMBS,ALAD
PXR/RXR Activation	3.03E+00	NaN	7.69E-02	CYP2B6,CYP1A2,CYP2C8,PAPSS2,CYP2A6 (includes others)
Tetrapyrrole Biosynthesis II	2.88E+00	NaN	4.00E-01	HMBS,ALAD
Th1 and Th2 Activation Pathway	2.84E+00	NaN	4.32E-02	IRF1,IL1RL1,CXCR4,HLA-A,HLA-DQB1,STAT1,TIMD4,CD274
SPINK1 General Cancer Pathway	2.65E+00	0.447213595	6.33E-02	PRSS1,Mt1,Mt2,Prss1 (includes others),PRSS2
LPS/IL-1 Mediated Inhibition of RXR Function	2.34E+00	1.341640786	3.59E-02	IL1RL1,CYP2B6,CYP4A11,CYP2C8,PAPSS2,CHST11,CYP2A6 (includes others),FABP2
Activation of IRF by Cytosolic Pattern Recognition Receptors	2.21E+00	-1	6.35E-02	STAT1,ISG15,ZBP1,IFIT2
Phagosome Maturation	2.12E+00	NaN	4.05E-02	CTSS,HLA-A,TUBB1,PRDX2,CTSE,TAP1
B Cell Development	2.08E+00	NaN	8.33E-02	HLA-A,HLA-DQB1,CD79A

Day 5 Female BDE-99

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
SPINK1 Pancreatic Cancer Pathway	7.91E+00	2.236067977	8.33E-02	CTRL,CPB1,Prss1 (includes others),PRSS2,2210010C04Rik
Bupropion Degradation	3.33E+00	NaN	8.00E-02	CYP2B6,CYP1A2
Acetone Degradation I (to Methylglyoxal)	3.17E+00	NaN	6.67E-02	CYP2B6,CYP1A2
Estrogen Biosynthesis	2.90E+00	NaN	4.88E-02	CYP2B6,CYP1A2
Transcriptional Regulatory Network in Embryonic Stem Cells	2.66E+00	NaN	3.70E-02	PAX6,HIST1H4B
Nicotine Degradation III	2.63E+00	NaN	3.57E-02	CYP2B6,CYP1A2
Melatonin Degradation I	2.50E+00	NaN	3.08E-02	CYP2B6,CYP1A2
Nicotine Degradation II	2.50E+00	NaN	3.08E-02	CYP2B6,CYP1A2
PXR/RXR Activation	2.50E+00	NaN	3.08E-02	CYP2B6,CYP1A2
Superpathway of Melatonin Degradation	2.44E+00	NaN	2.86E-02	CYP2B6,CYP1A2
SPINK1 General Cancer Pathway	2.34E+00	NaN	2.53E-02	Prss1 (includes others),PRSS2

Day 60 Male BDE-99

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
Superpathway of Cholesterol Biosynthesis	1.31E+01	-3.741657387	5.00E-01	EBP,HMGCS1,NSDHL,ACAT2,FDPS,HMGCR,MSMO1,PMVK,SQLE,IDI1,MVK,TM7SF2,CYP51A1,DHCR7
Cell Cycle Control of Chromosomal Replication	9.38E+00	NaN	2.68E-01	TOP2A,RPA2,POLA1,CDK14,MCM2,LIG1,PCNA,CDC7,POLE,MCM3,MCM4,MCM6,MCM5,PRIM1,CDK1
Acetone Degradation I (to Methylglyoxal)	7.46E+00	-1.264911064	3.33E-01	CYP4A22,CYP2C18,CYP2U1,CYP1A2,CYP4A11,CYP2C8,CYP3A5,CYP51A1,CYP2F1,CYP2A6 (includes others)
Cholesterol Biosynthesis I	7.10E+00	-2.645751311	5.38E-01	EBP,NSDHL,SQLE,TM7SF2,CYP51A1,MSMO1,DHCR7
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)	7.10E+00	-2.645751311	5.38E-01	EBP,NSDHL,SQLE,TM7SF2,CYP51A1,MSMO1,DHCR7
Cholesterol Biosynthesis III (via Desmosterol)	7.10E+00	-2.645751311	5.38E-01	EBP,NSDHL,SQLE,TM7SF2,CYP51A1,MSMO1,DHCR7
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)	6.10E+00	-2.645751311	4.12E-01	PMVK,HMGCS1,IDI1,MVK,ACAT2,FDPS,HMGCR
Glutathione-mediated Detoxification	6.06E+00	-3	2.81E-01	GSTA3,GSTM1,Gstm3,GSTM5,GSTM4,GSTP1,Gstt1,NAT8,Gsta4
Bupropion Degradation	5.92E+00	-1.414213562	3.20E-01	CYP2C18,CYP2U1,CYP1A2,CYP2C8,CYP3A5,CYP51A1,CYP2F1,CYP2A6 (includes others)
PXR/RXR Activation	5.73E+00	NaN	1.85E-01	PCK2,IGFBP1,GSTM1,CYP1A2,PRKAR2B,Aldh1a7,ALDH1A1,CYP2C8,CYP3A5,ABCC3,CYP2A6 (includes others),CYP7A1
Mevalonate Pathway I	5.65E+00	-2.449489743	4.62E-01	PMVK,HMGCS1,IDI1,MVK,ACAT2,HMGCR
LPS/IL-1 Mediated Inhibition of RXR Function	5.54E+00	0.447213595	1.03E-01	HMGCS1,CHST3,GSTA3,ALDH1L1,SMOX,CYP4A11,CHST11,SULT1C2,TNFRSF11B,IL1RN,GSTM1,ALDH1A1,Gstm3,CYP2C8,GSTM5,CYP3A5,GSTM4,FABP5,GSTP1,Cyp2a12/Cyp2a22,ABCC3,CYP2A6 (includes others),CYP7A1
Estrogen Biosynthesis	5.08E+00	-1	2.20E-01	CYP2C18,CYP2U1,CYP1A2,Akr1b7,CYP2C8,CYP3A5,CYP51A1,CYP2F1,CYP2A6 (includes others)
Retinoate Biosynthesis I	4.81E+00	-2.121320344	2.35E-01	RDH16,DHRS3,ADH1C,RDH11,ALDH1A1,RBP1,ADH4,SDR9C7
Nicotine Degradation III	4.74E+00	-1.897366596	1.79E-01	CYP2C18,CYP2U1,CYP1A2,CYP2C8,CYP3A5,AOX1,CYP51A1,CYP2F1,UGT2B28,CYP2A6 (includes others)
Zymosterol Biosynthesis	4.71E+00	-2	6.67E-01	NSDHL,TM7SF2,CYP51A1,MSMO1
Superpathway of Melatonin Degradation	4.60E+00	-0.904534034	1.57E-01	CYP2C18,SMOX,CYP2U1,CYP1A2,CYP2C8,CYP3A5,CYP51A1,CYP2F1,UGT2B28,CYP2A6 (includes others),SULT1C2
Aryl Hydrocarbon Receptor Signaling	4.51E+00	0.816496581	1.13E-01	GSTA3,POLA1,ALDH1L1,TGFB1,E2F1,CCND3,HSPB1,GSTM1,CYP1A2,ALDH1A1,CCND1,Gstm3,GSTM5,GSTM4,RBL1,GSTP1
Melatonin Degradation I	4.15E+00	-1.264911064	1.54E-01	CYP2C18,CYP2U1,CYP1A2,CYP2C8,CYP3A5,CYP51A1,CYP2F1,UGT2B28,CYP2A6 (includes others),SULT1C2
Nicotine Degradation II	4.15E+00	-1.897366596	1.54E-01	CYP2C18,CYP2U1,CYP1A2,CYP2C8,CYP3A5,AOX1,CYP51A1,CYP2F1,UGT2B28,CYP2A6 (includes others)
DNA Double-Strand Break Repair by Homologous Recombination	4.14E+00	NaN	3.57E-01	BRCA1,POLA1,GEN1,LIG1,RAD51
Retinol Biosynthesis	4.11E+00	-0.707106781	1.90E-01	DHRS3,Ces1e,RDH11,RBP1,LPL,Ces1g,CES1,BCO1
α-tocopherol Degradation	3.80E+00	NaN	7.50E-01	CYP4F3,CYP4A11,CYP4F12
Estrogen-mediated S-phase Entry	3.69E+00	1.632993162	2.31E-01	CCND1,E2F2,E2F1,RBL1,E2F7,CDK1
NER Pathway	3.66E+00	-0.333333333	1.17E-01	TOP2A,RPA2,POLA1,HIST1H4K,POLE,LIG1,HIST1H4H,HIST2H4B,PCNA,PRIM1,HIST1H4B,HIST1H4J
Xenobiotic Metabolism Signaling	3.54E+00	NaN	7.69E-02	CHST3,GSTA3,ALDH1L1,SMOX,Ces1g,CES1,CHST11,HMOX1,SULT1C2,GSTM1,Ces1e,CYP1A2,ALDH1A1,Gstm3,CYP2C8,GSTM5,CYP3A5,GSTM4,GRIP1,UGT2B28,GSTP1,PRKCZ,ABCC3
GADD45 Signaling	3.43E+00	NaN	2.63E-01	CCND3,BRCA1,CCND1,PCNA,CDK1
Mitotic Roles of Polo-Like Kinase	3.39E+00	0.377964473	1.36E-01	CDC7,PLK3,KIF23,TGFB1,ESPL1,PRC1,PLK4,KIF11,CDK1
BER pathway	3.26E+00	NaN	3.33E-01	FEN1,POLE,LIG1,PCNA
DNA Methylation and Transcriptional Repression Signaling	3.02E+00	NaN	1.76E-01	HIST1H4K,DNMT1,HIST1H4H,HIST2H4B,HIST1H4B,HIST1H4J
Leukocyte Extravasation Signaling	2.94E+00	2.672612419	7.98E-02	SPN,NCF1,Cldn13,ITGB2,ACTN1,CD44,VAV1,VCAM1,PLCG2,MMP8,ITGA4,ITGB3,ICAM1,CYBB,PRKCZ,MMP15,MMP14
Alanine Biosynthesis II	2.93E+00	NaN	1.00E+00	GPT2,GPT
Alanine Degradation III	2.93E+00	NaN	1.00E+00	GPT2,GPT

Role of BRCA1 in DNA Damage Response	2.78E+00	0.707106781	1.13E-01	BRIP1,BRCA1,FANCD2,E2F2,E2F1,BARD1,RBL1,RAD51,E2F7
Hepatic Fibrosis / Hepatic Stellate Cell Activation	2.70E+00	NaN	8.06E-02	MYH2,TGFB1,COL1A1,LEPR,COL5A1,VCAM1,IGF2,A2M,IGF1R,TNFRSF11B,IFNGR1,PROK1,MYH4,COL6A5,ICAM1
Cell Cycle: G1/S Checkpoint Regulation	2.69E+00	-1.133893419	1.19E-01	CCND3,TGFB1,CDKN2D,CCND1,E2F2,E2F1,RBL1,E2F7
Role of CHK Proteins in Cell Cycle Checkpoint Control	2.49E+00	-1.341640786	1.23E-01	BRCA1,E2F2,E2F1,CLSPN,PCNA,E2F7,CDK1
Methylglyoxal Degradation III	2.45E+00	0	2.11E-01	CYP4A22,Akr1b7,CYP4A11,ADH4
Ketogenesis	2.39E+00	NaN	3.00E-01	HMGCS1,ACAT2,BDH1
Granzyme A Signaling	2.36E+00	NaN	2.00E-01	HIST1H1C,HIST1H1D,HMGB2,Hist1h1e
Atherosclerosis Signaling	2.33E+00	NaN	8.59E-02	TNFRSF14,APOA4,IL1RN,TGFB1,LPL,ITGA4,ITGB2,COL1A1,PLA2G7,ICAM1,VCAM1
Ethanol Degradation II	2.24E+00	-2.236067977	1.47E-01	ADH1C,ALDH1L1,ALDH1A1,ACSS2,ADH4
Apelin Adipocyte Signaling Pathway	2.21E+00	-2.121320344	1.00E-01	PLIN1,GSTM1,PRKAR2B,PRKAA2,NOX4,GSTP1,CYBB,Gstt1
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.19E+00	-1.632993162	1.22E-01	TOP2A,BRCA1,AURKA,CKS1B,BORA,CDK1
Cyclins and Cell Cycle Regulation	2.18E+00	1.414213562	9.88E-02	CCND3,TGFB1,CDKN2D,CCND1,E2F2,E2F1,E2F7,CDK1
Pregnenolone Biosynthesis	2.15E+00	NaN	2.50E-01	CYP4A22,CYP7B1,CYP4A11
Cell Cycle Regulation by BTG Family Proteins	2.08E+00	1.341640786	1.35E-01	BTG2,CCND1,E2F2,E2F1,E2F7
Complement System	2.08E+00	NaN	1.35E-01	C1QC,C1QB,C7,ITGB2,CFD
Noradrenaline and Adrenaline Degradation	2.08E+00	-1.341640786	1.35E-01	ADH1C,ALDH1L1,SMOX,ALDH1A1,ADH4
Bile Acid Biosynthesis, Neutral Pathway	2.05E+00	NaN	2.31E-01	CYP8B1,CYP7A1,CYP27A1
Granulocyte Adhesion and Diapedesis	2.02E+00	NaN	7.22E-02	Cldn13,ITGB2,VCAM1,TNFRSF11B,HSPB1,CKLF,IL1RN,MMP8,ITGA4,ITGB3,ICAM1,MMP15,MMP14
Glioma Signaling	2.02E+00	1	8.20E-02	IGF1R,CDKN2D,CCND1,E2F2,E2F1,RBL1,PRKC2,E2F7,IGF2,PLCG2
Tryptophan Degradation X (Mammalian, via Tryptamine)	2.01E+00	-1	1.60E-01	ALDH1L1,SMOX,ALDH1A1,DDC

Day 60 Female BDE-99

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
EIF2 Signaling	3.27E+00	NaN	2.18E-02	RPS13,IRS2,CCND1,RPS15A,RPL19
Melanoma Signaling	3.09E+00	NaN	4.76E-02	IRS2,CCND1,CDH1
PXR/RXR Activation	3.05E+00	NaN	4.62E-02	IGFBP1,CYP3A5,G6PC
Endometrial Cancer Signaling	2.92E+00	NaN	4.17E-02	IRS2,CCND1,CDH1
Granzyme A Signaling	2.82E+00	NaN	1.00E-01	HIST1H1D,Hist1h1e
Sirtuin Signaling Pathway	2.80E+00	-2.236067977	1.71E-02	HIST1H1D,PFKFB3,ACSS2,Hist1h1e,CDH1
SPINK1 General Cancer Pathway	2.75E+00	NaN	3.66E-02	Mt1,IRS2,Mt2
IL-7 Signaling Pathway	2.60E+00	NaN	3.23E-02	BCL6,IRS2,CCND1
2-amino-3-carboxymuconate Semialdehyde Degradation to Glutaryl-CoA	2.54E+00	NaN	1.00E+00	ACMSD,
Superpathway of Cholesterol Biosynthesis	2.52E+00	NaN	7.14E-02	PMVK,DHCR7
TR/RXR Activation	2.51E+00	NaN	3.00E-02	IRS2,UCP1,G6PC
Oxidative Phosphorylation	2.40E+00	NaN	2.75E-02	COX6A1,ATP5MF,Cox8b
LPS/IL-1 Mediated Inhibition of RXR Function	2.39E+00	NaN	1.79E-02	Cyp4a14,FABP4,CYP3A5,FABP5
Retinoate Biosynthesis I	2.36E+00	NaN	5.88E-02	RDH16,RDH11
IGF-1 Signaling	2.36E+00	NaN	2.65E-02	IGFBP1,IRS2,IGFBP5
Retinol Biosynthesis	2.18E+00	NaN	4.76E-02	RDH11,PNLIP
Thyroid Cancer Signaling	2.10E+00	NaN	4.35E-02	CCND1,CDH1

Day 5 Male PCB

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
DNA Methylation and Transcriptional Repression Signaling	6.83E+00	NaN	1.47E-01	HIST1H4D,HIST1H4F,HIST1H4H,HIST1H4B,HIST1H4J
Transcriptional Regulatory Network in Embryonic Stem Cells	5.80E+00	NaN	9.26E-02	HIST1H4D,HIST1H4F,HIST1H4H,HIST1H4B,HIST1H4J
NER Pathway	4.42E+00	-2.236067977	4.85E-02	HIST1H4D,HIST1H4F,HIST1H4H,HIST1H4B,HIST1H4J
Acetone Degradation I (to Methylglyoxal)	3.75E+00	NaN	1.00E-01	CYP1A2,CYP4A11,CYP2A6 (includes others)
Nicotine Degradation III	2.94E+00	NaN	5.36E-02	CYP1A2,UGT3A1,CYP2A6 (includes others)
Melatonin Degradation I	2.76E+00	NaN	4.62E-02	CYP1A2,UGT3A1,CYP2A6 (includes others)
Nicotine Degradation II	2.76E+00	NaN	4.62E-02	CYP1A2,UGT3A1,CYP2A6 (includes others)
Superpathway of Melatonin Degradation	2.66E+00	NaN	4.29E-02	CYP1A2,UGT3A1,CYP2A6 (includes others)
4-hydroxybenzoate Biosynthesis	2.44E+00	NaN	1.00E+00	TAT,
4-hydroxyphenylpyruvate Biosynthesis	2.44E+00	NaN	1.00E+00	TAT,
Histamine Biosynthesis	2.44E+00	NaN	1.00E+00	HDC,
Bupropion Degradation	2.42E+00	NaN	8.00E-02	CYP1A2,CYP2A6 (includes others)
TGF-β Signaling	2.31E+00	NaN	3.23E-02	SERPINE1,SMAD9,INHBB
Estrogen Biosynthesis	2.00E+00	NaN	4.88E-02	CYP1A2,CYP2A6 (includes others)

Day 5 Female PCB

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
Th1 and Th2 Activation Pathway	3.21E+00	NaN	1.62E-02	JUN,STAT1,CD274
iNOS Signaling	3.11E+00	NaN	4.44E-02	JUN,STAT1
Activation of IRF by Cytosolic Pattern Recognition Receptors	2.82E+00	NaN	3.17E-02	JUN,STAT1
EGF Signaling	2.76E+00	NaN	2.94E-02	JUN,STAT1
IL-10 Signaling	2.74E+00	NaN	2.90E-02	JUN,IL1B
Thrombopoietin Signaling	2.72E+00	NaN	2.82E-02	JUN,STAT1
Toll-like Receptor Signaling	2.66E+00	NaN	2.63E-02	JUN,IL1B
Neuroinflammation Signaling Pathway	2.56E+00	NaN	9.65E-03	JUN,IL1B,STAT1
IL-3 Signaling	2.53E+00	NaN	2.25E-02	JUN,STAT1
JAK/Stat Signaling	2.53E+00	NaN	2.25E-02	JUN,STAT1
Prolactin Signaling	2.53E+00	NaN	2.25E-02	JUN,STAT1
IL-7 Signaling Pathway	2.51E+00	NaN	2.20E-02	JUN,STAT1
PDGF Signaling	2.46E+00	NaN	2.08E-02	JUN,STAT1
Glucocorticoid Receptor Signaling	2.44E+00	NaN	8.76E-03	JUN,IL1B,STAT1
PPAR Signaling	2.42E+00	NaN	1.98E-02	JUN,IL1B
Cholecystokinin/Gastrin-mediated Signaling	2.37E+00	NaN	1.87E-02	JUN,IL1B
Type I Diabetes Mellitus Signaling	2.34E+00	NaN	1.80E-02	IL1B,STAT1
UVA-Induced MAPK Signaling	2.34E+00	NaN	1.80E-02	JUN,STAT1
p38 MAPK Signaling	2.28E+00	NaN	1.68E-02	IL1B,STAT1
LXR/RXR Activation	2.27E+00	NaN	1.69E-02	IL1B,SCD
Renin-Angiotensin Signaling	2.22E+00	NaN	1.56E-02	JUN,STAT1
IL-6 Signaling	2.18E+00	NaN	1.49E-02	JUN,IL1B
Th1 Pathway	2.17E+00	NaN	1.48E-02	STAT1,CD274
HMGB1 Signaling	2.15E+00	NaN	1.44E-02	JUN,IL1B
Aryl Hydrocarbon Receptor Signaling	2.13E+00	NaN	1.41E-02	JUN,IL1B
IL-12 Signaling and Production in Macrophages	2.11E+00	NaN	1.37E-02	JUN,STAT1
Hepatic Cholestasis	2.03E+00	NaN	1.25E-02	JUN,IL1B

Day 60 Male PCB

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
PXR/RXR Activation	5.79E+00	NaN	7.69E-02	IGFBP1,CYP3A5,SULT2A1,CYP2A6 (includes others),NR0B2
Calcium Signaling	5.52E+00	NaN	3.40E-02	TNNC2,MYH1,MYH2,TNNT3,MYH4,Tpm2,TNNT1
LPS/IL-1 Mediated Inhibition of RXR Function	5.29E+00	NaN	3.14E-02	Sult3a1/Sult3a2,JUN,FABP1,CYP3A5,SULT2A1,CYP2A6 (includes others),NR0B2
Creatine-phosphate Biosynthesis	4.04E+00	NaN	4.00E-01	CKMT2,CKM
VDR/RXR Activation	4.03E+00	NaN	5.13E-02	PPARD,IGFBP1,SULT2A1,SPP1
SPINK1 Pancreatic Cancer Pathway	3.09E+00	NaN	5.00E-02	CTRL,PRSS3,CELA1
Melatonin Degradation I	2.99E+00	NaN	4.62E-02	CYP3A5,SULT2A1,CYP2A6 (includes others)
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)	2.92E+00	NaN	1.18E-01	PMVK,FDPS
Superpathway of Melatonin Degradation	2.90E+00	NaN	4.29E-02	CYP3A5,SULT2A1,CYP2A6 (includes others)
Tight Junction Signaling	2.76E+00	NaN	2.38E-02	JUN,MYH1,MYH2,MYH4
Bupropion Degradation	2.58E+00	NaN	8.00E-02	CYP3A5,CYP2A6 (includes others)
B Cell Receptor Signaling	2.54E+00	NaN	2.06E-02	JUN,BCL6,IGHM,EGR1
IL-7 Signaling Pathway	2.54E+00	NaN	3.23E-02	JUN,BCL6,IGHM
ILK Signaling	2.51E+00	-2	2.03E-02	JUN,MYH1,MYH2,MYH4
Superpathway of Cholesterol Biosynthesis	2.49E+00	NaN	7.14E-02	PMVK,FDPS
PPAR Signaling	2.44E+00	NaN	2.97E-02	PPARD,JUN,NR0B2
Acetone Degradation I (to Methylglyoxal)	2.43E+00	NaN	6.67E-02	CYP3A5,CYP2A6 (includes others)
Actin Cytoskeleton Signaling	2.27E+00	NaN	1.73E-02	MYH1,MYH2,MYH4,TTN
Fatty Acid Biosynthesis Initiation II	2.22E+00	NaN	5.00E-01	FASN,
Palmitate Biosynthesis I (Animals)	2.22E+00	NaN	5.00E-01	FASN,
FXR/RXR Activation	2.17E+00	NaN	2.38E-02	FASN,SULT2A1,NR0B2
Estrogen Biosynthesis	2.16E+00	NaN	4.88E-02	CYP3A5,CYP2A6 (includes others)
Protein Kinase A Signaling	2.14E+00	1	1.25E-02	HIST1H1D,MYH2,DUSP1,MYH4,TTN
Retinol Biosynthesis	2.14E+00	NaN	4.76E-02	PNLIPRP2,PNLIP
Cellular Effects of Sildenafil (Viagra)	2.13E+00	NaN	2.29E-02	MYH1,MYH2,MYH4
Dermatan Sulfate Biosynthesis (Late Stages)	2.06E+00	NaN	4.35E-02	Sult3a1/Sult3a2,SULT2A1
Biotin-carboxyl Carrier Protein Assembly	2.04E+00	NaN	3.33E-01	ACACB,
Chondroitin Sulfate Biosynthesis (Late Stages)	2.01E+00	NaN	4.08E-02	Sult3a1/Sult3a2,SULT2A1

Day 60 Female PCB

Ingenuity Canonical Pathways	-log(p-value)	zScore	Ratio	Molecules
PXR/RXR Activation	4.27E+00	NaN	4.62E-02	IGFBP1,CYP3A5,SULT2A1
VDR/RXR Activation	4.03E+00	NaN	3.85E-02	IGFBP1,IGFBP5,SULT2A1
Dermatan Sulfate Biosynthesis (Late Stages)	2.91E+00	NaN	4.35E-02	Sult3a1/Sult3a2,SULT2A1
Chondroitin Sulfate Biosynthesis (Late Stages)	2.85E+00	NaN	4.08E-02	Sult3a1/Sult3a2,SULT2A1
Chondroitin Sulfate Biosynthesis	2.72E+00	NaN	3.51E-02	Sult3a1/Sult3a2,SULT2A1
LPS/IL-1 Mediated Inhibition of RXR Function	2.70E+00	NaN	1.35E-02	Sult3a1/Sult3a2,CYP3A5,SULT2A1
Dermatan Sulfate Biosynthesis	2.69E+00	NaN	3.39E-02	Sult3a1/Sult3a2,SULT2A1
Melatonin Degradation I	2.61E+00	NaN	3.08E-02	CYP3A5,SULT2A1
Superpathway of Melatonin Degradation	2.55E+00	NaN	2.86E-02	CYP3A5,SULT2A1
Heparan Sulfate Biosynthesis (Late Stages)	2.48E+00	NaN	2.63E-02	Sult3a1/Sult3a2,SULT2A1
Heparan Sulfate Biosynthesis	2.40E+00	NaN	2.41E-02	Sult3a1/Sult3a2,SULT2A1
Xenobiotic Metabolism Signaling	2.34E+00	NaN	1.00E-02	Sult3a1/Sult3a2,CYP3A5,SULT2A1
Trehalose Degradation II (Trehalase)	2.25E+00	NaN	2.00E-01	GCK,
IGF-1 Signaling	2.14E+00	NaN	1.77E-02	IGFBP1,IGFBP5
FXR/RXR Activation	2.05E+00	NaN	1.59E-02	SULT2A1,A1BG

Table S3-3. Upstream regulators top 100

Day 5 Male BPA

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
NR1I3		ligand-dependent nuclear receptor	Inhibited	-2.958	bias	-0.674		1.61E-26	ABCC3,ALDH1A1,Aldh1a7,Ces2c,CYP1A2,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,DIO1,FASN,GSTM1,Gstm3,LRG1,Mt1,SCD,Slco1a4,THRSP	HNF4A,NR1I3
ciprofibrate		chemical drug	Activated	3.018		0.034	2.881	4.01E-19	BAAT,C9,CYP1A2,CYP27A1,Cyp2c54 (includes others),CYP2C8,CYP4F12,CYP7B1,DIO1,Mup1 (includes others),Nat8f2,Orm1 (includes others),SCD,SLC10A2,SLC22A25,Slco1a1,SLCO2B1	ACOX1,CEBPA,NR1H3,PPARA,RXRA,SREBF1,SREBF2,cholesterol,ciprofibrate
1,4-bis[2-(3,5-dichloropyridyloxy)]benzene		chemical toxicant		-1.784	bias	-0.529		4.39E-19	ABCC3,Ces2c,CYP1A2,CYP27A1,Cyp2b13/Cyp2b9,CYP2B6,CYP7B1,DIO1,FASN,LRG1,Mt1,SCD,Slco1a1,Slco1a4,THRSP,UCP1	1,4-bis[2-(3,5-dichloropyridyloxy)]benzene,HNF4A,NR1I3
NR1I2		ligand-dependent nuclear receptor	Inhibited	-2.791		-0.2	-2.055	4.62E-17	ABCC3,ALDH1A1,Aldh1a7,Ces2c,CYP1A2,CYP27A1,CYP2A6 (includes others),CYP2B6,CYP2C8,FASN,GSTM1,Gstm3,Mup1 (includes others),Nat8f2,SCD,Slco1a4	AHR,HNF4A,NR1I2,NR1I3,NR3C1,Rxr,dexamethasone
phenobarbital		chemical drug	Inhibited	-2.711	bias	-0.555		1.59E-16	ABCC3,CYP1A2,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,DIO1,GPT,Slco1a1,Slco1a4,THRSP	HNF4A,NR1I2,NR1I3,Rxr,phenobarbital
POR		enzyme		0	bias	0.298	-0.597	4.12E-16	ABCC3,ADH4,ALDH1A1,Aldh1a7,Ces2c,CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,CYP7B1,GCK,GSTM1,Gstm3,Mt1,SCD,Slco1a4	
RORA		ligand-dependent nuclear receptor		-1.103	bias	-0.433	-0.258	1.15E-15	Apoc3,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),CYP2C8,CYP7B1,FASN,Mt1,Mt2,Mup1 (includes others),RDH16,SCD,Slco1a1,Slco1a4	
ACOX1		enzyme	Inhibited	-3.212		0.155	-3.787	8.39E-15	BAAT,C9,CYP1A2,Cyp2c54 (includes others),CYP2C8,CYP4F12,CYP7B1,DIO1,FASN,Mup1 (includes others),Nat8f2,Orm1 (includes others),SLC22A25,SLCO2B1	ACOX1,CEBPA,NR1H3,PPARA,RXRA,SREBF1
pirinixic acid		chemical toxicant		-1.35	bias	-0.5	0.548	2.65E-14	ABCC3,ADH1C,ADH4,Apoc3,C9,CYP1A2,CYP27A1,CYP2B6,Cyp2c40 (includes others),Cyp2c54 (includes others),CYP2C8,CYP7B1,FASN,Mup1 (includes others),NUDT7,Orm1 (includes others),PRSS2,SCD,SLC10A2,UCP1	ACOX1,CEBPA,Insulin,JUN,NR1H3,NR1H4,NR1I3,PPARA,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,VDR,pirinixic acid
TO-901317		chemical reagent		-0.262	bias	-0.254	0.387	2.73E-14	ADH1C,C9,CYP7B1,DIO1,FASN,GCK,LIPG,Mt1,Mt2,Mug1/Mug2,Mup1 (includes others),Orm1 (includes others),RDH16,SCD,THRSP,UCP1	CEBPA,D-glucose,FOXO3,MLXIPL,NR1H3,PPARA,PPARD,RXRA,SREBF1,SREBF2,TO-901317,palmitic acid
STAT5B		transcription regulator		-1.521		-0.147	-0.973	3.31E-14	A2M,C9,CSRP3,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,GCK,Mup1 (includes others),MYH6,NUDT7,SCD,Slc22a26,Slco1a1,Slco1a4,THRSP,UCP1	CEBPA,FOXO1,IGF1,JUN,STAT5B
RXRA		ligand-dependent nuclear receptor		-1.694	bias	-0.368	-0.441	1.97E-13	ABCC3,ADH1C,ALDH1A1,Apoc3,BAAT,CYP1A2,CYP2B6,FASN,GCK,GPT,Orm1 (includes others),SCD,SLC10A2,Slco1a4,THRSP,UCP1	CEBPA,FOXO1,MED1,NR0B2,NR1H3,NR1H4,NRIP1,Ncoa6,PPARA,PPARD,PPARGC1A,RXRA,SREBF1,THRB,VDR,alitretinoin,fatty acid
PXR ligand-PXR-Retinoic acid-RXRα		complex	Inhibited	-2.937	bias	-0.767		2.33E-13	ABCC3,ALDH1A1,Aldh1a7,CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,GSTM1,SCD	
PPARA		ligand-dependent nuclear receptor		-0.586		-0.213	0.117	5.45E-13	Apoc3,C9,Clec2d (includes others),CYP27A1,CYP2B6,Cyp2c40 (includes others),Cyp2c54 (includes others),CYP2C8,CYP7B1,DIO1,FASN,GCK,GPT,LIPG,Mup1 (includes others),Orm1 (includes others),SCD,SLC10A2,UCP1	CEBPA,NR1H3,NR1H4,NR1I3,PPARA,PPARGC1A,RXRA,SREBF1,SREBF2,VDR,cholesterol,pirinixic acid
diethylnitrosamine		chemical toxicant	Activated	2.53		-0.08	2.782	1.11E-11	BAAT,C9,Cyp2c54 (includes others),CYP2C8,CYP4F12,CYP7B1,Mt1,Mup1 (includes others),SLC22A25,SLCO2B1	
RORC		ligand-dependent nuclear receptor						1.26E-11	CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),CYP2C8,CYP7B1,Mt1,Mt2,Mup1 (includes others),RDH16,SCD,Slco1a1,Slco1a4	
NR5A2		ligand-dependent nuclear receptor		-1.041	bias	-0.589		1.97E-11	ABCC3,BAAT,CELA1,CELA3B,CTRL,CYP7B1,FASN,Mt1,PLK3,SLC10A2	
carbon tetrachloride		chemical toxicant		-1.067	bias	-0.494	-0.088	2.80E-11	AOX1,Apoc3,C9,CA3,CELA1,CYP1A2,Cyp2b13/Cyp2b9,GSTM1,Mt1,Mt2,PRSS2,Slco1a1,Slco1a4	
clofibrate		chemical drug		0.387	bias	-0.396	1.617	4.63E-11	ABCC3,Apoc3,BAAT,CYP1A2,Cyp2b13/Cyp2b9,Mt1,Mt2,SCD,Slco1a1,SLCO2B1	
FECH		enzyme						1.16E-10	CYP1A2,CYP27A1,Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,Slco1a1	
ZBTB20		transcription regulator	Inhibited	-2.828		-0.048	-2.694	1.37E-10	ADH4,CYP1A2,Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),CYP2C8,FASN,GCK	
AHR		ligand-dependent nuclear receptor		-1.964		-0.08	-1.807	1.48E-10	A2M,CELA1,Ces2c,CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,DCLK3,DIO1,IDO2,Mt1,Mt2,RDH16,SCD,TDO2	AHR,IL6,RORC,STAT1
pregnenolone carbonitrile		chemical drug		-1.415	bias	-0.475	-0.208	6.55E-10	ABCC3,Cyp2b13/Cyp2b9,CYP2B6,SCD,Slco1a1,Slco1a4,SLCO2B1	
propylthiouracil		chemical drug						2.54E-09	ABCC3,Aldh1a7,CELA1,CSRP3,DIO1,LOC102724788/PRODH,MYH6,Orm1 (includes others),THRSP	
NR0B2		ligand-dependent nuclear receptor	Activated	2.185	bias	0.702		3.47E-09	BAAT,Ces2c,CYP7B1,FASN,GCK,GPT,SCD,SLC10A2	CEBPA,Insulin,JUN,NR0B2,NR1H3,NR1H4,NR1I3,NR5A2,Nr1h,PPARA,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,VDR
spironolactone		chemical drug		-0.335		0.22	-0.944	4.27E-09	ABCC3,FASN,KCNMA1,SCD,Slco1a1,Slco1a4,SLCO2B1,UCP1	
GPD1		enzyme						1.72E-08	C9,Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,Mug1/Mug2,Mup1 (includes others),NUDT7	
SLC25A13		transporter						2.03E-08	C9,Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,Mug1/Mug2,Mup1 (includes others),NUDT7	
FOXA2		transcription regulator		-1.4		-0.08	-1.224	3.19E-08	A2M,ADH1C,CYP2A6 (includes others),EPX,GCK,Mt1,PNLIPRP1,PYY,SCD,TDO2	CEBPA,FOXA2,FOXO1,Ins1,RXRA,SREBF1,USF2
ethanol		chemical - endogenous mammalian		-1.877		-0.24	-1.065	3.46E-08	ADH1C,ADH4,C9,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,FASN,GCK,GPT,Gstm3,PLK3,SCD	CEBPA,NR1H3,NR1H4,NR1I3,PPARA,PPARD,PPARGC1A,RXRA,SREBF1,VDR,ethanol,fatty acid
methylprednisolone		chemical drug		1.033		-0.159	1.494	4.21E-08	A2M,ALDH1A1,C9,CELA1,CYP1A2,Cyp2b13/Cyp2b9,DIO1,GCK,GPT,Mt1,PIGR,PLS3,SERPINA6,SLC10A2,TDO2	IFNG,NFKBIA,NR3C1,STAT1,USF1,methylprednisolone
bromobenzene		chemical toxicant						4.52E-08	ABCC3,CYP1A2,Cyp2b13/Cyp2b9,CYP2B6,GSTM1,Mt1,Mt2	
NCOA2		transcription regulator		-1.616	bias	-0.358	-0.78	5.93E-08	ADH4,CYP2B6,Cyp2c40 (includes others),FASN,GCK,IFIT1B,ISG15,LIPG	NCOA2,NFKBIA,STAT1
2,4,5,2',4',5'-hexachlorobiphenyl		chemical toxicant	Inhibited	-2.156		-0.25	-1.463	6.37E-08	ABCC3,AOX1,Ces2c,Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),FASN,Prss1 (includes others)	
cholic acid		chemical - endogenous mammalian		0.263		-0.162	0.683	7.34E-08	ABCC3,CYP27A1,CYP2B6,CYP7B1,SLC10A2,Slco1a1,Slco1a4	NR0B2,NR1H4,RXRA,bile salt,cholic acid
NR1H4		ligand-dependent nuclear receptor		1.896		0.011	1.863	1.15E-07	ABCC3,BAAT,CYP2B6,FASN,GPT,Orm1 (includes others),SLC10A2,Slco1a1,UCP1	Insulin,JUN,NR0B2,NR1H4,NR1I2,NR1I3,NR5A2,Nr1h,PPARA,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,VDR,chenodeoxycholic acid
POU2F1		transcription regulator						1.25E-07	A2M,Aldh1a7,AOX1,CYP2A6 (includes others),CYP2B6,CYP2C8,GSTM1,PRKAA2	
HNF4A		transcription regulator	Inhibited	-3.517	bias	-0.273	-2.558	1.29E-07	ABCC3,ALDH1A1,Apoc3,Apon,BAAT,CDC6,Ces2c,CYP1A2,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,DCK,DTL,GPT,LARS2,LOC102724788/PRODH,MOCOS,Mt1,Mt2,PNLIPRP1,SCD,Slc22a26,Slco1a1,Slco1a4,TDO2,UGT2A3	
lipopolysaccharide		chemical drug		1.341	bias	-0.403	3.333	1.29E-07	ABCC3,CYP1A2,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP2C8,CYP7B1,Ear2 (includes others),FASN,GPT,IDO2,IFIT1B,ISG15,LIPG,Mt1,Mt2,Orm1 (includes others),PIGR,PLK3,PRKAA2,Slco1a1,Slco1a4,TDO2,THRSP,TNNT3	CHUK,FOXO3,HNF1A,IKBKB,IL1B,IL6,NFKBIA,NR3C1,RORC,RXRA,SREBF2,STAT1,TNF,lipopolysaccharide
LIPE		enzyme		-1.342	bias	-0.184	-0.931	1.42E-07	ADH1C,ALDH1A1,CSRP3,FASN,INMT,SCD,THRSP,UCP1	CEBPA,FASN,FOXO1,Ins1,LIPE,NR1H3,PPARD,RXRA,SREBF1,USF2,fatty acid
FGF19		growth factor		1.982		0.097	1.79	1.76E-07	ALDH1A1,CYP7B1,FASN,GCK,SCD,SLC10A2,THRSP	ADIPOQ,FGF19,FOXO1,JINK1/2,MLXIPL,NR0B2,NR5A2,Nr1h,PPARA,PPARGC1A,RXRA
HNF1A		transcription regulator	Inhibited	-2.975	bias	-0.737		2.22E-07	ADH1C,ADH4,C9,CYP1A2,CYP27A1,DTL,GCK,PIGR,SLC10A2,Slco1a1,Slco1a4,TMED6,UGT2A3	
PPARGC1A		transcription regulator	Inhibited	-3.124	bias	-0.573		3.20E-07	Apoc3,CYP1A2,CYP2A6 (includes others),CYP2B6,DIO1,FASN,MYH6,PRKAA2,SCD,UCP1	AMPK,CEBPA,FOXO1,MED1,MLXIPL,NR1H3,NR1H4,NR1I3,PPARA,PPARGC1A,RXRA,SREBF1,THRA,THRB,VDR
NRIP1		transcription regulator		-0.277	bias	0.464	-1.307	4.78E-07	CDC6,CYP2C8,FASN,SCD,THRSP,UCP1	KAT2B,NFKBIA,NR3C1,NRIP1,SREBF2,TNF
GATA2		transcription regulator						4.93E-07	C9,Cyp2c40 (includes others),Ear2 (includes others),EPX,LIN28B,PNLIPRP1,PRG2,PRSS1,Prss1 (includes others),PRSS2,SERPINA6,SERPINI2	
ursodeoxycholic acid		chemical - endogenous mammalian		0.394		-0.182	0.792	7.00E-07	ABCC3,CYP27A1,CYP2B6,FASN,GPT,SLC10A2	HNF4A,NR0B2,NR1H4,NR1I2,RXRA,ursodeoxycholic acid
mercuric chloride		chemical toxicant						7.80E-07	GSTM1,Mt1,Mt2,Mup1 (includes others),Orm1 (includes others)	
alitretinoin		chemical drug		-1.693	bias	-0.348	-0.729	8.75E-07	ABCC3,CYP1A2,CYP2B6,FASN,ISG15,MYH6,SCD,UCP1	Insulin,JUN,MED1,NR0B2,NR1H4,NR1I3,Ncoa6,PPARA,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,VDR,alitretinoin
allyl sulfide		chemical drug		-1.181	bias	-0.303	-0.593	8.77E-07	ABCC3,CYP2B6,Slco1a1,Slco1a4	
xanthohumol		chemical - endogenous non-mammalian	Activated	2	bias	0.661		8.99E-07	CSRP3,CYP1A2,FASN,MYH6,SCD	
dexamethasone		chemical drug		-1.78		-0.082	-1.423	9.04E-07	ABCC3,ALDH1A1,Clec2d (includes others),CYP1A2,CYP27A1,CYP2A6 (includes others),CYP2B6,CYP2C8,DIO1,FASN,GCK,GPT,GSTM1,IFIT1B,ISG15,Mt1,Mt2,PNLIPRP2,PRKAA2,SCD,SERPINA6,SLC10A2,Slco1a1,Slco1a4,SLCO2B1,TDO2,THRSP	HNF4A,IL6,NFKBIA,NR1I2,NR1I3,NR3C1,RORC,SREBF2,STAT1,TNF,dexamethasone
ATP7B		transporter	Inhibited	-2.236		-0.109	-1.992	1.18E-06	Cyp2c40 (includes others),FASN,Mt1,Mt2,THRSP	
NR1H3		ligand-dependent nuclear receptor		-0.152		-0.102	0.111	1.74E-06	FASN,GCK,GPT,Mt1,Mt2,SCD,UCP1	CEBPA,FOXO1,NR1H3,NR1H4,NR1I3,PPARA,PPARD,PPARGC1A,RXRA,SREBF1,SREBF2,VDR,bezafibrate,fenofibrate
ethoxyquin		chemical toxicant		-1.067	bias	-0.723		1.85E-06	CYP1A2,CYP2B6,Slco1a1,SLCO2B1	
ABCB6		transporter	Inhibited	-2.23		-0.056	-2.104	1.94E-06	CYP1A2,CYP2A6 (includes others),CYP2B6,Cyp2c40 (includes others),Cyp2c54 (includes others)	
CYB5R4		enzyme		-0.247	bias	0.727		2.30E-06	FASN,Mt1,Mt2,SCD	CEBPA,CYB5R4,FOXO1,Ins1,NR1H3,PPARD,RXRA,SREBF1,USF2,fatty acid
MLX		transcription regulator		-1.982	bias	-0.808		2.30E-06	DIO1,FASN,SCD,THRSP	MLX,MLXIPL
IL6		cytokine	Activated	2.017	bias	-0.433	3.512	2.43E-06	A2M,ABCC3,CDC6,CYP1A2,CYP2B6,CYP2C8,DIO1,IFIT1B,LRG1,Mt1,Mt2,Orm1 (includes others),Slco1a1,Slco1a4,THRSP	HNF1A,IL1B,IL6,NFKBIA,NR3C1,RORC,RXRA,SREBF2,STAT1,TNF
HOXA10		transcription regulator		0.378	bias	0.269	-0.334	2.56E-06	ADH4,ALDH1A1,CA3,INMT,PIGR,SCD,TDO2,THRSP	
CYP1A2	-2.07E+00	enzyme		1.342		-0.035	1.42	2.73E-06	CYP2B6,Gstm3,Mt1,Mt2,Slco1a1	
fluconazole		chemical drug						2.83E-06	ADH1C,CYP2B6,Cyp2c40 (includes others),CYP2C8	
NOS2		enzyme		-1.414		-0.086	-1.172	3.54E-06	FASN,GPT,IFIT1B,ISG15,MYH6,Orm1 (includes others),PIGR,TNNT3	IFNG,NFKBIA,NOS2,NR3C1,STAT1,USF1
SLCO1B3		transporter						3.72E-06	GPT,Slco1a4,SLCO2B1	
triolein		chemical drug						3.72E-06	FASN,GCK,THRSP	
IKBKG		kinase		-0.736	bias	-0.59		4.25E-06	CYP7B1,GPT,IFIT1B,ISG15,Mt1,Mt2,MYH6	CHUK,FOXO3,IKBKB,IKBKG,NFKBIA,NR3C1,SREBF2,TNF
beta-naphthoflavone		chemical toxicant		-0.882	bias	-0.374	-0.146	4.59E-06	ABCC3,CYP1A2,GSTM1,Slco1a4,SLCO2B1	
cadmium chloride		chemical toxicant						4.59E-06	GSTM1,Mt1,Mt2,Mup1 (includes others),Orm1 (includes others)	
IL1B		cytokine	Activated	2.8	bias	-0.369	4.137	5.40E-06	A2M,ABCC3,CYP1A2,CYP2B6,DIO1,GCK,IFIT1B,ISG15,Mt1,Mt2,PIGR,PLK3,SLC10A2,Slco1a1,Slco1a4,THRSP	IFN Beta,IFNG,IL1B,IL6,NFKBIA,NR3C1,RORC,SREBF2,STAT1,TNF,USF1
SLC13A1		transporter		0		0.088	-0.215	5.44E-06	ALDH1A1,C9,Cyp2b13/Cyp2b9,INMT,Mt1,SCD	
NFE2L2		transcription regulator		-0.089	bias	-0.541		5.60E-06	ABCC3,AOX1,ATP6V0D2,CELA1,GSTM1,Gstm3,INMT,Mt1,SERPINA6,THRSP,UCP1	
CITCO		chemical reagent						5.94E-06	CYP2A6 (includes others),CYP2B6,THRSP	CITCO,HNF4A,NR1I3
THRSP	-7.81E+00	other						5.94E-06	DIO1,FASN,THRSP	
3-methylcholanthrene		chemical toxicant		-0.627	bias	-0.698		6.70E-06	CYP1A2,GSTM1,Mt1,Mt2,Orm1 (includes others)	
CYP1B1		enzyme		1.342		-0.058	1.471	7.33E-06	CYP2B6,Gstm3,Mt1,Mt2,Slco1a1	
LDLR		transporter						7.85E-06	CYP27A1,CYP7B1,FASN,GPT,SCD,UCP1	LDLR,NFKBIA,NR3C1,SREBF1,SREBF2,TNF,cholesterol
PEBP1		other	Inhibited	-2	bias	-0.329	-1.342	8.12E-06	Aldh1a7,FASN,SCD,UCP1	
CYP1A1		enzyme		1.664		-0.065	1.822	8.82E-06	CYP2B6,GPT,Gstm3,Mt1,Mt2,Slco1a1	
TNF		cytokine		0.148	bias	-0.287	1.442	9.51E-06	A2M,ABCC3,Aldh1a7,CYP27A1,CYP2C8,CYP7B1,DIO1,FASN,IFIT1B,ISG15,LRG1,Mt1,Mt2,Orm1 (includes others),PIGR,PLK3,RGL3,SCD,Slco1a1,Slco1a4,SLCO2B1,THRSP,UCP1	CHUK,FOXO3,HNF1A,IKBKB,IL1B,IL6,NFKBIA,NR3C1,RORC,RXRA,STAT1,TNF
LEP		growth factor		-0.716	bias	-0.312	0.221	9.87E-06	ABCC3,CA3,Cyp2c54 (includes others),CYP2C8,FASN,GCK,Gstm3,PRKAA2,SCD,THRSP,UCP1	ADIPOQ,CEBPA,FOXO1,GHRL,Ins1,Insulin,JUN,LEP,MLXIPL,NR1H3,PPARA,PPARD,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,fatty acid
TFE3		transcription regulator		0	bias	-0.527		1.09E-05	FASN,GCK,SCD,THRSP	
carbohydrate		chemical - endogenous mammalian						1.09E-05	FASN,GCK,SCD,THRSP	FOXO1,GHRL,Insulin,JUN,PPARGC1A,SREBF1,SREBF2,USF2,carbohydrate
CEBPA		transcription regulator	Inhibited	-2.244	bias	-0.276	-1.48	1.10E-05	A2M,ADH1C,Apoc3,CYP2A6 (includes others),CYP2B6,FASN,ISG15,Mup1 (includes others),Orm1 (includes others),SCD,UCP1	CEBPA,SREBF1,SREBF2
MED1		transcription regulator		-1.091	bias	-0.642		1.14E-05	CDC6,CYP1A2,CYP2B6,DIO1,FASN,GCK,UCP1	
MLXIPL		transcription regulator						1.25E-05	FASN,GCK,SCD,THRSP	MLXIPL,NR1H3,PPARD,SREBF1,fatty acid
SIK1/SIK1B		kinase						1.26E-05	FASN,SCD,THRSP	SIK1/SIK1B,SREBF1,SREBF2
L-triiodothyronine		chemical - endogenous mammalian	Inhibited	-2.102		-0.242	-1.354	1.30E-05	A2M,ALDH1A1,DIO1,FASN,GCK,Mup1 (includes others),MYH6,SCD,THRSP,UCP1	CEBPA,FOXO1,Ins1,L-triiodothyronine,MLXIPL,PPARGC1A,RXRA,SREBF1,THRA,THRB,USF2
butylated hydroxyanisol		chemical toxicant		-1.177		-0.234	-0.717	1.43E-05	GSTM1,Gstm3,Slco1a1,SLCO2B1	
SLC51A		transporter						1.73E-05	ABCC3,CYP2B6,SLC10A2	
oleic acid		chemical - endogenous mammalian		-0.97		-0.239	-0.39	1.87E-05	CYP4F12,FASN,Mt1,Mt2,SCD,THRSP	CEBPA,D-glucose,FOXO1,FOXO3,Ins1,MLXIPL,NR1H3,PPARD,RXRA,SREBF1,USF2,fatty acid,oleic acid,palmitic acid
Insulin		group		-1.775		-0.195	-1.206	1.87E-05	CA3,CYP1A2,FASN,GCK,Orm1 (includes others),PRKAA2,SCD,SLC10A2,THRSP,UCP1	ADIPOQ,CEBPA,D-glucose,FOXO1,FOXO3,GHRL,IGF1,Insulin,JUN,MLXIPL,NR1H3,PPARA,PPARD,PPARGC1A,RXRA,SREBF1,STAT5B,fatty acid
CDN1163		chemical reagent						2.30E-05	FASN,SCD,UCP1	AMPK,CDN1163,MED1,MLXIPL,PPARGC1A
NRG4		growth factor						2.30E-05	FASN,GCK,SCD	Insulin,JUN,NRG4,PPARGC1A,SREBF1,SREBF2,USF2
amiodarone		chemical drug						2.64E-05	CA3,MYH6,SCD,SLCO2B1	
NKX2-1		transcription regulator						2.94E-05	DCK,Ear2 (includes others),INMT,LRG1,PNLIPRP1,SCD,TFF2	
acetaminophen		chemical drug		-0.61	bias	-0.257	0.059	2.94E-05	A2M,ABCC3,CA3,CYP1A2,GPT,Mt1,Slco1a1	HNF1A,IFNG,IL1B,NFKBIA,NR3C1,RXRA,STAT1,USF1,acetaminophen
SREBF1		transcription regulator		-0.404	bias	-0.568		2.98E-05	ADH1C,CYP7B1,FASN,GCK,PLS3,SCD,THRSP,UCP1	CEBPA,D-glucose,FOXO1,FOXO3,Ins1,Insulin,JUN,MLX,MLXIPL,NR1H3,PPARA,PPARD,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,fatty acid
palmitic acid		chemical - endogenous mammalian		-0.768	bias	-0.355	0.16	3.15E-05	CYP4F12,FASN,GCK,Mt1,Mt2,Orm1 (includes others),SCD	CEBPA,D-glucose,FOXO1,FOXO3,Ins1,Insulin,JUN,MLXIPL,NR1H3,PPARD,PPARGC1A,RXRA,SREBF1,SREBF2,USF2,fatty acid,palmitic acid
MED13		transcription regulator						3.28E-05	CYP2A6 (includes others),FASN,SCD,THRSP	
CEBPB		transcription regulator		-0.98	bias	-0.518		3.38E-05	ADH1C,ALDH1A1,CDC6,CYP2A6 (includes others),INMT,Orm1 (includes others),PRG2,SCD,UCP1,XIST	CEBPA,CEBPB,SREBF1
N-ethyl-N-nitrosourea		chemical toxicant						4.71E-05	GSTM1,Mt1,Mt2	

Day 5 Female BPA

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset
GATA2		transcription regulator						3.62E-06	CYP2F1,Ear2 (includes others),EPX,GBP2,PNLIPRP1,PRG2,Prss1 (includes others)
diquat		chemical toxicant						5.62E-05	Mt1,Mt2
CYP1A2		enzyme						6.12E-05	Mt1,Mt2,RGS16
N-methyl-3,4-methylenedioxyamphetamine		chemical drug						7.49E-05	Mt1,Mt2
IKBKG		kinase		1.067		-0.162	1.389	7.53E-05	GBP2,Mt1,Mt2,RGS16
IL1B		cytokine		0.813		-0.102	1.094	8.76E-05	AQP4,CD274,GBP2,GBP6,Mt1,Mt2,PAX6,RGS16
CYP1B1		enzyme						1.10E-04	Mt1,Mt2,RGS16
HTT		transcription regulator						1.40E-04	FOLR1,Fxyd2,KCNQ2,Mt1,RGS16,SEZ6,TNNI2
bromobenzene		chemical toxicant						2.15E-04	Mt1,Mt2,TUBB2B
N-ethyl-N-nitrosourea		chemical toxicant						2.79E-04	Mt1,Mt2
PROCR		other						2.79E-04	GBP2,GBP6
FOXA2		transcription regulator						2.89E-04	EPX,Mt1,PAX6,PNLIPRP1
RORA		ligand-dependent nuclear receptor						2.89E-04	CAV3,CYP2F1,Mt1,Mt2
CHUK		kinase		1.103		-0.18	1.454	4.13E-04	GBP2,Mt1,Mt2,RGS16
DMD		other						4.20E-04	AQP4,Cmya5,OBSCN,SLN
CYB5R4		enzyme						5.02E-04	Mt1,Mt2
Zn2+		chemical - endogenous mammalian						5.02E-04	Mt1,Mt2
DMRT1		transcription regulator						5.60E-04	Ear2 (includes others),EPX,PRG2
APP		other						5.68E-04	FOLR1,GBP2,GBP6,Mt1,PAX6,Prss1 (includes others),TUBB2B
CYP1A1		enzyme						6.12E-04	Mt1,Mt2,RGS16
PARP1		enzyme						8.96E-04	CD274,GBP2,GBP6
NR3C2		ligand-dependent nuclear receptor						9.19E-04	AQP4,Cmya5,Hrc
SLC9A3		ion channel						9.21E-04	Mt1,Mt2
DNMT3A		enzyme						1.12E-03	Mt1,RGS16,SLN
IKBKB		kinase		1.154		-0.145	1.44	1.21E-03	GBP2,Mt1,Mt2,RGS16
IL6		cytokine		1.726		-0.119	2.008	1.25E-03	AQP4,CD274,GBP2,Mir124a-1hg,Mt1,Mt2
SU6656		chemical toxicant						1.55E-03	Mt1,Mt2
mercuric chloride		chemical toxicant						1.64E-03	Mt1,Mt2
NEB	-3.55E+00	other						1.66E-03	SLN
SU9597		chemical - kinase inhibitor						1.66E-03	PAX6
alectinib		chemical drug						1.66E-03	CD274
budesonide/formoterol		chemical drug						1.66E-03	CD274
cabozantinib		chemical drug						1.66E-03	CD274
fluticasone/salmeterol		chemical drug						1.66E-03	CD274
miR-1343-5p (and other miRNAs w/seed GGGGAGC)		mature microrna						1.66E-03	AQP4
miR-513a-5p (miRNAs w/seed UCACAGG)		mature microrna						1.66E-03	CD274
miR-668-3p (and other miRNAs w/seed GUCACUC)		mature microrna						1.66E-03	AQP4
mir-668		microrna						1.66E-03	AQP4
mir-939		microrna						1.66E-03	AQP4
trametinib		chemical drug						1.66E-03	CD274
ATP7B		transporter						1.92E-03	Mt1,Mt2
RORC		ligand-dependent nuclear receptor						2.21E-03	CYP2F1,Mt1,Mt2
nitric oxide		chemical - endogenous mammalian						2.37E-03	CAV3,Mt1,Mt2
STAT3		transcription regulator		0.152		-0.103	0.357	2.49E-03	CD274,GBP2,GBP6,Mt1,PAX6
dimethylnitrosamine		chemical toxicant						2.55E-03	Mt1,Mt2
STAT1		transcription regulator		1.214		-0.154	1.519	2.61E-03	CD274,GBP2,GBP6,PAX6
IFNA4		cytokine						2.66E-03	CD274,GBP2
SB203580		chemical - kinase inhibitor		-0.106		0.184	-0.466	3.13E-03	AQP4,CAV3,CD274,GBP2
cadmium chloride		chemical toxicant						3.26E-03	Mt1,Mt2
CCR3		g-protein coupled receptor						3.33E-03	PRG2
DTNA		other						3.33E-03	AQP4
SRD5A2		enzyme						3.33E-03	Mt1
ST8SIA2		enzyme						3.33E-03	PAX6
dicumarol		chemical drug						3.33E-03	Mt1
POR		enzyme						3.36E-03	GBP2,Mt1,TUBB2B
CEBPE		transcription regulator						3.52E-03	EPX,PRG2
EBI3		cytokine						3.52E-03	CD274,GBP2
palmitic acid		chemical - endogenous mammalian						3.57E-03	Mt1,Mt2,PAX6
3-methylcholanthrene		chemical toxicant						3.78E-03	Mt1,Mt2
MYOD1		transcription regulator						3.85E-03	Hrc,TNNI2,TTN
NPTX1		other						4.98E-03	KCNQ2
F2RL1		g-protein coupled receptor						5.09E-03	GBP2,GBP6
SOD1		enzyme						5.22E-03	CYP2F1,Mt1,Mt2
diethylstilbestrol		chemical drug						5.43E-03	AQP4,CYP2F1,SEZ6
NFKBIA		transcription regulator		1		-0.061	1.122	5.99E-03	GBP2,Mt1,Mt2,RGS16
STAT4		transcription regulator						6.08E-03	Mt1,RGS16,TUBB2B
epigallocatechin-gallate		chemical drug						6.23E-03	AQP4,EPX,PRG2
AKAP5		other						6.64E-03	KCNQ2
GZMB		peptidase						6.64E-03	CD274
SCTR		g-protein coupled receptor						6.64E-03	AQP4
SLC39A4		transporter						6.64E-03	Mt1
ammonia		chemical - endogenous mammalian						6.64E-03	AQP4
cadmium sulfate		chemical toxicant						6.64E-03	Mt1
lipopolysaccharide		chemical drug		1.596		-0.111	1.904	6.69E-03	AQP4,CD274,Ear2 (includes others),GBP2,GBP6,Mt1,Mt2,RGS16
Bvht		other						6.92E-03	Hrc,TTN
cadmium		chemical toxicant						6.92E-03	Mt1,Mt2
IL17A		cytokine						6.94E-03	CD274,GBP2,RGS16
TO-901317		chemical reagent						7.02E-03	CYP2F1,Mt1,Mt2
MBD3		enzyme						7.84E-03	Mt1,PAX6
FFAR3		g-protein coupled receptor						8.22E-03	GBP2,GBP6
L-homocysteine		chemical - endogenous mammalian						8.29E-03	FOLR1
WZ-4002		chemical - kinase inhibitor						8.29E-03	CD274
ZNF536		transcription regulator						8.29E-03	PAX6
carvacrol		chemical - endogenous non-mammalian						8.29E-03	AQP4
zinc chloride		chemical reagent						8.29E-03	Mt1
FGF19		growth factor						8.81E-03	AQP4,RGS16
MRTFB		transcription regulator						8.81E-03	EPX,PRG2
mir-21		microrna						9.14E-03	CD274,GBP2,GBP6
HDAC1		transcription regulator						9.53E-03	Mt1,Mt2,TNNI2
Ifnar		group						9.63E-03	CD274,GBP2
ZFHX3		transcription regulator						9.84E-03	RGS16,TUBB2B
CCL15		cytokine						9.94E-03	EPX
DIAPH1		other						9.94E-03	PAX6
DPPA3		other						9.94E-03	PAX6
EN2		transcription regulator						9.94E-03	PAX6
FUBP1		transcription regulator						9.94E-03	STMN3
GPR39		g-protein coupled receptor						9.94E-03	RGS16
MEIS2		transcription regulator						9.94E-03	PAX6
SIX3		transcription regulator						9.94E-03	PAX6
SOX15		transcription regulator						9.94E-03	Hrc

