dAKAP1: A mitochondrial AKAP that coordinates local translation

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Abstract

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A-Kinase anchoring proteins (AKAPs) are a structurally diverse family of proteins defined by the ability to bind protein kinase A (PKA). AKAPs process and integrate a variety of intracellular signals by sequestering PKA with other signaling enzymes such as kinases, phosphodiesterases, and phosphatases. dAKAP1 tethers both PKA and protein phosphatase 1 (PP1) to the outer mitochondrial membrane and contains RNA and protein interaction domains that permit the clustering of signaling enzymes with the post-transcriptional machinery. The function of RNA binding by dAKAP1 at the outer mitochondrial membrane, however, is largely unresolved.

I investigated two main questions: what are the protein and RNA binding partners of dAKAP1? and what is the physiological significance of the association of these molecules with dAKAP1? In order to answer the first question, I utilized mass spectrometry to identify protein interacting partners of dAKAP1 and discovered that dAKAP1 interacts with protein subcomplexes with RNA regulatory functions. I validated the interaction of one of these subcomplexes, LARP4/PABPC1, and determined that dAKAP1 binding of RNA is required for its localization to the outer mitochondrial membrane. I utilized RNA-Seq to identify RNA interacting partners of dAKAP1 and discovered that dAKAP1 can interact with RNAs that encode mitochondrial proteins. In order to answer the second question, I investigated the local translation of proteins

encoded by RNA interacting partners of dAKAP1 at the mitochondria. I observed that dAKAP1-mediated anchoring of the *SDHA* mRNA directly correlates with mitochondrial SDHA protein levels. Though alternation of this anchoring is not sufficient to drive metabolic change, I also correlate a decrease of SDHA with a decrease in dAKAP1 levels across four different breast cancer cell lines.

Collectively, my work suggests that dAKAP1 anchoring of both RNA and RNA-regulatory proteins is important for the local translation of at least one protein, SDHA, involved in the critical mitochondrial function of oxidative phosphorylation.

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Preface

Portions of the text and data from this dissertation are reproduced from the following work under fair use:

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This work is dedicated to you both.

Chapter 1: Introduction

"Metaphors play an essential role in establishing links between scientific language and the world. Those links are not, however, given once and for all. Theory change, in particular, is accompanied by a change in some of the relevant metaphors and in the corresponding parts of the network of similarities through which terms attach to nature." - Thomas Kuhn, "Metaphor and Thought"

Ask a middle school student about mitochondria, and a common reply might be, "The mitochondria is the powerhouse of the cell." The metaphor of the mitochondria as the powerhouse of the cell is a cliché but evokes an important core truth: mitochondria coordinate energy production for the cell.

This metaphor, however, does not encompass the multi-faceted, diverse functions of this key organelle, including roles in calcium signaling, cell differentiation, apoptosis, growth and the cell cycle.[1] The overarching goal of this work is to provide insight into the function of the mitochondrial protein dAKAP1. In exploring the functions of the mitochondria beyond energy, perhaps the central metaphor of mitochondrial biology – and indeed our fundamental understanding of mitochondrial biology – can be extended.

1.1 Overarching principles of cell signaling

Cell signaling requires integration of extracellular cues with the intracellular environment at subcellular locations in order to effect physiological changes. Due to the required specificity, signaling is controlled on multiple levels. These include post-transcriptional and post-translational mechanisms. Post-transcriptional mechanisms include the regulation of mRNA processing and stability. Post-translational mechanisms include addition of functional groups to proteins' amino acid side chains, such as phosphorylation or methylation.

One class of enzymes that performs post-translational modifications is the protein kinase family. Protein kinases catalyze the transfer of a phosphate group to amino acid side chains containing a hydroxyl group, such as serine and threonine (serine/threonine kinases) or tyrosine (tyrosine kinases). Protein kinase A (PKA), or adenosine 3',5'-

monophosphate (cyclic AMP)-dependent protein kinase, is a basophilic serine/threonine kinase that generally recognizes the motif R/K-R/K-X-**S/T** in substrate proteins.[2] PKA signaling plays a diverse role in many biological processes, including mitochondrial morphology and signaling.[3]

The spatiotemporal organization of enzymes that catalyze these modifications can be achieved in part through scaffolding or anchoring proteins. Errors in local cell signaling mechanisms not only compromise basic cellular function, but also underlie disorders such as cancer and autoimmunity.

1.2 Significance of the mitochondria

The mitochondrion is broadly divided into three “compartments”: the outer mitochondrial surface, which faces into and is congruent with the cytoplasm and is bounded by the outer mitochondrial membrane (OMM); the inner-membrane space (IMM) located between the outer and inner mitochondrial membranes (IMM); and the mitochondrial matrix (M). Mitochondrial dysfunction has been implicated in many diseases, including cancer, metabolic disorders, neurodegenerative diseases, and cardiac hypertrophy.[4] There is high heterogeneity in clinical presentation of mitochondrial disease and symptoms can be tissue specific. Thus, it is increasingly clear that the definitive linking of mitochondrial phenotypes to disease states will require a better understanding of mitochondrial biology, organization, and inheritance.[5]

1.3 Aims and overview

In order to elucidate the role of dAKAP1 at the outer mitochondrial membrane, I broadly asked two questions: first, **what are the protein and RNA binding partners of dAKAP1**? and second, **what is the physiological significance of the association of these molecules with dAKAP1**?

Chapter 2 provides context for the important signaling events that occur at the mitochondria and offers background on known molecular partners and physiological function of dAKAP1 particularly as it pertains to the interface with RNA. **Chapter 3** describes the generation of reagents.

Most of the work presented herein addresses the first question. **Chapter 4** describes proteomics experiments that identify protein interacting partners of dAKAP1, as well as the validation and investigation of one particular protein partner, LARP4. **Chapter 5** describes RNA pulldown and sequencing experiments that identify RNA interacting partners of dAKAP1.

In **Chapter 6**, I outline experiments that address the physiological of importance of both the protein and RNA interacting partners of dAKAP1 at the OMM. Outstanding questions and future directions are offered in **Chapter 7**.

Materials and methods are described in **Chapter 8**. Lastly, **Appendix A** includes selections from the large data sets generated in Chapters 4 and 5.

Chapter 2: dAKAP1: a mitochondrial A-Kinase Anchoring Protein

A-Kinase Anchoring Proteins (AKAPs) comprise a diverse family of anchoring proteins that integrate cAMP-responsive (PKA) signaling through the binding of phosphodiesterases, protein kinases, and protein phosphatases.[6] Our work focuses on a particular AKAP, dAKAP1, which is localized to the outer mitochondrial membrane.

First, in **Section 2.1**, I describe general features of the AKAP family. In **Section 2.2**, I elaborate on the architecture and known interacting partners dAKAP1. In **Section 2.3**, I also expand upon general properties of RNA Binding Proteins (RBPs), and how dAKAP1 in some ways can be considered a prototypical RBP. I contextualize the signaling role of dAKAP1 in **Section 2.4**, wherein I describe general principles of mitochondrial signaling as well as cAMP/PKA signaling at the outer mitochondrial membrane (OMM). Finally, I elucidate open questions about dAKAP1 as it pertains to RNA biology and mitochondrial signaling in **Section 2.5** to set the stage for the subsequent chapters of this work.

2.1 A-Kinase Anchoring Proteins

A-Kinase Anchoring proteins are defined by their ability to interact with the regulatory (R) subunit of PKA.[7] All AKAPs contain at least one conserved PKA anchoring domain, a 14-18 residue amphipathic helix which interacts with the N-terminal docking/dimerization (D/D) domain of the R subunit. Most well-characterized AKAPs exhibit high affinity for one form of the R subunit, RII. However, some AKAPs interact with RI, or are dual-affinity and can bind both RI and RII, typically at 10-100-fold lower affinity than for RII.[8,9]

AKAPs achieve compartmentalized signaling specificity through a localization signal which targets them to specific subcellular locations. AKAPs sequester signaling complexes through targeted expression, either through these targeting domains or differential, cell type-specific expression of splice variants through additional modification.

A hallmark of AKAPs is the ability to simultaneously associate with several binding partners to form multimeric signaling complexes; this confers the ability to facilitate rapid and efficient signal transmission in local environment through spatial integration of constituents of different signaling pathways. Moreover, AKAPs form complexes with other signaling effectors that directly couple it to cAMP signaling. For example, AKAPs can associate with G-Coupled Protein Receptors (GPCRs), which can activate adenylyl cyclase to produce a local gradient of cAMP. AKAPs can also couple with signaling terminators (e.g. protein phosphatases, phosphodiesterases) as well as other elements of signaling pathways (e.g. protein kinases, small GTPases, GTPase Activating Proteins (GAPs)/Guanine Nucleotide Exchange Factors (GEFs)).[6]

2.2 Dual-anchoring A-Kinase Anchoring Protein 1 (dAKAP1)

D-AKAP1c, or dAKAP1, is one of several anchoring protein isoforms encoded by the AKAP1 gene.[10] An atypical PKA anchoring protein of 903 residues (human) (857 residues [mouse]), dAKAP1 has the capability to bind both RI and RII through its PKA binding helix.[8] Various physiological roles for dAKAP1 have been examined: global knockouts of *AKAP1* resulted in failure of oocyte maturation,[11] and siRNA knockdown of dAKAP1 in rat cardiomyocytes resulted in hypertrophy.[12] It has also been demonstrated that dAKAP1 is involved in neuroprotective remodeling through promotion of mitochondrial fusion and elongation, thus promoting neuronal survival.[13,14] Mechanistically, these physiological effects proceed through a cohort of dAKAP1-binding partners.

2.2.1 dAKAP1 protein architecture

dAKAP1 is localized to the mitochondria by short mitochondrial targeting domain (MTD) comprised of a hydrophobic helix followed by a series of positively charged residues.[15,16] In addition to its PKA binding helix, dAKAP1 contains two highly conserved domains: a K homology (KH) domain followed closely by a Tudor domain at the C-terminus **(Figure 2.2.1A)**. KH domains typically function in RNA or ssDNA recognition modules;[17] Tudor domains recognize lysine or arginine methylation, including monomethylated and asymmetrically or symmetrically dimethylated arginine residues.[18]

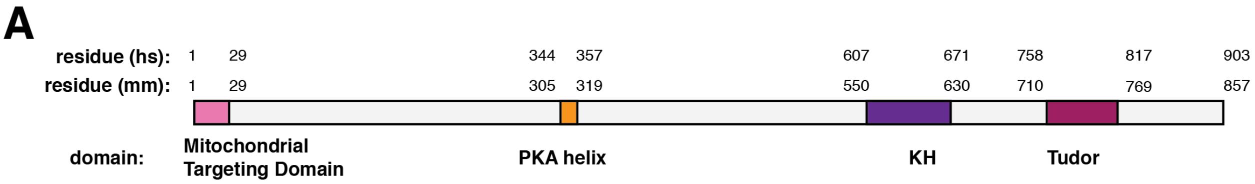

Figure 2.2.1.1 dAKAP1 domain architecture.

A. Schematic of dAKAP1 domain architecture. Domains are indicated by colored boxes, with residue numbering for both human (hs) and mouse (ms) above and domain below.

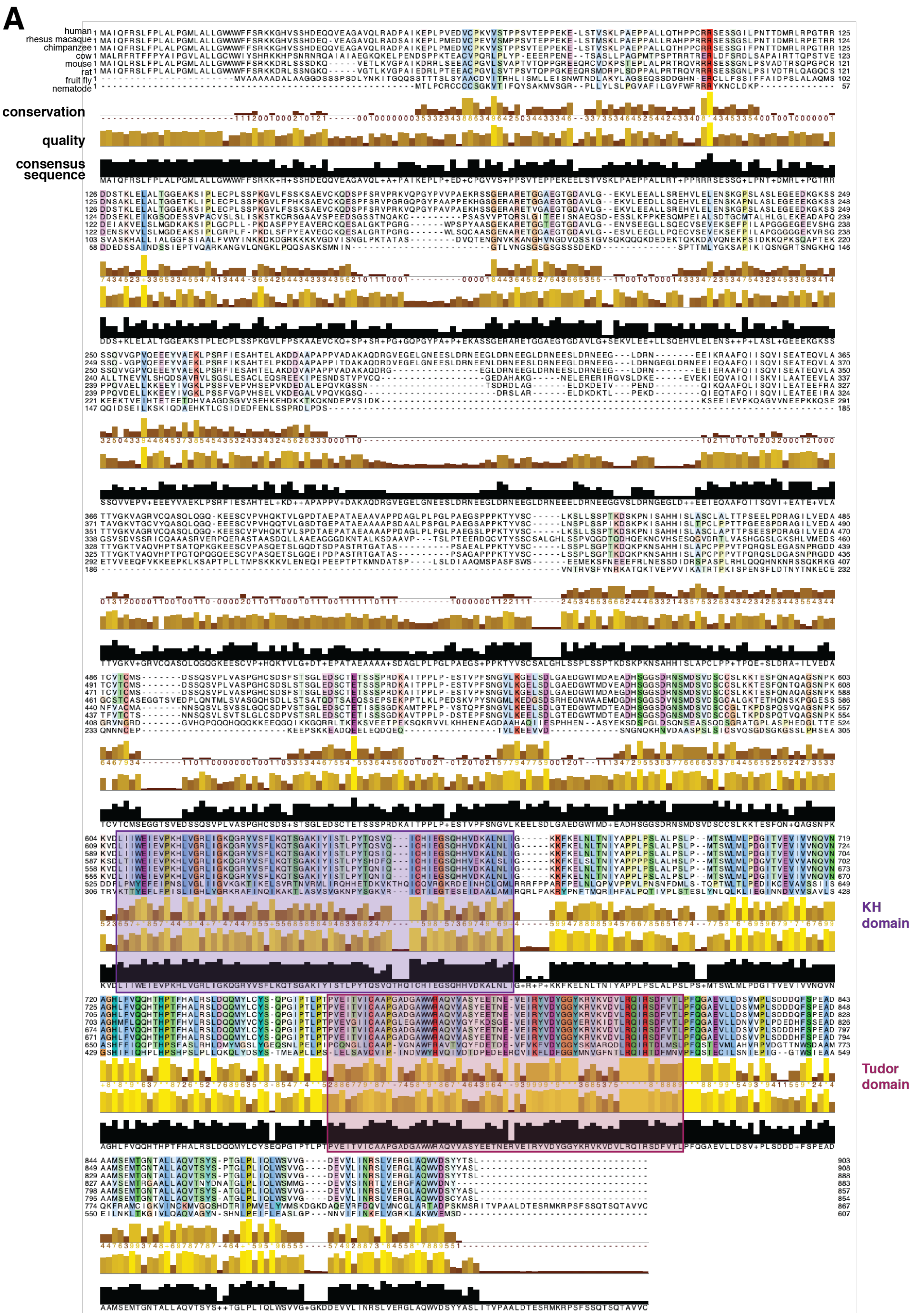
A
human
rhesus macaque
chimpanzee
cow
mouse
rat
fruit fly
nematode
conservation
quality
consensus sequence
KH domain
Tudor domain

Figure 2.2.1.2 dAKAP1 domain conservation.

A. Identity matrix of dAKAP1 across various species. Sequences of the following species are represented, top to bottom: *Homo sapiens* (human), *Macaca mulatta* (rhesus macaque), *Pan troglodytes* (chimpanzee), *Bos taurus* (cow), *Gallus gallus* (chicken), *Mus musculus* (mouse), *Rattus norvegicus* (rat), *Drosophila melanogaster* (fruit fly) and *Caenorhabditis elegans* (nematode). Sequences were retrieved from UniProt and aligned using the Clustal Omega[19] algorithm in Jalview.[20] Conservation and quality of alignment are indicated by yellow bars; consensus sequence is indicated in black bars, below. The KH and Tudor domains for human dAKAP1 are outlined in indicated boxes.

2.2.2 Known interacting partners of dAKAP1

In addition to binding PKA, dAKAP1 interacts with protein phosphatase 1 (PP1) through a conserved N-terminal RxVF motif (mouse residues ^{627}RYVSF^{631}) which is dependent on S^{630} phosphorylation by PKA. Interestingly, this motif is found in the KH domain.[21] However, PP1 targeting and RNA binding are regulated in a mutually exclusive manner through this phosphorylation event.[22] Additional protein binding partners that have been reported in large protein-protein interaction databases are summarized in **Table 2.2.2**.[23,24]

Multiple interactions between dAKAP1 and RNA have been reported. The 3' UTR of mRNAs for MnSOD and Fo-f mRNAs, the products of which are located in the mitochondria, were reported to be mediated by the KH domain;[25] interaction with the mRNA for lipoprotein lipase has also been reported.[26] AKAP1 interacts with argonaute 2 (Ago2), a member of the RNA-induced silencing complex (RISC) through its Tudor domain.[27] These associations may be necessary for post-transcriptional regulation of RNAs targeted to the mitochondria.

Table 2.2.2. List of known dAKAP1 interacting protein partners.

Known dAKAP1 interacting partners were retrieved from BioGrid or EMBL InTact, as indicated in “Source” column.

UniProt ID	Entry name	Protein names	Gene names	Source
Q71RC2	LARP4_HUMAN	La-related protein 4 (La ribonucleoprotein domain family member 4)	LARP4 PP13296	BioGrid, EMBL InTact
Q7Z4T9	CFA91_HUMAN	Cilia- and flagella-associated protein 91 (CFAP91) (AMY-1-associating protein expressed in testis 1) (AAT-1) (MYCBP/AMY-1-associated testis-expressed protein 1) (Protein MAATS1)	MAATS1 AAT1 C3orf15 CFAP91	BioGrid, EMBL InTact
O43255	SIAH2_HUMAN	E3 ubiquitin-protein ligase SIAH2 (EC 2.3.2.27) (RING-type E3 ubiquitin transferase SIAH2) (Seven in absentia homolog 2) (Siah-2) (hSiah2)	SIAH2	BioGrid, EMBL InTact
Q15599	NHRF2_HUMAN	Na(+)/H(+) exchange regulatory cofactor NHE-RF2 (NHERF-2) (NHE3 kinase A regulatory protein E3KARP) (SRY-interacting protein 1) (SIP-1) (Sodium-hydrogen exchanger regulatory factor 2) (Solute carrier family 9 isoform A3 regulatory factor 2) (Tyrosine kinase activator protein 1) (TKA-1)	SLC9A3R2 NHERF2	BioGrid, EMBL InTact
Q5HYA8	MKS3_HUMAN	Meckelin (Meckel syndrome type 3 protein) (Transmembrane protein 67)	TMEM67 MKS3	BioGrid, EMBL InTact
Q99417	MYCBP_HUMAN	c-Myc-binding protein (Associate of Myc 1) (AMY-1)	MYCBP AMY1	BioGrid, EMBL InTact
P04745	AMY1_HUMAN	Alpha-amylase 1 (EC 3.2.1.1) (1,4-alpha-D-glucan glucanohydrolase 1) (Salivary alpha-amylase)	AMY1A AMY1; AMY1B AMY1; AMY1C AMY1	BioGrid
Q92870	APBB2_HUMAN	Amyloid-beta A4 precursor protein-binding family B member 2 (Protein Fe65-like 1)	APBB2 FE65L FE65L1	BioGrid
P05067	A4_HUMAN	Amyloid-beta precursor protein (APP) (ABPP) (APPI) (Alzheimer disease amyloid protein) (Amyloid precursor protein) (Amyloid-beta A4 protein) (Cerebral vascular amyloid peptide) (CVAP) (PreA4) (Protease nexin-II) (PN-II) [Cleaved into: N-APP; Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99 (Beta-secretase C-terminal fragment) (Beta-CTF); Amyloid-beta protein 42 (Abeta42) (Beta-APP42); Amyloid-beta protein 40 (Abeta40) (Beta-APP40); C83 (Alpha-secretase C-terminal fragment) (Alpha-CTF); P3(42); P3(40); C80; Gamma-secretase C-terminal fragment 59 (Amyloid intracellular domain 59) (AICD-59) (AID(59)) (Gamma-CTF(59)); Gamma-secretase C-terminal fragment 57 (Amyloid intracellular domain 57) (AICD-57) (AID(57)) (Gamma-CTF(57)); Gamma-secretase C-terminal fragment 50 (Amyloid intracellular domain 50) (AICD-50) (AID(50)) (Gamma-CTF(50)); C31]	APP A4 AD1	BioGrid
Q14008	CKAP5_HUMAN	Cytoskeleton-associated protein 5 (Colonic and hepatic tumor overexpressed gene protein) (Ch-TOG)	CKAP5 KIAA0097	BioGrid

Q9H6Z9	EGLN3_HUMAN	Egl nine homolog 3 (EC 1.14.11.29) (HPH-1) (Hypoxia-inducible factor prolyl hydroxylase 3) (HIF-PH3) (HIF-prolyl hydroxylase 3) (HPH-3) (Prolyl hydroxylase domain-containing protein 3) (PHD3)	EGLN3	BioGrid
Q99613	EIF3C_HUMAN	Eukaryotic translation initiation factor 3 subunit C (eIF3c) (Eukaryotic translation initiation factor 3 subunit 8) (eIF3 p110)	EIF3C EIF3S8	BioGrid
Q92731	ESR2_HUMAN	Estrogen receptor beta (ER-beta) (Nuclear receptor subfamily 3 group A member 2)	ESR2 ESTRB NR3A2	BioGrid
Q9Y4F1	FARP1_HUMAN	FERM, ARHGEF and pleckstrin domain-containing protein 1 (Chondrocyte-derived ezrin-like protein) (FERM, RhoGEF and pleckstrin domain-containing protein 1) (Pleckstrin homology domain-containing family C member 2) (PH domain-containing family C member 2)	FARP1 CDEP PLEKHC2	BioGrid
Q9NWT6	HIF1N_HUMAN	Hypoxia-inducible factor 1-alpha inhibitor (EC 1.14.11.30) (EC 1.14.11.n4) (Factor inhibiting HIF-1) (FIH-1) (Hypoxia-inducible factor asparagine hydroxylase)	HIF1AN FIH1	BioGrid
Q6UB35	C1TM_HUMAN	Monofunctional C1-tetrahydrofolate synthase, mitochondrial (EC 6.3.4.3) (Formyltetrahydrofolate synthetase)	MTHFD1L FTHFSDC1	BioGrid
Q99742	NPAS1_HUMAN	Neuronal PAS domain-containing protein 1 (Neuronal PAS1) (Basic-helix-loop-helix-PAS protein MOP5) (Class E basic helix-loop-helix protein 11) (bHLHe11) (Member of PAS protein 5) (PAS domain-containing protein 5)	NPAS1 BHLHE11 MOP5 PASD5	BioGrid
P04629	NTRK1_HUMAN	High affinity nerve growth factor receptor (EC 2.7.10.1) (Neurotrophic tyrosine kinase receptor type 1) (TRK1-transforming tyrosine kinase protein) (Tropomyosin-related kinase A) (Tyrosine kinase receptor) (Tyrosine kinase receptor A) (Trk-A) (gp140trk) (p140-TrkA)	NTRK1 MTC TRK TRKA	BioGrid
P35232	PHB_HUMAN	Prohibitin	PHB	BioGrid
Q99623	PHB2_HUMAN	Prohibitin-2 (B-cell receptor-associated protein BAP37) (D-prohibitin) (Repressor of estrogen receptor activity)	PHB2 BAP REA	BioGrid
A4D1T9	PRS37_HUMAN	Probable inactive serine protease 37 (Probable inactive trypsin-X2)	PRSS37 TRYX2	BioGrid
Q00765	REEP5_HUMAN	Receptor expression-enhancing protein 5 (Polyposis locus protein 1) (Protein TB2)	REEP5 C5orf18 DP1 TB2	BioGrid
P30050	RL12_HUMAN	60S ribosomal protein L12 (Large ribosomal subunit protein uL11)	RPL12	BioGrid
Q9BUL9	RPP25_HUMAN	Ribonuclease P protein subunit p25 (RNase P protein subunit p25) (EC 3.1.26.5)	RPP25	BioGrid
P19429	TNNI3_HUMAN	Troponin I, cardiac muscle (Cardiac troponin I)	TNNI3 TNNC1	BioGrid
O15350	P73_HUMAN	Tumor protein p73 (p53-like transcription factor) (p53-related protein)	TP73 P73	BioGrid
Q9BRP8	PYM1_HUMAN	Partner of Y14 and mago (PYM homolog 1 exon junction complex-associated factor) (Protein wibg homolog)	PYM1 PYM WIBG	BioGrid
O95831	AIFM1_HUMAN	Apoptosis-inducing factor 1, mitochondrial (EC 1.1.1.-) (Programmed cell death protein 8)	AIFM1 AIF PDCD8	EMBL InTact
O75923	DYSF_HUMAN	Dysferlin (Dystrophy-associated fer-1-like protein) (Fer-1-like protein 1)	DYSF FER1L1	EMBL InTact
Q9NS69	TOM22_HUMAN	Mitochondrial import receptor subunit TOM22 homolog (hTom22) (1C9-2) (Translocase of outer membrane 22 kDa subunit homolog)	TOMM22 TOM22	EMBL InTact

2.3 dAKAP1 as an RBP

2.3.1 General features of RBPs

RNA binding proteins (RBPs) comprise a large, diverse classification of proteins that act to bind RNA at every stage of the RNA cycle, from nucleus to cytoplasm.[28] In addition to well-characterized functions of classical RBPs, such as splicing and regulation of RNA stability, much recent work on RBPs is converging to implicate RBPs in functions as diverse as metabolism, cell cycle regulation, and differentiation.[29] Indeed, the increasing evidence that RNA molecules themselves have both regulatory and structural roles in all structural functions suggests that it is equally likely that RBPs have additional regulatory functions beyond that of the RNA itself.

Recent efforts have focused on wide-scale identification of novel RBPs through high-throughput pulldown and screening efforts, greatly expanding both the number of known RBPs as well the structural and functional variety of RBPs.[30–33] RBPs have been traditionally defined by their presence of known RNA binding domains (RBDs). These include KH domains, RNA Recognition Motifs (RRMs), and PIWI domains, amongst others.[34]

Beyond recognizing and binding RNA, RNA binding domains have an important role in topologically positioning RNAs relative to other domains in the RNA binding protein, such as other RBDs and catalytic or functional domains.[34,35] Many RNA binding proteins contain multiple RNA binding domains, vastly improving the specificity of target interacting RNAs, as well as domains for the recruitment of other proteins.[36] Indeed, different RBDs, or RBDs in conjunction with other functional domains, can cooperatively recognize RNA through synergistic weak protein: RNA and protein: protein interactions.

2.3.2 dAKAP1 as a regulatory RBP

On the basis of its conserved domain architecture alone, dAKAP1 can be considered a “classical” RBP, in that it contains a known RBD and additional regulatory domains. The following vignette illustrates the additional regulation that dAKAP1 binding domains may have on a particular RNA, and could serve as a potential model for dAKAP1:KHT interactions:

dAKAP1 and type II PKA holoenzyme enhance steroidogenesis by directing the synthesis and activation of Steroidogenic Acute Regulator (StAR) at the mitochondria in response to cAMP.[37] (StAR) protein facilitates the transfer of cholesterol between mitochondrial membranes, providing a cholesterol substrate for steroidal precursors.[38] dAKAP1's KH domain interacts *in vitro* at micromolar affinity with the 3' UTR of *Star* mRNA.[27] A proposed co-translational import model for StAR expression suggests that nuclear-encoded mRNA of mitochondrially-localized proteins requires interaction with D-AKAP1 anchored RBPs.

2.4 Mitochondrial signaling

2.4.1 General mitochondrial signaling

General principles of mitochondrial signaling mirror the underlying principles of all cellular signaling: namely, mitochondria must integrate extracellular, as well as intracellular, cues in order to adapt and effect specific physiological change.[39] While mitochondrial signaling has traditionally been conceived of as primarily unidirectional, from nucleus to mitochondria, recent work has begun to highlight the importance of mitochondrial signaling to the nucleus.[40] Indeed, given that mitochondrial integrity is an essential component of signaling for apoptosis, it is increasingly appreciated that the mitochondria, too, signals its state to the rest of the cell.[41,42]

Broadly, mitochondrial signaling include, but is not limited to: uptake or release of calcium;[43] release of metabolites, such as TCA cycle products;[44] release of reactive oxygen species for thiol oxidation on cytosolic sensor proteins;[45] changes in energy production, and therefore AMP:ATP ratios, resulting in the activation of AMP kinase activity;[46] release of mitochondrial-specific compounds, such as cytochrome c[47] or mtDNA itself,[48] into the cytoplasm; and mitochondrial quality control, mediated by fission and fusion.[49]

Mitochondrial fission and fusion, collectively termed “mitochondrial dynamics,” are both a key readout for and regulator of a homeostatic response to metabolic or environmental stress.[50,51] Fission is mediated in part by the dynamin family member Drp1 and is an important mechanism for generating new mitochondria during cell division.[52]

Conversely, while fusion is also absolutely required for embryogenesis and development, it also provides one mechanism by which incompetent or mutated mitochondria can be fused to healthy bacteria in order to sequester them from the cell. Work from our lab, amongst others, has demonstrated that fission is inhibited when Drp1 is phosphorylation by PKA; more specifically, Drp1 phosphorylation by dAKAP1-anchored PKA at the OMM inhibits fission, thus promoting fusion.[13,53,54]

2.4.2 cAMP/PKA signaling at the OMM

Beyond regulating Drp1 phosphorylation, cAMP/PKA signaling has several other important roles at the OMM.[3,64] The mitochondrial proteome consists of proteins encoded by the mitochondrial genome itself, but primarily consists of nuclearly-encoded, cytoplasmically-translated proteins that are then imported to the appropriate mitochondrial compartment.[55,56] PKA phosphorylation on OMM proteins can prevent proper protein import: TOM70 phosphorylation prevents interaction with chaperon complexes (e.g. Hsp70)[57]; TOM22 phosphorylation inhibits import into the mitochondria;[58] and TOM40 phosphorylation prevents its integration into the OMM.[59]

Moreover, PKA phosphorylation at the OMM can also regulate apoptosis. PKA phosphorylation of the pro-apoptotic protein Bad can promote its sequestration in complex with PKA anchored at dAKAP1, inhibiting apoptosis.[61,62] Conversely, PKA phosphorylation of Bax can promote its translocation to the mitochondria,[63] enable the release of cytochrome c and thus promote apoptosis. These examples of cAMP/PKA signaling at one location, the OMM, highlight multifaceted roles of the same signaling paradigm and underscores the exquisite spatiotemporal control over signaling.

2.5 Open questions about dAKAP1

Though far from complete, the above introduction is meant to contextualize my work on dAKAP1 in the larger framework of known roles of dAKAP1 in mitochondria biology and physiology. However, while several specific roles have been elucidate for anchored dAKAP1 binding partners, the RNA anchoring function of dAKAP1 remains largely unexplored.

Reiterating the broad aims laid out in **Chapter** 1, I was interested in two main questions: first, **what are the protein and RNA binding partners of dAKAP1**? and second, **what is the physiological significance of the association of these molecules with dAKAP1**?