Day 60 Male BPA

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
TP53		transcription regulator	Inhibited	-2.102		0.15	-3.572	5.85E-27	A2M,ACACB,ACSF2,ACSS2,ADAM8,ADRB2,AFP,ALDH18A1,ANLN,ANXA1,AR,ASNS,ASPM,ATAD2,AURKA,BIRC5,BRCA1,BTG2,CCND3,CCNF,CD44,CDC25A,CDC6,CDK1,CDKN2D,CENPA,CENPE,CENPF,CERS6,CGREF1,CKAP2,CKMT2,CMBL,COL1A1,CORO1A,Cox8b,CSF2RA,CYFIP2,CYR61,DHCR7,DLGAP5,DNMT1,DTX1,[illegible],H19,H2AFX,Hist1h1b,HIST2H4B,HMGB2,Hmgn2 (includes others),HMMR,HMOX1,HSPB1,ID1,IGDCC4,IGF1R,IGF2,IGFBP2,IL1RN,KIF23,LOX,MCM3,MCM4,MCM5,MCM6,ME2,MKI67,MOCOS,Mt2,MYLK3,NCAPD3,NCAPH,NCF1,NDC8	[illegible]
ERBB2		kinase	Activated	4.174	bias	0.34	1.801	3.32E-23	ADAM8,Aldh1a7,AR,ASPM,AURKA,BARD1,BIRC5,BTG2,CCND3,CDC25A,CDC6,CDCA2,CDCA3,CDCA4,CDH11,CDK1,CENPA,CENPE,CENPF,CLEC3B,COL1A1,COL5A1,DTX1,E2F1,E2F2,Elf5,ESPL1,FASN,FEN1,FSTL1,FXYD3,GINS3,H19,HIST1H4C,HMGB2,HSPB1,HSPB8,ID1,IGF1R,IGF2,ITGB3,LCN2,LPCAT1,Marcks,MCM3,MCM4,[illegible],SOX4,SPAG5,TCEAL9,THBS1,Tmsb4x (includes others),TNC,TNNT3,TOP2A	[illegible]
YY1		transcription regulator		1.118		0.052	0.993	6.92E-20	ARID3A,AURKA,BIRC5,BRCA1,BTG2,CD93,CDC6,CDCA3,CENPA,CENPE,COL1A1,CXCR4,CYBB,FDPS,FEN1,GPC3,H2AFX,HIST1H4C,HMOX1,INCENP,KIF11,KIF23,LMNB1,MCM4,MCM5,MCM6,MKI67,MYH1,MYH2,MYH4,PCNA,PLAGL1,POLA1,PRC1,RAB8B,RAD18,RRM1,SLC25A4,TOP2A,UHRF1,VAV1	CDKN2A,E2F1,E2F4,E2f,MYC,RB1,RBL1,TP53,TP73,YY1
CSF2		cytokine	Activated	6.168	bias	0.522		1.01E-19	ADAM8,ANLN,ANXA1,AURKA,BIRC5,CCND3,CCNF,CD63,CDCA2,CDCA3,CDK1,CENPE,CSF2RA,CXCR4,CYBB,ELN,FIGNL1,GATA1,IL1RN,INPP5D,Ins1,ITGA4,ITGB3,KIF11,KLF1,LY75,MARCO,MCM3,MCM5,MCM6,MKI67,MKNK1,MMP14,NCAPH,NFE2,NUSAP1,POLE,PRC1,RBM3,RRM2,SLC1A5,Sfrn2,SMC2,SPAG5,SPC25,STMN1,T[illegible]	[illegible],HDAC1,HIF1A,IL6,MYC,NFkB (complex),P38 MAPK,RB1,RELA,SMAD4,SRF,STAT3,TGFB1,TP53,TP73,Vegf
CCND1		transcription regulator	Activated	3.476		0.094	2.983	2.30E-19	AR,ASPM,ATAD2,AURKA,BIRC5,BRCA1,C7,CCND3,CD44,CDC25A,CDC6,CDK1,CENPA,CENPF,CIP2A,CLSPN,COL1A1,DNMT1,DTL,E2F1,ESCO2,FAM83D,FLNA,GPC6,HIST1H4H,HSPB1,HSPB8,ID1,ITGB3,KIF11,KIF20B,KNL1,MCM4,MORC4,NCAPH,PCNA,PRSS1,RBL1,RRM2,SELENBP1,SOX4,SPC25,TPX2,TUBB,TUBB1,UHRF1	CBX3,CCND1,CCNE1,CDKN1A,E2F1,E2F2,E2F3,E2F4,E2f,RB1,RBL1,RBL2,TP53
dexamethasone		chemical drug		0.693		0.068	0.039	2.76E-19	AACS,ABHD2,ACSS2,ADAMTS15,ADRB2,AFP,Akr1b7,ALDH18A1,AMY2B,ANXA1,APOA4,ASNS,ATP2B4,BCL6,BEX3,BIRC5,BRCA1,BTG2,CA2,CAMP,CCND3,CD44,CDH11,CKLF,Clca3a1/Clca3a2,COL1A1,CTSE,CXCR4,CYBB,Cyp2a12/Cyp2a22,CYP2A6 (includes others),CYP2B6,CYP3A5,CYP4A11,CYR61,DLGAP5,DUSP5,E2F2,ECT2,[illegible],IGF2,IGFBP1,IGFBP2,IL1RN,INHBB,Ins1,ISG20,ITGA4,ITGB3,KNL1,LAD1,LAMC1,LCN2,LPL,LY75,LYVE1,MARCO,MCM4,MFGE8,MMP14,MMP8,MS4A6A,Mt1,Mt2,NCAPH,NDC80,NEIL3,NREP,NUF2,P	[illegible]
PPARA		ligand-dependent nuclear receptor	Activated	2.716		0.178	1.753	3.70E-19	ABCD2,ACSS2,Akr1b7,APCS,APOA4,ASNS,AURKA,Cd24a,CD63,CDK1,CTSE,CYBB,CYP2B6,Cyp2c54 (includes others),CYP4A11,DHCR7,ETHE1,FABP5,FASN,FDPS,GCK,GPT,GSTK1,GSTP1,H2AFX,HIST1H1C,Hmgn2 (includes others),HMOX1,IGFBP1,IGFBP2,IL1RN,Ins1,KHK,KRT23,LIPG,LPL,ME2,MKI67,Mup1 (includes others),NC[illegible]	[illegible],SREBF1,SREBF2,THRB,ciprofibrate,pirinixic acid
lipopolysaccharide		chemical drug	Activated	2.302	bias	0.337	-0.841	1.45E-18	ADRB2,AGER,ALOX12,ANXA1,APCS,APOA4,Apol7e (includes others),AR,BCL6,CAMP,CCND3,CCNF,Cd24a,CD300LF,CD44,CDC25A,CDH11,CHST3,COL1A1,COL5A1,CORO1A,CSF2RA,CUX2,CXCR4,CYBB,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP3A5,CYP4A11,CYR61,DNMT1,DUSP5,DUSP8,E2F1,Ear2 (includes oth[illegible],KCNK5,KIF23,LCN2,LIPG,LMNB1,LPL,Marcks,MARCKSL1,MARCO,MCM5,MFN2,MKI67,MMP14,MMP8,Mt1,Mt2,NCF1,NFE2,NID1,NNMT,NUSAP1,Orm1 (includes others),PCNA,PKM,PLA2G7,PLEK,POLA1	[illegible]
E2F4		transcription regulator						6.92E-18	ANLN,BARD1,BRCA1,CDC25A,CDC6,CDCA4,CDK1,CENPA,CENPE,E2F1,E2F2,ECT2,FANCD2,FEN1,H2AFX,HIST1H3D,HMMR,MCM3,MCM4,MCM5,MCM6,MKI67,NDC80,PCNA,POLA1,PRC1,PSAT1,RBL1,RRM1,RRM2,SMC2,STMN1,TOP2A,TPX2,UHRF1	E2F1,E2F3,E2F4,EP300,HDAC1,RB1,TP53
dextran sulfate		chemical drug						1.02E-17	ADAM8,ANLN,AURKA,BIRC5,CCNF,CDCA2,CDCA3,CDK1,CENPE,FIGNL1,HMOX1,IGF1R,KIF11,MCM3,MCM5,MCM6,MKI67,MMP14,NCAPH,NUSAP1,PCNA,POLE,PRC1,RRM2,Sfrn2,SMC2,SPAG5,SPC25,STMN1,THBS1,THBS2,TICRR,TOP2A,TPX2,UHRF1,VCAM1	Ap1,CAT,EGR1,FOXO1,FOXO3,HIF1A,Hif1,IGFBP3,IL6,JUN,LDL,MYC,NFKB1,NFKBIA,NFkB (complex),NR4A1,PPARA,RELA,STAT3,TP53,dextran sulfate,nitric oxide
E2F1	1.472	transcription regulator	Activated	4.583	bias	0.405	2.3	1.27E-17	AMY2B,AR,ATAD2,AURKA,BIRC5,BRCA1,CA2,CCND3,CCNF,CD44,CDC25A,CDC6,CDCA4,CDK1,CDKN2D,DNMT1,E2F1,E2F2,ECT2,FANCD2,FEN1,FHDC1,H19,HIST1H4H,HMGB2,Hmgn2 (includes others),IGF2,INMT,Ins1,KIF23,MCM3,MCM4,MCM5,MCM6,MYH2,MYH4,NDC80,NUSAP1,PCNA,POLA1,PSAT1,RBL1,RRM1,RRM2,STM[illegible]	[illegible],RB1,RBL1,Rb,TP53,TP73
E2F3		transcription regulator	Activated	3.968	bias	0.362	2.269	1.49E-17	AKNA,BIRC5,CCND3,CDC25A,CDC6,CDCA3,CDCA4,CDK1,E2F1,E2F2,HIST1H1C,HIST1H2BN,HIST1H3D,HIST1H4B,HIST3H2A,HMGB2,IGF2,LPL,MCM3,MCM4,MCM5,MCM6,NCAPG2,PCNA,POLA1,RBL1,RRM1,RRM2,TENT5A,THBS1,TPX2	CCNE1,CDK2,Cyclin E,E2F1,E2F2,E2F3,E2F4,E2f,IGF2,MYC,NFKBIA,RB1,RBL1,RELA,TP53,TP73
CDKN1A		kinase	Inhibited	-2.372		-0.209	-1.648	2.21E-17	ANLN,ASPM,ATAD2,AURKA,BIRC5,BRCA1,CCND3,CDC25A,CDC6,CDK1,CENPF,CYR61,DLGAP5,DTL,H2AFX,HMGB2,ITGB3,MCM3,MCM4,MCM6,MKI67,NCAPD3,NUSAP1,PCNA,PRC1,RBL1,RRM1,SERPINI2,SMC2,SPAG5,STMN1,TOP2A,TPX2,UHRF1	CCND1,CCNE1,CDKN1A,Cyclin E,E2F1,E2F4,E2f,ESR1,HDAC1,MYC,RB1,RBL1,Rb,TP53,TP73
calcitriol		chemical drug	Inhibited	-2.614		-0.067	-2.173	5.06E-17	ANLN,AR,BIRC5,BRCA1,CA2,CAMP,CCND3,CDC6,CDK1,CENPA,CYP2B6,CYR61,ECT2,ELN,ESPL1,FASN,FBN2,FDPS,FEN1,FIGNL1,Hmgn2 (includes others),ID1,IGF1R,IL1RN,INCENP,Ins1,ITGA4,KIF23,KRT23,LCN2,LPL,MCM3,MCM4,MCM5,NUSAP1,PCNA,PDK3,POLE,PRC1,RGCC,RRM2,SLC16A1,SLC8A1,SMC2,SPAG5,SPRY2,S[illegible]	[illegible],JUN,MYC,NFKBIA,NFkB (complex),RB1,RBL1,RELA,SP1,STAT3,TNF,TP53,beta-estradiol,calcitriol,prostaglandin E2
TCF3		transcription regulator		-1.482		0.073	-1.788	2.72E-16	ACACB,ANLN,AURKA,BCL6,BIRC5,CA2,CCND3,CDCA3,CDK1,CERK,CGREF1,CIP2A,CKAP4,COL1A1,CTSE,DTX1,EBF1,ECT2,ESCO2,GATA1,H2AFX,HMGB2,Hmgn2 (includes others),HMMR,Ins1,KIF11,MKI67,NDC80,NUF2,NUSAP1,PLCG2,PLK4,PRC1,PRSS3,RGS16,RRM2,SPC25,TCEAL9,TENT5C,TOP2A	
Vegf		group	Activated	5.332	bias	0.494	1.968	8.06E-16	A2M,ASNS,AURKA,BIRC5,CA2,CCNF,CD44,CD93,CDC25A,CDC6,CDK1,CENPF,CXCR4,CYP4A11,CYR61,DUSP5,EFNA1,ELN,FLNA,GATA1,GRB10,HMMR,HMOX1,ID1,INHBB,ISG20,KIF11,KIF20B,KLF1,LCN2,LY75,LYVE1,MCM5,MKI67,MMP14,Mt2,NDC80,NRROS,PLK4,PRC1,RGCC,SH3TC2,SLC7A1,SLCO2B1,SMC2,TGFB1,TNC,T[illegible]	[illegible],FOS,FOXO1,FOXO3,HIF1A,JUN,Jnk,MXI1,MYC,NFKB1,NFKBIA,NFkB (complex),RELA,SMAD4,TGFB1,TP53,VEGFA,Vegf
tretinoin		chemical - endogenous mammalian	Activated	2.075		0.241	0.005	8.66E-16	A2M,ABHD2,ACACB,ACSS2,AFP,ANXA1,APBB1IP,ASNS,ATP2A3,BCL6,BCO1,BIRC5,BRCA1,BTG2,CA2,CCND3,CD44,CD63,CD93,CDKN2D,Clca3a1/Clca3a2,COL1A1,COTL1,CXCR4,CYBB,CYP2B6,CYP2U1,CYP4A11,CYR61,DLGAP5,DNMT1,DTL,ELN,FABP5,FASN,GCK,GRB10,GSTP1,HK1,HLA-A,HMOX1,HSPB1,ID1,IFIT2,IFNGR1,[illegible],MTHFD2,MYO9A,NCF1,NFE2,PAK1,PEG10,PLA2G7,PLCB2,PLEK,PLEKHB1,PNLIPRP2,PRG2,RBL1,RBP1,RFLNB,RNASE1,S100A10,SIRPA,SLA,SLC16A1,SMOX,SOX4,TAL1,TFRC,TGFB1,THBS1,TNC,TOP2A,TSPAN33,V	[illegible]
TNF		cytokine	Activated	2.041		0.241	-0.197	2.36E-15	A2M,ABCD2,ADAM8,ADRB2,AGER,Aldh1a7,ANXA1,APCS,AR,ARHGDIB,ATP2B4,BCL6,BIRC5,BTG2,CA2,CCND3,CD44,CDH11,CERS6,CMBL,COL1A1,COTL1,CXCR4,CYBB,CYR61,DNMT1,DUSP5,DUSP9,E2F1,EFNA1,FABP5,FASN,FDPS,FRMD4A,GBP2,GSTP1,H19,HLA-A,Hmgn2 (includes others),HMOX1,ID1,IFNGR1,IGF1R,IGF2,[illegible],NID1,NNMT,NRROS,Orm1 (includes others),PCK2,PCNA,PDK3,PIK3CD,PKM,Ppbp,PPP1R3C,RBP1,RGCC,RGS16,RNASE1,RRM1,RRM2,SELPLG,SH3TC2,SLC14A1,SLC1A4,SLC7A1,SLC8A1,SLCO2B1,Sfrn2	[illegible]
let-7		microrna	Inhibited	-4.697	bias	-0.654		4.00E-15	AR,ARID3A,AURKA,BRCA1,BTG2,CCNF,CD44,CDC25A,CDC6,CDCA2,CDCA3,CDK1,COL1A1,E2F2,FANCD2,HBA1/HBA2,IGF1R,ITGA4,ITGB3,MCM3,MCM4,MCM5,MCM6,NUF2,PKM,PLAGL1,RBM38,RRM1,RRM2,THBS1	Akt,CEBPB,CREBBP,CTNNB1,EGR1,ERK1/2,JUN,MYC,PGR,RELA,let-7
GATA1	11.717	transcription regulator		1.712		0.169	0.851	1.31E-14	ALOX12,BIRC5,BTG2,CA2,CCND3,CDKN2D,Clca3a1/Clca3a2,CYBB,DMTN,GATA1,Gypa,HBA1/HBA2,HBB,IKZF1,INHBB,ITGB3,KLF1,LEPR,MCM3,MCM5,NFE2,PCNA,PLEK,PRG2,RBL1,RRM1,SLC4A1,SPTA1,TAL1,TFRC,TOP2A,TUBB1	E2F2,GATA1,Histone h3,RNA polymerase II,RUVBL1,RUVBL2,SP1
BNIP3L		other	Inhibited	-2.688		-0.175	-1.969	1.50E-14	AURKA,CCND3,CENPE,CENPF,CKAP2,E2F1,FANCD2,GSN,KIF11,NUF2,PIK3CD,RBL1,RRM2,SYK,TFRC,TGFB1,TOP2A	
doxorubicin		chemical drug		-0.044		0.238	-1.515	1.64E-14	A2M,AFP,ANXA1,AR,ASNS,AURKA,BARD1,BIRC5,BRCA1,BTG2,CA2,CAPN6,CD44,CDK1,CDK14,CENPA,CKAP4,CYBB,CYR61,DNMT1,DUSP5,E2F1,E2F2,H2AFX,HMOX1,ID1,IGFBP1,LCN2,MCM3,PCNA,PRC1,RBL1,RBM3,RGS16,RRM1,RRM2,S100A10,SLC25A4,STMN1,TGFB1,TOP2A,TUBB	Ap1,E2F1,E2F2,E2F3,E2F4,E2f,FOS,FOXO3,HDAC1,IL6,JUN,MYC,NFkB (complex),NR3C1,RB1,RELA,STAT3,TP53,TP73,doxorubicin
TGFB1	1.416	growth factor	Activated	4.546		0.211	2.856	2.21E-14	AFP,ALDH18A1,ALOX12,AMY2B,ARHGAP19,ASNS,ASPM,BARD1,BCL6,BIRC5,CAMP,CCND3,CD44,CDC25A,CDH11,CDK1,CENPA,CENPE,CENPF,Ces2c,CHST3,COL1A1,COL5A1,COTL1,CXCR4,CYBB,CYR61,DMTN,DNMT1,DOCK2,E2F1,ELN,ESPL1,FABP5,FASN,FLNA,FNDC3B,GATA1,GBP2,GCNT1,GGT6,GPT,GSN,HMOX1,HS[illegible],NDC80,NEU3,NNMT,PCNA,PIK3CD,PLAGL1,PPP1R3C,PRC1,PRSS1,PRSS3,RBL1,RBM3,RFLNB,RGCC,S100A10,SELENBP1,SELPLG,SLC13A3,SLC25A4,SLC4A1,SLC7A1,SMC2,SOX4,SPC25,TFRC,TGFB1	[illegible]
MYC		transcription regulator	Activated	4.412	bias	0.266	2.451	1.50E-13	AFP,ALDH18A1,AR,ASNS,ASPRV1,ATP5IF1,BCL6,BIRC5,BRCA1,CCND3,CD44,CDC25A,CDK1,CLEC3B,COL1A1,COL5A1,COX6A1,CYFIP2,DNMT1,DUSP5,E2F1,E2F2,Ear2 (includes others),EBF1,Elf5,FABP5,FASN,FBN2,FLNA,FSTL1,GBP2,GCK,GPC3,GPT,H19,HLA-A,Hmgn2 (includes others),HMOX1,HSPB1,ID1,IKZF1,Ins1,LOX,MC[illegible],TNNT3,ULBP1,UNC119,VCAM1	[illegible]
E2F2	3.652	transcription regulator	Activated	3	bias	0.555		1.54E-13	AMY2B,BIRC5,CCND3,CDC25A,CDC6,CDCA4,CDK1,CDKN2D,E2F1,Ins1,MCM3,MCM4,MCM5,MCM6,PCNA,POLA1,RBL1,RRM2	CCNE1,CDK2,E2F1,E2F2,E2F4,E2f,RB1,RBL1,TFDP1,TP53
HGF		growth factor	Activated	4.537	bias	0.46	1.655	1.67E-13	A2M,AFP,ASNS,AURKA,BIRC5,CCNF,CD44,CD93,CDC25A,CDC6,CDK1,CENPF,COL1A1,CXCR4,CYP2B6,CYR61,FEN1,FLNA,GRB10,HK1,HMMR,HMOX1,ID1,Ins1,ISG20,KIF11,KIF20B,LCN2,LY75,LYVE1,MCM5,MKI67,MMP14,MMP8,NDC80,PCNA,PLK4,PRC1,SLC7A1,SMC2,SPRY2,TGFB1,THBS1,TPX2,VCAM1	Ap1,CTNNB1,E2F1,EGR1,FOXO1,FOXO3,HGF,HIF1A,HRAS,IL6,JUN,MYC,NFKB1,NFKBIA,NFkB (complex),PPARG,PPARGC1A,RELA,SIRT1,STAT3,TP53,TP73,VEGFA,hyaluronic acid
RORC		ligand-dependent nuclear receptor						1.72E-13	ABCD2,ACACB,APOA4,ASNS,CKMT2,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),CYP3A5,CYP4A11,GSTM4,GSTP1,IGFBP1,KCNK5,LCN2,Mt1,Mt2,Mup1 (includes others),Nat8f5,NNMT,PPP1R3C,SELENBP1,SULT2A1,UBE2O	
thioacetamide		chemical toxicant	Activated	2.601	bias	0.571		2.02E-13	AACS,ANXA1,ASNS,B4GALT6,BARD1,BRCA1,CAPN6,Cd24a,CD44,COL1A1,ELN,FCGR2A,FSTL1,HIST1H3D,HK1,IGFBP1,LCN2,LOX,LYVE1,MCM3,MCM6,MMP14,PKM,POLE,RBM3,RGCC,RRM1,S100A10,SERPINA7,SLC13A3,TGFB1	CREBBP,ESR1,HIF1A,JUN,MYC,NFKBIA,NFkB (complex),RELA,SMAD4,TGFB1,TNF,TP53,thioacetamide
discodermolide		chemical drug						3.05E-13	BARD1,BRCA1,CDC25A,CDK1,E2F2,ESPL1,FANCD2,KIF11,KIF23,PLK4,PRC1,RBL1,SMC2,TOP2A	E2F1,E2F4,MYC,RB1,TP53,TP73,discodermolide
diethylnitrosamine		chemical toxicant	Activated	2.612		0.067	2.343	3.64E-13	AFP,APCS,CD63,Cyp2c54 (includes others),CYP4A11,E2F1,GSTP1,IGFBP1,IGFBP2,LCN2,LPL,Mt1,Mup1 (includes others),MYH1,PCNA,QPCT,SELENBP1,SLCO2B1,Vnn3	CREBBP,CTNNB1,E2F2,FOXO3,GLIS2,Histone h3,IL6,JUN,MYC,NFKB1,NFKBIA,NFkB (complex),RELA,RNA polymerase II,RUVBL1,RUVBL2,SP1,STAT3,TNF,diethylnitrosamine
IL6		cytokine	Activated	3.543	bias	0.361	1.22	4.32E-13	A2M,AFP,ANXA1,APCS,BCL6,BIRC5,BTG2,CD44,CDC6,CDK1,CDKN2D,CENPA,CENPE,COL1A1,CXCR4,CYBB,CYP2B6,CYP3A5,DNMT1,E2F1,E2F2,GATA1,GBP2,HLA-A,HMOX1,ID1,IFIT2,IGF2,IGFBP1,IL1RN,ITGB3,KIF11,LCN2,LPL,MCM3,MKI67,MMP8,Mt1,Mt2,NEU3,Orm1 (includes others),PCNA,PLK4,RRM2,SERPINA7,SLC14A1,[illegible]	[illegible],NFKBIA,NFkB (complex),RELA,STAT3,TNF,TP53,VEGFA,beta-estradiol
gefitinib		chemical drug						4.80E-13	ADAMTS15,AURKA,BIRC5,BRCA1,BTG2,CCNF,CDC6,CDKN2D,CKAP2,COL1A1,ECT2,EFNA1,HMOX1,HSPB1,ID1,KIF11,KIF23,MCM3,MKI67,PCNA,PRC1,RAD18,RBL1,SMC2,TOP2A	CCND1,CREB1,E2F1,E2f,EGFR,EGR1,ERBB2,ESR1,ESR2,FOXO1,FOXO3,MDM2,MYBL2,MYC,NR1H3,PGR,PPARA,PPARG,RARA,RB1,RXRA,Rb,SP1,SREBF1,TP53,gefitinib
LY294002		chemical - kinase inhibitor	Inhibited	-3.358	bias	-0.521		5.42E-13	ACSS2,ADRB2,AR,ATP2B2,AURKA,BCL6,BIRC5,CCND3,CD44,CDKN2D,COL1A1,CYR61,FASN,FEN1,GCK,GRB10,GSTP1,HIST1H4C,HMGB2,HMOX1,IGF1R,IGF2,IGFBP2,IL1RN,INHBB,ISG20,ITGB3,LCN2,MFN2,MMP14,NDC80,PCNA,RBL1,SLA,SMC2,SPAG5,SPN,SPRY2,SULT1C2,SYK,TGFB1,THBS1,TOP2A,TTN,VCAM1	AKT1,AR,Akt,CREBBP,CTNNB1,EGR1,EP300,FOXO1,FOXO3,HIF1A,IGF1,JUN,LY294002,NFkB (complex),PI3K (complex),PPARG,RELA,SP1
GATA2		transcription regulator	Activated	2.556		0.114	2.152	5.60E-13	AMY2B,AR,CAMP,Cldn13,CYBB,E2F2,Ear2 (includes others),GATA1,GBP2,GRAP2,Gypa,HBA1/HBA2,IKZF1,Ins1,KLF1,LCN2,MFSD2B,NFE2,Ngp,Ppbp,PRG2,PRSS1,Prss1 (includes others),PRSS3,SERPINA6,SERPINI2,SLC4A1,SPN,Stfa2/Stfa2l1,Stfa3,TAL1,TFRC,THBS1,TREM3,TRIM58,TSPAN32,TUBB1,VCAM1,Wfdc21	
beta-estradiol		chemical - endogenous mammalian	Activated	3.436		0.222	1.386	6.74E-13	A2M,ADRB2,AFP,AGER,ALDH18A1,ANXA1,APOA4,AR,ATAD2,ATP2B2,AURKA,BCL6,BIRC5,BRCA1,BTG2,CA2,CCND3,CD44,CDC25A,CDC6,CDH11,CDK1,COL1A1,CXCR4,CYBB,CYP2A6 (includes others),CYP2B6,CYR61,DHCR7,DMTN,DUSP5,E2F1,E2F2,EFNA1,ENC1,EPB41L3,FABP5,FAM111A,FASN,FCGR2A,FEN1,FSTL1,GBP2,[illegible],MCM3,MCM4,MCM5,MCM6,MKI67,PCNA,PKM,POLA1,PPP1R3C,PPP1R9B,PRC1,PSAT1,PSEN2,RGS16,RRM2,SELENBP1,SLA,SLC13A3,SLC14A1,SLC8A1,SLCO2B1,SMC2,SOX4,SPN,SPRY	[illegible]
phorbol myristate acetate		chemical drug		1	bias	0.337	-1.617	8.04E-13	ADAM8,AGER,ALOX12,ANXA1,ATP2A3,ATP2B4,AURKA,BIRC5,BTG2,CA2,CCND3,CD44,CDK1,CDKN2D,CERK,CSF2RA,CXCR4,CYBB,CYP2A6 (includes others),CYR61,DNMT1,DTL,DUSP5,DUSP8,E2F1,GATA1,GSTP1,H19,HIST1H4C,HMBS,ID1,IFNGR1,IGF2,IGFBP1,IGFBP2,IKZF1,IL1RN,INHBB,ITGB3,ITM2A,JCAD,LCN2,LEPR,[illegible],SPN,SST,TEAD2,TGFB1,THBS1,THRSP,VCAM1	[illegible]
butyric acid		chemical - endogenous mammalian		-1.605		0.065	-1.967	9.76E-13	A2M,ANXA1,AR,ATP2A3,ATP2B4,BIRC5,C7,CAMP,CD44,CDC25A,CDC6,CDH11,COL1A1,COL5A1,COX6A1,CXCR4,CYP2B6,CYP4A11,E2F1,FASN,FSTL1,GATA1,GBP2,GSN,GSTP1,HBA1/HBA2,HBB,HIST1H1C,HK1,HMGB2,IGF2,INPP5D,MKI67,NEU3,PCNA,PLCB2,PTPN7,RBL1,SYK,TGFB1,TOP2A	CCNE1,E2F1,E2F2,E2F4,E2f,ESR1,FOXO3,GATA3,HDAC1,HIF1A,Histone h4,IL2,IL6,MED1,MYC,NFKBIA,NFkB (complex),RB1,RBL1,RELA,SMAD4,STAT3,STAT5A,TGFB1,TP53,butyric acid
EP400		other	Activated	2.891	bias	0.559		9.98E-13	CCNF,CDC25A,CDC6,CDCA3,CENPF,E2F1,E2F2,INCENP,MCM3,MCM4,NCAPG2,PCNA,RBL1,UHRF1	E2F2,EP400,HDAC1,Histone h4,MED1
cycloheximide		chemical reagent		-0.982		-0.083	-0.506	1.56E-12	AFP,Akr1b7,APBB1IP,AR,ATP2B2,BEX3,BRCA1,BTG2,CCND3,CD44,CDKN2D,COL1A1,COL5A1,CXCR4,CYP2B6,CYP3A5,CYP4A11,CYR61,GATA1,HMOX1,IGF2,IGFBP1,IGFBP2,IL1RN,ISG20,ITGB3,LCN2,LPL,Mt1,MYLK3,PRKAR2B,PSEN2,RBM3,SST,TGFB1,THBS1,VCAM1	Akt,Ap1,CREBBP,CTNNB1,EGR1,FOS,FOXO3,HIF1A,Hif1,IL1B,IL6,JUN,MYC,NFKBIA,NFkB (complex),NR3C1,RELA,STAT3,TP53,VHL,cycloheximide
fulvestrant		chemical drug	Inhibited	-3.302		-0.141	-2.563	1.65E-12	ADRB2,ASNS,AURKA,BARD1,BIRC5,CDC25A,CDK1,CENPF,CYR61,E2F1,FEN1,GSTP1,H2AFX,ID1,IGF1R,INHBB,ITGB3,KIF11,LEPR,LPL,MCM3,MCM5,PCNA,POLE,PPP1R9B,RBL1,RRM1,STMN1,TFRC,TGFB1,VCAM1	CCND1,CDKN1A,CREB1,E2F1,E2F2,E2F3,E2F4,E2f,ESR1,ESR2,HDAC1,RARA,RB1,RBL1,SP1,TP53,fulvestrant
SMARCB1		transcription regulator		-1.934	bias	0.392	-3.734	1.66E-12	A2M,AURKA,CD44,CDC6,CDK1,CENPA,CENPE,COL1A1,CXCR4,Cyp2c54 (includes others),CYP4A11,Defb1,E2F1,FCGR2A,GSN,IGFBP2,KIF11,KIF23,MCM3,MCM4,MCM5,Mup1 (includes others),PLK4,POLA1,PPP1R3C	E2F1,E2F4,E2f,MDM2,MYBL2,MYC,RB1,Rb,SMARCA4,SMARCB1,SP1,SP3,STAT3,TP53,TP73
ZBTB20		transcription regulator	Inhibited	-2.673		0.04	-2.821	1.69E-12	ACSS2,AFP,Akr1b7,Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),CYP3A5,FASN,GCK,GPC3,GSTM4,IGFBP1,IGFBP2,Ins1,LEPR	CTNNB1,Ins1,LEP,NFKB1,NFkB (complex),PPARA,PPARG,RELA,RXRA,SP1,USF2,ZBTB20
methylselenic acid		chemical reagent						1.99E-12	AR,ATAD2,AURKA,BIRC5,BRCA1,CD44,CDC25A,CDC6,CDK1,CDKN2D,CENPA,CENPF,CORO1A,E2F1,HMMR,ID1,IGF1R,KIF11,KIF20B,MCM3,MCM5,MCM6,MKI67,NREP,PCNA,PEG3,POLA1,RRM1,RRM2,TOP2A	CCND1,CCNE1,CDKN2A,E2F1,E2F2,E2F3,E2F4,E2f,ESR1,ESR2,MYC,RB1,RBL1,RELA,TP53,beta-estradiol,methylselenic acid
methylprednisolone		chemical drug		0.589		0.134	-0.127	2.02E-12	A2M,ANXA1,ASNS,ATP5IF1,B4GALT6,Cd24a,CD44,Ces1e,COX6A1,CYBB,Cyp2a12/Cyp2a22,Cyp2b13/Cyp2b9,EFNA1,FABP5,FCGR2A,FSTL1,GBP2,GCK,GPT,GSTK1,GSTP1,HMBS,HMOX1,ID1,IFNGR1,IGFBP1,IL1RN,KCNAB2,LAD1,LOX,LPL,LYVE1,Mt1,PCNA,PSAT1,QDPR,RGCC,SERPINA6,SIRPA,SLC13A3,SLC16A1,SULT2A1,T[illegible]	[illegible],HIF1A,IFNG,IGF1,IL6,JUN,MED1,MYC,NFkB (complex),NOTCH1,NR3C1,RELA,SP1,STAT1,STAT3,methylprednisolone
RORA		ligand-dependent nuclear receptor						3.55E-12	ABCD2,ACACB,APOA4,ASNS,CKMT2,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,Cyp2c54 (includes others),CYP3A5,CYP4A11,FASN,GSTM4,GSTP1,IGFBP1,KCNK5,LCN2,Mt1,Mt2,Mup1 (includes others),Nat8f5,NNMT,PPP1R3C,SELENBP1,SULT2A1,UBE2O	
STAT5B		transcription regulator		-1.567		0.169	-2.193	9.20E-12	A2M,ABCD2,AR,BCL6,CA2,CCND3,CKMT2,Cox8b,CUX2,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2B6,CYP3A5,CYP4A11,EBF1,FAM126A,GCK,GSTP1,Mup1 (includes others),MYH1,NIPAL1,NNMT,PPP1R3C,STAMBPL1,SULT2A1,Sult2a2,SYBU,THRSP,TNFRSF14,TREM3	CEBPA,CREBBP,HNF4A,JUN,MED1,NFkB (complex),PPARGC1A,STAT1,STAT3,STAT5B,STAT6
PD98059		chemical - kinase inhibitor	Inhibited	-2.859	bias	-0.425	-0.117	1.08E-11	ANXA1,AR,BCL6,BIRC5,CA2,CAMP,CD44,CDC25A,COL1A1,CXCR4,DNMT1,DUSP5,E2F1,E2F2,ELN,FASN,HMOX1,IGF1R,IGF2,IGFBP1,IL1RN,Ins1,ITGA4,ITGB3,LAD1,LIPG,LPL,MKI67,MMP14,MYH1,MYH4,PCNA,PLAGL1,PRSS3,RRM2,S100A10,SELENBP1,SIRPA,SLC8A1,SPRY2,TEAD2,TGFB1,THBS1,TOP2A,VCAM1	Akt,CREBBP,CTNNB1,E2f,EGF,EGR1,FGF2,FOXO3,HIF1A,JUN,MYC,NFKBIA,NFkB (complex),PD98059,RAF1,RB1,RELA,TNF
ACOX1		enzyme	Inhibited	-4.139		-0.129	-3.552	1.32E-11	APCS,CD63,CTSE,Cyp2c54 (includes others),CYP4A11,FASN,GSTP1,IGFBP1,IGFBP2,KRT23,LCN2,LPL,MFGE8,Mup1 (includes others),MYH1,Orm1 (includes others),QPCT,RBM3,SELENBP1,SLC16A1,SLCO2B1,Vnn3	ACOX1,CEBPA,NR1H3,PPARA,PPARG,RXRA,SREBF1
NUPR1		transcription regulator	Inhibited	-4.529		-0.203	-3.232	1.54E-11	ADGRL3,ADRB2,ARHGAP11A,ASPM,ATAD5,AURKA,BRCA1,CCNF,CD63,CDCA2,CDCA3,CERK,CKAP2L,CXCR4,CYR61,DUSP5,DUSP8,ESPL1,FAM111A,FANCD2,GBP2,HIST1H2AJ,HIST1H2BB,HIST1H2BM,HIST1H3F,HIST2H3A,HIST2H3D,IFIT2,IGF1R,KIF11,KIF23,KNL1,LMNB1,MKI67,NEIL3,NRROS,NSL1,POLQ,SPAG5,SPC25,SU[illegible]	CCND1,CDK4,NUPR1
progesterone		chemical - endogenous mammalian		0.944		0.163	-0.026	1.83E-11	ADRB2,AR,AURKA,BCL6,BIRC5,CA2,CCND3,CDC25A,CDH11,CXCR4,CYP2A6 (includes others),CYP2B6,CYP3A5,E2F1,EFNA1,ENC1,ESPL1,FEN1,GRB10,H19,HUNK,ID1,IGFBP1,IGFBP2,INMT,ISG20,LCN2,LEPR,LPL,MCM3,MCM4,MCM5,MCM6,MKI67,NCAPH,PCNA,PDK3,PEG3,PKM,PLA2G7,RBP1,RRM2,SLC1A5,SPINK1,TGFB1,T[illegible]	[illegible],CREB1,CREBBP,CTNNB1,E2F2,EP300,ESR1,ESR2,HDAC1,Histone h4,Insulin,JUN,MED1,PGR,PPARG,RARA,RB1,RELA,RNA polymerase II,SP1,TP53,USF2,progesterone
SCAP		other	Inhibited	-2.95	bias	0.649		1.90E-11	AACS,ACACB,ACSS2,ASNS,CYP2B6,DHCR7,FABP5,FASN,FDPS,Gstm6,HES6,ID1,Mt2,MTHFD2,PMVK,SLC7A1,THRSP	ESR2,NFE2L2,NFkB (complex),PPARG,PPARGC1A,SCAP,SREBF1,SREBF2,STAT3,Srebp,cholesterol
KRAS		enzyme		-0.915		0.002	-0.927	2.14E-11	AGER,AOX1,BEX1,BIRC5,CCND3,CD44,CHSY1,COL1A1,DNMT1,DUSP5,E2F1,EFNA1,ELN,FASN,FSTL1,FXYD3,GPC3,GSN,HMOX1,HSPB1,ID1,IGF1R,IGF2,IGFBP2,ITGB3,ITM2A,LCN2,LIPG,LMNB1,LOX,PAK1,PEG3,PKM,PLAGL1,Ppbp,PRC1,SIRPA,Sfrn2,SPRY2,TEAD2,THBS1,TNC,TOP2A,Tpm2	AKT1,E2F1,E2F4,EGFR,EGR1,EP300,FOXO1,FOXO3,HIF1A,JUN,KRAS,MAX,MYC,Mek,PGR,PPARG,RB1,SP1,STAT3,TP53,TP73
D-glucose		chemical - endogenous mammalian		0.489		0.196	-0.755	2.24E-11	AGER,ANLN,ANXA1,ASNS,ATP2A3,ATP2B2,ATP2B4,BIRC5,CCND3,CDK1,COL1A1,CXCR4,CYBB,E2F1,FABP5,FASN,GCK,GSN,HIST1H4C,HK1,HMOX1,HSPB1,ID1,IGF1R,IGF2,INHBB,Ins1,LAMC1,LPL,MMP14,Mt1,Mt2,NCF1,Orm1 (includes others),PCK2,PCNA,PKM,RRM2,SLC25A4,SLC7A1,SLC8A1,SST,TFRC,TGFB1,THBS1,[illegible]	[illegible],D-glucose,EGR1,EP300,ESR1,HIF1A,IGF1,Insulin,JUN,NFKBIA,NFkB (complex),NR4A1,PDX1,PPARG,RELA,RNA polymerase II,SP1,TNF,USF2
FGF19		growth factor	Activated	2.59		-0.081	2.8	3.50E-11	ACACB,AFP,Akr1b7,BIRC5,CTSE,FABP5,FASN,FDPS,GCK,ID1,IGFBP1,IL1RN,LCN2,LEPR,PEG3,RGS16,THRSP	ADIPOQ,CTNNB1,FGF19,MLXIPL,MYC,NFKB1,NFkB (complex),PPARA,RELA,STAT1,STAT3,TP63
IGF1		growth factor	Activated	2.22	bias	0.327	0.348	3.74E-11	A2M,ACSS2,BIRC5,BRCA1,BTG2,CAMP,CCND3,CD44,CDK1,COL1A1,CYBB,CYFIP2,CYR61,E2F1,ELN,FASN,GCK,H2AFX,HBB,HMOX1,ID1,IGF1R,IGF2,IGFBP1,IGFBP2,Ins1,LCN2,LEPR,LPL,MKI67,MMP14,NFE2,PCK2,PCNA,PKM,SST,TGFB1,THBS1,THRSP,VCAM1	Akt,CREBBP,CTNNB1,EGR1,ESR1,ESR2,HIF1A,IGF1,Insulin,JUN,LEP,MYC,NFKB1,NFkB (complex),PPARG,RELA,SP1,STAT3,TP53,USF2,beta-estradiol
troglitazone		chemical drug	Inhibited	-2.907		0.062	-3.221	4.11E-11	ABCD2,ABHD2,AGER,Aldh1a7,AR,BIRC5,CCND3,CDC25A,COL1A1,CYP2B6,CYP3A5,E2F1,E2F2,ECT2,FABP5,FASN,GBP2,GCK,HBA1/HBA2,HMMR,HMOX1,HUNK,Ins1,ITM2A,LPL,MKI67,NCAPH,NCF1,NEIL3,NNMT,NUF2,PCNA,TGFB1,THRSP,VCAM1	ADIPOQ,Ap1,CCL2,CTNNB1,D-glucose,FOXO1,MLXIPL,MYC,NFKB1,NFkB (complex),NR1H3,NR1H4,PDX1,PPARA,PPARG,PPARGC1A,RELA,RXRA,SP1,SREBF1,THRB,troglitazone
estrogen		chemical drug	Activated	2.829	bias	0.437	0.71	4.56E-11	APCS,AR,AURKA,BARD1,BRCA1,CDC25A,COL1A1,COL5A1,CYBB,CYR61,DNMT1,E2F1,ESPL1,FEN1,IGF1R,IGF2,IGFBP2,ITM2A,LCN2,LPL,MCM3,MCM4,MCM5,PCNA,POLE,RRM2,SMC2,Tmsb4x (includes others),TOP2A,UHRF1	CCND1,CREB1,CTNNB1,E2F1,E2F2,E2F3,E2F4,E2f,EGF,EP300,ERBB2,HIF1A,JUN,MED1,MYC,RB1,RBL1,RELA,Rb,TP53,calcitriol,estrogen
RABL6		other	Activated	2.324	bias	0.342	0.997	5.77E-11	BTG2,CDC25A,CENPF,FEN1,FRMD4A,H2AFX,HMMR,HMOX1,KIF23,MCM5,NDC80,POLA1,PRC1,TOP2A,TPX2	E2F1,E2F4,MYC,RABL6,RB1,TP53,TP73
captopril		chemical drug		1.946		0.153	1.339	5.84E-11	A2M,ANXA1,ASNS,BIRC5,CAPN6,CD44,FCGR2A,HMOX1,IGFBP1,IL1RN,LCN2,MCM3,RBM3,S100A10,SLC8A1,TGFB1	AGT,AKT1,AMPK,Ap1,EGR1,EP300,FOXO1,FOXO3,HIF1A,JUN,NFE2L2,NFkB (complex),PPARG,RELA,SIRT1,SP1,captopril
cisplatin		chemical drug	Activated	3.051	bias	0.25	1.431	9.31E-11	A2M,ANXA1,ASNS,BIRC5,BRCA1,BTG2,CAPN6,CD44,CDC25A,CDK1,CMBL,COL1A1,E2F1,FAM117A,FASN,FCGR2A,FNDC3B,GSTP1,H2AFX,HBA1/HBA2,HK1,HMOX1,IGF1R,IGFBP1,INPP5D,KCNK5,LCN2,MCM3,Mt1,NCF1,NOL4L,NREP,PRG2,RAB8B,RBM3,RRM2,S100A10,SLC15A2,SLC25A4,SMOX,STMN1,SULT2A1,TGFB1,THBS[illegible]	[illegible],NFkB (complex),NR3C1,RB1,RELA,STAT3,TP53,TP73,cisplatin
EGF		growth factor	Activated	2.45	bias	0.415	-0.021	9.32E-11	AFP,ALOX12,AR,AURKA,BIRC5,BRCA1,BTG2,CCND3,CD44,CDH11,CDK1,COL1A1,CXCR4,CYP2B6,CYR61,DUSP5,E2F1,FASN,FSTL1,GSTP1,HMOX1,ID1,IGF1R,IGF2,IGFBP1,IGFBP2,Ins1,ITGB3,LCN2,NCF1,PCNA,PLAGL1,RRM1,RRM2,S100A10,SOX4,SPRY2,TGFB1,THBS1,TNC,VCAM1	Akt,Ap1,CREBBP,CTNNB1,EGF,EGR1,ESR1,ESR2,FOS,HIF1A,HRAS,JUN,MYC,NFKB1,NFkB (complex),NR3C1,RELA,STAT3,TP53,TP73,beta-estradiol
2-(4-amino-1-isopropyl-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-1H-indol-5-ol		chemical reagent	Inhibited	-2.35		-0.03	-2.233	1.15E-10	ACACB,AURKA,BIRC5,CCNF,CDC6,CDCA2,E2F2,HIST1H1C,HIST2H2BF,HIST3H2A,ID1,KNL1,MTHFD2,SMC2,TOP2A	
CDKN2A		transcription regulator	Inhibited	-4.172		-0.068	-3.839	1.16E-10	A2M,ATAD2,BARD1,BIRC5,BTG2,CCND3,CDC25A,CDCA4,CDK1,CDKN2D,E2F1,E2F2,EBF1,EFNA1,FAM111A,FEN1,H2AFX,HMGB2,HUNK,ITGB3,MCM4,MCM5,MKI67,PCNA,PEG3,PLAGL1,RBL1,RRM1,RRM2,TCF19	CCND1,CCNE1,CDKN1A,CDKN2A,Cyclin E,E2F1,E2F2,E2F3,E2F4,E2f,MYC,RB1,RBL1,TP53,TP73
SP1		transcription regulator	Activated	3.789	bias	0.587		1.34E-10	ABCD2,ABHD2,AGER,Akr1b7,ALOX12,AR,ASNS,ATP2A3,BIRC5,CAMP,CCND3,CDK1,CDKN2D,Ces2c,COL1A1,CXCR4,DIAPH3,E2F1,FASN,FLNA,GLTP,HBB,HMOX1,IFNGR1,IGF1R,IGF2,IGFBP1,ITGB3,KLF1,LPL,Marcks,MFN2,MMP14,Mt1,PKM,PRKAR2B,RBL1,SLC25A4,SLC7A1,SPN,TGFB1,THBS1,TNC,UBC	APP,AR,CCND1,CREB1,CREBBP,CTNNB1,EGR1,EP300,ESR1,ESR2,FOS,JUN,MAX,MYC,NFKBIA,NFkB (complex),NR4A1,PML,PPARG,RARA,RELA,RXRA,SP1,STAT3,TP53
PTGER2		g-protein coupled receptor	Activated	3.769	bias	0.45	1.867	1.37E-10	ASPM,AURKA,BRCA1,CENPE,CENPF,CKAP2L,CXCR4,ECT2,H2AFX,KIF11,MKI67,NUF2,NUSAP1,PRC1,SPAG5,Stfa2/Stfa2l1,THBS1,TPX2	CSF2,GATA1,PTGER2,Rb,TP53
INSR		kinase		-1.267	bias	0.52		1.38E-10	ATP2A3,ATP5MF,BIRC5,CDC6,CDK1,CKMT2,CORO1A,Cox8b,CXCR4,DHCR7,FASN,FDPS,FEN1,GCK,GRB10,H19,IGF1R,IGF2,IGFBP1,Ins1,LEPR,MARCKSL1,MCM4,MCM5,Meg3,MKNK1,PLAGL1,RGS16,RRM1,RRM2,TGFB1,THBS2,Tpm2,UHRF1,VCAM1	AKT1,D-glucose,EGR1,EP300,ESR1,FOXO1,FOXO3,IGF1R,IGF2,INSR,Ins1,JUN,MYC,NFKBIA,PDX1,PPARA,PPARG,RELA,RXRA,SP1,THRB,TP53,USF2
CEBPB		transcription regulator	Activated	3.034	bias	0.436	0.816	1.66E-10	Akr1b7,APCS,ASNS,CDC25A,CDC6,COL1A1,CXCR4,CYP2A6 (includes others),DHCR7,E2F1,HBB,HIST1H4B,HIST1H4D,HIST1H4H,HIST1H4J,HIST1H4K,HIST2H4B,HLA-A,ID1,IGFBP1,IL1RN,INMT,Ins1,LAMC1,LCN2,LEPR,MCM3,Orm1 (includes others),PCNA,PRG2,PRKAR2B,RAD18,SLC7A1,SST,SULT2A1,TGFB1	CEBPA,CEBPB,CREBBP,ESR2,FOXO3,HNF4A,IL6,JUN,MYC,NFkB (complex),PI3K (complex),PPARG,RELA,RNA polymerase II,SMARCA4,SP1,STAT3,TP53,cyclic AMP
IKBKB		kinase	Activated	2.004	bias	0.45	-0.148	1.84E-10	AFP,AGER,BRCA1,CD44,CDC6,CXCR4,ECT2,FASN,GBP2,H2AFX,HLA-A,HMOX1,IGFBP2,IL1RN,ITGB3,KIF23,LCN2,LMNB1,Mt1,NID1,RBP1,RGS16,Sfrn2,TGFB1,Tmsb4x (includes others),TNC,Tpm2,VCAM1	CHUK,CREBBP,FOXO3,HIF1A,IKBKB,IKBKG,JUN,MYC,NCOA3,NFKB1,NFKBIA,NFkB (complex),RELA,STAT1,STAT3,TNF
FOXO3		transcription regulator		-0.847	bias	0.278	-1.841	2.08E-10	ANXA1,AR,AURKA,BCL6,BIRC5,CCND3,CDC6,CXCR4,CYR61,DLGAP5,FABP5,FASN,IGF1R,IGFBP1,LCN2,MCM4,MKI67,Mt1,Mt2,MTHFD2,NCAPG2,PAK1,PCNA,SLC1A4,SLC7A1,SPAG5,TAL1,TGFB1,TPX2,UBC,VCAM1	AKT1,CCND1,CDKN1A,CREB1,CREBBP,E2F4,E2f,EP300,ESR1,ESR2,FOXO1,FOXO3,IL6,JUN,MYC,NFKBIA,NFkB (complex),PPARG,RARA,RB1,RELA,SP1,STAT3,TNF,TP53
imipramine blue		chemical drug	Inhibited	-3.286	bias	-0.388	-2.01	2.81E-10	AURKA,CCNF,CDC25A,CENPA,CENPE,CENPF,CERK,E2F2,PCNA,PLK4,STMN1	
RRP1B		transcription regulator						3.04E-10	AURKA,BIRC5,BRCA1,CCND3,CDC6,CDK1,CDKN2D,ESPL1,FEN1,KIF11,MCM3,MCM4,MCM5,MCM6,PCNA,RBL1,TGFB1,TOP2A	
mir-21		microrna	Inhibited	-3.172	bias	-0.466	-0.792	3.14E-10	ANLN,ASPM,ATAD2,BTG2,CDC25A,COL1A1,DLGAP5,ECT2,ELN,FCGR2A,GBP2,H2AFX,INPP5D,KIF23,LEPR,MARCO,MKI67,NUSAP1,Orm1 (includes others),PRC1,SLC25A37,Sfrn2,SMC2,SPRY2,STMN1,TGFB1,TOP2A,VCAM1	CTNNB1,FOXO1,FOXO3,IL6,MYC,NFKBIA,NFkB (complex),PTEN,RELA,STAT3,mir-21
MITF		transcription regulator	Activated	3.736	bias	0.6		3.70E-10	APOLD1,BRCA1,CCNF,CD44,CDCA3,CENPF,COL1A1,ECT2,FABP5,HMMR,HSPB1,LCN2,MCM4,MCM5,MCM6,MMP14,NCAPD3,NUSAP1,PSEN2,QDPR,SLC14A1,SPAG5,SPC25,TMCC2,TNFRSF14,TPX2	
FOXO1		transcription regulator	Activated	4.481	bias	0.42	2.32	4.97E-10	A2M,ANLN,AR,ASPM,BIRC5,CA2,CCNF,CDK1,CENPF,CKMT2,CTSE,DLGAP5,EBF1,FABP5,FASN,FDPS,GCK,GSTK1,HMOX1,IGF1R,IGFBP1,IKZF1,Ins1,KIF11,LPL,MCM5,NUSAP1,PAK1,PCK2,PRC1,SLC25A37,SPC25,SPRY2,TGFB1,THBS1,VCAM1	AKT1,Akt,CREBBP,CTNNB1,EGF,EGR1,EP300,FOXO1,FOXO3,HIF1A,JUN,MYC,NR1H3,PPARA,PPARD,PPARG,RELA,RXRA,SP1,SREBF1,TP53,fatty acid
medroxyprogesterone acetate		chemical drug		-1.392		-0.077	-1.063	5.48E-10	ANLN,ASPM,BIRC5,BTG2,CD44,CDK1,CENPF,CXCR4,CYR61,DLGAP5,FASN,IGFBP1,KIF11,MCM5,NUSAP1,PRC1,SPC25,TGFB1,TNC	CCND1,E2F1,EGR1,ERBB2,ESR1,ESR2,FOXO1,FOXO3,HDAC1,IL6,MYC,NFkB (complex),PPARG,PPARGC1A,RB1,RELA,Rb,SIRT1,SRF,STAT3,TP53,Vegf,beta-estradiol,medroxyprogesterone acetate
CDK4		kinase						5.71E-10	AURKA,BRCA1,CCNF,CDC6,CDCA2,E2F2,CENPF,CIP2A,DTL,ELN,FAM83D,GPC6,HIST1H4H,Ins1,KIF11,KIF20B,KNL1,MORC4,NCAPH,SPC25,TPX2	CCND1,CCNE1,CDK4,CDKN1A,E2F1,E2F4,E2f,ESR1,RB1,TP53
indomethacin		chemical drug		0.512		0.193	-0.392	5.83E-10	A2M,ADAM8,ANXA1,ASNS,BIRC5,BTG2,CAPN6,CD44,CXCR4,CYP2B6,FASN,FCGR2A,HMOX1,ID1,IGFBP1,IGF1R,LCN2,LOXL2,LPL,MCM3,MMP14,PCNA,Ppbp,RBM3,S100A10,TNFRSF21,TUBB	CREBBP,CTNNB1,EGF,EGR1,FOXO3,HIF1A,IGF1,IL6,JUN,MYC,NFKBIA,NFkB (complex),PPARG,PTGS2,RELA,SP1,STAT3,TNF,indomethacin
TBX2		transcription regulator	Activated	3.873		0.207	3.072	6.12E-10	ANLN,AURKA,CDC6,CDCA3,CDK1,CKAP2,DNMT1,E2F1,MCM4,MCM5,MCM6,NCAPG2,PRC1,RBL1,SMC2	CCND1,CDKN1A,E2F1,E2F3,E2F4,E2f,HDAC1,RB1,TBX2,TP53
ciprofibrate		chemical drug	Activated	3.621		-0.028	3.745	8.31E-10	APCS,CD63,Cyp2c54 (includes others),CYP4A11,GSTP1,IGFBP1,IGFBP2,Ins1,LCN2,LPL,Mup1 (includes others),MYH1,Orm1 (includes others),QPCT,RBM3,SELENBP1,SLC16A1,SLCO2B1,SULT2A1,Vnn3	ACOX1,CEBPA,CREBBP,CTNNB1,Ins1,JUN,LEP,NFKB1,NFKBIA,NFkB (complex),NR1H3,PPARA,PPARG,RELA,RXRA,SP1,SREBF1,TNF,USF2,ciprofibrate
Akt		group	Activated	2.471		0.221	1.42	9.20E-10	A2M,AR,BCL6,BIRC5,BRCA1,BTG2,CCND3,CD44,COL1A1,CXCR4,E2F2,GCK,GSTK1,HMOX1,IGF1R,IGF2,IGFBP2,LCN2,LPL,MFN2,MMP14,PCNA,RRM2,SLC8A1,SOX4,THBS1,THBS2,TNC,VCAM1	AKT1,Akt,CREBBP,CTNNB1,EGFR,EGR1,EP300,ESR1,ESR2,FOXO1,FOXO3,JUN,MYC,NFKBIA,NFkB (complex),PGR,PPARG,PTEN,RELA,SP1,TNF,TP53,beta-estradiol
IL1B		cytokine	Activated	3.358	bias	0.308	1.379	1.10E-09	A2M,ADAM8,ADRB2,AGER,ANXA1,APCS,BCL6,BTG2,Cd24a,CD44,COL1A1,CXCR4,CYBB,CYP2B6,CYP3A5,DNMT1,DUSP5,E2F1,E2F2,E2F4,EFNA1,FABP5,GBP2,GCK,H19,HLA-A,Hmgn2 (includes others),HMOX1,HSPB1,IFNGR1,IGFBP1,IL1RN,Ins1,ISG20,ITGB3,LCN2,LOX,MARCKSL1,MMP14,MMP8,Mt1,Mt2,MYLK3,Ppbp,RGS16,R[illegible]	[illegible]
CEBPA		transcription regulator		1.665		0.23	0.516	1.17E-09	A2M,ANXA1,APOA4,ASNS,ASPRV1,BTG2,CA2,CAMP,CKAP4,COL1A1,CSF2RA,CXCR4,CYP2A6 (includes others),CYP2B6,CYP3A5,DHCR7,E2F1,EBF1,Elf5,FASN,GSTP1,HMOX1,ID1,IL1RN,LCN2,LEPR,LPL,MMP8,Mup1 (includes others),Orm1 (includes others),PCNA,PPP1R3C,RBL1,SULT2A1,Sult2a2,THBS1	ADIPOQ,Ap1,CEBPA,CTNNB1,FOS,HNF4A,JUN,MED1,MLXIPL,MYC,NFKB1,NFkB (complex),NR3C1,PPARA,PPARGC1A,RELA,SMARCA4,SP1,SP3,STAT1,STAT3,TP63
RB1		transcription regulator	Inhibited	-4.195		0.166	-4.911	1.43E-09	ATAD2,BARD1,BIRC5,BRCA1,CCND3,CDC25A,CDCA4,CDK1,COX6A1,DNMT1,E2F1,FAM111A,FEN1,HMGB2,HUNK,ID1,IGF1R,MCM3,MCM4,MCM5,MCM6,MFN2,MYH2,MYH4,PCNA,PSEN2,RBL1,RRM1,RRM2,TCF19,TGFB1,Tpm2	CCNE1,CDK2,Cyclin E,E2F1,E2F2,E2F3,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TFDP1,TP53
KDM5B		transcription regulator	Inhibited	-3.483	bias	-0.327	-2.073	1.57E-09	AURKA,BRCA1,CDCA3,CDK1,DLGAP5,E2F1,ECT2,Elf5,FABP5,HMMR,IGFBP2,MCM3,MIA3,NCAPH,NDC80,SMOX,TAL1,TGFB1,TOP2A	E2F1,E2F4,E2f,KDM5B,RB1,RBL1,TP53
JUN		transcription regulator	Activated	2.776	bias	0.358	0.967	2.00E-09	A2M,AFP,ATAD2,ANXA1,AR,ASNS,BRCA1,CAMP,CCND3,CD44,CDK1,Clca3a1/Clca3a2,COL1A1,CYR61,DNMT1,DUSP5,GPT,GSTP1,HMOX1,IGF1R,IGFBP1,IGFBP2,MMP8,PLAGL1,S100A10,SLC7A1,SLC8A1,SST,STMN1,SULT2A1,SYK,TGFB1,THBS1,Tmsb4x (includes others),TNC,VCAM1	Akt,Ap1,CREBBP,CTNNB1,EGR1,FOS,FOXO1,HIF1A,IGF1,JUN,MYC,NFE2L2,NFKB1,NFKBIA,NFkB (complex),RELA,SP1,STAT1,STAT3,TNF
cholesterol		chemical - endogenous mammalian	Activated	3.176		0.209	2.186	2.16E-09	ACSS2,APCS,COL1A1,CYBB,CYP3A5,DHCR7,FABP5,FASN,FDPS,HES6,IL1RN,LEPR,LPL,MMP14,MMP8,OCSTAMP,Orm1 (includes others),PMVK,PSAT1,RGCC,RGS16,TGFB1,THBS1,VCAM1	CREBBP,IL1B,INSIG1,JUN,KEAP1,MYC,NFE2L2,NFKB1,NFKBIA,NFkB (complex),RELA,SMAD3,SREBF1,SREBF2,STAT3,Srebp,TNF,cholesterol
trichostatin A		chemical drug	Activated	2.13	bias	0.364	0.114	2.24E-09	AFP,AR,ATAD2,BRCA1,CAMP,CD44,CDC6,CDK1,CDKN2D,CGREF1,CLEC3B,CXCR4,CYBB,CYP2A6 (includes others),CYP3A5,DNMT1,FASN,GINS3,GSN,GSTM4,HBA1/HBA2,HBB,ID1,IGFBP1,IKZF1,LEPR,MCM3,MCM6,PCNA,PLAGL1,PRG2,PTPN7,RIMS2,S100A10,SLC8A1,SPN,STMN1,SULT2A1,TGFB1,THBS1,TOP2A,TSKU,VCAM1	Ap1,EGR1,FOS,FOXO3,HIF1A,IL6,JUN,MAX,MYC,NFkB (complex),NR3C1,PPARG,RELA,SNAI1,STAT3,TP53,TP63,TP73,decitabine,trichostatin A
E2f		group	Activated	3.206	bias	0.535		2.26E-09	BRCA1,CDC25A,CDC6,CDK1,E2F1,E2F2,FANCD2,HIST1H2AG,MCM3,MCM4,MCM5,MCM6,NUSAP1,PCNA,POLA1,RBL1,RRM2,TPX2	CCNE1,Cyclin E,E2F1,E2F2,E2F4,E2f,MDM2,MYBL2,RB1,RBL1,Rb,TFDP1,TP53
ESR1		ligand-dependent nuclear receptor	Activated	2.385		0.101	1.667	2.39E-09	ABHD2,ANLN,AR,ASPM,ATP2A3,AURKA,BCL6,BIRC5,BRCA1,CA2,CCND3,CDK1,CENPA,CENPE,CENPF,CLSPN,COTL1,Cox8b,CYFIP2,CYR61,DHCR7,DIAPH3,DMTN,DUSP5,DUSP9,E2F1,EFNA1,FASN,FLNA,GSN,H19,HIST1H4C,ID1,IGF1R,IGF2,IGFBP2,INCENP,INHBB,ISG20,KIF23,KLF1,KNL1,LCN2,LEPR,LPL,MKI67,NCAPH,PAK1,[illegible],TFRC,TGFB1,TSKU,UNC119	[illegible]
MED1		transcription regulator		1.569	bias	0.537		3.39E-09	AURKA,BCL11A,BCL6,BIRC5,CDC6,CDK1,CENPA,CYP2B6,CYP3A5,CYP4A11,E2F1,EBF1,FASN,GCK,GSTP1,IGFBP1,IKZF1,LAD1,SULT2A1,THBS1	CEBPA,FOS,FOXO1,HNF4A,JUN,MED1,NFkB (complex),NR1H3,NR1I3,NR3C1,PPARA,PPARG,PPARGC1A,RXRA,SREBF1,STAT1
Rb		group	Inhibited	-2.556	bias	-0.304	-1.612	4.10E-09	BIRC5,CDC6,CDK1,DNMT1,E2F1,E2F2,ECT2,H19,MCM3,MCM5,Ngp,PCNA,RBL1,TOP2A	CCND1,CDKN1A,Cyclin E,E2F1,E2F2,E2F3,E2F4,E2f,HDAC1,Histone h4,MED1,MYC,RB1,Rb,TP53,TP73
ZFP36		transcription regulator	Inhibited	-2.961	bias	-0.647		5.17E-09	CAMP,CDC6,CENPA,CYBB,E2F1,KIF11,LCN2,Ngp,NUF2,PRC1,TFRC,TMCC2,TOP2A,VCAM1,Wfdc21	FOXO3,HIF1A,IL6,JUN,MYC,NFKB1,NFKBIA,NFkB (complex),NOTCH1,RELA,STAT3,TP53,ZFP36
INSIG1		other		0.277	bias	-0.661		5.59E-09	AACS,ACACB,ACSS2,CXCR4,DHCR7,FABP5,FASN,FDPS,LCN2,LIPG,LPL,MARCO,PLA2G7,PMVK,SELPLG,TGFB1	ESR2,INSIG1,NFE2L2,NFkB (complex),PPARG,PPARGC1A,SREBF1,SREBF2,STAT3,Srebp,cholesterol
ABCB6		transporter		-0.533		0.047	-0.685	6.63E-09	ATP5IF1,Cyp2a12/Cyp2a22,CYP2A6 (includes others),CYP2B6,Cyp2c54 (includes others),CYP3A5,CYP4A11,HK1,HMBS,KLF1,SLC25A37	
FOXM1		transcription regulator	Activated	3.429	bias	0.578		7.08E-09	ANXA1,AR,BIRC5,CCNF,CDC25A,CDCA2,CDK1,CENPA,CENPE,CENPF,IL1RN,LOX,MKI67,PCNA,PLK4,PRC1,STMN1,TOP2A	CCND1,CDKN1A,E2F1,E2F4,E2f,FOXM1,FOXO1,FOXO3,HDAC1,MYC,NFkB (complex),RB1,RELA,SRF,STAT1,STAT3,TP53,TP63,TP73,Vegf
AHR		ligand-dependent nuclear receptor		-1.117		0.067	-1.377	7.75E-09	A2M,BTG2,CCND3,CCNF,CDK1,CDKN2D,Ces2c,CGREF1,COL1A1,COL5A1,CYP2A6 (includes others),CYP2B6,DCLK3,E2F1,FBN2,HUNK,IGFBP1,MMD2,Mt1,Mt2,Nat8f5,NID1,NNMT,POLA1,RBL1,RBP1,SERPINA7,SLC1A4,TGFB1,THBS1	AHR,CEBPB,E2F1,E2F2,E2F3,E2f,EGR1,EP300,ESR1,FOXO3,HDAC1,Histone h4,IL1B,IL6,MED1,MYC,NFKBIA,NFkB (complex),NR4A1,RB1,RELA,SP1,STAT3,TP53
CCNE1		transcription regulator		-0.113	bias	0.482	-1.468	8.30E-09	AR,BARD1,BRCA1,CD44,CDC6,E2F1,MCM4,PCNA,RBL1	CCNE1,CDK2,Cyclin E,E2F1,E2F2,E2F3,E2F4,E2f,HDAC1,RB1,RBL1,Rb,TFDP1,TP53
PI3K (complex)		complex	Activated	3.488	bias	0.465	1.36	8.56E-09	ADRB2,BIRC5,CCND3,CD44,COL1A1,CXCR4,CYBB,E2F1,FABP5,FRY,GSTP1,H19,HK1,HMOX1,IGF1R,IGF2,IGFBP1,IGFBP2,IL1RN,LCN2,MMP14,MTHFD2,PRKAR2B,SST,STMN1,THBS1,VCAM1	AKT1,Akt,CREBBP,CTNNB1,EGR1,EP300,FOXO1,FOXO3,HIF1A,JUN,LY294002,NFKBIA,NFkB (complex),PI3K (complex),PPARG,RELA,SP1,STAT3,TNF,TP53,prostaglandin E2
HIF1A		transcription regulator	Activated	3.334	bias	0.481	0.997	8.58E-09	AFP,ASNS,AURKA,BIRC5,BRCA1,CD44,CORO1A,CXCR4,CYR61,DTX1,GATA1,GCK,H2AFX,HES6,HIST1H1C,HIST2H2AC,HIST2H4B,HMOX1,HSPB1,ID1,IGF2,IGFBP2,INHBB,ITGB3,LOX,LOXL2,PKM,SLC25A37,TFRC,TGFB1,THBS1,TTN,VCAM1	Akt,Ap1,CREBBP,CTNNB1,E2F1,E2F4,EGR1,EPAS1,HIF1A,Hif1,JUN,MYC,NFKB1,NFkB (complex),RB1,RELA,STAT3,TP53,TP73,VEGFA,VHL

Day 60 Female BPA

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
PTGER2		g-protein coupled receptor	Activated	4.025	bias	0.636		1.32E-23	ASPM,AURKA,BRCA1,BUB1B,CCNB2,CENPE,CENPF,CKAP2L,EGR1,H2AFX,KIF11,KIF2C,MKI67,NUF2,NUSAP1,PLK1,RACGAP1,Stfa2/Stfa2l1,THBS1,TPX2,TROAP	BRCA1,CREB1,CSF2,MYC,NFkB (complex),PTGER2,RB1,RNA polymerase II,Rb,STAT3,TP53
dextran sulfate		chemical drug						5.61E-23	AURKA,BIRC5,BUB1B,CCNB1,CDK1,CENPE,FIGNL1,KIF11,MCM3,MCM5,MCM6,MKI67,NCAPH,NUSAP1,PLK1,POLE,RACGAP1,RRM2,S100A9,SPC25,STMN1,THBS1,THBS2,TOP2A,TPX2,UHRF1,VCAM1	FOXO1,FOXO3,IL6,MYC,NFkB (complex),STAT3,dextran sulfate
CDKN1A		kinase	Inhibited	-2.192	bias	-0.296	-1.393	7.52E-23	ASPM,ATAD2,AURKA,AURKB,BIRC5,BRCA1,BUB1B,CCNB1,CDK1,CENPF,DLGAP5,H2AFX,KIF20B,KIF2C,MCM3,MCM6,MIS18BP1,MKI67,NUSAP1,PLK1,RACGAP1,SMC4,STMN1,TOP2A,TPX2,UHRF1,WDHD1	CCND1,CDKN1A,CDKN2A,E2F1,E2F4,E2f,FOXO3,HDAC1,MYC,RB1,RBL1,RBL2,TBX2,TP53
E2F1		transcription regulator	Activated	3.322	bias	0.573		6.86E-20	ATAD2,AURKA,AURKB,BIRC5,BRCA1,CA2,CCNB1,CCNB2,CDK1,DBF4,DNMT1,E2F2,EGR1,FEN1,H19,HIST1H4H,IGF2,KIF23,MCM3,MCM5,MCM6,NDC80,NUSAP1,PSAT1,RACGAP1,RRM2,SMC4,STMN1,THBS1,TOP2A,UHRF1,VCAM1	BRCA1,CDKN2A,E2F1,E2F2,E2F4,E2f,MYC,RB1,RBL1,Rb,TBX2,TP53,TP73,doxorubicin
TP53		transcription regulator	Inhibited	-3.289		0.211	-4.657	1.30E-19	AFP,ANK1,ASPM,ATAD2,AURKA,AURKB,BIRC5,BRCA1,BUB1B,CCNB1,CCNB2,CDK1,CENPE,CENPF,DBF4,DLGAP5,DNMT1,DSN1,E2F2,EGR1,FABP5,FEN1,FIGNL1,H19,H2AFX,Hist1h1b,HMMR,IGDCC4,IGF2,KCNN4,KIF23,MCM3,MCM5,MCM6,MIS18BP1,MKI67,NCAPH,NDC80,NUSAP1,PEG10,PEG3,PLK1,PPIC,RACGAP1,RGS16,R[illegible]	[illegible],RB1,RBL1,Rb,TP53
YY1		transcription regulator						6.76E-18	ARID3A,AURKA,AURKB,BIRC5,BRCA1,BUB1B,CCNB1,CCNB2,CENPE,EGR1,FEN1,GPC3,H2AFX,INCENP,KIF11,KIF23,KIF2C,MCM6,MKI67,PLK1,SLC25A4,TOP2A,UHRF1	CDKN2A,E2F1,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TBX2,TP53,YY1
E2F4		transcription regulator						1.25E-17	AURKB,BRCA1,CDK1,CENPE,DBF4,E2F2,FEN1,H2AFX,HMMR,MCM3,MCM5,MCM6,MKI67,NDC80,PLK1,PSAT1,RRM2,SMC4,STMN1,TOP2A,TPX2,UHRF1	E2F1,E2F3,E2F4,HDAC1,HDAC2,RB1,TP53
TCF3		transcription regulator	Inhibited	-3.357		0.095	-3.726	3.42E-17	AURKA,BIRC5,CA2,CCNB1,CCNB2,CDK1,CIP2A,FAM129C,H2AFX,HMMR,KCNN4,KIF11,KIF2C,MKI67,NDC80,NUF2,NUSAP1,PLK4,RACGAP1,RGS16,RRM2,SPC25,TCEAL9,TENT5C,TOP2A	
CSF2		cytokine	Activated	5.16	bias	0.739		8.38E-17	AURKA,BIRC5,BUB1B,CCNB1,CDK1,CENPE,EGR1,ELN,FIGNL1,KIF11,MARCO,MCM3,MCM5,MCM6,MKI67,NCAPH,NUSAP1,PLK1,POLE,RACGAP1,RRM2,SLC1A5,SPC25,STMN1,THBS1,TOP2A,TPX2,UHRF1	CDKN2A,CREB1,CSF2,CTNNB1,E2F1,E2F4,E2f,FOXO1,FOXO3,IL6,MYC,NFkB (complex),RB1,RBL1,STAT3,TBX2,TP53,Vegf
methylselenic acid		chemical reagent						1.68E-15	ATAD2,AURKA,BIRC5,BRCA1,BUB1B,CCNB1,CCNB2,CDK1,CENPF,HMMR,KIF11,KIF20B,MCM3,MCM5,MCM6,MKI67,MXD1,PEG3,PLK1,RRM2,TOP2A	CCND1,CDKN2A,E2F1,E2F2,E2f,HDAC1,MYC,PGR,RB1,RBL1,Rb,TBX2,TP53,YY1,beta-estradiol,methylselenic acid
RABL6		other	Activated	3.606	bias	0.485	1.858	4.86E-15	AURKB,BUB1B,CCNB1,CENPF,FEN1,H2AFX,HMMR,KIF23,MCM5,NDC80,PLK1,TOP2A,TPX2	CDKN2A,E2F1,E2F4,MYC,RABL6,RB1,TP53
Vegf		group	Activated	3.829	bias	0.699		8.82E-15	AQP4,AURKA,AURKB,BIRC5,BUB1B,CA2,CCNB1,CDK1,CENPF,CYP4A11,DBF4,EGR1,ELN,GRB10,HMMR,INHBB,ISG20,KIF11,KIF20B,KIF2C,LCN2,MCM5,MKI67,NDC80,PLK1,PLK4,TPX2,VCAM1	AR,CTNNB1,E2F1,ERBB2,FOXM1,FOXO1,FOXO3,HDAC1,HRAS,MXI1,MYC,NFkB (complex),PPARG,RB1,Rb,TP53,TP73,Vegf
doxorubicin		chemical drug		-1.341	bias	0.336	-2.914	4.40E-14	AFP,AURKA,AURKB,BIRC5,BUB1B,CA2,CAPN6,CCNB1,CCNB2,CDK1,DNMT1,E2F2,EGR1,H2AFX,IGFBP1,LCN2,MCM3,PLK1,RGS16,RRM2,SLC25A4,STMN1,TOP2A	CDKN2A,E2F1,E2F2,E2F4,E2f,FOXO3,HDAC1,MYC,RB1,RBL1,RBL2,Rb,TBX2,TP53,YY1,doxorubicin
HGF		growth factor	Activated	3.354	bias	0.651		5.05E-14	AFP,AURKA,AURKB,BIRC5,BUB1B,CCNB1,CDK1,CENPF,DBF4,EGR1,FEN1,GRB10,HMMR,ISG20,KIF11,KIF20B,KIF2C,LCN2,MCM5,MKI67,NDC80,PLK1,PLK4,S100A9,THBS1,TPX2,VCAM1	AR,BRCA1,CTNNB1,E2F4,ERBB2,FOXM1,FOXO1,FOXO3,HDAC1,HGF,IL6,MYC,NFkB (complex),RB1,Rb,STAT3,TP53
GATA1		transcription regulator		1.558		0.239	0.651	9.37E-14	ANK1,BIRC5,CA2,DMTN,EGR1,GP9,HBA1/HBA2,HBB,IKZF1,INHBB,MCM3,MCM5,PRG2,SLC4A1,SPTA1,TAL1,TFRC,TOP2A	E2F2,GATA1,Histone h3,RNA polymerase II
FOXO3		transcription regulator		1.019	bias	0.385	-0.125	2.15E-13	AQP4,AURKA,BIRC5,BUB1B,CCNB1,CCNB2,DLGAP5,EGR1,FABP5,IGFBP1,KIF2C,LCN2,MKI67,MXD1,NCAPG2,PLK1,SLC1A4,SLIT2,TAL1,TPX2,VCAM1	CTNNB1,E2F1,FOXO1,FOXO3,IL6,MYC,NFKBIA,NFkB (complex),PPARG,STAT3,TCF3,Vegf,cytokine
KDM5B		transcription regulator	Inhibited	-3.833	bias	-0.462	-2.061	3.55E-13	AURKA,BRCA1,BUB1B,CCNB1,CDK1,DLGAP5,EGR1,FABP5,HMMR,KIF2C,MCM3,NCAPH,NDC80,TAL1,TOP2A	E2F1,E2f,KDM5B,RB1,RBL1,TBX2,TP53
CCND1		transcription regulator	Activated	3		0.134	2.599	4.38E-13	ASPM,ATAD2,AURKA,BIRC5,BRCA1,CCNB1,CENPF,CIP2A,DNMT1,HIST1H4H,KIF11,KIF20B,KIF2C,KNL1,MORC4,NCAPH,PLK1,RACGAP1,RRM2,SPC25,TPX2,UHRF1	CCND1,CDKN1A,E2F1,E2F2,E2F4,E2f,FOXO3,HDAC1,RB1,RBL1,RBL2,Rb,TBX2,TP53
discodermolide		chemical drug						5.00E-13	BRCA1,CCNB1,CCNB2,CDK1,E2F2,KIF11,KIF23,PLK1,PLK4,TOP2A	CDKN2A,E2F1,E2F4,MYC,RB1,TP53,discodermolide
NUPR1		transcription regulator	Inhibited	-4.491	bias	-0.287	-3.087	5.05E-13	ANK1,ARHGAP11A,ASPM,AURKA,BRCA1,BUB1B,CCNB2,CKAP2L,DSN1,HIST1H2AJ,HIST1H2BB,HIST1H2BM,HIST1H3A,HIST2H3A,HIST2H3D,KIF11,KIF23,KIF2C,KNL1,LARS2,MKI67,MXD1,NEIL3,PLK1,SPC25	CCND1,CDK4,NUPR1
IL6		cytokine		1.451	bias	0.511		9.75E-13	AFP,AQP4,BIRC5,BUB1B,CCNB1,CCNB2,CDK1,CENPE,CYP3A5,DNMT1,E2F2,EGR1,IGF2,IGFBP1,KIF2C,LCN2,LPL,MCM3,MKI67,PLK4,RRM2,S100A9,SERPINA7,SPC25,TAL1,TFRC,THBS1,TOP2A,VCAM1	Akt,CTNNB1,E2F1,EGR1,ERBB2,FOXM1,FOXO1,FOXO3,HDAC1,HIF1A,IL6,MXI1,MYC,NFkB (complex),NRAS,PGR,RB1,Rb,TP53,beta-estradiol
E2F3		transcription regulator	Activated	3.244	bias	0.513		1.28E-12	BIRC5,CCNB1,CCNB2,CDK1,E2F2,HIST1H2BN,IGF2,LPL,MCM3,MCM5,MCM6,NCAPG2,PLK1,RRM2,THBS1,TPX2	CDKN2A,E2F1,E2F3,E2F4,E2f,MYC,RB1,RBL1,TBX2,TP53
LIN9		other	Activated	2.779	bias	0.764		3.00E-12	AURKA,BIRC5,BUB1B,CCNB1,CDK1,CENPE,DLGAP5,PLK1	
MYBL2		transcription regulator		1.92	bias	0.585		5.05E-12	AURKA,BIRC5,CCNB1,CDK1,CENPE,ELN,PLK1,SLC1A5,TOP2A	
RRP1B		transcription regulator						5.72E-12	AURKA,BIRC5,BRCA1,CCNB2,CDK1,DBF4,FEN1,KIF11,MCM3,MCM5,MCM6,PLK1,TOP2A	
AREG		growth factor	Activated	3.45	bias	0.304	2.402	6.78E-12	ARHGAP11A,AURKB,BIRC5,CCNB1,CCNB2,CENPF,EGR1,IQGAP3,MKI67,PLK1,RRM2,TOP2A	AREG,CREB1,E2F1,ERBB2,ESR1,FOXO1,FOXO3,HDAC1,IL6,MAPK1,MYC,NFkB (complex),PPARG,RB1,Rb,STAT3,TP53
let-7		microrna	Inhibited	-3.831	bias	-0.926		8.33E-12	ARID3A,AURKA,AURKB,BRCA1,BUB1B,CCNB1,CDK1,DBF4,E2F2,HBA1/HBA2,MCM3,MCM5,MCM6,NUF2,RRM2,THBS1	Akt,CTNNB1,E2F1,EGR1,HIF1A,let-7
CDK4		kinase						1.15E-11	AURKA,BRCA1,CENPF,CIP2A,ELN,HIST1H4H,KIF11,KIF20B,KIF2C,KNL1,MORC4,NCAPH,SPC25,TPX2	CCND1,CDK4,E2F1,RB1
Rb		group		-1.753	bias	-0.43	-0.65	1.99E-11	AURKB,BIRC5,CDK1,DNMT1,E2F2,H19,MCM3,MCM5,Ngp,PLK1,TOP2A	CCND1,CDKN1A,CDKN2A,E2F1,E2F2,E2F3,E2F4,E2f,MYBL2,MYC,RB1,Rb,TP53
RBL2		other	Inhibited	-2.93	bias	-0.842		3.59E-11	AURKA,AURKB,BRCA1,BUB1B,CCNB1,CCNB2,CDK1,CDR2,DNMT1,PLK1,RRM2,STMN1	E2F1,E2F2,E2F3,E2F4,E2f,FOXM1,FOXO1,FOXO3,HDAC1,MXI1,MYC,NFkB (complex),RB1,RBL2,Rb,TP53
calcitriol		chemical drug	Inhibited	-2.416		-0.094	-1.994	4.06E-11	BIRC5,BRCA1,BUB1B,CA2,CCNB1,CDK1,EGR1,ELN,FEN1,FIGNL1,INCENP,KIF23,LCN2,LPL,MCM3,MCM5,NUSAP1,POLE,RACGAP1,RRM2,S100A9,STMN1,THBS1,TPX2	Akt,CTNNB1,E2F1,E2f,EGR1,FOXO1,FOXO3,HDAC2,HIF1A,IL6,MYC,NFkB (complex),PGR,RB1,RBL1,STAT3,TBX2,TP53,beta-estradiol,calcitriol
FOXM1		transcription regulator	Activated	3.528	bias	0.818		6.55E-11	AURKB,BIRC5,BUB1B,CCNB1,CCNB2,CENPE,CENPF,MKI67,PLK1,PLK4,STMN1,TOP2A	CCND1,CDKN1A,CDKN2A,CTNNB1,E2F1,E2F4,E2f,FOXM1,FOXO1,FOXO3,MYC,RB1,TP53,Vegf
fulvestrant		chemical drug	Inhibited	-2.073		-0.2	-1.259	6.85E-11	AURKA,BIRC5,CCNB1,CDK1,CENPF,EGR1,FEN1,H2AFX,INHBB,KIF11,LPL,MCM3,MCM5,POLE,STMN1,TFRC,VCAM1	AR,CREB1,CTNNB1,E2F1,E2F2,E2f,FOXO1,FOXO3,HIF1A,IGF1,NFkB (complex),RB1,RBL1,Rb,SP1,STAT3,TBX2,TP53,fulvestrant
MYC		transcription regulator	Activated	4.533	bias	0.377	2.474	7.60E-11	ABCG4,AFP,AURKB,BIRC5,BRCA1,BUB1B,CCNB1,CCNB2,CDK1,COX6A1,DNMT1,E2F2,EGR1,FABP5,GPC3,H19,IKZF1,MCM5,MCM6,MKI67,PEG10,PEG3,PLK1,PSAT1,RRM2,SLC1A5,SPN,STMN1,TFRC,THBS1,THBS2,UNC119,VCAM1	CDKN2A,E2F1,E2F4,E2f,ESR2,FOXO3,HDAC1,MYC,PGR,RB1,RBL1,RBL2,TBX2,TP53,TP73,YY1,beta-estradiol
ESR1		ligand-dependent nuclear receptor	Activated	3.007		0.142	2.294	1.14E-10	AFP,ASPM,ATP2A3,AURKA,BIRC5,BUB1B,CA2,CCNB1,CDK1,CDKN3,CENPF,DIAPH3,DMTN,EGR1,H19,HSD3B2,IGF2,INCENP,INHBB,ISG20,KIF23,KNL1,LCN2,LPL,MKI67,NCAPH,PLK4,PSAT1,RGS16,S100A9,SAMD11,SLC1A4,SLC25A4,SMC4,TFRC,UNC119	4-hydroxytamoxifen,CCND1,EGF,ESR1,ESR2,FOS,HIF1A,MYC,NFKBIA,PPARG,RARA,RB1,SP1,STAT3,tamoxifen
FGF19		growth factor						9.38E-11	AFP,Akr1b7,AQP4,BIRC5,EGR1,FABP5,HSD3B2,IGFBP1,LCN2,PEG3,RGS16	
GATA2		transcription regulator		1.912		0.162	1.488	9.84E-11	Cldn13,E2F2,GP9,HBA1/HBA2,IKZF1,LCN2,MFSD2B,Ngp,PRG2,S100A9,SLC4A1,SNCA,SPN,Stfa2/Stfa2l1,Stfa3,TAL1,TFRC,THBS1,TSPAN32,VCAM1	
ZFP36		transcription regulator	Inhibited	-2	bias	-0.916		1.38E-10	ABCG4,KIF11,LCN2,MXD1,Ngp,NUF2,S100A9,TFRC,TMCC2,TOP2A,VCAM1	FOXO1,FOXO3,IL6,MYC,NFkB (complex),STAT3,ZFP36
2-(4-amino-1-isopropyl-1H-pyrazolo[3,4-d]pyrimidin-3-yl)-1H-indol-5-ol		chemical reagent	Inhibited	-2.474		-0.043	-2.341	1.87E-10	AURKA,AURKB,BIRC5,CCNB1,E2F2,EGR1,HIST2H2BF,KNL1,TOP2A,TROAP	
imipramine blue		chemical drug	Inhibited	-2.768	bias	-0.55		1.88E-10	AURKA,CCNB1,CENPE,CENPF,E2F2,PLK1,PLK4,STMN1	
FOXO1		transcription regulator	Activated	3.859	bias	0.594		4.49E-10	ASPM,BIRC5,CA2,CCNB1,CCNB2,CDK1,CENPF,DLGAP5,EGR1,FABP5,IGFBP1,IKZF1,KIF11,LPL,MCM5,NUSAP1,SLC25A37,SPC25,THBS1,VCAM1	AKT1,AR,E2F1,E2F2,E2f,EGF,FOXO1,FOXO3,HIF1A,IL6,MYC,NFKBIA,NFkB (complex),PPARA,PPARG,RB1,RXRA,Rb,SP1,STAT3,TCF3,TP53,YAP1
ERBB2		kinase	Activated	3.444	bias	0.48	1.455	4.99E-10	ASPM,AURKA,AURKB,BIRC5,BRCA1,CCNB1,CCNB2,CDK1,CENPE,EGR1,FEN1,H19,IGF2,KCNN4,LCN2,MCM3,MCM5,MCM6,MKI67,NDC80,POLE,RRM2,TCEAL9,THBS1,TOP2A	AR,CDKN2A,E2F1,E2F3,E2F4,E2f,EGFR,ERBB2,FOXO1,FOXO3,HDAC1,IL6,MYC,NFkB (complex),RB1,RBL1,STAT3,TBX2,TP53,YAP1
BNIP3L		other	Inhibited	-3		-0.247	-2.258	5.77E-10	ANK1,AURKA,CENPE,CENPF,KIF11,NUF2,RRM2,TFRC,TOP2A	
medroxyprogesterone acetate		chemical drug	Inhibited	-2.77		-0.11	-2.396	5.92E-10	ASPM,BIRC5,CCNB1,CCNB2,CDK1,CENPF,DLGAP5,EGR1,IGFBP1,KIF11,MCM5,NUSAP1,SPC25	CCND1,E2F1,ERBB2,FOXO1,FOXO3,HDAC1,IL6,MYC,NFkB (complex),PGR,PPARG,RB1,RNA polymerase II,Rb,STAT3,TP53,medroxyprogesterone acetate
mir-21		microrna	Inhibited	-2.557	bias	-0.659		7.71E-10	ASPM,ATAD2,CCNB1,DLGAP5,ELN,H2AFX,KIF23,MARCO,MKI67,NUSAP1,RACGAP1,SLC25A37,STMN1,TOP2A,VCAM1,ZWILCH	
TCF4		transcription regulator						1.03E-09	BIRC5,CCNB2,CDK1,CIP2A,FAM129C,HMMR,KCNN4,MKI67,NDC80,NUF2,RACGAP1,RRM2,SPC25,TENT5C	
lipopolysaccharide		chemical drug	Activated	3.092	bias	0.477	0.428	1.51E-09	AQP4,AURKB,CCNB1,CCNB2,Cd24a,Cyp2b13/Cyp2b9,CYP3A5,CYP4A11,DNMT1,EGR1,FABP5,H19,IGFBP1,INHBB,ISG20,KCNAB2,KCNN4,KIF23,LCN2,LPL,MARCO,MCM5,MKI67,MXD1,NUSAP1,PLK1,PROK1,RGS16,S100A9,SLC1A5,SLFN13,STMN1,TFRC,THBS1,THBS2,TNFRSF13B,TOP2A,TREML2,UNC119,VCAM1	CDKN2A,CHUK,EGR1,FOXO3,IL1B,MYC,NFKBIA,NFkB (complex),PPARA,PPARG,RB1,RBL1,RXRA,Rb,STAT3,TP53,lipopolysaccharide
cycloheximide		chemical reagent		-1.03		-0.118	-0.569	1.71E-09	AFP,Akr1b7,AQP4,BEX3,BIRC5,CYP3A5,CYP4A11,EGR1,IGF2,IGFBP1,ISG20,LCN2,LPL,MXD1,PLK1,PRKAR2B,THBS1,VCAM1	Akt,CTNNB1,E2F1,EGR1,F2R,FOS,HIF1A,IKBKB,IL1B,LDLR,NFKBIA,NFkB (complex),RB1,STAT3,TP53,cycloheximide
4-nitroquinoline-1-oxide		chemical toxicant	Activated	2.449	bias	0.808		1.97E-09	AURKA,AURKB,CCNB1,CCNB2,CDK1,EGR1	4-nitroquinoline-1-oxide,CDKN2A,E2F1,E2F4,MYC,RB1,TP53
KLF1		transcription regulator		0.541		-0.064	0.682	3.23E-09	ADD2,Cd24a,DMTN,E2F2,GP9,HBB,KCNN4,TFRC	
HDAC1		transcription regulator		-0.928		-0.154	-0.558	4.51E-09	CCNB1,CCNB2,CDK1,E2F2,EGR1,H2AFX,LCN2,MCM3,MCM5,PLK1,RRM2,S100A9,TAL1,TOP2A,UHRF1	CDKN2A,E2F1,E2F2,E2F3,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TBX2,TP53
E2f		group	Activated	2.941	bias	0.757		5.66E-09	BRCA1,CCNB1,CDK1,DBF4,E2F2,MCM3,MCM5,MCM6,NUSAP1,RRM2,TPX2	E2F1,E2F4,E2f,MYBL2,RB1,RBL1,Rb,TBX2,TP53
progesterone		chemical - endogenous mammalian		-0.257		0.231	-1.261	6.49E-09	AURKA,BRCA1,CA2,CCNB1,CCNB2,CYP3A5,EGR1,FEN1,GRB10,H19,IGFBP1,INHBB,ISG20,LCN2,LPL,MCM3,MCM5,MCM6,MKI67,NCAPH,PEG3,RRM2,SLC1A5	CREB1,E2F1,ESR1,ESR2,FOXO1,FOXO3,IL6,MYC,NFkB (complex),PGR,PPARA,PPARG,RARA,RNA polymerase II,RXRA,SMARCE1,SP1,STAT3,progesterone
trichostatin A		chemical drug	Activated	2.773	bias	0.515		6.69E-09	AFP,ATAD2,AURKB,BRCA1,CCNB2,CDK1,CYP3A5,DNMT1,HBA1/HBA2,HBB,IGFBP1,IKZF1,MCM3,MCM6,MXD1,PLK1,PRG2,SPN,STMN1,THBS1,TOP2A,VCAM1	CDKN2A,E2F2,E2F4,E2f,HDAC1,Histone h4,MED1,MYC,RB1,RBL1,RNA polymerase II,Rb,TP53,trichostatin A
TERC		other						7.39E-09	AURKA,Cyp2b13/Cyp2b9,CYP4A11,EGR1,H19,Ngp,S100A9	
AGN194204		chemical drug						1.01E-08	Akr1b7,AURKA,CCNB1,Cd24a,CDK1,H2AFX,KIF2C,LPL,MKI67,PLK1,SMC4,TOP2A	
TBX2		transcription regulator	Activated	3	bias	0.293	2.122	1.12E-08	AURKA,AURKB,CCNB1,CDK1,DNMT1,MCM5,MCM6,NCAPG2,PLK1	CCND1,CDKN1A,E2F1,E2F3,E2F4,E2f,FOXO1,FOXO3,HDAC1,HIF1A,NFkB (complex),PTEN,RB1,TBX2,TP53
L-methionine		chemical - endogenous mammalian						1.22E-08	AURKA,BIRC5,CCNB1,CCNB2,CDK1,IGFBP1,NUSAP1,TOP2A	
estrogen		chemical drug	Activated	3.057	bias	0.619		1.26E-08	AURKA,BRCA1,CCNB2,DNMT1,EGR1,FEN1,IGF2,LCN2,LPL,MCM3,MCM5,POLE,RRM2,TOP2A,UHRF1	CEBPA,CREB1,E2F1,E2F2,E2F3,E2F4,E2f,ERBB2,HDAC1,HDAC2,MYC,RB1,RBL1,Rb,TBX2,TP53,calcitriol,estrogen
CDKN2A		transcription regulator	Inhibited	-3.261		-0.097	-2.922	2.09E-08	ATAD2,AURKB,BIRC5,BUB1B,CCNB1,CDK1,E2F2,EGR1,FEN1,H2AFX,MCM5,MKI67,PEG3,PLK1,RRM2	CDKN2A,E2F1,E2F3,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TBX2,TP53,TP73,YY1
beta-estradiol		chemical - endogenous mammalian	Activated	2.51	bias	0.315	0.771	3.02E-08	AFP,ANK1,ATAD2,AURKA,BIRC5,BRCA1,CA2,CCNB1,CCNB2,CDK1,DMTN,E2F2,EGR1,FABP5,FEN1,GRB10,H19,HBA1/HBA2,HBB,HSD17B6,IGF2,IGFBP1,INHBB,LCN2,LPL,MCM3,MCM5,MCM6,MKI67,MXD1,PSAT1,RGS16,RRM2,SLC13A3,SLIT2,SPN,THBS1,TOP2A,TREML2,VCAM1	CREB1,E2F1,E2F2,E2f,ERBB2,ESR1,ESR2,FOXO1,FOXO3,HDAC1,HDAC2,HIF1A,IGF1,MYC,PGR,PPARG,RB1,Rb,SP1,STAT3,TP53,beta-estradiol,estrogen,progesterone
PPARA		ligand-dependent nuclear receptor		0.442	bias	0.251	-0.186	3.57E-08	Akr1b7,AURKA,CCNB1,Cd24a,CDK1,CYP4A11,FABP5,H2AFX,IGFBP1,KIF2C,LPL,MKI67,Mup1 (includes others),PLK1,S100A9,SMC4,TOP2A,VCAM1	FOXO1,FOXO3,IL6,MED1,MYC,NFKBIA,NFkB (complex),PPARA,PPARG,RXRA,STAT3,pirinixic acid
EP400		other	Activated	2.621	bias	0.791		4.39E-08	CENPF,E2F2,INCENP,MCM3,NCAPG2,PLK1,UHRF1	
RBX1		enzyme		1	bias	0.636		6.23E-08	BIRC5,BRCA1,CCNB1,CDK1	BRCA1,CREB1,ESR1,ESR2,MYC,NFkB (complex),PML,RARA,RBX1,RNA polymerase II,SMARCE1,SP1,STAT3,TP53,TP73
MED1		transcription regulator	Activated	2.945	bias	0.759		7.09E-08	AURKA,AURKB,BIRC5,CCNB1,CDK1,CYP3A5,CYP4A11,IGFBP1,IKZF1,PLK1,THBS1	
gefitinib		chemical drug						9.76E-08	AURKA,AURKB,BIRC5,BRCA1,CCNB1,KIF11,KIF23,MCM3,MKI67,S100A9,TOP2A	CREB1,E2F1,E2f,ERBB2,ESR1,ESR2,HDAC1,MAPK1,MYBL2,MYC,NFkB (complex),RARA,RB1,Rb,SMARCE1,SP1,STAT3,TP53,gefitinib
E2F2	5.46E+00	transcription regulator						1.24E-07	BIRC5,CCNB1,CCNB2,CDK1,MCM3,MCM5,MCM6,RRM2	E2F1,E2F2,E2f,RB1,RBL1,TBX2,TP53
E2F7		transcription regulator						1.36E-07	CCNB1,CDK1,E2F2,KIF23,RACGAP1	
IGF2	8.61E+00	growth factor						1.41E-07	BIRC5,CDK1,EGR1,FEN1,H19,IGF2,MCM5,RGS16,RRM2,THBS2,UHRF1	AKT1,AR,Akt,CTNNB1,E2F1,EGFR,EGR1,FOXO1,FOXO3,HIF1A,IGF2,MYC,NFkB (complex),SP1,STAT3,YAP1
INSR		kinase		1.039	bias	0.735		1.55E-07	ATP2A3,BIRC5,CDK1,EGR1,FEN1,GRB10,H19,IGF2,IGFBP1,MCM5,Meg3,RGS16,RRM2,THBS2,UHRF1,VCAM1	Akt,CTNNB1,D-glucose,E2F1,EGR1,ESR1,FOXO1,FOXO3,HIF1A,HMGA1,IGF1,INSR,IRS1,MYC,NFkB (complex),PI3K (complex),SP1,STAT3
SMARCB1		transcription regulator		-1.944	bias	0.554		1.69E-07	AURKA,CDK1,CENPE,CYP4A11,KIF11,KIF23,MCM3,MCM5,Mup1 (includes others),PLK4,SMC4	
YAP1		transcription regulator		1.969	bias	0.664		1.77E-07	AURKA,BIRC5,CDK1,DIAPH3,IGF2,MCM6,PLK1,UHRF1,VCAM1	AKT1,AR,FOXO1,FOXO3,NFkB (complex),SP1,YAP1
RBL1		transcription regulator	Inhibited	-2.414	bias	-0.67		1.90E-07	AURKB,CDK1,MCM3,MCM5,MCM6,PLK1,RRM2,THBS1	CDKN2A,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TP53,TP73
LY294002		chemical - kinase inhibitor	Inhibited	-2.777	bias	-0.737		2.40E-07	AURKA,AURKB,BIRC5,BUB1B,CCNB1,EGR1,FEN1,GRB10,HSD17B6,IGF2,INHBB,ISG20,LCN2,MXD1,NDC80,SPN,THBS1,TOP2A,VCAM1	CSF1,CTNNB1,E2F1,EGR1,FOXO1,FOXO3,HRAS,KRAS,LY294002,MDM2,MYBL2,MYC,NFKBIA,NFkB (complex),RB1,STAT3,TP53,TP73,Vegf
BMS-690514		chemical drug	Inhibited	-2.449	bias	-0.434	-1.387	2.43E-07	BRCA1,CCNB1,CDK1,MCM3,MCM5,MCM6	BMS-690514,ERBB2,HDAC1,MYC,RB1,Rb,TP53
TGFB1		growth factor		1.343	bias	0.298	-0.008	2.88E-07	AFP,ASPM,BIRC5,BUB1B,CCNB1,CCNB2,CDK1,CENPE,CENPF,DMTN,DNMT1,EGR1,ELN,FABP5,HSD17B6,IGF2,INHBB,KLRC1,LCN2,LPL,MKI67,NDC80,RACGAP1,SLC13A3,SLC25A4,SLC4A1,SMC4,SPC25,TENM4,TFRC,THBS1,THBS2,TOP2A,UNC119,VCAM1	CREB1,CTNNB1,E2F1,EGR1,ERBB2,ESR1,ESR2,FGF2,FOXO1,FOXO3,HDAC1,IL6,MYC,NFkB (complex),PPARG,RARA,RB1,Rb,SMARCE1,SP1,STAT3,TGFB1,TP53
ACTB		other	Activated	2.236		-0.064	2.378	3.54E-07	AURKA,AURKB,CCNB2,RACGAP1,STMN1	
troglitazone		chemical drug		-1.115		0.088	-1.369	4.99E-07	BIRC5,CCNB1,CYP3A5,E2F2,EGR1,FABP5,HBA1/HBA2,HMMR,LPL,MKI67,NCAPH,NEIL3,NUF2,RACGAP1,STMN1	CCL2,CREB1,D-glucose,EGR1,ESR1,FOXO1,HIF1A,MAPK1,NFKBIA,NFkB (complex),PPARA,PPARG,RXRA,SP1,STAT3,troglitazone
PBRM1		other						5.13E-07	CCNB1,CDK1,CENPE,CENPF	
MITF		transcription regulator	Activated	3.464	bias	0.848		5.74E-07	AURKB,BRCA1,CCNB1,CENPF,DSN1,MCM5,MCM6,NUF2,PLK1,SPC25,TMCC2,TPX2	E2F1,E2f,MITF,RB1,RBL1,TBX2,TP53
SMARCE1		transcription regulator		-1.342		0.064	-1.484	6.11E-07	BRCA1,CCNB1,CDK1,CENPE,CENPF	
hydroxyurea		chemical drug		0.485	bias	0.653		6.23E-07	CCNB1,E2F2,H2AFX,HBB,MCM5,RRM2,UHRF1	BRCA1,CDKN2A,E2F1,E2F4,E2F6,MYC,NFkB (complex),RB1,RNA polymerase II,STAT3,TP53,hydroxyurea
cisplatin		chemical drug		1.554	bias	0.354	0.145	6.69E-07	ANK1,BIRC5,BRCA1,CAPN6,CCNB1,CDK1,EGR1,H2AFX,HBA1/HBA2,IGFBP1,LCN2,MCM3,PLK1,PRG2,RRM2,SLC25A4,STMN1,THBS1,TOP2A,UHRF1,VCAM1	BRCA1,CEBPD,CREB1,CSF2,E2F1,E2F2,E2F3,E2F4,E2f,FOXO1,HDAC1,Histone h4,RB1,Rb,SP1,STAT3,TP53,cisplatin,prostaglandin E2
RB1		transcription regulator	Inhibited	-3.277		0.235	-4.047	7.16E-07	ATAD2,AURKB,BIRC5,BRCA1,CCNB1,CDK1,COX6A1,DNMT1,EGR1,FEN1,MCM3,MCM5,MCM6,PLK1,RRM2	CDKN2A,E2F1,E2F2,E2F3,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TBX2,TP53,TP73
dihydrotestosterone		chemical - endogenous mammalian		0.664	bias	0.463	-0.786	7.27E-07	Akr1b7,ATAD2,BUB1B,CCNB1,CYP4A11,EGR1,ELN,GRB10,HSD3B2,INHBB,LPL,MCM5,Mup1 (includes others),SLC1A4,SLC1A5,SLC25A37,THBS1,VCAM1	AR,BRCA1,CAV1,CTNNB1,EGR1,ESR1,FOXO1,FOXO3,MDM2,MYC,NFYA,TGFB1,TP53,Vegf,dihydrotestosterone
O6-benzylguanine		chemical drug		-1.285		-0.191	-0.91	8.50E-07	CCNB1,CCNB2,H2AFX,MKI67	
SMOC2		other	Activated	2	bias	0.764		8.50E-07	AURKB,CCNB1,CDK1,CENPF	
dexamethasone		chemical drug		1.033		0.096	0.539	1.01E-06	AFP,Akr1b7,BEX3,BIRC5,BRCA1,CA2,CYP3A5,CYP4A11,DLGAP5,E2F2,EGR1,ELN,FABP5,GPC3,HMMR,IGF2,IGFBP1,INHBB,ISG20,KNL1,LCN2,LPL,MARCO,NCAPH,NDC80,NEIL3,NUF2,PRKAR2B,RACGAP1,S100A9,SLC13A3,SLC25A37,SLC4A1,SPECC1,TFRC,THBS1,TOP2A,VCAM1	Akt,CREB1,CTNNB1,E2F1,EGR1,ESR1,FOXO1,FOXO3,HIF1A,IGF1,MYC,NFYA,NFkB (complex),PPARA,PPARG,RXRA,SP1,STAT3,TCF4,TGFB1,TP53,dexamethasone,troglitazone
E2F8		transcription regulator						1.33E-06	CCNB1,CDK1,KIF23,RACGAP1	
miR-24-3p (and other miRNAs w/seed GGCUCAG)		mature microrna	Inhibited	-2.2	bias	-0.955		1.55E-06	AURKB,CDK1,E2F2,FEN1	
BRCA1	2.32E+00	transcription regulator		-1.711	bias	0.286	-2.391	1.83E-06	BIRC5,BRCA1,CCNB1,CCNB2,Cd24a,EGR1,FEN1,H2AFX,HBB,PLK1	BRCA1,CDKN2A,E2F1,E2F4,FOXO1,MED1,MYC,NFKBIA,NFkB (complex),RB1,RBL1,RNA polymerase II,Rb,STAT3,TP53
IGF1		growth factor	Activated	2.614	bias	0.463	0.995	1.93E-06	AQP4,BIRC5,BRCA1,CCNB1,CDK1,EGR1,ELN,H2AFX,HBB,IGF2,IGFBP1,LCN2,LPL,MKI67,THBS1,VCAM1	CREB1,CTNNB1,E2F1,EGR1,FGF2,FOXO1,FOXO3,HDAC1,IGF1,IL6,MYC,NFYA,NFkB (complex),PGR,RB1,STAT3,TP53,TP73,beta-estradiol,cisplatin,hydrogen peroxide
phorbol myristate acetate		chemical drug		0.115	bias	0.477	-2.089	2.01E-06	ACHE,AQP4,ATP2A3,AURKA,AURKB,BIRC5,CA2,CDK1,DNMT1,EGR1,H19,IGF2,IGFBP1,IKZF1,INHBB,KCNN4,KIF2C,LCN2,LPL,NEIL3,PRKAR2B,S100A9,SPN,THBS1,TNFRSF13B,VCAM1	AR,E2F1,EGF,EGFR,FOXO1,FOXO3,HIF1A,IGF1,IL6,MYC,NFKBIA,NFkB (complex),PI3K (complex),RB1,SP1,STAT3,YAP1,phorbol myristate acetate
NFYB		transcription regulator						2.17E-06	ARHGAP11A,CCNB1,CCNB2,CDK1,CENPF,CIP2A,IGDCC4,PLK1,RRM2,SPECC1,TOP2A,UHRF1	
FOS		transcription regulator		0.063	bias	0.281	-0.76	2.49E-06	ADD2,ARID3A,CA2,DNMT1,EGR1,HBA1/HBA2,HMMR,HSD3B2,IGFBP1,KCNN4,LPL,MCM5,MXD1,S100A9,STMN1,TAL1,VCAM1	ESR1,ESR2,FOS,NFkB (complex),PPARG,SP1,STAT3,cytokine
PD98059		chemical - kinase inhibitor	Inhibited	-2.371	bias	-0.602		3.74E-06	BIRC5,CA2,CCNB1,DNMT1,E2F2,EGR1,ELN,IGF2,IGFBP1,LPL,MKI67,MXD1,RRM2,THBS1,TNFRSF13B,TOP2A,VCAM1	Akt,CREB1,CTNNB1,E2F1,EGF,EGR1,FGF2,FOXO1,FOXO3,HIF1A,IL6,MYC,NFKBIA,NFkB (complex),PD98059,RB1,STAT3,TP53,VEGFA
ZBTB20		transcription regulator	Inhibited	-2.236		0.056	-2.362	3.93E-06	AFP,Akr1b7,Cyp2b13/Cyp2b9,CYP3A5,GPC3,IGFBP1	
SP600125		chemical - kinase inhibitor		-1.321	bias	-0.275	-0.376	4.08E-06	CCNB1,Cd24a,CDK1,DNMT1,EGR1,FABP5,GRB10,H2AFX,H19,HIST1H2BN,THBS1,THBS2,VCAM1	CREB1,E2F1,EGR1,ESR1,FOXO1,IL1B,MYC,NFKBIA,NFYA,NFkB (complex),PPARG,SP600125,STAT3,TGFB1,TP53,VEGFA
SRSF1		other						4.78E-06	AURKA,AURKB,BIRC5,PLK1,RRM2	

TP73		transcription regulator	Inhibited	-3.021	bias	0.298	-4.064	4.80E-06	AFP,AURKA,BIRC5,CCNB1,CDK1,EGR1,FEN1,KIF23,MCM6,Meg3,STMN1,THBS1,THBS2,TPX2	CCND1,CDKN1A,CDKN2A,E2F1,E2F4,E2f,FOXO1,MED1,MYC,RB1,RBL1,Rb,STAT3,TBX2,TP53,TP73