More specifically, I was interested in dAKAP1 protein partners that may be involved in RNA regulation at the mitochondrial membrane, as well as identification of the RNA binding partners themselves. To my knowledge, no work has yet been published that provides a comprehensive look at the RNA binding partners of dAKAP1, beyond large-scale, genome-wide RBP pulldown and RNA sequencing studies that provide a more global picture of RBP:RNA interactions. What type of RNA does dAKAP1 anchor – mature mRNA, microRNA, lncRNA, rRNA? Is the specificity of RNA binding enhanced by the proximal Tudor domain, or is dAKAP1 capable of binding RNA relatively promiscuously and instead is a passive scaffold or platform for RNAs that are target to the OMM by some other mechanism?

In investigating the physiological significance of dAKAP1 anchoring of RBPs and RNAs, I also hope to start to answer the question of why these functions are evolutionarily conserved in the context of an AKAP. The AKAP family of proteins is a prototypical anchoring family which helps regulate cell signaling via the classical post-translational paradigm of phosphorylation and dephosphorylation. Why, then, would an AKAP also bind RNA in this context? Does post-translational modification of dAKAP1 itself, or of its protein binding partners, influence the specificity of RNA binding?

My hope is that, at least in part, this work demonstrates a relatively novel function for AKAPs – namely, RNA anchoring – and highlights the importance of local translation.

Chapter 3: Generation of in vivo and in vitro reagents for studying dAKAP1

3.1 Introduction

In order to comprehensively study dAKAP1, it was first necessary to generate tools and reagents to examine different parts of the molecule.

First, I used *E. coli* to express recombinant protein fusions of a Maltose Binding Protein (MBP) tag and various subdomains of dAKAP1 **(Section 3.2.1)**. I also generated expressed purified protein components of Protein Kinase A (PKA) **(Section 3.2.2)**. Second, in collaboration with Stacey Aggarwal, we generated a knockout HEK293T cell line **(Section 3.3.1**). We also developed plasmids containing dAKAP1 with various mutations for transient expression of rescue of dAKAP1 **(Section 3.3.2)**. Lastly, I also re-established a colony of dAKAP1 knockout mice that had previously been generated at the University of Washington **(Section 3.3.3)**.

3.2 Recombinant protein purification

3.2.1 AKAP1 subdomains

Certain subdomains of dAKAP1 are predicted to form stable secondary structures **(Figure 3.2.1.1A,B)**;[65] these regions generally corresponded to identified domains of biological interest, and were thus chosen as good candidates for recombinant protein expression in *E. coli*. Subdomains of the mouse version of dAKAP1 were expressed in *E. coli* as His-tagged MBP fusion proteins **(Figure 3.2.1.1C)**; and purified on nickel resin. Further uniformity of purified protein was achieved by gel filtration chromatography. **(Figure 3.2.1.1D)**; For structural studies, purification tags were cleaved by the HRV 3C protease and removed by further gel filtration chromatography.

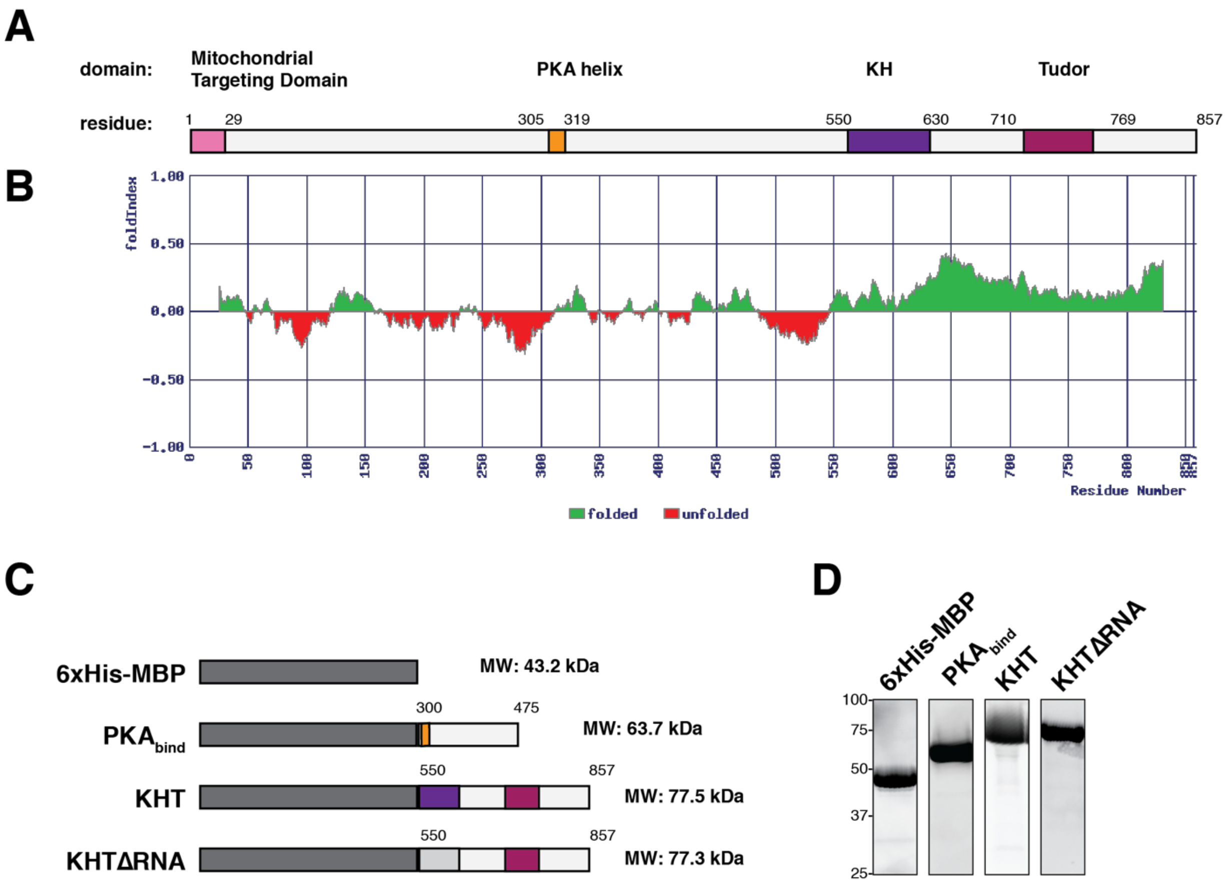

Figure 3.2.1.1: dAKAP1 subdomains.

A. Schematic of mouse dAKAP1, with domains and residues annotated above, to scale with **B.** FoldIndex plot of predicted regions of order (folded; green) and disorder (unfolded; red). Predicted folded regions correspond to regions of biological interest and known domains, including the PKA binding helix, the KH domain and the Tudor domain. **C.** Schematic of constructs used in subsequent studies, with 6xHis-Maltose Binding Protein (MBP) tag indicated by grey box. Predicted molecular weight indicated to the right of each construct. **D.** Stainfree gels of peak fraction of indicated construct following size exclusion chromatography.

Homology modeling of KH domain in dAKAP1 was performed in order to determine which residues were important for RNA binding and stailization **(Figure 3.2.1.2A)**.[66] In many KH domains, a GxxG motif forms a binding loop for RNA; this corresponds to residues **Gly**$^{\mathbf{571}}$-Lys-Gln-**Gly**$^{\mathbf{571}}$ in mouse dAKAP1.[67] These residues form an electrostatically positive surface, stabilizing an interaction with the negatively-charged phosphate backbone of RNA **(Figure 3.2.1.2B)**. Substituting aspartic acids in GxxG loop introduces an electrostatically negative surface that should prevent RNA binding but does not significantly affect the overall stability of the domain **(Figure 3.2.1.2C)**. This mutation was made in the context of the KHT subdomain construct, designated KHTΔRNA.

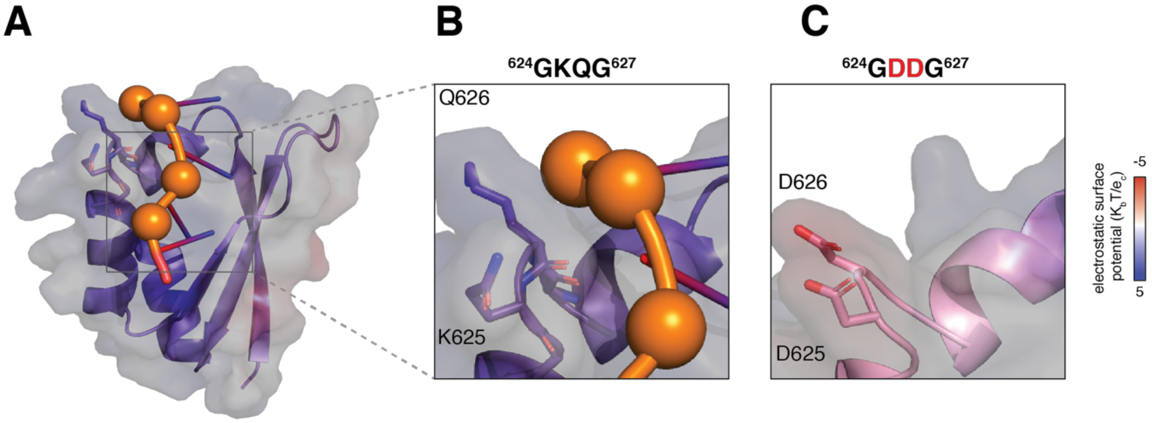

Figure 3.2.1.2: Homology model of dAKAP1 KH domain.

A. Ribbon diagram of PHYRE homology model of human dAKAP1 KH domain, overlaid with electrostatic potential map. Negative charge is indicated in red, positive charge in blue. RNA depicted as ball and stick in orange **B.** Magnification of GxxG loop of dAKAP1. RNA position was determined by averaging the position of RNA included in the crystal structures on which the PHYRE model was based. Positive charge from K625 and Q526 stabilize the negatively-charged phosphate backbone of RNA. **C.** Substituting two aspartic acids in the GxxG loop results in a negative surface, which should make electrostatic interactions unstable with RNA. The overall architecture of the KH domain, however, remains folded.

3.2.2 PKA RII and PKAc

Protocols for PKA RIIα and PKAc recombinant protein expression have been well-established in the Scott lab.[68,69] Briefly, both proteins were expressed as 6xHis-tagged proteins and purified on nickel resin, followed by gel filtration chromatography **(Figure 3.2.2)**. Work from our lab has previously demonstrated that deleting a flexible linker region of RIIα produces a rigid, stable AKAP:PKA holoenzyme complex suitable for EM and potentially for crystallographic analysis. This construct, RIIαΔlinker, was also expressed and purified in the course of this study.

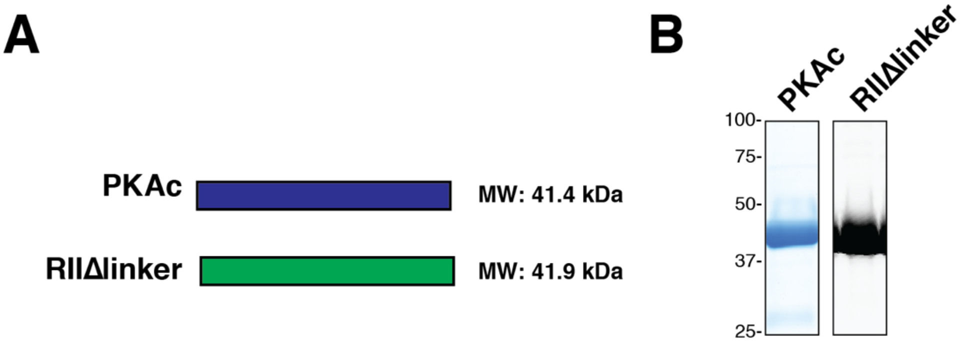

Figure 3.2.2.2: Purification of PKA.

A. Schematic of PKA catalytic and RIIΔlinker constructs, with molecular weights as indicated. **B.** Coomassie or stain-free gel of peak fraction of indicated protein following size exclusion chromatography.

3.3 Knockout cell line generation and rescue

Knockout cell lines are a common tool to investigate the effect of a particular gene or protein by looking for physiological effects in the absence of the gene or gene product. We utilized CRISPR-Cas9 genome editing to genetically delete dAKAP1 from HEK293T cells. The genetic knockout mouse was created via homologous recombination with a Neo resistance cassette in place of *AKAP1* exon 2.[11]

3.3.1 CRISPR

We deleted the *AKAP1* gene in HEK293T cells via CRISPR-Cas9 genome editing. Guide RNAs were designed to target exon 2 before the start of the KH and Tudor domains **(Figure 3.3.1A)**. Editing of the *AKAP1* gene was validated via sequencing **(Figure 3.3.1B)** and elimination of dAKAP1 protein expression was confirmed by immunoblot **(Figure 3.3.1C)**. Three clonal dAKAP1 null cell lines were derived; clone B9 is used in all subsequent experiments and is hereafter designated “HEK$^{dAKAP1-/-}$.” This cell line served as a valuable reagent for rescue experiments that monitored how modified forms of dAKAP1 forms altered the scaffolding, RNA binding properties, and mitochondrial localization of the protein.

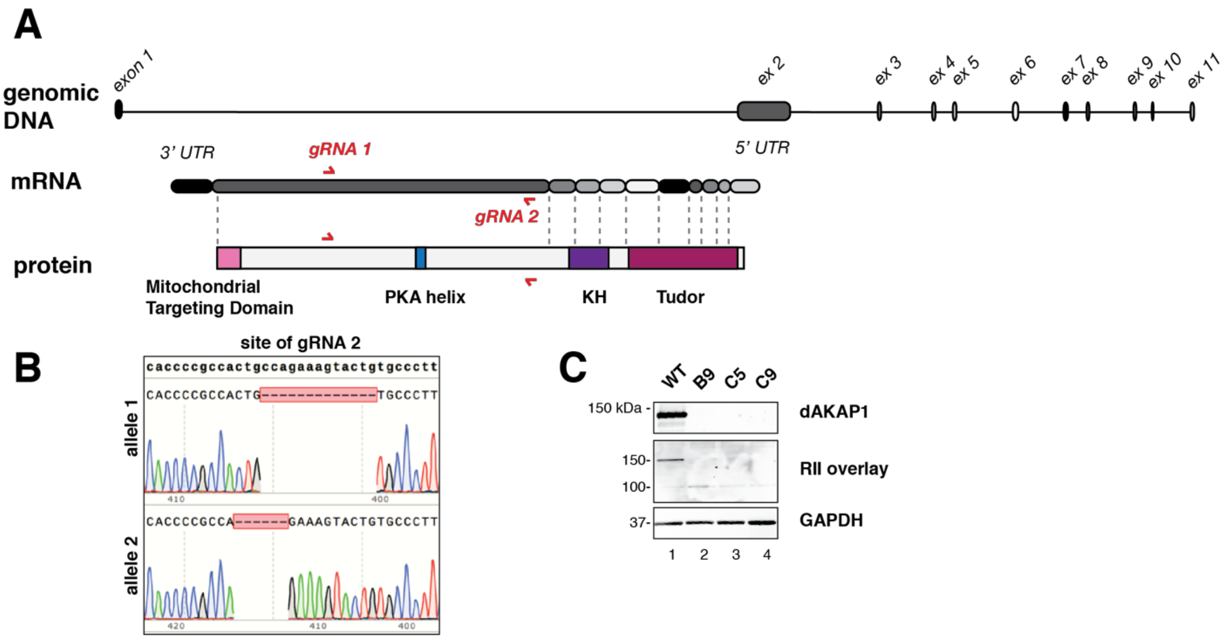

Figure 3.3.1: CRISPR knockout of dAKAP1 in HEK293T cells.

A. Schematic of genomic DNA, mRNA and protein of dAKAP1, to scale. Position of guide RNAs (gRNAs) indicated by red arrows on mRNA and corresponding location in the protein. **B.** Sequencing trace from at site of gRNA 2 from both alleles of clone B9. Allele 1 contains a 13 bp deletion causing a frameshift mutation that introduces a premature stop codon; allele 2 contains an insertion of 6 bp at gRNA site 1 (not shown) and an insertion of 1bp, resulting in a frameshift mutation that introduces a premature stop codon. **C.** Immunoblot for dAKAP1 and RII overlay from HEK^{WT} and three HEK$^{dAKAP1-/-}$ clones. GAPDH is shown as a loading control.

3.3.2 Rescue constructs

Rescue constructs with various forms of human dAKAP1 were cloned into transient expression vectors with N-terminal V5 epitope tags **(Figure 3.3.2A-C)**. Expression of the intact, WT form of human dAKAP1 was designated “control” in experiments. Rescue of HEK$^{dAKAP1-/-}$ cells with various forms of dAKAP1 was validated by immunoprecipitation (IP) of dAKAP1 complexes with anti-V5 antibodies, and subsequent immunoblot (IB) for dAKAP1 in both V5 immune complexes and input cell lysate; GAPDH expression served as a loading control.

Interaction with PKA was abrogated via site-directed mutagenesis of two residues in the PKA binding helix to generate dAKAP1ΔPKA **(Figure 3.3.2D)**. Loss of PKA anchoring was validated by RII overlay. Equivalent expression of both proteins was evident in cell lysate.

A non-mitochondrial form of dAKAP1 was created by deleting the MTD via site-directed mutagenesis (dAKAPΔMTD) **(Figure 3.3.2E)**. Mitochondrial fractions were isolated by differential centrifugation. Only the control dAKAP1 was present in mitochondrial fractions, whereas dAKAP1ΔMTD form was only detected in total lysates. IB detection TOM20 of served as a mitochondrial marker. Collectively, these results indicate that the ΔMTD dAKAP1 is not enriched in mitochondria.

Finally, a form of dAKAP1 unable to interact with RNA was generated by site-directed mutagenesis of the GxxG loop, as performed in the purified protein constructs. For human dAKAP1, **Gly^{624}**-Lys-Gln-**Gly^{627}** was mutated to GDDG. Stable protein expression and immunoprecipitation were validated by IB **(Figure 3.3.2F)**.

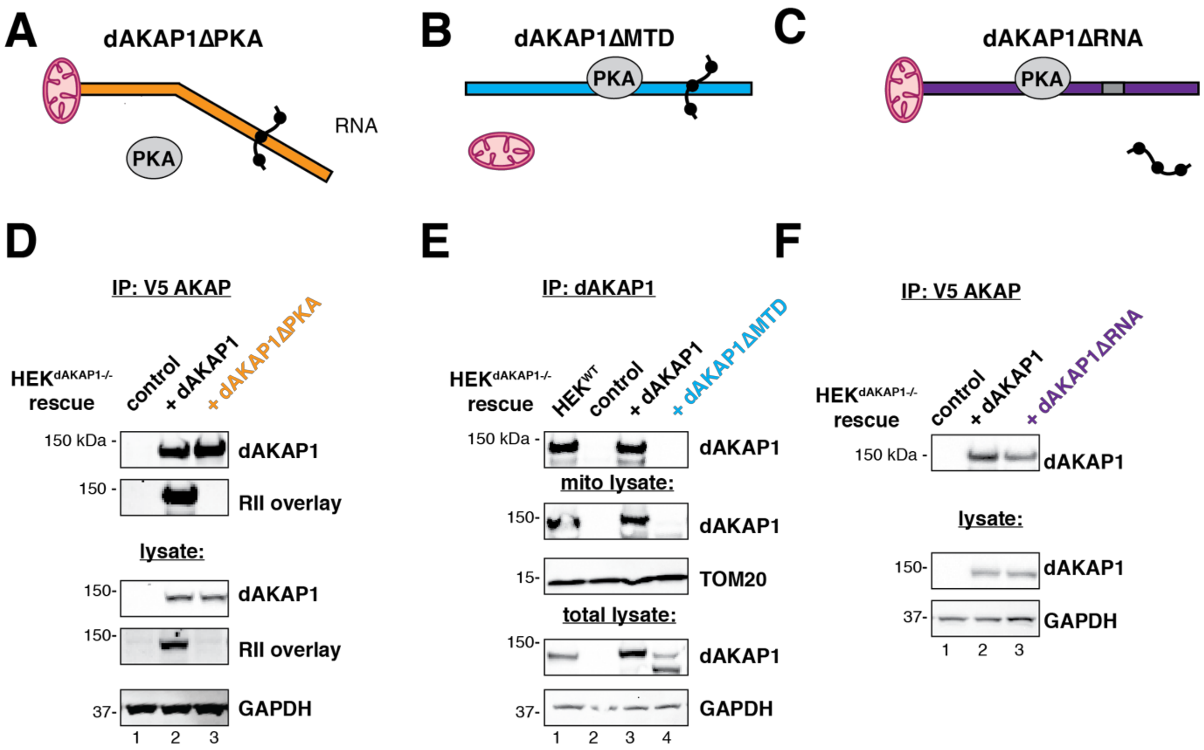

Figure 3.3.2: dAKAP1 rescue constructs.

A-C. Schematic of rescue constructs, indicating mitochondrial localization, PKA binding, and RNA binding of each. **D**. IP with anti-V5 antibody for rescue with dAKAP1 or dAKAP1ΔPKA, IB for dAKAP1 and RII overlay, showing that dAKAP1ΔPKA does not interact with PKA. **E.** IP with anti-dAKAP1 antibody for endogenous and rescue dAKAP1from mitochondrial lysate, IB for dAKAP1 in IP, mito lysate and total lysate fractions. dAKAP1 is IPed and present in HEK^{WT} and HEK$^{dAKAP1-/-}$ rescue, but not in HEK$^{dAKAP1-/-}$ rescue with dAKAP1ΔMTD. **F.** IP with anti-V5 antibody for rescue with dAKAP1 or dAKAP1ΔRNA, IB for dAKAP1 indicating that the dAKAP1ΔRNA construct can be IPed and recognized by the dAKAP1 antibody.

3.3.3 Knockout mouse and pMEF generation

In order to investigate the physiological consequences of dAKAP1 knockout, I re-generated *AKAP1 -/-* (knockout) mice **(Figure 3.3.3A)**. Male knockout mice were obtained and bred to female C57Bl/6 (wild-type) mice to produce heterozygous *AKAP1* +/- pups. Knockout females are subfertile, so the subsequent breeding strategy entailed breeding knockout males to heterozygous females such that half the resulting pups were knockout.[11]

In order to obtain primary cells from a knockout background, primary fibroblasts (pMEFs) were generated.[70] Heterozygous females were crossed with knockout males, and pregnancy timing was monitored by checking breeding mice for vaginal mucus plugs. Individual embryos were harvested at E13.5 and isolated primary fibroblasts were cultured **(Figure 3.3.3B)**. Knockout was validated by: PCR for *AKAP1* exon 2 of DNA extracted from eviscerated embryonic tissue **(Figure 3.3.3C)**; PCR for *AKAP1* exon 2 of DNA from cultured fibroblasts at passage 2 (not shown); and RII overlay from cell lysates at passage 3 of pMEFs **(Figure 3.3.3D)**.

3.4 Discussion

In vitro and *in vivo* reagents were generated to study dAKAP1. Purified KHT, KHTΔRNA and MBP were used as bait in protein pulldowns for proteomics experiments **(Chapter 4)** and bait in RNA pulldown for RNA sequencing experiments **(Chapter 5)**. Knockout HEK293T cells were used to validate proteomics results **(Chapter 4)** and to explore the physiological consequences of dAKAP1 anchoring **(Chapter 6)**.

Reagent availability, including lack of commercial antibodies that reliably detected dAKAP1 in mouse tissue, precluded comprehensive analysis of mouse tissue samples and physiological relevance of dAKAP1 anchoring. These reagents, however, may prove useful in future studies **(**discussed in **Chapter 7)**.

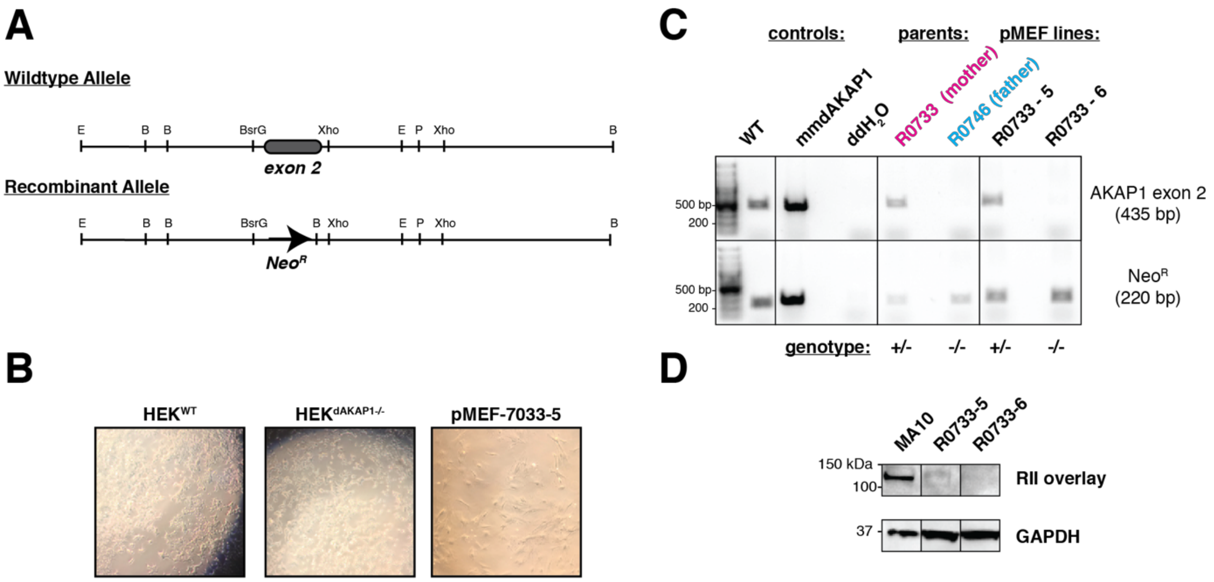

Figure 3.3.3: dAKAP1 knockout mouse and generation of primary embryonic fibroblasts.

A. Schematic knockout strategy of *AKAP1* mouse adapted from original publication, with exon 2 replaced by a Neo resistance cassette. Restriction sites: E = EcoRI; B = BamHI; BsrG = BsrGI; P = Pac. **B.** Representative 4x images of cell lines, showing that pMEF lines exhibit fibroblast morphology. **C.** Genotyping PCRs. Controls include: WT = AKAP1 WT mouse with Neo^R knocked in at a separate genomic site; mmdAKAP1 = pcDNA3.1-AKAP121 CDS (plasmid); ddH$_2$O = water used in all PCR reactions. Primer pairs for *AKAP1* exon 2 (product size: 435 bp) and Neo^R (product size: 220 bp) were for amplification. Heterozygous mice are positive for both *AKAP1* exon 2 and Neo^R; knockout mice are positive for only Neo. Genotyping gels from parents of the embryos used to derive pMEF lines R0733-5 (heterozygous) and -6 (knockout). **D.** RII overlay of protein lysate from passage 3 of pMEF lines R0733-5 and -6. MA10, a mouse Leydig cell line, is used as a positive control; GAPDH shown as loading control.

Chapter 4: Identifying and validating protein partners of dAKAP1

4.1 Introduction

I reasoned that RNA binding and the recruitment of RNA binding proteins occur through the tandem KH and Tudor domains (KHT) of dAKAP1.

First, in collaboration with Ho-Tak Lau and Shao-En Ong at the Unviersity of Washington, we performed mass spectrometry in order to identify protein binding partners of this region of dAKAP1 **(Section 4.2)**. I chose MA10 cells, a mouse Leydig cell line, because they represent a physiological cell type in which known dAKAP1/RNA binding function has been reported.[25,35]

Second, I analyzed the findings of our proteomic screen and determined that many of the *in vitro* protein interacting partners of dAKAP1 had annotated RNA binding and regulatory function **(Section 4.3)**. Moreover, I utilized bioinformatic databases to reveal that many of these proteins were predicted to form subcomplexes.

Lastly, I validated that protein components of one of these subcomplexes, the RNPs PABPC1 and LARP4, associate with dAKAP1 *in vivo* **(Section 4.4)**. I discovered that LARP4 is phosphorylated by PKA in the context of dAKAP1 complexes. I also determined that RNA contributes to the recruitment of LARP4 and possibly PABC1 to mitochondrial dAKAP1 signaling complexes.

4.2 Proteomics

We utilized purified KHT and MBP proteins as bait to capture protein interacting partners from MA10 cell lysate **(Figure 4.2.1A-C)**. Analysis by LC-MS/MS mass spectrometry identified 1181 putative interacting proteins. Five replicates were performed in order to account for the variability of lysate pulldown experiments. Peptides corresponding to 527 of these proteins were present in all five replicates **(Figure 4.2.1D)**. Of these, 40 proteins were significantly enriched ($p < 0.05$), with a normalized intensity of fivefold in the KHT pulldown condition over the MBP control **(Figure 4.2.1D, E red circles).**

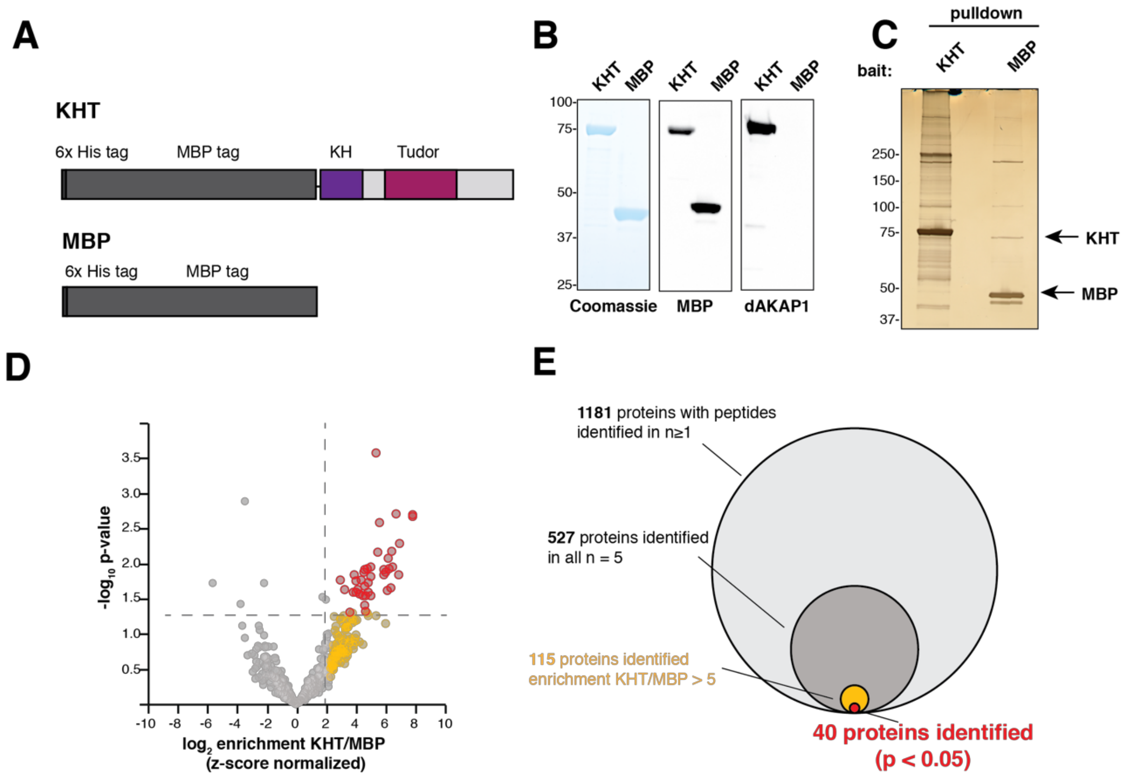

Figure 4.2.1: Proteomics of dAKAP1 KHT domains.