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Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
TRIM24		transcription regulator	Activated	3.997	bias	-0.301	5.321	2.71E-19	Apol9a/Apol9b,Bst2,CA2,GBP2,GBP3,GBP4,IFIT1B,IFIT2,IFIT3,Igtp,Iigp1,IRF1,IRGM,Irgm1,ISG15,PSMB8,SAMHD1,STAT1,TAP1,Tgtp1/Tgtp2	
IFNB1		cytokine	Inhibited	-4.216		0.15	-4.897	8.88E-19	Bst2,Cd24a,CD274,CYP1A2,GBP2,GBP3,GBP4,GBP5,GBP6,GBP7,Gvin1 (includes others),HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,Igtp,IRF1,IRGM,Irgm1,ISG15,ITGB3,SLFN13,STAT1,Tgtp1/Tgtp2,THBS1,TNFSF10,Trim30a/Trim30d,ZBP1	
STAT1	-1.94E+00	transcription regulator	Inhibited	-4.843		0.224	-5.995	1.83E-18	A2M,C1R,CD274,CTSS,CYP1A2,CYP2C8,CYP4A11,EGR1,GBP2,GBP3,GBP4,GBP5,GBP6,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,IRF1,Irgm1,ISG15,NLRC5,PSMB8,SAMHD1,Serpina3g (includes others),SLFN13,STAT1,TAP1,Tgtp1/Tgtp2,TNFSF10	
IFNG		cytokine	Inhibited	-3.54		0.143	-4.562	3.12E-18	A2M,AQP1,Bst2,C1R,Cd24a,CD274,CD5L,CHST11,CSF1,CTSS,CXCR4,CYP1A2,DUSP1,E2F4,EGR1,EPOR,GBP2,GBP3,GBP4,GBP5,GBP6,GBP7,Gvin1 (includes others),HLA-A,HLA-DQB1,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,Iigp1,IL1RL1,IRF1,IRGM,Irgm1,ISG15,ITGB3,JUNB,KLF1,KLF10,Mt1,MYB,NLRC5,PLA2G7,PRDX2,PSMB8,SAMHD1,Serpina3g (includes others),SERPINB9,SLC14A1,STAT1,TAP1,Tgtp1/Tgtp2,THBS1,TNFRSF14,TNFSF10,TSPAN33	
Ifnar		group	Inhibited	-4.17	bias	0.294	-5.395	1.41E-17	Bst2,CD274,GBP2,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,IRF1,Irgm1,ISG15,NLRC5,PSMB8,STAT1,TAP1,TNFSF10,ZBP1	
IL6		cytokine		0.744		0.173	-0.281	9.90E-17	A2M,AQP4,BTG2,CD274,CD79A,CDC6,CDKN2D,CSF1,CXCR4,CYP1A2,CYP2B6,CYP2C8,DUSP1,E2F4,EGR1,ENO2,FGL1,GATA1,GBP2,GBP3,HLA-A,IFI16,IFIT1B,IFIT2,IFITM3,IL1RL1,IRF1,ITGB3,JUNB,Mt1,Mt2,MYB,PROM1,PSMB8,RRM2,SLC14A1,STAT1,TAL1,TAP1,THBS1,TNFSF10	
STAT3		transcription regulator		1.445		0.15	0.694	2.23E-16	A2M,CD274,CDKN2D,CXCR4,EGR1,GBP2,GBP3,GBP5,GBP6,HBB,HIST2H2AA3/HIST2H2AA4,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,IRF1,Irgm1,ISG15,JUNB,Mt1,MYB,PROM1,PSMB8,Serpina3g (includes others),SERPINB9,SLFN13,SMAD9,STAT1,TAP1,TFF3,Tgtp1/Tgtp2,THBS1,TNFSF10	
lipopolysaccharide		chemical drug	Inhibited	-2.158		0.161	-3.362	4.31E-15	ADRB2,AQP1,AQP4,CCNF,Cd24a,CD274,CSF1,CXCR4,CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,CYP4A11,DUSP1,Ear2 (includes others),EGR1,FABP2,FGF21,GATA1,GBP2,GBP3,GBP4,GBP5,GBP6,HLA-A,HLA-DQB1,IFI16,IFIT1B,IFIT2,IFIT3,Igtp,Iigp1,INHBB,IRF1,IRGM,Irgm1,ISG15,JUNB,KCNN4,KLF10,LPIN1,MARCO,Mt1,Mt2,NLRC5,PAPSS2,PLA2G7,PLK3,PSMB8,PTPRU,SERPINB9,SLFN13,SPHK1,STAT1,TAP1,Tgtp1/Tgtp2,THBS1,TIMD4,TNFSF10,TNNT2,Trim30a/Trim30d	
IL10RA		transmembrane receptor	Activated	4.584		0.009	4.537	5.17E-15	CA2,Cd24a,CDKN2D,Ces2g,CTSE,CYP2F1,GBP2,GBP5,GBP6,HLA-A,IFI16,Iigp1,IRF1,IRGM,Irgm1,MYB,NLRC5,PSMB8,SAMHD1,Serpina3g (includes others),SERPINB9,STAT1,TAP1,Tgtp1/Tgtp2,TNFRSF14,ZBP1	
GATA1	9.49E-01	transcription regulator		0.986		0.081	0.652	1.02E-14	AQP1,BTG2,CA1,CA2,CDKN2D,EGR1,EPOR,GATA1,GFI1B,Gypa,HBB,IL1RL1,INHBB,ITGB3,JUNB,KLF1,MYB,PRG2,SPTA1,SPTB,TAL1,TFF3,TUBB1	
IRF7		transcription regulator	Inhibited	-4.36	bias	0.323	-5.767	1.28E-14	GBP3,GBP4,GBP5,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,IRF1,IRGM,Irgm1,ISG15,PARP14,PSMB8,STAT1,TAP1,TNFSF10,Trim30a/Trim30d,ZBP1	
IRF3		transcription regulator	Inhibited	-4.444		0.246	-5.537	2.46E-14	Bst2,CD274,GBP5,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,IRF1,IRGM,Irgm1,ISG15,JUNB,NLRC5,PARP14,STAT1,TAP1,TNFSF10,Trim30a/Trim30d,ZBP1	
GATA2		transcription regulator		1.851		0.055	1.683	3.67E-14	Cldn13,CYP2F1,Ear2 (includes others),GATA1,GBP2,GFI1B,Gypa,HEMGN,IL1RL1,KEL,KLF1,MFSD2B,MYB,PNLIPRP1,Ppbp,PRG2,PRSS1,Prss1 (includes others),PRSS2,RHAG,RHCE/RHD,SERPINA6,SLC22A4,TAL1,THBS1,TSPAN32,TUBB1,UGT2B7	
dexamethasone		chemical drug	Activated	2.594		0.033	2.36	1.85E-13	ADRB2,AQP1,BTG2,CA2,CD274,Clec2d (includes others),CSF1,CTSE,CXCR4,CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,CYP4A11,DUSP1,E2F4,EGR1,ENO2,FGF21,FILIP1L,GATA1,GBP2,GBP3,GBP5,HEMGN,HILPDA,HLA-A,HLA-DQB1,IFIT1B,IFIT2,IFIT3,IFITM3,IL1RL1,INHBB,IRF1,ISG15,ITGB3,JUNB,LPIN1,MARCO,Mt1,Mt2,MYB,PARP14,Ppbp,PRDX2,RFX2,RGCC,RGS5,RHAG,SAMHD1,SERPINA6,SERPINB9,SLC14A1,SPHK1,SPIB,STAT1,Tgtp1/Tgtp2,THBS1,TNFRSF19,TNFSF10,Trim30a/Trim30d,TSPAN33,TUBB1	
IL1B		cytokine		0.182		0.147	-0.629	2.87E-13	A2M,ACHE,ADRB2,AQP4,BTG2,C1R,Cd24a,CD274,CSF1,CTSS,CXCR4,CYP1A2,CYP2B6,DUSP1,EGR1,GBP2,GBP3,GBP6,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,IL1RL1,IRF1,ISG15,ITGB3,JUNB,KLF10,Mt1,Mt2,PLK3,Ppbp,PSMB8,SERPINB9,SLC14A1,SLC22A4,STAT1,Tgtp1/Tgtp2,THBS1,TNFSF10	
poly rI:rC-RNA		biologic drug	Inhibited	-3.628		0.243	-4.873	2.96E-13	Bst2,CD274,Clec2d (includes others),CSF1,CXCR4,DUSP1,EGR1,GBP2,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,Iigp1,IRF1,ISG15,JUNB,MARCO,MYB,NLRC5,PSMB8,STAT1,TAP1,THBS1,TNFSF10,Trim30a/Trim30d,ZBP1	
KCNK9		ion channel	Activated	2.72		-0.071	2.954	1.09E-12	A2M,CA1,Cldn13,CTSE,Gypa,HEMGN,KEL,RHAG,RHCE/RHD,SLC14A1,SPTA1	
ABCB6		transporter		-1.745		0.023	-1.818	1.94E-12	ALAD,CYP1A2,CYP2A6 (includes others),CYP2B6,Cyp2c54 (includes others),CYP4A11,HK1,HMBS,KLF1,PRDX2,UROD	
PTGER4		g-protein coupled receptor	Activated	3.826		-0.076	4.117	2.48E-11	CXCR4,EGR1,GBP2,GBP4,GBP6,IFI16,IFIT1B,IFIT2,Igtp,IRF1,IRGM,Irgm1,PARP14,SLFN13,Tgtp1/Tgtp2,TNFSF10	
mir-21		microrna	Activated	3.385		-0.218	4.35	3.71E-11	BTG2,C1R,CD274,GBP2,GBP3,GBP5,GBP6,GBP7,Gvin1 (includes others),H2AFX,IFI16,Iigp1,IRF1,IRGM,Irgm1,MARCO,NLRC5,STAT1,TAP1,Tgtp1/Tgtp2	
tretinoin		chemical - endogenous mammalian		-1.299		0.116	-2.039	7.07E-11	A2M,AQP1,BTG2,CA2,CD274,CDKN2D,CTSS,CXCR4,CYP1A2,CYP2B6,CYP4A11,DTL,DUSP1,E2F4,EGR1,GBP4,HK1,HLA-A,HSD17B6,IFI16,IFIT1B,IFIT2,IFIT3,INMT,IRF1,ISG15,ITGB3,KLF1,Mt1,MYB,PARP14,PLA2G7,PLK3,PRDX2,PRG2,PROM1,PSMB8,PTPRU,PYCR2,RGS5,SAMHD1,SERPINB9,SMAD9,STAT1,TAL1,TAP1,THBS1,TNFRSF19,TNFSF10,TSPAN33,XK	
Interferon alpha		group	Inhibited	-3.526		0.205	-4.458	5.23E-10	Bst2,BTG2,CDKN2D,CYP1A2,E2F4,GBP2,GBP3,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,IRF1,ISG15,PARP14,PSMB8,SERPINB9,SLFN13,STAT1,TAP1,Tgtp1/Tgtp2,TNFSF10,ZBP1	
SOCS1		other	Activated	2.765		-0.237	3.635	5.85E-10	A2M,DUSP1,GBP5,GBP6,Gvin1 (includes others),IFI16,IFIT1B,IFIT2,IFIT3,Iigp1,IRF1,IRGM,ISG15,STAT1	
butyric acid		chemical - endogenous mammalian		0.435		0.031	0.299	6.26E-10	A2M,ACHE,ALAD,AQP1,CDC6,CSF1,CXCR4,CYP2B6,CYP4A11,DUSP1,E2F4,EPOR,FGF21,GATA1,GBP2,HBB,HIST1H1C,HK1,IFI16,IFIT3,IL1RL1,IRF1,MYB,TFF3	
MAPK1		kinase	Activated	2.998		-0.005	3.021	9.49E-10	BCL11A,CCNF,DUSP1,EGR1,ENDOD1,GBP2,GBP5,HBB,IFI16,IFIT2,IFIT3,IFITM3,ISG15,ITGB3,JUNB,PSMB8,SAMHD1,Serpina3g (includes others),STAT1,TAP1,TNFSF10	
IFN Beta		group	Inhibited	-2.501		0.234	-3.355	1.05E-09	CD274,CYP1A2,DUSP1,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,IRF1,ISG15,Mt2,STAT1,TNFSF10,ZBP1	
NRAS		enzyme		-1.183		-0.005	-1.163	1.20E-09	CDC6,CTSE,EGR1,GBP2,HLA-A,IFI16,IFIT1B,Iigp1,Irgm1,ISG15,PRDX2,PSMB8,RBM38,STAT1,TAP1,Tgtp1/Tgtp2	
E. coli B4 lipopolysaccharide		chemical toxicant	Inhibited	-2.877		0.209	-3.769	1.23E-09	AQP1,CD274,CYP2C8,GBP2,GBP4,Gm4951,HLA-A,IFI16,IFIT1B,IFIT3,IFITM3,Igtp,Iigp1,PSMB8,SLC14A1,TAP1,TNFSF10,Trim30a/Trim30d,ZBP1	
SPI1		transcription regulator	Inhibited	-2.659		0.131	-3.118	2.68E-09	BCL11A,BCL7A,CD79A,CSF1,CTSE,CTSS,GATA1,HMBS,IFIT1B,IFIT2,IFIT3,IFITM3,ISG15,MYB,PRG2,PSMB8,TNFRSF14,TNFSF10	
APP		other	Inhibited	-3.36		0.107	-3.863	5.19E-09	ACHE,C1R,CD5L,CSF1,CXCR4,EGR1,ENO2,FXYD1,GBP2,GBP4,GBP6,HIST1H2AD,HIST1H2BD,HIST1H4I,HK1,IFI16,IFIT1B,IFIT2,Igtp,IRF1,IRGM,Irgm1,ITGB3,JUNB,Mt1,PARP14,PRDX2,Prss1 (includes others),SLC25A38,SLFN13,SMARCA2,Tgtp1/Tgtp2,TNFSF10	
NFE2		transcription regulator	Activated	2.2	bias	0.323	1.49	5.91E-09	ERMAP,GATA1,HBB,HMBS,KLF1,SPTA1,TUBB1	
AREG		growth factor		0.194		0.103	-0.145	6.79E-09	CCNF,CXCR4,EGR1,HIST1H2AC,HIST1H2BD,HIST1H2BG,HIST1H2BK,HIST2H2AA3/HIST2H2AA4,IFIT2,IFIT3,RRM2	
IRF9		transcription regulator		-1.348		0.06	-1.503	9.30E-09	IFIT2,IFIT3,IFITM3,IRF1,ISG15,STAT1,Tgtp1/Tgtp2,TNFSF10	
IRF1	-1.62E+00	transcription regulator	Inhibited	-3.201		0.231	-3.941	1.15E-08	C1R,CD274,CTSS,GBP2,IFIT2,IFIT3,IFITM3,IRF1,ISG15,MYB,PSMB8,STAT1,TAP1,TNFSF10	
TLR3		transmembrane receptor	Inhibited	-2.197	bias	0.292	-3.304	1.25E-08	CD274,CD300E,DUSP1,GBP2,GBP3,GBP4,IFI16,IFIT2,IFIT3,Iigp1,IRF1,ISG15,JUNB,SERPINB9,STAT1,TNFSF10,TSPAN33	
TNF		cytokine		-1.06		0.115	-1.798	1.46E-08	A2M,ADRB2,ALAD,AQP1,BTG2,CA2,CD274,CHST11,CSF1,CTSS,CXCR4,CYP2C8,DUSP1,EGR1,GBP2,GBP3,GBP6,HLA-A,IFI16,IFIT1B,IFIT3,IL1RL1,IRF1,ISG15,ITGB3,JUNB,KLF10,Mt1,Mt2,PARP14,PLK3,Ppbp,PPP1R3C,PSMB8,RFX2,RGCC,RGS5,RRM2,SERPINB9,SH3TC2,SLC14A1,SLC22A4,SLC7A1,SPHK1,STAT1,TAP1,Tgtp1/Tgtp2,THBS1,TNFSF10	
SIRT1		transcription regulator	Activated	4.451		-0.121	4.989	1.50E-08	CYP2B6,FGF21,GBP3,GBP6,HLA-A,HLA-DQB1,IFIT1B,IFIT3,IFITM3,Igtp,Iigp1,IRGM,Irgm1,NLRC5,PARP14,STAT1,TAL1,TAP1,Tgtp1/Tgtp2,Trim30a/Trim30d	
TICAM1		other	Inhibited	-2.842	bias	0.304	-3.855	1.59E-08	DUSP1,EGR1,IFI16,IFIT1B,IFIT2,IFIT3,Igtp,IRF1,IRGM,Irgm1,ISG15,SAMHD1,STAT1,TNFSF10	
IFNA2		cytokine	Inhibited	-3.909	bias	0.271	-4.967	2.03E-08	C1R,GBP2,GBP4,HLA-A,IFI16,IFIT2,IFIT3,IFITM3,IRF1,ISG15,SAMHD1,SERPINB9,STAT1,TAP1,TNFSF10,ZBP1	
IFNAR1		transmembrane receptor		-1.498		0.191	-1.917	2.04E-08	Apol9a/Apol9b,CSF1,GBP4,HLA-A,IFI16,IFIT1B,IFIT2,IFIT3,ISG15,PLA2G7,STAT1,THBS1,TNFSF10	
RNASEH2A		enzyme						2.21E-08	GBP2,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,IRF1,ISG15	
IL21		cytokine	Inhibited	-3.207		0.216	-4.017	2.42E-08	EGR1,GBP5,GBP6,IFI16,IFIT1B,IFIT2,IFIT3,Igtp,Irgm1,ISG15,Serpina3g (includes others),SLFN13,TAP1,Tgtp1/Tgtp2	
IFN alpha/beta		group	Inhibited	-3.095		0.243	-3.848	3.77E-08	HLA-A,IFI16,IFIT2,IFIT3,IRF1,Irgm1,SERPINB9,STAT1,Tgtp1/Tgtp2,TNFSF10	
AHR		ligand-dependent nuclear receptor		-1.941		0.032	-2.049	4.23E-08	A2M,BTG2,CCNF,CDKN2D,CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,DCLK3,FGF21,IRF1,JUNB,Mt1,Mt2,RDH16,SLC16A10,TFF3,THBS1,TNFRSF19	
IKBKB		kinase		-1.603		0.211	-2.406	4.60E-08	CDC6,CSF1,CXCR4,EGR1,GBP2,GBP3,H2AFX,HLA-A,IFI16,IFIT1B,IFIT3,IRF1,ISG15,ITGB3,JUNB,Mt1,Mt2,MYO1D	
IFNA4		cytokine	Inhibited	-2.758	bias	0.323	-3.649	5.74E-08	Bst2,CD274,GBP2,GBP5,IFIT2,Irgm1,ISG15,ZBP1	
stallimycin		biologic drug	Inhibited	-2.759	bias	0.309	-3.611	5.74E-08	CSF1,IFI16,IFIT2,IFIT3,IRF1,ISG15,STAT1,TNFSF10	
PARP9		enzyme		-1.455	bias	0.289	-2.156	5.89E-08	HLA-DQB1,IFIT2,IFIT3,IRF1,ISG15,STAT1	
AGN194204		chemical drug		-1.406	bias	0.286	-2.254	7.54E-08	Cd24a,Cyp2c54 (includes others),DUSP1,FABP2,GBP2,GBP3,H2AFX,HIST1H1C,IFITM3,Igtp,IRF1,TAP1,Tgtp1/Tgtp2	
IFN type 1		group	Inhibited	-2.567		0.181	-3.032	8.13E-08	Bst2,IFI16,IFIT1B,IFIT2,IRF1,ISG15,STAT1,TNFSF10	
STAT6		transcription regulator		1.248		0.063	1.032	9.25E-08	ANKRD55,Cd24a,CTSS,CYP4A11,EGR1,FGF21,GBP2,GBP3,IFI16,IFIT3,IRF1,ISG15,MYB,SPHK1,STAT1,TFF3,Tgtp1/Tgtp2,Trim30a/Trim30d	
SAMSN1		other	Inhibited	-2.53	bias	0.287	-3.439	1.16E-07	IFIT1B,IFIT3,Iigp1,IRF1,IRGM,ISG15,MARCO,RGCC,STAT1	
TLR4		transmembrane receptor	Inhibited	-2.588		0.238	-3.486	1.34E-07	CD274,GBP2,IFI16,IFIT1B,IFIT2,IFIT3,IFITM3,Igtp,Iigp1,IRF1,IRGM,Irgm1,ISG15,MARCO,RGCC,SPHK1,STAT1,TNFSF10,TSPAN33	
SASH1		other	Inhibited	-3	bias	0.323	-3.969	1.45E-07	IFIT1B,IFIT2,IFIT3,Iigp1,IRF1,IRGM,ISG15,MARCO,STAT1	
EBI3		cytokine	Inhibited	-2.21		0.194	-2.746	1.82E-07	CD274,CTSE,GBP2,IFI16,IRF1,STAT1,TAP1,TNFSF10	
bromodeoxyuridine		chemical drug	Inhibited	-2.759	bias	0.311	-3.613	1.82E-07	CSF1,IFI16,IFIT2,IFIT3,IRF1,ISG15,STAT1,TNFSF10	
CHUK		kinase	Inhibited	-2.145	bias	0.262	-3.053	2.30E-07	CSF1,GBP2,GBP3,GBP4,HLA-A,IFI16,IFIT1B,IFIT2,ISG15,ITGB3,JUNB,KLF10,Mt1,Mt2	
POR		enzyme	Activated	2.157		-0.119	2.491	2.39E-07	CYP1A2,CYP2A6 (includes others),CYP2B6,CYP2C8,CYP4A11,FABP2,FGL1,GBP2,HLA-A,HLA-DQB1,Mt1,PLA2G7,STAT1	
NFKBIA		transcription regulator		-0.233		0.089	-0.601	2.99E-07	A2M,BCL11A,BTG2,CDC6,CDKN2D,CITED4,CSF1,CXCR4,GBP2,GBP3,HLA-A,IFI16,IFIT1B,IRF1,ISG15,JUNB,KCNN4,Mt1,Mt2,TNFSF10	
EPO		cytokine		1.643		0.171	1.11	4.19E-07	CA1,CA2,CXCR4,EGR1,EPOR,GATA1,GFI1B,HBB,IL1RL1,JUNB,KLF1,MYB,RHAG,TAL1,TNFSF10,TUBB1	
STAT4		transcription regulator		0.039	bias	0.323	-1.154	4.50E-07	ENO2,EPOR,HILPDA,HIST2H2AA3/HIST2H2AA4,HLA-DQB1,IFIT1B,IFIT2,IRF1,ISG15,LPIN1,Mt1,RGCC,STAT1,Trim30a/Trim30d	
DDX58		enzyme	Inhibited	-2.738	bias	0.301	-3.561	4.88E-07	GBP3,IFIT1B,IFIT2,IFIT3,IRF1,ISG15,STAT1,TNFSF10	
cycloheximide		chemical reagent		1.115		-0.04	1.272	5.06E-07	AQP4,BTG2,CDKN2D,CSF1,CXCR4,CYP1A2,CYP2B6,CYP4A11,DUSP1,EGR1,GATA1,IL1RL1,ITGB3,JUNB,Mt1,Tgtp1/Tgtp2,THBS1,TNFSF10	
CEBPB		transcription regulator	Activated	2.14		0.207	1.297	5.77E-07	CDC6,CXCR4,CYP2A6 (includes others),HBB,HIST1H4A,HIST1H4B,HIST1H4D,HIST1H4F,HIST1H4H,HIST1H4I,HIST1H4J,HIST1H4K,HIST2H4A,HLA-A,IFITM3,INMT,PRG2,SLC7A1,TNFRSF19	
SLC9A3		ion channel						5.94E-07	Igtp,Mt1,Mt2,PSMB8,STAT1,Tgtp1/Tgtp2	
IKBKG		kinase		-1.902		0.236	-2.666	6.29E-07	CSF1,GBP2,GBP3,HLA-A,IFI16,IFIT1B,ISG15,JUNB,Mt1,Mt2,TNFSF10	
ACKR2		g-protein coupled receptor	Activated	2.646	bias	-0.273	3.368	6.36E-07	IFI16,IFIT1B,IFIT2,IFIT3,Iigp1,ISG15,STAT1	
KITLG		growth factor	Activated	2.484	bias	0.258	1.722	6.52E-07	CA2,Cd24a,CSF1,CXCR4,EGR1,EPOR,GATA1,IL1RL1,ITGB3,KLF1,MARCO,MYB,RHAG,TAL1	
NCOA2		transcription regulator		-0.7		0.143	-1.121	6.99E-07	CYP2B6,EGR1,IFIT1B,IFIT2,ISG15,LECT2,LPIN1,MYB,PPP1R3C,Sult2a2	
Irgm1	-1.32E+00	other		1.134	bias	-0.323	1.988	7.49E-07	DTL,IFI16,IFIT1B,IFIT2,IFIT3,Iigp1,RRM2	
TLR9		transmembrane receptor	Inhibited	-2.227	bias	0.263	-3.202	7.61E-07	CD274,CD300E,CSF1,DUSP1,EGR1,IFI16,IFIT1B,IFIT2,IFIT3,IRF1,ISG15,SPHK1,STAT1,TNFSF10	
IFNA1/IFNA13		cytokine	Inhibited	-2.187		0.231	-2.818	8.11E-07	CYP1A2,IFIT2,IFIT3,IRF1,ISG15,STAT1,Tgtp1/Tgtp2,ZBP1	
IRF2		transcription regulator						8.11E-07	CTSS,HIST1H4C,HIST2H4A,IRF1,ISG15,PSMB8,TAP1,TNFSF10	
CA4		enzyme	Inhibited	-2.449	bias	-0.271	-1.785	9.35E-07	CA1,CA2,HEMGN,KEL,RHCE/RHD,SPTB	
PARP1		enzyme	Inhibited	-3.128		0.17	-3.66	9.73E-07	CD274,GBP2,GBP4,GBP6,GBP7,Igtp,Iigp1,IRGM,STAT1,Tgtp1/Tgtp2	
RPSA		translation regulator	Activated	2.449		-0.194	2.924	1.16E-06	DUSP1,GBP3,GBP4,ISG15,STAT1,TAP1	
CNOT7		transcription regulator						1.42E-06	ISG15,PSMB8,SLC14A1,STAT1,TAP1,TFF3	
DOCK8		other	Inhibited	-2.828	bias	0.323	-3.742	1.46E-06	IFIT1B,IFIT2,IFIT3,Iigp1,IRF1,IRGM,ISG15,STAT1	
IL4		cytokine		1.538		0.197	0.765	1.66E-06	ANKRD55,BCL11A,CA2,Cd24a,CD274,CD79A,CSF1,CXCR4,GBP2,GBP3,GBP7,IFI16,IFIT1B,IFIT3,Iigp1,IL1RL1,IRF1,ISG15,ITGB3,JUNB,MARCO,PSMB8,Serpina3g (includes others),SPHK1,STAT1,TFF3,Tgtp1/Tgtp2,Trim30a/Trim30d	
phorbol myristate acetate		chemical drug		-0.137		0.161	-0.974	1.80E-06	ABCA7,ACHE,AQP4,BTG2,CA2,CDKN2D,CXCR4,CYP1A2,CYP2A6 (includes others),DTL,DUSP1,E2F4,EGR1,EPOR,FAM83G,GATA1,HIST1H4C,HIST2H4A,HMBS,INHBB,IRF1,ISG15,ITGB3,JUNB,KCNN4,KEL,SERPINB9,SLC7A1,SPHK1,STAT1,THBS1,TNFSF10	
17-alpha-ethinylestradiol		chemical drug		-1.283		0.104	-1.606	2.16E-06	CD5L,CTSS,CYP2B6,Gm15807/Hmgn5,H2AFX,IFI16,INHBB,LPIN1,MARCO,PLK3,TFF3	
NPAT		transcription regulator						2.23E-06	HIST1H2AC,HIST1H2BD,HIST1H4C,HIST2H4A	
HIF1A		transcription regulator		1.403		0.228	0.56	2.39E-06	AQP4,CD274,CSF1,CXCR4,ENO2,EPOR,GATA1,H2AFX,HILPDA,HIST1H1C,HIST1H2AC,HIST1H2BK,HIST2H2AC,INHBB,ITGB3,PROM1,SPHK1,THBS1	
STAT2		transcription regulator		-1.602		0.219	-2.126	2.41E-06	IFIT1B,IFIT2,IFIT3,IRF1,ISG15,PSMB8,TNFSF10	
RORC		ligand-dependent nuclear receptor						2.45E-06	CYP2A6 (includes others),CYP2B6,Cyp2c54 (includes others),CYP2C8,CYP2F1,CYP4A11,Mt1,Mt2,PPP1R3C,RDH16,SLC16A10	
NUPR1		transcription regulator		0		-0.097	0.433	2.51E-06	ADRB2,CCNF,CXCR4,ENO2,FAM83G,GBP2,HILPDA,HIST1H2AJ,HIST1H2BB,HIST1H2BM,HIST1H3A,HIST1H3F,HIST1H4A,HIST2H3A,HIST2H3D,IFIT2,LARS2,PLK3,SAMHD1,SLC16A10	
DNASE2		enzyme		1.951	bias	0.323	2.581	2.52E-06	Apol9a/Apol9b,IFIT1B,IFIT3,ISG15,TNFSF10,ZBP1	
IL3		cytokine		1.757		0.225	1.091	2.73E-06	BTG2,CSF1,CXCR4,EGR1,GATA1,HK1,HLA-A,IL1RL1,ITGB3,JUNB,KLF1,Mt1,PLA2G7,PRG2,Serpina3g (includes others),TNFSF10	
epigallocatechin-gallate		chemical drug		1.357		-0.115	1.759	2.94E-06	AQP4,CA2,EGR1,GBP3,GBP4,IRF1,ISG15,ITGB3,JUNB,PRG2,STAT1,TAP1,TNFSF10	
SU6656		chemical toxicant		-1.633	bias	-0.284	-0.938	3.01E-06	CSF1,EGR1,IL1RL1,JUNB,Mt1,Mt2	
arsenite		chemical toxicant		1.473		0.144	1.159	5.65E-06	CYP2B6,DUSP1,EGR1,FGF21,INHBB,IRF1,Mt2,PPP1R3C,THBS1	
pomalidomide		chemical drug		-1.991	bias	-0.269	-1.455	8.53E-06	BCL11A,GATA1,HBB,KLF1	
SP600125		chemical - kinase inhibitor		-0.602		-0.139	-0.127	9.18E-06	AQP1,DUSP1,EGR1,H2AFX,HIST1H2BE,HIST1H2BN,HIST2H2AA3/HIST2H2AA4,ISG15,JUNB,SPHK1,THBS1,TNNT2	
TCF3		transcription regulator		-0.391		0.035	-0.468	1.02E-05	CA2,CD79A,Clec2d (includes others),CTSE,E2F4,GATA1,GFI1B,H2AFX,IFI16,KCNN4,PRDX2,PTPRU,RRM2,Serpina3g (includes others),ZBP1	
PLK2		kinase		-0.447		0.248	-1.003	1.15E-05	IFIT2,Iigp1,IRF1,MARCO,RGCC	
ethanol		chemical - endogenous mammalian		0.602		0.096	0.226	1.16E-05	AQP4,CXCR4,CYP2A6 (includes others),CYP2B6,CYP2C8,CYP4A11,DUSP1,EGR1,FABP2,HLA-A,LPIN1,PLK3,PPP1R3C,RGCC,STAT1,TFF3	
RUNX1		transcription regulator	Activated	2.728		0.097	2.408	1.19E-05	ACHE,BTG2,CD79A,CSF1,GATA1,GFI1B,ITGB3,Mt1,RGCC,SLC22A4,TAL1	
IFNLR1		transmembrane receptor						1.20E-05	CSF1,IFIT1B,IFIT2,IFIT3,ISG15,THBS1	
SLC4A1		transporter		1.961		0.088	1.788	1.22E-05	AQP1,Gypa,RHAG,RHCE/RHD	
TREX1		enzyme						1.22E-05	IFI16,IFIT1B,IFIT2,ISG15	

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Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
GATA2		transcription regulator						2.81E-08	Ear2 (includes others),EPX,GBP2,Hbq1a,PNLIPRP1,PRG2,Prss1 (includes others),PRSS2	
IL1B		cytokine		0.177		-0.033	0.267	1.13E-06	A2M,AQP4,CD274,CYP1A2,CYP2B6,GBP2,PAX6,RGS16,RORC	IFNG,IL1B,STAT1,STAT3
IL6		cytokine		1.378		-0.038	1.483	2.99E-06	A2M,AQP4,CD274,CYP1A2,CYP2B6,GBP2,Mir124a-1hg,RORC	IL1B,IL6,STAT1
FOXA2		transcription regulator						4.46E-06	A2M,EPX,PAX6,PNLIPRP1,RORC	
STAT1		transcription regulator		0.651		-0.05	0.761	4.71E-06	A2M,CD274,CYP1A2,GBP2,PAX6,RORC	IFNG,STAT1,STAT3
decabromobiphenyl ether		chemical toxicant						4.84E-06	CYP1A2,CYP2B6	
FECH		enzyme						8.52E-06	APOA4,CYP1A2,CYP2B6	
ABCB6		transporter						2.31E-05	CYP1A2,CYP2B6,Cyp2c54 (includes others)	
bergamottin		chemical - endogenous non-mammalian						2.42E-05	CYP1A2,CYP2B6	
ZBTB20		transcription regulator						4.11E-05	CYP1A2,CYP2B6,Cyp2c54 (includes others)	
EBI3		cytokine						4.36E-05	CD274,GBP2,RORC	
RORC	-9.09E-01	ligand-dependent nuclear receptor						4.65E-05	APOA4,CYP2B6,Cyp2c54 (includes others),RORC	
STAT3		transcription regulator		0.128		-0.033	0.206	7.86E-05	A2M,APOA4,CD274,GBP2,PAX6,RORC	IFNG,STAT1,STAT3
POR		enzyme						8.29E-05	APOA4,CYP1A2,CYP2B6,GBP2	
RORA		ligand-dependent nuclear receptor						1.06E-04	APOA4,CYP2B6,Cyp2c54 (includes others),RORC	
1-chloro-2-(2,2,2-trichloro-1-(4-chlorophenyl)ethyl)benzene		chemical toxicant						1.25E-04	APOA4,CYP2B6	
dehydroisoandrosterone		chemical - endogenous mammalian						1.44E-04	APOA4,CYP2B6,RORC	
meclizine		chemical drug						1.46E-04	CYP1A2,CYP2B6	NR1I3,meclizine
aroclor 1254		chemical toxicant						1.92E-04	CYP1A2,CYP2B6	
pirinixic acid		chemical toxicant						2.30E-04	APOA4,CYP1A2,CYP2B6,Cyp2c54 (includes others),PRSS2	
CREB3L3		transcription regulator						2.44E-04	APOA4,CYP2B6	
DMRT1		transcription regulator						2.64E-04	Ear2 (includes others),EPX,PRG2	
ethoxyquin		chemical toxicant						2.72E-04	CYP1A2,CYP2B6	
berberine		chemical drug						3.72E-04	CYP1A2,CYP2B6,RORC	
2,4,5,2',4',5'-hexachlorobiphenyl		chemical toxicant						3.92E-04	CYP2B6,Cyp2c54 (includes others),Prss1 (includes others)	
POU2F1		transcription regulator						5.05E-04	A2M,CYP2B6,GBP2	
IL2		cytokine		1.371		-0.047	1.474	7.13E-04	CD274,CYP1A2,CYP2B6,RGS16,RORC	IL1B,IL2,STAT1
IL27		cytokine						7.88E-04	CD274,GBP2,RORC	
IL7		cytokine						8.54E-04	CD274,RGS16,RORC	
rifampin		chemical drug						9.07E-04	CYP1A2,CYP2B6,GBP2	
FOXA1		transcription regulator						1.02E-03	GBP2,PAX6,RORC	
nafenopin		chemical drug						1.05E-03	APOA4,Prss1 (includes others)	
AHR		ligand-dependent nuclear receptor						1.05E-03	A2M,CYP1A2,CYP2B6,RORC	
NR1I2		ligand-dependent nuclear receptor						1.09E-03	APOA4,CYP1A2,CYP2B6	
mevalonic acid		chemical - endogenous mammalian						1.10E-03	CYP2B6,RORC	
lipopolysaccharide		chemical drug		1.357		-0.036	1.449	1.22E-03	APOA4,AQP4,CD274,CYP1A2,CYP2B6,Ear2 (includes others),GBP2,RGS16	
PXR ligand-PXR-Retinoic acid-RXRα		complex						1.22E-03	CYP1A2,CYP2B6	
6beta-hydroxyestradiol-17beta		chemical - endogenous non-mammalian						1.29E-03	CYP2B6	
NSC 659687		chemical reagent						1.29E-03	CYP1A2	
SU9597		chemical - kinase inhibitor						1.29E-03	PAX6	
alectinib		chemical drug						1.29E-03	CD274	
budesonide/formoterol		chemical drug						1.29E-03	CD274	
cabozantinib		chemical drug						1.29E-03	CD274	
fluticasone/salmeterol		chemical drug						1.29E-03	CD274	
miR-1343-5p (and other miRNAs w/seed GGGGAGC)		mature microrna						1.29E-03	AQP4	
miR-513a-5p (miRNAs w/seed UCACAGG)		mature microrna						1.29E-03	CD274	
miR-668-3p (and other miRNAs w/seed GUCACUC)		mature microrna						1.29E-03	AQP4	
mir-668		microrna						1.29E-03	AQP4	
mir-939		microrna						1.29E-03	AQP4	
trametinib		chemical drug						1.29E-03	CD274	
JAK3		kinase						1.35E-03	CD274,RORC	
STK11		kinase						1.52E-03	A2M,CD274,CYP2B6	RELA,STK11
CYP1A2	-2.11E+00	enzyme						1.61E-03	CYP2B6,RGS16	
IFNA4		cytokine						1.61E-03	CD274,GBP2	
omeprazole		chemical drug						1.76E-03	A2M,CYP1A2	
CEBPE		transcription regulator						2.14E-03	EPX,PRG2	
carboplatin		chemical drug						2.14E-03	A2M,CD274	
RELA		transcription regulator		-0.625		-0.049	-0.53	2.14E-03	A2M,CD274,CYP2B6,RORC	
CYP1B1		enzyme						2.38E-03	CYP2B6,RGS16	
3-hydroxykynurenine		chemical - endogenous mammalian						2.59E-03	RORC	
CCR3		g-protein coupled receptor						2.59E-03	PRG2	
DTNA		other						2.59E-03	AQP4	
ST8SIA2		enzyme						2.59E-03	PAX6	
Tgf beta receptor		complex						2.59E-03	RORC	
allocryptopine		chemical - endogenous non-mammalian						2.59E-03	CYP1A2	
cyproconazole		chemical drug						2.59E-03	CYP2B6	
protopine		chemical - endogenous non-mammalian						2.59E-03	CYP1A2	
retinoyl glucuronide		chemical - endogenous mammalian						2.59E-03	CYP1A2	
epigallocatechin-gallate		chemical drug						3.04E-03	AQP4,EPX,PRG2	
IL1A		cytokine						3.08E-03	CD274,CYP1A2,CYP2B6	
tretinoin		chemical - endogenous mammalian		0.659		-0.026	0.715	3.15E-03	A2M,CD274,CYP1A2,CYP2B6,PAX6,PRG2,RORC	IFNG,RELA,STAT1,STAT3,tretinoin
OTX2		transcription regulator						3.19E-03	A2M,PAX6	
IL17A		cytokine						3.39E-03	CD274,GBP2,RGS16	IL17A,NFkB (complex)
bromobenzene		chemical toxicant						3.69E-03	CYP1A2,CYP2B6	
3-nitrobenzanthrone		chemical toxicant						3.88E-03	CYP1A2	
FKHR		group						3.88E-03	A2M	
S-efavirenz		chemical drug						3.88E-03	CYP2B6	
Stat1-Stat3		complex						3.88E-03	A2M	
avasimibe		chemical drug						3.88E-03	CYP2B6	
barbiturate		chemical drug						3.88E-03	CYP2B6	
devazepide		chemical drug						3.88E-03	PRSS2	
dichlorodiphenyl dichloroethylene		chemical toxicant						3.88E-03	CYP2B6	
dipyrone		chemical drug						3.88E-03	CYP2B6	
isradipine		chemical drug						3.88E-03	CYP2B6	
sulfinpyrazone		chemical drug						3.88E-03	CYP2B6	
PPARGC1A		transcription regulator						3.90E-03	APOA4,CYP1A2,CYP2B6	
U0126		chemical - kinase inhibitor		-1.238		0.047	-1.33	3.96E-03	CD274,CYP2B6,PAX6,RORC	
E. coli B5 lipopolysaccharide		chemical - endogenous non-mammalian						4.50E-03	CD274,Cyp2c54 (includes others),GBP2	
CTCF		transcription regulator						4.68E-03	PAX6,RORC	
RXRA		ligand-dependent nuclear receptor						4.90E-03	CYP1A2,CYP2B6,RORC	
GZMB		peptidase						5.17E-03	CD274	
SCTR		g-protein coupled receptor						5.17E-03	AQP4	
USP17L9P		other						5.17E-03	RORC	
USP4		peptidase						5.17E-03	RORC	
ammonia		chemical - endogenous mammalian						5.17E-03	AQP4	
benoxaprofen		chemical drug						5.17E-03	CYP1A2	
di-n-propyl disulfide		chemical reagent						5.17E-03	CYP2B6	
ethylbenzene		chemical toxicant						5.17E-03	CYP2B6	
nevirapine		chemical drug						5.17E-03	CYP2B6	
nitrendipine		chemical drug						5.17E-03	CYP2B6	

Day 60 Male BDE-99

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
PPARA		ligand-dependent nuclear receptor		1.236		0.114	0.419	8.95E-35	ABCD2,Acaa1b,ACAT2,Acot1,ACSS2,ADIPOQ,AHCY,Akr1b7,APCS,APOA4,Apoc3,AQP8,ASNS,AURKA,C1QB,CCND1,Cd24a,CD63,CDK1,CTSE,CYB5B,CYBB,CYP27A1,Cyp2c54 (includes others),CYP2C8,CYP4A11,CYP51A1,CYP7A1,CYP7B1,CYP8B1,DHCR7,DIO1,ELOVL3,ETHE1,FABP5,FASN,FDPS,GLS,GLUL,GPAM,GPT,Gsta4,…	[illegible]
POR		enzyme	Activated	2.561		-0.159	3.336	1.13E-31	ABCC3,ACAT2,ACLY,Acot1,ADH4,ALDH1A1,Aldh1a7,APOA4,AQP8,ASNS,BDH1,Ces2c,CYB5B,CYP1A2,CYP2A6 (includes others),CYP2C18,CYP2C8,CYP4A11,CYP51A1,CYP7A1,CYP7B1,CYP8B1,DHCR7,ELOVL3,ETHE1,FDPS,FGL1,FLVCR2,GBP2,GSTA3,GSTM1,Gstm3,GSTM5,Gstm6,HLA-A,HMGCR,HMGCS1,HMOX1,IDI1,INSIG1,LPL,MSMO1,Mt1,MVK,NSDHL,PLA2G7,PMVK,RETSAT,Scd2,SQLE,TM7SF2	
dexamethasone		chemical drug		-1.055		0.043	-1.555	4.22E-27	AACS,ABCC3,ABHD2,ACSS2,ADAMTS1,ADAMTS15,ADIPOQ,ADRB2,AFP,Akr1b7,ALDH1A1,ALDH1L1,ANXA1,APOA4,ASF1B,ASNS,ATP2B4,BEX3,BIRC5,BRCA1,BTG2,C1QB,CA2,CAMP,CAVIN2,…	[illegible]
TP53		transcription regulator	Inhibited	-2.333		0.096	-3.358	2.29E-26	A2M,ACACB,ACLY,ACSF2,ACSS2,ACTN1,ADAM8,ADRB2,AFP,AHCY,ANK1,ANLN,ANXA1,AR,ASF1B,ASNS,ASPM,ATAD2,AURKA,BIRC5,BRCA1,BTG2,C1QC,CCND1,CCND3,CCNF,CD44,CDC7,…	[illegible]
cholesterol		chemical - endogenous mammalian	Activated	3.614		0.134	2.707	3.18E-26	Acaa1b,ACLY,Acot1,ACSS2,ADAM11,APCS,AQP8,C1QC,CD5L,CES1,COL1A1,CYB5B,CYBB,CYP27A1,CYP3A5,CYP7A1,CYP7B1,CYP8B1,DDC,DHCR7,FABP5,FASN,FDPS,HES6,HMGCR,HMGCS1,…	[illegible]
SCAP		other	Inhibited	-4.351	bias	0.415	-6.317	2.45E-25	AACS,ACACB,ACLY,ACSS2,ASNS,CYP51A1,DHCR7,FABP5,FASN,FDPS,GPAM,Gstm6,HES6,HMGCR,HMGCS1,IDI1,IDI1,INSIG1,MSMO1,Mt2,MVK,NSDHL,OLR1,PCSK9,PMVK,RDH11,REG1A,Scd2,SLC7A1,SQLE,THRSP,TM7SF2	HNF4α dimer,MBTPS1,NFE2L2,NR5A2,Nr1h,PPARG,PPARGC1A,SCAP,SREBF1,SREBF2,cholesterol,lipid
ERBB2		kinase	Activated	4.622		0.217	2.988	2.83E-24	Acaa1b,ADAM8,Aldh1a7,AR,ASPM,AURKA,BARD1,BIRC5,BRIP1,BTG2,CAVIN2,CCND1,CCND3,CDC7,CDCA2,CDCA3,CDCA4,CDCA8,CDK1,CENPA,CENPE,CENPF,CES1,CKS1B,CLEC3B,COL1A…	[illegible]
FGF19		growth factor	Activated	3.081		-0.052	3.24	1.56E-23	ACACB,ACLY,AFP,Akr1b7,ALDH1A1,AQP4,AQP8,BIRC5,CCND1,CTSE,Cyp2d9 (includes others),CYP7A1,CYP7B1,CYP8B1,ELOVL3,FABP5,FASN,FDPS,HMGCR,HSD3B2,ID1,IGFBP1,IL1RN,LCN2,LEPR,MME,PEG3,RGS16,Scd2,SQLE,THRSP	ADIPOQ,FGF19,HNF4A,HNF4α dimer,JUN,NCOA2,NCOR1,NFKB1,NFkB (complex),NR0B2,NR5A2,PPARA,RELA,SP1,STAT1,STAT3
lipopolysaccharide		chemical drug	Activated	4.115		0.215	1.761	2.00E-23	ABCC3,ACLY,ACO1,Acot1,ADIPOQ,ADRB2,AGER,ANXA1,APCS,APOA4,Apol7e (includes others),AQP4,AR,ATP1A2,CAMP,CCND1,CCND3,CCNF,Cd24a,CD274,CD300LF,CD44,CD83,CENPI,CFD,…	[illegible]
calcitriol		chemical drug	Inhibited	-3.625		-0.043	-3.289	5.18E-23	ABCC3,ACAT2,ANLN,AR,BIRC5,BRCA1,CA2,CAMP,CCND1,CCND3,CDCA8,CDK1,CENPA,CES1,CFD,CYP7A1,CYR61,DUSP1,ECT2,ELN,ESPL1,EZH2,FASN,FBN2,FDPS,FEN1,FIGNL1,Hmgn2 (i…	[illegible]
ATP7B		transporter	Inhibited	-4.264		0.058	-4.537	2.79E-22	AACS,ACLY,CKS1B,CYP51A1,CYP7A1,FABP5,FASN,FDPS,H19,HIST1H1C,HMGCR,HMGCS1,IDI1,MAD2L1,MSMO1,Mt1,Mt2,RAD51,SMC2,SQLE,THRSP,TRIP13	
NR1I3		ligand-dependent nuclear receptor	Inhibited	-2.687	bias	0.36	-4.619	5.17E-22	ABCC3,ALDH1A1,Aldh1a7,APCS,Ces2c,CYP1A2,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2C8,CYP2F1,CYP3A5,CYP7A1,CYP7B1,CYP8B1,DIO1,FASN,Gsta4,GSTM1,Gstm3,GSTM4,GSTM5,GSTP1,Gstt1,ICAM1,INSIG1,LEAP2,LRG1,Mt1,RARRES1,RPA2,THRSP,UGT2B28	CEBPA,ESR1,HNF1A,HNF4A,NCOA6,NR1I3,NR4A1
dextran sulfate		chemical drug		0.689		0.244	0.211	1.20E-21	ADAM8,ADAMTS1,ANLN,AURKA,BIRC5,CCNF,CD83,CDCA2,CDCA3,CDCA8,CDK1,CENPE,CKS1B,E2F7,FIGNL1,GSTM5,HMOX1,ICAM1,IGF1R,KIF11,MCM3,MCM5,MCM6,MKI67,MMP14,NCAPD…	[illegible]…JUN,LDL,MYC,NFKB1,NFKBIA,NFkB (complex),NOS3,NR4A1,RELA,STAT3,dextran sulfate
CCND1	1.213	transcription regulator	Activated	4.928		0.06	4.591	3.89E-20	AR,ARMCX1,ASPM,ATAD2,AURKA,BIRC5,BRCA1,BRIP1,C7,CCND1,CCND3,CD44,CDCA2,CDCA8,CENPF,CIP2A,CLSPN,COL1A1,DNMT1,DTL,E2F1,E2F7,ESCO2,FAM83D,FLNA,GPC6,HIST1H4…	[illegible]…RB1,RBL1,RBL2,Rb,TP53
IL6		cytokine	Activated	3.722		0.231	1.922	4.44E-20	A2M,ABCC3,ADAMTS1,AFP,ANXA1,APCS,AQP4,BIRC5,BTG2,CCND1,CD274,CD44,CD83,CDK1,CDKN2D,CENPA,CENPE,CES1,CFD,COL1A1,CYBB,CYP1A2,CYP2C8,CYP3A5,DIO1,DNMT1,DPP…	[illegible]
IFNG		cytokine	Activated	4.027		0.191	2.142	5.94E-20	A2M,ACLY,ACO1,Acot1,ADGRG2,ADIPOQ,AGER,AHCY,ALDH1L1,ASNS,BRIP1,Bst2,C1QB,C1QC,CCND1,CCND3,Cd24a,CD274,CD44,CD5L,CD63,CD83,CELSR1,CERS6,CGAS,CHST11,CHST3…	[illegible]
CSF2		cytokine	Activated	6.313	bias	0.334	3.84	1.11E-19	ADAM8,ANLN,ANXA1,AURKA,BIRC5,CCND1,CCND3,CCNF,CD63,CD83,CDCA2,CDCA3,CDCA8,CDK1,CENPE,CHST11,CKS1B,CLEC7A,CYBB,E2F7,ELN,FIGNL1,ICAM1,IDO2,IL1RN,INPP5D,ITG…	[illegible]
TCF3		transcription regulator	Inhibited	-2.559		0.047	-2.769	1.84E-19	ACACB,ADIPOQ,ANLN,ASF1B,AURKA,BIRC5,CA2,CCND3,CDCA3,CDK1,CERK,CIP2A,CKAP4,COL1A1,CTSE,DCK,DTX1,EBF1,ECT2,ESCO2,GM2A,GPAM,H2AFX,HMGB2,Hmgn2 (includes others…	[illegible]
E2F3		transcription regulator	Activated	4.511		0.232	3.309	2.24E-19	AKNA,BIRC5,CCND1,CCND3,CDCA3,CDCA4,CDK1,E2F1,E2F2,EZH2,FST,HIST1H1C,HIST1H2BN,HIST1H3D,HIST1H4B,HIST3H2A,HMGB2,IGF2,LPL,MAD2L1,MCM2,MCM3,MCM4,MCM5,MCM6…	CCNE1,CDKN2A,E2F1,E2F3,E2F4,E2f,EP300,IGF2,MYC,NFKBIA,RB1,RBL1,RELA,TP53
TNF		cytokine	Activated	2.765		0.154	1.093	3.06E-19	A2M,ABCC3,ABCD2,ADAM8,ADIPOQ,ADRB2,AGER,Aldh1a7,ANXA1,APCS,AR,ARHGDIB,ATP2B4,BIRC5,BTG2,CA2,CCND1,CCND3,CD274,CD44,CD83,CERS6,CFD,CHST11,CMBL,COL1A1,CO…	[illegible]
SREBF2		transcription regulator	Inhibited	-3.471	bias	0.344	-5.157	3.91E-19	AACS,ACLY,ACSS2,CYP51A1,CYP7B1,CYP8B1,DHCR7,EBP,FABP5,FASN,FDPS,HES6,HMGCR,HMGCS1,IDI1,INSIG1,MSMO1,MVK,NSDHL,PCSK9,PMVK,RDH11,REG1A,SQLE,THRSP,TM7SF2	CEBPB,FOXO1,HDAC3,HNF4α dimer,NCOR1,NFE2L2,NR5A2,Nr1h,PPARA,PPARG,PPARGC1A,RXRA,SREBF1,SREBF2,Srebp,USF1,cholesterol,lipid
pirinixic acid		chemical toxicant		0.916	bias	0.267	-0.819	1.42E-18	ABCC3,Acaa1b,ACACB,ACAT2,Acot1,ACSS2,ADH1C,ADH4,AFP,APCS,APOA4,Apoc3,ASNS,CCND1,CCND3,Cd24a,CD5L,CD63,CDK1,COL1A1,CYP1A2,CYP27A1,Cyp2c54 (includes others),CYP2…	[illegible]
progesterone		chemical - endogenous mammalian		-0.45		0.104	-0.335	1.92E-18	Acot1,ADAMTS1,ADIPOQ,ADRB2,ALDH1A1,AR,ATP1A2,AURKA,BRCA1,CA2,CCND1,CCND3,Cdkn1c,CES1,CFD,CYP2A6 (includes others),CYP2C8,CYP2F1,CYP3A5,E2F1,ENC1,ESPL1,FEN1,FK…	[illegible]
CDKN1A		kinase	Inhibited	-2.213		-0.134	-1.714	2.00E-18	ANLN,ASPM,ATAD2,AURKA,BIRC5,BRCA1,CCND1,CCND3,CDK1,CENPF,CIT,CKS1B,CYR61,DLGAP5,DTL,DUSP1,H2AFX,HMGB2,ITGB3,KNSTRN,MAD2L1,MCM2,MCM3,MCM4,MCM6,MKI67,NASP,NDC80,NUSAP1,PCNA,PRC1,PTPRC,RACGAP1,RAD51,RBL1,RRM1,SMC2,STMN1,TOP2A,TPX2,TYMS,UHRF1	BRCA1,CCND1,CCNE1,CDKN1A,CDKN2A,E2F1,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TP53
E2F1	1.33	transcription regulator	Activated	4.212	bias	0.259	2.599	4.55E-18	ADIPOQ,AR,ATAD2,AURKA,BIRC5,BRCA1,CA2,CCND1,CCND3,CCNF,CD44,CDCA4,CDK1,CDKN2D,DNMT1,DUSP1,E2F1,E2F2,ECT2,EZH2,FANCD2,FEN1,FHDC1,GM2A,H19,HELLS,HIST1H4…	[illegible]
STAT5B		transcription regulator	Inhibited	-2.162		0.108	-2.614	6.26E-18	A2M,ABCD2,Acot1,Adh6-ps1,AR,CA2,CCND1,CCND3,Cdkn1c,CKMT2,Cox8b,CSRP3,CUX2,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP2C8,Cyp2d9 (includes others),CYP3…	[illegible]
TGFB1	1.208	growth factor	Activated	3.103		0.135	1.798	7.63E-18	ACLY,Acot1,ACTN1,ADGRG2,ADIPOQ,AFP,Apon,AQP8,ASNS,ASPM,BARD1,BDH1,BIRC5,BRIP1,C1QB,C1QC,CAMP,CAVIN2,CCND1,CCND3,CD44,CD83,CDC7,CDK1,Cdkn1c,CENPA,CENPE,C…	[illegible]
RORC	-0.927	ligand-dependent nuclear receptor						1.09E-17	ABCD2,ACACB,APOA4,AQP8,ASNS,CKMT2,CYP2A6 (includes others),Cyp2b13/Cyp2b9,Cyp2c54 (includes others),CYP2C8,CYP2F1,CYP3A5,CYP4A11,CYP7B1,CYP8B1,DDC,ELOVL3,GSTM4,GS…	
NR1I2		ligand-dependent nuclear receptor		-1.872		0.106	-2.454	1.66E-17	ABCC3,AHCY,ALDH1A1,Aldh1a7,APOA4,CES1,Ces2c,CYP1A2,CYP27A1,CYP2A6 (includes others),CYP2C8,Cyp2d9 (includes others),CYP3A5,CYP4A11,CYP7A1,DHCR7,E2F1,FASN,GLUL,Gsta4,…	CEBPA,FOS,HNF1A,HNF4A,JUN,NFE2L2,NFKB1,NFkB (complex),NR1H4,NR1I2,NR3C1,NR5A2,Nr1h,RELA,SREBF1,SREBF2,STAT3,cholesterol,dexamethasone,glucocorticoid,lithocholic acid
E2F4		transcription regulator		1.982		0.118	1.749	3.46E-17	ANLN,ASF1B,BARD1,BRCA1,CCND1,CDCA4,CDK1,CENPA,CENPE,CKS1B,E2F1,E2F2,ECT2,FANCD2,FEN1,H2AFX,HIST1H3D,HMMR,MAD2L1,MCM3,MCM4,MCM5,MCM6,MKI67,MYB,NASP,ND…	E2F1,E2F4,EP300,HDAC1,HDAC2,RB1,TP53
AGN194204		chemical drug	Activated	2.429	bias	0.382	1.174	5.59E-17	Acaa1b,ACAT2,Acot1,Akr1b7,AURKA,Cd24a,CDK1,COTL1,Cyp2c54 (includes others),CYP51A1,CYP7B1,DHCR7,DUSP1,ELOVL3,EZH2,FDPS,GBP2,GPR65,Gzmb,H2AFX,HIST1H1C,Hmgn2 (inclu…	[illegible]
Vegf		group	Activated	5.355	bias	0.316	2.964	6.64E-17	A2M,ADAMTS1,AQP4,ASNS,AURKA,BIRC5,CA2,CCNF,CD44,CD93,CDK1,CELSR1,CENPF,CKS1B,CYP4A11,CYR61,DUSP5,EBP,ELN,FKBP5,FLNA,FST,GRB10,HELLS,HMMR,HMOX1,ICAM1,ID1…	[illegible]…TGFB1,TP53,VEGFA,Vegf
atorvastatin		chemical drug	Inhibited	-5.05		-0.065	-4.658	7.20E-17	ABCC3,ADIPOQ,AGER,COL1A1,CYBB,CYP27A1,CYP51A1,CYP7A1,CYP8B1,CYR61,DHCR7,DUSP1,FDPS,GPAM,HBA1/HBA2,HBB,HMGCR,HMGCS1,HMOX1,ICAM1,IDI1,ITGB2,LPL,MAP1LC3A,…	APOE,CEBPA,CTNNB1,EGR1,FOS,JUN,Jnk,MAPK8,MYC,NFATC1,NFKB1,NFKBIA,NFkB (complex),NR1H3,PPARA,PPARG,RELA,RXRA,SMAD3,SP1,SREBF1,STAT3,TNF,atorvastatin
TBX2		transcription regulator	Activated	4.899		0.132	4.251	7.57E-17	ANLN,ASF1B,AURKA,CDCA3,CDK1,CKAP2,CKS1B,DNMT1,E2F1,E2F7,EZH2,HELLS,LIG1,MAD2L1,MCM2,MCM4,MCM5,MCM6,NCAPD2,NCAPG2,NFIL3,PRC1,RBL1,SMC2	CCND1,CDKN1A,E2F4,E2f,RB1,TBX2,TP53
YY1		transcription regulator		0.671		0.033	0.585	8.14E-17	ARID3A,AURKA,BIRC5,BRCA1,BTG2,CBX3,CD93,CDCA3,Cdkn1c,CENPA,CENPE,COL1A1,CYBB,FDPS,FEN1,GPC3,H2AFX,HELLS,HMGCR,HMOX1,INCENP,KIF11,KIF23,LMNB1,MAD2L1,MCM…	CDKN2A,E2F1,E2F4,E2f,MYC,RB1,RBL1,Rb,TP53,YY1
1,4-bis[2-(3,5-dichloropyridyloxy)]benzene		chemical toxicant		-0.32	bias	0.282	-1.783	1.14E-16	ABCC3,APCS,CCND1,CDK1,Ces2c,CKAP4,CYP1A2,CYP27A1,Cyp2b13/Cyp2b9,CYP2F1,CYP3A5,CYP7A1,CYP7B1,CYP8B1,DIO1,FASN,GSTP1,ICAM1,INSIG1,LEAP2,LRG1,MAD2L1,MCM5,MCM…	1,4-bis[2-(3,5-dichloropyridyloxy)]benzene,ESR1,HNF4A,JUN,MYC,NCOA6,NR1I3,NR4A1,Rb,SP1,STAT3,TP53
TO-901317		chemical reagent		-1.248		0.132	-1.89	1.65E-16	Acaa1b,ACLY,Acot1,ADAM11,ADH1C,Akr1b7,APCS,CCND1,CD5L,Cox8b,Cyp2d9 (includes others),CYP2F1,CYP3A5,CYP4A11,CYP7A1,CYP7B1,CYP8B1,DDC,DHCR7,DIO1,ELOVL3,FABP5,FASN…	CEBPA,HNF4α dimer,NFE2L2,NR1H3,NR5A2,Nr1h,PPARA,PPARG,PPARGC1A,RORA,RXRA,SREBF1,SREBF2,TO-901317,cholesterol
RORA		ligand-dependent nuclear receptor		-0.625		0.234	-1.136	2.38E-16	ABCD2,ACACB,APOA4,Apoc3,AQP8,ASNS,CKMT2,CYP27A1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,Cyp2c54 (includes others),CYP2C8,CYP2F1,CYP3A5,CYP4A11,CYP7B1,CYP8B1,DDC,EL…	
SREBF1		transcription regulator	Inhibited	-2.625	bias	0.303	-4.346	2.64E-16	AACS,ABCD2,ACACB,ACLY,ACSS2,ADH1C,ADIPOQ,AR,CFD,CYP51A1,CYP7A1,CYP7B1,CYP8B1,DHCR7,ETHE1,FABP5,FASN,FDPS,GPAM,Gstm6,HMGCR,HMGCS1,HMOX1,IDI1,INSIG1,LPL,…	CEBPA,EGR1,FOXO1,Insulin,NFE2L2,NR5A2,Nr1h,PPARG,PPARGC1A,SCAP,SP1,SREBF1,SREBF2,Srebp,cholesterol,lipid
methylprednisolone		chemical drug		-0.506		0.085	-1.068	2.68E-16	A2M,ADRA1B,AHCY,ALDH1A1,ANXA1,AQP8,ASNS,ATP5IF1,B4GALT6,BDH1,C1QB,CCND1,Cd24a,CD44,Ces1e,COX6A1,CYB5B,CYBB,CYP1A2,Cyp2a12/Cyp2a22,Cyp2b13/Cyp2b9,CYP4F3,DIO…	[illegible]
estrogen		group	Activated	2.825	bias	0.28	1.271	9.56E-16	APCS,AR,AURKA,BARD1,BRCA1,CCND1,CKS1B,COL1A1,COL5A1,CYBB,CYR61,DNMT1,DUSP1,E2F1,ESPL1,FBLN1,FEN1,HMGCR,ICAM1,Il27,IGF1R,IGF2,IGFBP2,ITM2A,LCN2,LIG1,LPL,MCM…	CCND1,CREB1,E2F1,E2F2,E2F3,EGF,EGR1,EP300,ERBB2,ESR1,HDAC1,HDAC2,HIF1A,IGF1,JUN,MYC,RB1,RELA,Rb,SP1,TP53,calcitriol,estrogen
SMARCB1		transcription regulator	Inhibited	-2.275	bias	0.25	-3.598	1.80E-15	A2M,AURKA,CCND1,CD44,CDC7,CDK1,CENPA,CENPE,COL1A1,Cyp2c54 (includes others),CYP2C8,Cyp2d9 (includes others),CYP4A11,CYP8B1,Defb1,E2F1,FCGR2A,GSN,IFI16,IGFBP2,KIF11,K…	BRCA1,CCND1,CDKN1A,CDKN2A,E2F1,E2F4,E2f,MDM2,MYBL2,MYC,RB1,RBL1,Rb,SMARCA4,SMARCB1,SP1,SP3,STAT3,TP53
doxorubicin		chemical drug		-0.593		0.152	-1.545	1.96E-15	A2M,ABCC3,ADAMTS1,AFP,ANXA1,AR,ASNS,AURKA,BARD1,BIRC5,BRCA1,BTG2,CA2,CAPN6,CCND1,CD44,CDK1,CDK14,CENPA,CENPE,CYBB,CYR61,DNMT1,DUSP1,DUSP5,E2F1,E2F2,FBL…	[illegible]…RELA,Rb,STAT3,TP53,doxorubicin
gefitinib		chemical drug		-1.982		-0.138	-1.626	2.42E-15	ADAMTS1,ADAMTS15,ALDH1A1,AURKA,BIRC5,BRCA1,BTG2,CCND1,CCNF,CD274,CDKN2D,CKAP2,COL1A1,CYP2F1,ECT2,EPSTI1,HMOX1,HSPB1,ID1,KIF11,KIF23,MCM3,MKI67,MMP15,NOX…	Akt,BRCA1,CCND1,CEBPA,E2F1,E2f,EGR1,ERBB2,FOXO1,HDAC1,JUN,MDM2,MYBL2,NFkB (complex),PPARA,PPARG,RB1,RELA,RXRA,Rb,SREBF1,STAT3,TP53,gefitinib
beta-estradiol		chemical - endogenous mammalian		1.688		0.142	0.213	3.29E-15	A2M,Acot1,ADAMTS1,ADGRG2,ADH1C,ADIPOQ,ADRB2,AFP,AGER,ANK1,ANXA1,APOA4,AR,ATAD2,AURKA,BIRC5,BRCA1,BTG2,C8orf44-SGK3/SGK3,CA2,CCND1,CCND3,CD274,CD44,CDK1,…	[illegible]
let-7		microrna	Inhibited	-5.18	bias	0.418	-2.794	4.79E-15	AR,ARID3A,AURKA,BRCA1,BTG2,CCND1,CCNF,CD44,CDCA2,CDCA3,CDCA8,CDK1,CKS1B,COL1A1,E2F2,EZH2,FANCD2,HBA1/HBA2,IGF1R,ITGA4,ITGB3,MAD2L1,MCM2,MCM3,MCM4,MCM5…	[illegible]
IL10RA		transmembrane receptor	Inhibited	-2.881		0.013	-2.964	4.87E-15	ACSS2,ADH1C,B4GALNT3,CA2,Cd24a,CD300LF,CDKN2D,Ces1f,Ces1g,CTSE,CYFIP2,CYP2C18,CYP2F1,CYR61,FABP5,FSTL1,GAS6,GBP2,GBP5,GBP6,Gsta4,GSTM1,Gstm3,GSTM5,Gstm6,HK…	[illegible]…NFkB (complex),RELA,STAT1,STAT3,STAT6
AGT		growth factor	Activated	2.056		0.215	0.536	6.38E-15	ACAT2,ADH1C,ADIPOQ,AGER,ANXA1,BRCA1,CCND1,CCND3,CD44,CDK1,CIT,COL1A1,COLEC10,CYBB,CYP4A11,DUSP1,EBP,FASN,GSTA3,GSTM5,Gstm6,GSTP1,HMGB2,HMGCR,HMGCS1,…	[illegible]
MYC		transcription regulator	Activated	4.515		0.17	3.111	8.02E-15	ABCC3,ACTN1,ADAMTS1,AFP,AHCY,AR,ASNS,ASPRV1,ATP5IF1,BIRC5,BRCA1,CCND1,CCND3,CD274,CD44,CDK1,CLEC3B,COL1A1,COL5A1,COX6A1,CYFIP2,DNMT1,DUSP1,DUSP5,E2F1,E2…	[illegible]
methylselenic acid		chemical reagent						9.00E-15	ADAMTS1,AR,ATAD2,AURKA,BIRC5,BRCA1,CCND1,CD44,CDC7,CDK1,CDKN2D,CENPA,CENPF,E2F1,FKBP5,HMMR,ID1,IGF1R,ITGB4,KIF11,KIF20B,MAP1B,MCM2,MCM3,MCM5,MCM6,MKI67,…	[illegible]
LY294002		chemical - kinase inhibitor	Inhibited	-2.791	bias	-0.333	-0.354	9.23E-15	ACSS2,ADAMTS1,ADH1C,ADRB2,AR,AURKA,BIRC5,CCND1,CCND3,CD274,CD44,CD83,CDKN2D,COL1A1,CYR61,DUSP1,FASN,FEN1,GRB10,Gsta4,GSTP1,HMGB2,HMGCR,HMGCS1,HMOX1,…	[illegible]
tretinoin		chemical - endogenous mammalian		1.858		0.154	0.387	9.50E-15	A2M,ABHD2,ACACB,ACSS2,ADAM11,AFP,ALDH1A1,ANXA1,APBB1IP,ASNS,ATP2A3,BCO1,BIRC5,BRCA1,BTG2,CA2,CCND1,CCND3,CD274,CD44,CD63,CD93,CDKN2D,CES1,Clca3a1/Clca3a2,C…	[illegible]
INSIG1	-1.286	other		1.682	bias	-0.422	3.751	1.27E-14	AACS,ACACB,ACLY,ACSS2,CLEC7A,CYP51A1,DHCR7,FABP5,FASN,FDPS,GPAM,HMGCR,HMGCS1,IDI1,LCN2,LPL,MARCO,MVK,OLR1,PLA2G7,PMVK,Scd2,SQLE,TGFB1,TM7SF2	[illegible]
mir-21		microrna	Inhibited	-4.514	bias	0.298	-2.682	2.07E-14	ANLN,ASPM,ATAD2,BTG2,C8orf44-SGK3/SGK3,CD274,COL1A1,DLGAP5,ECT2,ELN,FCGR2A,GBP2,GBP5,GBP6,GBP7,Gvin1 (includes others),Gzmb,H2AFX,ICAM1,IFI16,INPP5D,KIF23,LEPR,M…	[illegible]
E. coli B4 lipopolysaccharide		chemical toxicant	Activated	4.772	bias	0.279	3.03	2.10E-14	ANXA1,ARHGAP30,C1QB,CD274,CD83,CENPA,Clca3a1/Clca3a2,CYP27A1,CYP2C8,CYP3A5,CYP7A1,CYP8B1,Defb1,EMB,GBP2,GBP4,HLA-A,HMOX1,ICAM1,IFI16,IL1RN,INPP5D,KIF20B,KLHL6,…	CHUK,E. coli B4 lipopolysaccharide,IL1B,IL6,IRF1,IRF3,JUN,MYC,NCOA3,NFKB1,NFKBIA,NFkB (complex),RELA,STAT1,STAT3,STAT6,TLR4
thioacetamide		chemical toxicant	Activated	2.809	bias	0.365	1.333	2.42E-14	AACS,ADAMTS1,ADH4,ANXA1,AQP8,ASNS,B4GALT6,BARD1,BRCA1,BRIP1,CAPN6,Cd24a,CD44,COL1A1,CYP1A2,CYP8B1,ELN,FCGR2A,FSTL1,HIST1H3D,IGFBP1,ITGB4,LCN2,LOX,LYVE1,M…	JUN,MYC,RELA,SNAI1,TGFB1,TP53,thioacetamide
D-glucose		chemical - endogenous mammalian		0.86		0.125	-0.09	3.16E-14	ACLY,ACTN1,ADIPOQ,AGER,ANLN,ANXA1,ASNS,ATP2A3,ATP2B4,BIRC5,C8orf44-SGK3/SGK3,CCND1,CCND3,CDK1,COL1A1,CYBB,CYP7A1,DUSP1,E2F1,FABP5,FASN,FST,GLUL,GPAM,GSN…	[illegible]
RABL6		other	Activated	3.578		0.219	2.599	5.07E-14	BTG2,CENPF,CKS1B,EZH2,FEN1,H2AFX,HMMR,HMOX1,KIF23,MAD2L1,MCM2,MCM5,MELK,NDC80,POLA1,PRC1,PRIM1,TOP2A,TPX2,VRK1	CDKN2A,E2F1,E2F4,MYC,RABL6,RB1,TP53
fulvestrant		chemical drug	Inhibited	-3.637		-0.09	-3.102	6.23E-14	ADRB2,ASNS,AURKA,BARD1,BIRC5,CCDC34,CCND1,CDK1,CENPF,CKS1B,CYR61,E2F1,FEN1,GSTP1,H2AFX,ICAM1,ID1,Il27,IGF1R,INHBB,ITGB3,KIF11,LEPR,LPL,MCM2,MCM3,MCM5,MYB,P…	CCND1,CDKN1A,E2F1,E2F2,E2F3,E2F4,E2f,EGR1,HDAC1,HIF1A,IGF1,JUN,RB1,RBL1,RELA,Rb,SP1,TP53,fulvestrant
ZBTB20		transcription regulator	Inhibited	-3.153		0.025	-3.258	9.19E-14	ACSS2,ADH4,AFP,Akr1b7,CYP1A2,Cyp2b13/Cyp2b9,Cyp2c54 (includes others),CYP2C8,CYP2F1,CYP3A5,FASN,GAS6,GPC3,GSTM4,GSTM5,IGFBP1,IGFBP2,LEPR	CTNNB1,LEP,MED1,NFKB1,PPARG,RELA,ZBTB20
ACOX1		enzyme	Inhibited	-4.796		-0.083	-4.37	1.75E-13	ADAMTS1,APCS,CD63,CTSE,CYP1A2,Cyp2c54 (includes others),CYP2C8,Cyp2d9 (includes others),CYP4A11,CYP4F12,CYP7B1,DIO1,ELOVL3,FASN,GSTP1,IGFBP1,IGFBP2,KRT23,LCN2,LPL,M…	ACOX1,CEBPA,NR1H3,PPARA,PPARG,RXRA,SREBF1
diethylnitrosamine		chemical toxicant	Activated	3.072		0.043	2.885	1.92E-13	AFP,APCS,CCND1,CD63,Cyp2c54 (includes others),CYP2C8,CYP4A11,CYP4F12,CYP7B1,E2F1,ELOVL3,GSTP1,IGFBP1,IGFBP2,LCN2,LPL,Mt1,Mup1 (includes others),PCNA,QPCT,SELENBP1,S…	CEBPA,CREBBP,CTNNB1,E2F2,GATA3,GLIS2,Histone h3,IL6,JUN,MED1,MYC,NFKB1,NFKBIA,NFkB (complex),PPARG,RELA,RNA polymerase II,RUVBL2,SP1,STAT3,TNF,diethylnitrosamine
AKT1		kinase		1.644		0.198	0.735	2.08E-13	ACAT2,ACLY,ADIPOQ,AR,BIRC5,C1QC,CCND1,CCND3,CYP7A1,DHCR7,DIAPH3,E2F1,EBP,FABP5,FASN,FSTL1,GSTM5,Gstt1,HMGB2,HMGCR,HMGCS1,HMOX1,HUNK,IGF1R,IGF2,IGFBP1,L…	AKT1,Akt,BRCA1,CEBPA,CEBPB,E2F1,EGR1,ESR1,FOXO1,Insulin,JUN,NCOA3,NR4A1,PPARG,PPARGC1A,RELA,SIRT1,SP1,SREBF1,TP53,beta-estradiol
IL1B		cytokine	Activated	4.101		0.197	2.59	2.09E-13	A2M,ABCC3,ADAM8,ADAMTS1,ADRB2,AGER,ANXA1,APCS,AQP4,BTG2,Cd24a,CD274,CD44,CD83,Cdkn1c,COL1A1,CYBB,CYP1A2,CYP3A5,CYP7A1,CYP8B1,DIO1,DNMT1,DUSP1,DUSP5,E2F1…	[illegible]
cycloheximide		chemical reagent		-0.896		-0.053	-0.558	2.20E-13	ADRA1B,AFP,Akr1b7,APBB1IP,AQP4,AR,ATP2B4,BEX3,BRCA1,BTG2,CCND1,CCND3,CD44,CDKN2D,COL1A1,COL5A1,CYP1A2,CYP3A5,CYP4A11,CYR61,DIO1,DUSP1,FST,HMOX1,ICAM1,IGF…	[illegible]…FOS,IL1B,IL6,JUN,MYC,NFATC1,NFKB1,NFKBIA,NFkB (complex),RELA,SMAD3,SP1,STAT3,cycloheximide
RB1		transcription regulator	Inhibited	-4.204		0.106	-4.716	2.33E-13	ASF1B,ATAD2,BARD1,BIRC5,BRCA1,CCND1,CCND3,CDCA4,CDK1,Cdkn1c,COX6A1,DCK,DNMT1,E2F1,EZH2,FAM111A,FEN1,FST,GPT2,HMGB2,HUNK,ID1,IGF1R,LIG1,MCM2,MCM3,MCM4,M…	CCNE1,CDKN2A,E2F1,E2F2,E2F3,E2F4,E2f,HDAC1,MYC,RB1,RBL1,Rb,TP53
LEP		growth factor	Activated	2.267		0.167	1.186	2.49E-13	ABCC3,ACLY,ACO1,ADAM8,ADIPOQ,APOA4,AR,BIRC5,CCND1,CD63,CFD,COL1A1,CYBB,Cyp2a12/Cyp2a22,CYP2C18,Cyp2c54 (includes others),CYP2C8,Cyp2d9 (includes others),CYP2F1,CYF…	[illegible]
dihydrotestosterone		chemical - endogenous mammalian		1.481		0.209	0.253	2.52E-13	ACLY,ADAMTS1,ADH1C,ADIPOQ,Akr1b7,Apoc3,AR,ATAD2,BRIP1,BTG2,CCND1,CCND3,CD63,CYBB,Cyp2d9 (includes others),CYP4A11,CYP4A22,DTL,ELN,FASN,FKBP5,FST,GAS6,GLUL,GRB…	[illegible]
BNIP3L		other	Inhibited	-3.308		-0.112	-2.835	2.81E-13	ANK1,AURKA,CCND3,CENPE,CENPF,CKAP2,E2F1,FANCD2,GSN,KIF11,NUF2,PRIM1,RBL1,RRM2,SYK,TFRC,TGFB1,TOP2A	
FOXO3		transcription regulator		-1.021		0.178	-1.808	3.44E-13	ACLY,Acot1,ANXA1,AQP4,AR,AURKA,BIRC5,CCND1,CCND3,CDCA8,CYR61,DLGAP5,FABP5,FASN,GLUL,GSTM5,HMGCR,ICAM1,IGF1R,IGFBP1,ITGB2,KIF15,LCN2,MAP1LC3A,MCM2,MCM4,M…	AKT1,CDKN2A,CEBPA,E2F1,E2F4,EGR1,FOXO1,FOXO3,FOXO4,JUN,MYC,NCOA3,NFKB1,NFKBIA,NFkB (complex),NR4A1,PPARG,PPARGC1A,RB1,RELA,SIRT1,SP1,STAT3,TNF,TP53,cytokine
INSR		kinase	Inhibited	-2.175	bias	0.332	-3.809	4.09E-13	ATP2A3,ATP5MF,BIRC5,CCND1,CD83,CDK1,CKMT2,Cox8b,CYP51A1,DHCR7,DUSP1,FASN,FBLN1,FDPS,FEN1,GRB10,H19,HELLS,HMGCR,HMGCS1,IDI1,IGF1R,IGF2,IGFBP1,LEPR,MARCKS…	[illegible]
E2F2	3.353	transcription regulator	Activated	3	bias	0.355	1.936	4.42E-13	BIRC5,CCND1,CCND3,CDCA4,CDK1,CDKN2D,E2F1,EZH2,MCM2,MCM3,MCM4,MCM5,MCM6,MYB,NPAT,PCNA,POLA1,RAD51,RBL1,RRM2	BRCA1,CCNE1,CDK2,E2F1,E2F2,E2F4,E2f,RB1,RBL1,TFDP1,TP53
AHR		ligand-dependent nuclear receptor		-1.216		0.043	-1.417	4.65E-13	A2M,ACTN1,Adh6-ps1,BTG2,CCND1,CCND3,CCNF,CDK1,CDKN2D,Ces2c,COL1A1,COL5A1,CYP1A2,CYP2A6 (includes others),CYP2C8,DIO1,E2F1,FBN2,GAS6,GPAM,GSTM5,HMGCR,HUNK,I…	AHR,CEBPA,CREB1,EGR1,ESR1,FOXO1,HDAC1,Histone h4,IL1B,IL6,JUN,MED1,MYC,NFKB1,NFkB (complex),NR4A1,PI3K (complex),RELA,SP1,STAT3,TP53
GATA2		transcription regulator	Activated	2.546		0.073	2.256	5.91E-13	AR,C1QC,CAMP,CCND1,CES1,Cldn13,CSTA,CYBB,CYP2F1,E2F2,Ear2 (includes others),FCHO1,GBP2,GPR65,GRAP2,Gypa,Gzmb,HBA1/HBA2,HHEX,KLF1,LCN2,MFSD2B,MYB,NFIL3,Ngp,PPP1…	[illegible]
FECH		enzyme						6.88E-13	APOA4,CCND1,CYP1A2,CYP27A1,Cyp2b13/Cyp2b9,CYP2C8,Cyp2d9 (includes others),CYP2F1,CYP3A5,CYP4A11,CYP51A1,CYP7A1,CYP7B1,HMOX1	
ESR1		ligand-dependent nuclear receptor	Activated	2.202		0.065	1.646	7.81E-13	ABCC3,ABHD2,ANLN,AR,ARL4D,ASPM,ATP2A3,AURKA,BIRC5,BRCA1,CA2,CASP8AP2,CCND1,CCND3,CD83,CDCA8,CDK1,CENPA,CENPE,CENPF,CIT,CLEC7A,CLSPN,COTL1,Cox8b,CYFIP2,C…	[illegible]
ritonavir		chemical drug		-1.172		-0.013	-1.143	8.31E-13	ABHD2,ACAT2,ADIPOQ,BIRC5,CYP2C8,CYP3A5,DHCR7,ECT2,FDPS,GBP2,HMGCR,HMMR,HUNK,ICAM1,IDI1,ME1,MME,MSMO1,MVK,MYB,NCAPH,NEIL3,NUF2,RACGAP1,RDH11,SQLE,VCAM…	ADIPOQ,NCOR1,NFKB1,NFYA,PPARA,PPARG,RELA,SP1,SREBF1,SREBF2,Srebp,lipid,ritonavir,sterol
phorbol myristate acetate		chemical drug		1.659		0.216	-0.169	1.09E-12	ACO1,ADAM8,ADAMTS1,AGER,ANXA1,AQP4,ATP2A3,ATP2B4,AURKA,BIRC5,BTG2,CA2,CCND1,CCND3,CD44,CDK1,CDKN2D,CERK,CES1,CSTA,CYBB,CYP1A2,CYP2A6 (includes others),CYP7…	[illegible]
mir-223		microrna		0.778		0.093	0.319	1.12E-12	ASPRV1,C7,CD274,CD93,E2F1,GPR65,Gstm3,GSTM5,HMGCS1,ICAM1,IFI16,IGF1R,IL1RN,LPL,MMP8,MREG,MSMO1,Mt2,POSTN,PRTN3,Serpina3g (includes others),SLC40A1,Stfa2/Stfa2l1,Stfa3…	JUN,NFKB1,NFkB (complex),RELA,STAT1,STAT3,mir-223
GATA1		transcription regulator		1.91		0.108	1.333	1.13E-12	ACTN1,ANK1,BIRC5,BTG2,CA2,CCND1,CCND3,CDKN2D,Clca3a1/Clca3a2,CYBB,DMTN,Gypa,HBA1/HBA2,HBB,HHEX,INHBB,ITGB3,KLF1,LEPR,MCM3,MCM5,MYB,NFIL3,PCNA,PLEK,PRG2,RB…	CREBBP,E2F2,GATA1,Histone h3,MED1,MYB,MYC,RNA polymerase II,RUVBL2,SP1
HGF		growth factor	Activated	4.01	bias	0.294	1.98	1.31E-12	A2M,ADAMTS1,AFP,ASNS,AURKA,BIRC5,CCND1,CCNF,CD44,CD93,CDK1,CELSR1,CENPF,CKS1B,COL1A1,CYR61,EBP,FEN1,FKBP5,FLNA,GRB10,HELLS,HMMR,HMOX1,ICAM1,ID1,INSIG1,IS…	[illegible]
SP1		transcription regulator	Activated	3.323	bias	0.375	1.379	1.31E-12	ABCD2,ABHD2,ADAMTS1,ADRA1B,AGER,Akr1b7,ANK1,AR,ASNS,ATP2A3,ATP7A,BIRC5,CAMP,CCND1,CCND3,CDK1,CDKN2D,CES1,Ces2c,COL1A1,Cyp2d9 (includes others),CYP51A1,CYP7B1…	[illegible]
ciprofibrate		chemical drug	Activated	4.339		-0.018	4.431	1.66E-12	ADAMTS1,APCS,CD63,CYP1A2,CYP27A1,Cyp2c54 (includes others),CYP2C8,Cyp2d9 (includes others),CYP4A11,CYP4F12,CYP7A1,CYP7B1,DIO1,ELOVL3,GSTP1,IGFBP1,IGFBP2,LCN2,LPL,Mup…	ACOX1,CEBPA,CTNNB1,HNF4A,LEP,MED1,N-cor,NCOA6,NFKB1,NR1H3,NR1I3,NR3C1,PPARA,PPARG,RELA,RXRA,SREBF1,THRA,THRAP3,ciprofibrate
discodermolide		chemical drug						1.80E-12	BARD1,BRCA1,CDC7,CDK1,E2F2,ESPL1,FANCD2,KIF11,KIF23,PLK4,PRC1,RAD51,RBL1,SMC2,TOP2A	CDKN2A,E2F1,E2F4,MYC,RB1,TP53,discodermolide
IKBKB		kinase	Activated	2.075	bias	0.287	0.466	1.89E-12	AFP,AGER,BRCA1,CCND1,CD44,CKS1B,CYP7B1,ECT2,EZH2,FASN,GBP2,GM2A,Gstt1,H2AFX,HLA-A,HMOX1,ICAM1,IFI16,IGFBP2,IL1RN,ITGB3,KIF23,LCN2,LMNB1,Mt1,Mt2,NID1,PLIN1,POST…	CEBPA,CHUK,IKBKB,IKBKG,IL1B,JUN,MYC,NCOA3,NFKB1,NFKBIA,NFkB (complex),RELA,STAT1,STAT3,TNF
PDGF BB		complex		1.637	bias	0.264	0.049	2.69E-12	ACAT2,ADRB2,BRCA1,CCND1,CCND3,CD44,CDK1,CYR61,DUSP1,DUSP5,FASN,FLNA,GBP2,GLUL,H19,HMGCR,HMGCS1,HMOX1,IGF1R,IGF2,MCM6,MMP14,Mt1,Mt2,NFIL3,NOX4,NPR3,OLR…	APP,Akt,BRCA1,E2F1,EGR1,ERK1/2,FOXO1,JUN,Jnk,MYC,NFkB (complex),NOTCH1,PDGF BB,PGR,PI3K (complex),RELA,SP1,STAT3,TP53
IGF1		growth factor		1.335		0.209	-0.003	2.75E-12	A2M,ACSS2,ADIPOQ,AQP4,BIRC5,BRCA1,BTG2,CAMP,CAVIN2,CCND1,CCND3,CD44,CDK1,COL1A1,CYBB,CYFIP2,CYR61,DUSP1,E2F1,ELN,FASN,H2AFX,HBB,HMGCR,HMOX1,ICAM1,ID1,IG…	[illegible]
FOXO1		transcription regulator	Activated	2.938	bias	0.269	1.462	3.68E-12	A2M,ACLY,ADIPOQ,ANLN,Apoc3,AR,ASPM,BIRC5,BRIP1,CA2,CCND1,CCNF,CDK1,Cdkn1c,CENPF,CKMT2,CTSE,CYP7A1,DLGAP5,EBF1,FABP5,FASN,FDPS,GPAM,Gzmb,HMGCR,HMOX1,ICA…	[illegible]…CEBPA,EGR1,EP300,FGF21,FOXO1,FOXO3,FOXO4,JUN,NR4A1,PPARA,PPARG,RELA,RXRA,SIRT1,SP1,SREBF1,TP53,lipid
cardiotoxin		chemical - other		1.89	bias	0.431	0.749	3.81E-12	Bex1,BIRC5,CAPN6,CCND1,CCND3,Cdkn1c,E2F1,E2F2,FEN1,GM2A,H19,IGF2,IL1RN,ITGA4,ITGB2,KPNA2,MCM2,MCM3,MEST,MMP15,NASP,PCNA,PEG3,PLAGL1,PTPRC,RBL1,SNRPD1	[illegible]
EGF		growth factor		1.623	bias	0.265	-0.153	3.83E-12	ACTN1,AFP,AR,AURKA,BIRC5,BRCA1,BTG2,CAVIN2,CCND1,CCND3,CD44,CDK1,COL1A1,CYR61,DUSP1,DUSP5,E2F1,ENAH,FASN,FST,FSTL1,Gsta4,GSTP1,HMGCS1,HMOX1,HSD3B2,ICAM1…	[illegible]
PD98059		chemical - kinase inhibitor	Inhibited	-2.183	bias	-0.272	-0.243	4.24E-12	ACAT2,ADIPOQ,ANXA1,AR,BDH1,BIRC5,CA2,CAMP,CCND1,CD44,CD83,COL1A1,DHRS3,DNMT1,DUSP1,DUSP5,E2F1,E2F2,ELN,FASN,FKBP5,HMOX1,ICAM1,IGF1R,IGF2,IGFBP1,IL1RN,INSIG…	[illegible]…NFkB (complex),PD98059,RAF1,RELA,STAT3,TNF,TP53
troglitazone		chemical drug	Inhibited	-3.232		0.04	-3.451	4.94E-12	ABCD2,ABHD2,Acot1,ADIPOQ,AGER,Aldh1a7,AR,BIRC5,CCND1,CCND3,CFD,COL1A1,CYP3A5,CYP7A1,DHRS3,E2F1,E2F2,ECT2,FABP5,FASN,GBP2,GPAM,HBA1/HBA2,HMMR,HMOX1,HUNK,I…	ADIPOQ,CCL2,CEBPA,D-glucose,FOXO1,FOXO3,JUN,MYC,NCOR1,NFATC1,NFKB1,NFKBIA,NFkB (complex),PPARA,PPARG,RELA,RXRA,SMAD3,SP1,SREBF1,STAT3,TNF,TP53,troglitazone
SH3TC2		other						5.22E-12	AACS,ACLY,CYP51A1,DHCR7,EBP,FDPS,HMGCR,HMGCS1,IDI1,MVK,NSDHL,PMVK,SQLE	
NCOA2		transcription regulator		-0.629		0.24	-1.442	5.25E-12	ADH4,ADIPOQ,APOA4,AR,CCND1,CFD,CYP51A1,CYP7A1,FASN,FST,GBE1,HMGCR,HMGCS1,IDI1,IFIT2,KHK,LPL,Mx1,MYB,NSDHL,OASL,PLIN1,PPP1R3B	ADIPOQ,CEBPA,CTNNB1,CYP19A1,ESRRA,FOXO1,NCOA2,NCOR1,NCOR2,NFKB1,PPARA,PPARG,RELA,RXRA,SP1,SREBF1,STAT5A,THRA,THRB
lovastatin		chemical drug	Inhibited	-2.824		0.172	-3.551	5.45E-12	ACAT2,ADAMTS1,ADIPOQ,AR,BIRC5,CCND1,CCND3,COTL1,DHCR7,ENC1,FASN,FDPS,HBA1/HBA2,HELLS,HMGCR,HMGCS1,HMOX1,MKI67,MVK,NOX4,PCSK9,PMVK,PPARD,RBL1,TGFB1,TNFRSF11B	AKT1,APOE,CDKN2A,CEBPA,CTNNB1,E2F1,E2F4,FOXO1,FOXO3,JUN,MYC,NFKB1,NFKBIA,NFkB (complex),NR4A1,NR5A2,PPARGC1A,RB1,RELA,SP1,SREBF1,SREBF2,STAT3,TNF,TP53,lovastatin
PI3K (complex)		complex	Activated	3.01	bias	0.297	1.453	6.17E-12	ADRB2,BIRC5,CCND1,CCND3,CD274,CD44,COL1A1,CYBB,CYP7A1,DUSP1,E2F1,FABP5,FRY,GSTM5,GSTP1,H19,HMGCR,HMOX1,ICAM1,IGF1R,IGF2,IGFBP1,IGFBP2,IL1RN,ITGB2,LCN2,LTB…	AKT1,Akt,BRCA1,CEBPA,E2F1,EGR1,FOXO1,FOXO3,Insulin,JUN,LY294002,NFKBIA,NFkB (complex),NR4A1,PI3K (complex),PPARG,RELA,SP1,SREBF1,TNF,TP53
cisplatin		chemical drug	Activated	2.109		0.16	0.953	6.36E-12	A2M,ABCC3,ADAMTS1,ANK1,ANXA1,ASNS,BIRC5,BRCA1,BTG2,CABYR,CAPN6,CCND1,CD44,CDK1,CMBL,COL1A1,DHRS3,DUSP1,E2F1,E2F7,FAM117A,FASN,FCGR2A,FNDC3B,GSTM1,GST…	[illegible]
CDKN2A		transcription regulator	Inhibited	-4.897		-0.044	-4.649	7.60E-12	A2M,ASF1B,ATAD2,BARD1,BIRC5,BTG2,CCND1,CCND3,CDCA4,CDK1,CDKN2D,DCK,DUSP1,E2F1,E2F2,EBF1,EZH2,FAM111A,FEN1,FST,H2AFX,HMGB2,HUNK,ITGB3,MAD2L1,MCM4,MCM5,M…	CCND1,CDKN1A,CDKN2A,E2F1,E2F2,E2F3,E2F4,E2f,MDM2,MYBL2,MYC,RB1,RBL1,Rb,TP53
Akt		group	Activated	2.211		0.141	1.434	9.25E-12	A2M,ADIPOQ,AMOT,AR,BIRC5,BRCA1,BTG2,CCND1,CCND3,CD274,CD44,E2F2,EZH2,FKBP5,HMOX1,IGF1R,IGF2,IGFBP2,LCN2,LPL,MFN2,MMP14,MYB,NFIL3,NOX4,PCNA,PPARD,PPP1R1B,…	AKT1,Akt,CEBPA,CREB1,CTNNB1,E2F1,ESR1,FOS,FOXO1,FOXO3,JUN,MYC,NFKBIA,NFkB (complex),NR4A1,PTEN,RELA,SP1,TNF,TP53,beta-estradiol
E2f		group	Activated	3.24	bias	0.342	1.856	1.04E-11	BRCA1,CDC7,CDK1,E2F1,E2F2,FANCD2,ITGB4,LIG1,MAD2L1,MCM2,MCM3,MCM4,MCM5,MCM6,MYB,NASP,NUSAP1,PCNA,POLA1,RAD51,RBL1,RRM2,TPX2,TYMS	E2F1,E2F4,E2f,MDM2,MYBL2,RB1,RBL1,Rb,TBX2,TP53

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Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
TO-901317		chemical reagent		-0.193		0.028	-0.275	3.77E-16	CCND1,Cox8b,CYP3A5,Cyp4a14,DHCR7,FABP4,FABP5,G6PC,GCK,Mt1,Mt2,Mup1 (includes others),PFKFB3,RDH16,UCP1	D-glucose,FOXO1,JUN,MYC,NR1H3,PDX1,PPARA,PPARG,RORA,RORC,RXRA,SREBF1,THRB,TO-901317
PPARA		ligand-dependent nuclear receptor		0.909		0.024	0.832	3.59E-13	ACSS2,CCND1,Cyp4a14,DHCR7,FABP4,FABP5,G6PC,GCK,IGFBP1,IGFBP5,Mup1 (includes others),PHLDA1,PMVK,RETSAT,SLC10A2,UCP1	ADIPOQ,CEBPB,CEBPD,CREBBP,FOS,FOXO1,Ins1,JUN,NR1H4,PGR,PPARA,PPARG,PPARGC1A,RXRA,VDR,pirinixic acid
Growth hormone		group		1.183		0.038	1.067	4.55E-12	BCL6,CCND1,CDH1,Cyp4a14,FABP4,G6PC,HBB,IGFBP1,IGFBP5,KLF10,ONECUT1,PFKFB3	CEBPB,CREBBP,EP300,ESR2,FOS,FOXO1,FOXO3,Growth hormone,IRS2,JUN,MYC,PGR,PPARA,PPARG,SMARCA4,STAT3,STAT5A
SREBF1		transcription regulator		0.611		0.064	0.397	1.27E-11	ACSS2,BHLHE40,DHCR7,FABP4,FABP5,G6PC,GCK,IRS2,LPIN1,PMVK,RDH11,UCP1	CEBPB,FOXO1,Insulin,JUN,NR1H4,PPARA,PPARG,PPARGC1A,SCAP,SREBF1,SREBF2,THRB,cholesterol
pirinixic acid		chemical toxicant		1.735		0.056	1.537	5.02E-11	ACMSD,ACSS2,CCND1,CYP3A5,Cyp4a14,FABP4,FABP5,G6PC,KLF10,MBD1,Mup1 (includes others),PHLDA1,SLC10A2,UCP1	ACOX1,ADIPOQ,JUN,NR1H4,PPARA,PPARG,PPARGC1A,RXRA,SREBF1,VDR,pirinixic acid
PPARG		ligand-dependent nuclear receptor		0.217		0.028	0.133	1.30E-10	ARL4D,BCL6,CCND1,CDH1,Cyp4a14,FABP4,FABP5,G6PC,GCK,IGFBP1,IGFBP5,IRS2,PFKFB3,UCP1	AKT1,AR,CEBPB,CREB1,FOS,FOXA2,FOXO1,FOXO3,HIF1A,INS,IRS1,JUN,LEP,MED1,PPARA,PPARG,PPARGC1A,SIRT1,STAT5B,STAT6
Ins1		other	Activated	2.191		0.035	2.077	1.64E-10	ATP1A2,CCND1,Cox8b,FABP4,G6PC,GCK,IGFBP1,IGFBP5,IRS2,Mt1,RETSAT,UCP1	ADIPOQ,CEBPB,CEBPD,CREB1,FOS,FOXO1,FOXO3,IRS1,IRS2,Ins1,PPARA,PPARG,PPARGC1A,SIRT1,STAT3,cyclic AMP
INSR		kinase		-0.239		0.07	-0.423	1.72E-10	ATP5MF,CCND1,Cox8b,DHCR7,FABP4,GCK,H19,IGFBP1,KLF10,MBD1,PHLDA1,RGS16,UCP1	ADIPOQ,CREB1,ESR1,FOXO1,FOXO3,IGF1R,INSR,IRS1,IRS2,PPARA,PPARGC1A
rosiglitazone		chemical drug		0.561		0.033	0.455	4.59E-10	ACSS2,CCND1,CDH1,Cox8b,FABP4,FABP5,GCK,IGFBP1,IGFBP5,IRS2,LPIN1,Mup1 (includes others),UCP1	CEBPB,CREB1,CREBBP,FOS,FOXA1,FOXA2,FOXO1,FOXO3,HIF1A,IGF1,INS,IRS1,JUN,PGR,PPARA,PPARG,PPARGC1A,RB1,RXRA,rosiglitazone
INS		other		1.357		0.013	1.323	1.01E-09	CCND1,CDH1,G6PC,GCK,IGFBP1,IGFBP5,IRS2,RDH16,UCP1	AKT1,AR,CEBPB,CREB1,FOS,FOXA1,FOXA2,FOXO1,FOXO3,HIF1A,IGF1,INS,IRS1,IRS2,JUN,PPARG,PPARGC1A,SIRT1
MED1		transcription regulator		0.692		0.072	0.532	1.20E-09	BCL6,BHLHE40,CCND1,CYP3A5,Cyp4a14,FABP4,GCK,IGFBP1,UCP1	CEBPB,CREBBP,EP300,FOXO1,JUN,MED1,NCOR1,NR3C1,PGR,PPARA,PPARG,RB1,STAT3
cadmium		chemical toxicant		-1.095		0.037	-1.191	2.95E-09	CCND1,CYP26B1,G6PC,HBB,Mt1,Mt2,RETSAT	
progesterone		chemical - endogenous mammalian		-0.319		0.022	-0.389	3.93E-09	ATP1A2,BCL6,BHLHE40,CCND1,CDH1,CYP3A5,H19,ID3,IGFBP1,IGFBP5,IRS2,KLF10,LPIN1,PFKFB3	APP,CTNNB1,FOS,FOXO3,HIF1A,IL6,JUN,MYB,NCOR1,NR3C1,PGR,SIN3A,SNAI1,STAT3,TGFB1,progesterone,testosterone
IRS1		enzyme	Activated	2.201		0.039	2.093	3.98E-09	CCND1,CDH1,FABP4,G6PC,GCK,IGFBP1,IRS2,UCP1	CEBPB,CEBPD,CREB1,FOS,FOXA2,FOXO1,INS,IRS1,IRS2,Ins1,insulin,JUN,PPARA,PPARG,PPARGC1A,SIRT1
FOXA2		transcription regulator		-1.165		0.009	-1.183	6.98E-09	CCND1,CDH1,FABP5,G6PC,GCK,IGFBP1,IGFBP5,Mt1,ONECUT1	CEBPB,CEBPD,FOS,FOXA1,FOXA2,FOXO1,FOXO3,IL6,Ins1,NCOR1,NR3C1,PPARA,PPARG,STAT3
FGF19		growth factor						7.17E-09	CCND1,Cyp4a14,FABP5,GCK,IGFBP1,RGS16,SLC10A2	
RICTOR		other	Activated	2.254		-0.065	2.449	7.29E-09	ATP5MF,COX6A1,FABP5,G6PC,GCK,IGFBP1,IRS2,RGS16,RPS13,SLC10A2	AKT1,AR,CEBPB,FOXO1,HIF1A,PPARG,PPARGC1A,RICTOR,SIRT1
IL1B		cytokine		-1.156		0.041	-1.302	7.59E-09	BCL6,CYP3A5,FABP5,GCK,H19,ID3,IGFBP1,IGFBP5,IRS2,KLF10,Mt1,Mt2,PHLDA1,PIM3,RGS16,SLC10A2	FOS,FOXO3,FOXO4,HDAC1,HIF1A,IFNG,IL1B,IL6,JUN,MED1,MYC,NCOR1,NR3C1,PPARG,STAT3,TNF,TP53
bucladesine		chemical toxicant		-1.336		0.051	-1.494	8.34E-09	CCND1,CYP3A5,G6PC,GCK,H19,IGFBP1,IGFBP5,IRS2,Mt1,RGS16,UCP1	CEBPB,CEBPD,FOS,FOXO1,FOXO3,IL6,Ins1,NCOR1,NR3C1,PGR,PPARA,PPARG,STAT3,bucladesine,cyclic AMP,hydrocortisone
AKT1		kinase	Activated	2.409		0.042	2.297	1.11E-08	CCND1,CDH1,DHCR7,FABP5,G6PC,GCK,IGFBP1,IGFBP5,IRS2,PHLDA1	AKT1,CEBPB,CEBPD,CREB1,CREBBP,FOS,FOXO1,FOXO3,IRS1,JUN,PGR,PPARA,PPARG,PPARGC1A,SIRT1,STAT3,TP53,beta-estradiol,cyclic AMP
STAT5B		transcription regulator		0.298		0.023	0.248	1.46E-08	BCL6,CCND1,CDH1,Cox8b,CYP26B1,CYP3A5,GCK,HAO2,Mup1 (includes others),UCP1	
IGF1		growth factor		1.682		0.044	1.545	1.93E-08	ACSS2,BHLHE40,CCND1,CDH1,FABP4,GCK,HBB,IGFBP1,IGFBP5,IRS2,PHLDA1,UCP1	AKT1,AR,Akt,CEBPB,CREB1,CREBBP,FOS,FOXA1,FOXA2,FOXO1,FOXO3,HIF1A,IGF1,INS,IRS1,IRS2,JUN,PPARA,PPARG,PPARGC1A,RB1,RXRA
HTT		transcription regulator						2.19E-08	ATP5MF,BCL6,BHLHE40,CCND1,COX6A1,Cox8b,DHCR7,GSN,HBA1/HBA2,IGFBP5,Mt1,Mup1 (includes others),RGS16,UCP1	
forskolin		chemical toxicant		0.036		0.044	-0.119	2.27E-08	BHLHE40,CCND1,CYP3A5,DHCR7,G6PC,H19,ID3,IGFBP1,IGFBP5,IRS2,Mt1,Mt2,PIM3,UCP1	CEBPA,CEBPB,CREB1,CREBBP,FOS,FOXO3,FOXO4,HDAC1,IL1B,IL6,JUN,NCOR1,NR3C1,PPARG,STAT3,TNF,TP53,forskolin
RORC		ligand-dependent nuclear receptor						2.43E-08	CYP3A5,Cyp4a14,G6PC,IGFBP1,Mt1,Mt2,Mup1 (includes others),RDH16	
INSIG1		other		0.557		-0.089	0.772	2.58E-08	ACSS2,DHCR7,FABP4,FABP5,IRS2,LPIN1,PMVK	INSIG1,PPARGC1A,SREBF1,SREBF2,cholesterol
streptozocin		chemical drug	Inhibited	-2.267		0.017	-2.317	2.85E-08	ACMSD,ATP1A2,Cyp4a14,FABP4,G6PC,GCK,IGFBP1,IRS2,UCP1	CEBPB,CEBPD,CREB1,FOS,FOXO1,HIF1A,IGF1,IRS2,Insulin,JUN,LEP,MED1,PPARA,PPARG,STAT3,STAT6,cyclic AMP,streptozocin
Insulin		group		1.362		0.023	1.294	2.88E-08	CCND1,FABP4,G6PC,GCK,IGFBP1,IRS2,LPIN1,PFKFB3,RETSAT,SLC10A2,UCP1	ADIPOQ,CREB1,FOS,FOXA1,FOXO1,FOXO3,IRS1,IRS2,Insulin,JUN,PPARA,PPARG,PPARGC1A,RB1,RXRA,SIRT1
beta-estradiol		chemical - endogenous mammalian		0.063		0.03	-0.058	3.05E-08	BCL6,BHLHE40,CCND1,CDH1,CYP26B1,DHCR7,FABP4,FABP5,G6PC,H19,HBA1/HBA2,HBB,HSD17B6,IGFBP1,IGFBP5,IRS2,KLF10,LPIN1,PHLDA1,RGS16,RPS13,SPOCK2	AKT1,AR,CEBPB,FOS,FOXO1,FOXO4,HDAC1,HIF1A,JUN,PGR,PPARG,STAT3,TNF,TP53,beta-estradiol
D-glucose		chemical - endogenous mammalian		1.029		0.026	0.945	5.90E-08	CCND1,FABP5,G6PC,GCK,GSN,IRS2,KLF10,MAFB,Mt1,Mt2,PFKFB3,RDH16,UCP1	ADIPOQ,CREB1,CREBBP,D-glucose,EP300,FOS,FOXA2,FOXO1,INS,MYC,PDX1,PPARA,PPARG,PPARGC1A,SIRT1
methylprednisolone		chemical drug		-0.677		0.018	-0.727	6.91E-08	CCND1,CDH1,COX6A1,FABP5,G6PC,GCK,ID3,IGFBP1,MAFB,Mt1,PIM3,SLC10A2	CREBBP,EP300,FOS,FOXO3,HIF1A,IFNG,IL6,JUN,MED1,MYC,NCOR1,NR3C1,PPARG,SMARCA4,STAT3,methylprednisolone,prostaglandin E2
E. coli B5 lipopolysaccharide		chemical - endogenous non-mammalian		0.05		0.044	-0.08	9.14E-08	BCL6,BHLHE40,CCND1,CYP3A5,G6PC,IGFBP1,Mup1 (includes others),PHLDA1,UCP1	Akt,CREBBP,E. coli B5 lipopolysaccharide,EP300,FOS,FOXO1,FOXO3,HIF1A,IL6,JUN,NCOR1,NR3C1,RB1,SMARCA4,STAT3
palmitic acid		chemical - endogenous mammalian		-0.394		0.04	-0.505	9.51E-08	ATP5MF,FABP4,G6PC,GCK,IGFBP1,IRS2,Mt1,Mt2	CEBPB,CEBPD,CREB1,FOS,FOXA1,FOXA2,FOXO1,FOXO3,HDAC2,IRS1,IRS2,Ins1,MYC,PPARA,PPARG,PPARGC1A,SIRT1,palmitic acid
PDX1		transcription regulator		-0.314		0.023	-0.364	1.03E-07	ARL4D,CCND1,G6PC,GCK,ID3,IRS2,KLF10,Mt1	CEBPB,FOXO1,Ins1,PDX1,PPARA,PPARG
cholic acid		chemical - endogenous mammalian		1.004		0.018	0.962	1.08E-07	CYP3A5,Cyp4a14,DHCR7,G6PC,IGFBP5,SLC10A2	NR1H4,RXRA,cholic acid
SREBF2		transcription regulator	Inhibited	-2.236		0.072	-2.398	1.17E-07	ACSS2,DHCR7,FABP5,IRS2,PMVK,RDH11	PPARGC1A,SREBF1,SREBF2,cholesterol
ATP7B		transporter		1.342		0.012	1.314	1.19E-07	FABP5,H19,LPIN1,Mt1,Mt2	
RORA		ligand-dependent nuclear receptor						1.26E-07	CYP3A5,Cyp4a14,G6PC,IGFBP1,Mt1,Mt2,Mup1 (includes others),RDH16	FOS,FOXO3,IL6,NCOR1,NR3C1,RORA,STAT3
lipopolysaccharide		chemical drug		-0.649		0.045	-0.843	1.33E-07	ATP1A2,BCL6,CCND1,CDH1,CYP3A5,FABP4,FABP5,GSN,H19,ID3,IGFBP1,IGFBP5,KLF10,LPIN1,MAFB,Mt1,Mt2,PFKFB3,PHLDA1,RGS16	AR,FOS,FOXO1,FOXO3,FOXO4,HDAC1,HDAC2,IL1B,JUN,MYC,NR3C1,PGR,TNF,TP53,lipopolysaccharide,progesterone
MYC		transcription regulator		-1.676		0.036	-1.796	1.47E-07	BCL6,CCND1,CDH1,COX6A1,FABP4,FABP5,G6PC,GCK,H19,ID3,KLF10,Mt1,Mt2,PFKFB3,RPL19,RPS15A	Akt,CEBPB,CREBBP,EP300,FOXO1,HIF1A,IL6,JUN,MYC,NOTCH1,PPARG,RB1,STAT3
IRS2	-6.59E-01	enzyme	Activated	2.158		0.019	2.116	1.55E-07	CCND1,FABP4,G6PC,GCK,IGFBP1	AKT1,AR,CEBPB,CEBPD,CREB1,FOXO1,FOXO3,HIF1A,IRS1,IRS2,Ins1,Insulin,JUN,PPARA,PPARG,PPARGC1A,SIRT1
PGR		ligand-dependent nuclear receptor		0.053		0.057	-0.106	1.66E-07	BCL6,CCND1,G6PC,H19,HBA1/HBA2,IGFBP1,IGFBP5,IRS2,PFKFB3	CEBPB,CEBPD,CREBBP,EP300,FOS,FOXO1,FOXO3,Ins1,NR3C1,PGR,PPARA,PPARG,SMARCA4,STAT3,dexamethasone
TNF		cytokine		1.622		0.032	1.491	1.76E-07	BCL6,BHLHE40,CCND1,CDH1,CYP26B1,FABP4,FABP5,H19,ID3,IGFBP1,IGFBP5,IRS2,KLF10,Mt1,Mt2,PHLDA1,PIM3,RGS16,RPS13,UCP1	CEBPB,CREB1,CTNNB1,FOS,FOXO3,IL1B,IL6,JUN,NR3C1,PGR,PRL,RB1,STAT3,TNF,TP53,beta-estradiol,forskolin,testosterone
SCAP		other	Inhibited	-2		0.087	-2.175	1.85E-07	ACSS2,DHCR7,FABP5,Mt2,PMVK,RDH11	PPARGC1A,SCAP,SREBF1,SREBF2,cholesterol
FGF21		growth factor		0.219		0.037	0.141	2.79E-07	Cox8b,G6PC,IGFBP1,IRS2,UCP1	CEBPB,CEBPD,CREBBP,FGF21,FOXO1,Ins1,JUN,PGR,PPARA,PPARG
RXRA		ligand-dependent nuclear receptor		1.762		0.047	1.662	2.82E-07	CCND1,CYP3A5,FABP4,FABP5,GCK,IGFBP1,ONECUT1,SLC10A2,UCP1	CREBBP,FOS,FOXA1,FOXO1,JUN,L-triiodothyronine,MED1,NCOA2,NR1H4,PGR,PPARA,PPARG,RB1,RXRA,SREBF1,THRB
TP53		transcription regulator		1.922		0.02	1.841	2.93E-07	ACSS2,BHLHE40,CCND1,CDH1,Cox8b,CYP26B1,DHCR7,FABP4,FABP5,G6PC,GSN,H19,ID3,IGFBP5,LPIN1,MAFB,Mt2,PFKFB3,PHLDA1,RGS16	AKT1,AR,CEBPB,ESR1,ESR2,FOS,FOXO1,FOXO4,HDAC1,HIF1A,IL6,JUN,MYC,PPARG,TNF,TP53
ciprofibrate		chemical drug		0.379		-0.004	0.389	3.04E-07	Cyp4a14,FABP4,G6PC,IGFBP1,Mup1 (includes others),PHLDA1,SLC10A2	ACOX1,JUN,PPARA,PPARG,RXRA,SREBF1,ciprofibrate
NR5A2		ligand-dependent nuclear receptor		0.774		0.066	0.63	3.22E-07	CCND1,IGFBP1,Mt1,ONECUT1,PNLIP,SLC10A2	
dexamethasone		chemical drug		-0.446		0.009	-0.486	3.76E-07	ACSS2,BCL6,BHLHE40,CCND1,CYP3A5,FABP4,FABP5,FOXQ1,G6PC,GCK,IGFBP1,IGFBP5,IRS2,LPIN1,Mt1,Mt2,PFKFB3,PHLDA1,RDH11,SLC10A2,SPOCK2	CEBPB,FOS,FOXO1,FOXO3,HDAC2,IL6,Insulin,JUN,MED1,MYC,NCOR1,NR3C1,PPARA,PPARG,STAT3,dexamethasone
LY294002		chemical - kinase inhibitor	Inhibited	-2.178		-0.07	-1.955	4.21E-07	ACSS2,BCL6,BHLHE40,CCND1,CDH1,GCK,HSD17B6,IGFBP5,IRS2,KLF10,PHLDA1	AKT1,AR,Akt,CEBPB,CREBBP,FOS,FOXA1,FOXA2,FOXO1,FOXO3,HIF1A,IGF1,JUN,LY294002,PIK3CA,PPARG,RB1,Rb,VHL
ZBTB20		transcription regulator		0.447		0.005	0.435	5.22E-07	ACSS2,CYP3A5,G6PC,GCK,IGFBP1	
FOXO3		transcription regulator	Inhibited	-2.158		0.037	-2.238	5.55E-07	BCL6,CCND1,CDH1,FABP4,FABP5,IGFBP5,IRS2,Mt1,Mt2	CREBBP,EP300,FOS,FOXO1,FOXO3,FOXO4,HDAC1,IL6,JUN,MTOR,MYC,NCOR1,NR3C1,PPARG,PPARGC1A,RORC,SIRT1,STAT3,TNF,TP53
GW501516		chemical drug		0.849		0.061	0.729	7.18E-07	CCND1,Cox8b,IGFBP1,IGFBP5,LPIN1,UCP1	CEBPB,CEBPD,FOXO1,GW501516,Ins1,PPARA,PPARD,PPARG,RXRA,SIRT1
methotrexate		chemical drug		-0.896		0.014	-0.93	7.30E-07	ACSS2,CCND1,CDH1,GSN,HBA1/HBA2,IGFBP5,LPIN1,Mt1	
FOS		transcription regulator		-0.305		0.027	-0.356	7.33E-07	CCND1,CDH1,FABP4,G6PC,HBA1/HBA2,IGFBP1,IGFBP5,IRS2,Mt2,PHLDA1,SLC10A2	CEBPA,CEBPB,CREB1,CREBBP,FOS,FOXA1,JUN,PPARG,RB1,RXRA
IGF2		growth factor		1.114		0.037	1.042	8.19E-07	CCND1,DHCR7,H19,IGFBP5,PHLDA1,RGS16,UCP1	CEBPD,EP300,IGF2,P38 MAPK,PPARG,RB1,SMARCA4
dihydrotestosterone		chemical - endogenous mammalian		1.066		0.044	0.961	8.91E-07	CCND1,CDH1,FABP4,FOXQ1,GSN,IGFBP5,IRS2,Mt1,Mup1 (includes others),PHLDA1,RPL19	AR,CTNNB1,ESR1,ESR2,FOXO1,FOXO3,MTOR,SIRT1,TP53,dihydrotestosterone
SMARCB1		transcription regulator		-1.325		0.053	-1.45	9.22E-07	CCND1,CDH1,Cyp4a14,FABP4,G6PC,GSN,Mup1 (includes others)	
CEBPA		transcription regulator		-0.651		0.031	-0.741	9.86E-07	CCND1,CDH1,CYP3A5,DHCR7,FABP4,G6PC,IRS2,Mup1 (includes others),ONECUT1,UCP1	ADIPOQ,CEBPA,CEBPB,CREBBP,EP300,FOS,FOXA1,FOXO1,HDAC1,JUN,NR4A1,NR4A3,PGR,PPARA,PPARG,PPARGC1A,RB1,RXRA,STAT3
NR4A3		ligand-dependent nuclear receptor						1.27E-06	CCND1,FABP4,G6PC,LPIN1,UCP1	Akt,CEBPB,CREB1,CREBBP,FOXO1,FOXO3,HIF1A,IRS1,Insulin,JUN,NR4A3,PPARA,PPARG,PPARGC1A,RB1
testosterone		chemical - endogenous mammalian		0.141		0.042	0.026	1.34E-06	CCND1,CDH1,CYP26B1,FABP4,ID3,IGFBP1,IGFBP5,IRS2,Mt1	APP,CEBPB,CTNNB1,FGF2,FOS,FOXA1,FOXO1,FOXO3,HDAC2,HIF1A,JUN,MYC,RB1,RXRA,testosterone
CG		complex		0.397		0.06	0.22	1.47E-06	BHLHE40,CDH1,DHCR7,FABP4,FABP5,G6PC,IRS2,PFKFB3,PHLDA1	AR,CEBPB,CG,FOS,JUN,PGR,STAT3,TP53,beta-estradiol
IGF1R		transmembrane receptor		0.244		0.06	0.078	1.56E-06	ATP5MF,CDH1,Cox8b,GCK,H19,IGFBP5,IRS2,UCP1	CEBPB,CEBPD,CREB1,ESR1,ESR2,FOS,FOXO1,FOXO3,HIF1A,IGF1,IGF1R,IRS1,Ins1,JUN,PIK3CA,PPARA,PPARG,PPARGC1A,Rb,TP53
HNF1B		transcription regulator		-0.724		0.007	-0.739	1.60E-06	BHLHE40,CDH1,ID3,IGFBP1,MAFB,ONECUT1	
BSCL2		other						1.61E-06	CCND1,FABP4,GCK,IGFBP5,LPIN1	
TSC2		other		-1.067		-0.049	-0.971	2.03E-06	ACSS2,CCND1,GSN,IGFBP5,IRS2,Mt1	AR,CTNNB1,FOXO3,HIF1A,PTEN,RB1,TSC2
L-triiodothyronine		chemical - endogenous mammalian		-0.161		0.027	-0.24	2.33E-06	CCND1,FABP4,G6PC,GCK,HBA1/HBA2,ID3,IGFBP1,Mup1 (includes others),UCP1	CEBPB,CEBPD,EP300,FOXO1,Ins1,Insulin,JUN,L-triiodothyronine,P38 MAPK,PPARA,PPARG,PPARGC1A,RB1,SIRT1,SMARCA4,THRB
deferoxamine		chemical drug		0.218		0.05	0.086	2.44E-06	BHLHE40,CCND1,CDH1,CYP3A5,IGFBP5,PFKFB3,SPRY4	CTNNB1,EPAS1,HIF1A,PPARG,Rb,TP53,VHL,deferoxamine
BMP2		growth factor		1.054		0.052	0.918	2.97E-06	BHLHE40,CCND1,CDH1,FABP4,ID3,IGFBP5,KLF10	Akt,BMP2,CEBPD,CREBBP,CTNNB1,Ca2+,EP300,FOS,FOXO1,HIF1A,JUN,MYB,P38 MAPK,PPARG,RB1,SIN3A,SMARCA4,SNAI1,TGFB1
tretinoin		chemical - endogenous mammalian		0.64		0.032	0.515	3.09E-06	ACSS2,BCL6,BHLHE40,CCND1,CDH1,CYP26B1,Cyp4a14,FABP4,FABP5,GCK,HSD17B6,ID3,IGFBP5,MAFB,Mt1,PHLDA1,UCP1	Akt,CEBPB,CEBPD,CREBBP,EP300,FOS,FOXO1,FOXO4,HDAC1,HIF1A,IGF1,JUN,MED1,NCOR1,NR3C1,P38 MAPK,PPARG,RB1,SMARCA4,TNF,TP53,tretinoin
LCOR		transcription regulator						3.19E-06	CDH1,CYP26B1,IGFBP1	
SU6656		chemical toxicant		0		-0.08	0.16	3.83E-06	CCND1,Mt1,Mt2,PHLDA1	MAP2K1/2,STAT3,SU6656
dehydroisoandrosterone		chemical - endogenous mammalian		1.057		-0.016	1.09	4.25E-06	CCND1,CYP3A5,Cyp4a14,FABP4,IGFBP1	AHR,CREB1,ERK,FOS,FOXO3,JUN,LEP,MED1,PPARG,STAT3,STAT6,dehydroisoandrosterone
mercuric chloride		chemical toxicant						4.29E-06	CDH1,Mt1,Mt2,Mup1 (includes others)	FOS,FOXO3,IL6,NCOR1,NR3C1,STAT3,mercuric chloride
cholesterol		chemical - endogenous mammalian		1.937		0.028	1.863	4.87E-06	ACSS2,CYP3A5,DHCR7,FABP5,PMVK,RDH11,RGS16	INSIG1,PPARGC1A,SCAP,SREBF1,SREBF2,cholesterol
ACOX1		enzyme		0		-0.017	0.042	5.07E-06	Cyp4a14,FABP4,G6PC,IGFBP1,Mup1 (includes others),PHLDA1	ACOX1,JUN,PPARA,PPARG,RXRA,SREBF1
EPCAM		other						5.82E-06	CCND1,CDH1,FABP5	
HMGA1		transcription regulator		0.785		0.028	0.725	6.42E-06	CCND1,DHCR7,GSN,H19,ID3,IGFBP1	
diethylnitrosamine		chemical toxicant		0.555		0.009	0.535	6.46E-06	CCND1,IGFBP1,Mt1,Mup1 (includes others),PHLDA1	
MEN1		transcription regulator						6.60E-06	CCND1,CDH1,FABP4,IRS2	Akt,CREBBP,CTNNB1,ERK1/2,FOS,FOXA1,FOXO1,HDAC1,HDAC2,HIF1A,JUN,MEN1,PPARG,RB1,RXRA
PDGF BB		complex		1.147		0.056	1.002	6.77E-06	BHLHE40,CCND1,H19,ID3,KLF10,Mt1,Mt2,PHLDA1	
PD98059		chemical - kinase inhibitor		-0.485		-0.057	-0.308	7.49E-06	BCL6,CCND1,CDH1,FABP4,ID3,IGFBP1,PHLDA1,RETSAT,TSPOAP1,UCP1	Akt,CEBPB,CREBBP,CTNNB1,EP300,FGF2,FOS,FOXA1,FOXO1,FOXO3,FOXO4,HDAC1,HIF1A,JUN,MYC,PD98059,PPARG,RB1,RXRA,STAT3,TNF,TP53
LEP		growth factor		0.674		0.035	0.579	8.44E-06	CCND1,CDH1,CYP3A5,Cyp4a14,FABP4,G6PC,GCK,IRS2,UCP1	ADIPOQ,CREB1,CREBBP,FOS,FOXA2,FOXO1,FOXO3,INS,IRS1,JUN,LEP,MED1,NR3C1,PGR,PPARA,PPARG,PPARGC1A
STAT3		transcription regulator		0.92		0.043	0.826	9.42E-06	BCL6,CCND1,CDH1,G6PC,HBB,IGFBP1,IGFBP5,MAFB,Mt1,PHLDA1	CEBPB,CREBBP,EP300,FOS,FOXO3,IL6,JUN,NCOR1,NR3C1,PPARG,RB1,RNA polymerase II,RORC,SMARCA4,STAT3,prostaglandin E2
FOXO4		transcription regulator						1.00E-05	BCL6,CCND1,FABP4,FABP5,IGFBP1	Akt,CREBBP,FOXO1,FOXO4,HIF1A,JUN,RB1
PPARGC1A		transcription regulator		0.841		0.064	0.688	1.01E-05	ATP5MF,CYP3A5,FABP4,G6PC,IRS2,LPIN1,UCP1	CEBPB,CREB1,FGF21,FOXO1,FOXO3,IRS1,Insulin,JUN,PDX1,PPARA,PPARG,PPARGC1A,SIRT1,palmitic acid
TXNIP		other		0.152		-0.004	0.161	1.06E-05	BCL6,CCND1,Cyp4a14,DHCR7	
dimethylnitrosamine		chemical toxicant						1.06E-05	CDH1,IGFBP5,Mt1,Mt2	FOS,FOXO4,HDAC1,JUN,TNF,TP53,dimethylnitrosamine
CYP1A2		enzyme		0		0.004	-0.008	1.16E-05	CCND1,Mt1,Mt2,RGS16	
FNDC5		other						1.20E-05	Cox8b,FABP4,UCP1	
clofibrate		chemical drug		-1.231		0.045	-1.33	1.29E-05	CCND1,Cyp4a14,IGFBP1,Mt1,Mt2	AHR,CYP1A1,clofibrate
SB-431542		chemical reagent		0.555		-0.03	0.622	1.42E-05	ATP1A2,CCND1,CDH1,ID3,MAFB	PGR,SB-431542,progesterone
RETN		other		-1		0.052	-1.104	1.50E-05	FABP4,FABP5,G6PC,UCP1	CREB1,FOXO1,FOXO3,IRS1,JUN,LEP,MED1,PPARG,PPARGC1A,RETN,STAT6
HDAC1		transcription regulator		1.982		-0.015	2.011	1.55E-05	BCL6,CCND1,CDH1,FABP4,Mt1,Mt2,PFKFB3	CEBPA,CREBBP,FOXO1,HDAC1,HDAC2,JUN,NR4A1,NR4A3,PGR,PPARA,PPARG,RB1,SIN3A
cycloheximide		chemical reagent		-1.2		-0.011	-1.171	1.75E-05	CCND1,CYP3A5,IGFBP1,IGFBP5,IRS2,Mt1,PFKFB3,UCP1	CEBPB,CEBPD,CREBBP,FOS,FOXA1,FOXO1,FOXO3,IL6,Insulin,JUN,NCOR1,NR3C1,PGR,PPARA,PPARG,RB1,RXRA,STAT3,cyclic AMP,cycloheximide
NR4A1		ligand-dependent nuclear receptor						1.76E-05	CCND1,FABP4,G6PC,LPIN1,Mt1,UCP1	CEBPB,CREB1,FOXO1,FOXO3,IRS1,Insulin,JUN,NR4A1,PPARA,PPARG,PPARGC1A

cadmium chloride		chemical toxicant						1.76E-05	CCND1,Mt1,Mt2,Mup1 (includes others)	
CTBP2		transcription regulator						1.78E-05	CDH1,HBB,SPRY4	
4-hydroxytamoxifen		chemical drug		-0.232		0.046	-0.343	1.87E-05	BHLHE40,CCND1,CDH1,FABP4,IGFBP1,RGS16	4-hydroxytamoxifen,AHR,Akt,CEBPB,CREBBP,FOS,FOXA1,FOXO1,HIF1A,IGF1,JUN,RB1,RNA polymerase II,RXRA