A. Schematic of constructs used as bait in proteomics experiments: KHT (6xHis tag - MBP tag – mouse dAKAP1 KH and Tudor domains) or MBP (6xHis tag – MBP tag). **B.** Validation of bait proteins. Coomassie gel for integrity of bait; IB for MBP is positive for both MBP and KHT; IB for dAKAP1 is positive only for KHT. **C.** Silver stain of representative pulldowns for KHT or MBP. Bait protein is indicated with arrows. **D.** Volcano plot of n=5 biological replicates. The x-axis represents the log2 enrichment score, calculated as the z-score normalized intensity of peptides corresponding to a known protein for KHT divided by that the corresponding intensity for MBP. **E.** Circle plot representing the number of proteins with peptides identified in at least one replicate (largest gray circle: 1181); proteins with peptides in n=5 biological replicates (medium gray circle: 527); proteins enriched at least 5-fold KHT/MBP (yellow circle: 115); and statistically significant enriched proteins (red circle: 40; $p < 0.05$, $FDR < 0.5$). Area of circles is proportional to number of proteins.

4.3 GO Analysis and model of protein-protein interactions

I examined the putative function of these KHT-binding partners through search of the Gene Ontology (GO) database for annotated molecular function and biological process.[71–73] Statistically significantly overrepresented molecular functions were associated with RNA, such as mRNA 3' UTR binding, single-strand RNA binding, and poly(U) RNA binding **(Figure 4.3.1A)**. Statistically significantly overrepresented molecular processes were also associated with RNA biology, including: regulation of cytoplasmic mRNA processing body assembly, negative regulation of mRNA splicing, and mRNA stabilization and destabilization **(Figure 4.3.1B)**.

A logical extension of this strategy was to query the STRING database to identify prospective protein-protein between the cohort of KHT-binding partners **(Figure 4.3.1C)**.[74,75] Interactions solely between the input proteins were examined at high stringency (minimum interaction score >= 0.80). This database identified three subcomplexes: components of spliceosome, the ribosome and ribornucleoprotein granules (RNPs). Since this latter group was the most enriched in our KHT-domain proteomic screen, I decided to further investigate the association of the PABPC1 and LARP4 with the dAKAP1.

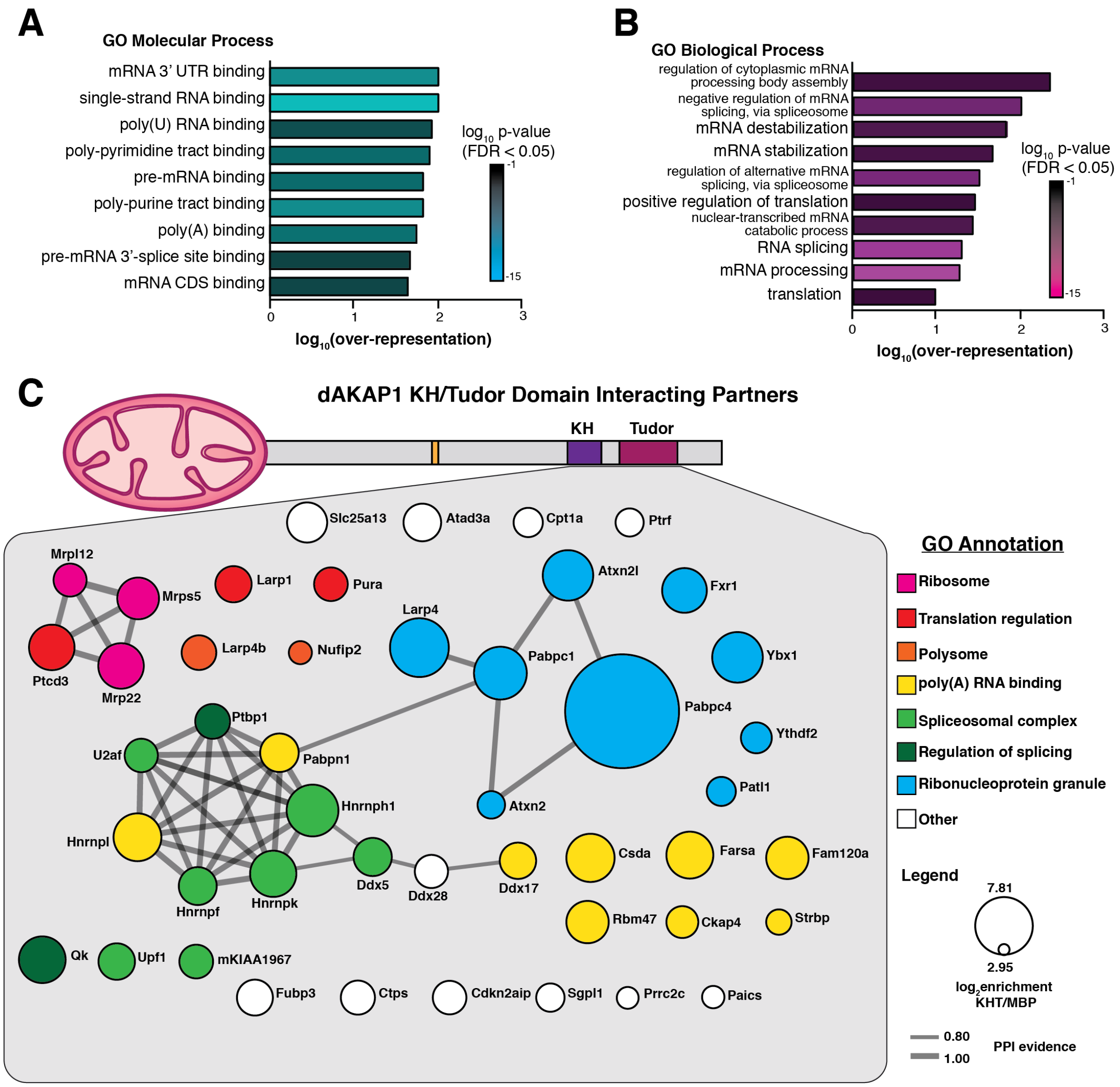

Figure 4.3.1: KHT associated proteins form sub-complexes of RNA-regulatory proteins.

A. Top ten GO Molecular Process terms overrepresented in the pool of significant KHT interacting proteins. Length of bar corresponds to log-fold overrepresentation; color represents p-value for significance of the overrepresentation by Fisher's test, with False Discover Rate (FDR) < 0.05. **B.** Top ten GO Biological process overrepresented in the dataset. **C.** Schematized protein-protein interactions in the dataset, with evidence of protein-protein interaction as predicted by STRING indicted by width of bar connecting proteins. Manual annotation of GO term indicated by color.

4.4 Validating and investigating LARP4 as a dAKAP1 binding partner

4.4.1 LARP4 coimmunoprecipitates with dAKAP1

I first validated the *in vivo* interaction of dAKAP1 with PABPC1 and LARP4 through co-immunoprecipitation (coIP). Lysates from HEK$^{dAKAP1-/-}$ with or without rescue with control V5-tagged dAKAP1 were prepared, and dAKAP1 complexes were IPed with anti-V5 antibody. Immune complexes were probed for co-IP of endogenous PABPC1 **(Figure 4.4.1A)** and LARP4 **(Figure 4.4.1B)**. IB for LARP4 revealed that LARP4 coIPed with dAKAP1-V5. Lysates were also probed to monitor expression levels of endogenous PABC1, rescue with V5-dAKAP1 and GAPDH loading controls.

Reciprocal coIP experiments determined that dAKAP1 coIPed with LARP4. HEK^{WT} and HEK$^{dAKAP1-/-}$ were transfected with FLAG-tagged LARP4, and lysates from these cells were IPed with anti-FLAG antibody. Subsequent immunoblot of LARP4 immune complexes revealed that dAKAP1 IPed in HEK^{WT}, but not HEK$^{dAKAP1-/-}$, cells **(Figure 4.4.2C)**. Together, these results indicate that that dAKAP1 and LARP4 interact *in vivo*.

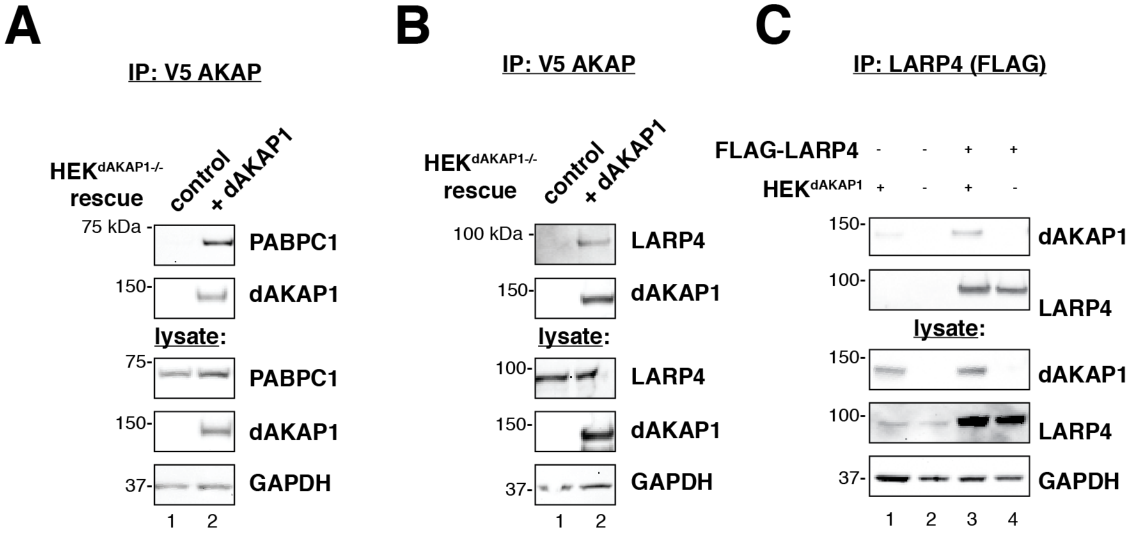

Figure 4.4.1: Coimmunoprecipitation of PABPC1, LARP4, and dAKAP1.

A. IP with anti-V5 antibody for dAKAP1 rescue and IB for endogenous PABPC. **B.** IP with anti-V5 antibody for dAKAP1 rescue and IB for endogenous LARP4. **C.** IP for FLAG for transfected FLAG-LARP4 and IB for endogenous dAKAP1.

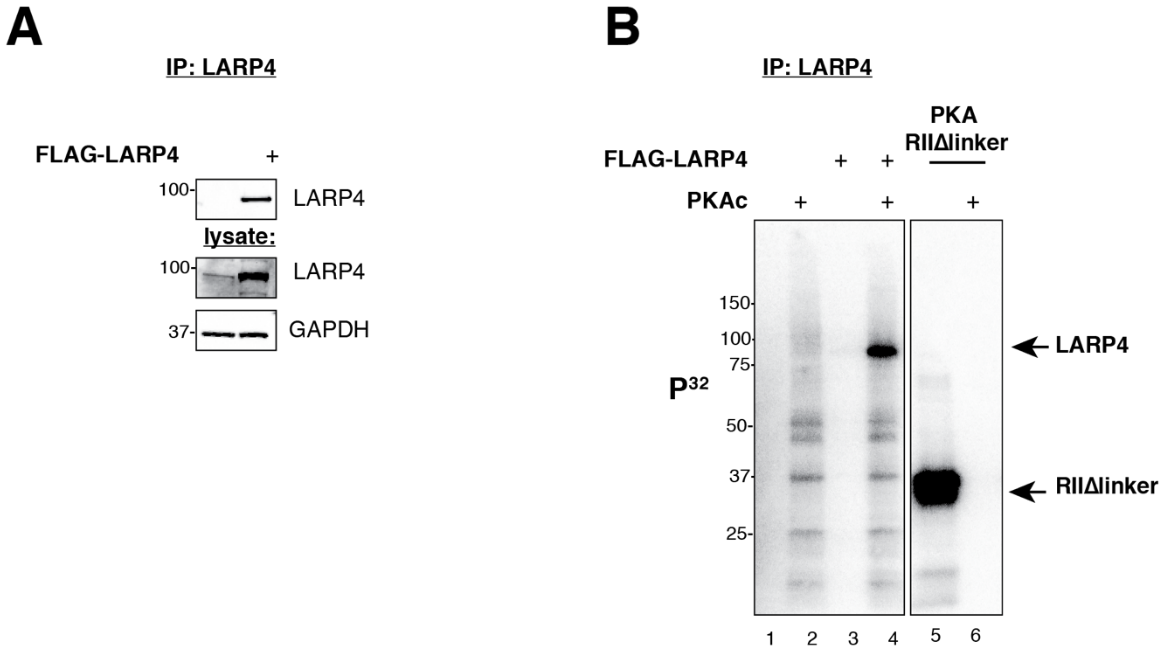

Figure 4.4.2.1*: In vitro phosphorylation* of LARP4 by exogenous PKAc.

A. IP with anti-FLAG antibody to isolate LARP4 from whole cell lysates; WB for endogenous LARP4 demonstrates specificity of IP with no background endogenous LARP4 binding in non-transfected conditions. **B.** IPed fractions from transfected and untransfected cells were incubated with or without PKAc in the presence of [Y32-P] ATP. A strong signal was observed at the molecular weight of LARP4. RIIΔlinker was used as a control for PKA phosphorylation.

4.4.2 LARP4 as a PKA substrate

LARP4 has been reported to form complexes with PKAc *in vivo*. LARP4 is also predicted to contain several PKA phosphorylation sites in several databases **(Table 4.4.2).**[76–81] I validated phosphorylation by PKA through *in vitro* phosphorylation. HEK^{WT} cells were transfected with FLAG-tagged LARP4, and LARP4 was IPed by an anti-FLAG antibody **(Figure 4.4.2.1A)**. IPed fractions were incubated with [γ-32 ATP], with or without purified PKAc, and exposed to a phosphoimager screen overnight; purified RIIα was used as a positive control for PKA phosphorylation **(Figure 4.2.2.1B)**. A very strong band at molecular weight of LARP4 was observed, indicating that LARP4 is indeed capable of being phosphorylated by PKAc.

More sophisticated studies examined this phosphorylation event within intact dAKAP1-PKA signaling complexes by serial coIP **(Figure 4.4.2.2A)**. Intact dAKAP1 complexes were IPed from $HEK^{dAKAP1-/-}$ cells rescued with either a control dAKAP1 or dAKAP1ΔPKA by anti-V5 antibody. These complexes were eluted from beads with molar excess of V5 peptide. Reformation of dAKAP1 with partner proteins in solution was prevented in solution by increasing the SDS concentration in the IP buffer. The V5 eluate was the incubated with anti-phospho-PKA substrates antibody to enrich proteins that were phosphorylated in the context of dAKAP1 complexes. Control experiments included IPing the input lysate with anti-V5 antibody (i.e. the first step of the serial coIP) and anti-phospho-PKA substrates antibody **(Figure 4.4.2.2D**).

From the serial coIP, increased levels of LARP4 were detected by immunoblot in the presence of full length dAKAP1 (**Figure 4.4.2.2B**). Importantly, this signal was reduced when the experiment was repeated upon rescue with the anchoring defective dAKAP1ΔPKA form. Immunoblot analysis of cell lysates monitored expression levels of endogenous dAKAP1, LARP4 and GAPDH loading controls (**Figure 4.4.2C, E)**.

Table 4.4.2: List of putative LARP4 phosphorylation sites.

PhosphoSitePlus, NetPhos, ScanSite and Peptide Atlas were all queried for predicted and reported phosphorylation sites. Residue number corresponds to human LARP4; predicted kinase, where known, is indicated; consensus sequence, with phosphorylated residue bolded and in red.

Residue	Amino Acid	Source	Predicted kinase	Consensus
195	S	PhosphoSite Plus		KVRP**s**HKRC
		NetPhos		
276	T	PhosphoSite Plus		
		ScanSite	PKC zeta (PKC_zeta)	ARIKAIN**t**FFAKNGY
382	S	PhosphoSite Plus	Aurora B (AuroB)	VKPQFRS**s**GGSEHST
		ScanSite		
		NetPhos		
392	S	PhosphoSite Plus		STEG**s**VSLG
		UniProt		
		NetPhos		
		Peptide Atlas		
404	S	PhosphoSite Plus		LNRYS**s**RNF
		NetPhos		
406	S	Phosphidia	PKA site	LVLENRM**s**DVVKGVY
431	S	ScanSite	PKC epsilon (PKC_epsilon)	TYLQKET**s**TLQVEQN
		ScanSite	AMP Kinase (AMPK)	
461	S	PhosphoSite Plus		RREDDRI**s**RPHPstA
		NetPhos		
505	S	PhosphoSite Plus		LVLENrM**s**DVVKGVY
		UniProt		
		Peptide Atlas		
578	T	PhosphoSite Plus		QKdGLNQ**t**tIPVsPP
		UniProt		
		Peptide Atlas		
579	T	PhosphoSite Plus		KdGLNQt**t**IPVsPPs
		UniProt		
		Peptide Atlas		
583	S	PhosphoSite Plus		NQttIPV**s**PPsttKP
		UniProt		
594	S	PhosphoSite Plus		ttKPsRA**s**tAsPCNN
		NetPhos		
595	T	PhosphoSite Plus	Akt Kinase (Akt_Kin)	tKPsRAs**t**AsPCNNN
		ScanSite		
597	S	PhosphoSite Plus		PsRAstA**s**PCNNNIN
		UniProt		
		Peptide Atlas		
618	S	PhosphoSite Plus	Protein Kinase A (PKA_Kin)	LQEPRKL**s**YAEVCQK
		ScanSite		
		NetPhos		
647	S	PhosphoSite Plus		REQRRQF**s**HRAIPQG
		UniProt		
		Peptide Atlas		
649	T	PhosphoSite Plus		RsNVVsP**t**KNEDNGA
		UniProt		
		Peptide Atlas		
722	S	PhosphoSite Plus		EQyVPPR**s**PK_____
		UniProt		
		Peptide Atlas		

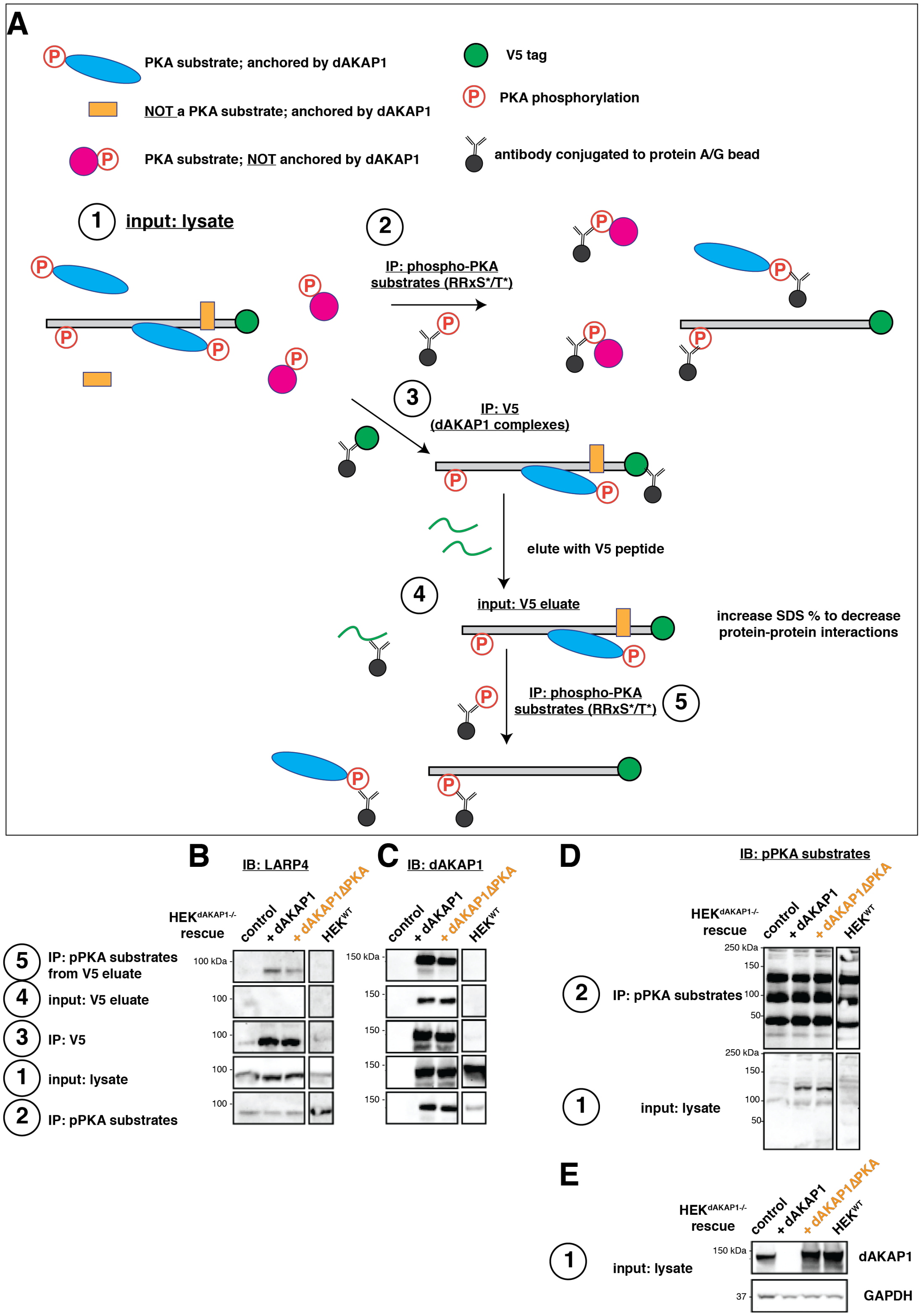

Figure 4.4.2.2: Serial coIP reveals LARP4 is phosphorylated by dAKAP1-anchored PKA.

A. Schematic of experiment. Numbers indicate fraction that is immunoblotted below. **B.** Immunoblot for LARP4. CoIP (5) reveals that less LARP4 was IPed by anti-pPKA substrates from input dAKAP1 complexes that cannot bind PKA than from intact WT dAKAP1 complexes. **C.** Immunoblot for dAKAP1 validates that dAKAP1 immune complexes were IPed at the expected experimental stages. Signal appears in (2) because dAKAP1 contains known PKA phosphorylation sites. **D.** Immunoblot of pPKA substrates from IPs for pPKA substrates validates the antibody is capable of IPing pPKA substrates. **E.** Immunoblots for dAKAP1 and GAPDH from input lysate confirm equivalent rescue of the different V5-tagged dAKAP1 forms and equal starting lysate concentration.

4.4.3 LARP4 localization

I next investigated whether LARP4 was recruited to the dAKAP1 signaling complex through association with RNA. In order to test this hypothesis, I used a co-immunoprecipitation approach in the HEK$^{dAKAP1-/-}$ genetic background to evaluate LARP4 interaction upon rescue with dAKAP1ΔRNA form. Capture of LARP4 was significantly reduced in the presence of the dAKAP1ΔRNA form as compared to control experiments conducted with the wildtype anchoring protein (**Figure 4.4.3A**). Immunoblot analysis of cell lysates monitored expression levels of V5-dAKAP1, LARP4 and GAPDH loading controls.

Subcellular fractionation of mitochondria confirmed that enrichment of the dAKAP1/LARP4 subcomplex in cells was rescued with the full-length dAKAP1, but not dAKAP1ΔMTD or dAKAP1ΔRNA (**Figure 4.4.3B)**. Reduced levels of LARP4 were detected in parallel mitochondrial fractions expressing dAKAP1ΔMTD and the dAKAP1ΔRNA forms of the anchoring protein. Detection of the marker TOM20 and Ponceau staining evaluated the quality of mitochondrial fractions.

Further validation was provided by immunofluorescent staining. Endogenous LARP4 was visualized by staining with anti-LARP4 (green); mitochondria were visualized through transfection of a mitochondrially-localized fluorophore (red). In HE^{KWT}, LARP4 signal was observed as green punctate decorating the surface of the mitochondria **(Figure 4.4.3C)**; in contrast, in HEK$^{dAKAP1-/-}$, LARP4 signal more evenly distributed throughout the cytoplasm **(Figure 4.4.3D)**. Furthermore, co-distribution of the LARP4 (green) and dAKAP1 (red) signals tightly correlated with dAKAP1 mitochondrial localization (cyan) **(Figure 4.4.2E)**. By contrast, the subcellular distribution of LARP4 was more evenly distributed throughout the cytoplasm in cells rescued with the dAKAP1ΔMTD form **(Figure 4.4.3F)**.

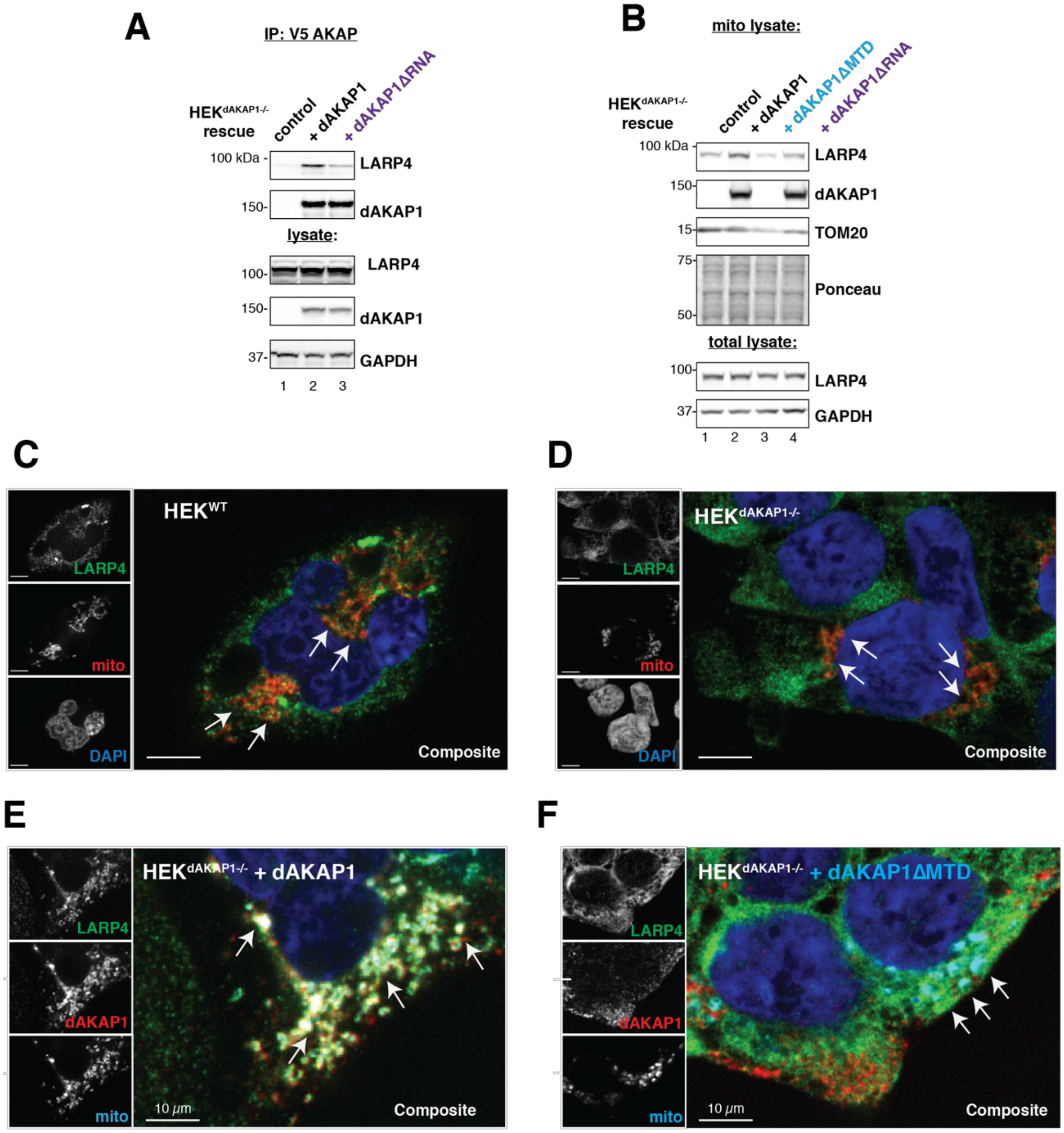

Figure 4.4.3: LARP4 localization to the mitochondria requires dAKAP1.

A. IP with anti-V5 antibody and IB for endogenous LARP4 demonstrate that less LARP4 is coIPed in dAKAP1ΔRNA rescue than WT rescue. **B.** Immunoblot for endogenous LARP4 from total and mitochondrial lysates demonstrate that less LARP4 is present in HEK$^{dAKAP1-/-}$ fractions. Localization to the mitochondrial is restored upon rescue with dAKAP1, but not dAKAP1ΔMTD or dAKAP1ΔRNA.

4.5 Discussion

Collectively, the proteomic studies and confirmation of the RNA-dependent association of dAKAP1 with LARP4 and PABPC1 at the OMM support my hypothesis that dAKAP1 is involved in local RNA recruitment and biology. More specifically, I validated dAKAP1 interaction with LARP4 due to the role of LARP proteins in promoting RNA stability and regulation.

The Lupus Antigen and related RNA-binding Proteins (LARP) proteins comprise a family of RBPs containing a common La Motif (LaM).[82] Cytoplasmic LARP family members broadly influence mRNA stability to regulate translation. Members include LARP1, LARP4, LARP4B, and LARP6, of which all but LARP6 were significantly enriched in our proteomics screen. The cytoplasmic LARPs share common functionality of mRNA binding, translation, and influencing mRNA stability.[84] LARPs 1, 4 and 6 interact with Poly A Binding Protein (PABP), the multifunctional protein that binds to the 3' poly(A) tails of mature mRNA. [84,85] PABP also acts as a platform for interaction with other proteins that influence translation initiation (e.g. Paip 1/2), poly(A) deadenylases (e.g. PAN3, CCR4 complexes) and translation termination (e.g. eRF3). [86–88]

Recent work suggests that LARP1 associates with and stabilizes 5' terminal oliogopyrimidine tract (5'TOP) transcripts, in which the 5' terminal regions act as a regulator of translation for mRNAs that encode elongation factors and ribosomal proteins.[89,90] Moreover, in *Drosophila*, LARP1 was recently identified as a stimulator of translation that associates with MDI, the fly ortholog of dAKAP1, at the OMM. [83]

LARP4 and 4B have also been shown to interact with PABP and RACK1, an important component of the 40S ribosome.[84,91,92] Both proteins associate with polysomes for the promotion of mRNA translation and localize to RNA granules (RNPs, as noted in our GO annotation) such as stress granules.[93–95] The proteins differ in their additional RNA Recognition Motifs (RRMs), suggesting that their RNA binding preferences differ.

I validated that LARP4 interacts with dAKAP1 specifically at the OMM *in vivo*. Given the established role of LARPs 1, 4 and 4B in promoting RNA stability and translation, we further hypothesize that dAKAP1 acts as a platform for local translation through the RNA-dependent recruitment of proteins necessary for RNA stability and translation initiation and regulation **(Figure 4.5.1)**.