Day 5 Male PCB

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset
ABCB6		transporter		0.069		0.013	0.038	1.25E-08	CYP1A2,CYP2A6 (includes others),Cyp2c54 (includes others),Cyp2d9 (includes others),CYP4A11,KLF1
CEBPB		transcription regulator		1.614		0.119	1.242	4.43E-07	CYP2A6 (includes others),Cyp2d9 (includes others),HDC,HIST1H4B,HIST1H4D,HIST1H4F,HIST1H4H,HIST1H4J,IGFBP3,SERPINE1,SLC7A1
ACOX1		enzyme		-1.102		-0.035	-1.009	1.15E-06	CYP1A2,Cyp2c54 (includes others),Cyp2d9 (includes others),CYP4A11,Cyp4a14,GOT1,Nat8f2
ciprofibrate		chemical drug		1.171		-0.008	1.191	1.26E-06	CYP1A2,Cyp2c54 (includes others),Cyp2d9 (includes others),CYP4A11,Cyp4a14,GOT1,Nat8f2
17-alpha-ethinylestradiol		chemical drug		-0.232		0.06	-0.375	1.81E-06	Cyp2d9 (includes others),H2AFX,INHBB,LPIN1,MARCO,PLK3,TFF3
dibutyl phthalate		chemical toxicant		1.948		0.04	1.869	2.17E-06	CYP4A11,INHBB,JUNB,SERPINE1
SASH1		other		-1.342		0.185	-1.756	6.97E-06	HDC,IFIT1B,Iigp1,ISG15,MARCO
ethanol		chemical - endogenous mammalian		0.88		0.055	0.722	1.21E-05	AQP4,CYP2A6 (includes others),CYP4A11,LPIN1,PLK3,PPP1R3C,SERPINE1,TAT,TFF3
clofibric acid		chemical drug						1.41E-05	CYP4A11,Cyp4a14,SERPINE1
TBK1		kinase		-0.577		0.157	-0.849	1.59E-05	HDC,IFIT1B,Iigp1,ISG15,MARCO
H-7		chemical - kinase inhibitor		-0.927		-0.157	-0.614	1.66E-05	HDC,ISG15,JUNB,SERPINE1
lipopolysaccharide		chemical drug		-1.087		0.092	-1.465	1.66E-05	AQP4,CYP1A2,CYP2A6 (includes others),CYP4A11,GBP4,GBP6,HDC,IFIT1B,IGFBP3,Iigp1,INHBB,ISG15,JUNB,LPIN1,MARCO,PLK3,PROK1,SAA2-SAA4,SERPINE1
PROCR		other						2.23E-05	GBP4,GBP6,Iigp1
SAMSN1		other		-1.342		0.165	-1.71	2.35E-05	HDC,IFIT1B,Iigp1,ISG15,MARCO
HIF1A		transcription regulator		1.082		0.131	0.746	2.58E-05	AQP4,EPOR,H2AFX,HIF3A,HIST1H2AC,HIST1H2BK,IGFBP3,INHBB,SERPINE1
NR1I2		ligand-dependent nuclear receptor		0.391		0.046	0.289	2.85E-05	CYP1A2,CYP2A6 (includes others),Cyp2d9 (includes others),CYP4A11,GOT1,Nat8f2
TRIM24		transcription regulator		1.982		-0.172	2.324	3.70E-05	GBP4,IFIT1B,Iigp1,ISG15,SERPINE1
CSNK1E		kinase						4.14E-05	PER1,SERPINE1
cyclic AMP		chemical - endogenous mammalian	Activated	2.588		0.118	2.282	5.58E-05	CYP2A6 (includes others),GOT1,IGFBP3,JUNB,PER1,SERPINE1,TAT
staurosporine		chemical - kinase inhibitor		-0.068		-0.026	-0.017	7.84E-05	CYP2A6 (includes others),HDC,INHBB,ISG15,SERPINE1
benoxaprofen		chemical drug						8.27E-05	CYP1A2,CYP4A11
Hif1		complex						8.62E-05	EPOR,HIF3A,LPIN1,TFF3
RORA		ligand-dependent nuclear receptor						8.69E-05	CYP2A6 (includes others),Cyp2c54 (includes others),CYP4A11,Cyp4a14,GOT1,PPP1R3C
Ifn		group		-1.103		0.127	-1.351	9.19E-05	CFH,CYP4A11,ISG15,SERPINE1,ZBP1
IFNB1		cytokine		-1.988		0.086	-2.208	1.06E-04	CYP1A2,GBP4,GBP6,GBP7,IFIT1B,ISG15,ZBP1
DOCK8		other		-1		0.185	-1.37	1.31E-04	HDC,IFIT1B,Iigp1,ISG15
GCG		other		1.154		0.098	0.962	1.55E-04	LPIN1,PLK3,PPP1R3C,TAT
diethylstilbestrol		chemical drug		0.958		0.082	0.797	1.57E-04	AQP4,CYP2A6 (includes others),HDC,IGFBP3,INHBB,RIDA
STAT4		transcription regulator		1.104		0.185	0.654	1.96E-04	EPOR,IFIT1B,ISG15,LPIN1,PER1,SERPINE1
FECH		enzyme						2.11E-04	CYP1A2,Cyp2d9 (includes others),CYP4A11
pirinixic acid		chemical toxicant		1.101		0.115	0.831	2.45E-04	CFH,CYP1A2,Cyp2c54 (includes others),CYP4A11,Cyp4a14,GOT1,JUNB,SERPINE1
GATA1		transcription regulator		0.492		0.046	0.39	2.78E-04	CA1,EPOR,INHBB,JUNB,KLF1,TFF3
DNASE2		enzyme						2.78E-04	IFIT1B,ISG15,ZBP1
RORC		ligand-dependent nuclear receptor						3.01E-04	CYP2A6 (includes others),Cyp2c54 (includes others),CYP4A11,Cyp4a14,PPP1R3C
phorbol myristate acetate		chemical drug		1.086		0.093	0.784	3.13E-04	AQP4,CYP1A2,CYP2A6 (includes others),EPOR,HDC,IGFBP3,INHBB,ISG15,JUNB,PER1,SERPINE1,SLC7A1,TAT
STAT1		transcription regulator		-1.963		0.129	-2.215	3.35E-04	CYP1A2,Cyp2d9 (includes others),CYP4A11,GBP4,GBP6,IFIT1B,ISG15
PPAR ligand-PPAR-Retinoic acid-RXRα		complex						3.82E-04	CYP4A11,Cyp4a14
diltiazem		chemical drug						3.82E-04	CYP4A11,Cyp4a14
MERTK		kinase						3.88E-04	EPOR,HDC,MARCO
E. coli B5 lipopolysaccharide		chemical - endogenous non-mammalian		0.816		0.089	0.598	4.35E-04	Cyp2c54 (includes others),Cyp2d9 (includes others),INHBB,JUNB,SERPINE1,TAT
raloxifene		chemical drug		0.555		0	0.555	4.59E-04	EPOR,INHBB,PLK3,PPP1R3C,SERPINE1
SMARCB1		transcription regulator		0.555		0.107	0.316	4.71E-04	Cyp2c54 (includes others),Cyp2d9 (includes others),CYP4A11,Cyp4a14,PPP1R3C
IL1B		cytokine		0.758		0.085	0.51	4.78E-04	AQP4,CYP1A2,EFNA1,GBP6,IFIT1B,IGFBP3,ISG15,JUNB,PLK3,SAA2-SAA4,SERPINE1
E2F3		transcription regulator	Activated	2		0.1	1.801	5.37E-04	HIST1H2BG,HIST1H3D,HIST1H4B,HIST3H2A,SERPINE1
ACKR2		g-protein coupled receptor						5.60E-04	IFIT1B,Iigp1,ISG15
ADAM12		peptidase						6.11E-04	JUNB,SERPINE1
RNASEH2B		enzyme						6.11E-04	IFIT1B,ISG15
nicardipine		chemical drug						6.11E-04	CYP4A11,Cyp4a14
Vegf		group		1.348		0.135	0.97	6.19E-04	AQP4,CYP4A11,EFNA1,HDC,IGFBP3,INHBB,KLF1,SLC7A1
TMEM173		other						6.41E-04	HDC,IFIT1B,ISG15
Insulin		group		0.633		0.045	0.517	6.49E-04	CYP1A2,HIF3A,IGFBP3,LPIN1,SERPINE1,SLC7A1,TAT
EPHB1		kinase						7.45E-04	JUNB,SERPINE1
mifepristone		chemical drug		-0.714		-0.037	-0.632	7.57E-04	HDC,IGFBP3,INHBB,JUNB,SERPINE1,TAT
NCOA2		transcription regulator		-1.177		0.082	-1.338	7.79E-04	IFIT1B,ISG15,LPIN1,PPP1R3C
PAF1		other						8.23E-04	HIST1H2AC,ISG15,SERPINE1
glucocorticoid		chemical drug		1.372		-0.008	1.39	8.72E-04	GOT1,IGFBP3,LPIN1,PER1,SERPINE1,TAT
PARP1		enzyme		-1.98		0.098	-2.173	8.90E-04	GBP4,GBP6,GBP7,Iigp1
trientine		chemical drug						8.92E-04	IGFBP3,SERPINE1
trans-hydroxytamoxifen		chemical drug		0		-0.043	0.085	9.81E-04	EFNA1,EPOR,INHBB,PPP1R3C
MAPKAPK2		kinase						1.04E-03	HDC,Iigp1,MARCO
PTPRJ		phosphatase						1.04E-03	HDC,Iigp1,MARCO
bromodeoxyuridine		chemical drug						1.04E-03	IGFBP3,ISG15,SERPINE1
6-aminopyrazolopyrimidine derivative compound II		chemical - kinase inhibitor						1.05E-03	IFIT1B,ISG15
TREX1		enzyme						1.05E-03	IFIT1B,ISG15
dehydroepiandrosterone sulfate		chemical - endogenous mammalian						1.05E-03	CYP4A11,Cyp4a14
salmonella minnesota R595 lipopolysaccharides		chemical - endogenous non-mammalian		-0.392		0.185	-0.755	1.11E-03	IFIT1B,ISG15,JUNB,SERPINE1
Ins1		other		1.729		0.072	1.56	1.14E-03	Cyp2d9 (includes others),IGFBP3,JUNB,PER1,SERPINE1,TAT
IFNA10		cytokine						1.22E-03	ISG15,ZBP1
IFNA14		cytokine						1.22E-03	ISG15,ZBP1
IFNA21		cytokine						1.22E-03	ISG15,ZBP1
IFNA5		cytokine						1.22E-03	ISG15,ZBP1
IFNA6		cytokine						1.22E-03	ISG15,ZBP1
IFNA7		cytokine						1.22E-03	ISG15,ZBP1
DMD		other						1.23E-03	AQP4,ATP1B2,IFIT1B,LPIN1,PPP1R3C
SP600125		chemical - kinase inhibitor		-1.009		-0.08	-0.834	1.26E-03	H2AFX,ISG15,JUNB,PER1,SERPINE1
Pkc(s)		group		1.934		0.106	1.729	1.39E-03	AQP4,CYP2A6 (includes others),JUNB,PER1,SERPINE1
LEP		growth factor		1.569		0.072	1.4	1.40E-03	Cyp2c54 (includes others),Cyp2d9 (includes others),CYP4A11,Cyp4a14,IGFBP3,JUNB,SERPINE1
CGAS		enzyme						1.41E-03	IFIT1B,ISG15
CRKL		kinase						1.41E-03	HDC,Iigp1
EHHADH		enzyme						1.41E-03	CYP4A11,Cyp4a14
IFNA16		cytokine						1.41E-03	ISG15,ZBP1
IFNA8		cytokine						1.41E-03	ISG15,ZBP1
valproic acid		chemical drug		-0.169		-0.001	-0.168	1.56E-03	CITED4,CYP2A6 (includes others),Cyp2c54 (includes others),CYP4A11,Cyp4a14,SERPINE1,SMAD9
SOCS1		other		1.982		-0.136	2.252	1.58E-03	GBP6,IFIT1B,Iigp1,ISG15
epigallocatechin-gallate		chemical drug		1.432		-0.066	1.578	1.60E-03	AQP4,GBP4,ISG15,JUNB,SERPINE1
streptozocin		chemical drug		1.29		0.036	1.22	1.60E-03	ATP1B2,CYP4A11,Cyp4a14,SERPINE1,TAT
hydrocortisone		chemical - endogenous mammalian		1.982		0.023	1.937	1.66E-03	AQP4,IGFBP3,SERPINE1,TAT
F2RL1		g-protein coupled receptor						1.79E-03	GBP4,GBP6,Iigp1
IFNA1/IFNA13		cytokine						1.79E-03	CYP1A2,ISG15,ZBP1
FZD9		g-protein coupled receptor						1.82E-03	IFIT1B,ISG15
SMAD6		transcription regulator						1.82E-03	KLF1,SERPINE1
Smad2/3-Smad4		complex						1.82E-03	IGFBP3,SERPINE1
IFN Beta		group		-1.282		0.134	-1.545	1.85E-03	CYP1A2,IFIT1B,ISG15,ZBP1
aldosterone		chemical - endogenous mammalian		0.784		0.128	0.536	1.85E-03	AQP4,PER1,SERPINE1,TAT
entinostat		chemical drug						1.87E-03	H2AFX,IGFBP3,SERPINE1
TO-901317		chemical reagent						1.93E-03	CFH,Cyp2d9 (includes others),CYP4A11,Cyp4a14,SAA2-SAA4
NFIA		transcription regulator						2.04E-03	CYP1A2,CYP2A6 (includes others)
mannitol		chemical - endogenous mammalian						2.04E-03	AQP4,HDC
AHR		ligand-dependent nuclear receptor						2.10E-03	CYP1A2,CYP2A6 (includes others),GOT1,JUNB,SERPINE1,TFF3
trovafloxacin		chemical drug						2.13E-03	JUNB,SERPINE1,TAT

Day 5 Female PCB

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	
STAT1	1.55E+00	transcription regulator		1.178		-0.11	1.465	1.14E-08	CD274,GBP2,IL1B,JUN,PAX6,Serpina3g (includes others),STAT1	IFNG,STAT1,STAT3
PARP1		enzyme		1.088		-0.083	1.271	4.08E-08	CD274,GBP2,IL1B,JUN,STAT1	IFNG,PARP1,STAT1,STAT3
MAPK1		kinase		-1.387		0.003	-1.393	3.65E-07	GBP2,IL1B,JUN,RGS16,Serpina3g (includes others),STAT1	MAPK1,NFKBIA,NFkB (complex)
IL1B	-2.04E+00	cytokine		-0.663		-0.072	-0.466	4.08E-07	AQP4,CD274,GBP2,IL1B,JUN,PAX6,RGS16,STAT1	
SB203580		chemical - kinase inhibitor		0.359		0.131	0.047	5.15E-07	AQP4,CD274,GBP2,IL1B,JUN,STAT1	IFNB1,IL4,IRF1,IRF3,RELA,SB203580,STAT1,STAT3
Ifnar		group		1.982		-0.144	2.267	9.89E-07	CD274,GBP2,IL1B,STAT1	IFNB1,IRF1,IRF3,Ifnar,STAT1,STAT3,poly rI:rC-RNA
IL17A		cytokine		-0.775		-0.116	-0.52	1.49E-06	CD274,GBP2,IL1B,JUN,RGS16	IL17A,NFKBIA,NFkB (complex)
TAB1		enzyme						1.86E-06	GBP2,IL1B,JUN	MAP3K7,NFKBIA,TAB1
BTK		kinase	Inhibited	-2		-0.025	-1.951	2.86E-06	CD274,IL1B,JUN,STAT1	Akt,BTK,JUN,PI3K (complex),RELA
RAS		group						4.64E-06	CD274,GBP2,JUN,STAT1	
IL27		cytokine		1.687		-0.083	1.827	6.21E-06	CD274,GBP2,IL1B,STAT1	IL27,STAT1,STAT3
STAT3		transcription regulator		-0.074		-0.073	0.084	6.94E-06	CD274,GBP2,IL1B,PAX6,Serpina3g (includes others),STAT1	IFNG,STAT1,STAT3
Inflammasome (Nalp3, Asc, Casp1)		complex						7.30E-06	IL1B,SCD	
isoproterenol		chemical drug		-0.832		-0.099	-0.639	7.73E-06	AQP4,IL1B,JUN,SCD	LEP,PPARG,isoproterenol
TMEM173		other						7.96E-06	IL1B,RGS16,Serpina3g (includes others)	
IRF1		transcription regulator		0.94		-0.113	1.158	1.21E-05	CD274,GBP2,IL1B,STAT1	IRF1,STAT1,STAT3
IL10		cytokine		0.721		-0.017	0.759	1.29E-05	CD274,IL1B,JUN,RGS16,STAT1	
CD3 group		group						1.31E-05	GBP2,IL1B,SCD	
EBI3		cytokine						1.31E-05	CD274,GBP2,STAT1	EBI3,IL27,STAT3
ethanol		chemical - endogenous mammalian		-1.522		-0.047	-1.435	1.53E-05	AQP4,IL1B,JUN,SCD,STAT1	CEBPB,CTNNB1,IGF1,ethanol
manidipine		chemical drug						1.53E-05	IL1B,JUN	
TLR4		transmembrane receptor						1.55E-05	CD274,GBP2,IL1B,RGS16,STAT1	IFNB1,IRF1,IRF3,NFkB (complex),STAT3,TLR4,lipopolysaccharide
AQP4	-9.87E-01	transporter						2.04E-05	AQP4,IL1B	
25-hydroxycholesterol		chemical reagent						2.31E-05	IL1B,JUN,SCD	
HIF1A		transcription regulator		-1.253		-0.112	-1.006	2.42E-05	AQP4,CD274,IL1B,JUN,TTN	
Map3k7		kinase						2.42E-05	IL1B,JUN,SCD	
FAT1		other						2.62E-05	IL1B,JUN	
rosiglitazone		chemical drug		-0.464		-0.058	-0.352	2.68E-05	GBP2,IL1B,Mup1 (includes others),SCD,Serpina3g (includes others)	
cyclosporin A		biologic drug		1.96		0.047	1.868	3.26E-05	IL1B,JUN,Kap,SCD,TTN	
IRAK4		kinase						3.73E-05	IL1B,JUN,RGS16	IRAK4,NFKBIA,NFkB (complex)
JUN	-1.01E+00	transcription regulator		-1.047		-0.084	-0.881	3.75E-05	CD274,IL1B,JUN,SCD,STAT1	
epigallocatechin-gallate		chemical drug		0		0.056	-0.112	3.97E-05	AQP4,IL1B,JUN,STAT1	RARB,epigallocatechin-gallate
Mek		group		-1.398		-0.054	-1.295	4.11E-05	GBP2,IL1B,JUN,PAX6	
MAP3K7		kinase						4.19E-05	GBP2,IL1B,JUN	MAP3K7,NFKBIA,NFkB (complex)
poly rI:rC-RNA		biologic drug		0.601		-0.119	0.862	4.20E-05	CD274,GBP2,IL1B,JUN,STAT1	IFNB1,IL4,IRF1,IRF3,RELA,STAT1,STAT3,TLR3,poly rI:rC-RNA
fenretinide		chemical drug						4.35E-05	IL1B,JUN,STAT1	RARB,fenretinide
Gsk3		group						4.52E-05	IL1B,JUN,STAT1	
pentylenetetrazol		chemical drug						4.80E-05	IL1B,JUN	Ap1,pentylenetetrazol
imiquimod		chemical drug						4.87E-05	CD274,IL1B,STAT1	IRF1,IRF3,TLR7,imiquimod
FGF19		growth factor						5.42E-05	AQP4,RGS16,SCD	
hydroquinone		chemical - endogenous mammalian						5.67E-05	IL1B,JUN	
SOCS3		phosphatase						6.01E-05	IL1B,JUN,SCD	LEP,PPARG,SOCS3
U0126		chemical - kinase inhibitor		0.022		0.104	-0.185	6.26E-05	CD274,FOLR1,IL1B,JUN,PAX6	
TNFSF11		cytokine						6.55E-05	IL1B,JUN,RGS16,STAT1	MAPK1,NFKBIA,TNFSF11
MVP		other						6.61E-05	IL1B,JUN	Ap1,MVP
gamma-tocotrienol		chemical drug						6.61E-05	IL1B,JUN	
ATF3		transcription regulator						6.64E-05	GBP2,IL1B,JUN	
RARB		ligand-dependent nuclear receptor						6.64E-05	IL1B,JUN,STAT1	
TNF		cytokine		-0.054		-0.056	0.102	6.73E-05	CD274,GBP2,IL1B,JUN,PAX6,RGS16,SCD,STAT1	
TLR3		transmembrane receptor						6.75E-05	CD274,GBP2,IL1B,STAT1	IFN Beta,IFNB1,IRF1,IRF3,Interferon alpha,STAT1,STAT3,TLR3,poly rI:rC-RNA
LY294002		chemical - kinase inhibitor		0.533		0.121	0.309	6.80E-05	CD274,IL1B,JUN,SCD,TTN	
E. coli B5 lipopolysaccharide		chemical - endogenous non-mammalian		0.607		-0.076	0.754	6.85E-05	CD274,GBP2,IL1B,Mup1 (includes others)	
mir-21		microrna		-1		0.107	-1.213	6.85E-05	CD274,GBP2,IL1B,STAT1	IL4,IRF1,RELA,STAT1,STAT3,mir-21
SLC13A1		transporter						6.86E-05	GBP2,Kap,SCD	
IL4		cytokine		0.559		-0.096	0.786	7.47E-05	CD274,GBP2,IL1B,JUN,Serpina3g (includes others),STAT1	IFNG,IL4,IRF1,MAPK1,NFKBIA,STAT1,STAT3
IL18R1		transmembrane receptor						7.62E-05	IL1B,STAT1	
selumetinib		chemical drug						7.62E-05	CD274,JUN	
DPH5		enzyme						8.70E-05	IL1B,STAT1	
S1PR3		g-protein coupled receptor						8.70E-05	IL1B,JUN	
UCP2		transporter						8.70E-05	IL1B,SCD	NR1H3,UCP2,fatty acid
silicon dioxide		chemical drug						8.70E-05	IL1B,JUN	Ap1,MAPK8,TNFRSF1A,silicon dioxide
TNFSF10		cytokine						8.80E-05	IL1B,JUN,STAT1	
IFNG		cytokine		0.748		-0.07	0.929	9.43E-05	CD274,GBP2,IL1B,JUN,PAX6,Serpina3g (includes others),STAT1	IFNG,IL4,IRF1,RELA,STAT1,STAT3
GFI1		transcription regulator						9.61E-05	IL1B,JUN,STAT1	
E. coli B4 lipopolysaccharide		chemical toxicant		-0.398		-0.102	-0.2	9.65E-05	CD274,FOLR1,GBP2,IL1B	
IL2		cytokine		-0.553		-0.103	-0.323	1.02E-04	CD274,IL1B,JUN,RGS16,Serpina3g (includes others)	
IFNB1		cytokine		1.958		-0.074	2.102	1.03E-04	CD274,GBP2,IL1B,STAT1	IFNB1,IL27,IRF1,IRF3,Interferon alpha,STAT1,STAT3
MET		kinase						1.08E-04	CD274,IL1B,JUN	Akt,MET,PI3K (complex),RELA
Mapk		group						1.08E-04	IL1B,JUN,STAT1	
RAC1		enzyme						1.08E-04	IL1B,JUN,STAT1	
ADRB3		g-protein coupled receptor						1.11E-04	IL1B,JUN	
PDCD4		other						1.11E-04	IL1B,JUN	Ap1,PDCD4
S100B		other						1.11E-04	IL1B,JUN	Ap1,FOSL1,MAP2K1/2,S100B,nitric oxide
lisinopril		biologic drug						1.11E-04	IL1B,JUN	
mannitol		chemical - endogenous mammalian						1.11E-04	AQP4,JUN	
paclitaxel		chemical drug						1.16E-04	CD274,FOLR1,IL1B,JUN	Akt,PI3K (complex),RELA,paclitaxel
vemurafenib		chemical drug						1.24E-04	CD274,IL1B	
benzyloxycarbonyl-Leu-Leu-Leu aldehyde		chemical - protease inhibitor		-0.38		-0.075	-0.234	1.34E-04	IL1B,JUN,PAX6,STAT1	
IL10RA		transmembrane receptor		-1		-0.005	-0.991	1.37E-04	GBP2,IL1B,Serpina3g (includes others),STAT1	IL10RA,STAT1,STAT3
LY6E		other						1.38E-04	CD274,IL1B	
ammonium chloride		chemical drug						1.38E-04	AQP4,IL1B	
chitin		chemical - endogenous non-mammalian						1.38E-04	CD274,IL1B	
Tlr		group						1.40E-04	IL1B,RGS16,STAT1	
MAPK12		kinase						1.52E-04	IL1B,JUN	Ap1,MAPK12
IL12 (family)		group						1.55E-04	CD274,IL1B,STAT1	
ERN1		kinase						1.63E-04	IL1B,JUN,SCD	
PDGF BB		complex						1.66E-04	GBP2,IL1B,JUN,SCD	CEBPB,FGF2,FOXO1,PDGF BB
GADD45A		other						1.67E-04	IL1B,JUN	Ap1,GADD45A,MAPK8
Mt2		other						1.67E-04	IL1B,JUN	
resolvin D2		chemical - endogenous mammalian						1.67E-04	IL1B,JUN	
JAK2		kinase						1.71E-04	GBP2,IL1B,STAT1	
Pam3-Cys-Ser-Lys4		chemical reagent						1.75E-04	CD274,IL1B,STAT1	
NFkB (complex)		complex		-0.311		-0.136	-0.048	1.76E-04	CD274,GBP2,IL1B,JUN,RGS16	NFKBIA,NFkB (complex)
TCF3		transcription regulator						1.78E-04	IL1B,JUN,RGS16,Serpina3g (includes others)	
hydrochloric acid		chemical - endogenous mammalian						1.83E-04	IL1B,JUN	
lipoarabinomannan		chemical - endogenous non-mammalian						1.83E-04	IL1B,STAT1	
poly dA-dT		chemical reagent						1.83E-04	IL1B,STAT1	
zidovudine		chemical drug						1.83E-04	IL1B,STAT1	
medroxyprogesterone acetate		chemical drug						1.83E-04	IL1B,JUN,SCD	FOXO1,medroxyprogesterone acetate
dexamethasone		chemical drug		0.274		-0.016	0.31	1.85E-04	CD274,GBP2,IL1B,JUN,PAX6,SCD,STAT1,SYNGR4	

Day 60 Male PCB

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
MYOD1		transcription regulator	Inhibited	-2.236		-0.195	-1.7	5.72E-13	ACACB,BCL6,CKM,DUSP1,Hrc,JUNB,MAFB,MYH4,TNNC2,TNNT1,TNNT3,TTN	
HTT		transcription regulator						2.97E-12	BCL6,CKM,Cox8b,EGR1,FASN,FDPS,HBA1/HBA2,JUN,JUNB,Mup1 (includes others),MYH1,PPARD,RGS16,Sik1,SPP1,THRSP,TNNT3,Tpm2	ATF2,CEBPA,CREB1,CREBBP,ELK1,EP300,ESR1,FOS,FOSL1,FOXO1,FOXO3,HTT,Ins1,LEP,Mapk,NFkB (complex),PPARA,PPARG,RNA polymerase II,RXRA,SMAD3,SP1,YY1
STAT5B		transcription regulator		0.788		-0.086	1.029	3.60E-12	BCL6,CKMT2,Cox8b,CYP26B1,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,Mup1 (includes others),MYH1,SULT2A1,Sult3a1/Sult3a2,THRSP,TNNT1	
SCAP		other	Inhibited	-2.156	bias	-0.33	-1.239	3.62E-12	ACACB,ACSS2,FASN,FDPS,IGHM,PCSK9,PMVK,REG1A,THRSP	SCAP,SREBF1,SREBF2,cholesterol
atorvastatin		chemical drug	Inhibited	-2.042		0.052	-2.21	3.92E-11	DUSP1,EGR1,FDPS,HBA1/HBA2,HBB,JUN,JUNB,NR0B2,PCSK9,PMVK,SPP1	ATF2,CREB1,CREBBP,Ca2+,EGR1,ELK1,ERK1/2,ESR2,ETS2,FOS,FOSL1,JUN,JUNB,LDL,MAPK1,MYC,NFkB (complex),SMAD3,SP1,TP53,atorvastatin
carbon tetrachloride		chemical toxicant		-0.86		-0.211	-0.354	4.82E-11	CELA1,Cyp2b13/Cyp2b9,DUSP1,FABP1,IGFBP1,JUN,JUNB,NR0B2,PPARD,REG1A,SPP1	CEBPA,ESR1,FOS,FOXO3,HNF4A,IL6,JUN,NFkB (complex),NR3C1,PPARG,RXRA,SMAD3,SP1,SRF,TNF,TP53,carbon tetrachloride
RORC		ligand-dependent nuclear receptor						4.87E-11	ACACB,CKMT2,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,IGFBP1,Mup1 (includes others),SULT2A1,Sult3a1/Sult3a2,ZBTB16	
FGF19		growth factor		1.501		0.041	1.411	2.16E-10	ACACB,EGR1,FASN,FDPS,IGFBP1,NR0B2,RGS16,THRSP	
SREBF1		transcription regulator		-1.193		-0.242	-0.406	2.93E-10	ACACB,ACSS2,FASN,FDPS,IGHM,LPIN1,NR0B2,PCSK9,PMVK,THRSP,TTN	SCAP,SREBF1,SREBF2,cholesterol
NR5A2		ligand-dependent nuclear receptor		0.478		-0.249	1.133	3.44E-10	CELA1,CTRL,FASN,IGFBP1,JUN,JUNB,NR0B2,PNLIP	
RORA		ligand-dependent nuclear receptor						3.96E-10	ACACB,CKMT2,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,FASN,IGFBP1,Mup1 (includes others),SULT2A1,Sult3a1/Sult3a2	
SREBF2		transcription regulator		-1.976	bias	-0.274	-1.272	3.61E-09	ACSS2,FASN,FDPS,PCSK9,PMVK,REG1A,THRSP	SREBF1,SREBF2,cholesterol
lipopolysaccharide		chemical drug		-0.183		-0.172	0.561	6.04E-09	BCL6,CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,DUSP1,EGR1,FASN,IGFBP1,IGHM,JUN,JUNB,LPIN1,MAFB,NR0B2,PPARD,RGS16,SPP1,SULT2A1,THRSP,TNNT3,Tpm2,TSC22D3	CEBPA,ESR1,ESR2,FOS,FOXO3,HDAC1,HNF4A,IL1B,IL6,JUN,MYC,NFkB (complex),NR3C1,PPARG,SMAD3,TGFB1,TP53,lipopolysaccharide,progesterone
SRF		transcription regulator	Inhibited	-2.187		-0.139	-1.884	7.75E-09	CKM,EGR1,IGHM,JUN,JUNB,MYH1,MYH2,MYH4,TNNT1,Tpm2,TTN	CEBPA,HNF4A,NFkB (complex),SMAD3,SP1,SRF
TNF		cytokine		-1.669		-0.123	-1.109	8.25E-09	BCL6,CKM,CYP26B1,DUSP1,EFNA1,EGR1,FABP1,FASN,FDPS,IGFBP1,JUN,JUNB,MFSD2A,NR0B2,PCSK9,PPARD,RGS16,RNASE1,SPP1,SULT2A1,THRSP,TSC22D3	CEBPA,EGF,EGR1,ELK1,ESR1,FOS,HDAC1,HNF4A,IL1B,JUN,MYC,NFkB (complex),NR3C1,POU2F2,PPARA,PPARG,RXRA,SMAD3,SP1,TNF,TP53
IL1B		cytokine		-1.806		-0.157	-1.219	9.60E-09	BCL6,CYP3A5,DUSP1,EFNA1,EGR1,FABP1,IGFBP1,JUN,JUNB,NR0B2,RGS16,RNASE1,SLC25A25,SPP1,THRSP,TSC22D3	CEBPA,EGR1,ELK1,ESR1,FOS,FOXO1,FOXO3,HDAC1,HNF4A,IGF1,IL1B,IL6,JUN,NFkB (complex),NR3C1,POU2F2,PPARG,SMAD3,SP1,TNF,TP53
TP53		transcription regulator		-0.565		-0.076	-0.254	1.47E-08	ACACB,ACSS2,CKM,CKMT2,Cox8b,CYP26B1,DUSP1,EFNA1,EGR1,FASN,FDPS,JUN,JUNB,LPIN1,MAFB,NR0B2,PPARD,RGS16,SPP1,Tpm2,TSC22D3,TTN	CEBPA,CREB1,ELK1,ESR1,FOS,FOSL1,HNF4A,IGF2,JUN,MAPK14,Mapk,NFkB (complex),NR3C1,PPARG,SMAD3,SP1,SRF,TNF,TP53
PD98059		chemical - kinase inhibitor		1.155		0.216	0.461	1.53E-08	BCL6,DUSP1,EGR1,FASN,IGFBP1,JUN,JUNB,PPARD,PRSS3,SPP1,TSC22D3	ATF2,CEBPB,CREB1,EGF,EGFR,EGR1,ELK1,ERK,FOS,FOSL1,FOXO3,HTT,IFNG,JUN,MYC,PD98059,SMAD3,SP1,SRF,TNF,TP53,VitaminD3-VDR-RXR
triamcinolone acetonide		chemical drug		1.468		-0.008	1.492	1.74E-08	DUSP1,EGR1,JUN,JUNB,RGS16,SPP1,SULT2A1,TSC22D3,ZBTB16	ATF1,ATF2,ESR1,HDAC1,JUN,Jnk,MYC,NFkB (complex),NR3C1,POU2F2,RARA,SMAD3,triamcinolone acetonide
dexamethasone		chemical drug		-0.591		-0.035	-0.439	2.12E-08	ACSS2,BCL6,CYP2A6 (includes others),CYP3A5,DUSP1,EFNA1,EGR1,FASN,IGFBP1,IGHM,JUN,JUNB,LPIN1,PCSK9,PNLIPRP2,PPARD,REG1A,SPP1,SULT2A1,THRSP,TNNT1,TSC22D3,ZBTB16	CEBPA,CREB1,ESR1,FOS,FOXO3,HDAC1,HNF4A,IL6,Insulin,JUN,MYC,NFkB (complex),NR3C1,POU2F2,PPARG,SP1,USF1,USF2,dexamethasone
ethanol		chemical - endogenous mammalian		0.668		-0.102	0.977	2.17E-08	CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,DUSP1,EGR1,FASN,IGHM,JUN,LPIN1,Sik1,TSC22D3	ATF2,ATM,CREB1,CREM,ELK1,EP300,FOS,MAPK8,MYC,NR3C1,PRKCB,SMAD3,SP1,TP53,ethanol,prostaglandin E2
sterol		chemical - endogenous mammalian		-0.072		0.172	-0.402	2.26E-08	ACSS2,FASN,FDPS,LPIN1,PCSK9	INSIG1,SCAP,SREBF1,SREBF2,Srebp,sterol
RXRA		ligand-dependent nuclear receptor		0.794		-0.178	1.112	2.50E-08	ACACB,CYP3A5,FABP1,FASN,IGFBP1,NR0B2,PPARD,SPP1,SULT2A1,THRSP	CEBPA,HNF4A,MYC,NCOA3,NR0B2,NR1H4,NR1I3,PPARA,PPARG,RARA,RXRA,RXRB,VitaminD3-VDR-RXR,alitretinoin
glucocorticoid		chemical drug		-0.016		0.016	-0.062	2.50E-08	CYP3A5,DUSP1,FASN,IGFBP1,IGHM,LPIN1,Mup1 (includes others),SPP1,TSC22D3,ZBTB16	
cholesterol		chemical - endogenous mammalian		1.669		-0.106	1.982	2.59E-08	ACSS2,CYP3A5,FASN,FDPS,NR0B2,PCSK9,PMVK,RGS16,Sult3a1/Sult3a2	INSIG1,SCAP,SREBF1,SREBF2,Srebp,cholesterol
Growth hormone		group		-0.529		-0.142	-0.163	3.66E-08	BCL6,EGR1,FASN,FDPS,HBB,IGFBP1,JUN,JUNB,SPP1	CEBPA,CEBPB,CREB1,EGR1,ELK1,ESR2,FOS,FOSL1,FOXO1,FOXO3,GH1,Growth hormone,IGF1,INS,JUN,MYC,NFkB (complex),NR3C1,SMAD3,SP1,STAT3,VitaminD3-VDR-RXR
beta-estradiol		chemical - endogenous mammalian	Inhibited	-3.005		-0.113	-2.503	4.16E-08	BCL6,CKM,CYP26B1,CYP2A6 (includes others),DUSP1,EFNA1,EGR1,FASN,HBA1/HBA2,HBB,IGFBP1,JUN,JUNB,LPIN1,NR0B2,RGS16,THRSP,TNNC2,TNNT1,TNNT3,TSC22D3,TTN	ATF1,ATF2,CREB1,EGFR,EGR1,ELK1,ESR1,ESR2,FOS,FOSL1,FOXO1,FOXO3,HDAC1,HNF4A,HTT,IL1B,INS,JUN,MYC,NFkB (complex),NR3C1,PPARG,TNF,TP53,beta-estradiol,cyclic AMP
TO-901317		chemical reagent		-1.555		-0.105	-1.325	4.57E-08	Cox8b,CYP3A5,FASN,FDPS,Mup1 (includes others),NR0B2,PCSK9,SULT2A1,THRSP	NCOA3,NR0B1,NR1H2,NR1H3,NR1H4,NR1I3,NR5A1,PPARA,PPARG,RXRA,SREBF1,SREBF2,TO-901317,cholesterol
LY294002		chemical - kinase inhibitor	Activated	2.346	bias	0.265	1.504	5.45E-08	ACSS2,BCL6,DUSP1,EGR1,FASN,IGHM,JUN,JUNB,PPARD,SPP1,TTN,ZBTB16	ATF2,CREB1,EGFR,EGR1,ELK1,ERK1/2,ETS2,FOS,FOSL1,FOXO3,HRAS,HTT,JUN,KRAS,LY294002,MYC,NFkB (complex),SMAD3,TP53,nitric oxide
methotrexate		chemical drug		-1.342		-0.052	-1.226	5.87E-08	ACACB,ACSS2,DUSP1,FABP1,FASN,HBA1/HBA2,LPIN1,PPARD,SPP1	NFkB (complex),SMAD3,TP53,WT1,methotrexate
TEAD4		transcription regulator						7.33E-08	CKM,JUN,JUNB,MYH1,MYH4	
MEF2C		transcription regulator	Inhibited	-2.415		-0.23	-1.859	9.36E-08	CKM,JUN,JUNB,MYH1,MYOZ1,TNNT1,TTN	
E. coli B5 lipopolysaccharide		chemical - endogenous non-mammalian		-0.376		-0.166	0.113	1.04E-07	BCL6,CYP3A5,DUSP1,FABP1,FASN,IGFBP1,JUNB,Mup1 (includes others),SPP1	E. coli B5 lipopolysaccharide,ESR1,FOS,FOXO3,HDAC1,HNF4A,IL1B,IL6,JUN,NFkB (complex),NR3C1,PPARG,TNF,TP53
MAPK14		kinase		-0.236		-0.203	0.29	1.12E-07	CKM,DUSP1,EFNA1,FASN,FDPS,JUN,JUNB,Tpm2	CREB1,ELK1,ESR1,FOS,FOSL1,HDAC6,MAPK14,MYC,Mek,NFkB (complex),PPARG,RNA polymerase II,RPS6KA4,RPS6KA5,SMAD3,SRF,TGFB1,TP53,WT1
MED13		transcription regulator						1.13E-07	CYP2A6 (includes others),FASN,PCSK9,Sik1,THRSP	
RNA polymerase II		complex						1.63E-07	CKM,DUSP1,HBB,IGFBP1,JUN,JUNB,SPP1,TNNT1,XIST	
IGF1		growth factor	Inhibited	-2.498		-0.167	-1.962	2.26E-07	ACSS2,DUSP1,EGR1,FASN,HBB,IGFBP1,JUN,JUNB,SLC25A25,SPP1,THRSP	CEBPA,CEBPB,CREB1,EGR1,ELK1,ESR1,FOS,FOSL1,FOXO1,FOXO3,GH1,Growth hormone,IGF1,INS,LEP,NFkB (complex),NR3C1,SMAD3,SP1,STAT3,VitaminD3-VDR-RXR
NFYA		transcription regulator		-1	bias	-0.252	-0.497	2.34E-07	EGR1,FASN,JUN,JUNB,LPIN1,THRSP	
EPO		cytokine		-1.295		-0.179	-0.828	2.63E-07	BCL6,EGR1,FABP1,HBA1/HBA2,HBB,JUN,JUNB,SPP1,TSC22D3	ATF2,ELK1,ELK4,EPO,ESR2,ETS2,FOS,GATA1,HDAC6,Hdac,JUN,MAPK1,MAPK3,MYC,NFkB (complex),SP1
L-triiodothyronine		chemical - endogenous mammalian		-2		-0.103	-1.684	2.68E-07	DUSP1,EFNA1,EGR1,FABP1,FASN,HBA1/HBA2,IGFBP1,Mup1 (includes others),THRSP,TTN	AGT,ATF2,CREB1,FOS,Insulin,L-triiodothyronine,MYC,NCOR1,SP1,TP53,USF1,USF2
CREBBP		transcription regulator		-1.59		-0.227	-1.036	3.31E-07	BCL6,CKM,DUSP1,EGR1,FDPS,HBB,JUN,MYH1,THRSP,XIST	ATF2,CREBBP,EP300,MYC,PML,RB1,RNA polymerase II,SP1,YY1
DMD		other						3.37E-07	CKMT2,LPIN1,Mup1 (includes others),MYH1,MYH2,MYH4,MYOZ1,OBSCN	
okadaic acid		chemical toxicant		0.092		-0.112	0.361	3.53E-07	BCL6,EGR1,JUN,JUNB,SPP1,THRSP	ATF2,EGR1,ELK1,ELK4,ERK1/2,ETS2,FOS,FOSL1,HDAC6,MAPK3,Mapk,NFkB (complex),Pkc(s),RARA,RARB,SMAD3,SP1,okadaic acid
INSR		kinase						3.55E-07	CKMT2,Cox8b,DUSP1,EGR1,FASN,FDPS,IGFBP1,JUNB,RGS16,Tpm2	ATF2,CREB1,D-glucose,EGR1,ELK1,ERK,FOS,FOSL1,FOXO1,FOXO3,IGF2,INS,INSR,Ins1,JUN,MYC,NFkB (complex),SMAD3,SP1,TP53
prostaglandin E2		chemical - endogenous mammalian		0.314		-0.124	0.599	4.87E-07	DUSP1,EGR1,FASN,IGFBP1,JUN,MAFB,MYOZ1,THRSP,TSC22D3	ATF2,EGR1,ELK1,ERK,FOS,FOSL1,FOXO1,FOXO3,IGF1,Ins1,JUN,SMAD3,SP1,arachidonic acid,prostaglandin E2
Ins1		other		-1.517		-0.133	-1.133	5.00E-07	CKM,Cox8b,EGR1,FASN,IGFBP1,JUN,JUNB,PPARD,THRSP	ATF1,CEBPA,D-glucose,EGR1,ELK1,ESR2,FOS,FOXO1,GH1,HNF4A,IRS2,Ins1,MYC,NFkB (complex),NR3C1,SMAD3,SP1,SRF,STAT3,TP53,cyclic AMP
6,7-dinitroquinoxaline-2,3-dione		chemical reagent						5.61E-07	EGR1,JUN,JUNB	6,7-dinitroquinoxaline-2,3-dione,EGR1,FOS,GNRH1,NFkB (complex)
6-cyano-7-nitroquinoxaline-2,3-dione		chemical reagent						5.61E-07	EGR1,JUN,JUNB	
GPER1		g-protein coupled receptor		-1.459	bias	-0.316	-0.773	5.63E-07	DUSP1,EGR1,FASN,JUN,RGS16	ATF2,CREB1,Ca2+,EGR1,ELK1,ERK1/2,ETS2,FOS,FOSL1,GPER1,Insulin,JUNB,MAP2K1,MAPK1,MYC,NFkB (complex),SMAD3,SP1,THRA,USF1,USF2
ZBTB20		transcription regulator		-0.447		-0.02	-0.402	5.63E-07	ACSS2,Cyp2b13/Cyp2b9,CYP3A5,FASN,IGFBP1	
NR1I2		ligand-dependent nuclear receptor		-1.417		-0.085	-1.202	5.77E-07	CYP2A6 (includes others),CYP3A5,FASN,JUN,Mup1 (includes others),NR0B2,SULT2A1	
MAP3K1		kinase		-1.922		-0.247	-1.447	6.82E-07	DUSP1,EGR1,JUN,MYH2,PPARD	ATF1,ATF2,ELK1,Jnk,MAP2K1/2,MAP3K1,MAPK8,MYC,NR3C1,RARA,RAS,SMAD3,SP1,TP53
INSIG1		other		1.72	bias	0.336	0.92	7.41E-07	ACACB,ACSS2,FASN,FDPS,LPIN1,PMVK	INSIG1,SREBF1,SREBF2,Srebp,cholesterol
anisomycin		chemical - endogenous non-mammalian	Inhibited	-2.202		-0.124	-1.928	7.49E-07	DUSP1,EGR1,JUN,JUNB,SPP1	ATF2,EGR1,ELK1,ELK4,ERK1/2,ETS2,FOS,FOSL1,HDAC6,Hdac,MAPK1,MAPK3,Mapk,NFkB (complex),SMAD3,SP1,anisomycin
TCF3		transcription regulator		0.66		-0.034	0.726	8.37E-07	ACACB,BCL6,CELA1,CKM,IGHM,JUN,NR0B2,PRSS3,RGS16	
NR3C1		ligand-dependent nuclear receptor		-0.401		-0.054	-0.263	9.16E-07	BCL6,CYP2A6 (includes others),CYP3A5,DUSP1,EFNA1,EGR1,IGFBP1,JUN,MFSD2A,NR0B2,SPP1,TSC22D3	CEBPA,ESR1,FOS,FOXO3,HNF4A,IL6,JUN,MED1,NFkB (complex),NR3C1,PPARG,RNA polymerase II,RXRA,SMAD3,TNF,TP53,dexamethasone
PPARGC1A		transcription regulator		-2		-0.243	-1.318	9.28E-07	ACACB,CKMT2,CYP2A6 (includes others),CYP3A5,FASN,LPIN1,MYH1,SULT2A1	
KMT5B		enzyme						9.80E-07	DUSP1,IGFBP1,TSC22D3	
NR1I3		ligand-dependent nuclear receptor		-1.559	bias	-0.287	-0.937	1.10E-06	CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,FASN,SULT2A1,THRSP	CEBPA,HNF4A,JUN,NR1H4,NR1I3,PPARG,lithocholic acid
CEBPA		transcription regulator		0.012		-0.117	0.354	1.14E-06	CYP2A6 (includes others),CYP3A5,FASN,JUN,JUNB,Mup1 (includes others),PPARD,SPP1,SULT2A1,TSC22D3	CEBPA,ESR1,FOS,HNF4A,Histone h3,JUN,NFkB (complex),NR3C1,PPARA,PPARG,RXRA,SP1
MAPK1		kinase		-0.426		0.006	-0.443	1.15E-06	DUSP1,EGR1,HBA1/HBA2,HBB,JUN,JUNB,MYH4,RGS16,SPP1	CEBPA,CREB1,EGR1,ELK1,ELK4,ERK1/2,ETS2,FOS,FOSL1,HDAC6,HNF4A,Hdac,JUN,MAPK1,MAPK3,NFkB (complex),SMAD3,TP53,nitric oxide
TAF4B		transcription regulator						1.18E-06	IGHM,JUN,SPP1,ZBTB16	
8-bromo-cAMP		chemical reagent	Inhibited	-2.528		-0.189	-2.049	1.39E-06	DUSP1,EGR1,IGFBP1,JUN,PPARD,SPP1,SULT2A1	8-bromo-cAMP,ATF1,ATF2,CEBPB,CG,CREB1,EGR1,ELK1,ERK,FOS,FOSL1,JUN,Jnk,MYC,NFkB (complex),NR3C1,RARA,RXRA,SMAD3,SP1,VitaminD3-VDR-RXR
A23187		chemical reagent		-0.806		-0.221	-0.272	1.50E-06	EGR1,JUN,JUNB,MYH1,MYH2,THRSP	A23187,ATF1,ATF2,CREB1,CREBBP,Ca2+,EGR1,ELK1,EP300,ESR2,FOS,FOSL1,JUN,JUNB,NFkB (complex),P38 MAPK,RARG,RNA polymerase II,YY1,cyclic AMP,lysophosphatidic acid
GH1		growth factor		-0.555		-0.058	-0.425	1.50E-06	EGR1,FASN,IGFBP1,JUN,JUNB,SPP1	EGR1,ELK1,ELK4,ESR2,FOS,FOXO1,GH1,Growth hormone,HDAC6,Hdac,IGF1,JUN,MAPK3,MYC,NFkB (complex),SP1,STAT3
acetic acid		chemical - endogenous mammalian						1.56E-06	EGR1,JUN,JUNB	ATF2,ERK,FOSL1,JUN,SMAD3,SP1,acetic acid
aplidine		biologic drug						1.56E-06	DUSP1,JUN,JUNB	ATF1,ATF2,CREB1,EGFR,EGR1,ELK1,FADD,FOXO3,HTT,Jnk,MYC,NFkB (complex),P38 MAPK,RAC1,RARA,RARG,SMAD3,aplidine
MEF2		group						1.62E-06	CKM,JUN,MYH1,MYH4	
PPARG		ligand-dependent nuclear receptor		-1.178		-0.107	-0.887	1.85E-06	BCL6,FABP1,FASN,FDPS,IGFBP1,JUN,PPARD,SPP1,Tpm2,TSC22D3	Akt,CEBPB,EGR1,ELK1,ESR1,JUN,MYC,NR3C1,PPARA,PPARD,PPARG,SMAD3,SP1,TGFB1,TNF,TP53,VitaminD3-VDR-RXR,indomethacin
ARRB1		other						1.87E-06	EGR1,FASN,JUNB,SPP1	ARRB1,CEBPA,EGR1,ELK1,ELK4,ERK1/2,ETS2,FOS,FOSL1,FOXO3,HDAC6,HNF4A,IRS1,MAPK3,Mapk,NFkB (complex),SMAD3,SP1,TP53
PTCH1		transmembrane receptor	Activated	2		0.165	1.669	1.87E-06	MYH1,TNNT1,TNNT3,Tpm2	
SMTNL1		other	Activated	2		0.178	1.645	1.87E-06	MYH4,TNNC2,TNNT3,Tpm2	
MLXIPL		transcription regulator						2.15E-06	ACACB,FASN,RGS16,THRSP	
cycloheximide		chemical reagent		-1.439		0.042	-1.554	2.18E-06	CKM,CYP3A5,DUSP1,EGR1,FABP1,IGFBP1,JUN,JUNB,SPP1	EGR1,ELK1,ELK4,ERK1/2,ETS2,FOS,FOSL1,FOXO3,HDAC1,HDAC6,HNF4A,IGF2,IL1B,IL6,JUN,MAPK3,NFkB (complex),NR3C1,SMAD3,cycloheximide
LIPE		enzyme						2.22E-06	ACSS2,BCL6,EGR1,FASN,MYH4,THRSP	
tamoxifen		chemical drug		-0.264		-0.041	-0.151	2.25E-06	CYP3A5,FABP1,FASN,JUN,JUNB,NR0B2,SPP1,SULT2A1	CEBPA,ELK1,ELK4,ESRRA,FOS,HDAC1,HDAC6,HNF4A,IL1B,JUN,MAPK3,NFkB (complex),NR1I2,NR3C1,SMAD3,TP53,tamoxifen
Gm15807/Hmgn5	1.21E+00	other						2.81E-06	Mup1 (includes others),TNNC2,TNNT3,Tpm2	
Calcineurin protein(s)		complex		-0.068		-0.195	0.317	2.89E-06	CKM,CKMT2,DUSP1,EGR1,SPP1	ATF2,CREB1,Ca2+,Calcineurin protein(s),EGR1,ELK1,ERK1/2,ETS2,FOS,FOSL1,JUN,JUNB,MYC,MYD88,NFkB (complex),SMAD3,SRC
GCG		other		0.73		-0.181	1.127	2.89E-06	FASN,FDPS,IGFBP1,LPIN1,Sik1	
Sik1	-1.12E+00	kinase						3.34E-06	DUSP1,FASN,THRSP	
pCPT-cAMP		chemical - kinase inhibitor						3.34E-06	EGR1,JUN,JUNB	CREB1,CREM,ELK1,ELK4,FOS,GLI3,HDAC6,MAPK3,NFkB (complex),Pka,RARA,pCPT-cAMP
Insulin		group	Inhibited	-2.302		-0.085	-2.052	3.48E-06	DUSP1,EGR1,FASN,IGFBP1,JUN,LPIN1,PCSK9,PPARD,THRSP	ATF1,ATF2,D-glucose,EGR1,ELK1,ERK,FOSL1,FOXO1,IRS2,Insulin,JUN,Jnk,MYC,NFYA,NR3C1,RARA,SMAD3,SP1,TP53,cisplatin
tretinoin		chemical - endogenous mammalian		-0.681		-0.123	-0.205	3.86E-06	ACACB,ACSS2,BCL6,CYP26B1,DUSP1,EGR1,FASN,IGHM,JUN,MAFB,NR0B2,PNLIPRP2,PPARD,RNASE1,SPP1,TSC22D3,ZBTB16	ATF2,Akt,CREB1,EP300,ESR1,FOS,IFNG,JUN,MYC,NFkB (complex),PPARG,RARA,SMAD3,SP1,TGFB1,TP53,WT1,tretinoin
NR0B2	7.87E-01	ligand-dependent nuclear receptor						4.04E-06	EGR1,FASN,LPIN1,NR0B2,SPP1	AGT,ATF2,CREB1,ESR1,ESR2,FOS,FOXO3,IRS1,MYC,NCOA1,NCOA2,NR0B2,SMAD3,TP53
mercuric chloride		chemical toxicant						4.56E-06	JUN,JUNB,Mup1 (includes others),SPP1	
EPHB1		kinase						4.58E-06	EGR1,JUN,JUNB	ATF2,CREB1,EGR1,ELK1,ELK4,EPHB1,ERK,ERK1/2,ETS2,FOS,FOSL1,HDAC6,HRAS,JUN,MAPK3,MYC,NFkB (complex),P38 MAPK,RARG,SMAD3,SP1,TP53
SLC51A		transporter						4.58E-06	CYP3A5,NR0B2,SULT2A1	
MAP2K1/2		group		-1.949		-0.2	-1.559	4.88E-06	DUSP1,EGR1,JUN,MYH2,Sik1	ATF1,ATF2,CREB1,EGR1,ELK1,EP300,ERK,ERK1/2,ETS2,FOSL1,JUN,Jnk,MAP2K1/2,MYC,P38 MAPK,RARA,RARG,SMAD3,SP1
PPARD	-1.38E+00	ligand-dependent nuclear receptor		-0.346		-0.135	-0.05	4.93E-06	ACACB,FABP1,FASN,IGFBP1,MFSD2A,PCSK9,PPARD	CREB1,Insulin,MYC,NCOA3,NR1H4,NR1I3,PPARA,PPARD,PPARG,RXRA,SP1,USF1,USF2,linoleic acid,palmitic acid
4-methylnitrosoamino-1-(3-pyridinyl)-1-butanone		chemical toxicant		-0.866		-0.206	-0.462	5.10E-06	FASN,JUN,JUNB,SPP1	4-methylnitrosoamino-1-(3-pyridinyl)-1-butanone,CEBPA,EGR1,ELK1,ELK4,ERK1/2,ESR1,ESR2,ETS2,FOS,FOSL1,HDAC6,HNF4A,MAPK3,Mapk,NFkB (complex),SMAD3,SP1,TP53
lovastatin		chemical drug		-1.964		-0.137	-1.695	5.11E-06	FASN,FDPS,HBA1/HBA2,PCSK9,PMVK,PPARD	SREBF1,SREBF2,lovastatin
CASZ1		enzyme		-1.131		0.108	-1.346	5.69E-06	CKM,MYOZ1,Sik1,TNNT1	
kainic acid		chemical toxicant		-1.405		-0.236	-0.844	5.77E-06	DUSP1,EGR1,JUN,JUNB,Sik1,SPP1	ATF2,BDNF,CREB1,CREM,Ca2+,EGR1,ELK1,EP300,ERK1/2,ETS2,FOS,FOSL1,JUNB,NFkB (complex),NR3C1,Pkc(s),RARA,RARB,SMAD3,kainic acid
NCOA1		transcription regulator						6.00E-06	EGR1,JUNB,LPIN1,NR0B2,PPARD,THRSP	CEBPA,HNF4A,NCOA1,NFkB (complex),SMAD3,SP1,SRF
DBI		other						6.09E-06	ACSS2,FASN,PPARD	
RPS6KA4		kinase						6.09E-06	DUSP1,JUN,JUNB	CREB1,CREM,EP300,FOS,FOXO3,IL6,JUN,NFkB (complex),NR3C1,RPS6KA4
chenodeoxycholic acid		chemical - endogenous mammalian		0.733		-0.092	0.904	6.20E-06	CYP3A5,EGR1,FASN,NR0B2,SULT2A1	ESR1,HNF4A,Histone h3,NR0B2,NR1H4,NR1I2,RXRA,SP1,chenodeoxycholic acid
phenobarbital		chemical drug	Inhibited	-2.191		-0.236	-1.675	6.20E-06	CYP2A6 (includes others),Cyp2b13/Cyp2b9,CYP3A5,SULT2A1,THRSP	CEBPA,NR1I2,NR1I3,phenobarbital
ATP7B		transporter		-1		-0.046	-0.907	6.32E-06	FASN,FDPS,LPIN1,THRSP	
FOXO1		transcription regulator		-1.255		-0.214	-0.708	7.43E-06	CKMT2,EGR1,FASN,FDPS,IGFBP1,JUN,JUNB,SLC25A25,TNNT1	EGF,EGR1,FOS,FOXO1,FOXO3,Ins1,JUN,MYC,NCOA1,SMAD3,SP1

Day 60 Female PCB

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Notes	Bias Term	Bias-corrected z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
RORC		ligand-dependent nuclear receptor						2.58E-08	CYP3A5,IGFBP1,LCN2,Mup1 (includes others),SULT2A1,Sult3a1/Sult3a2	
STAT5B		transcription regulator						3.36E-08	A1BG,CYP3A5,GCK,Mup1 (includes others),SULT2A1,Sult2a2,Sult3a1/Sult3a2	
FGF19		growth factor						5.08E-08	EGR1,GCK,IGFBP1,LCN2,RGS16	ERK,FGF19,FOXO3
RORA		ligand-dependent nuclear receptor						9.16E-08	CYP3A5,IGFBP1,LCN2,Mup1 (includes others),SULT2A1,Sult3a1/Sult3a2	
NR1I2		ligand-dependent nuclear receptor		1.498		0.076	1.336	1.12E-06	CYP3A5,LCN2,Mup1 (includes others),SULT2A1,Sult2a2	
RXRA		ligand-dependent nuclear receptor						1.15E-06	CYP3A5,GCK,IGFBP1,LCN2,ONECUT1,SULT2A1	
bucladesine		chemical toxicant		-1.446		0.172	-1.824	3.03E-06	CYP3A5,EGR1,GCK,IGFBP1,IGFBP5,RGS16	
IL1B		cytokine		-0.946		0.14	-1.331	6.54E-06	CYP3A5,EGR1,GCK,IGFBP1,IGFBP5,LCN2,RGS16,SAA2-SAA4	AKT1,FOXO3,IGF1,IL1B,IL6
TO-901317		chemical reagent						8.01E-06	CYP3A5,GCK,Mup1 (includes others),SAA2-SAA4,SULT2A1	
CEBPA		transcription regulator		0.849		0.105	0.641	1.24E-05	CYP3A5,LCN2,Mup1 (includes others),ONECUT1,SULT2A1,Sult2a2	
PPARA		ligand-dependent nuclear receptor						1.34E-05	ETHE1,GCK,IGFBP1,IGFBP5,Mup1 (includes others),SULT2A1	
IRS2		enzyme						1.59E-05	EGR1,GCK,IGFBP1	AKT1,FOXO3,IRS2
NANOG		transcription regulator						1.62E-05	EGR1,GCK,IGFBP1,ONECUT1	
AKT1		kinase		1.25		0.141	0.966	1.74E-05	EGR1,GCK,IGFBP1,IGFBP5,LCN2	AKT1,ERK,FOXO3,IL6
ZMPSTE24		peptidase						2.10E-05	IGFBP1,IGFBP5,RGS16	
CYP1A2		enzyme						2.25E-05	ETHE1,RGS16,Sult3a1/Sult3a2	
VitaminD3-VDR-RXR		complex						2.25E-05	IGFBP1,IGFBP5,SULT2A1	
H89		chemical - kinase inhibitor		0.038		-0.216	0.46	2.30E-05	EGR1,IGFBP1,IGFBP5,SULT2A1	
ciprofibrate		chemical drug		0.132		-0.013	0.158	2.63E-05	IGFBP1,LCN2,Mup1 (includes others),SULT2A1	
ZBTB20		transcription regulator						3.26E-05	CYP3A5,GCK,IGFBP1	
INS		other						3.33E-05	EGR1,GCK,IGFBP1,IGFBP5	AKT1,FOXO3,IGF1,INS
MED1		transcription regulator						3.59E-05	CYP3A5,GCK,IGFBP1,SULT2A1	
EGLN		group		-0.132	bias	-0.296	0.456	3.96E-05	A1BG,IGFBP1,LCN2,Mup1 (includes others)	
CYP1B1		enzyme						4.07E-05	ETHE1,RGS16,Sult3a1/Sult3a2	
CSHL1		growth factor						4.77E-05	CYP3A5,IGFBP1,ONECUT1	
cycloheximide		chemical reagent		-1.309		-0.038	-1.227	7.27E-05	CYP3A5,EGR1,IGFBP1,IGFBP5,LCN2	AKT1,ERK,FOXO3,IL6,cycloheximide
SLC51A		transporter						7.56E-05	CYP3A5,SULT2A1	
FOXA2		transcription regulator						7.82E-05	GCK,IGFBP1,IGFBP5,ONECUT1	
deferoxamine		chemical drug		-1		0.171	-1.341	8.80E-05	CYP3A5,EGR1,IGFBP5,LCN2	
betamethasone		chemical drug						9.07E-05	CYP3A5,SULT2A1	
cholesterol		chemical - endogenous mammalian		0.152		0.095	-0.037	1.32E-04	CYP3A5,RGS16,SAA2-SAA4,Sult3a1/Sult3a2	
chenodeoxycholic acid		chemical - endogenous mammalian						1.37E-04	CYP3A5,EGR1,SULT2A1	
rosiglitazone		chemical drug		0.314		0.112	0.068	1.37E-04	GCK,IGFBP1,IGFBP5,LCN2,Mup1 (includes others)	AKT1,FOXO3,IGF1,rosiglitazone
diethylnitrosamine		chemical toxicant						1.47E-04	IGFBP1,LCN2,Mup1 (includes others)	
potassium chloride		chemical drug						1.47E-04	EGR1,IGFBP1,IGFBP5	
Growth hormone		group		0.8		0.128	0.55	1.54E-04	EGR1,IGFBP1,IGFBP5,ONECUT1	
NR5A2		ligand-dependent nuclear receptor						1.68E-04	IGFBP1,ONECUT1,PNLIP	
IGF1		growth factor		0.515		0.149	0.182	2.29E-04	EGR1,GCK,IGFBP1,IGFBP5,LCN2	AKT1,ERK,FOXO3,IGF1,IL6
CYP1A1		enzyme						2.29E-04	ETHE1,RGS16,Sult3a1/Sult3a2	
cyclic AMP		chemical - endogenous mammalian		-0.05		0.197	-0.44	2.49E-04	EGR1,GCK,IGFBP1,IGFBP5	AKT1,FOXO3,cyclic AMP
HOXA5		transcription regulator						2.59E-04	EGR1,IGFBP1	
RICTOR		other		0.927		-0.221	1.366	2.64E-04	EGR1,GCK,IGFBP1,RGS16	
fluconazole		chemical drug						2.87E-04	CYP3A5,SULT2A1	
NCOA2		transcription regulator						3.04E-04	EGR1,GCK,Sult2a2	
PRKAA2		kinase						3.04E-04	CYP3A5,EGR1,Foxp2	
selenomethylselenocysteine		chemical - endogenous mammalian						3.15E-04	CYP3A5,EGR1	
GW7647		chemical drug						3.76E-04	IGFBP1,IGFBP5	
KN-62		chemical - kinase inhibitor						4.08E-04	CYP3A5,EGR1	
IRS1		enzyme						4.32E-04	EGR1,GCK,IGFBP1	AKT1,FOXO3,IRS1
MAC		complex						4.42E-04	EGR1,RGS16	
lithocholic acid		chemical - endogenous mammalian						4.77E-04	CYP3A5,SULT2A1	
Ins1		other		0.918		0.119	0.681	4.96E-04	EGR1,GCK,IGFBP1,IGFBP5	AKT1,FOXO3,IGF1,Ins1
HNF4A		transcription regulator		0.507		0.104	0.28	5.19E-04	A1BG,CYP3A5,EGR1,IGFBP1,LARS2,LCN2,ONECUT1,SULT2A1,Sult2a2	
MLXIPL		transcription regulator						5.90E-04	GCK,RGS16	
hydrocortisone		chemical - endogenous mammalian						5.90E-04	IGFBP1,IGFBP5,SULT2A1	
ACOX1		enzyme						6.68E-04	IGFBP1,LCN2,Mup1 (includes others)	
lipopolysaccharide		chemical drug		-0.697		0.154	-1.117	7.35E-04	CYP3A5,EGR1,IGFBP1,IGFBP5,LCN2,RGS16,SAA2-SAA4,SULT2A1	FOXO3,IL6,lipopolysaccharide
progesterone		chemical - endogenous mammalian		-0.058		0.074	-0.202	7.37E-04	CYP3A5,EGR1,IGFBP1,IGFBP5,LCN2	AKT1,ERK,FOXO3,IL6,progesterone
STAT1		transcription regulator						7.47E-04	CYP3A5,EGR1,GCK,LCN2	
EZH2		transcription regulator						7.96E-04	EGR1,IGFBP1,LCN2,ONECUT1	
GNRH		group						8.04E-04	EGR1,IGFBP5	
ethionine		chemical toxicant						9.98E-04	IGFBP1,LCN2	
pregnenolone carbonitrile		chemical drug						9.98E-04	CYP3A5,SULT2A1	
NR1H4		ligand-dependent nuclear receptor						1.03E-03	CYP3A5,LCN2,SULT2A1	
PXR ligand-PXR-Retinoic acid-RXRα		complex						1.05E-03	CYP3A5,SULT2A1	
RUVBL1		transcription regulator						1.05E-03	HIST1H2BK,HIST2H2AC	
L-triiodothyronine		chemical - endogenous mammalian		-0.849		0.092	-1.031	1.06E-03	EGR1,GCK,IGFBP1,Mup1 (includes others)	
IGF2		growth factor						1.06E-03	EGR1,IGFBP5,RGS16	
LEPR		transmembrane receptor						1.12E-03	GCK,LCN2,Mup1 (includes others)	
GHR		transmembrane receptor						1.16E-03	IGFBP1,ONECUT1	
phenacetin		chemical drug						1.16E-03	IGFBP1,LCN2	
INSR		kinase						1.18E-03	EGR1,GCK,IGFBP1,RGS16	
3,7,12-trihydroxycoprostane		chemical - endogenous mammalian						1.20E-03	CYP3A5	
CHRM2		g-protein coupled receptor						1.20E-03	EGR1	
CML advanced glycation end products		chemical reagent						1.20E-03	EGR1	
RPS6KA2		kinase						1.20E-03	EGR1	
TMED10		transporter						1.20E-03	TMED9	
TRPM3		ion channel						1.20E-03	EGR1	
arachidonyl-2-chloroethylamide		chemical reagent						1.20E-03	EGR1	
beclomethasone dipropionate		chemical drug						1.20E-03	CYP3A5	
cAMP-dependent protein kinase inhibitor		chemical drug						1.20E-03	CYP3A5	
cyclothiazide		chemical drug						1.20E-03	EGR1	
desmethoxyyangonin		chemical - endogenous non-mammalian						1.20E-03	CYP3A5	
dihydrokawain		chemical - endogenous non-mammalian						1.20E-03	CYP3A5	
dihydromethysticin		chemical - endogenous non-mammalian						1.20E-03	CYP3A5	
hispidulin		chemical drug						1.20E-03	EGR1	
miR-495-3p (and other miRNAs w/seed AACAAAC)		mature microrna						1.20E-03	ONECUT1	
troleandomycin		chemical drug						1.20E-03	CYP3A5	
STK11		kinase						1.25E-03	Foxp2,IGFBP1,IGFBP5	
8-bromo-cAMP		chemical reagent						1.27E-03	EGR1,IGFBP1,SULT2A1	
4-hydroxytamoxifen		chemical drug						1.29E-03	EGR1,IGFBP1,RGS16	
TMEM173		other						1.33E-03	LCN2,RGS16	
doxorubicin		chemical drug		0		0.108	-0.215	1.38E-03	EGR1,IGFBP1,LCN2,RGS16	ERK,FOXO3,IKBKB,NFkB (complex),doxorubicin
FGF21		growth factor						1.39E-03	EGR1,IGFBP1	
BAPTA-AM		chemical reagent						1.45E-03	CYP3A5,EGR1	

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chemical drug
chemical reagent
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1.46E-03 GCK.HIST1H3BK.HIST2H3AC.ACRBP5
1.51E-03 CCP7&S23CP5
1.57E-03 ADRP1L1.CIN7
1.57E-03 H1FNA.CNNDUC1

Table S3-4. Diseases and Biofunctions

Day 5 Male BPA

Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	modification	Modification of retinaldehyde	8.92E-15	Decreased
	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	metabolism	Metabolism of terpenoid	3.43E-14	Decreased
	Drug Metabolism, Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	metabolism	Metabolism of retinoic	2.03E-12	Decreased
	Energy Production, Lipid Metabolism, Small Molecule Biochemistry	oxidation	Oxidation of lipid	1.63E-11	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	conversion	Conversion of lipid	3.91E-10	Decreased
	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	conversion	Conversion of retinol	7.42E-10	Decreased
	Drug Metabolism, Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	synthesis	Synthesis of tretinoin	2.05E-09	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	metabolism	Fatty acid metabolism	3.64E-09	Decreased
	Drug Metabolism	metabolism	Metabolism of xenobiotic	1.91E-08	Decreased
	Vitamin and Mineral Metabolism	metabolism	Metabolism of vitamin	4.62E-08	Decreased
	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	conversion	Conversion of retinaldehyde	4.72E-08	Decreased
	Molecular Transport, Small Molecule Biochemistry	transport	Transport of alkyl sulfonic acid	5.18E-08	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	hydroxylation	Hydroxylation of lipid	1.49E-07	Decreased
	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	uptake	Uptake of lipid	3.47E-06	Decreased
	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	transport	Transport of lipid	9.04E-06	Decreased
	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	synthesis	Synthesis of terpenoid	1.24E-05	Decreased
	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	transport	Transport of steroid	2.32E-05	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	synthesis	Synthesis of lipid	4.80E-05	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	conversion	Conversion of fatty acid	6.38E-05	Decreased
	Molecular Transport	transport	Transport of carboxylic acid	2.81E-04	Decreased
	Molecular Transport	transport	Transport of molecule	3.87E-04	Decreased
	Carbohydrate Metabolism, Molecular Transport	transport	Transport of carbohydrate	4.25E-03	Decreased

Day 5 Female BPA

Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Neurological Disease	damage	Damage of nervous system	2.18E-03	Decreased

Day 60 Male BPA

Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cellular Movement	cell movement	Cell movement	5.83E-16	Increased
	Cellular Movement	migration	Migration of cells	1.26E-14	Increased
	Cell Cycle	cell cycle progression	Cell cycle progression	6.41E-14	Increased
	Cellular Movement	cell movement	Cell movement of myeloid cells	6.88E-14	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	cell movement	Cell movement of phagocytes	1.11E-13	Increased
	Cellular Growth and Proliferation, Lymphoid Tissue Structure and Development	proliferation	Proliferation of lymphatic system cells	1.11E-13	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Lymphoid Tissue Structure and Development	proliferation	Proliferation of immune cells	6.27E-13	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Lymphoid Tissue Structure and Development	proliferation	Proliferation of mononuclear leukocytes	6.30E-13	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Lymphoid Tissue Structure and Development	proliferation	Proliferation of lymphocytes	9.88E-13	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of leukocytes	1.32E-12	Increased
	Hematological System Development and Function	hemostasis	Hemostasis	3.09E-12	Increased
	Cellular Movement	cell movement	Cell movement of blood cells	5.50E-12	Increased
	Cellular Development, Cellular Growth and Proliferation	proliferation	Proliferation of blood cells	5.59E-12	Increased
	Cellular Movement, Immune Cell Trafficking	migration	Leukocyte migration	8.51E-12	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	cell movement	Cell movement of neutrophils	1.17E-11	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of granulocytes	4.10E-11	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Lymphoid Tissue Structure and Development	cell proliferation	Cell proliferation of T lymphocytes	5.21E-11	Increased
	Hematological System Development and Function	coagulation	Coagulation	9.09E-11	Increased
	Hematological System Development and Function, Organismal Functions	coagulation	Coagulation of blood	1.76E-10	Increased
	Cellular Assembly and Organization, Cellular Function and Maintenance	organization	Organization of cytoskeleton	3.48E-10	Increased
	Inflammatory Response	inflammatory response	Inflammatory response	3.61E-10	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of phagocytes	3.88E-10	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Hematological System Development and Function	phagocytosis	Phagocytosis of myeloid cells	4.30E-10	Increased
	Cellular Function and Maintenance	engulfment	Engulfment of phagocytes	5.15E-10	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of blood cells	6.24E-10	Increased
	Cancer, Organismal Injury and Abnormalities	growth	Growth of tumor	6.63E-10	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	immune response	Immune response of phagocytes	6.91E-10	Increased
	Cell Morphology, Cellular Movement	cell spreading	Cell spreading	8.28E-10	Increased
	Cell-To-Cell Signaling and Interaction	response	Response of myeloid cells	9.34E-10	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	response	Response of phagocytes	1.27E-09	Increased
	Cellular Function and Maintenance	engulfment	Engulfment of blood cells	1.81E-09	Increased
	Cellular Movement	cell movement	Cell movement of tumor cell lines	2.48E-09	Increased
	Cell Death and Survival	survival	Cell survival	2.68E-09	Increased
	Cardiovascular System Development and Function, Organismal Development	angiogenesis	Angiogenesis	4.07E-09	Increased
	Cellular Movement	chemotaxis	Chemotaxis	5.50E-09	Increased
	Cancer, Organismal Injury and Abnormalities	metastatic solid tumor	Metastatic solid tumor	8.25E-09	Increased
	Cardiovascular System Development and Function	development	Development of vasculature	9.27E-09	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	chemotaxis	Chemotaxis of phagocytes	1.13E-08	Increased
	Cell Death and Survival	cell viability	Cell viability	1.15E-08	Increased
	Cellular Movement	homing	Homing of cells	1.26E-08	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Hematological System Development and Function	phagocytosis	Phagocytosis of granulocytes	1.54E-08	Increased
	Cellular Function and Maintenance	endocytosis	Endocytosis	1.72E-08	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	homing	Homing of leukocytes	1.84E-08	Increased
	Cell-To-Cell Signaling and Interaction	response	Response of myeloid leukocytes	2.38E-08	Increased
	Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Inflammatory Response	immune response	Immune response of neutrophils	2.72E-08	Increased
	Cardiovascular System Development and Function, Organismal Development	vasculogenesis	Vasculogenesis	2.78E-08	Increased
	Cellular Development, Cellular Growth and Proliferation	cell proliferation	Cell proliferation of breast cancer cell lines	3.01E-08	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Tissue Development	hematopoiesis	Hematopoiesis of mononuclear leukocytes	3.22E-08	Increased
	Cellular Function and Maintenance	internalization	Internalization of cells	3.69E-08	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	chemotaxis	Chemotaxis of leukocytes	4.11E-08	Increased
	Cell-To-Cell Signaling and Interaction	activation	Activation of cells	4.57E-08	Increased
	Cell Cycle	G1 phase	G1 phase	4.92E-08	Increased
	DNA Replication, Recombination, and Repair	repair	Repair of DNA	5.41E-08	Increased
	Cellular Development, Cellular Growth and Proliferation, Connective Tissue Development and Function	proliferation	Proliferation of fibroblast cell lines	6.08E-08	Increased
	Cell-To-Cell Signaling and Interaction	response	Response of granulocytes	6.49E-08	Increased
	Cellular Movement	chemotaxis	Chemotaxis of myeloid cells	6.88E-08	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Tissue Development	leukopoiesis	Leukopoiesis	7.29E-08	Increased
	Cellular Movement	migration	Migration of tumor cell lines	8.27E-08	Increased
	Free Radical Scavenging	metabolism	Metabolism of reactive oxygen species	9.09E-08	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Hematological System Development and Function, Inflammatory Response	phagocytosis	Phagocytosis of neutrophils	1.09E-07	Increased
	Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis	1.14E-07	Increased
	Cardiovascular System Development and Function	neovascularization	Neovascularization	1.88E-07	Increased
	Cellular Movement, Immune Cell Trafficking	cell movement	Cell movement of lymphatic system cells	2.19E-07	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	immune response	Immune response of leukocytes	2.36E-07	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of mononuclear leukocytes	2.38E-07	Increased
	DNA Replication, Recombination, and Repair	metabolism	Metabolism of DNA	2.47E-07	Increased
	Free Radical Scavenging	synthesis	Synthesis of reactive oxygen species	2.47E-07	Increased
	Cellular Movement	migration	Migration of myeloid cells	2.81E-07	Increased
	Connective Tissue Development and Function, Tissue Development	growth	Growth of connective tissue	3.13E-07	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	migration	Migration of phagocytes	3.44E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Hematological System Development and Function, Inflammatory Response	phagocytosis	Phagocytosis by macrophages	3.71E-07	Increased
	Tissue Development	growth	Growth of epithelial tissue	4.21E-07	Increased
	Cellular Movement	invasion	Invasion of cells	4.23E-07	Increased
	Cellular Movement	cell movement	Cell movement of connective tissue cells	4.24E-07	Increased
	Cellular Function and Maintenance	engulfment	Engulfment of antigen presenting cells	6.39E-07	Increased
	Cellular Growth and Proliferation, Connective Tissue Development and Function, Tissue Development	proliferation	Proliferation of connective tissue cells	6.76E-07	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	migration	Migration of mononuclear leukocytes	7.56E-07	Increased
	Inflammatory Response	immune response	Immune response of cells	8.25E-07	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of antigen presenting cells	8.57E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of cells	1.03E-06	Increased
	Cellular Development, Cellular Growth and Proliferation, Embryonic Development, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Organ Development, Organismal Development, Tissue Development	lymphopoiesis	Lymphopoiesis	1.03E-06	Increased
	DNA Replication, Recombination, and Repair	replication	DNA replication	1.27E-06	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of lymphocytes	1.32E-06	Increased
	Cellular Movement, Immune Cell Trafficking	migration	Migration of lymphatic system cells	1.37E-06	Increased
	Hematological System Development and Function, Humoral Immune Response, Lymphoid Tissue Structure and Development, Tissue Morphology	quantity	Quantity of B lymphocytes	1.49E-06	Increased
	Cellular Movement	extravasation	Extravasation	1.53E-06	Increased
	Cellular Movement	invasion	Invasion of tumor cell lines	1.75E-06	Increased
	Cellular Function and Maintenance	homeostasis	Cellular homeostasis	1.83E-06	Increased
	Cellular Function and Maintenance	endocytosis	Endocytosis by eukaryotic cells	1.84E-06	Increased
	Cellular Development, Cellular Growth and Proliferation, Embryonic Development, Hematological System Development and Function, Hematopoiesis, Humoral Immune Response, Lymphoid Tissue Structure and Development, Organ Development, Organismal Development, Tissue Development	differentiation	Differentiation of B lymphocytes	3.08E-06	Increased
	Cellular Movement	migration	Migration of connective tissue cells	3.54E-06	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	chemotaxis	Chemotaxis of granulocytes	4.03E-06	Increased
	Cellular Movement	invasion	Invasion of breast cancer cell lines	4.05E-06	Increased
	Cellular Development, Cellular Growth and Proliferation, Connective Tissue Development and Function, Tissue Development	cell proliferation	Cell proliferation of fibroblasts	6.74E-06	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	chemotaxis	Chemotaxis of neutrophils	6.75E-06	Increased
	Cellular Movement, Connective Tissue Development and Function	cell movement	Cell movement of fibroblasts	7.03E-06	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	response	Response of macrophages	7.24E-06	Increased
	Organismal Development	size	Size of body	7.36E-06	Increased

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Organismal Survival	mortality or mortality	Mortality or mortality	7.95E-15	Decreased
	Organismal Survival	organismal death	Organismal death	5.56E-14	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	lymphoma	Lymphoma	7.17E-12	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	lymphoid cancer	Lymphoid cancer	1.71E-11	Decreased
	Hematological Disease, Immunological Disease	lymphoproliferative disorder	Lymphoproliferative disorder	2.06E-11	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	lymphocytic neoplasm	Lymphocytic neoplasm	3.62E-11	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	neoplasia	Neoplasia of leukocytes	3.80E-11	Decreased
	Hematological System Development and Function, Tissue Morphology	quantity	Quantity of myeloid cells	2.50E-10	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	lymphocytic cancer	Lymphocytic cancer	3.51E-10	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	hematologic cancer	Hematologic cancer of cells	1.05E-09	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	hematological neoplasia	Hematopoietic neoplasm	2.30E-08	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	hematologic cancer	Hematologic cancer	4.67E-08	Decreased
	Cancer, Organismal Injury and Abnormalities	incidence	Incidence of tumor	5.43E-08	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	T-cell non-Hodgkin disease	T-cell non-Hodgkin lymphoma	1.20E-07	Decreased
	Cancer, Organismal Injury and Abnormalities	frequency	Frequency of tumor	1.48E-07	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	T-cell malignant neoplasm	T-cell malignant neoplasm	3.29E-07	Decreased
	Cardiovascular Disease, Hematological Disease, Organismal Injury and Abnormalities	anemia	Anemia	5.03E-07	Decreased
	Cancer, Organismal Injury and Abnormalities	development	Development of malignant tumor	1.08E-06	Decreased
	Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Tissue Morphology	quantity	Quantity of megakaryocytes	1.24E-06	Decreased
	Infectious Diseases	infection	Infection of mammalia	2.90E-06	Decreased
	Developmental Disorder	chorioallantoic membrane fusion failure	Chorioallantoic membrane fusion failure	4.58E-06	Decreased
	Developmental Disorder	aplasia or hypoplasia	Aplasia or hypoplasia	6.85E-06	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cell Cycle, Cellular Assembly and Organization, DNA Replication, Recombination, and Repair	segregation	Segregation of chromosomes	1.13E-24	Increased
	Cell Cycle	cell cycle progression	Cell cycle progression	1.15E-10	Increased
	Cellular Development, Cellular Growth and Proliferation	cell proliferation	Cell proliferation of tumor cell lines	4.12E-08	Increased
	Cell Death and Survival	survival	Cell survival	2.94E-07	Increased
	Cancer, Organismal Injury and Abnormalities	growth	Growth of tumor	4.99E-07	Increased
	Cell Death and Survival	cell viability	Cell viability	3.81E-06	Increased
	Organismal Survival	survival	Survival of organism	7.16E-06	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Lymphoid Tissue Structure and Development	cell proliferation	Cell proliferation of T lymphocytes	1.40E-05	Increased
	Cellular Movement	cell movement	Cell movement	2.25E-05	Increased
	Cell Death and Survival	cell viability	Cell viability of myeloma cell lines	3.84E-05	Increased
	Cellular Development, Cellular Growth and Proliferation	cell proliferation	Cell proliferation of breast cancer cell lines	1.41E-04	Increased
	Hematological System Development and Function, Organismal Functions	coagulation	Coagulation of blood	1.86E-04	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Lymphoid Tissue Structure and Development	proliferation	Proliferation of immune cells	2.36E-04	Increased
	Cell Cycle	cycling	Cycling of centrosome	4.04E-04	Increased
	Cellular Development, Cellular Growth and Proliferation	proliferation	Proliferation of blood cells	4.13E-04	Increased
	Cellular Movement	migration	Migration of cells	4.54E-04	Increased
	Cellular Movement	invasion	Invasion of cells	5.09E-04	Increased
	Cell Death and Survival	cell viability	Cell viability of tumor cell lines	5.12E-04	Increased
	Connective Tissue Development and Function, Tissue Development	growth	Growth of connective tissue	5.56E-04	Increased
	Cell Cycle	interphase	Entry into interphase	5.84E-04	Increased

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cardiovascular Disease, Hematological Disease, Organismal Injury and Abnormalities	anemia	Anemia	1.72E-09	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	incidence	Incidence of lymphoma	6.07E-09	Decreased
	Organismal Injury and Abnormalities, Renal and Urological Disease	renal lesion	Renal lesion	6.84E-08	Decreased
	Cancer, Organismal Injury and Abnormalities	development	Development of malignant tumor	2.89E-07	Decreased
	Hematological Disease, Immunological Disease	lymphoproliferative disorder	Lymphoproliferative disorder	4.57E-07	Decreased
	Cell Death and Survival	apoptosis	Apoptosis of cervical cancer cell lines	6.12E-07	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	lymphoma	Lymphoma	1.15E-05	Decreased
	Organismal Survival	organismal death	Organismal death	1.98E-05	Decreased
	Cardiovascular System Development and Function, Hematological System Development and Function	diastolic pressure	Diastolic pressure	2.65E-04	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Infectious Diseases	infection	Viral infection	1.49E-08	Increased
	Cellular Function and Maintenance	ion homeostasis	Ion homeostasis of cells	4.62E-05	Increased
	Hematological System Development and Function, Lymphoid Tissue Structure and Development, Tissue Morphology	quantity	Quantity of helper T lymphocytes	8.51E-04	Increased
	Infectious Diseases	replication	Replication of virus	1.12E-03	Increased
	Cell-To-Cell Signaling and Interaction	binding	Binding of tumor cell lines	1.99E-03	Increased

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cellular Development, Hematopoiesis, Tissue Development	differentiation	Differentiation of bone marrow cells	2.74E-16	Decreased
	Cardiovascular Disease, Hematological Disease, Organismal Injury and Abnormalities	anemia	Anemia	2.77E-10	Decreased
	Cell Death and Survival	cytolysis	Cytolysis	1.56E-08	Decreased
	Connective Tissue Development and Function, Hematological System Development and Function, Hematopoiesis, Organismal Development, Tissue Morphology	quantity	Quantity of reticulocytes	7.37E-08	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	conversion	Conversion of lipid	3.92E-05	Decreased
	Cell Death and Survival	cell death	Cell death	1.32E-04	Decreased
	Cell Death and Survival, Organismal Injury and Abnormalities	necrosis	Necrosis of epithelial tissue	1.39E-04	Decreased
	Hematological System Development and Function, Tissue Morphology	quantity	Quantity of myeloid cells	1.63E-04	Decreased
	Organismal Survival	mortality or mortality	Mortality or mortality	1.54E-03	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cell Cycle	cell cycle progression	Cell cycle progression	1.10E-17	Increased
	Cellular Development, Cellular Growth and Proliferation	cell proliferation	Cell proliferation of tumor cell lines	1.47E-17	Increased
	Cellular Movement	cell movement	Cell movement	1.13E-15	Increased
	Cellular Movement	migration	Migration of cells	1.32E-15	Increased
	Cell Death and Survival	cell viability	Cell viability	1.47E-15	Increased
	Cell Death and Survival	survival	Cell survival	2.85E-15	Increased
	Cancer, Organismal Injury and Abnormalities	growth	Growth of tumor	8.40E-13	Increased
	Cancer, Organismal Injury and Abnormalities	abdominal neoplasm	Abdominal neoplasm	2.56E-11	Increased
	Cellular Development, Cellular Growth and Proliferation	cell proliferation	Cell proliferation of breast cancer cell lines	2.65E-11	Increased

	Cellular Assembly and Organization, Cellular Function and Maintenance	organization	Organization of cytoskeleton	4.46E-11	Increased
	Embryonic Development, Organismal Development	development	Development of body trunk	5.81E-11	Increased
	Free Radical Scavenging	metabolism	Metabolism of reactive oxygen species	8.48E-11	Increased
	Cell Death and Survival	cell viability	Cell viability of tumor cell lines	9.93E-11	Increased
	DNA Replication, Recombination, and Repair	repair	Repair of DNA	1.63E-10	Increased
	Cellular Movement	cell movement	Cell movement of myeloid cells	2.27E-10	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Tissue Development	leukopoiesis	Leukopoiesis	2.39E-10	Increased
	Cancer, Organismal Injury and Abnormalities	growth	Growth of malignant tumor	3.26E-10	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	cell movement	Cell movement of phagocytes	3.58E-10	Increased
	Free Radical Scavenging	synthesis	Synthesis of reactive oxygen species	4.27E-10	Increased
	Cancer, Gastrointestinal Disease, Organismal Injury and Abnormalities	neoplasia	Gastrointestinal tumor	4.59E-10	Increased
	Connective Tissue Development and Function, Tissue Development	growth	Growth of connective tissue	7.23E-10	Increased
	Cellular Development, Cellular Growth and Proliferation, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Tissue Development	hematopoiesis	Hematopoiesis of mononuclear leukocytes	1.05E-09	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of leukocytes	1.62E-09	Increased
	Cellular Movement	cell movement	Cell movement of blood cells	2.04E-09	Increased
	Inflammatory Response	inflammatory response	Inflammatory response	2.36E-09	Increased
	Cellular Movement, Immune Cell Trafficking	migration	Leukocyte migration	2.55E-09	Increased
	Cardiovascular System Development and Function	development	Development of vasculature	3.18E-09	Increased
	Cell-To-Cell Signaling and Interaction	aggregation	Aggregation of cells	4.26E-09	Increased
	Organismal Development	size	Size of body	4.94E-09	Increased
	Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis	5.95E-09	Increased
	Cardiovascular System Development and Function, Organismal Development	angiogenesis	Angiogenesis	9.68E-09	Increased
	DNA Replication, Recombination, and Repair	double-stranded DNA break repair	Double-stranded DNA break repair	1.13E-08	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	cell movement	Cell movement of neutrophils	1.42E-08	Increased
	Cellular Movement	invasion	Invasion of breast cancer cell lines	1.42E-08	Increased
	DNA Replication, Recombination, and Repair	metabolism	Metabolism of DNA	1.77E-08	Increased
	Cellular Movement	invasion	Invasion of cells	2.20E-08	Increased
	Cellular Movement	cell movement	Cell movement of tumor cell lines	2.28E-08	Increased
	Cardiovascular Disease, Organismal Injury and Abnormalities	vaso-occlusion	Vaso-occlusion	2.44E-08	Increased
	Cellular Movement	migration	Migration of tumor cell lines	2.69E-08	Increased
	Inflammatory Response	immune response	Immune response of cells	2.70E-08	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking, Inflammatory Response	cell movement	Cell movement of macrophages	3.17E-08	Increased
	Cell-To-Cell Signaling and Interaction	response	Response of myeloid cells	3.43E-08	Increased
	Cellular Development, Cellular Growth and Proliferation, Embryonic Development, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Organ Development, Organismal Development, Tissue Development	lymphopoiesis	Lymphopoiesis	3.47E-08	Increased
	Free Radical Scavenging	production	Production of reactive oxygen species	3.54E-08	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	response	Response of phagocytes	4.69E-08	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	immune response	Immune response of phagocytes	6.87E-08	Increased
	Cellular Function and Maintenance	endocytosis	Endocytosis	8.13E-08	Increased
	Cellular Movement	invasion	Invasion of tumor cell lines	9.05E-08	Increased
	Cellular Growth and Proliferation, Connective Tissue Development and Function, Tissue Development	proliferation	Proliferation of connective tissue cells	9.16E-08	Increased
	Cellular Function and Maintenance	engulfment	Engulfment of phagocytes	9.24E-08	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of leukocytes	1.09E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of blood cells	1.11E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of cells	1.87E-07	Increased
	Cell-To-Cell Signaling and Interaction	activation	Activation of cells	1.87E-07	Increased
	Cellular Development, Cellular Growth and Proliferation	cell proliferation	Cell proliferation of carcinoma cell lines	2.14E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Inflammatory Response	phagocytosis	Phagocytosis of phagocytes	2.28E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Hematological System Development and Function	phagocytosis	Phagocytosis of myeloid cells	2.50E-07	Increased
	Cell-To-Cell Signaling and Interaction, Inflammatory Response	immune response	Immune response of leukocytes	2.64E-07	Increased
	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	cell movement	Cell movement of granulocytes	2.72E-07	Increased
	Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Inflammatory Response	immune response	Immune response of neutrophils	2.95E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Movement	recruitment	Recruitment of blood cells	3.31E-07	Increased
	Cell Death and Survival	cytotoxicity	Cytotoxicity	3.40E-07	Increased
	Cellular Assembly and Organization, Cellular Function and Maintenance	organization	Microtubule dynamics	3.79E-07	Increased
	Cellular Function and Maintenance	engulfment	Engulfment of blood cells	3.83E-07	Increased
	Hematological System Development and Function, Humoral Immune Response, Lymphoid Tissue Structure and Development, Tissue Morphology	quantity	Quantity of B lymphocytes	4.41E-07	Increased
	Cell-To-Cell Signaling and Interaction, Cellular Function and Maintenance, Hematological System Development and Function	phagocytosis	Phagocytosis of granulocytes	6.31E-07	Increased
	Cell-To-Cell Signaling and Interaction	response	Response of myeloid leukocytes	6.40E-07	Increased
	Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Inflammatory Response	aggregation	Aggregation of blood platelets	6.60E-07	Increased
	Cellular Function and Maintenance	homeostasis	Lymphocyte homeostasis	7.48E-07	Increased
	Cardiovascular System Development and Function, Organismal Development	vasculogenesis	Vasculogenesis	7.51E-07	Increased
	Cellular Function and Maintenance	internalization	Internalization of cells	8.39E-07	Increased
	Cell-To-Cell Signaling and Interaction	response	Response of granulocytes	9.79E-07	Increased
	Cellular Function and Maintenance	homeostasis	Homeostasis of blood cells	1.07E-06	Increased

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Organismal Survival	morbidity or mortality	Morbidity or mortality	6.55E-21	Decreased
	Organismal Survival	organismal death	Organismal death	1.42E-19	Decreased
	Hematological Disease, Immunological Disease	lymphoproliferative disorder	Lymphoproliferative disorder	1.38E-15	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	lymphocytic neoplasm	Lymphocytic neoplasm	2.26E-15	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	neoplasia	Neoplasia of leukocytes	5.15E-15	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	lymphocytic cancer	Lymphocytic cancer	1.77E-13	Decreased
	Cancer, Hematological Disease, Organismal Injury and Abnormalities	hematologic cancer	Hematologic cancer of cells	4.33E-12	Decreased
	Cancer, Hematological Disease, Immunological Disease, Organismal Injury and Abnormalities	lymphoma	Lymphoma	1.21E-11	Decreased
	Hematological System Development and Function, Tissue Morphology	quantity	Quantity of myeloid cells	1.28E-10	Decreased
	Cardiovascular Disease, Hematological Disease, Organismal Injury and Abnormalities	anemia	Anemia	1.98E-10	Decreased
	Infectious Diseases	infection	Infection of mammalia	4.38E-10	Decreased
	Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	modification	Modification of retinaldehyde	4.32E-09	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	conversion	Conversion of lipid	4.12E-08	Decreased
	Drug Metabolism	conjugation	Conjugation of glutathione	1.64E-07	Decreased
	Connective Tissue Disorders, Organismal Injury and Abnormalities, Skeletal and Muscular Disorders	abnormal bone density	Abnormal bone density	4.14E-07	Decreased
	Infectious Diseases	infection	Parasitic infection	7.02E-07	Decreased
	Vitamin and Mineral Metabolism	metabolism	Metabolism of vitamin	7.12E-07	Decreased
	Developmental Disorder	growth failure	Growth Failure	8.28E-07	Decreased
	Cellular Assembly and Organization, DNA Replication, Recombination, and Repair	formation	Formation of gamma H2AX nuclear focus	9.18E-07	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Carbohydrate Metabolism	metabolism	Metabolism of carbohydrate	4.74E-06	Increased
	Protein Synthesis	quantity	Quantity of protein in blood	3.61E-05	Increased
	Cancer, Organismal Injury and Abnormalities	growth	Growth of tumor	8.60E-05	Increased
	Endocrine System Development and Function, Molecular Transport, Small Molecule Biochemistry	concentration	Concentration of hormone	1.56E-04	Increased
	Cell Death and Survival, Gastrointestinal Disease, Hepatic System Disease, Organismal Injury and Abnormalities	necrosis	Necrosis of liver	2.89E-04	Increased
	Cancer, Cellular Development, Cellular Growth and Proliferation, Organismal Injury and Abnormalities, Tumor Morphology	proliferation	Proliferation of tumor cells	2.39E-03	Increased

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cellular Development, Cellular Growth and Proliferation, Embryonic Development, Hematological System Development and Function, Hematopoiesis, Lymphoid Tissue Structure and Development, Organ Development, Organismal Development, Tissue Development	megakaryocytopoiesis	Megakaryocytopoiesis	1.76E-10	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Cellular Development, Cellular Growth and Proliferation, Connective Tissue Development and Function, Skeletal and Muscular System Development and Function, Tissue Development	formation	Formation of osteoclasts	9.51E-06	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Inflammatory Response	inflammation	Inflammation of body cavity	1.88E-07	Increased

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	Skeletal and Muscular System Development and Function	contractility	Contractility of muscle	3.43E-08	Decreased
	Lipid Metabolism, Small Molecule Biochemistry	synthesis	Synthesis of lipid	1.05E-05	Decreased
	Cell Death and Survival	cell viability	Cell viability	1.70E-04	Decreased
	Cell Death and Survival	cell viability	Cell viability of tumor cell lines	2.15E-04	Decreased
	Cell Death and Survival	cell viability	Cell viability of breast cancer cell lines	1.81E-03	Decreased

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Increased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Decreased	Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State
	NA				

Table S3-5. Tox lists p < 0.01

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Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Fatty Acid Metabolism	1.13E+01	9.40E-02	ADH1C,CYP2B6,CYP1A2,ALDH1A1,Aldh1a7,Cyp2c40 (includes others),CYP2C8,Cyp2b13/Cyp2b9,ADH4,CYP4F12,CYP2A6 (includes others)
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	1.10E+01	2.92E-01	Cyp2c54 (includes others),CYP2B6,CYP1A2,Cyp2c40 (includes others),CYP2C8,Cyp2b13/Cyp2b9,CYP2A6 (includes others)
PXR/RXR Activation	1.09E+01	1.38E-01	CYP2B6,GSTM1,CYP1A2,ALDH1A1,Aldh1a7,SCD,CYP2C8,ABCC3,CYP2A6 (includes others)
Xenobiotic Metabolism Signaling	8.06E+00	3.59E-02	ADH1C,ADH4,CYP4F12,Cyp2c54 (includes others),CYP2B6,GSTM1,CYP1A2,ALDH1A1,Gstm3,CYP2C8,Cyp2b13/Cyp2b9,ABCC3,CYP2A6 (includes others)
NRF2-mediated Oxidative Stress Response	6.70E+00	3.97E-02	Cyp2c54 (includes others),CYP2B6,GSTM1,CYP1A2,Gstm3,Cyp2c40 (includes others),CYP2C8,Cyp2b13/Cyp2b9,AOX1,CYP2A6 (includes others)
LPS/IL-1 Mediated Inhibition of RXR Function	6.65E+00	3.92E-02	Cyp2c54 (includes others),CYP2B6,GSTM1,ALDH1A1,Gstm3,Cyp2c40 (includes others),CYP2C8,Cyp2b13/Cyp2b9,ABCC3,CYP2A6 (includes others)
Aryl Hydrocarbon Receptor Signaling	6.18E+00	4.97E-02	Cyp2c54 (includes others),GSTM1,CYP1A2,ALDH1A1,Gstm3,Cyp2c40 (includes others),CYP2C8,FASN
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	5.95E+00	2.22E-01	CYP2B6,CYP1A2,CYP2C8,CYP2A6 (includes others)
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	5.35E+00	1.60E-01	CYP2B6,CYP1A2,CYP2C8,CYP2A6 (includes others)
Glutathione Depletion - Hepatocellular Hypertrophy	5.32E+00	3.75E-01	CYP2B6,Gstm3,ABCC3
CAR/RXR Activation	5.08E+00	1.38E-01	CYP2B6,ALDH1A1,CYP2C8,ABCC3
Nongenotoxic Hepatocarcinogenicity Biomarker Panel	3.90E+00	1.36E-01	Mt1,ALDH1A1,LOC102724788/PRODH
Genes Upregulated in Response to Chronic Renal Failure (Rat)	3.70E+00	4.00E-01	Slco1a4,ABCC3
FXR/RXR Activation	3.58E+00	3.97E-02	BAAT,FASN,C9,SLC10A2,CYP27A1
TR/RXR Activation	3.00E+00	4.08E-02	THRSP,UCP1,FASN,DIO1
Glutathione Depletion - CYP Induction and Reactive Metabolites	2.89E+00	1.67E-01	ALDH1A1,ABCC3
Decreases Respiration of Mitochondria	2.82E+00	1.54E-01	Mt1,UCP1
PPARα/RXRα Activation	2.79E+00	2.65E-02	Cyp2c54 (includes others),Cyp2c40 (includes others),CYP2C8,PRKAA2,FASN
RAR Activation	2.78E+00	2.63E-02	RDH16,ADH1C,ALDH1A1,Aldh1a7,ADH4
Cytochrome P450 Panel - Substrate is a Sterol (Human)	2.76E+00	1.43E-01	CYP7B1,CYP27A1
Cytochrome P450 Panel - Substrate is a Sterol (Mouse)	2.76E+00	1.43E-01	CYP7B1,CYP27A1
Cytochrome P450 Panel - Substrate is a Sterol (Rat)	2.76E+00	1.43E-01	CYP7B1,CYP27A1
Acute Renal Failure Panel (Rat)	2.56E+00	4.84E-02	A2M,Mt1,Slco1a1
Glutathione Depletion - Phase II Reactions	2.44E+00	1.00E-01	GSTM1,Gstm3
Hepatic Cholestasis	2.20E+00	2.45E-02	CYP7B1,SLC10A2,ABCC3,CYP27A1
Renal Proximal Tubule Toxicity Biomarker Panel (Rat)	2.19E+00	7.41E-02	Slco1a4,Slco1a1
Positive Acute Phase Response Proteins	2.10E+00	6.67E-02	A2M,C9

Day 5 Female BPA

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
NA			

Day 60 Male BPA

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Hepatic Fibrosis	5.73E+00	1.23E-01	TGFB1,IGFBP2,ELN,COL1A1,THBS1,COL5A1,A2M,NID1,IGFBP1,THBS2,TNC,MMP8,MMP14
Acute Renal Failure Panel (Rat)	5.63E+00	1.61E-01	A2M,IGFBP1,Mt1,TUBB,COL1A1,CD44,LCN2,HMOX1,VCAM1,ANXA1
Liver Proliferation	5.60E+00	8.20E-02	GPC3,Mt1,CYR61,TGFB1,Mt2,NCF1,E2F1,COL1A1,LEPR,THBS1,IGF2,Ins1,IGF1R,CCND3,IFNGR1,IGFBP1,CXCR4,IL1RN,ITGB3,MMP14
Cardiac Necrosis/Cell Death	5.37E+00	7.41E-02	SST,ADRB2,CYR61,BIRC5,SLC8A1,HSPB8,E2F1,FASN,LEPR,MYLK3,FSTL1,LCN2,HMOX1,AR,HSPB1,CXCR4,MFN2,IL1RN,THBS2,GSN,CYBB,HK1
Increases Liver Hyperplasia/Hyperproliferation	4.78E+00	1.01E-01	GPC3,HMMR,PEG10,CYR61,TGFB1,CENPA,ACSS2,E2F1,IGFBP2,IGF1R,RRM2,CXCR4,TPX2
LPS/IL-1 Mediated Inhibition of RXR Function	4.75E+00	7.45E-02	CHST3,SMOX,CYP2U1,CYP4A11,ALDH18A1,GSTK1,SULT1C2,Cyp2c54 (includes others),IL1RN,CYP2B6,Cyp2b13/Cyp2b9,CYP3A5,GSTM4,FABP5,SULT2A1,GSTP1,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Gstm6
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	4.72E+00	2.50E-01	Cyp2c54 (includes others),CYP2B6,Cyp2b13/Cyp2b9,CYP3A5,Cyp2a12/Cyp2a22,CYP2A6 (includes others)
PXR/RXR Activation	4.57E+00	1.38E-01	Ins1,PCK2,IGFBP1,CYP2B6,PRKAR2B,Aldh1a7,CYP3A5,SULT2A1,CYP2A6 (includes others)
Aryl Hydrocarbon Receptor Signaling	4.38E+00	8.70E-02	POLA1,TGFB1,E2F1,FASN,ALDH18A1,GSTK1,CCND3,Cyp2c54 (includes others),HSPB1,CYP3A5,GSTM4,RBL1,GSTP1,Gstm6
Persistent Renal Ischemia-Reperfusion Injury (Mouse)	4.13E+00	2.00E-01	HSPB1,LOX,COL1A1,LCN2,VCAM1,MMP14
NRF2-mediated Oxidative Stress Response	3.75E+00	6.69E-02	CYP2U1,CYP4A11,HSPB8,GSTK1,HMOX1,ENC1,Cyp2c54 (includes others),PIK3CD,CYP2B6,Cyp2b13/Cyp2b9,CYP3A5,AOX1,GSTM4,GSTP1,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Gstm6
Xenobiotic Metabolism Signaling	3.58E+00	5.77E-02	CHST3,MEST,SMOX,ALDH18A1,Ces1g,GSTK1,HMOX1,SULT1C2,Cyp2c54 (includes others),PIK3CD,CYP2B6,Ces1e,Cyp2b13/Cyp2b9,CYP3A5,GSTM4,GRIP1,SULT2A1,GSTP1,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Gstm6
Renal Necrosis/Cell Death	3.54E+00	5.01E-02	GRB10,AGER,Mt1,TGFB1,Mt2,SLC8A1,THBS1,RGS16,Ins1,ATP2B2,GSTP1,TFRC,BRCA1,PAK1,BIRC5,CD44,LCN2,HMOX1,STMN1,IGF1R,AR,HSPB1,BCL6,GSN,PSEN2,CYBB,HK1,CDK1
Increases Renal Proliferation	3.50E+00	8.00E-02	SYK,PIK3CD,Mt1,TGFB1,Mt2,E2F1,DLGAP5,CAMP,Tpm2,LCN2,IGF2,MMP14
Cardiac Fibrosis	2.92E+00	6.28E-02	ADRB2,TGFB1,SLC8A1,NCF1,HSPB8,MYLK3,HMOX1,IGF1R,AR,BCL6,THBS2,LPL,CYBB,SLC4A1
Cell Cycle: G1/S Checkpoint Regulation	2.84E+00	1.01E-01	CCND3,TGFB1,CDKN2D,E2F2,CDC25A,E2F1,RBL1
Genes associated with Chronic Allograft Nephropathy (Human)	2.82E+00	1.90E-01	TGFB1,TNC,THBS1,VCAM1
Liver Necrosis/Cell Death	2.69E+00	5.38E-02	SST,AGER,Mt1,TGFB1,FLNA,Mt2,NCF1,E2F1,HMOX1,AR,IFNGR1,IGFBP1,IL1RN,GSN,SLC25A4,ITGB3,Meg3
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	2.53E+00	1.60E-01	CYP2B6,CYP3A5,Cyp2a12/Cyp2a22,CYP2A6 (includes others)
Renal Proximal Tubule Toxicity Biomarker Panel (Rat)	2.41E+00	1.48E-01	HSPB1,IGFBP1,SLC15A2,GSTP1
Increases Liver Steatosis	2.38E+00	7.62E-02	ID1,PRKAR2B,RGCC,PKM,CCDC3,CD44,RGS16,HMOX1
Decreases Respiration of Mitochondria	2.37E+00	2.14E-01	Mt1,TGFB1,PKM
Cholesterol Biosynthesis	2.20E+00	1.88E-01	PMVK,FDPS,DHCR7
p53 Signaling	2.17E+00	7.02E-02	BRCA1,PIK3CD,BIRC5,E2F1,PLAGL1,FASN,THBS1,PCNA
Increases Renal Damage	2.11E+00	7.53E-02	TGFB1,SLC8A1,RGCC,THBS1,CYBB,CD44,FCGR2A
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	2.05E+00	1.67E-01	CYP2B6,CYP3A5,CYP2A6 (includes others)

Day 60 Female BPA

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	6.77E+00	1.35E-01	BRCA1,TOP2A,AURKA,CCNB2,CDK1,CCNB1,PLK1
Acute Renal Failure Panel (Rat)	2.83E+00	6.45E-02	IGFBP1,EGR1,LCN2,VCAM1
Increases Liver Hyperplasia/Hyperproliferation	2.44E+00	3.88E-02	GPC3,RRM2,HMMR,PEG10,TPX2
Renal Necrosis/Cell Death	2.30E+00	1.97E-02	GRB10,BRCA1,SNCA,BIRC5,THBS1,TFRC,LCN2,RGS16,CDK1,CCNB1,STMN1

Day 5 Male BDE-99

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	6.59E+00	2.50E-01	Cyp2c54 (includes others),CYP2B6,CYP1A2,CYP2C8,CYP2F1,CYP2A6 (includes others)
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	5.82E+00	2.78E-01	CYP2B6,CYP1A2,CYP2C8,CYP2F1,CYP2A6 (includes others)
Nongenotoxic Hepatocarcinogenicity Biomarker Panel	3.96E+00	1.82E-01	BTG2,Mt1,CITED4,TAP1
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	3.74E+00	1.60E-01	CYP2B6,CYP1A2,CYP2C8,CYP2A6 (includes others)
Acute Renal Failure Panel (Rat)	3.12E+00	8.06E-02	A2M,Mt1,SPHK1,EGR1,AQP1
LPS/IL-1 Mediated Inhibition of RXR Function	3.09E+00	3.92E-02	Cyp2c54 (includes others),IL1RL1,CYP2B6,CYP4A11,CYP2C8,CYP2F1,PAPSS2,CHST11,CYP2A6 (includes others),FABP2
PXR/RXR Activation	3.03E+00	7.69E-02	CYP2B6,CYP1A2,CYP2C8,PAPSS2,CYP2A6 (includes others)
Fatty Acid Metabolism	2.61E+00	5.13E-02	CYP2B6,CYP1A2,CYP4A11,CYP2C8,CYP2F1,CYP2A6 (includes others)
CAR/RXR Activation	2.35E+00	1.03E-01	CYP2B6,CYP2C8,PAPSS2
NRF2-mediated Oxidative Stress Response	2.03E+00	3.17E-02	Cyp2c54 (includes others),CYP2B6,CYP1A2,CYP4A11,CYP2C8,CYP2F1,CYP2A6 (includes others),JUNB

Day 5 Female BDE-99

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	5.43E+00	1.25E-01	Cyp2c54 (includes others),CYP2B6,CYP1A2
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	3.62E+00	1.11E-01	CYP2B6,CYP1A2
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	3.33E+00	8.00E-02	CYP2B6,CYP1A2
PXR/RXR Activation	2.50E+00	3.08E-02	CYP2B6,CYP1A2
NRF2-mediated Oxidative Stress Response	2.40E+00	1.19E-02	Cyp2c54 (includes others),CYP2B6,CYP1A2
Fatty Acid Metabolism	2.01E+00	1.71E-02	CYP2B6,CYP1A2