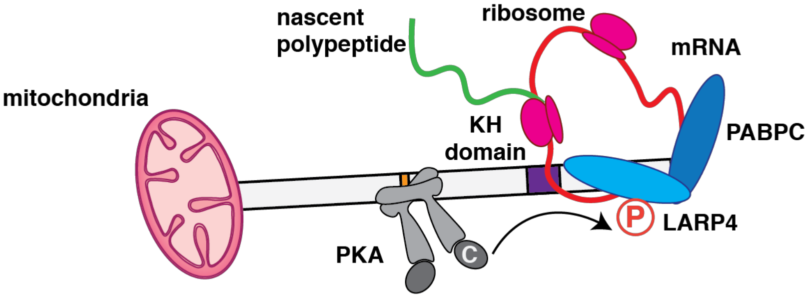

Figure 4.5.1: Model of dAKAP1 as a platform for local translation.
dAKAP1 is localized to the OMM and faces the cytoplasm. PKA interacts with the PKA helix of dAKAP1, and can localize catalytic subunit to phosphorylate LARP4. LARP4 interacts with PABPC and promotes the circularization of mRNAs that are recruited to the dAKAP1 KH domain. Ribosomes translate nascent polypeptides, which can be transported to the nearby mitochondria.

These results set the stage for me to both explore RNAs with which dAKAP1 KHT interacts **(Chapter 5)** and whether their translation and function is influenced by loss of dAKAP1 **(Chapter 6)**.

Chapter 5: Identifying and analyzing RNA interacting partners of dAKAP1

5.1 Introduction

RNA sequencing (RNA-Seq) is a powerful, next-generation sequencing platform which allows users to identify and quantify specific RNAs from biological samples.[96] Given the published interaction of dAKAP1 with the mRNA for the StAR protein (Steroidogenic Acute Regulatory Protein),[25] as well the high number of RNA regulatory proteins and RBPs identified in our protein pulldowns, I decided to pursue RNA-Seq for RNA interacting partners of the dAKAP1 KH-Tudor domains from the same physiological cell type as our protein pulldowns, MA10 mouse Leydig cells. These studies were performed in collaboration with Lauren Saunders and Cole Trapnell at the Unviersity of Washington,

At the time at which these studies were initiated, RNA-Seq had achieved neither the ubiquity nor the accessibility for it to be practical for our lab to undertake these studies *in vivo*. Therefore, I chose an *in vitro* appr oach to more broadly identify a cohort of RNAs to which the dAKAP1 KHT domain *could* bind **(Section 5.2)**. I validated that our pulldown approach would achieve RNA binding with low background. I also performed multiple bioinformatic analyses to explore the functions of the proteins encoded by the RNAs that interact with the dAKAP1 KHT **(Section 5.3)**.

5.2 RIP-Seq

In an analogous approach to our purified protein pulldowns, we performed RNA immunoprecipitation (RIP) experiments in order to identify potential RNA interacting partners of the dAKAP1 KH domain. Briefly, purified RNA from MA10 cells was incubated with KHT protein; empty beads, MBP and KHT$^{\Delta RNA}$ were used as background binding controls. RNA-protein complexes were IPed by anti-MBP antibody, RNA was eluted with Trizol, and total RNA isolated from pulldowns was sequenced following depletion of ribosomal rRNA **(Figure 5.2.1A)**.

Preliminary RNA pulldown experiments were first performed to determine background binding. Input bait and beads post-RNA elution were resolved by SDS-PAGE to confirm that the bait protein was being equally recovered between conditions **(Figure**

5.2.1B). We performed RT-PCR for exon 2 of the *Star* mRNA, a published interactor of dAKAP1's KH domain. Exon 2 of *Star* mRNA was amplified from the input, and only amplified in KHT IPs, with significantly low background binding from empty beads, MBP, or KHT$^{\Delta RNA}$ **(Figure 5.2.1C, D)**. Amplification reactions in which no reverse transcriptase was added were used as control.

We also generated a standard curve of *Star* mRNA and used qPCR to determine the order of magnitude enrichment of KHT over background controls. The *Star* CDS was cloned under a T7 promoter and expressed using an *in vitro* expression system to generate known quantities of RNA, which were used as input into RT-PCR reactions. RNA eluted from pulldowns was also amplified. These measurements more quantitaively determined that KHT associated with *Star* mRNA on the order of 10^5 to 10^6-fold more than background controls.

Having validated the low background binding and therefore the specificity of our pulldown strategy, we proceeded to perform pulldown experiments followed by RNA-Seq. Three biological replicates were performed, and three technical replicates of each sample were sequenced. In order to stringently define a pool of RNAs to which KHT bound, RNAs that only came down in the KHT condition in all three biological replicates were considered **(Figure 5.2.1F).** Sequence reads were aligned to the mouse genome in R using TopHat[138] and enrichment by read count was calculated using custom scripts and the Kallisto package[139] in R. From these analyses, we defined a pool of 315 "KHT associated RNAs" **(Appendix A, Table 1)**.

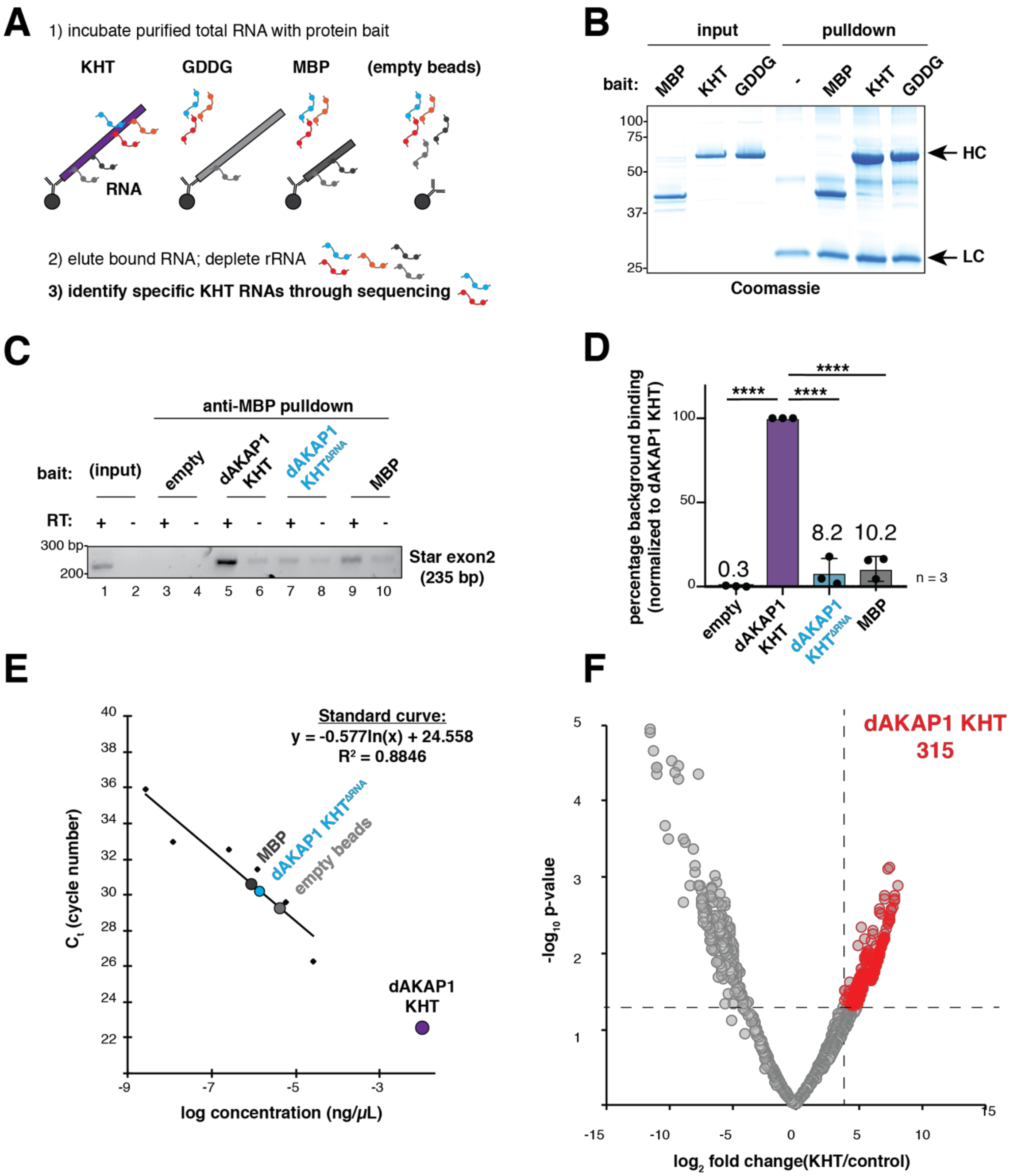

Figure 5.2.1: dAKAP1 KHT RNA-Seq.

A. Schematic of RNA pulldown strategy. **B.** Coomassie gel of input bait and bait recovered post-pulldown by anti-MBP beads. Antibody heavy chain (HC) and light chain (LC) are indicated with arrows. **C.** RT-PCR for *Star* exon 2, quantified in **D.** Background binding of negative control conditions, by densitometry of signal of RT+ minus signal of RT- lane for each sample. Three biological replicates were performed. Statistical significance was determined by unpaired student's t-test (**** = p-value < 0.00001). **E.** Quantification of *Star* mRNA determined by qPCR. Standard dilutions of RNA were prepared and plotted against C_t. A standard curve was generated by logarithmic regression ($R^2 = 0.8846$) and concentrations for negative controls and KHT were calculated with C_t. **F.** Volcano plot of RNA-Seq results. The x-axis represents the log2 enrichment score as calculated by "differential expression" between KHT pulldowns and pooled negative control reads. Red circles represent "KHT associated RNAs."

5.3 Analysis

Significantly enriched RNAs underwent bioinformatics analysis in order to parse out the physiological significance of dAKAP1 anchoring. GO Molecular Component and Function were examined **(Figure 4.3.1A, B).** Intriguingly, many of the proteins encoded by these RNAs are involved in functions such as RNA binding and regulation of translation, similar to our proteomics results.

We were also interested in determining if the dAKAP1 KH domain anchored RNAs that encoded mitochondrially-localized proteins or proteins that were found in our proteomics screen **(Figure 4.3.1C)**. A list of mitochondrial proteins was compiled from Mouse MitoCarta 2.0[58,97] and the GO database for proteins with mitochondrial annotated localization **(Appendix A, Table 2)**. Of the 315 RNA interacting partners, 63 encoded mitochondrial proteins. We reduced the stringency of our defined pool of KHT protein interactors to encompass proteins that were pulled down in all n=5 experimental replicates and were enriched 2.5-fold over background binding **(Appendix A, Table 3)**; we pulled down the RNA encoding the protein for 22 of the proteomics targets.

Lastly, we identified 5 RNAs which encoded mitochondrial proteins that were also pulled down in our proteomics screen: HADHA (*HADHA*), heterogeneous ribonucleoprotein K (*HNRNPK*), Heat Shock 60kD Protein 1 (HSP60, chaperonin; *HSPD1*), formyltetrahydrofolate synthetase (*MTHFD1*), and transketolase (*TKT*).

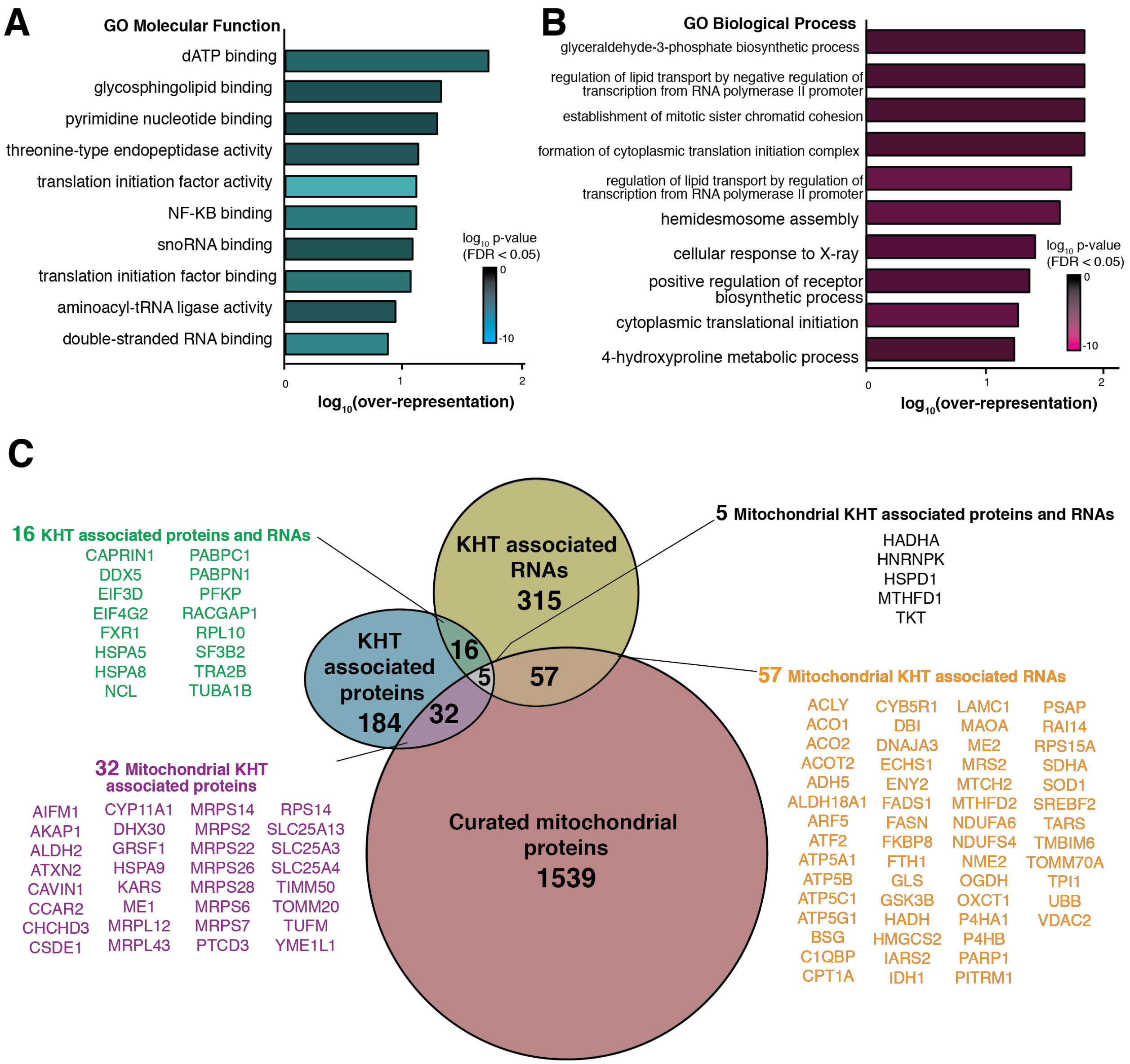

Figure 5.3.1 Bioinformatic analysis of KHT associated RNAs.

A. Top ten GO Molecular Process terms overrepresented in KHT associated RNAs. Length of bar corresponds to log-fold overrepresentation; color represents p-value for significance of the overrepresentation by Fisher's test, with False Discover Rate (FDR) < 0.05.) **B.** Top ten GO Biological Process terms overrepresented in KHT associated RNAs. **C.** Venn diagram of KHT associated RNAs (yellow; total number, including intersections, 315), KHT associated proteins (blue; total number, 184), and curated mitochondrial proteins (red; total number, 1539). Area of ellipses and intersections proportional to numbers represented.

5.4 Discussion

This *in vitro* RNA pulldown and sequencing strategy allowed me to identify 315 potential interacting partners of the dAKAP1 KH domain. There are several important caveats to consider when interpreting the data, however.

Firstly, my strategy allowed me to find a cohort of putative RNAs to which the dAKAP1 *could* bind. The kinetics and dynamics of these RNA-protein interactions, however, are highly dependent on the *in vitro*, including: type of salt, salt concentration, detergent concentration, temperature, length of incubation, and maintenance of RNase-free working conditions.[29] Because I only had surrogate for specificity of KHT pulldowns – namely, RT-PCR amplification of the StAR mRNA – I chose buffer conditions that afforded maximum stringency and specificity of RNA pulldown for this one mRNA. In so doing, I may have artificially constrained the pool of energetically favorable RNA-protein interactions.

As a corollary, it is also important to note that just because I observed that the dAKAP1 KH domain was capable of binding a certain RNA *in vitro* does not mean that it can or does *in vivo*. Moreover, I can say nothing about the affinity of the dAKAP1 KH domain for certain RNAs *in vivo* because these interactions are so highly dependent on reaction conditions, as discussed above. Therefore, it was important to consider fold enrichment over background controls when defining our pool of RNAs, but not as a metric for selecting as follow-up candidates.

Secondly, I chose a cell type in which dAKAP1-RNA interactions had already been observed (MA10 cells). In limiting input RNA to one cell type, I absolutely restricted potential interactions to a cell-type and cell-state dependent pool of RNAs. Although there were published data that indicated dAKAP1-RNA interactions were biologically relevant in MA10 cells, it is possible that dAKAP1 anchoring of specific RNAs is less important or irrelevant in other cell types. I consider this to be unlikely given the highly conserved nature of the KH domain, particularly in tandem with the Tudor domain, however.

Thirdly, I chose to use the purified dAKAP1 KH and Tudor domains as opposed to the KH domain alone because we had identified dAKAP1 protein interacting partners with RNA binding function. In our *in vitro* system, however, we did not expose the dAKAP1

KHT to other RBPs in complex with RNA. I consider it possible, and even likely, that dAKAP1 binds and recruits RNA through its interaction with RBPs including LARP4 and PABPC. The dAKAP1 KH domain may be capable of binding these RNAs and stabilizing their interaction in the context of larger protein-protein-RNA complexes, but it may not be energetically favorable for the RNA to interact with the dAKAP1 KH domain alone, in the absence of these factors.

Nevertheless, my *in vitro* pulldown strategy has allowed us to stringently define a cohort of RNAs to which the dAKAP1 could potentially interact *in vivo*. My bioinformatic analysis suggests that this cohort is, indeed, biologically relevant, including the presence of 63 of the RNAs encoding mitochondrial proteins. I explore the relevance of this RNA anchoring in the next chapter, **Chapter 6.**

Chapter 6: Physiological significance of dAKAP1 anchoring of RNA

6.1 Introduction

I hypothesized that dAKAP1-anchored RNA could be regulated, and translation thereof promoted, by the validated interacting partner LARP4, whose function includes mRNA stabilization and translation.

First, I monitored the local translation of proteins encoded by these mRNAs at the mitochondria in our HEK$^{dAKAP1-/-}$ cell line with the various rescue constructs **(Section 6.2)**. I also performed preliminary experiments to monitor overall translation at the mitochondria. Next, I examined the specific physiological importance of the anchoring of specific RNAs by dAKAP1 at the mitochondria by re-examining our RNA-Seq dataset and finding a significant enrichment of TCA cycle enzymes in the mitochondrial KHT RNAs **(Section 6.3)**. Lastly, I extended my investigation into the anchoring of these RNAs in various breast cancer lines on which the Scott lab has recently published work suggesting that dAKAP1 expression levels correlate with metabolic state (i.e. glycolytic or OXPHOS) **(Section 6.4)**.

6.2 Local translation of KHT associated RNAs in HEK$^{dAKAP1-/-}$ cells

In order to examine local translation, I performed subcellular fractionation to isolate mitochondria and investigated protein level through immunoblotting for specific proteins of both total and mitochondrial fractions.

6.2.1 Expression of proteins encoded by KHT associated RNAs

I focused my attention on a subset of RNAs whose encoded proteins were mitochondrial. I reasoned that if dAKAP1 anchoring of these RNAs was necessary for local translation, I should see a corresponding change in protein levels in mitochondrial fractions in HEK$^{dAKAP1-/-}$ cells. Protein levels should be restored upon rescue with dAKAP1, but not rescue with dAKAP1ΔMTD or dAKAP1ΔRNA.

I was interested in proteins that had also been pulled down in our proteomics screen, including: HADHA, HSPD1, MTHFD1, and TKT. I also examined RNAs whose encoded proteins had known important function at the mitochondria, such as SOD1 (superoxide dismutase).[98] I included a non-mitochondrial protein encoded by the CALR RNA to control for specific mitochondrial enrichment and translation. Other experimental controls include monitoring protein levels of: dAKAP1; TOM20, as a surrogate measure of mitochondrial enrichment; GAPDH and β-actin as loading controls for total lysate; and LARP4, whose localization we had previously demonstrated was dependent on dAKAP1.

Representative immunoblots of three biological replicates of subcellular fractionation revealed that levels of certain proteins remained consistent regardless of dAKAP1 status **(Figure 6.2.1)**. Quantification of the mitochondrial lysate **(Figure 6.2.1B-K)** revealed that rescue with different constructs dAKAP1 constructs was not consistent across replicates, which most likely contributed to the lack of overall statistical significance for most of these genes.

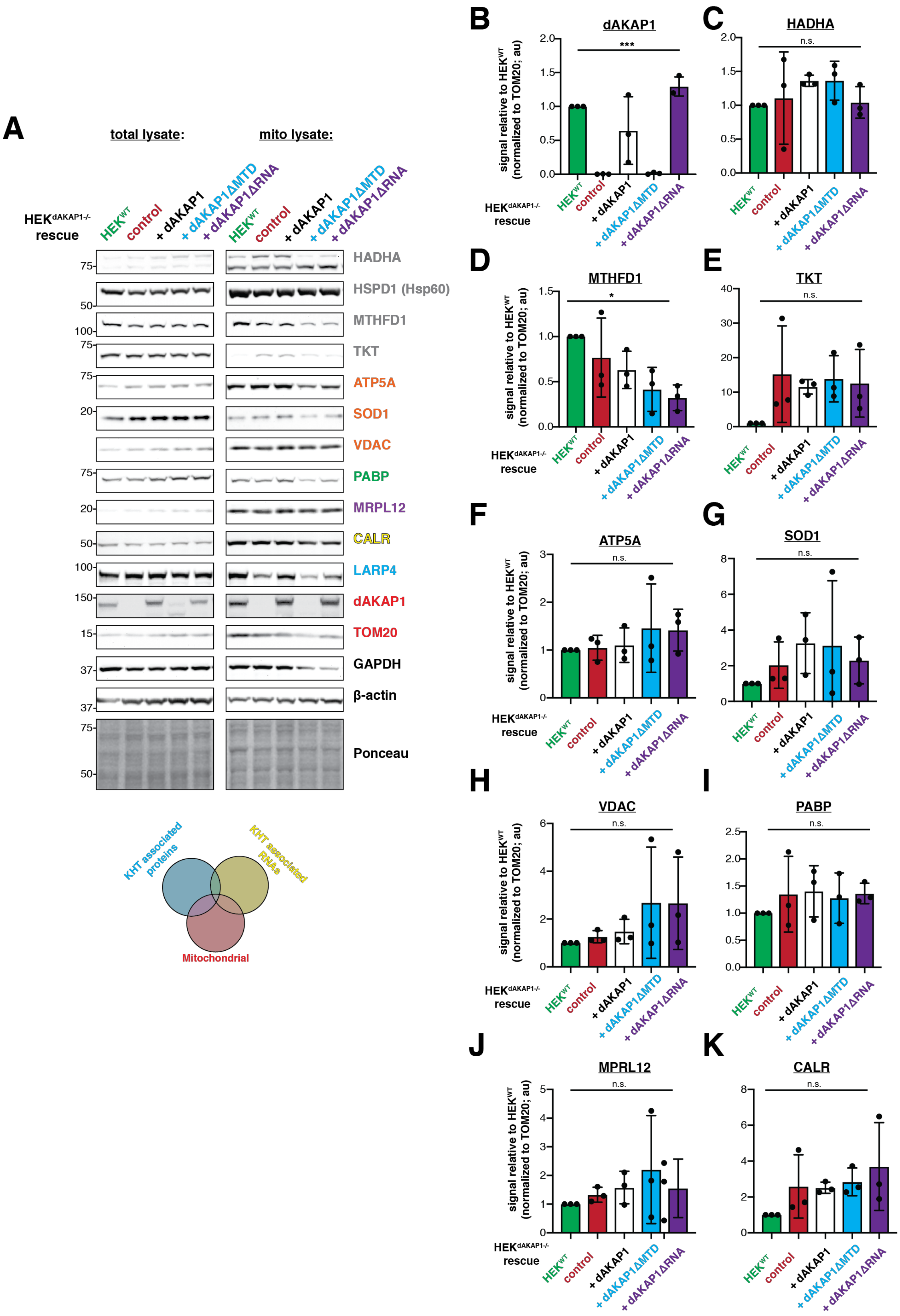

Figure 6.2.1: Local levels of proteins encoded by KHT associated RNAs.

A. Immunoblots of total and mitochondrial lysates from HEK^{WT}, HEK$^{dAKAP1-/-}$ and various rescues, with protein target indicated to the right. Legend for color of protein target text corresponds to **Figure 5.3.1** (cyan = KHT associated protein; yellow = KHT associated RNA; red = mitochondrial). **B-K.** Quantification of mitochondrial lysate signal by densitometry of three biological replicates. Statistical significance was determined by ordinary one-way ANOVA (* indicates p-value < 0.05, *** indicates p-value < 0.001).

6.2.2 Puromycin labeling of actively translating ribosomes

I initiated preliminary studies to more directly investigate local translation. Puromycin, an antibiotic that prematurely terminates translation, has previously been used to label actively translating ribosomes; because puromycin resembles the 3' end of aminoacylated-tRNA, it is able to enter the ribosome A site, where it transfers to a nascent polypeptide and causes the premature release of the chain.[99] Puromycylated peptides can be monitored by immunoblot with an antibody against puromycin.

I transiently treated HEK$^{dAKAP1-/-}$ control and rescue cells with a low dose of puromycin and examined either the total or mitochondrial protein fractions for the presence of puromycylated proteins as a surrogate for local translation **(Figure 6.2.2A)**. As a control, cells were treated with either vehicle (PBS) or pre-treated with cycloheximide, a small molecule that blocks translation by inhibiting elongation. [100] Somewhat contrary to my expectations, there did not seem to be an appreciable difference in puromycin signal in mitochondrial lysates. Immunoblot for dAKAP1 from total lysates, however, revealed an unequal rescue of dAKAP1 between the various different constructs **(Figure 6.2.2B)**. Imaging of cells treated from the same set of experiments were also inconclusive (data not shown), suggesting that this method of local protein detection will require future optimization.

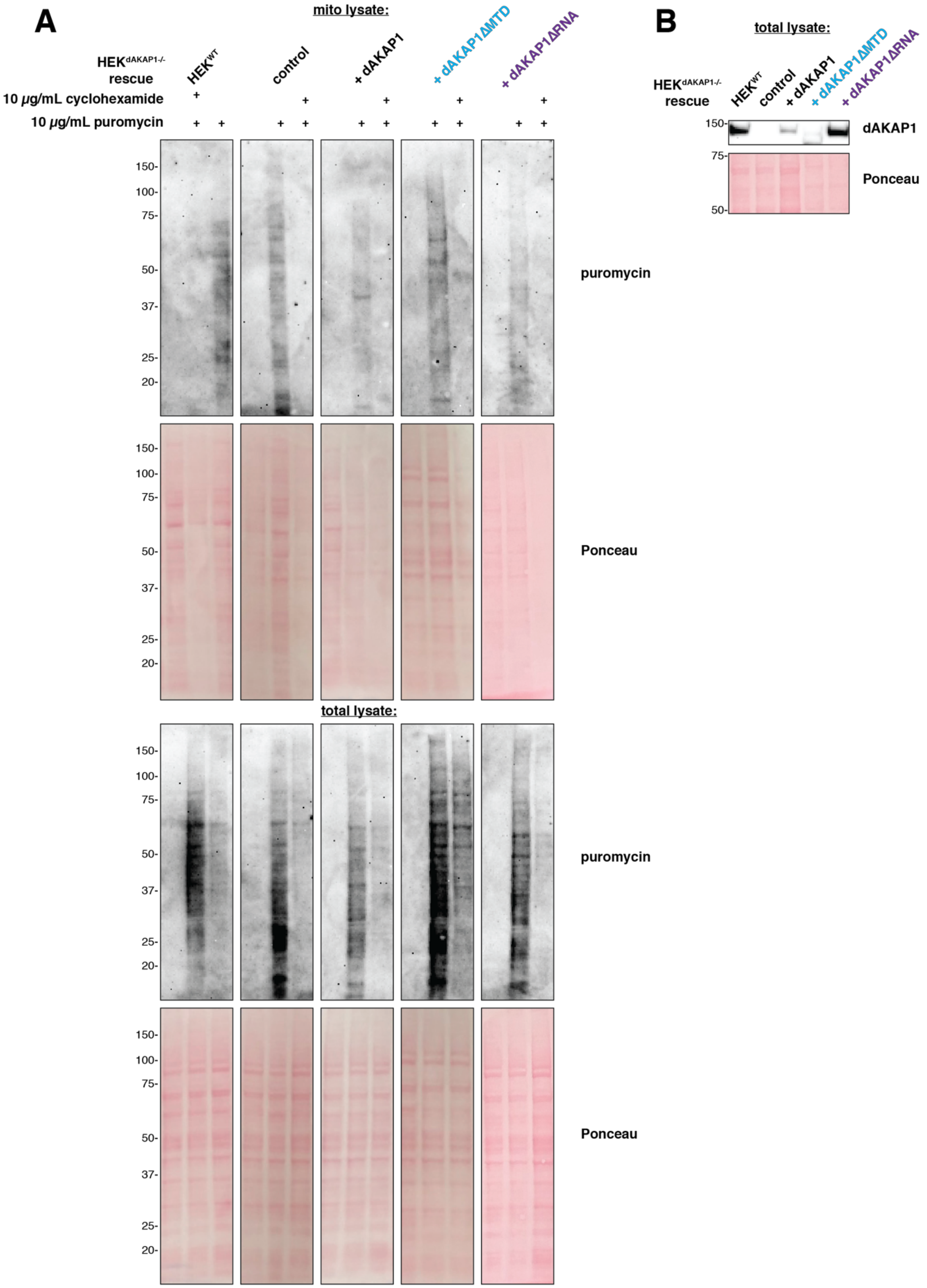
A
mito lysate:
HEK$^{dAKAP1-/-}$
rescue
10 µg/mL cyclohexamide
10 µg/mL puromycin
HEK^{WT}
control
+ dAKAP1
+ dAKAP1ΔMTD
+ dAKAP1ΔRNA
+ + + + + + + + + +
+ + + + +
150-
100-
75-
50-
37-
25-
20-
puromycin
Ponceau
total lysate:
puromycin
Ponceau
B
total lysate:
HEK$^{dAKAP1-/-}$
rescue
HEK^{WT}
control
+ dAKAP1
+ dAKAP1ΔMTD
+ dAKAP1ΔRNA
150-
75-
50-
dAKAP1
Ponceau

Figure 6.2.2: Puromycin labeling of actively translating ribosomes.

A. Immunoblots of mitochondrial (top) and total (bottom) lysate of HEK^{WT} and $\text{HEK}^{\text{dAKAP1-/-}}$ and various rescues for puromycin. Treatments indicated above, including 10 μg/mL puromycin in cell media for 10 minutes, or pre-treatment with 10 μg/mL cycloheximide for 10 minutes followed by treatment with both puromycin and cycloheximide for 10 minutes. Corresponding Ponceaus shown below to demonstrate to protein loading. **B.** Immunoblot for dAKAP1 from total cell lysate to demonstrate degree of rescue of various dAKAP1 constructs in $\text{HEK}^{\text{dAKAP1-/-}}$ background.