Day 60 Male BDE-99

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Cholesterol Biosynthesis	1.08E+01	6.25E-01	EBP,PMVK,HMGCS1,SQLE,IDI1,MVK,ACAT2,FDPS,HMGCR,DHCR7
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	8.56E+00	4.17E-01	Cyp2c54 (includes others),CYP2C18,CYP1A2,CYP2C8,Cyp2b13/Cyp2b9,CYP3A5,CYP2F1,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Cyp2d9 (includes others)
Xenobiotic Metabolism Signaling	8.35E+00	1.02E-01	ADH4,CYP2F1,Gstt1,Gsta4,Cyp2c54 (includes others),GSTM1,Ces1e,ALDH1A1,GSTM5,GRIP1,GSTP1,PRKCZ,Cyp2a12/Cyp2a22,ABCC3,CYP2A6 (includes others),Gstm6,Cyp2d9 (includes others),CHST3,GSTA3,MEST,ADH1C,ALDH1L1,SMOX,Ces1g,CES1,CYP4F12,CHST11,HMOX1,SULT1C2,CYP1A2,Gstm3,CYP2C8,Cyp2b13/Cyp2b9,CYP3A5,GSTM4,CYP51A1,UGT2B28
LPS/IL-1 Mediated Inhibition of RXR Function	8.34E+00	1.18E-01	CYP2U1,CYP4A11,CYP2F1,Cyp2c54 (includes others),IL1RN,CYP2C18,GSTM1,ALDH1A1,GSTM5,FABP5,GSTP1,Cyp2a12/Cyp2a22,ABCC3,CYP2A6 (includes others),Gstm6,Cyp2d9 (includes others),HMGCS1,CHST3,GSTA3,ALDH1L1,SMOX,CHST11,SULT1C2,TNFRSF11B,Gstm3,CYP2C8,Cyp2b13/Cyp2b9,CYP3A5,GSTM4,CYP7A1
Persistent Renal Ischemia-Reperfusion Injury (Mouse)	7.46E+00	3.33E-01	HSPB1,C1QC,LOX,Serpina3g (includes others),C1QB,COL1A1,LCN2,LTBP2,VCAM1,MMP14
Aryl Hydrocarbon Receptor Signaling	7.44E+00	1.37E-01	GSTA3,POLA1,ALDH1L1,TGFB1,E2F1,FASN,CCND3,Cyp2c54 (includes others),HSPB1,CYP2C18,GSTM1,CYP1A2,ALDH1A1,CCND1,Gstm3,CYP2C8,GSTM5,CYP3A5,GSTM4,RBL1,GSTP1,Gstm6
Fatty Acid Metabolism	7.00E+00	1.54E-01	ADH1C,CYP4A11,ACAT2,ADH4,CYP2F1,CYP4F12,CYP4A22,CYP2C18,CYP1A2,Aldh1a7,ALDH1A1,CYP2C8,Cyp2b13/Cyp2b9,CYP3A5,CYP51A1,Acaa1b,Cyp2a12/Cyp2a22,CYP2A6 (includes others)
Hepatic Fibrosis	6.18E+00	1.51E-01	TGFB1,IGFBP2,ELN,COL1A1,THBS1,COL5A1,SPARC,A2M,NID1,IGFBP1,THBS2,TNC,MMP8,ICAM1,LTBP2,MMP14
NRF2-mediated Oxidative Stress Response	6.11E+00	1.02E-01	CYP2U1,CYP4A11,CYP2F1,ENC1,Cyp2c54 (includes others),FKBP5,CYP2C18,GSTM1,DNAJC9,GSTM5,AOX1,GSTP1,PRKCZ,Cyp2a12/Cyp2a22,CYP2A6 (includes others),Gstm6,Cyp2d9 (includes others),GSTA3,HMOX1,CYP4A22,CYP1A2,Gstm3,CYP2C8,Cyp2b13/Cyp2b9,CYP3A5,GSTM4
PXR/RXR Activation	5.73E+00	1.85E-01	PCK2,IGFBP1,GSTM1,CYP1A2,PRKAR2B,Aldh1a7,ALDH1A1,CYP2C8,CYP3A5,ABCC3,CYP2A6 (includes others),CYP7A1
Liver Proliferation	5.39E+00	9.84E-02	GPC3,Mt1,CYR61,TGFB1,Mt2,NCF1,E2F1,COL1A1,LEPR,THBS1,ADIPOQ,IGF2,IGF1R,CCND3,PPARD,IFNGR1,IGFBP1,IL1RN,CCND1,CIT,FGL1,ITGB3,FST,MMP14
Liver Necrosis/Cell Death	4.84E+00	8.54E-02	AGER,Mt1,TGFB1,Mt2,NCF1,E2F1,ITGB2,CD274,ADIPOQ,IFNGR1,IL1RN,TYROBP,ITGB3,TLR7,MME,FLNA,HMOX1,AR,IGFBP1,GSN,CCND1,SLC25A4,CIT,PRKAA2,Meg3,PTPRC,CYP7A1
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	4.68E+00	3.33E-01	CYP2C18,CYP1A2,CYP2C8,CYP3A5,CYP2F1,CYP2A6 (includes others)
Increases Liver Hyperplasia/Hyperproliferation	4.42E+00	1.16E-01	GPC3,HMMR,PEG10,CYR61,TGFB1,CENPA,HMGCR,ACSS2,E2F1,IGFBP2,IGF1R,RRM2,CCND1,SDR9C7,TPX2
Glutathione Depletion - Phase II Reactions	4.38E+00	3.00E-01	GSTA3,GSTM1,Gstm3,GSTM5,GSTM4,GSTP1
CAR/RXR Activation	4.35E+00	2.41E-01	GSTA3,CYP2C18,ALDH1A1,CCND1,CYP2C8,CES1,ABCC3
Renal Necrosis/Cell Death	4.25E+00	6.80E-02	GRB10,AGER,Mt1,TGFB1,Mt2,SLC8A1,THBS1,RGS16,SNCA,DUSP1,GSTM5,GSTP1,TFRC,ABCC3,BRCA1,SLC40A1,BIRC5,MELK,MAP1LC3A,CD44,LCN2,HMOX1,HELLS,OLR1,STMN1,IGF1R,AR,HSPB1,PPARD,GSN,PSEN2,RAD51,RGS4,ICAM1,CYBB,CDK1,VOPP1,GLS
Cytochrome P450 Panel - Substrate is a Sterol (Human)	4.14E+00	3.57E-01	CYP7B1,CYP51A1,CYP8B1,CYP7A1,CYP27A1
Cytochrome P450 Panel - Substrate is a Sterol (Mouse)	4.14E+00	3.57E-01	CYP7B1,CYP51A1,CYP8B1,CYP7A1,CYP27A1
Cytochrome P450 Panel - Substrate is a Sterol (Rat)	4.14E+00	3.57E-01	CYP7B1,CYP51A1,CYP8B1,CYP7A1,CYP27A1
Cytochrome P450 Panel - Substrate is a Fatty Acid (Human)	3.61E+00	4.00E-01	CYP4A22,CYP4F3,CYP4A11,CYP4F12
Acute Renal Failure Panel (Rat)	3.60E+00	1.45E-01	A2M,IGFBP1,Mt1,COL1A1,CD44,LCN2,HMOX1,VCAM1,ANXA1
Cardiac Necrosis/Cell Death	3.58E+00	7.74E-02	ADRB2,BMP10,CYR61,BIRC5,SLC8A1,E2F1,FASN,NOX4,LEPR,MYLK3,FSTL1,LCN2,HMOX1,ADIPOQ,AR,HSPB1,MFN2,IL1RN,THBS2,GSN,PRKAA2,S100A1,CYBB
Cytochrome P450 Panel - Substrate is a Fatty Acid (Rat)	3.42E+00	3.64E-01	CYP4A22,CYP4F3,CYP4A11,CYP4F12
Glutathione Depletion - CYP Induction and Reactive Metabolites	3.26E+00	3.33E-01	FEN1,ALDH1A1,GSTM4,ABCC3
Genes associated with Chronic Allograft Nephropathy (Human)	3.22E+00	2.38E-01	TGFB1,TNC,THBS1,ICAM1,VCAM1
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	2.85E+00	2.00E-01	CYP1A2,CYP2C8,CYP3A5,Cyp2a12/Cyp2a22,CYP2A6 (includes others)
Cytochrome P450 Panel - Substrate is a Fatty Acid (Mouse)	2.74E+00	2.50E-01	CYP4A22,CYP4F3,CYP4A11,CYP4F12
Increases Renal Proliferation	2.69E+00	8.67E-02	GAS6,Mt1,TGFB1,Mt2,E2F1,DLGAP5,CAMP,LCN2,IGF2,SYK,VTCN1,Tpm2,MMP14
Cell Cycle: G1/S Checkpoint Regulation	2.61E+00	1.16E-01	CCND3,TGFB1,CDKN2D,CCND1,E2F2,E2F1,RBL1,E2F7
Oxidative Stress	2.49E+00	1.23E-01	BRCA1,GSTM1,DUSP1,ME1,ICAM1,VCAM1,Gstm6
Increases Cardiac Dysfunction	2.40E+00	1.19E-01	ADRB2,TGFB1,NCF1,E2F1,NOX4,S100A1,CYBB
Cardiac Fibrosis	2.34E+00	7.17E-02	ADRB2,TGFB1,SLC8A1,NCF1,NOX4,MYLK3,HMOX1,IGF1R,POSTN,AR,PPP1R13L,THBS2,LPL,CYBB,CSRP3,SLC4A1
Increases Renal Damage	2.33E+00	9.68E-02	TGFB1,SLC8A1,THBS1,Mbl1,ICAM1,CYBB,POU2F2,CD44,FCGR2A
Cardiac Hypertrophy	2.13E+00	6.08E-02	ADRB2,BMP10,ADRA1B,TGFB1,HMGCR,PLIN5,BIRC5,SLC8A1,NCF1,NOX4,MYLK3,ADIPOQ,CA2,DUSP5,CKMT2,DUSP1,PRKAA2,ITGB3,S100A10,RGS4,CSRP3,TTN
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.07E+00	1.15E-01	TOP2A,BRCA1,AURKA,CKS1B,BORA,CDK1
Long-term Renal Injury Pro-oxidative Response Panel (Rat)	2.05E+00	2.31E-01	NCF1,NOX4,CYBB
Irreversible Glomerulonephritis Biomarker Panel (Rat)	2.05E+00	2.31E-01	LAMC1,COL1A1,NPR3

Day 60 Female BDE-99

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Acute Renal Failure Panel (Rat)	4.50E+00	6.45E-02	IGFBP1,Cyp4a14,Mt1,IGFBP5
Reversible Glomerulonephritis Biomarker Panel (Rat)	4.19E+00	1.11E-01	Cyp4a14,IGFBP5,HBB
Liver Necrosis/Cell Death	3.51E+00	1.90E-02	IGFBP1,Mt1,GSN,CCND1,Mt2,G6PC
Liver Proliferation	3.14E+00	2.05E-02	IGFBP1,Mt1,CCND1,Mt2,PIM3
Decreases Respiration of Mitochondria	3.13E+00	1.43E-01	Mt1,UCP1
PXR/RXR Activation	3.05E+00	4.62E-02	IGFBP1,CYP3A5,G6PC
Cholesterol Biosynthesis	3.01E+00	1.25E-01	PMVK,DHCR7
TR/RXR Activation	2.51E+00	3.00E-02	IRS2,UCP1,G6PC
Renal Necrosis/Cell Death	2.25E+00	1.07E-02	BCL6,Mt1,GSN,Mt2,MAFB,RGS16
Increases Liver Hyperplasia/Hyperproliferation	2.20E+00	2.33E-02	CCND1,ACSS2,PIM3
LPS/IL-1 Mediated Inhibition of RXR Function	2.19E+00	1.57E-02	Cyp4a14,FABP4,CYP3A5,FABP5

Day 5 Male PCB

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	5.78E+00	1.67E-01	Cyp2c54 (includes others),CYP1A2,CYP2A6 (includes others),Cyp2d9 (includes others)
NRF2-mediated Oxidative Stress Response	4.41E+00	2.78E-02	Cyp2c54 (includes others),Cyp4a14,CYP1A2,CYP4A11,CYP2A6 (includes others),JUNB,Cyp2d9 (includes others)
Cytochrome P450 Panel - Substrate is a Fatty Acid (Rat)	3.15E+00	1.82E-01	Cyp4a14,CYP4A11
Fatty Acid Metabolism	3.04E+00	3.42E-02	Cyp4a14,CYP1A2,CYP4A11,CYP2A6 (includes others)
Cytochrome P450 Panel - Substrate is a Fatty Acid (Mouse)	2.81E+00	1.25E-01	Cyp4a14,CYP4A11
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	2.71E+00	1.11E-01	CYP1A2,CYP2A6 (includes others)
LPS/IL-1 Mediated Inhibition of RXR Function	2.61E+00	1.96E-02	Cyp2c54 (includes others),Cyp4a14,CYP4A11,CYP2A6 (includes others),Cyp2d9 (includes others)
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	2.42E+00	8.00E-02	CYP1A2,CYP2A6 (includes others)
Reversible Glomerulonephritis Biomarker Panel (Rat)	2.36E+00	7.41E-02	Cyp4a14,IGFBP3
TGF-β Signaling	2.28E+00	3.12E-02	SERPINE1,SMAD9,INHBB

Day 5 Female PCB

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Increases Glomerular Injury	4.21E+00	3.53E-02	Kap,IL1B,CD274
Increases Liver Steatosis	3.95E+00	2.88E-02	IL1B,SCD,RGS16
Liver Necrosis/Cell Death	3.78E+00	1.28E-02	JUN,STAT1,SCD,CD274
Liver Proliferation	2.86E+00	1.23E-02	JUN,IL1B,STAT1
Cardiac Necrosis/Cell Death	2.62E+00	1.01E-02	IL1B,STAT1,SCD
Mechanism of Gene Regulation by Peroxisome Proliferators via PPARα	2.47E+00	2.11E-02	JUN,IL1B
Cardiac Hypertrophy	2.38E+00	8.31E-03	JUN,IL1B,TTN
LXR/RXR Activation	2.25E+00	1.63E-02	IL1B,SCD
Increases Liver Damage	2.24E+00	1.60E-02	IL1B,STAT1
Vasopressin-induced Genes in Inner Medullary Renal Collecting Duct Cells (Rat)	2.14E+00	1.25E-01	AQP4
Increases Renal Proliferation	2.10E+00	1.35E-02	JUN,IL1B
Aryl Hydrocarbon Receptor Signaling	2.03E+00	1.24E-02	JUN,IL1B
Hepatic Cholestasis	2.02E+00	1.23E-02	JUN,IL1B

Day 60 Male PCB

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
LPS/IL-1 Mediated Inhibition of RXR Function	5.98E+00	3.14E-02	Sult3a1/Sult3a2,JUN,FABP1,CYP3A5,Cyp2b13/Cyp2b9,SULT2A1,CYP2A6 (includes others),NR0B2
PXR/RXR Activation	5.79E+00	7.69E-02	IGFBP1,CYP3A5,SULT2A1,CYP2A6 (includes others),NR0B2
Mechanism of Gene Regulation by Peroxisome Proliferators via PPARα	4.98E+00	5.26E-02	PPARD,JUN,FABP1,DUSP1,NR0B2
Increases Liver Steatosis	4.77E+00	4.76E-02	LPIN1,TSC22D3,DUSP1,MFSD2A,RGS16
Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse)	4.28E+00	1.25E-01	CYP3A5,Cyp2b13/Cyp2b9,CYP2A6 (includes others)
VDR/RXR Activation	4.03E+00	5.13E-02	PPARD,IGFBP1,SULT2A1,SPP1
Acute Renal Failure Panel (Rat)	3.05E+00	4.84E-02	JUN,IGFBP1,EGR1
NRF2-mediated Oxidative Stress Response	2.98E+00	1.97E-02	JUN,CYP3A5,Cyp2b13/Cyp2b9,CYP2A6 (includes others),JUNB
Cholesterol Biosynthesis	2.97E+00	1.25E-01	PMVK,FDPS
Cytochrome P450 Panel - Substrate is a Xenobiotic (Human)	2.87E+00	1.11E-01	CYP3A5,CYP2A6 (includes others)
Aryl Hydrocarbon Receptor Signaling	2.83E+00	2.48E-02	JUN,CYP3A5,FASN,NR0B2
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	2.58E+00	8.00E-02	CYP3A5,CYP2A6 (includes others)
Renal Proximal Tubule Toxicity Biomarker Panel (Rat)	2.52E+00	7.41E-02	IGFBP1,SPP1
Cardiac Fibrosis	2.32E+00	1.79E-02	BCL6,IGHM,EGR1,SPP1
Cardiac Hypertrophy	2.31E+00	1.38E-02	JUN,DUSP1,CKMT2,CKM,TTN
Xenobiotic Metabolism Signaling	2.30E+00	1.37E-02	Sult3a1/Sult3a2,CYP3A5,Cyp2b13/Cyp2b9,SULT2A1,CYP2A6 (includes others)
Fatty Acid Metabolism	2.26E+00	2.56E-02	CYP3A5,Cyp2b13/Cyp2b9,CYP2A6 (includes others)
Liver Proliferation	2.19E+00	1.64E-02	PPARD,JUN,IGFBP1,SPP1
FXR/RXR Activation	2.17E+00	2.38E-02	FASN,SULT2A1,NR0B2
Renal Necrosis/Cell Death	2.15E+00	1.07E-02	PPARD,BCL6,DUSP1,MAFB,SPP1,RGS16

Day 60 Female PCB

Ingenuity Toxicity Lists	-log(p-value)	Ratio	Molecules
Acute Renal Failure Panel (Rat)	6.16E+00	6.45E-02	IGFBP1,IGFBP5,EGR1,LCN2
PXR/RXR Activation	4.27E+00	4.62E-02	IGFBP1,CYP3A5,SULT2A1
VDR/RXR Activation	4.03E+00	3.85E-02	IGFBP1,IGFBP5,SULT2A1
LPS/IL-1 Mediated Inhibition of RXR Function	2.53E+00	1.18E-02	Sult3a1/Sult3a2,CYP3A5,SULT2A1
Hepatic Fibrosis	2.19E+00	1.89E-02	IGFBP1,IGFBP5
Xenobiotic Metabolism Signaling	2.10E+00	8.24E-03	Sult3a1/Sult3a2,CYP3A5,SULT2A1
FXR/RXR Activation	2.05E+00	1.59E-02	SULT2A1,A1BG

Day 5 Male BPA

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Cholestasis	cholestasis	Cholestasis	1.06E-12				
Liver Cholestasis	progressive familial intrahepatic cholestasis type 1	Progressive familial intrahepatic cholestasis type 1	8.31E-09				
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	6.24E-05				
Liver Enlargement	hepatomegaly	Hepatomegaly	9.24E-04				
Liver Hyperplasia/Hyperproliferation	cancer	Liver cancer	1.37E-03				
Liver Hyperplasia/Hyperproliferation	size	Size of liver tumor	1.51E-03				
Glutathione Depletion In Liver	conjugation	Conjugation of glutathione	3.59E-03				
Renal Degeneration	degeneration	Degeneration of kidney	4.34E-03				
Liver Cholestasis	cholestasis	Advanced stage cholestasis	4.49E-03				
Congenital Heart Anomaly	atrial septal defect type 3	Atrial septal defect type 3	4.49E-03				
Cardiac Dilation	dilated cardiomyopathy 1m	Dilated cardiomyopathy 1m	4.49E-03				
Cardiac Dilation	dilated cardiomyopathy type 1EE	Dilated cardiomyopathy type 1EE	4.49E-03				
Cardiac Enlargement	hypertrophy	Hypertrophy of cardiac anterior wall	4.49E-03				
Cardiac Arrythmia	sick sinus syndrome type 3	Sick sinus syndrome type 3	4.49E-03				
Kidney Failure	end stage renal disease	End stage renal disease	6.69E-03				
Renal Degeneration	degeneration	Degeneration of tubular cells	8.96E-03				
Liver Hyperbilirubinemia	Dubin-Johnson syndrome	Dubin-Johnson syndrome	8.96E-03				
Liver Hemorrhaging	bleeding	Bleeding of liver	9.06E-03				
Liver Degeneration	degeneration	Degeneration of liver	9.61E-03				
Liver Hyperplasia/Hyperproliferation	quantity	Quantity of liver tumor	9.61E-03				

Day 5 Female BPA

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Hyperplasia/Hyperproliferation	size	Size of liver tumor	2.15E-04				
Renal Degeneration	degeneration	Degeneration of kidney	6.32E-04				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	9.71E-04				
Liver Hemorrhaging	bleeding	Bleeding of liver	1.34E-03				
Liver Degeneration	degeneration	Degeneration of liver	1.43E-03				
Liver Hyperplasia/Hyperproliferation	quantity	Quantity of liver tumor	1.43E-03				
Cardiac Dilation	dilated cardiomyopathy 1g	Dilated cardiomyopathy 1g	1.69E-03				
Cardiac Dysfunction	left ventricular noncompaction type 2	Left ventricular noncompaction type 2	1.69E-03				
Cardiac Arrythmia, Congenital Heart Anomaly	susceptibility to acquired long QT syndrome type 9	Susceptibility to acquired long QT syndrome type 9	1.69E-03				
Renal Atrophy	atrophy of kidney	Atrophy of kidney	2.88E-03				
Renal Degeneration	degeneration	Degeneration of tubular cells	3.39E-03				
Cardiac Arrythmia, Congenital Heart Anomaly	digenic long QT syndrome 2/9	Digenic long QT syndrome 2/9	3.39E-03				
Renal Necrosis/Cell Death	apoptosis	Apoptosis of renal tubule	3.65E-03				
Glomerular Injury, Kidney Failure, Renal Fibrosis	interstitial fibrosis	Interstitial fibrosis of kidney	4.65E-03				
Cardiac Arrythmia	familial arrhythmogenic right ventricular dysplasia type 1	Familial arrhythmogenic right ventricular dysplasia type 1	5.07E-03				
Renal Enlargement	nephromegaly	Nephromegaly	5.93E-03				
Liver Regeneration	regeneration	Regeneration of liver	9.76E-03				

Day 60 Male BPA

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	4.72E-10		0.726		0.844
Liver Hyperplasia/Hyperproliferation	liver carcinoma	Liver carcinoma	1.65E-08		0.396		0.578
Liver Hyperplasia/Hyperproliferation	cancer	Liver cancer	8.56E-08		1.412		1.538
Liver Hyperplasia/Hyperproliferation	liver tumor	Liver tumor	1.22E-07		0.853		1.09
Liver Steatosis	hepatic steatosis	Hepatic steatosis	9.50E-07		1.179		2.093
Liver Proliferation	proliferation	Proliferation of liver cells	1.16E-06		1.254		0.542
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	2.70E-06				
Cardiac Necrosis/Cell Death	necrosis	Necrosis of cardiac muscle	4.92E-06		-1.255		-0.613
Renal Proliferation	cell proliferation	Cell proliferation of kidney cell lines	9.31E-06		0.209		-0.141
Cardiac Necrosis/Cell Death	cell death	Cell death of cardiomyocytes	1.23E-05		-1.101		-0.495
Renal Inflammation, Renal Nephritis	glomerulonephritis	Glomerulonephritis	2.54E-05		-0.194 bias		0.834
Renal Inflammation, Renal Nephritis	nephritis	Nephritis	5.20E-05		-0.738 bias		0.552
Renal Necrosis/Cell Death	cell death	Cell death of renal tubule	6.18E-05		-1.066		-0.558
Liver Proliferation	proliferation	Proliferation of hepatocytes	1.49E-04		-0.079		-0.574
Cardiac Necrosis/Cell Death	apoptosis	Apoptosis of cardiomyocytes	1.96E-04		-1.228		-0.664
Cardiac Arteriopathy	disorder of coronary artery	Disorder of coronary artery	2.66E-04				
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Refractory hepatosplenic T-cell lymphoma	2.73E-04				
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Relapsed hepatosplenic T-cell lymphoma	2.73E-04				
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Resectable liver cholangiocarcinoma	2.73E-04				
Renal Necrosis/Cell Death	apoptosis	Apoptosis of renal tubule	3.23E-04		-1.134		-0.767
Liver Hyperplasia/Hyperproliferation	growth	Growth of liver tumor	3.23E-04		1.998 bias		1.298
Kidney Failure	failure	Failure of kidney	3.28E-04		-1.316 bias		-0.211
Liver Inflammation/Hepatitis	inflammation	Inflammation of liver	3.68E-04		-0.937		-0.129
Liver Hyperplasia/Hyperproliferation	hepatic adenocarcinoma	Hepatic adenocarcinoma	4.53E-04				
Renal Proliferation	proliferation	Proliferation of renal tubular epithelial cells	4.68E-04				
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Hepatosplenic T-cell lymphoma	7.27E-04				
Increased Levels of Red Blood Cells	quantity	Increased Levels of Red Blood Cells	1.00E-03	Increased	2.958 bias		
Renal Necrosis/Cell Death	necrosis	Necrosis of renal tubule	1.01E-03		-0.82		-0.336
Cardiac Damage	cardiotoxicity	Cardiotoxicity	1.17E-03				
Cardiac Enlargement	enlargement	Enlargement of heart	1.32E-03				
Renal Enlargement	nephromegaly	Nephromegaly	1.32E-03				
Renal Necrosis/Cell Death	cell death	Cell death of kidney cells	1.56E-03		0.742		0.187
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Liver cholangiocarcinoma	1.61E-03				
Liver Necrosis/Cell Death	necrosis	Necrosis of liver	1.81E-03		-0.213		0.338
Liver Fibrosis, Liver Proliferation	proliferation	Proliferation of hepatic stellate cells	1.95E-03		1.964		1.526
Cardiac Arteriopathy	coronary artery disease	Coronary artery disease	1.98E-03				
Cardiac Fibrosis	fibrosis	Fibrosis of heart	1.98E-03		-0.614		0.047
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	growth	Growth of hepatocellular carcinoma	2.14E-03		1.98 bias		
Increased Levels of Hematocrit	hematocrit	Increased Levels of Hematocrit	2.56E-03	Increased	2.76 bias		
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	childhood type hepatocellular carcinoma	Childhood type hepatocellular carcinoma	2.75E-03				
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Metastatic liver cholangiocarcinoma	3.43E-03				
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Unresectable liver cholangiocarcinoma	3.43E-03				
Cardiac Dysfunction	systolic dysfunction	Systolic dysfunction	4.19E-03				
Cardiac Dysfunction	diastolic dysfunction	Diastolic dysfunction of heart	4.29E-03				
Biliary Hyperplasia	proliferation	Proliferation of cholangiocytes	4.29E-03				
Kidney Failure	acute renal failure	Acute renal failure	4.42E-03				
Renal Necrosis/Cell Death	cell death	Cell death of kidney cell lines	5.41E-03		0.652		0.059
Glutathione Depletion In Liver, Liver Fibrosis	generation	Generation of reactive oxygen species in liver	5.65E-03				
Cardiac Dysfunction	diastolic dysfunction	Diastolic dysfunction	6.52E-03				
Cardiac Enlargement	hypertrophy	Hypertrophy of heart	6.73E-03				
Liver Hyperplasia/Hyperproliferation	liver metastasis	Liver metastasis	7.17E-03	Increased	2		1.638
Congenital Heart Anomaly	ventricular septal defect	Ventricular septal defect	7.45E-03		-1.98 bias		
Cardiac Dilation, Cardiac Enlargement	dilated cardiomyopathy	Dilated cardiomyopathy	7.82E-03				
Liver Hyperplasia/Hyperproliferation	hepatoblastoma	Hepatoblastoma	7.89E-03				
Liver Hyperplasia/Hyperproliferation	quantity	Quantity of liver tumor	8.16E-03				
Renal Inflammation, Renal Nephritis	systemic lupus erythematosus nephritis	Systemic lupus erythematosus nephritis	8.16E-03				
Cardiac Hemorrhaging	bleeding	Bleeding of heart	8.34E-03				
Renal Proliferation	cytostasis	Cytostasis of kidney cell lines	8.34E-03				
Liver Hyperplasia/Hyperproliferation	liver tumor	Metastatic liver tumor	9.07E-03				
Liver Necrosis/Cell Death	cell death	Cell death of liver cells	9.53E-03		1.59		1.762
Cardiac Dysfunction	dysfunction	Dysfunction of heart	9.53E-03		1.715		1.827

Day 60 Female BPA

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	1.32E-08				
Liver Hyperplasia/Hyperproliferation	hepatic adenocarcinoma	Hepatic adenocarcinoma	5.79E-06				
Liver Hyperplasia/Hyperproliferation	liver tumor	Liver tumor	6.98E-06		1.383		1.59
Liver Hyperplasia/Hyperproliferation	liver carcinoma	Liver carcinoma	9.41E-06		0.651		0.844
Liver Hyperplasia/Hyperproliferation	cancer	Liver cancer	1.97E-05		0.97		1.092
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Liver cholangiocarcinoma	7.57E-04				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	growth	Growth of hepatocellular carcinoma	7.64E-04				
Renal Necrosis/Cell Death	apoptosis	Apoptosis of renal tubule	8.74E-04		-1		-0.606
Liver Hyperplasia/Hyperproliferation	growth	Growth of liver tumor	8.74E-04		1.997 bias		1.237
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Refractory hepatosplenic T-cell lymphoma	9.11E-04				
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Relapsed hepatosplenic T-cell lymphoma	9.11E-04				
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Resectable liver cholangiocarcinoma	9.11E-04				
Kidney Failure	acute tubular necrosis	Acute tubular necrosis	1.27E-03				
Renal Proliferation	proliferation	Proliferation of renal tubular epithelial cells	1.27E-03				
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Hepatosplenic T-cell lymphoma	1.68E-03				
Liver Hyperplasia/Hyperproliferation	liver tumor	Metastatic liver tumor	2.42E-03				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	childhood type hepatocellular carcinoma	Childhood type hepatocellular carcinoma	3.86E-03				
Kidney Failure	failure	Failure of kidney	3.87E-03		-1 bias		
Renal Necrosis/Cell Death	apoptosis	Apoptosis of tubular cells	4.14E-03				
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Metastatic liver cholangiocarcinoma	4.57E-03				
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Unresectable liver cholangiocarcinoma	4.57E-03				
Renal Necrosis/Cell Death	cell death	Cell death of kidney cells	4.68E-03		0.38		-0.101
Liver Regeneration	regeneration	Regeneration of liver	5.24E-03				
Glomerular Injury, Renal Fibrosis	fibrosis	Fibrosis of kidney component	6.09E-03				
Renal Atrophy	atrophy of kidney	Atrophy of kidney	6.45E-03				
Increased Levels of Hematocrit	hematocrit	Increased Levels of Hematocrit	7.37E-03		1.944 bias		
Liver Hyperplasia/Hyperproliferation	hepatoblastoma	Hepatoblastoma	7.64E-03				
Cardiac Dilation, Cardiac Enlargement	dilated cardiomyopathy	Advanced stage dilated cardiomyopathy	7.90E-03				
Cardiac Stenosis	supravalvular aortic stenosis	Autosomal dominant supravalvular aortic stenosis	7.90E-03				
Increased Levels of Albumin	flux	Increased flux of albumin	7.90E-03				
Heart Failure	heart failure	Progressive heart failure	7.90E-03				
Kidney Failure	septic acute kidney injury	Septic acute kidney injury	7.90E-03				

Day 5 Male BDE-99

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Increased Levels of Hematocrit	hematocrit	Increased Levels of Hematocrit	1.92E-06	Increased	2.941 bias		1.933
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	1.05E-04				
Liver Damage	damage	Damage of hepatocytes	5.09E-04				
Renal Damage	damage	Damage of kidney	6.72E-04		0.478		0.232
Liver Damage	injury	Injury of hepatocytes	7.90E-04				
Kidney Failure	failure	Failure of kidney	8.40E-04		-1.633		-1.13
Liver Damage	damage	Damage of liver	1.09E-03		-1.604		-1.6
Increased Levels of Red Blood Cells	quantity	Increased Levels of Red Blood Cells	1.28E-03	Increased	2.412 bias		1.586
Heart Failure	chronic heart failure	Chronic heart failure	1.66E-03				
Cardiac Infarction	myocardial infarction	Myocardial infarction	2.67E-03				
Kidney Failure	stage V chronic kidney disease	Stage V chronic kidney disease	2.70E-03				
Kidney Failure	end stage renal disease	End stage renal disease	3.29E-03				
Renal Necrosis/Cell Death	apoptosis	Apoptosis of renal tubule	3.30E-03		0		0.164
Cardiac Infarction	ST-elevation myocardial infarction	ST-elevation myocardial infarction	4.86E-03				
Liver Hematopoiesis	erythropoiesis	Erythropoiesis of liver	5.66E-03				
Renal Damage	injury	Injury of kidney	7.66E-03		0		-0.159
Cardiac Dysfunction, Cardiac Enlargement	hypertrophy	Hypertrophy of left ventricle	9.17E-03				
Liver Hyperplasia/Hyperproliferation	size	Size of liver tumor	9.59E-03				
Cardiac Arrythmia	tachyarrhythmia	Tachyarrhythmia	9.59E-03				

Day 5 Female BDE-99

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Enlargement	hypertrophy	Hypertrophy of liver	6.40E-03				
Kidney Failure	acute tubular necrosis	Acute tubular necrosis	8.94E-03				

Day 60 Male BDE-99

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	7.74E-16		-0.122		-0.041
Liver Hyperplasia/Hyperproliferation	cancer	Liver cancer	5.92E-13		0.192		0.275
Liver Hyperplasia/Hyperproliferation	liver carcinoma	Liver carcinoma	1.10E-12		-0.372		-0.248
Liver Hyperplasia/Hyperproliferation	liver tumor	Liver tumor	2.06E-11		0.478		0.643
Glutathione Depletion In Liver	conjugation	Conjugation of glutathione	1.64E-07	Decreased	-2.605 bias		-3.644
Liver Steatosis	hepatic steatosis	Hepatic steatosis	5.16E-06		-0.194		0.42
Liver Proliferation	proliferation	Proliferation of liver cells	5.65E-06		1.666		1.185
Liver Necrosis/Cell Death	necrosis	Necrosis of liver	1.15E-05		0.368		0.82
Kidney Failure	failure	Failure of kidney	1.62E-05		-0.323		0.482
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	1.73E-05				
Renal Necrosis/Cell Death	cell death	Cell death of renal tubule	3.28E-05		-1.035		-0.687
Liver Inflammation/Hepatitis	inflammation	Inflammation of liver	4.97E-05		0.064		0.721
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Hepatosplenic T-cell lymphoma	5.61E-05				
Renal Inflammation, Renal Nephritis	nephritis	Nephritis	5.66E-05		-0.703		0.153
Cardiac Dysfunction	dysfunction	Dysfunction of heart	6.77E-05		1.931		2.019
Cardiac Dysfunction	diastolic dysfunction	Diastolic dysfunction	7.03E-05				
Renal Proliferation	cell proliferation	Cell proliferation of kidney cell lines	8.80E-05		-0.535		-0.76
Cardiac Necrosis/Cell Death	necrosis	Necrosis of cardiac muscle	9.45E-05		-1.011		-0.603
Renal Enlargement	nephromegaly	Nephromegaly	1.04E-04				
Renal Inflammation, Renal Nephritis	systemic lupus erythematosus nephritis	Systemic lupus erythematosus nephritis	1.08E-04				
Cardiac Enlargement	hypertrophy	Hypertrophy of heart	1.13E-04				
Kidney Failure	acute renal failure	Acute renal failure	1.39E-04				
Renal Inflammation, Renal Nephritis	glomerulonephritis	Glomerulonephritis	1.52E-04		-0.194		0.444
Cardiac Necrosis/Cell Death	apoptosis	Apoptosis of cardiomyocytes	1.60E-04		-0.915		-0.534
Cardiac Necrosis/Cell Death	cell death	Cell death of cardiomyocytes	1.84E-04		-0.86		-0.474

Liver Necrosis/Cell Death	cell death	Cell death of liver cells	1.88E-04		1.874	2.019
Renal Damage	damage	Damage of kidney	2.02E-04	increased	2.122	1.767
Cardiac Damage	cardiotoxicity	Cardiotoxicity	2.43E-04			
Cardiac Enlargement	enlargement	Enlargement of heart	3.08E-04			
Congenital Heart Anomaly	ventricular septal defect	Ventricular septal defect	3.40E-04		-0.347	bias 0.718
Renal Necrosis/Cell Death	necrosis	Necrosis of renal tubule	3.64E-04		-0.739	-0.397
Cardiac Dysfunction	ventricular dysfunction	Ventricular dysfunction	3.80E-04		1.751	1.809
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	childhood type hepatocellular carcinoma	Childhood type hepatocellular carcinoma	3.81E-04			
Cardiac Inflammation	endocarditis	Endocarditis	3.84E-04			
Renal Necrosis/Cell Death	apoptosis	Apoptosis of renal tubule	4.81E-04		-1.414	-1.171
Liver Hyperplasia/Hyperproliferation	growth	Growth of liver tumor	4.81E-04		1.264	0.804
Cardiac Arteriopathy	disorder of coronary artery	Disorder of coronary artery	5.06E-04			
Cardiac Dysfunction	left ventricular dysfunction	Left ventricular dysfunction	5.38E-04		1.236	1.286
Heart Failure	chronic heart failure	Chronic heart failure	6.96E-04			
Cardiac Dysfunction	systolic dysfunction	Systolic dysfunction	6.96E-04			
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Refractory hepatosplenic T-cell lymphoma	7.48E-04			
Liver Hyperplasia/Hyperproliferation	hepatosplenic T-cell lymphoma	Relapsed hepatosplenic T-cell lymphoma	7.48E-04			
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Resectable liver cholangiocarcinoma	7.48E-04			
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Metastatic liver cholangiocarcinoma	7.72E-04			
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Unresectable liver cholangiocarcinoma	7.72E-04			
Cardiac Infarction	myocardial infarction	Myocardial infarction	8.45E-04		0.034	0.275
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	growth	Growth of hepatocellular carcinoma	9.50E-04		0.967	bias 0.271
Liver Hyperplasia/Hyperproliferation	liver tumor	Metastatic liver tumor	9.53E-04			
Renal Enlargement	hypertrophy	Hypertrophy of kidney	1.04E-03			
Cardiac Arrythmia	arrhythmia	Arrhythmia	1.05E-03		0.391	0.401
Cardiac Arrythmia	atrial fibrillation	Atrial fibrillation	1.07E-03			
Renal Necrosis/Cell Death	cell death	Cell death of kidney cells	1.12E-03		1.033	0.634
Kidney Failure	acute tubular necrosis	Acute tubular necrosis	1.28E-03			
Renal Proliferation	proliferation	Proliferation of renal tubular epithelial cells	1.28E-03			
Renal Damage	injury	Injury of kidney	1.36E-03		0.97	0.697
Cardiac Arrythmia	cardiac fibrillation	Cardiac fibrillation	1.43E-03			
Renal Hydronephrosis	hydronephrosis	Hydronephrosis	1.70E-03		-1.109	bias -0.315
Liver Hyperplasia/Hyperproliferation	hepatoblastoma	Hepatoblastoma	1.71E-03			
Heart Failure	cardiac decompensation	Cardiac decompensation	1.81E-03			
Increased Levels of Hematocrit	hematocrit	Increased Levels of Hematocrit	1.84E-03	increased	2.525	bias 1.286
Congenital Heart Anomaly	double outlet right ventricle	Double outlet right ventricle	1.92E-03			
Cardiac Dysfunction, Heart Failure	diastolic heart failure	Diastolic heart failure	1.99E-03			
Renal Enlargement	hypertrophy	Hypertrophy of renal glomerulus	2.00E-03			
Renal Proliferation	proliferation	Proliferation of kidney cells	2.17E-03		0.115	-0.152
Cardiac Arteriopathy	coronary artery disease	Coronary artery disease	2.33E-03			
Liver Fibrosis, Liver Proliferation	proliferation	Proliferation of hepatic stellate cells	2.39E-03	increased	2.236	1.927
Increased Levels of Red Blood Cells	quantity	Increased Levels of Red Blood Cells	3.09E-03	increased	3.12	bias 1.876
Liver Hyperplasia/Hyperproliferation	hepatic adenocarcinoma	Hepatic adenocarcinoma	3.27E-03			
Cardiac Fibrosis	interstitial fibrosis	Interstitial fibrosis of heart	3.30E-03		1.387	1.197
Cardiac Proliferation	proliferation	Proliferation of adventitial fibroblasts	3.46E-03			
Liver Damage	damage	Damage of liver	3.92E-03		0.246	0.239
Liver Proliferation	proliferation	Proliferation of hepatocytes	4.01E-03		-0.162	-0.469
Cardiac Inflammation	carditis	Carditis	4.16E-03			
Heart Failure	acute heart failure	Acute heart failure	4.20E-03			
Cardiac Enlargement	ventricular hypertrophy	Ventricular hypertrophy	4.22E-03			
Cardiac Dysfunction, Cardiac Enlargement	hypertrophy	Hypertrophy of left ventricle	4.62E-03			
Congenital Heart Anomaly	single ventricle defect	Single ventricle defect	5.19E-03			
Cardiac Dysfunction, Heart Failure	systolic heart failure	Systolic heart failure	5.19E-03			
Renal Damage, Renal Tubule Injury	damage	Damage of renal tubule	5.22E-03		0.849	0.616
Liver Cholestasis	secretion	Secretion of bile acid	5.42E-03			
Congenital Heart Anomaly	conotruncal heart malformations	Conotruncal heart malformations	5.71E-03			
Cardiac Dysfunction	left ventricular dilation	Left ventricular dilation	5.80E-03			
Cardiac Infarction	acute myocardial infarction	Acute myocardial infarction	6.59E-03			
Liver Hyperplasia/Hyperproliferation	liver metastasis	Inoperable liver metastasis	6.76E-03			
Renal Inflammation, Renal Nephritis	crescentic glomerulonephritis	Progressive crescentic glomerulonephritis	6.76E-03			
Cardiac Fibrosis	fibrosis	Fibrosis of heart	7.49E-03		0.254	0.713
Liver Hyperplasia/Hyperproliferation	liver cholangiocarcinoma	Liver cholangiocarcinoma	8.57E-03			
Liver Necrosis/Cell Death	cell death	Cell death of hepatocytes	8.71E-03		1.415	1.546
Heart Failure	cardiorenal syndrome	Cardiorenal syndrome	9.84E-03			

Day 60 Female BDE-99

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Steatosis	hepatic steatosis	Hepatic steatosis	2.58E-07		-0.323		-0.414
Liver Necrosis/Cell Death	necrosis	Necrosis of liver	2.89E-04	increased	2.176		2.117
Liver Inflammation/Hepatitis	inflammation	Inflammation of liver	3.45E-04		-1.159		-1.242
Renal Atrophy	atrophy of kidney	Atrophy of kidney	3.68E-04				
Renal Necrosis/Cell Death	apoptosis	Apoptosis of renal tubule	5.22E-04				
Liver Proliferation	proliferation	Proliferation of liver cells	5.71E-04		0.853		0.916
Liver Inflammation/Hepatitis	infection	Infection by Hepatitis C virus genotype 1	6.35E-04				
Liver Hyperplasia/Hyperproliferation	size	Size of liver tumor	6.35E-04				
Liver Hyperplasia/Hyperproliferation	liver tumor	Liver tumor	8.92E-04		1.664		1.641
Renal Enlargement	nephromegaly	Nephromegaly	1.02E-03				
Liver Hyperplasia/Hyperproliferation	cancer	Liver cancer	1.33E-03				
Liver Steatosis	nonalcoholic fatty liver disease	Nonalcoholic fatty liver disease	1.41E-03				
Renal Degeneration	degeneration	Degeneration of kidney	1.85E-03				
Liver Proliferation	proliferation	Proliferation of hepatocytes	1.91E-03		0.471		0.518
Liver Regeneration	regeneration	Regeneration of liver	2.15E-03				
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	2.52E-03				
Liver Enlargement	hepatomegaly	Hepatomegaly	2.76E-03				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	3.11E-03				
Liver Hyperplasia/Hyperproliferation	liver carcinoma	Liver carcinoma	3.56E-03				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	development	Development of hepatocellular carcinoma	3.74E-03				
Liver Hemorrhaging	bleeding	Bleeding of liver	3.90E-03				
Liver Hyperplasia/Hyperproliferation	quantity	Quantity of liver tumor	4.14E-03				
Glomerular Injury	abnormal morphology	Abnormal morphology of renal glomerulus	4.15E-03				
Liver Degeneration	degeneration	Degeneration of liver	4.65E-03				
Liver Inflammation/Hepatitis	infection	Infection by Hepatitis C virus	5.52E-03				
Renal Degeneration	degeneration	Degeneration of tubular cells	5.80E-03				
Renal Necrosis/Cell Death	apoptosis	Apoptosis of tubular cells	6.33E-03				

Day 5 Male PCB

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Hematopoiesis	hematopoiesis	Arrest in hematopoiesis of liver	3.66E-03				
Pulmonary Hypertension	primary pulmonary hypertension 2	Primary pulmonary hypertension 2	3.66E-03				
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	4.85E-03				
Renal Inflammation, Renal Nephritis	membranoproliferative glomerulonephritis type II	Membranoproliferative glomerulonephritis type II	7.31E-03				

Day 5 Female PCB

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Damage	damage	Damage of liver	1.52E-05				
Liver Necrosis/Cell Death	apoptosis	Apoptosis of liver cells	2.51E-05		1.969		1.979
Cardiac Dysfunction	diastolic dysfunction	Diastolic dysfunction of heart	7.20E-05				
Liver Necrosis/Cell Death	apoptosis	Apoptosis of hepatocytes	4.16E-04				
Liver Steatosis	hepatic steatosis	Hepatic steatosis	4.42E-04				
Liver Fibrosis	fibrosis	Fibrosis of liver	4.55E-04				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	6.66E-04				
Liver Inflammation/Hepatitis	inflammation	Inflammation of liver	6.74E-04				
Liver Necrosis/Cell Death	apoptosis	Apoptosis of hepatoblasts	9.16E-04				
Cardiac Dilation	dilated cardiomyopathy 1g	Dilated cardiomyopathy 1g	9.16E-04				
Increased Levels of Albumin	release	Increased release of albumin	9.16E-04				
Cardiac Dysfunction	left ventricular noncompaction type 2	Left ventricular noncompaction type 2	9.16E-04				
Liver Proliferation	proliferation	Proliferation of liver cells	1.18E-03				
Cardiac Dysfunction	dysfunction	Dysfunction of heart	1.45E-03				
Cardiac Necrosis/Cell Death	cell death	Cell death of heart	2.28E-03				
Liver Damage	hepatic injury	Hepatic injury	2.48E-03				
Cardiac Arrythmia	familial arrhythmogenic right ventricular dysplasia type 1	Familial arrhythmogenic right ventricular dysplasia type 1	2.75E-03				
Decreased Levels of Albumin	secretion	Decreased secretion of albumin	3.66E-03				
Liver Hyperplasia/Hyperproliferation	liver cancer	Early stage liver cancer	3.66E-03				
Kidney Failure	acute tubular necrosis	Acute tubular necrosis	6.39E-03				
Cardiac Dysfunction, Cardiac Fibrosis	interstitial fibrosis	Interstitial fibrosis of left ventricle	6.39E-03				
Increased Levels of ALT	release	Increased release of ALT	7.30E-03				
Cardiac Enlargement	hypertrophy	Hypertrophy of heart	8.50E-03				
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	size	Size of hepatocellular carcinoma	9.12E-03				

Day 60 Male PCB

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	3.90E-07				
Liver Steatosis	hepatic steatosis	Hepatic steatosis	4.03E-07		1.172		0.879
Liver Inflammation/Hepatitis	inflammation	Inflammation of liver	1.11E-06		1.706		1.347
Liver Damage	damage	Damage of liver	1.18E-04		0.492		0.497
Hepatocellular Carcinoma, Liver Hyperplasia/Hyperproliferation	hepatocellular carcinoma	Hepatocellular carcinoma	3.53E-04				
Cardiac Inflammation	myocarditis	Myocarditis	3.96E-04				
Kidney Failure	failure	Failure of kidney	4.11E-04				
Cardiac Enlargement	hypertrophy	Hypertrophy of heart	5.91E-04				
Renal Damage	damage	Damage of kidney	7.61E-04				
Renal Damage	injury	Injury of kidney	2.17E-03				
Liver Regeneration	regeneration	Regeneration of liver	2.45E-03				
Liver Necrosis/Cell Death	apoptosis	Apoptosis of hepatoblasts	3.04E-03				
Cardiac Dilation, Cardiac Enlargement	dilated cardiomyopathy 1g	Dilated cardiomyopathy 1g	3.04E-03				
Renal Damage	injury	Injury of outer medulla	3.04E-03				
Cardiac Dysfunction, Heart Failure	left ventricular failure	Left ventricular failure	3.04E-03				
Cardiac Dysfunction	left ventricular noncompaction type 2	Left ventricular noncompaction type 2	3.04E-03				
Renal Necrosis/Cell Death	cell death	Cell death of kidney cells	3.23E-03		0.577		0.729
Cardiac Dysfunction, Cardiac Enlargement	hypertrophy	Hypertrophy of left ventricle	4.60E-03				
Liver Proliferation	proliferation	Proliferation of liver cells	5.47E-03		1		1.208
Cardiac Fibrosis	fibrosis	Fibrosis of heart	5.72E-03	increased	2		1.765
Renal Damage	injury	Injury of renal cortex	6.07E-03				
Renal Damage, Renal Tubule Injury	injury	Injury of tubulointerstitium	6.07E-03				
Liver Inflammation/Hepatitis	infection	Infection by Hepatitis C virus	6.27E-03				
Cardiac Dysfunction	dysfunction	Dysfunction of heart	7.39E-03				
Renal Inflammation, Renal Nephritis	proliferative nephritis	Proliferative nephritis	8.65E-03				
Liver Steatosis	hepatic steatosis	Advanced stage hepatic steatosis	9.10E-03				
Renal Proliferation	contact growth inhibition	Contact growth inhibition of kidney cell lines	9.10E-03				
Cardiac Arrythmia	familial arrhythmogenic right ventricular dysplasia type 1	Familial arrhythmogenic right ventricular dysplasia type 1	9.10E-03				
Pulmonary Hypertension	chronic thromboembolic pulmonary hypertension	Inoperable chronic thromboembolic pulmonary hypertension	9.10E-03				
Cardiac Dysfunction	left ventricular dilation	Left ventricular dilation	9.39E-03				

Day 60 Female PCB

Categories	Functions	Diseases or Functions Annotation	p-Value	Predicted Activation State	Activation z-score	Notes	Bias-corrected z-score
Liver Steatosis	hepatic steatosis	Hepatic steatosis	8.22E-05		-0.254		-0.171
Kidney Failure	septic acute kidney injury	Septic acute kidney injury	1.13E-03				
Liver Inflammation/Hepatitis	inflammation	Inflammation of liver	1.61E-03				
Renal Damage	ischemic injury	Ischemic injury of kidney	2.27E-03				
Liver Regeneration	regeneration	Regeneration of liver	4.46E-03				
Liver Damage	injury	Injury of hepatocytes	4.53E-03				
Renal Damage, Renal Tubule Injury	proximal tubular toxicity	Proximal tubular toxicity	4.97E-03				
Kidney Failure	acute tubular necrosis	Acute tubular necrosis	7.92E-03				
Renal Proliferation	proliferation	Proliferation of renal tubular epithelial cells	7.92E-03				

Table S3-8. Day 60 top 10 upstream regulators

	BPA	BDE-99	PCB			
Male	Trp53	Ppara	Myod1	Trp53	Ppara	Rorc
	Erbb2	Por	Htt	Erbb2	Por	Htt
	Yy1	Trp53	STAT5B	Csf2	Trp53	Scap
	Csf2	Scap	Scap	Yy1	Scap	Fgf15
	Ccnd1	Erbb2	Rorc	Ppara	Fgf15	Myod1
	Ppara	Fgf15	Fgf15	Ccnd1	Atp7b	Nr5a2
	E2f4	Atp7b	Srebf2	E2f3	Erbb2	Rora
	E2f1	Nr1i3	Nr5a2	Cdkn1a	Il6	Srebf1
	E2f3	Ccnd1	Rora	E2f4	Nr1i3	Srf
	Cdkn1a	Il6	Srebf2	E2f1	Tnf	Insr
Female	Ptger2	Ppara	Rorc	Ptger2	Ppara	Rorc
	Cdkn1a	Srebf1	STAT5B	Cdkn1a	Srebf1	Rora
	E2f1	Pparg	Fgf15	Yy1	Med1	Fgf15
	Trp53	Ins1	Rora	Trp53	Rorc	Cyp1a2
	Yy1	Insr	Nr1i2	E2f4	Pparg	Il1b
	E2f4	Ins	Rxra	E2f1	Fgf15	Cyp1b1
	Tcf3	Med1	Il1b	Csf2	Rora	Nr1i2
	Csf2	Irs1	Cebpa	Tcf3	Ins	Foxa2
	Rabl6	Foxa2	Ppara	Il6	Igf1	Nr5a2
	Hgf	Fgf15	Irs2	Hgf	Insr	Cyp1a1

Table S3-7. Day 5 top 10 upstream regulators

	BPA	BDE-99	PCB
Male	Nr1i3	Trim24	Abcb6
	Nr1i2	Ifnb1	Cebpb
	Por	Stat1	Acox1
	Rora	Ifng	Sash1
	Acox1	Il6	Tbk1
	Stat5b	Stat3	H-7
	Rxra	Il10ra	Procr
	PXR ligand-PXR-Retinoic acid-RXRα	Gata1	Samsn1
	Ppara	Irf7	Hif1a
	Rorc	Irf3	Nr1i2
Female	Gata2	Gata2	Stat1
	Cyp1a2	Il1b	Parp1
	Ikbkg	Il6	Mapk1
	Il1b	Foxa2	Il1b
	Cyp1b1	Stat1	Il17a
	Htt	Fech	Tab1
	Procr	Abcb6	Btk
	Fox2a	Zbtb20	RAS
	Rora	Ebi3	Il27
	Chuk	Rorc	Stat3

Table S4. List of gene ontology (GO) categories used to visualize and cluster GO terms

Category
Amino acid metabolism
Blood and immune response
Carbohydrate metabolism
Cell adhesion and motility
Cell cycle and DNA synthesis
Chromatin epigenetic modification
Cofactors
Cytoplasmic translation
Drug metabolism
Energy metabolism
Epinephrine
Glutathione metabolism
GTPase
Hypoxia
Lipid metabolism
Metals
miRNA transcription
Mitochondrial energy metabolism
Signal transduction
Nucleotide metabolism
Nutrient & vitamins
Organelle fission
Protein modification
Secondary messenger
Stress response
Tau protein
Thioester metabolism
Transporters
One carbon metabolism
Folic acid metabolism
Cell membrane
Hormone metabolism/ transport
Cell signaling
Dietary factors
Collagen synthesis

Chapter 4

Conclusion and Future work

Persistent environmental chemicals, such as polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) have been utilized in industry for their useful properties, such as chemical stability and flame-retardant properties. However, for their chemical nature, including lipophilicity and bio-accumulative properties, these chemicals are now considered as contaminants and have been present in the environment for decades, even though they have been phased-out in most areas worldwide. These contaminants will likely exist in the future and long-term exposure to humans, such as from dust, old household products, meat, breast milk, fish, and other consumables. Although the acute and chronic toxicities on the liver from exposure to PCBs and PBDEs have been well-documented from previous investigations, the role of the gut microbiome in the liver responses and whether early-life exposure to these contaminants produce long-term effects were unknown. The works in my thesis were focused to answer these two questions critical to toxicology and public health.

The gut microbiome has multiple critical roles in the body, ranging from producing short-chain fatty acids (SCFAs), converting primary bile acids (BAs) to secondary BAs, modulating immune response, to directly and indirectly metabolizing xenobiotics. As the main route of exposure to PCBs is the oral route, the first major bio-compartment that can metabolize PCBs would be the gut, where the majority of the microbiome resides. Therefore, in Chapter 2, using conventional mice (with normal microbiome colonization [CV]) and germ-free mice (without microbiome colonization [GF]) and oral PCB exposure, I hypothesized that the gut microbiome critically impacts the effect of PCBs in the liver. I used two doses of PCBs (the Fox River PCB mixture, 6 and 30 mg/kg) and utilized RNA sequencing (RNA-seq),

metabolomics to detect endogenous aqueous metabolites, and 16s rDNA sequencing (16s rDNA-seq) to compare the effect of oral exposure to PCBs in CV and GF mice. I found that the majority of differentially expressed genes (DEGs) were unique to each enterotype, the presence or absence of microbiome, and only 5 genes were commonly differentially regulated. The prototypical targets of known key transcription factors from PCB exposure, namely, the aryl hydrocarbon receptor (AhR), constitutive androstane receptor (CAR), and pregnane X receptor (PXR) were attenuated in GF mice exposed to PCBs, compared to CV mice. Using the DEGs, I performed gene ontology (GO) enrichment to summarize and estimate the biological value of the differentially regulated genes from PCB exposure. The top 5 up-regulated GO results comprised of GO terms related to xenobiotic metabolism. Consistent with the prototypical targets, CV mice exposed to PCBs had higher significance values than GF mice at the same exposure dose. The relative expression of DEGs important in xenobiotic metabolism and immune response also followed this trend; at the same PCB dose, CV mice tended to have higher induction of genes encoding enzymes important in xenobiotic metabolism and immune response. The top down-regulated GO terms in CV mice were related to response to incorrect and misfolded proteins, which are hallmarks of endoplasmic reticulum (ER) stress. However, these results were not observed for GF mice exposed to PCBs, suggesting that PCB-induced ER stress is a mechanism that is dependent on the gut microbiome.

In PCB-exposed CV mice, most of the differentially abundant (DA) liver metabolites, such as acetylcarnitine and adenylosuccinate, were related to amino acid metabolism, whereas the DA metabolites of GF mice exposed to PCBs were primarily related to nucleotide and carbohydrate metabolism, suggesting key metabolic differences present upon PCB exposure in CV and GF mice. I used correlation to estimate the relationship between DA

bacteria and DA metabolites and DEGs and found that *Ruminiclostridium 6 and Family XIII UCG-001* were positively correlated with aminoisobutyric acid and dimethylglycine, which are involved in inflammation and oxidative stress. Furthermore, the same bacteria, in addition to *Roseburia spp.*, were positively correlated with DEGs in the Cyp1 and 2 families, which are linked to oxidative stress. Lastly, using the gut microbiome-dependent DEGs and the Library of Integrated Network-based Cellular Signatures (LINCS) L1000 database as the reference, I predicted that specific drugs have the potential to mitigate the ER stress- and inflammation-related signatures from exposure to PCBs. These results warrant future experiments that investigate the cellular machinery of the significantly correlated bacteria, as well as the therapeutics predicted from the LINCS database.

The developmental origins of health and disease (DOHaD) hypothesis states that there is a sensitive developmental time window for toxic exposures to chemicals that lead to delayed onset of diseases in adulthood. The prenatal liver is a major source of hematopoeisis which drastically changes to a central organ responsible for functions including xenobiotic metabolism, nutrient homeostasis, and endocrine signaling. During this transition, at this critical time, if there are exposure to certain xenobiotics, the developmental trajectory may be altered via the epigenetic reprogramming of the liver. Previous work from Dr. Dana Dolinoy's lab showed that exposure to BPA produced an increased likelihood of liver cancer in mice for pups which the mothers were exposed to BPA. PBDEs and PCBs are persistent in the environment and are ubiquitously detected in humans. Extending Dr. Dolinoy's result and combining with the DOHaD hypothesis, I hypothesized that in addition to BPA, exposure to PBDEs (using the BDE-99 congener) or PCBs (the Fox River PCB mixture) also lead to persistent liver responses in xenobiotic biotransformation in adult age. Two-day-old pups were orally exposed to BPA, BDE-99, or PCBs once daily for three consecutive days and the

liver, blood, and intestines were collected at postnatal day (PND) 5 (acute response) and PND 60 (persistent response), when the exposed pups became sexually mature (adulthood). To test this hypothesis, I took an unbiased approach using sequencing methods (RNA-seq, SCFA metabolomics, and 16s rDNA-seq). The number of differentially regulated PCGs in adulthood were greater than those at PND 5, in particular in males neonatally exposed to BPA and BDE-99, suggesting that the transcriptomic responses were amplified in adulthood. Using Ingenuity Pathway Analysis (IPA), I predicted, using the persistently DEGs, that important cell regulators (i.e. P53, E2f1, E2f3), sterol regulator (i.e. Scap), and lipid and xenobiotic sensing transcription factors (i.e. PPARs, RORs, CAR) were the important upstream regulators that influenced the observed DEGs.

GO enrichment using DEGs at PND 5 showed up-regulated GO terms related to drug and lipid metabolism and down-regulated terms related to cell cycle and epigenetic modification. However, at PND 60, these changes were reversed; drug and lipid metabolism-related GO terms were persistently down-regulated and cell cycle and lipid metabolism-related terms were persistently up-regulated. Long non-coding RNAs (lncRNAs) have distinct functions, such as cell cycle regulation, as well as the ability to modify DNA and RNA. Persistent up-regulation of cell cycle and epigenetic modification-related GO terms were further evidenced by the persistent up-regulation of lncRNAs that are involved in cancer progression (i.e. H19, Meg3, Snhg1, Snhg4) in males neonatally exposed to BPA or BDE-99. Furthermore, in males neonatally exposed to BDE-99, lactate and succinate, which are used in histone epigenetic modification, were persistently up-regulated and acetate, although not significantly different from the control, tended to have higher abundance.

Neonatal exposure to BPA or BDE-99 produced greater number of dysregulated genes compared to those of PCBs in both males and females. The majority of genes that encode phase-I and -II enzymes were persistently down-regulated in males exposed to BPA or BDE-

99, providing addition evidence for the persistent down-regulation of drug and lipid metabolism-related GO terms. In females, neonatal exposure to BPA or BDE-99 tended to persistently up-regulate genes in the phase-I category, suggesting sex-dependent persistent responses from early-life exposure. In males neonatally exposed to BPA or BDE-99 and females neonatally exposed to BPA, most dysregulated transporters were persistently up-regulated, which may indicate a compensatory response from the early-life exposure.

In the colon, neonatal exposure to BDE-99 resulted in persistent dysbiosis with important SCFA-producing bacteria, such as *Akkermansia muciniphila* and *Lachnospiraceae spp.* being up-regulated. *A. muciniphila* and *Lachnospiraceae spp.* were, negatively and positively correlated, respectively, with the persistently down-regulated genes in the phase-I category. In females neonatally exposed to BDE-99, differentially abundant bacteria, such as *Ruminiclostridium, Family XIII*, and *Clostridium spp.* were positively correlated with genes in the cytochrome P450 (Cyp) 3a family, which are involved in xenobiotic metabolism, and negatively correlated with Cyp4a14, which is involved in lipid metabolism. These results suggest that, from early-life exposure to BDE-99, there is persistent alteration of the gut-liver axis, which may influence the liver transcriptomic persistent responses. Neonatal exposure to BPA, BDE-99, and to a lesser extent PCBs, amplified the liver transcriptomic changes in adulthood, with males being more sensitive than females. The altered hepatic transcriptomic signatures related to drug and lipid metabolism implicate altered liver metabolic capacity, which may increase the risk for chronic diseases. Future studies are warranted using GF mice to investigate the role of the microbiome, applying a gene or lncRNA knockdown/knockout approach to test whether the persistent signatures can be mitigated, and using modeling techniques to investigate the mechanistic gene-protein-reaction relationship of the persistent responses from early-life exposures to these environmental contaminants.

Through utilizing a multi-omics approach, the two studies generated novel hypotheses and insights that warrant additional mechanistic investigations. Overall, the work presented in this thesis provides insights into the role of the gut microbiome in toxicant-induced liver responses, as well as the persistent liver responses from early-life exposure to environmental contaminants. These studies extend knowledge in the toxicity testing techniques used by regulatory agencies, which generally seek for specific endpoints in only certain organs and consider less regarding the systemic interactions among different organs. Furthermore, the early-life exposure model can also be utilized in toxicity testing, as these agencies tend to focus on only acute and chronic endpoints. The persistent transcriptomic changes related to metabolic processes suggest that early-life exposure to certain environmental contaminants may partially explain the increasing number of patients with metabolic diseases, such as type II diabetes.

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