6.3 Examining metabolism and the TCA cycle in HEK$^{dAKAP1-/-}$ cells

Because the local translation experiments were inconclusive, I returned to our KHT associated RNAs dataset, and specifically focused on the 63 RNAs that encoded mitochondrial proteins. As before, I performed GO Enrichment analysis for molecular function on this subset of 63 RNAs, and discovered that there was significant overrepresentation for the TCA cycle **(Figure 6.3.1A)** as well as other bioenergetic pathways. Six of the genes (*ACO1, ACO2, IDH1, IDH2, ODGH,* and *SDHA*) encoded enzymes in the TCA cycle **(Figure 6.3.1B, genes in red)**.

I broadly surveyed the TCA cycle by immunoblotting mitochondrial fractions from our HEK$^{dAKAP1-/-}$ and various rescue lines. Having seen that dAKAP1 was rescued unequally between cell lines in our previous experiments **(Figure 6.2.2B)**, we instead focused on interpreting representative immunoblots of mitochondrial lysate from one replicate in which dAKAP1 constructs rescued equally **(Figure 6.2.C)**.

Levels of four of the six TCA enzymes were monitored by immunoblot **(Figure 6.3.1C,** KHT associated RNAs denoted in red**)**. Of these, SDHA levels appeared substantially lower in HEK$^{dAKAP1-/-}$ compared to HEK^{WT}. Rescue with dAKAP1, but not dAKAP1ΔRNA, restored SDHA levels comparable to the HEK^{WT}. These results demonstrate that, at least for the enzyme SDHA, dAKAP1 anchoring of the RNA correlates with mitochondrial protein levels, implying that this RNA is translated locally.

I reasoned that protein levels of SDHA, a component of Complex II of the respiratory chain, could manifest as a global metabolic shift away from OXPHOS to glycolysis in HEK$^{dAKAP1-/-}$ cells.[101101] In order to start to test this hypothesis, I performed growth curve assays on HEK^{WT} or HEK$^{dAKAP1-/-}$ cells in growth media which either supported glycolysis (control media) or forced cells towards OXPHOS (2-deoxy-d-glucose or galactose) for energy production and growth **(Figure 6.3.1D)**.[130] 2-deoxy-d-glycose is a form of glycose in which the 2' hydroxyl group is replaced by hydrogen and cannot be phosphorylated by hexokinase to generate glucose-6-phosphate, inhibiting glycolysis.[102] Galactose requires conversion to glucose-6-phosphate through various enzymatic steps and has been demonstrated to slow cellular growth rates.[103]

In two biological replicates, with four technical replicates per biological replicate, I [103103]did not observe appreciable differences between HEK$^{\mathrm{WT}}$ and HEK$^{\mathrm{dAKAP1-/-}}$ cells. Cell growth was monitored by MTS assay. Due to the low initial cell number plated (2500 cells/well), I did not observe cell growth as assayed by MTS signal until 48 hours post-media change. It is likely that I will need to repeat these measurements

I was also interested in possible differences in subcellular distribution of SDHA protein between HEK$^{\mathrm{WT}}$ and HEK$^{\mathrm{dAKAP1-/-}}$ cells. Immunostaining validated our immunoblot results that SDHA signal (green) was decreased overall in both the mitochondria (red) and cytoplasm compartments in HEK$^{\mathrm{dAKAP1-/-}}$ as compared to HEK$^{\mathrm{WT}}$ **(Figure 6.3.1E, F)**. In co-staining the mitochondria by TOM20 (red), we observed that the mitochondria of HEK$^{\mathrm{dAKAP1-/-}}$ appeared to be more fragmented.

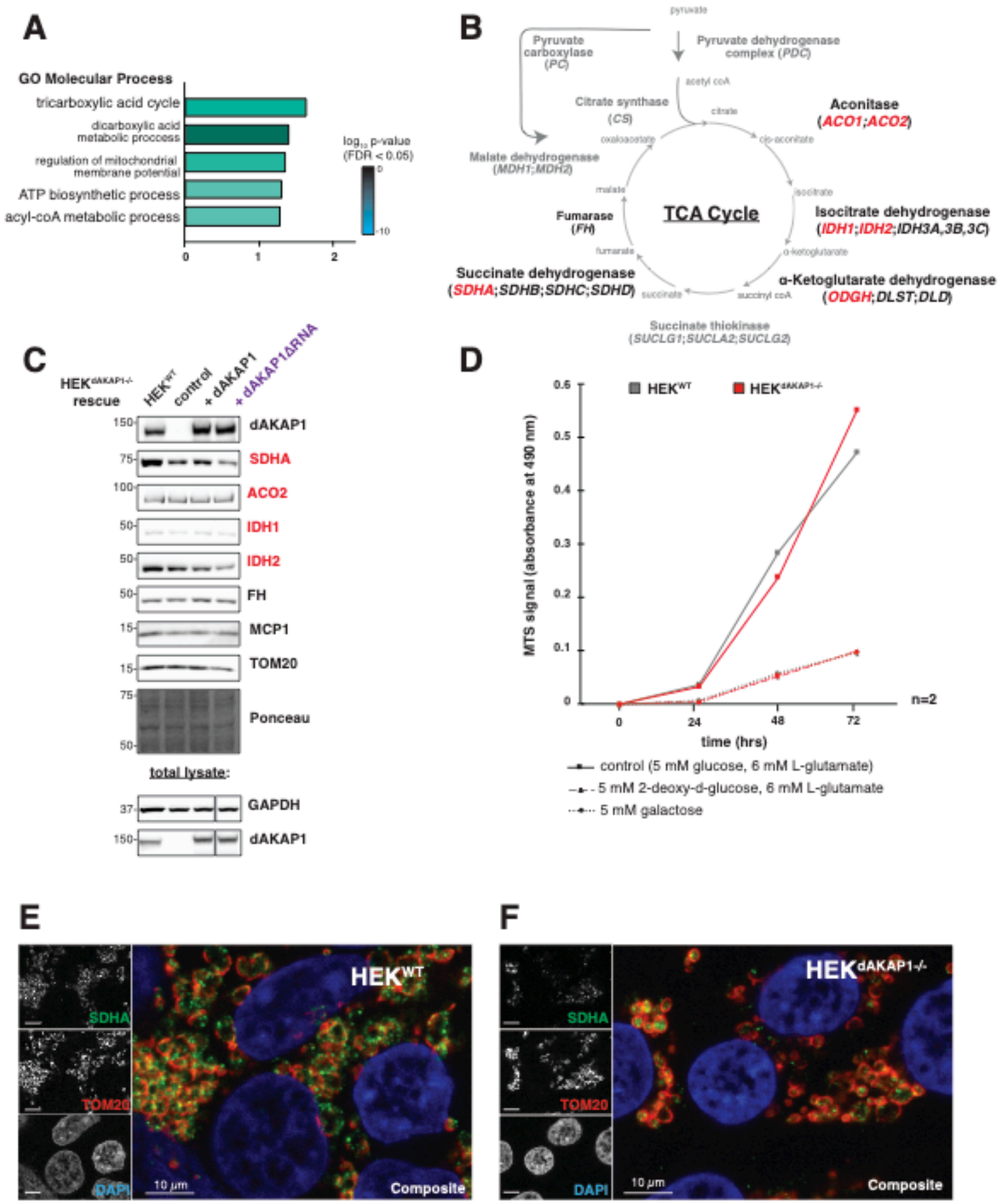

Figure 6.3.1. Examining TCA cycle components in HEK^{WT} and HEK$^{dAKAP1-/-}$ cells.

A. Top five GO Molecular Process terms overrepresented 63 mitochondrial KHT associated RNAs. Length of bar corresponds to log-fold overrepresentation; color represents p-value for significance of the overrepresentation by Fisher's test, with False

Discover Rate (FDR) < 0.05). **B.** Schematic of TCA cycle, with KHT associated RNAs indicated in red. **C.** Representative immunoblots of one of three biological replicates for members of the TCA cycle from mitochondrial lysates, with proteins encoded by KHT associated RNAs indicated in red. **D.** Growth curves of two biological replicates of HEK^{WT} (grey) and $\text{HEK}^{\text{dAKAP1-/-}}$ as assayed by MTS signal. Growth media, with corresponding concentrations of glucose, 2-deoxy-d-glucose, or galactose, represented in legend below. **E.** Immunostaining of HEK^{WT} and **F.** $\text{HEK}^{\text{dAKAP1-/-}}$ cells for SDHA (green) and TOM20 (red), with nuclei counterstained by DAPI (blue). Scale bar = 10 μm.

6.4 Local translation in breast cancer lines

I repeated our immunostaining experiments for TOM20 (green) and dAKAP1 (red) to confirm, on average, the mitochondria in HEK$^{dAKAP1-/-}$ cells appeared smaller and more fragmented than HEK^{WT} **(Figure 6.4.1A, B)**. These observations aligned with the recently published findings from the Scott lab that dAKAP1 levels correlate with mitochondrial fragmentation in various breast cancer lines.[53]

As with the HEK lines, I first decided to immunoblot total cell lysates of four different breast cancer cell lines for a subset of proteins encoded by RNAs identified we identified as dAKAP1 KHT associated **(representative blots shown in Figure 6.4.1C)**. Immunoblot for dAKAP1 validated that two of the cell lines, MCF10A and MCF7 (magenta), could be classified as “dAKAP1-high”, and the other two, MD-MBA-231 and HS578 (grey), could be classified as “dAKAP1-low” (quantification in **Figure 6.4.1D**). Across three biological replicates, SDHA was significantly different between the dAKAP1-high and dAKAP1-low breast cancer lines **(Figure 6.4.1G)**, with other proteins following the trend **(Figures 6.4.1E-H)**.

Previous work from the Scott lab and others has established that metabolically, dAKAP1-high breast cancer lines are more OXPHOS and dAKAP1-low breast cancer lines are more glycolytic.[104104,105] As with the HEK lines, I monitored the mitochondrial lysate for protein levels of TCA enzymes **(Figure 6.4.1I)**. Intriguingly, dAKAP1 expression at the mitochondria was not absolutely correlated with dAKAP1 levels in total cell lysate for the nominally dAKAP1-high breast cancer line MCF-10A, even when accounting for greater mitochondrial lysate loaded as determined by TOM20 signal. I did observe on average, across three biological replicates (quantification not shown), higher expression of TCA enzymes in dAKAP1-high cell lines, including SDHA.

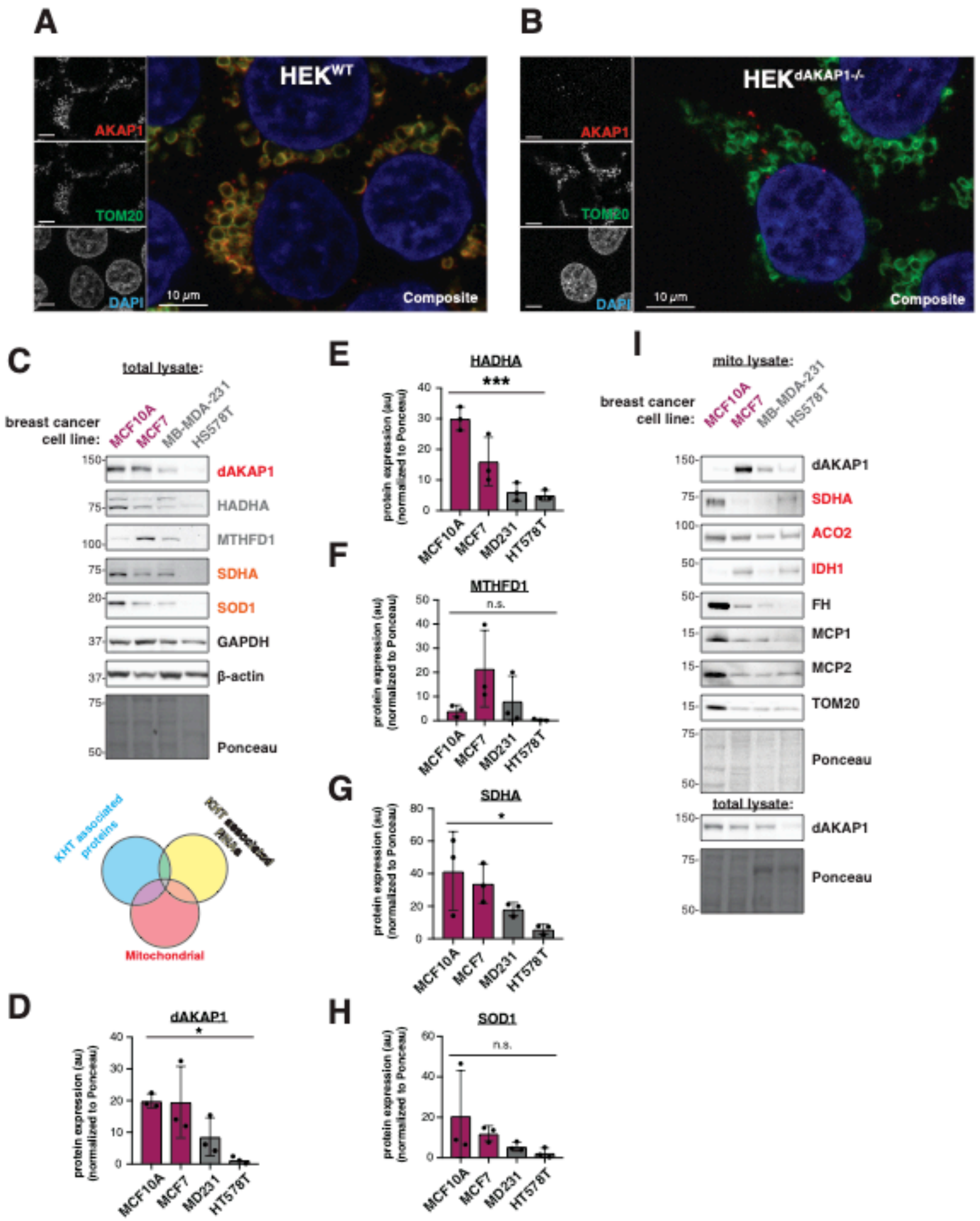

Figure 6.4.1: Local levels of proteins encoded by KHT associated RNAs and TCA cycle components in breast cancer cell lines.

A. Immunostaining of $\mathrm{HEK}^{\mathrm{WT}}$ and **B.** $\mathrm{HEK}^{\mathrm{dAKAP1-/-}}$ cells for AKAP1 (red) and TOM20 (green), with nuclei counterstained by DAPI (blue). Scale bar = 10 μm. **B.** Immunoblots of total lysates from breast cancer lines MCF10A, MCF7, MD-MBA-231 (MD231) and HST578T, with protein target indicated to the right. Legend for color of protein target text corresponds to **Figure 5.3.1** (cyan = KHT associated protein; yellow = KHT associated RNA; red = mitochondrial). **C-H.** Quantification of total lysate signal by densitometry of three biological replicates. Statistical significance was determined by ordinary one-way ANOVA (* indicates p-value < 0.05, *** indicates p-value < 0.001). **I.** Representative immunoblots of one of three biological replicates for members of the TCA cycle from mitochondrial lysates, with proteins encoded by KHT associated RNAs indicated in red. Total lysate below.

6.5 Discussion

Collectively, these preliminary studies suggest that dAKAP1 anchoring of RNA is important for the local translation of at least one protein, SDHA, involved in the critical mitochondrial function of oxidative phosphorylation.

I individually examined mitochondrial levels of proteins encoded by KHT associated RNAs in order to define a range of potential physiological consequences of dAKAP1 anchoring of RNA. This manual approach was necessarily circumscribed by constraints such availability of commercial antibodies, meaning that there are many other potential physiological consequences that I overlooked or have yet to test. Moreover, as discussed in **Chapter 6**, *in vitro* interaction of an RNA with the dAKAP1 KHT does not require either *in vivo* interaction or physiological consequence of its anchoring. Therefore, non-statistically significant changes in protein level (as seen for many of the proteins which I examined) do not universally invalidate the hypothesis that dAKAP1 anchoring of RNA supports local protein translation.

However, I did identify one such interaction – namely, dAKAP1 anchoring of the *SDHA* mRNA – that was that was consistent across both HEK lines and in physiological breast cancer cell lines. As previously noted, SDHA is a component of Complex II of the electron transport chain (succinate dehydrogenase; SDH). Mutations in the all of the genes which encode the protein components of SDH – *SDHA*, *SDHB*, *SDHC*, and *SDHD* – have been reported in various types of cancer. Their loss results in succinate accumulation, a metabolite indicative of pseudohypoxia. Whether the loss of dAKAP1 anchoring of the *SDHA* mRNA is necessary or sufficient to lead to a shift in metabolic profile, however, remains to be determined, as do many future directions discussed in the next chapter, **Chapter 7**.

Chapter 7: Conclusions, open questions, and future directions

7.1 Conclusions

The main findings of my work are threefold:

First, dAKAP1 robustly interacts with RNA binding proteins via its KH and Tudor domains. These KHT associated RBPs likely interact with dAKAP1 as protein subcomplexes with distinct functions, including RNA sequestration RNP granules, splicing, and regulation translation. Moreover, the localization of these RBPs to dAKAP1, and thus the OMM, may be regulated by PKA phosphorylation and/or RNA interaction with the dAKAP1 KH domain itself.

Second, dAKAP1 can interact with a cohort of RNAs that encode both cytoplasmic and mitochondrial proteins. The cohort of RNAs encoding mitochondrial proteins is greatly enriched for molecular functions in the TCA cycle and cell metabolism.

Third, dAKAP1-mediated anchoring of the *SDHA* mRNA directly correlates with mitochondrial SDHA protein levels. Though alternation of this anchoring is not sufficient to drive metabolic change, I also correlate a decrease of SDHA with a decrease in dAKAP1 levels across four different breast cancer cell lines. Whether this change is a cause of, or is caused by, overall change in tumor metabolism remains an open question. The consistent observation of this finding across cell lines, with physiological changes in mitochondrial dynamics and metabolism, both validates our pulldown strategy for at least one target and and also suggests that this pool of RNAs may provide other insight into the role of RNA anchoring at the OMM.

7.2 Open questions and future directions

While we succeeded in addressing of our first aim of identifying protein and RNA binding partners of dAKAP1, there remains much work to be done to address the second aim of uncovering physiological consequences of dAKAP1 RNA anchoring. Indeed, many of the outstanding questions presented at the end of **Chapter 2** remain unanswered.

First, we have yet to demonstrate the direct association of dAKAP1 and our RNAs *in vitro*. We have initiated preliminary fRIP-Seq (formaldehyde crosslinked RNA

Immunoprecipitation)[106] studies in our HEK$^{dAKAP1-/-}$ cells rescued with the various V5-tagged dAKAP1 constructs, including dAKAP1ΔMTD and dAKAP1ΔRNA, and plan to conclude qPCR validation of this strategy imminently. Rapid advances in the field of RNA-Seq make this work far more feasible in cell models than when this work was begun.

Moreover, we have yet to directly demonstrate that local translation of dAKAP1-anchored RNAs occurs at the OMM. While our puromycin experiments can approximate local active ribosomes, crude subcellular fractionation may not be sensitive enough to detect small changes in levels of the translation of particular RNAs that, furthermore, may only change upon specific physiological conditions.

Newer large-scale labeling techniques, including but not limited to APEX-RIP[107] or APEX-Seq,[108] could allow us to directly label RNAs at the OMM, nascent polypeptides being translated at the OMM, and/or both. We would be able to compare these datasets with our *in vitro* RNA cohort, to allow us to narrow our range of potential follow-up candidates. We might also utilize co-localization imaging techniques like FLARIM,[109] which label both ribosomal rRNA and specific mRNAs; while published sets of probe that work with this technique, or for RNA-FISH, are currently limited, newer computational techniques could enable us to design and rapidly screen probes and provide the direct confirmation of local translation.[110,111]

While we are in some ways no closer to understanding why these RNA functions are conserved in the context of an AKAP, a broader look at the RNP literature may suggest an additional tier of regulation we have yet to consider. RNP granules, including stress granules[93–95,112–115], processing bodies (p-bodies)[116–124] and glycolytic bodies (g-bodies) [125], represent a new liquid-phase separated organelle.[118,126–129] Indeed, that membrane-associated RBPs orchestrate local translation is increasingly appreciated as a generalized paradigm for protein localization to specific organelles.[131–134] As new large-scale studies are published that identify the protein and RNA components of these compartments under specific physiological stresses and conditions, we can start to draw on these resources – along with our known protein interacting partners – to potential post-translational regulatory mechanisms, including but not limited to PKA phosphorylation.

Lastly, we have yet to translate our findings to an animal model, in spite of re-establishing the *AKAP1* knockout mouse colony. The *AKAP1* knockout mice represent a rich resource of various metabolic and physiological states of mitochondria, including the brain, heart, skeletal muscle and testes. While we have been stymied by the lack of a commercial antibody that can reliably detect the mouse form of dAKAP1 for basic biochemical applications such as immunoblot and immunostaining, we have nevertheless amassed a backlog of tissues which can hopefully be analyzed in the future. We might also conceivably consider broader questions about the role dAKAP1 might play in RNA anchoring at the mitochondria, such as during development, that could only be addressed [131–134]in an animal model.

Chapter 8: Materials and Methods

In vitro KHT pulldowns

Recombinant protein purification

N'-terminal MBP-6xHis tagged fusion constructs of AKAP1 domains were cloned into a modified pMAL c5x backbone (NEB) using Gateway cloning (ThermoFisher). BL21 (DE3) pLys cells were chemically transformed with 1 μg of plasmid and grown to confluence overnight in Lysogeny Broth (LB) at 37°C; cells were diluted and grown to OD_{600} ~ 0.5 before the being induced with 1 μM IPTG for 16 hrs at 16°C. Following induction, cells were pelleted and frozen at -20°C. Cell pellets from 0.66 L induced cell culture volume were thawed on ice and re-suspended in 50 mL Buffer A (50 mM sodium phosphate buffer, 100 mM NaCl, 5 mM imidazole, pH 7.6) supplemented with 2 mM tris(2-carboxyethyl)phosphine (TCEP), 2 mM $MgCl_2$, 4 mg/mL lysozyme, 1 mM AEBSF, 2 µg/mL leupeptin, 16 µg/mL benzamidine. Re-suspended cell pellets were lysed with the addition of 0.5% final Triton X-100 buffer and 1/10,000x dilution of benzonase; following lysis for 20 mins at 4°C, lysate was cleared by centrifugation at 10000 *xg*. Clarified lysate was incubated with 5 mL (CV = 1/10 lysis volume) nickel affinity resin (Roche) for 1 hr at 4°C and beads were collected by gravity on disposable columns. 3 1 CV washes in Buffer B (50 mM sodium phosphate buffer, 500 mM NaCl, pH 7.6) at 50 mM imidazole and 5 0.5 CV elutions in Buffer B at 500 mM imidazole were collected and analyzed by SDS-PAGE resolution followed by Coomassie staining. Appropriate fractions were combined, concentrated by spin centrifugation (Millipore) to a volume < 5mL, and separated by HiLoad 16/600 Superdex 200 gel filtration column in Buffer C (20 mM Tris-HCl, 200 mM NaCl, pH 7.6) at 0.5 mL/min. Peaks corresponding to soluble protein were pooled, concentrated to 2-5 mg/mL, flash-frozen in liquid nitrogen, and stored at -80˚C.

Protein pulldowns

MA10 cells were grown to confluence on 150 mm plates (Falcon), rinsed once with Phosphate Buffered Saline (PBS), lifted by 0.25% Trypsin-EDTA (Gibco), and pelleted at 500 x*g*. Pellets were lysed in 2 mL of IP Lysis Buffer (20 mM HEPES pH 7.4, 150 mM

NaCl, 1 mM EDTA, 1% Triton X-100) supplemented with protease inhibitors and incubated on ice for 15 mins before being cleared at 150000 *xg*, 4˚C. Protein concentrations were determined by BCA assay (Pierce). 2 mg cleared cell lysate was incubated with 25 *μ*g protein bait with gentle rocking for 1 hr at 4˚C; bait-prey complexes were recaptured by incubation with 15 *μ*L amylose beads (NEB). Beads were pelleted twice in High Salt IP Lysis Buffer (IP Lysis Buffer, 250 mM NaCl), thrice in IP Lysis Buffer, and once in PBS at 500 x*g*, 4˚C.

Mass Spectrometry

Proteins were eluted from beads in 1X LDS buffer with 1 mM TCEP and 2 mM chloroacetamide. The eluents were resolved by electrophoresis and gel lanes corresponding to each pulldown condition were excised and cut into 8 separate section. In-gel protein digestion was performed as previously described

For LC-MS/MS analysis, samples were loaded to self-pulled (P2000 Sutter Laser puller, Sutter Instrument, Novato, CA) 360 µm OD × 100 µm ID 10 cm columns with a 7 µm tip and packed with 3 µm Reprosil C18 resin (Dr. Maisch, Germany) using a pressure cell (NextAdvance, Averill Park, NY). Peptides were analyzed with 90 min gradients of 8–35% acetonitrile at 300 nL/min nanoLC–MS (Thermo Dionex RSLCnano, Sunnyvale, CA) on an Orbitrap Elite (Thermo, Bremen Germany). Orbitrap FTMS spectra (R = 30,000 at 400 m/z; m/z 350–1600; 3e6 target; max 500 ms ion injection time) and Top15 data dependent CID MS/MS spectra (1e4 target; max 250 ms injection time) were collected with dynamic exclusion for 30 s and an exclusion list size of 50. The normalized collision energy applied for CID was 35% for 10 ms.

MaxQuant v.1.5.7.4 and the associated Andromeda search engine was used to search a UniProt mouse database downloaded in July 2016.[135,136] Resulting data were analyzed using Perseus.[137]

RNA purification

Total RNA was purified by TRIzol (Invitrogen), followed by two chloroform extractions; in immunoprecipitation experiments, RNA was eluted by TRIzol, followed by two chloroform extractions. 10 μg glycogen was added to the aqueous phase as a carrier, followed by isopropanol precipitation. RNA was quantified by NanoDrop (Thermo Fischer).

RNA immunoprecipitation (RIP)

Protein bait was pre-incubated with anti-MBP antibody magnetic beads (NEB) in 10-fold molar excess in RNA coIP (RIP) buffer (20 mM Tris pH 7.4, 150 mM NaCl, 1 mM EDTA, 0.5% IPEGAL, 100 U/mL RNase OUT), 100 μL total reaction volume, with gentle rocking for 1 hr at 4°C. During bead incubation, total RNA from MA10 cells was heated to 90^{o}C on a thermal cycler (Bio-Rad) for 2 mins, cooled rapidly on ice 2 mins, and shifted to RT for 20 mins to allow for proper secondary structure formation. Beads were washed 3 times in RIP buffer and incubated with 15 nM total RNA from MA10 cells in 100 μL total, with gentle rocking for 1 hr at 4°C. Beads were washed 5 times in RIP buffer and RNA was eluted as described above.

In vitro transcription

The *StAR* CDS, including 5' and 3' UTR, was amplified from MA10 total cDNA using the following primers: 5' UTR (5' ACTCAGGACCTTGAAAGGCTCAGG 3') and 3' UTR (5' GATGCCCTCTTCTGGAGTATCTGAGG 3').[25] The resulting PCR product was cloned under a T7 promoter using the Zero Blunt TOPO PCR Cloning Kit (ThermoFisher) and orientation was verified by sequencing. RNA was transcribed using MAXIscript T7 Transcription Kit (ThermoFisher) and purified by TRIzol, as above.

RT-PCR and qPCR

cDNA was generated from RNA using the SuperScript IV Kit (ThermoFisher) and random hexamer priming. RNA reactions minus reverse transcriptase (RT) were carried throughout subsequent reactions as controls. Following first strand synthesis and RNAse digestion, PCR amplification for *Star* exon2 was performed using the following primers: F (5' AGCTCAACTGGAGAGCACTG 3'); R (5' AGCTCAACTGGAGAGCACTG 3'). qPCR was performed using TaqMan Fast Universal PCR Master Mix, No AmpErase UNG and the associated protocol (ThermoFisher), Taqman probes for *Star* (Probe number: Mm00441558_m1; ThermoFisher) and GAPDH (Probe Mm99999915_g1; ThermoFisher) were used.

RNA sequencing

Prior to RNA sequencing, integrity of RNA isolated from RNA pulldowns was analyzed by BioAnalyzer using RNA 6000 Pico chips according to manufacturer's protocol (Agilent). Libraries were generated using TruSeq Stranded Total RNA Kit with Ribo Zero Depletion (Illumina); each biological replicate was barcoded individually. Libraries were sequenced on Illumina NextSeq 500.

Cell line generation and culture; knockout mouse re-generation

Cell lines and culture

HEK 293T cell lines were grown in Dulbecco's modified Eagle's medium (DMEM; Gibco) supplemented with 10% fetal bovine serum (FBS; Gibco) and 1% Pen-Strep (PS; Gibco). MA10 cells were a generous gift from Dr. Joseph Beavo (University of Washington) and were grown in Roswell Park Memorial Institute 1640 Medium (RPMI 1640; Gibco) supplemented with 10% horse serum (HS; Gibco) and 1% PS. HEK 293T cells were transfected at 50% confluence with TransIT-LT1 (Mirus) for 48 hrs before further experiments were performed. Breast cancer lines were grown according to AT-CC recommendations.

AKAP1 knockout mouse generation and genotyping

Knockout male mice were a generous gift of Dr. Stefan Strack (University of Iowa), originally created in the lab of Dr. G. Stan McKnight (University of Washington).[11] Knockout male mice were bred with female C57BL/6J mice to generate heterozygotes. Offspring were genotyped by PCR from tail DNA extracts (PfuUltra II Hotstart PCR Master Mix; Agilent): Neo cassette (forward: 5' GGATGATCTGGACGAAGAGC 3'; reverse: 5' AATATCACGGGTAGCCAACG 3'; product: 220 bp); and AKAP1 exon 2 (forward: 5' ATGGCAATCCAGTTGCGTTCG 3'; reverse: 5' GCGGACATCCAAGAGGAATA 3';

product: 433 bp). Heterozygous animals were identified by the presence of PCR products present in both Neo and AKAP2 reactions, whereas homozygotes (WT or KO) were positive for only the WT or Neo allele. Knockouts were generated by crossing knockout males with heterozygous females. All of the animals were handled according to approved Institutional Animal Care and Use Committee (IACUC) protocols (#4196-01) of the University of Washington.

pMEF generation

Heterozygous female and homozygous male breeding pairs were co-housed and embryo timing was estimated by monitoring for the appearance of a vaginal mucus plug on each morning.[70] At ~E13.5, pregnant female mice were euthanized with carbon dioxide, and uterine horns were quickly dissected and placed in PBS on ice. Individual embryos were excised from the uterus placed in individual dishes of PBS before vivisection by forceps. Carcasses were rinsed in fresh PBS and placed in a dish containing 0.25% trypsin before mincing with two sterile blades. Tissue was dissociated for 5 minutes at 37˚C before neutralization with standard HEK media (see above); debris was allowed to settle for 5 minutes and supernatant was incubated at 37˚C overnight before changing media. Individual cell lines were numbered based on maternal mouse number and were genotyped by PCR and RII overlay.

Tissue lysis

Animal tissues were flash-frozen in liquid nitrogen and stored at -80˚C. Frozen tissue was powdered in a mortar under liquid nitrogen on dry ice and transferred to a dounce homogenizer on ice. Powdered tissue was re-suspended in RIPA buffer (50 mM Tris-HCl, pH 7.6, 150 mM NaCl, 1% Triton X-100, 0.5% sodium deoxycholate, 0.1% sodium dodecyl sulfate, 1 mM ehylenediaminetetraacetic acid [EDTA]) supplemented with protease/phosphatase inhibitors and was lysed by 10 strokes of pestle A followed by 10 strokes of pestle B, with care being taken to avoid foaming. Lysate was transferred to a tube and incubated on a rocker at 4°C for 30 mins before being cleared at 10,000 *xg* for 20 mins at 4°C.

Growth curves and MTS assays

Media conditions included: low glucose (25 mM glucose, 6 mM L-glutamine); 2-deoxy-d-glucose (5 μm 2-deoxy-d-glucose, 6 mM L-glutamine); and 5 μM galactose (5 μM galactose, 0 μM L-glutamine). Basal DMEM media lacking glucose, glutamine and phenol red (Gibco; A1443001) was supplemented with dialyzed FBS (Sigma-Aldrich; F0392). Carbon sources were restored by adding indicated amounts of of glucose (Sigma), galactose (Sigma), 2-deoxy-d-glucose (CalBioChem) or L-glutamine (Gibco).

For each biological replicate, 2500 cells/well of HEK^{WT} or $HEK^{dAKAP1-/-}$ cells were plated per media condition, with 4 technical replicates per cell line. Cells plated in normal HEK media and incubated 37˚C for 12 hrs to adhere before changing media. Assays were performed using CellTiter 96 AQueous One Solution Cell Proliferation Assay Kit (Promega) following manufacturer's protocol; at indicated time points, media was replaced with media containing MTS reagent and incubated for 4 hours at 37˚C before reading signal on plate reader.

Biochemical experiments

Immunofluorescence

Cells were seeded on poly-L-lysine coverslips (Corning). Following transfection, cells were fixed and stained according to antibody manufacturer's guidelines. Generally, cells were fixed in 4% paraformaldehyde (PFA) in PBS for 10 minutes at RT. Cells were washed 2 times in PBS and permeabilized in 0.1% Triton X-100 in PBS for 10 minutes at RT. Slides were blocked in 1% Bovine Serum Albumin (BSA) in PBS for 1 hr before incubation with primary antibody. For TOM20-FITC labeling, coverslips were incubated with antibody overnight in a dark, humified chamber. Following all co-staining, cells were washed 10 times rapidly in PBS and counterstained with DAPI for 10 minutes before a further 10 washes in PBS. Stained coverslips were mounted using Prolong Diamond Anti-Fade (Molecular Probes) and were allowed to harden at RT for at least 24 hours before imaging.

Immunoprecipitation

Cells were harvested on ice in PBS by scraping and washed once in cold PBS. Cell pellets were suspended in RIPA buffer and before incubation in ice for 15 minutes, with occasionally agitation by vortexer. Lysate was cleared by centrifugation at top speed, 4˚C, for 20 minutes; supernatant was transferred to a new tube and protein concentration as assayed by BCA. For most IP reactions, 1 μg of appropriate antibody was incubated with 1 mg lysate per reaction; depending on the antibody, reactions were carried out at 4˚C with gentle agitation for either 1 hour or overnight. Following primary antibody incubation, 15 μL 50% 1:1 Protein A:G suspension

In vitro phosphorylation

In vitro phosphorhylation experiments were performed as previously described.[140,141] Briefly, following immunoprecipitation of substrate, beads were re-suspended in kinase reaction kinase assay buffer (25 mM Tris (pH 7.5), 0.1 mM EGTA, 100 nM okadaic acid, 0.1 mM Na_3VO_4, 0.03% Brij-35, 10 mM $MgCl_2$, 0.1 mM ATP, ~10 μCi [γ-32P] ATP) supplemented with 0.2 μg PKAc for 30 min at 30°C. Reactions were stopped by resuspension in 2× Laemmli sample buffer and resolved by SDS-PAGE before transfer to nitrocellulose membrane. Membranes were exposed to phosphorscreen (Molecular Dynamics) for up to 48 hrs before imaging on Personal Molecular Imager (BioRad).

Subcellular fractionation and mitochondria isolation

Mitochondria were isolated following published methods.[142] Briefly, cells were grown to confluence and harvested in cold PBS by scraping. Cell pellets were washed once in PBS, and 1/10th of the total cell pellet was saved for total cell lysate. Remaining pellets were re-suspended in RBS Hypo Buffer (10 mM NaCl, 1.5 $MgCl_2$, 10 mM Tris-HCl pH 7.5) and allowed to swell for 10 minutes before lysis in a Dounce Homogenizer with 15 strokes of a B pestle. Mitochondria were separated from cell lysate by three 5 minute washes, 4˚C, 1500 *xg* in 1x MS Homogenization Buffer (210 mM mannitol, 70 mM sucrose, 5 mM Tris-HCl, 1 mM EDTA pH 7.5), before 2 collection at for 15 minutes, 4˚C, 15000 *xg*. Isolated mitochondria were lysed in RIPA buffer and incubated on ice for 15 minutes; lysate was cleared by centrifugation at top speed, 4˚C, 20 minutes, before further analysis was performed.

Puromycin labeling of ribosomes

Puromycin labeling protocols were adapted from published methods.[101] Cells were plated, transfected, and media was changed to antibiotic-free media (DMEM, 10% FBS) or ~1 hr before labeling. Treatments included control (antibiotic-free base media); puromycin (puro: media + 10 μg/mL puromycin); cycloheximide (CHX) pre-treatment (CHX-Pre: media + 10 μM CHX); and cycloheximide and puromycin (CHX+puro: media + 10 μg/mL puromycin + 10 μM CHX). For puromycin labeling, media was changed and cells incubated with puro media for 10 minutes. For cycloheximide (CHX) pre-treatment, media was changed to CHX-Pre for 10 mins before replacement with CHX+puro for a further 10 minute incubation. After treatment, cells were harvested by scraping in PBS and washing once with PBS before subsequent analysis.

Appendix A: Select Data Sets

Table A.1. RNAs enriched by dAKAP1 KHT.

Entry name, protein names, and gene names were retrieved from UniProt.[81] These comprise the “KHT associated RNAs” represented in **Figure 5.3.1**, as defined in **Chapter 5.2.**

Entry	Entry name	Protein names	Gene names
P00520	ABL1_MOUSE	Tyrosine-protein kinase ABL1 (EC 2.7.10.2) (Abelson murine leukemia viral oncogene homolog 1) (Abelson tyrosine-protein kinase 1) (Proto-oncogene c-Abl) (p150)	Abl1 Abl
Q91V92	ACLY_MOUSE	ATP-citrate synthase (EC 2.3.3.8) (ATP-citrate (pro-S-)-lyase) (Citrate cleavage enzyme)	Acly
P28271	ACOC_MOUSE	Cytoplasmic aconitate hydratase (Aconitase) (EC 4.2.1.3) (Citrate hydro-lyase) (Iron regulatory protein 1) (IRP1) (Iron-responsive element-binding protein 1) (IRE-BP 1)	Aco1 Ireb1 Irebp
Q99KI0	ACON_MOUSE	Aconitate hydratase, mitochondrial (Aconitase) (EC 4.2.1.3) (Citrate hydro-lyase)	Aco2
Q9QYR9	ACOT2_MOUSE	Acyl-coenzyme A thioesterase 2, mitochondrial (Acyl-CoA thioesterase 2) (EC 3.1.2.2) (Acyl coenzyme A thioester hydrolase) (MTE-I) (Very-long-chain acyl-CoA thioesterase)	Acot2 Mte1
Q99JY9	ARP3_MOUSE	Actin-related protein 3 (Actin-like protein 3)	Actr3 Arp3
P28474	ADHX_MOUSE	Alcohol dehydrogenase class-3 (EC 1.1.1.1) (Alcohol dehydrogenase 2) (Alcohol dehydrogenase 5) (Alcohol dehydrogenase B2) (ADH-B2) (Alcohol dehydrogenase class-III) (Glutathione-dependent formaldehyde dehydrogenase) (FALDH) (FDH) (GSH-FDH) (EC 1.1.1.-) (S-(hydroxymethyl)glutathione dehydrogenase) (EC 1.1.1.284)	Adh5 Adh-2 Adh2
Q91VH1	PAQR1_MOUSE	Adiponectin receptor protein 1 (Progestin and adipoQ receptor family member 1) (Progestin and adipoQ receptor family member I)	Adipor1 Parq1
Q8CJF7	ELYS_MOUSE	Protein ELYS (Embryonic large molecule derived from yolk sac) (Protein MEL-28) (Putative AT-hook-containing transcription factor 1)	Ahctf1 Elys
Q80SW1	SAHH2_MOUSE	S-adenosylhomocysteine hydrolase-like protein 1 (IP3R-binding protein released with inositol 1,4,5-trisphosphate) (Putative adenosylhomocysteinase 2) (S-adenosyl-L-homocysteine hydrolase 2) (AdoHcyase 2)	Ahcyl1 Irbit
Q9Z110	P5CS_MOUSE	Delta-1-pyrroline-5-carboxylate synthase (P5CS) (Aldehyde dehydrogenase family 18 member A1) [Includes: Glutamate 5-kinase (GK) (EC 2.7.2.11) (Gamma-glutamyl kinase); Gamma-glutamyl phosphate reductase (GPR) (EC 1.2.1.41) (Glutamate-5-semialdehyde dehydrogenase) (Glutamyl-gamma-semialdehyde dehydrogenase)]	Aldh18a1 P5cs Pycs
P53995	APC1_MOUSE	Anaphase-promoting complex subunit 1 (APC1) (Cyclosome subunit 1) (Mitotic checkpoint regulator) (Testis-specific gene 24 protein)	Anapc1 Mcpr Tsg24
Q9EST5	AN32B_MOUSE	Acidic leucine-rich nuclear phosphoprotein 32 family member B (Proliferation-related acidic leucine-rich protein PAL31)	Anp32b Pal31
P48036	ANXA5_MOUSE	Annexin A5 (Anchorin CII) (Annexin V) (Annexin-5) (Calphobindin I) (CBP-I) (Endonexin II) (Lipocortin V) (Placental anticoagulant protein 4) (PP4) (Placental anticoagulant protein I) (PAP-I) (Thromboplastin inhibitor) (Vascular anticoagulant-alpha) (VAC-alpha)	Anxa5 Anx5
P84091	AP2M1_MOUSE	AP-2 complex subunit mu (AP-2 mu chain) (Adaptor protein complex AP-2 subunit mu) (Adaptor-related protein complex 2 subunit mu) (Clathrin assembly protein complex 2 mu medium chain) (Clathrin coat assembly protein AP50) (Clathrin coat-associated protein AP50) (Mu2-adaptin) (Plasma membrane adaptor AP-2 50 kDa protein)	Ap2m1 Clapm1
P84084	ARF5_MOUSE	ADP-ribosylation factor 5	Arf5
Q99PT1	GDIR1_MOUSE	Rho GDP-dissociation inhibitor 1 (Rho GDI 1) (GDI-1) (Rho-GDI alpha)	Arhgdia C87222 Gdi1
Q60875	ARHG2_MOUSE	Rho guanine nucleotide exchange factor 2 (Guanine nucleotide exchange factor H1) (GEF-H1) (LBC'S first cousin) (Lymphoid blast crisis-like 1) (Oncogene LFC) (Rhobin)	Arhgef2 Kiaa0651 Lbcl1 Lfc

Q9D898	ARP5L_MOUSE	Actin-related protein 2/3 complex subunit 5-like protein (Arp2/3 complex 16 kDa subunit 2) (ARC16-2)	Arpc5l
Q8CDM1	ATAD2_MOUSE	ATPase family AAA domain-containing protein 2 (EC 3.6.1.3)	Atad2
P16951	ATF2_MOUSE	Cyclic AMP-dependent transcription factor ATF-2 (cAMP-dependent transcription factor ATF-2) (EC 2.3.1.48) (Activating transcription factor 2) (MXBP protein) (cAMP response element-binding protein CRE-BP1)	Atf2
F6VAN0	ATF6A_MOUSE	Cyclic AMP-dependent transcription factor ATF-6 alpha (cAMP-dependent transcription factor ATF-6 alpha) (Activating transcription factor 6 alpha) (ATF6-alpha) [Cleaved into: Processed cyclic AMP-dependent transcription factor ATF-6 alpha]	Atf6
Q91YH5	ATLA3_MOUSE	Atlastin-3 (EC 3.6.5.-)	Atl3
Q5XF89	AT133_MOUSE	Probable cation-transporting ATPase 13A3 (EC 3.6.3.-)	Atp13a3 Gm542
Q03265	ATPA_MOUSE	ATP synthase subunit alpha, mitochondrial (ATP synthase F1 subunit alpha)	Atp5f1a Atp5a1
P56480	ATPB_MOUSE	ATP synthase subunit beta, mitochondrial (EC 7.1.2.2) (ATP synthase F1 subunit beta)	Atp5f1b Atp5b
Q91VR2	ATPG_MOUSE	ATP synthase subunit gamma, mitochondrial (ATP synthase F1 subunit gamma) (F-ATPase gamma subunit)	Atp5f1c Atp5c1
Q9CR84	AT5G1_MOUSE	ATP synthase F(0) complex subunit C1, mitochondrial (ATP synthase lipid-binding protein) (ATP synthase membrane subunit c locus 1) (ATP synthase proteolipid P1) (ATPase protein 9) (ATPase subunit c)	Atp5mc1 Atp5g1
O88738	BIRC6_MOUSE	Baculoviral IAP repeat-containing protein 6 (EC 2.3.2.27) (BIR repeat-containing ubiquitin-conjugating enzyme) (BRUCE) (RING-type E3 ubiquitin transferase BIRC6) (Ubiquitin-conjugating BIR domain enzyme apollon) (APOLLON)	Birc6 Kiaa1289
P18572	BASI_MOUSE	Basigin (Basic immunoglobulin superfamily) (HT7 antigen) (Membrane glycoprotein gp42) (CD antigen CD147)	Bsg
Q64152	BTF3_MOUSE	Transcription factor BTF3 (Nascent polypeptide-associated complex subunit beta) (NAC-beta) (RNA polymerase B transcription factor 3)	Btf3
O35658	C1QBP_MOUSE	Complement component 1 Q subcomponent-binding protein, mitochondrial (GC1q-R protein) (Glycoprotein gC1qBP) (C1qBP)	C1qbp Gc1qbp
P14211	CALR_MOUSE	Calreticulin (CRP55) (Calregulin) (Endoplasmic reticulum resident protein 60) (ERp60) (HACBP)	Calr
Q60865	CAPR1_MOUSE	Caprin-1 (Cytoplasmic activation- and proliferation-associated protein 1) (GPI-anchored membrane protein 1) (GPI-anchored protein p137) (GPI-p137) (p137GPI) (Membrane component chromosome 11 surface marker 1) (RNA granule protein 105)	Caprin1 Gpiap Gpiap1 Gpip137 M11s1 Rng105 G5E5
P80316	TCPE_MOUSE	T-complex protein 1 subunit epsilon (TCP-1-epsilon) (CCT-epsilon)	Cct5 Ccte Kiaa0098
P42932	TCPQ_MOUSE	T-complex protein 1 subunit theta (TCP-1-theta) (CCT-theta)	Cct8 Cctq
Q8C172	CERS6_MOUSE	Ceramide synthase 6 (CerS6) (LAG1 longevity assurance homolog 6)	Cers6 Lass6
P40201	CHD1_MOUSE	Chromodomain-helicase-DNA-binding protein 1 (CHD-1) (EC 3.6.4.12) (ATP-dependent helicase CHD1)	Chd1 Chd-1
O54804	CHKA_MOUSE	Choline kinase alpha (CK) (EC 2.7.1.32) (CHETK-alpha) (Ethanolamine kinase) (EK) (EC 2.7.1.82)	Chka Chk
Q61245	COBA1_MOUSE	Collagen alpha-1(XI) chain	Col11a1
Q9WUM3	COR1B_MOUSE	Coronin-1B (Coronin-2)	Coro1b
Q8C0P5	COR2A_MOUSE	Coronin-2A	Coro2a
P97742	CPT1A_MOUSE	Carnitine O-palmitoyltransferase 1, liver isoform (CPT1-L) (EC 2.3.1.21) (Carnitine O-palmitoyltransferase I, liver isoform) (CPT I) (CPTI-L) (Carnitine palmitoyltransferase 1A)	Cpt1a Cpt-1 Cpt1
P07141	CSF1_MOUSE	Macrophage colony-stimulating factor 1 (CSF-1) (MCSF) [Cleaved into: Processed macrophage colony-stimulating factor 1]	Csf1 Csfm
Q8VCN5	CGL_MOUSE	Cystathionine gamma-lyase (EC 4.4.1.1) (Cysteine-protein sulfhydrase) (Gamma-cystathionase)	Cth

P06797	CATL1_MOUSE	Cathepsin L1 (EC 3.4.22.15) (Cathepsin L) (Major excreted protein) (MEP) (p39 cysteine proteinase) [Cleaved into: Cathepsin L1 heavy chain; Cathepsin L1 light chain]	Ctsl Ctsl1
Q9DB73	NB5R1_MOUSE	NADH-cytochrome b5 reductase 1 (b5R.1) (EC 1.6.2.2) (NAD(P)H:quinone oxidoreductase type 3 polypeptide A2)	Cyb5r1 Nqo3a2
P31786	ACBP_MOUSE	Acyl-CoA-binding protein (ACBP) (Diazepam-binding inhibitor) (DBI) (Endozepine) (EP)	Dbi
Q3U1J4	DDB1_MOUSE	DNA damage-binding protein 1 (DDB p127 subunit) (Damage-specific DNA-binding protein 1) (UV-damaged DNA-binding factor)	Ddb1
P35639	DDIT3_MOUSE	DNA damage-inducible transcript 3 protein (DDIT-3) (C/EBP zeta) (C/EBP-homologous protein) (CHOP) (C/EBP-homologous protein 10) (CHOP-10) (CCAAT/enhancer-binding protein homologous protein) (Growth arrest and DNA-damage-inducible protein GADD153)	Ddit3 Chop Chop10 Gadd153
Q9Z1N5	DX39B_MOUSE	Spliceosome RNA helicase Ddx39b (EC 3.6.4.13) (56 kDa U2AF65-associated protein) (DEAD box protein UAP56) (HLA-B-associated transcript 1 protein)	Ddx39b Bat1 Bat1a Uap56
Q61656	DDX5_MOUSE	Probable ATP-dependent RNA helicase DDX5 (EC 3.6.4.13) (DEAD box RNA helicase DEAD1) (mDEAD1) (DEAD box protein 5) (RNA helicase p68)	Ddx5 Tnz2
Q7TNV0	DEK_MOUSE	Protein DEK	Dek
Q99J56	DERL1_MOUSE	Derlin-1 (Degradation in endoplasmic reticulum protein 1) (Der1-like protein 1)	Derl1 Der1
Q3UH60	DIP2B_MOUSE	Disco-interacting protein 2 homolog B (DIP2 homolog B)	Dip2b Kiaa1463
Q811D0	DLG1_MOUSE	Disks large homolog 1 (Embryo-dlg/synapse-associated protein 97) (E-dlg/SAP97) (Synapse-associated protein 97) (SAP-97) (SAP97)	Dlg1 Dlgh1
Q99M87	DNJA3_MOUSE	DnaJ homolog subfamily A member 3, mitochondrial (DnaJ protein Tid-1) (mTid-1) (Tumorous imaginal discs protein Tid56 homolog)	Dnaja3 Tid1
P13864	DNMT1_MOUSE	DNA (cytosine-5)-methyltransferase 1 (Dnmt1) (Met-1) (EC 2.1.1.37) (DNA methyltransferase MmuI) (DNA MTase MmuI) (M.MmuI) (MCMT)	Dnmt1 Dnmt Met1 Uim
Q91ZU6	DYST_MOUSE	Dystonin (Bullous pemphigoid antigen 1) (BPA) (Dystonia musculorum protein) (Hemidesmosomal plaque protein) (Microtubule actin cross-linking factor 2)	Dst Bpag1 Macf2
Q8BH95	ECHM_MOUSE	Enoyl-CoA hydratase, mitochondrial (EC 4.2.1.17) (Enoyl-CoA hydratase 1) (Short-chain enoyl-CoA hydratase) (SCEH)	Echs1
O70251	EF1B_MOUSE	Elongation factor 1-beta (EF-1-beta)	Eef1b Eef1b2
P23116	EIF3A_MOUSE	Eukaryotic translation initiation factor 3 subunit A (eIF3a) (Centrosomin) (Eukaryotic translation initiation factor 3 subunit 10) (eIF-3-theta) (eIF3 p167) (eIF3 p180) (eIF3 p185) (p162)	Eif3a Csma Eif3 Eif3s10
O70194	EIF3D_MOUSE	Eukaryotic translation initiation factor 3 subunit D (eIF3d) (Eukaryotic translation initiation factor 3 subunit 7) (eIF-3-zeta) (eIF3 p66)	Eif3d Eif3s7
Q91WK2	EIF3H_MOUSE	Eukaryotic translation initiation factor 3 subunit H (eIF3h) (Eukaryotic translation initiation factor 3 subunit 3) (eIF-3-gamma) (eIF3 p40 subunit)	Eif3h Eif3s3
Q99JX4	EIF3M_MOUSE	Eukaryotic translation initiation factor 3 subunit M (eIF3m) (PCI domain-containing protein 1)	Eif3m Pcid1
P10630	IF4A2_MOUSE	Eukaryotic initiation factor 4A-II (eIF-4A-II) (eIF4A-II) (EC 3.6.4.13) (ATP-dependent RNA helicase eIF4A-2)	Eif4a2 Ddx2b
P63073	IF4E_MOUSE	Eukaryotic translation initiation factor 4E (eIF-4E) (eIF4E) (mRNA cap-binding protein) (eIF-4F 25 kDa subunit)	Eif4e
Q62448	IF4G2_MOUSE	Eukaryotic translation initiation factor 4 gamma 2 (eIF-4-gamma 2) (eIF-4G 2) (eIF4G 2) (Novel APOBEC-1 target 1) (Translation repressor NAT1) (p97)	Eif4g2 Nat1
P59325	IF5_MOUSE	Eukaryotic translation initiation factor 5 (eIF-5)	Eif5
Q05D44	IF2P_MOUSE	Eukaryotic translation initiation factor 5B (eIF-5B) (EC 3.6.5.3) (Translation initiation factor IF-2)	Eif5b If2
Q03173	ENAH_MOUSE	Protein enabled homolog (NPC-derived proline-rich protein 1) (NDPP-1)	Enah Mena Ndpp1
Q9JIX0	ENY2_MOUSE	Transcription and mRNA export factor ENY2 (Enhancer of yellow 2 transcription factor homolog)	Eny2
Q8CGC7	SYEP_MOUSE	Bifunctional glutamate/proline--tRNA ligase (Bifunctional aminoacyl-tRNA synthetase) [Includes: Glutamate--tRNA ligase (EC 6.1.1.17) (Glutamyl-tRNA synthetase) (GluRS); Proline--tRNA ligase (EC 6.1.1.15) (Prolyl-tRNA synthetase) (ProRS)]	Eprs Qprs
P42567	EPS15_MOUSE	Epidermal growth factor receptor substrate 15 (Protein Eps15) (Protein AF-1p)	Eps15

Q8R180	ERO1A_MOUSE	ERO1-like protein alpha (ERO1-L) (ERO1-L-alpha) (EC 1.8.4.-) (Endoplasmic reticulum oxidoreductase alpha) (Endoplasmic reticulum oxidoreductin-1-like protein) (Oxidoreductin-1-L-alpha)	Ero1a Ero1l
Q9R0P3	ESTD_MOUSE	S-formylglutathione hydrolase (FGH) (EC 3.1.2.12) (Esterase 10) (Esterase D) (Sid 478)	Esd Es10 Sid478
Q8BWY3	ERF1_MOUSE	Eukaryotic peptide chain release factor subunit 1 (Eukaryotic release factor 1) (eRF1)	Etf1
Q920L1	FADS1_MOUSE	Acyl-CoA (8-3)-desaturase (EC 1.14.19.44) (Delta(5) fatty acid desaturase) (D5D) (Delta(5) desaturase) (Delta-5 desaturase) (Fatty acid desaturase 1)	Fads1
Q3UW53	NIBAN_MOUSE	Protein Niban (Protein FAM129A)	Fam129a Niban
P19096	FAS_MOUSE	Fatty acid synthase (EC 2.3.1.85) [Includes: [Acyl-carrier-protein] S-acetyltransferase (EC 2.3.1.38); [Acyl-carrier-protein] S-malonyltransferase (EC 2.3.1.39); 3-oxoacyl-[acyl-carrier-protein] synthase (EC 2.3.1.41); 3-oxoacyl-[acyl-carrier-protein] reductase (EC 1.1.1.100); 3-hydroxyacyl-[acyl-carrier-protein] dehydratase (EC 4.2.1.59); Enoyl-[acyl-carrier-protein] reductase (EC 1.3.1.39); Oleoyl-[acyl-carrier-protein] hydrolase (EC 3.1.2.14)]	Fasn
Q91ZT5	FGD4_MOUSE	FYVE, RhoGEF and PH domain-containing protein 4 (Actin filament-binding protein frabin) (FGD1-related F-actin-binding protein)	Fgd4
O35465	FKBP8_MOUSE	Peptidyl-prolyl cis-trans isomerase FKBP8 (PPIase FKBP8) (EC 5.2.1.8) (38 kDa FK506-binding protein) (38 kDa FKBP) (FKBP-38) (mFKBP38) (FK506-binding protein 8) (FKBP-8) (FKBPR38) (Rotamase)	Fkbp8 Fkbp38 Sam11
P09528	FRIH_MOUSE	Ferritin heavy chain (Ferritin H subunit) (EC 1.16.3.1) [Cleaved into: Ferritin heavy chain, N-terminally processed]	Fth1 Fth
Q91WJ8	FUBP1_MOUSE	Far upstream element-binding protein 1 (FBP) (FUSE-binding protein 1)	Fubp1 D3Ertd330e
Q61584	FXR1_MOUSE	Fragile X mental retardation syndrome-related protein 1 (mFxr1p)	Fxr1 Fxr1h
P70699	LYAG_MOUSE	Lysosomal alpha-glucosidase (EC 3.2.1.20) (Acid maltase)	Gaa
Q6PAR5	GAPD1_MOUSE	GTPase-activating protein and VPS9 domain-containing protein 1 (GAPex-5) (Rab5-activating protein 6)	Gapvd1 Gapex5 Kiaa1521
Q61598	GDIB_MOUSE	Rab GDP dissociation inhibitor beta (Rab GDI beta) (GDI-3) (Guanosine diphosphate dissociation inhibitor 2) (GDI-2)	Gdi2 Gdi3
D3Z7P3	GLSK_MOUSE	Glutaminase kidney isoform, mitochondrial (GLS) (EC 3.5.1.2)	Gls Gls1 Kiaa0838
Q3THK7	GUAA_MOUSE	GMP synthase [glutamine-hydrolyzing] (EC 6.3.5.2) (GMP synthetase) (Glutamine amidotransferase)	Gmps
P27601	GNA13_MOUSE	Guanine nucleotide-binding protein subunit alpha-13 (G alpha-13) (G-protein subunit alpha-13)	Gna13 Gna-13
P63094	GNAS2_MOUSE	Guanine nucleotide-binding protein G(s) subunit alpha isoforms short (Adenylate cyclase-stimulating G alpha protein)	Gnas Gnas1 MNCb-5546
Q6R0H6	ALEX_MOUSE	Protein ALEX (Alternative gene product encoded by XL-exon)	Gnas Gnas1
Q6R0H7	GNAS1_MOUSE	Guanine nucleotide-binding protein G(s) subunit alpha isoforms XLas (Adenylate cyclase-stimulating G alpha protein) (Extra large alphas protein) (XLalphas)	Gnas Gnas1
Q9Z0F1	GNAS3_MOUSE	Neuroendocrine secretory protein 55 (NESP55) [Cleaved into: LHAL tetrapeptide; GPIPIRRH peptide]	Gnas Gnas1
Q9ESF4	LFG1_MOUSE	Protein lifeguard 1 (Glutamate [NMDA] receptor-associated protein 1) (NMDA receptor glutamate-binding subunit)	Grina Lag Lfg1 Nmdara1
Q9WV60	GSK3B_MOUSE	Glycogen synthase kinase-3 beta (GSK-3 beta) (EC 2.7.11.26) (Serine/threonine-protein kinase GSK3B) (EC 2.7.11.1)	Gsk3b
Q3UJK4	GTPB2_MOUSE	GTP-binding protein 2 (GTP-binding-like protein 2)	Gtpbp2
Q61425	HCDH_MOUSE	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial (HCDH) (EC 1.1.1.35) (Medium and short-chain L-3-hydroxyacyl-coenzyme A dehydrogenase) (Short-chain 3-hydroxyacyl-CoA dehydrogenase)	Hadh Hadhsc Mschad Schad
Q8BMS1	ECHA_MOUSE	Trifunctional enzyme subunit alpha, mitochondrial (TP-alpha) [Includes: Long-chain enoyl-CoA hydratase (EC 4.2.1.17); Long chain 3-hydroxyacyl-CoA dehydrogenase (EC 1.1.1.211)]	Hadha
P70288	HDAC2_MOUSE	Histone deacetylase 2 (HD2) (EC 3.5.1.98) (YY1 transcription factor-binding protein)	Hdac2 Yy1bp
Q61221	HIF1A_MOUSE	Hypoxia-inducible factor 1-alpha (HIF-1-alpha) (HIF1-alpha) (ARNT-interacting protein)	Hif1a

Q9ERH7	HIPK3_MOUSE	Homeodomain-interacting protein kinase 3 (EC 2.7.11.1) (Androgen receptor-interacting nuclear protein kinase) (ANPK) (Fas-interacting serine/threonine-protein kinase) (FIST) (Nuclear body-associated kinase 3) (Nbak3)	Hipk3 Fist3
P54869	HMCS2_MOUSE	Hydroxymethylglutaryl-CoA synthase, mitochondrial (HMG-CoA synthase) (EC 2.3.3.10) (3-hydroxy-3-methylglutaryl coenzyme A synthase)	Hmgcs2
Q99020	ROAA_MOUSE	Heterogeneous nuclear ribonucleoprotein A/B (hnRNP A/B) (CArG-binding factor-A) (CBF-A)	Hnrnpab Cbf-a Cgbfa Hnrpab
P61979	HNRPK_MOUSE	Heterogeneous nuclear ribonucleoprotein K (hnRNP K)	Hnrnpk Hnrpk
P07901	HS90A_MOUSE	Heat shock protein HSP 90-alpha (Heat shock 86 kDa) (HSP 86) (HSP86) (Tumor-specific transplantation 86 kDa antigen) (TSTA)	Hsp90aa1 Hsp86 Hsp86-1 Hspca
P11499	HS90B_MOUSE	Heat shock protein HSP 90-beta (Heat shock 84 kDa) (HSP 84) (HSP84) (Tumor-specific transplantation 84 kDa antigen) (TSTA)	Hsp90ab1 Hsp84 Hsp84-1 Hspcb
P20029	BIP_MOUSE	Endoplasmic reticulum chaperone BiP (EC 3.6.4.10) (78 kDa glucose-regulated protein) (GRP-78) (Binding-immunoglobulin protein) (BiP) (Heat shock protein 70 family protein 5) (HSP70 family protein 5) (Heat shock protein family A member 5) (Immunoglobulin heavy chain-binding protein)	Hspa5 Grp78
P63017	HSP7C_MOUSE	Heat shock cognate 71 kDa protein (Heat shock 70 kDa protein 8)	Hspa8 Hsc70 Hsc73
P63038	CH60_MOUSE	60 kDa heat shock protein, mitochondrial (EC 3.6.4.9) (60 kDa chaperonin) (Chaperonin 60) (CPN60) (HSP-65) (Heat shock protein 60) (HSP-60) (Hsp60) (Mitochondrial matrix protein P1)	Hspd1 Hsp60
Q7TMY8	HUWE1_MOUSE	E3 ubiquitin-protein ligase HUWE1 (EC 2.3.2.26) (E3Histone) (HECT, UBA and WWE domain-containing protein 1) (HECT-type E3 ubiquitin transferase HUWE1) (Upstream regulatory element-binding protein 1) (URE-B1) (URE-binding protein 1)	Huwe1 Kiaa0312 Ureb1
Q8BIJ6	SYIM_MOUSE	Isoleucine--tRNA ligase, mitochondrial (EC 6.1.1.5) (Isoleucyl-tRNA synthetase) (IleRS)	Iars2
O88844	IDHC_MOUSE	Isocitrate dehydrogenase [NADP] cytoplasmic (IDH) (EC 1.1.1.42) (Cytosolic NADP-isocitrate dehydrogenase) (IDP) (NADP(+)-specific ICDH) (Oxalosuccinate decarboxylase)	Idh1
P09055	ITB1_MOUSE	Integrin beta-1 (Fibronectin receptor subunit beta) (VLA-4 subunit beta) (CD antigen CD29)	Itgb1
O70309	ITB5_MOUSE	Integrin beta-5	Itgb5
Q920Q8	NS1BP_MOUSE	Influenza virus NS1A-binding protein homolog (NS1-BP) (NS1-binding protein homolog) (Kelch family protein Nd1-L) (ND1-L2) (Nd1-S)	Ivns1abp Kiaa0850 Nd1 Nd1L Nd1S Ns1 Ns1bp
P52332	JAK1_MOUSE	Tyrosine-protein kinase JAK1 (EC 2.7.10.2) (Janus kinase 1) (JAK-1)	Jak1
Q61768	KINH_MOUSE	Kinesin-1 heavy chain (Conventional kinesin heavy chain) (Ubiquitous kinesin heavy chain) (UKHC)	Kif5b Khcs Kns1
O35343	IMA3_MOUSE	Importin subunit alpha-3 (Importin alpha Q1) (Qip1) (Karyopherin subunit alpha-4)	Kpna4 Qip1
P02469	LAMB1_MOUSE	Laminin subunit beta-1 (Laminin B1 chain) (Laminin-1 subunit beta) (Laminin-10 subunit beta) (Laminin-12 subunit beta) (Laminin-2 subunit beta) (Laminin-6 subunit beta) (Laminin-8 subunit beta)	Lamb1 Lamb-1 Lamb1-1
P02468	LAMC1_MOUSE	Laminin subunit gamma-1 (Laminin B2 chain) (Laminin-1 subunit gamma) (Laminin-10 subunit gamma) (Laminin-11 subunit gamma) (Laminin-2 subunit gamma) (Laminin-3 subunit gamma) (Laminin-4 subunit gamma) (Laminin-6 subunit gamma) (Laminin-7 subunit gamma) (Laminin-8 subunit gamma) (Laminin-9 subunit gamma) (S-laminin subunit gamma) (S-LAM gamma)	Lamc1 Lamb-2 Lamc-1
Q8BMJ2	SYLC_MOUSE	Leucine--tRNA ligase, cytoplasmic (EC 6.1.1.4) (Leucyl-tRNA synthetase) (LeuRS)	Lars
P48678	LMNA_MOUSE	Prelamin-A/C [Cleaved into: Lamin-A/C]	Lmna Lmn1
Q91YX5	LGAT1_MOUSE	Acyl-CoA:lysophosphatidylglycerol acyltransferase 1 (EC 2.3.1.-)	Lpgat1 Fam34a
Q9ESE1	LRBA_MOUSE	Lipopolysaccharide-responsive and beige-like anchor protein (Beige-like protein)	Lrba Bgl Lba

Q91VN0	LRP5_MOUSE	Low-density lipoprotein receptor-related protein 5 (LRP-5) (Low-density lipoprotein receptor-related protein 7) (LRP-7)	Lrp5 Lr3 Lrp7
P97412	LYST_MOUSE	Lysosomal-trafficking regulator (Beige protein) (CHS1 homolog)	Lyst Bg Chs1
P27046	MA2A1_MOUSE	Alpha-mannosidase 2 (EC 3.2.1.114) (Golgi alpha-mannosidase II) (AMan II) (Man II) (Mannosidase alpha class 2A member 1) (Mannosyl-oligosaccharide 1,3-1,6-alpha-mannosidase)	Man2a1 Mana2
Q64133	AOFA_MOUSE	Amine oxidase [flavin-containing] A (EC 1.4.3.4) (Monoamine oxidase type A) (MAO-A)	Maoa
Q9JKP5	MBNL1_MOUSE	Muscleblind-like protein 1 (Triplet-expansion RNA-binding protein)	Mbnl1 Exp Mbnl
Q8C181	MBNL2_MOUSE	Muscleblind-like protein 2	Mbnl2 Kiaa4072
P49717	MCM4_MOUSE	DNA replication licensing factor MCM4 (EC 3.6.4.12) (CDC21 homolog) (P1-CDC21)	Mcm4 Cdc21 Mcmd4
P97311	MCM6_MOUSE	DNA replication licensing factor MCM6 (EC 3.6.4.12) (Mis5 homolog)	Mcm6 Mcmd6 Mis5
P15806	TFE2_MOUSE	Transcription factor E2-alpha (Immunoglobulin enhancer-binding factor E12/E47) (Transcription factor 3) (TCF-3) (Transcription factor A1)	Tcf3 Alf2 Me2 Tcfe2a
Q99KE1	MAOM_MOUSE	NAD-dependent malic enzyme, mitochondrial (NAD-ME) (EC 1.1.1.38) (Malic enzyme 2)	Me2
Q9DCS2	MTL26_MOUSE	Methyltransferase-like 26	Mettl26
Q8C3P7	MTA70_MOUSE	N6-adenosine-methyltransferase subunit METTL3 (EC 2.1.1.348) (Methyltransferase-like protein 3) (N6-adenosine-methyltransferase 70 kDa subunit) (MT-A70)	Mettl3 Mta70
Q8VBX6	MPDZ_MOUSE	Multiple PDZ domain protein (Multi-PDZ domain protein 1)	Mpdz Mupp1
Q5NCE8	MRS2_MOUSE	Magnesium transporter MRS2 homolog, mitochondrial (MRS2-like protein)	Mrs2 Gm902 Mrs2l
Q791V5	MTCH2_MOUSE	Mitochondrial carrier homolog 2	Mtch2
Q80WJ7	LYRIC_MOUSE	Protein LYRIC (3D3/LYRIC) (Lysine-rich CEACAM1 co-isolated protein) (Metadherin) (Metastasis adhesion protein)	Mtdh Lyric
Q922D8	C1TC_MOUSE	C-1-tetrahydrofolate synthase, cytoplasmic (C1-THF synthase) [Cleaved into: C-1-tetrahydrofolate synthase, cytoplasmic, N-terminally processed] [Includes: Methylenetetrahydrofolate dehydrogenase (EC 1.5.1.5); Methenyltetrahydrofolate cyclohydrolase (EC 3.5.4.9); Formyltetrahydrofolate synthetase (EC 6.3.4.3)]	Mthfd1
P18155	MTDC_MOUSE	Bifunctional methylenetetrahydrofolate dehydrogenase/cyclohydrolase, mitochondrial [Includes: NAD-dependent methylenetetrahydrofolate dehydrogenase (EC 1.5.1.15); Methenyltetrahydrofolate cyclohydrolase (EC 3.5.4.9)]	Mthfd2 Nmdmc
P01108	MYC_MOUSE	Myc proto-oncogene protein (Proto-oncogene c-Myc) (Transcription factor p64)	Myc
Q8VDD5	MYH9_MOUSE	Myosin-9 (Cellular myosin heavy chain, type A) (Myosin heavy chain 9) (Myosin heavy chain, non-muscle IIa) (Non-muscle myosin heavy chain A) (NMMHC-A) (Non-muscle myosin heavy chain IIa) (NMMHC II-a) (NMMHC-IIA)	Myh9
Q6PGB6	NAA50_MOUSE	N-alpha-acetyltransferase 50 (EC 2.3.1.258) (N-acetyltransferase NAT13) (N-epsilon-acetyltransferase 50) (EC 2.3.1.-) (NatE catalytic subunit)	Naa50 Mak3 Nat13
Q8BLF1	NCEH1_MOUSE	Neutral cholesterol ester hydrolase 1 (NCEH) (EC 3.1.1.-) (Arylacetamide deacetylase-like 1) (Chlorpyrifos oxon-binding protein) (CPO-BP)	Nceh1 Aadacl1 Kiaa1363
P28660	NCKP1_MOUSE	Nck-associated protein 1 (NAP 1) (Brain protein H19) (MH19) (Membrane-associated protein HEM-2) (p125Nap1)	Nckap1 Hem2 Kiaa0587 Nap1
P09405	NUCL_MOUSE	Nucleolin (Protein C23)	Ncl Nuc
Q60974	NCOR1_MOUSE	Nuclear receptor corepressor 1 (N-CoR) (N-CoR1) (Retinoid X receptor-interacting protein 13) (RIP13)	Ncor1 Rxrip13
Q9CQZ5	NDUA6_MOUSE	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6 (Complex I-B14) (CI-B14) (NADH-ubiquinone oxidoreductase B14 subunit)	Ndufa6
Q9CXZ1	NDUS4_MOUSE	NADH dehydrogenase [ubiquinone] iron-sulfur protein 4, mitochondrial (Complex I-18 kDa) (CI-18 kDa) (Complex I-AQDQ) (CI-AQDQ) (NADH-ubiquinone oxidoreductase 18 kDa subunit)	Ndufs4
Q9ES70	NEK6_MOUSE	Serine/threonine-protein kinase Nek6 (EC 2.7.11.1) (Never in mitosis A-related kinase 6) (NimA-related protein kinase 6)	Nek6

Q60795	NF2L2_MOUSE	Nuclear factor erythroid 2-related factor 2 (NF-E2-related factor 2) (NFE2-related factor 2) (Nuclear factor, erythroid derived 2, like 2)	Nfe2l2 Nrf-2 Nrf2
Q6KCD5	NIPBL_MOUSE	Nipped-B-like protein (Delangin homolog) (SCC2 homolog)	Nipbl Scc2
Q01768	NDKB_MOUSE	Nucleoside diphosphate kinase B (NDK B) (NDP kinase B) (EC 2.7.4.6) (Histidine protein kinase NDKB) (EC 2.7.13.3) (P18) (nm23-M2)	Nme2
O35710	NOCT_MOUSE	Nocturnin (EC 3.1.13.4) (Carbon catabolite repression 4-like protein) (Circadian deadenylase NOC)	Noct Ccr4 Ccrn4l Noc
Q9CQS2	NOP10_MOUSE	H/ACA ribonucleoprotein complex subunit 3 (Nucleolar protein 10) (Nucleolar protein family A member 3) (snoRNP protein NOP10)	Nop10 Nola3
Q9D6Z1	NOP56_MOUSE	Nucleolar protein 56 (Nucleolar protein 5A)	Nop56 Nol5a
Q6DFW4	NOP58_MOUSE	Nucleolar protein 58 (MSSP) (Nucleolar protein 5) (SIK-similar protein)	Nop58 Nol5
O35516	NOTC2_MOUSE	Neurogenic locus notch homolog protein 2 (Notch 2) (Motch B) [Cleaved into: Notch 2 extracellular truncation; Notch 2 intracellular domain]	Notch2
P33242	STF1_MOUSE	Steroidogenic factor 1 (SF-1) (STF-1) (Adrenal 4-binding protein) (Embryonal LTR-binding protein) (ELP) (Embryonal long terminal repeat-binding protein) (Fushi tarazu factor homolog 1) (Nuclear receptor subfamily 5 group A member 1) (Steroid hormone receptor Ad4BP) (Steroid hydroxylase positive regulator)	Nr5a1 Ftzf1
Q80XU3	NUCKS_MOUSE	Nuclear ubiquitous casein and cyclin-dependent kinase substrate 1 (JC7)	Nucks1 Nucks
Q8R2U6	NUDT4_MOUSE	Diphosphoinositol polyphosphate phosphohydrolase 2 (DIPP-2) (EC 3.6.1.52) (Diadenosine 5',5'''-P1,P6-hexaphosphate hydrolase 2) (EC 3.6.1.-) (Nucleoside diphosphate-linked moiety X motif 4) (Nudix motif 4)	Nudt4 Dipp2
Q60597	ODO1_MOUSE	2-oxoglutarate dehydrogenase, mitochondrial (EC 1.2.4.2) (2-oxoglutarate dehydrogenase complex component E1) (OGDC-E1) (Alpha-ketoglutarate dehydrogenase)	Ogdh Kiaa4192
B9EJ86	OSBL8_MOUSE	Oxysterol-binding protein-related protein 8 (ORP-8) (OSBP-related protein 8)	Osbpl8 Kiaa1451 Orp8
Q91ZD1	OSR2_MOUSE	Protein odd-skipped-related 2	Osr2
Q9D0K2	SCOT1_MOUSE	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial (EC 2.8.3.5) (3-oxoacid CoA-transferase 1) (Somatic-type succinyl-CoA:3-oxoacid CoA-transferase) (SCOT-s)	Oxct1 Oxct Scot
Q60715	P4HA1_MOUSE	Prolyl 4-hydroxylase subunit alpha-1 (4-PH alpha-1) (EC 1.14.11.2) (Procollagen-proline,2-oxoglutarate-4-dioxygenase subunit alpha-1)	P4ha1
P09103	PDIA1_MOUSE	Protein disulfide-isomerase (PDI) (EC 5.3.4.1) (Cellular thyroid hormone-binding protein) (Endoplasmic reticulum resident protein 59) (ER protein 59) (ERp59) (Prolyl 4-hydroxylase subunit beta) (p55)	P4hb Pdia1
P50580	PA2G4_MOUSE	Proliferation-associated protein 2G4 (IRES-specific cellular trans-acting factor 45 kDa) (ITAF45) (Mpp1) (Proliferation-associated protein 1) (Protein p38-2G4)	Pa2g4 Ebp1 Plfap
P29341	PABP1_MOUSE	Polyadenylate-binding protein 1 (PABP-1) (Poly(A)-binding protein 1)	Pabpc1 Pabp1
Q8CCS6	PABP2_MOUSE	Polyadenylate-binding protein 2 (PABP-2) (Poly(A)-binding protein 2) (Nuclear poly(A)-binding protein 1) (Poly(A)-binding protein II) (PABII) (Polyadenylate-binding nuclear protein 1)	Pabpn1 Pab2 Pabp2
Q9WVE8	PACN2_MOUSE	Protein kinase C and casein kinase substrate in neurons protein 2 (Syndapin-2) (Syndapin-II)	Pacsin2
Q8VE62	PAIP1_MOUSE	Polyadenylate-binding protein-interacting protein 1 (PABP-interacting protein 1) (PAIP-1) (Poly(A)-binding protein-interacting protein 1)	Paip1
Q8CIN4	PAK2_MOUSE	Serine/threonine-protein kinase PAK 2 (EC 2.7.11.1) (Gamma-PAK) (p21-activated kinase 2) (PAK-2) [Cleaved into: PAK-2p27; PAK-2p34]	Pak2
P97467	AMD_MOUSE	Peptidyl-glycine alpha-amidating monooxygenase (PAM) [Includes: Peptidylglycine alpha-hydroxylating monooxygenase (PHM) (EC 1.14.17.3); Peptidyl-alpha-hydroxyglycine alpha-amidating lyase (EC 4.3.2.5) (Peptidylamidoglycolate lyase) (PAL)]	Pam
Q7TPH6	MYCB2_MOUSE	E3 ubiquitin-protein ligase MYCBP2 (EC 2.3.2.-) (Myc-binding protein 2) (Pam/highwire/rpm-1 protein) (Protein Magellan) (Protein associated with Myc)	Mycbp2 Pam Phr1
Q61183	PAPOA_MOUSE	Poly(A) polymerase alpha (PAP-alpha) (EC 2.7.7.19) (Polynucleotide adenylyltransferase)	Papola Pap Plap
P11103	PARP1_MOUSE	Poly [ADP-ribose] polymerase 1 (PARP-1) (EC 2.4.2.30) (ADP-ribosyltransferase diphtheria toxin-like 1) (ARTD1) (DNA ADP-ribosyltransferase PARP1) (EC 2.4.2.-) (NAD(+) ADP-ribosyltransferase 1) (ADPRT 1) (Poly[ADP-ribose] synthase 1) (msPARP) (Protein poly-ADP-ribosyltransferase PARP1) (EC 2.4.2.-)	Parp1 Adprp Adprt Adprt1

Q9ES46	PARVB_MOUSE	Beta-parvin	Parvb
P17918	PCNA_MOUSE	Proliferating cell nuclear antigen (PCNA) (Cyclin)	Pcna
P49586	PCY1A_MOUSE	Choline-phosphate cytidylyltransferase A (EC 2.7.7.15) (CCT-alpha) (CTP:phosphocholine cytidylyltransferase A) (CCT A) (CT A) (Phosphorylcholine transferase A)	Pcyt1a Ctpct Pcyt1
Q8VE70	PDC10_MOUSE	Programmed cell death protein 10 (TF-1 cell apoptosis-related protein 15)	Pdcd10 Tfar15
Q08481	PECA1_MOUSE	Platelet endothelial cell adhesion molecule (PECAM-1) (CD antigen CD31)	Pecam1 Pecam Pecam-1
Q9WUA3	PFKAP_MOUSE	ATP-dependent 6-phosphofructokinase, platelet type (ATP-PFK) (PFK-P) (EC 2.7.1.11) (6-phosphofructokinase type C) (Phosphofructo-1-kinase isozyme C) (PFK-C) (Phosphohexokinase)	Pfkp Pfkc
P62962	PROF1_MOUSE	Profilin-1 (Profilin I)	Pfn1
Q9JJV2	PROF2_MOUSE	Profilin-2 (Profilin II)	Pfn2
O55022	PGRC1_MOUSE	Membrane-associated progesterone receptor component 1 (mPR)	Pgrmc1 Pgrmc
P07934	PHKG1_MOUSE	Phosphorylase b kinase gamma catalytic chain, skeletal muscle/heart isoform (EC 2.7.11.19) (Phosphorylase kinase subunit gamma-1) (Serine/threonine-protein kinase PHKG1) (EC 2.7.11.1) (EC 2.7.11.26)	Phkg1 Phkg
P70181	PI51B_MOUSE	Phosphatidylinositol 4-phosphate 5-kinase type-1 beta (PIP5K1-beta) (PtdIns(4)P-5-kinase 1 beta) (EC 2.7.1.68) (Phosphatidylinositol 4-phosphate 5-kinase type I alpha) (PIP5KIalpha) (Phosphatidylinositol 4-phosphate 5-kinase type I beta) (PIP5KIbeta)	Pip5k1b Pip5k1a
P70182	PI51A_MOUSE	Phosphatidylinositol 4-phosphate 5-kinase type-1 alpha (PIP5K1-alpha) (PtdIns(4)P-5-kinase 1 alpha) (EC 2.7.1.68) (68 kDa type I phosphatidylinositol 4-phosphate 5-kinase) (Phosphatidylinositol 4-phosphate 5-kinase type I alpha) (PIP5KIalpha) (Phosphatidylinositol 4-phosphate 5-kinase type I beta) (PI4P5KIbeta)	Pip5k1a Pip5k1b
Q8K411	PREP_MOUSE	Presequence protease, mitochondrial (EC 3.4.24.-) (Pitrilysin metalloproteinase 1)	Pitrm1 Kiaa1104 Ntup1
Q9QXS1	PLEC_MOUSE	Plectin (PCN) (PLTN) (Plectin-1) (Plectin-6)	Plec Plec1
O35691	PININ_MOUSE	Pinin	Pnn
P33609	DPOLA_MOUSE	DNA polymerase alpha catalytic subunit (EC 2.7.7.7) (DNA polymerase alpha catalytic subunit p180)	Pola1 Pola
P49443	PPM1A_MOUSE	Protein phosphatase 1A (EC 3.1.3.16) (Protein phosphatase 2C isoform alpha) (PP2C-alpha) (Protein phosphatase IA)	Ppm1a Pppm1a
Q6PD03	2A5A_MOUSE	Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit alpha isoform (PP2A B subunit isoform B'-alpha) (PP2A B subunit isoform B56-alpha) (PP2A B subunit isoform PR61-alpha) (PR61alpha) (PP2A B subunit isoform R5-alpha)	Ppp2r5a
Q9CQR6	PPP6_MOUSE	Serine/threonine-protein phosphatase 6 catalytic subunit (PP6C) (EC 3.1.3.16)	Ppp6c
Q922D4	PP6R3_MOUSE	Serine/threonine-protein phosphatase 6 regulatory subunit 3 (SAPS domain family member 3)	Ppp6r3 D19Ertd703e Kiaa1558 Pp6r3 Saps3
P97313	PRKDC_MOUSE	DNA-dependent protein kinase catalytic subunit (DNA-PK catalytic subunit) (DNA-PKcs) (EC 2.7.11.1) (p460)	Prkdc Xrcc7
Q61136	PRP4B_MOUSE	Serine/threonine-protein kinase PRP4 homolog (EC 2.7.11.1) (PRP4 pre-mRNA-processing factor 4 homolog) (Pre-mRNA protein kinase)	Prpf4b Cbp143 Prp4h Prp4k Prp4m Prpk
Q99PV0	PRP8_MOUSE	Pre-mRNA-processing-splicing factor 8 (Splicing factor Prp8)	Prpf8 Prp8
Q61207	SAP_MOUSE	Prosaposin (Sulfated glycoprotein 1) (SGP-1) [Cleaved into: Saposin-A; Saposin-B-Val; Saposin-B; Saposin-C; Saposin-D]	Psap Sgp1
Q99JF8	PSIP1_MOUSE	PC4 and SFRS1-interacting protein (Lens epithelium-derived growth factor) (mLEDGF)	Psip1 Ledgf
Q9QUM9	PSA6_MOUSE	Proteasome subunit alpha type-6 (EC 3.4.25.1) (Macropain iota chain) (Multicatalytic endopeptidase complex iota chain) (Proteasome iota chain)	Psma6
Q9Z2U0	PSA7_MOUSE	Proteasome subunit alpha type-7 (EC 3.4.25.1) (Proteasome subunit RC6-1)	Psma7

Q60692	PSB6_MOUSE	Proteasome subunit beta type-6 (EC 3.4.25.1) (Low molecular mass protein 19) (Macropain delta chain) (Multicatalytic endopeptidase complex delta chain) (Proteasome delta chain) (Proteasome subunit Y)	Psmb6 Lmp19
P70195	PSB7_MOUSE	Proteasome subunit beta type-7 (EC 3.4.25.1) (Macropain chain Z) (Multicatalytic endopeptidase complex chain Z) (Proteasome subunit Z)	Psmb7 Mmc14
Q8VDM4	PSMD2_MOUSE	26S proteasome non-ATPase regulatory subunit 2 (26S proteasome regulatory subunit RPN1) (26S proteasome regulatory subunit S2) (26S proteasome subunit p97)	Psmd2
Q8BJY1	PSMD5_MOUSE	26S proteasome non-ATPase regulatory subunit 5 (26S protease subunit S5 basic) (26S proteasome subunit S5B)	Psmd5 Kiaa0072
P26350	PTMA_MOUSE	Prothymosin alpha [Cleaved into: Prothymosin alpha, N-terminally processed; Thymosin alpha]	Ptma
Q63739	TP4A1_MOUSE	Protein tyrosine phosphatase type IVA 1 (EC 3.1.3.48) (Protein-tyrosine phosphatase 4a1) (Protein-tyrosine phosphatase of regenerating liver 1) (PRL-1)	Ptp4a1 Prl1
Q9CQJ7	PTTG1_MOUSE	Securin (Pituitary tumor-transforming gene 1 protein)	Pttg1 Pttg
P61027	RAB10_MOUSE	Ras-related protein Rab-10	Rab10
Q91V41	RAB14_MOUSE	Ras-related protein Rab-14	Rab14
P62821	RAB1A_MOUSE	Ras-related protein Rab-1A (YPT1-related protein)	Rab1A Rab1
Q9WVM1	RGAP1_MOUSE	Rac GTPase-activating protein 1 (Male germ cell RacGap) (MgcRacGAP)	Racgap1 Mgcracgap
Q61550	RAD21_MOUSE	Double-strand-break repair protein rad21 homolog (mHR21) (Pokeweed agglutinin-binding protein 29) (PW29) (SCC1 homolog) [Cleaved into: 64-kDa C-terminal product (64-kDa carboxy-terminal product)]	Rad21 Hr21 Scc1
P54726	RD23A_MOUSE	UV excision repair protein RAD23 homolog A (HR23A) (mHR23A)	Rad23a Mhr23a
Q9EP71	RAI14_MOUSE	Ankycorbin (Ankyrin repeat and coiled-coil structure-containing protein) (Novel retinal pigment epithelial cell protein) (Retinoic acid-induced protein 14) (p125)	Rai14 Kiaa1334 Norpeg
P63321	RALA_MOUSE	Ras-related protein Ral-A	Rala Ral Ral-a
B2RY56	RBM25_MOUSE	RNA-binding protein 25 (RNA-binding motif protein 25)	Rbm25
Q8VH51	RBM39_MOUSE	RNA-binding protein 39 (Coactivator of activating protein 1 and estrogen receptors) (Coactivator of AP-1 and ERs) (RNA-binding motif protein 39) (RNA-binding region-containing protein 2) (Transcription coactivator CAPER)	Rbm39 Caper Rnpc2
P70336	ROCK2_MOUSE	Rho-associated protein kinase 2 (EC 2.7.11.1) (Rho-associated, coiled-coil-containing protein kinase 2) (Rho-associated, coiled-coil-containing protein kinase II) (ROCK-II) (p164 ROCK-2)	Rock2
Q6ZWV3	RL10_MOUSE	60S ribosomal protein L10 (Protein QM homolog) (Ribosomal protein L10)	Rpl10 Qm
Q9CR57	RL14_MOUSE	60S ribosomal protein L14	Rpl14
P84099	RL19_MOUSE	60S ribosomal protein L19	Rpl19
P99027	RLA2_MOUSE	60S acidic ribosomal protein P2	Rplp2
P62245	RS15A_MOUSE	40S ribosomal protein S15a	Rps15a
P62849	RS24_MOUSE	40S ribosomal protein S24	Rps24
P62855	RS26_MOUSE	40S ribosomal protein S26	Rps26
P62983	RS27A_MOUSE	Ubiquitin-40S ribosomal protein S27a (Ubiquitin carboxyl extension protein 80) [Cleaved into: Ubiquitin; 40S ribosomal protein S27a]	Rps27a Uba80 Ubcep1
P97351	RS3A_MOUSE	40S ribosomal protein S3a (Protein TU-11)	Rps3a Rps3a1
P62754	RS6_MOUSE	40S ribosomal protein S6 (Phosphoprotein NP33)	Rps6
Q9DA37	SAMD8_MOUSE	Sphingomyelin synthase-related protein 1 (SMSr) (EC 2.7.8.-) (Ceramide phosphoethanolamine synthase) (CPE synthase) (Sterile alpha motif domain-containing protein 8) (SAM domain-containing protein 8)	Samd8
Q80UK7	SAS6_MOUSE	Spindle assembly abnormal protein 6 homolog	Sass6 Sas6

P48026	SAT1_MOUSE	Diamine acetyltransferase 1 (EC 2.3.1.57) (Polyamine N-acetyltransferase 1) (Putrescine acetyltransferase) (Spermidine/spermine N(1)-acetyltransferase 1) (SSAT) (SSAT-1)	Sat1 Sat
P58735	S26A1_MOUSE	Sulfate anion transporter 1 (SAT-1) (Solute carrier family 26 member 1)	Slc26a1 Sat1
P13011	ACOD2_MOUSE	Acyl-CoA desaturase 2 (EC 1.14.19.1) (Delta(9)-desaturase 2) (Delta-9 desaturase 2) (Fatty acid desaturase 2) (Stearoyl-CoA desaturase 2)	Scd2
Q8K2B3	SDHA_MOUSE	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial (EC 1.3.5.1) (Flavoprotein subunit of complex II) (Fp)	Sdha
Q9R0P6	SC11A_MOUSE	Signal peptidase complex catalytic subunit SEC11A (EC 3.4.21.89) (Endopeptidase SP18) (Microsomal signal peptidase 18 kDa subunit) (SPase 18 kDa subunit) (SEC11 homolog A) (SEC11-like protein 1) (SPC18) (Sid 2895)	Sec11a Sec11l1 Sid2895 Spc18
A8Y5H7	S14L1_MOUSE	SEC14-like protein 1	Sec14l1 Kiaa4251
Q8BU14	SEC62_MOUSE	Translocation protein SEC62 (Translocation protein 1) (TP-1)	Sec62 Tloc1
Q9Z1W5	SERP1_MOUSE	Stress-associated endoplasmic reticulum protein 1 (Ribosome-attached membrane protein 4)	Serp1 D3Ucla1 Ramp4
Q99NB9	SF3B1_MOUSE	Splicing factor 3B subunit 1 (Pre-mRNA-splicing factor SF3b 155 kDa subunit) (SF3b155) (Spliceosome-associated protein 155) (SAP 155)	Sf3b1 Sap155
P51881	ADT2_MOUSE	ADP/ATP translocase 2 (ADP,ATP carrier protein 2) (Adenine nucleotide translocator 2) (ANT 2) (Solute carrier family 25 member 5) [Cleaved into: ADP/ATP translocase 2, N-terminally processed]	Slc25a5 Ant2
Q9JIM1	S29A1_MOUSE	Equilibrative nucleoside transporter 1 (Equilibrative nitrobenzylmercaptopurine riboside-sensitive nucleoside transporter) (Equilibrative NBMPR-sensitive nucleoside transporter) (Nucleoside transporter, es-type) (Solute carrier family 29 member 1)	Slc29a1 Ent1
Q8CFE6	S38A2_MOUSE	Sodium-coupled neutral amino acid transporter 2 (Amino acid transporter A2) (Solute carrier family 38 member 2) (System A amino acid transporter 2) (System A transporter 1) (System N amino acid transporter 2)	Slc38a2 Ata2 Kiaa1382 Sat2 Snat2
P10852	4F2_MOUSE	4F2 cell-surface antigen heavy chain (4F2hc) (Solute carrier family 3 member 2) (CD antigen CD98)	Slc3a2 Mdu1
Q9WTR6	XCT_MOUSE	Cystine/glutamate transporter (Amino acid transport system xc-) (Solute carrier family 7 member 11) (xCT)	Slc7a11
P62315	SMD1_MOUSE	Small nuclear ribonucleoprotein Sm D1 (Sm-D1) (Sm-D autoantigen) (snRNP core protein D1)	Snrpd1
Q9D8U8	SNX5_MOUSE	Sorting nexin-5	Snx5
P08228	SODC_MOUSE	Superoxide dismutase [Cu-Zn] (EC 1.15.1.1)	Sod1
Q9QX47	SON_MOUSE	Protein SON (Negative regulatory element-binding protein) (NRE-binding protein)	Son Nrebp
O70494	SP3_MOUSE	Transcription factor Sp3	Sp3
Q58A65	JIP4_MOUSE	C-Jun-amino-terminal kinase-interacting protein 4 (JIP-4) (JNK-interacting protein 4) (JNK-associated leucine-zipper protein) (JLP) (JNK/SAPK-associated protein 2) (JSAP2) (Mitogen-activated protein kinase 8-interacting protein 4) (Sperm-associated antigen 9)	Spag9 Jip4 Jsap2 Kiaa0516 Mapk8ip4
P52019	ERG1_MOUSE	Squalene monooxygenase (EC 1.14.14.17) (Squalene epoxidase) (SE)	Sqle Erg1
Q64337	SQSTM_MOUSE	Sequestosome-1 (STONE14) (Ubiquitin-binding protein p62)	Sqstm1 A170 STAP
Q3U1N2	SRBP2_MOUSE	Sterol regulatory element-binding protein 2 (SREBP-2) (Sterol regulatory element-binding transcription factor 2) [Cleaved into: Processed sterol regulatory element-binding protein 2]	Srebf2 Srebp2
P49962	SRP09_MOUSE	Signal recognition particle 9 kDa protein (SRP9)	Srp9
Q8BL97	SRSF7_MOUSE	Serine/arginine-rich splicing factor 7 (Splicing factor, arginine/serine-rich 7)	Srsf7 Sfrs7
Q9CY50	SSRA_MOUSE	Translocon-associated protein subunit alpha (TRAP-alpha) (Signal sequence receptor subunit alpha) (SSR-alpha)	Ssr1
Q9DCF9	SSRG_MOUSE	Translocon-associated protein subunit gamma (TRAP-gamma) (Signal sequence receptor subunit gamma) (SSR-gamma)	Ssr3
Q08943	SSRP1_MOUSE	FACT complex subunit SSRP1 (Facilitates chromatin transcription complex subunit SSRP1) (Recombination signal sequence recognition protein 1) (Structure-specific recognition protein 1) (T160)	Ssrp1

Q99L47	F10A1_MOUSE	Hsc70-interacting protein (Hip) (Protein FAM10A1) (Protein ST13 homolog)	St13 Fam10a1 Hip
O35638	STAG2_MOUSE	Cohesin subunit SA-2 (SCC3 homolog 2) (Stromal antigen 2)	Stag2 Sa2 Sap2
Q60864	STIP1_MOUSE	Stress-induced-phosphoprotein 1 (STI1) (mSTI1) (Hsc70/Hsp90-organizing protein) (Hop)	Stip1
P11031	TCP4_MOUSE	Activated RNA polymerase II transcriptional coactivator p15 (Positive cofactor 4) (PC4) (SUB1 homolog) (Single-stranded DNA-binding protein p9) (p14)	Sub1 Pc4 Rpo2tc1
P61957	SUMO2_MOUSE	Small ubiquitin-related modifier 2 (SUMO-2) (SMT3 homolog 2) (Ubiquitin-like protein SMT3B) (Smt3B)	Sumo2 Smt3b Smt3h2
Q5F2E8	TAOK1_MOUSE	Serine/threonine-protein kinase TAO1 (EC 2.7.11.1) (Thousand and one amino acid protein 1)	Taok1 Kiaa1361
Q9D0R2	SYTC_MOUSE	Threonine--tRNA ligase, cytoplasmic (EC 6.1.1.3) (Threonyl-tRNA synthetase) (ThrRS)	Tars
Q6NXY1	TBC31_MOUSE	TBC1 domain family member 31 (Protein 4-B-3) (WD repeat-containing protein 67)	Tbc1d31 Wdr67
Q8BHJ5	TBL1R_MOUSE	F-box-like/WD repeat-containing protein TBL1XR1 (Nuclear receptor corepressor/HDAC3 complex subunit TBLR1) (TBL1-related protein 1) (Transducin beta-like 1X-related protein 1)	Tbl1xr1 Ira1 Tblr1
Q9JLC6	TEF_MOUSE	Thyrotroph embryonic factor	Tef
Q62351	TFR1_MOUSE	Transferrin receptor protein 1 (TR) (TfR) (TfR1) (Trfr) (CD antigen CD71)	Tfrc Trfr
P40142	TKT_MOUSE	Transketolase (TK) (EC 2.2.1.1) (P68)	Tkt
Q62371	DDR2_MOUSE	Discoidin domain-containing receptor 2 (Discoidin domain receptor 2) (EC 2.7.10.1) (CD167 antigen-like family member B) (Neurotrophic tyrosine kinase, receptor-related 3) (Receptor protein-tyrosine kinase TKT) (Tyrosine-protein kinase TYRO10) (CD antigen CD167b)	Ddr2 Ntrkr3 Tkt Tyro10
P26039	TLN1_MOUSE	Talin-1	Tln1 Tln
P58021	TM9S2_MOUSE	Transmembrane 9 superfamily member 2	Tm9sf2
Q9ET30	TM9S3_MOUSE	Transmembrane 9 superfamily member 3	Tm9sf3 Smbp
Q9D2C7	BI1_MOUSE	Bax inhibitor 1 (BI-1) (Testis-enhanced gene transcript protein) (Transmembrane BAX inhibitor motif-containing protein 6)	Tmbim6 Tegt
Q9DCS1	T176A_MOUSE	Transmembrane protein 176A (Gene signature 188) (Kidney-expressed gene 2 protein)	Tmem176a Gs188 Keg2
Q61029	LAP2B_MOUSE	Lamina-associated polypeptide 2, isoforms beta/delta/epsilon/gamma (Thymopoietin isoforms beta/delta/epsilon/gamma) (TP beta/delta/epsilon/gamma)	Tmpo Lap2
Q61033	LAP2A_MOUSE	Lamina-associated polypeptide 2, isoforms alpha/zeta (Thymopoietin isoforms alpha/zeta) (TP alpha/zeta)	Tmpo Lap2
Q9CZW5	TOM70_MOUSE	Mitochondrial import receptor subunit TOM70 (Mitochondrial precursor proteins import receptor) (Translocase of outer membrane 70 kDa subunit) (Translocase of outer mitochondrial membrane protein 70)	Tomm70 D16Wsu109e Tomm70a
Q01320	TOP2A_MOUSE	DNA topoisomerase 2-alpha (EC 5.99.1.3) (DNA topoisomerase II, alpha isozyme)	Top2a Top-2 Top2
P17751	TPIS_MOUSE	Triosephosphate isomerase (TIM) (EC 5.3.1.1) (Methylglyoxal synthase) (EC 4.2.3.3) (Triose-phosphate isomerase)	Tpi1 Tpi
P21107	TPM3_MOUSE	Tropomyosin alpha-3 chain (Gamma-tropomyosin) (Tropomyosin-3)	Tpm3 Tpm-5 Tpm5
P62996	TRA2B_MOUSE	Transformer-2 protein homolog beta (TRA-2 beta) (TRA2-beta) (Silica-induced gene 41 protein) (SIG-41) (Splicing factor, arginine/serine-rich 10) (Transformer-2 protein homolog B)	Tra2b Sfrs10 Silg41
G5E870	TRIPC_MOUSE	E3 ubiquitin-protein ligase TRIP12 (EC 2.3.2.26) (HECT-type E3 ubiquitin transferase TRIP12) (Thyroid receptor-interacting protein 12) (TR-interacting protein 12) (TRIP-12)	Trip12
Q923J1	TRPM7_MOUSE	Transient receptor potential cation channel subfamily M member 7 (EC 2.7.11.1) (Channel-kinase 1) (Long transient receptor potential channel 7) (LTrpC-7) (LTrpC7) (Transient receptor potential-phospholipase C-interacting kinase) (TRP-PLIK)	Trpm7 Chak Ltrpc7
P62500	T22D1_MOUSE	TSC22 domain family protein 1 (Regulatory protein TSC-22) (TGFB-stimulated clone 22 homolog) (TSC22-related inducible leucine zipper 1b) (Transforming growth factor beta-1-induced transcript 4 protein)	Tsc22d1 Kiaa1994 Tgfb1i4 Tilz1b Tsc22

P05213	TBA1B_MOUSE	Tubulin alpha-1B chain (Alpha-tubulin 2) (Alpha-tubulin isotype M-alpha-2) (Tubulin alpha-2 chain) [Cleaved into: Detyrosinated tubulin alpha-1B chain]	Tuba1b Tuba2
P0CG49	UBB_MOUSE	Polyubiquitin-B [Cleaved into: Ubiquitin]	Ubb
P63147	UBE2B_MOUSE	Ubiquitin-conjugating enzyme E2 B (EC 2.3.2.23) (E2 ubiquitin-conjugating enzyme B) (E214K) (RAD6 homolog B) (HR6B) (mHR6B) (Ubiquitin carrier protein B) (Ubiquitin-protein ligase B)	Ube2b Rad6b
P52483	UB2E3_MOUSE	Ubiquitin-conjugating enzyme E2 E3 (EC 2.3.2.23) (E2 ubiquitin-conjugating enzyme E3) (UbcM2) (Ubiquitin carrier protein E3) (Ubiquitin-conjugating enzyme E2-23 kDa) (Ubiquitin-protein ligase E3)	Ube2e3 Ubce4 Ubcm2
O08759	UBE3A_MOUSE	Ubiquitin-protein ligase E3A (EC 2.3.2.26) (HECT-type ubiquitin transferase E3A) (Oncogenic protein-associated protein E6-AP)	Ube3a
Q9JKB1	UCHL3_MOUSE	Ubiquitin carboxyl-terminal hydrolase isozyme L3 (UCH-L3) (EC 3.4.19.12) (Ubiquitin thioesterase L3)	Uchl3
P52623	UCK1_MOUSE	Uridine-cytidine kinase 1 (UCK 1) (EC 2.7.1.48) (Cytidine monophosphokinase 1) (Uridine monophosphokinase 1)	Uck1 Umpk
Q3UJD6	UBP19_MOUSE	Ubiquitin carboxyl-terminal hydrolase 19 (EC 3.4.19.12) (Deubiquitinating enzyme 19) (Ubiquitin thioesterase 19) (Ubiquitin-specific-processing protease 19)	Usp19 Kiaa0891
B1AY13	UBP24_MOUSE	Ubiquitin carboxyl-terminal hydrolase 24 (EC 3.4.19.12) (Deubiquitinating enzyme 24) (Ubiquitin thioesterase 24) (Ubiquitin-specific-processing protease 24)	Usp24
Q9Z1Q9	SYVC_MOUSE	Valine--tRNA ligase (EC 6.1.1.9) (Protein G7a) (Valyl-tRNA synthetase) (ValRS)	Vars Bat6 G7a Vars2
Q60930	VDAC2_MOUSE	Voltage-dependent anion-selective channel protein 2 (VDAC-2) (mVDAC2) (Outer mitochondrial membrane protein porin 2) (Voltage-dependent anion-selective channel protein 6) (VDAC-6) (mVDAC6)	Vdac2 Vdac6
Q6DID7	WLS_MOUSE	Protein wntless homolog (Integral membrane protein GPR177) (Protein evenness interrupted homolog) (EVI)	Wls Gpr177
P23475	XRCC6_MOUSE	X-ray repair cross-complementing protein 6 (EC 3.6.4.-) (EC 4.2.99.-) (5'-deoxyribose-5-phosphate lyase Ku70) (5'-dRP/AP lyase Ku70) (ATP-dependent DNA helicase 2 subunit 1) (ATP-dependent DNA helicase II 70 kDa subunit) (CTC box-binding factor 75 kDa subunit) (CTC75) (CTCBF) (DNA repair protein XRCC6) (Ku autoantigen protein p70 homolog) (Ku70)	Xrcc6 G22p1 Ku70
P62259	1433E_MOUSE	14-3-3 protein epsilon (14-3-3E)	Ywhae
P63101	1433Z_MOUSE	14-3-3 protein zeta/delta (Protein kinase C inhibitor protein 1) (KCIP-1) (SEZ-2)	Ywhaz
Q00899	TYY1_MOUSE	Transcriptional repressor protein YY1 (Delta transcription factor) (NF-E1) (UCR-motif DNA-binding protein) (Yin and yang 1) (YY-1)	Yy1 Ucrbp
Q8K0L9	ZBT20_MOUSE	Zinc finger and BTB domain-containing protein 20 (BTB/POZ domain zinc finger factor HOF) (Zinc finger protein 288)	Zbtb20 Zfp288
Q3TIV5	ZC3HF_MOUSE	Zinc finger CCCH domain-containing protein 15 (DRG family-regulatory protein 1) (Epo-immediate response gene protein FM22)	Zc3h15 Dfrp1
O88878	ZFAN5_MOUSE	AN1-type zinc finger protein 5 (Zinc finger A20 domain-containing protein 2) (Zinc finger protein 216)	Zfand5 Za20d2 Zfp216 Znf216
O88466	ZN106_MOUSE	Zinc finger protein 106 (Zfp-106) (H3a minor histocompatibility antigen) (Son of insulin receptor mutant) (Zinc finger protein 474)	Znf106 H3a Sh3bp3 Sirm Zfp106 Znf474
Q61624	ZN148_MOUSE	Zinc finger protein 148 (Beta enolase repressor factor 1) (G-rich box-binding protein) (Transcription factor BFCOL1) (Transcription factor ZBP-89) (Zinc finger DNA-binding protein 89)	Znf148 Zbp89 Zfp148
Q62511	ZFP91_MOUSE	E3 ubiquitin-protein ligase ZFP91 (EC 2.3.2.27) (Penta Zf protein) (RING-type E3 ubiquitin transferase ZFP91) (Zinc finger protein 91 homolog) (Zfp-91) (Zinc finger protein PZF)	Zfp91 Pzf
O88532	ZFR_MOUSE	Zinc finger RNA-binding protein	Zfr
Q8R5C8	ZMY11_MOUSE	Zinc finger MYND domain-containing protein 11	Zmynd11
Q9R020	ZRAB2_MOUSE	Zinc finger Ran-binding domain-containing protein 2 (Zinc finger protein 265) (Zinc finger, splicing)	Zranb2 Zfp265 Zis Znf265

Table A.2. Mitochondrial proteins identified from GO database.

Proteins from the GO database with annotated mitochondrial localization (mitochondria, mitochondrial outer membrane, mitochondrial inner membrane, mitochondrial matrix, etc.) were retrieved.[71] UniProt ID was used to identify duplicates from the Mouse MitoCarta 2.0[99] dataset, and unique "GO Mitochondrial" proteins are represented below, with associated entry name, protein names, and gene names from UniProt. These proteins, in addition to the Mouse MitoCarta 2.0 dataset, comprise the 1539 "Curated mitochondrial proteins" represented in **Figure 5.3.1.**

UniProt ID	Entry name	Protein names	Gene names
P26149	3BHS2_MOUSE	3 beta-hydroxysteroid dehydrogenase/Delta 5-->4-isomerase type 2 (3 beta-hydroxysteroid dehydrogenase/Delta 5-->4-isomerase type II) (3-beta-HSD II) [Includes: 3-beta-hydroxy-Delta(5)-steroid dehydrogenase (EC 1.1.1.145) (3-beta-hydroxy-5-ene steroid dehydrogenase) (Progesterone reductase); Steroid Delta-isomerase (EC 5.3.3.1) (Delta-5-3-ketosteroid isomerase)]	Hsd3b2
Q61694	3BHS5_MOUSE	NADPH-dependent 3-keto-steroid reductase Hsd3b5 (3 beta-hydroxysteroid dehydrogenase type 5) (3 beta-hydroxysteroid dehydrogenase type V) (3 beta-HSD V) (EC 1.1.1.270) (Dihydrotestosterone 3-ketoreductase) (EC 1.1.1.210)	Hsd3b5
O35469	3BHS6_MOUSE	3 beta-hydroxysteroid dehydrogenase/Delta 5-->4-isomerase type 6 (EC 1.1.1.-) (3 beta-hydroxysteroid dehydrogenase/Delta 5-->4-isomerase type VI) (3-beta-HSD VI) [Includes: 3-beta-hydroxy-Delta(5)-steroid dehydrogenase (EC 1.1.1.145) (3-beta-hydroxy-5-ene steroid dehydrogenase) (Progesterone reductase); Steroid Delta-isomerase (EC 5.3.3.1) (Delta-5-3-ketosteroid isomerase)]	Hsd3b6
Q9Z131	3BP5_MOUSE	SH3 domain-binding protein 5 (SH3BP-5) (SH3 domain-binding protein that preferentially associates with BTK)	Sh3bp5 Sab
Q04841	3MG_MOUSE	DNA-3-methyladenine glycosylase (EC 3.2.2.21) (3-alkyladenine DNA glycosylase) (3-methyladenine DNA glycosidase) (ADPG) (N-methylpurine-DNA glycosylase)	Mpg Mid1
P56379	68MP_MOUSE	6.8 kDa mitochondrial proteolipid	Mp68
Q8K442	ABC8A_MOUSE	ATP-binding cassette sub-family A member 8-A	Abca8a
Q7TMS5	ABCG2_MOUSE	ATP-binding cassette sub-family G member 2 (Breast cancer resistance protein 1 homolog) (Urate exporter) (CD antigen CD338)	Abcg2 Abcp Bcrp1
Q99LR1	ABD12_MOUSE	Monoacylglycerol lipase ABHD12 (EC 3.1.1.23) (2-arachidonoylglycerol hydrolase) (Abhydrolase domain-containing protein 12)	Abhd12
Q8R2Y0	ABHD6_MOUSE	Monoacylglycerol lipase ABHD6 (EC 3.1.1.23) (2-arachidonoylglycerol hydrolase) (Abhydrolase domain-containing protein 6)	Abhd6
Q2XU92	ACBG2_MOUSE	Long-chain-fatty-acid--CoA ligase ACSBG2 (EC 6.2.1.3) (Acyl-CoA synthetase bubblegum family member 2) (Bubblegum-related protein)	Acsbg2 Bgr
Q9CQJ0	ACO15_MOUSE	Acyl-coenzyme A thioesterase THEM5 (Acyl-CoA thioesterase THEM5) (EC 3.1.2.2) (Acyl-coenzyme A thioesterase 15) (Thioesterase superfamily member 5)	Them5 Acot15
O55137	ACOT1_MOUSE	Acyl-coenzyme A thioesterase 1 (Acyl-CoA thioesterase 1) (EC 3.1.2.2) (CTE-I) (Inducible cytosolic acyl-coenzyme A thioester	Acot1 Cte1

		hydrolase) (Long chain acyl-CoA thioester hydrolase) (Long chain acyl-CoA hydrolase)	
P58137	ACOT8_MOUSE	Acyl-coenzyme A thioesterase 8 (Acyl-CoA thioesterase 8) (EC 3.1.2.27) (Choloyl-coenzyme A thioesterase) (Peroxisomal acyl-CoA thioesterase 2) (PTE-2) (Peroxisomal acyl-coenzyme A thioester hydrolase 1) (PTE-1) (Peroxisomal long-chain acyl-CoA thioesterase 1)	Acot8 Pte1 Pte2
Q9CZW4	ACSL3_MOUSE	Long-chain-fatty-acid--CoA ligase 3 (EC 6.2.1.3) (Long-chain acyl-CoA synthetase 3) (LACS 3)	Acsl3 Acs3 Facl3
Q9JLN6	ADA28_MOUSE	Disintegrin and metalloproteinase domain-containing protein 28 (ADAM 28) (EC 3.4.24.-) (Thymic epithelial cell-ADAM) (TECADAM)	Adam28
Q8R2V5	ADAP2_MOUSE	Arf-GAP with dual PH domain-containing protein 2 (Centaurin-alpha-2) (Cnt-a2)	Adap2 Centa2
Q8C0I1	ADAS_MOUSE	Alkyldihydroxyacetonephosphate synthase, peroxisomal (Alkyl-DHAP synthase) (EC 2.5.1.26) (Alkylglycerone-phosphate synthase)	Agps
P28474	ADHX_MOUSE	Alcohol dehydrogenase class-3 (EC 1.1.1.1) (Alcohol dehydrogenase 2) (Alcohol dehydrogenase 5) (Alcohol dehydrogenase B2) (ADH-B2) (Alcohol dehydrogenase class-III) (Glutathione-dependent formaldehyde dehydrogenase) (FALDH) (FDH) (GSH-FDH) (EC 1.1.1.-) (S-(hydroxymethyl)glutathione dehydrogenase) (EC 1.1.1.284)	Adh5 Adh-2 Adh2
Q6PDY2	AEDO_MOUSE	2-aminoethanethiol dioxygenase (EC 1.13.11.19) (Cysteamine dioxygenase)	Ado Gm237
Q3UHD9	AGAP2_MOUSE	Arf-GAP with GTPase, ANK repeat and PH domain-containing protein 2 (AGAP-2) (Centaurin-gamma-1) (Cnt-g1) (Phosphatidylinositol 3-kinase enhancer) (PIKE)	Agap2 Centg1 Kiaa0167
Q91VJ1	AIM2_MOUSE	Interferon-inducible protein AIM2 (Interferon-inducible protein 210) (Ifi-210) (Interferon-inducible protein p210)	Aim2 Gm1313 Ifi210
Q8K1E6	ALKB3_MOUSE	Alpha-ketoglutarate-dependent dioxygenase alkB homolog 3 (EC 1.14.11.54) (Alkylated DNA repair protein alkB homolog 3) (mAbh3)	Alkbh3 Abh3
A2AH22	AMRA1_MOUSE	Activating molecule in BECN1-regulated autophagy protein 1	Ambra1 Kiaa1736
Q61839	ANFC_MOUSE	C-type natriuretic peptide [Cleaved into: CNP-22; CNP-29; CNP-53]	Nppc Cnp
Q8C8R3	ANK2_MOUSE	Ankyrin-2 (ANK-2) (Ankyrin-B) (Brain ankyrin)	Ank2 AnkB
Q9QZ10	ANX10_MOUSE	Annexin A10 (Annexin-10)	Anxa10
P10107	ANXA1_MOUSE	Annexin A1 (Annexin I) (Annexin-1) (Calpactin II) (Calpactin-2) (Chromobindin-9) (Lipocortin I) (Phospholipase A2 inhibitory protein) (p35)	Anxa1 Anx1 Lpc-1 Lpc1
Q9D385	AR2BP_MOUSE	ADP-ribosylation factor-like protein 2-binding protein (ARF-like 2-binding protein) (Binder of ARF2 protein 1)	Arl2bp Bart Bart1
Q61176	ARGI1_MOUSE	Arginase-1 (EC 3.5.3.1) (Liver-type arginase) (Type I arginase)	Arg1
Q8CG72	ARHL2_MOUSE	ADP-ribose glycohydrolase ARH3 (ADP-ribosylhydrolase 3) (O-acetyl-ADP-ribose deacetylase ARH3) (EC 3.5.1.-) (Poly(ADP-ribose) glycohydrolase ARH3) (EC 3.2.1.143) ([Protein ADP-ribosylarginine] hydrolase-like protein 2) ([Protein ADP-ribosylserine] hydrolase) (EC 3.2.2.-)	Adprhl2 Arh3
Q8CG76	ARK72_MOUSE	Aflatoxin B1 aldehyde reductase member 2 (EC 1.1.1.n11) (Succinic semialdehyde reductase) (SSA reductase)	Akr7a2 Afar Akr7a5
Q91YI0	ARLY_MOUSE	Argininosuccinate lyase (ASAL) (EC 4.3.2.1) (Arginosuccinase)	Asl
Q6A058	ARMX2_MOUSE	Armadillo repeat-containing X-linked protein 2	Armcx2 Kiaa0512
Q8BHS6	ARMX3_MOUSE	Armadillo repeat-containing X-linked protein 3	Armcx3 Alex3
Q8K3A6	ARMX6_MOUSE	Protein ARMCX6	Armcx6
Q91ZT8	ASB9_MOUSE	Ankyrin repeat and SOCS box protein 9 (ASB-9)	Asb9
Q8R1K4	AT2L2_MOUSE	5-phosphohydroxy-L-lysine phospho-lyase (EC 4.2.3.134) (Alanine--glyoxylate aminotransferase 2-like 2)	Phykpl Agxt2l2

P16951	ATF2_MOUSE	Cyclic AMP-dependent transcription factor ATF-2 (cAMP-dependent transcription factor ATF-2) (EC 2.3.1.48) (Activating transcription factor 2) (MXBP protein) (cAMP response element-binding protein CRE-BP1)	Atf2
Q8QZR1	ATTY_MOUSE	Tyrosine aminotransferase (TAT) (EC 2.6.1.5) (L-tyrosine:2-oxoglutarate aminotransferase)	Tat
Q8BVM4	AZIN2_MOUSE	Antizyme inhibitor 2 (AzI2) (Arginine decarboxylase-like protein) (ADC) (ARGDC) (Ornithine decarboxylase-like protein) (ODC-like protein) (ornithine decarboxylase paralog) (ODC-p)	Azin2 Adc Odcp
O54918	B2L11_MOUSE	Bcl-2-like protein 11 (Bcl2-L-11) (Bcl2-interacting mediator of cell death)	Bcl2l11 Bim
Q60739	BAG1_MOUSE	BAG family molecular chaperone regulator 1 (BAG-1) (Bcl-2-associated athanogene 1)	Bag1
Q8CI32	BAG5_MOUSE	BAG family molecular chaperone regulator 5 (BAG-5) (Bcl-2-associated athanogene 5)	Bag5
P18572	BASI_MOUSE	Basigin (Basic immunoglobulin superfamily) (HT7 antigen) (Membrane glycoprotein gp42) (CD antigen CD147)	Bsg
Q99ML1	BBC3_MOUSE	Bcl-2-binding component 3 (p53 up-regulated modulator of apoptosis)	Bbc3 Puma
A2AG58	BCLA3_MOUSE	BCLAF1 and THRAP3 family member 3	Bclaf3
Q9D2C7	BI1_MOUSE	Bax inhibitor 1 (BI-1) (Testis-enhanced gene transcript protein) (Transmembrane BAX inhibitor motif-containing protein 6)	Tmbim6 Tegt
O35425	BOK_MOUSE	Bcl-2-related ovarian killer protein (Apoptosis activator Mtd) (Protein matador)	Bok Mtd
Q920N2	BPL1_MOUSE	Biotin--protein ligase (EC 6.3.4.-) (Biotin apo-protein ligase) [Includes: Biotin--[methylmalonyl-CoA-carboxytransferase] ligase (EC 6.3.4.9); Biotin--[propionyl-CoA-carboxylase [ATP-hydrolyzing]] ligase (EC 6.3.4.10) (Holocarboxylase synthetase) (HCS); Biotin--[methylcrotonoyl-CoA-carboxylase] ligase (EC 6.3.4.11); Biotin--[acetyl-CoA-carboxylase] ligase (EC 6.3.4.15)]	Hlcs
Q8R3B7	BRD8_MOUSE	Bromodomain-containing protein 8	Brd8
Q8BXV2	BRI3B_MOUSE	BRI3-binding protein (I3-binding protein)	Bri3bp
Q499E0	BRNP3_MOUSE	BMP/retinoic acid-inducible neural-specific protein 3	Brinp3 Fam5c
Q9WUF3	C8AP2_MOUSE	CASP8-associated protein 2 (FLICE-associated huge protein)	Casp8ap2 Flash
O35350	CAN1_MOUSE	Calpain-1 catalytic subunit (EC 3.4.22.52) (Calcium-activated neutral proteinase 1) (CANP 1) (Calpain mu-type) (Calpain-1 large subunit) (Micromolar-calpain) (muCANP)	Capn1 Canp1 Capa1
Q05A80	CAPR2_MOUSE	Caprin-2 (C1q domain-containing protein 1) (Cytoplasmic activation/proliferation-associated protein 2) (RNA granule protein 140)	Caprin2 C1qdc1 Kiaa1873 Rng140
P29594	CASP2_MOUSE	Caspase-2 (CASP-2) (EC 3.4.22.55) (Neural precursor cell expressed developmentally down-regulated protein 2) (NEDD-2) (Protease ICH-1) [Cleaved into: Caspase-2 subunit p18; Caspase-2 subunit p13; Caspase-2 subunit p12]	Casp2 Ich1 Nedd-2 Nedd2
Q8C3Q9	CASP9_MOUSE	Caspase-9 (CASP-9) (EC 3.4.22.62) (Apoptotic protease Mch-6) (Apoptotic protease-activating factor 3) (APAF-3) (ICE-like apoptotic protease 6) (ICE-LAP6) [Cleaved into: Caspase-9 subunit p35; Caspase-9 subunit p10]	Casp9 Mch6
P10605	CATB_MOUSE	Cathepsin B (EC 3.4.22.1) (Cathepsin B1) [Cleaved into: Cathepsin B light chain; Cathepsin B heavy chain]	Ctsb
P18242	CATD_MOUSE	Cathepsin D (EC 3.4.23.5)	Ctsd
P49817	CAV1_MOUSE	Caveolin-1	Cav1 Cav
O54724	CAVN1_MOUSE	Caveolae-associated protein 1 (Cav-p60) (Cavin-1) (Polymerase I and transcript release factor)	Cavin1 Ptrf
Q8VDP4	CCAR2_MOUSE	Cell cycle and apoptosis regulator protein 2 (Cell division cycle and apoptosis regulator protein 2)	Ccar2
P24860	CCNB1_MOUSE	G2/mitotic-specific cyclin-B1	Ccnb1 Ccn-2 Ccnb1-rs13 Cycb Cycb1

Q08857	CD36_MOUSE	Platelet glycoprotein 4 (Glycoprotein IIIb) (GPIIIB) (PAS IV) (PAS-4) (Platelet glycoprotein IV) (GPIV) (CD antigen CD36)	Cd36
P11440	CDK1_MOUSE	Cyclin-dependent kinase 1 (CDK1) (EC 2.7.11.22) (EC 2.7.11.23) (Cell division control protein 2 homolog) (Cell division protein kinase 1) (p34 protein kinase)	Cdk1 Cdc2 Cdc2a Cdkn1
Q8BTE5	CEBOS_MOUSE	Protein CEBPZOS	Cebpzos
Q9JKC6	CEND_MOUSE	Cell cycle exit and neuronal differentiation protein 1 (BM88 antigen)	Cend1 Bm88
Q8K4Q7	CERK1_MOUSE	Ceramide kinase (mCERK) (EC 2.7.1.138) (Acylsphingosine kinase)	Cerk
Q6IQX7	CHSS2_MOUSE	Chondroitin sulfate synthase 2 (EC 2.4.1.175) (EC 2.4.1.226) (Chondroitin glucuronyltransferase 2) (Chondroitin-polymerizing factor) (ChPF) (Glucuronosyl-N-acetylgalactosaminyl-proteoglycan 4-beta-N-acetylgalactosaminyltransferase II) (N-acetylgalactosaminyl-proteoglycan 3-beta-glucuronosyltransferase II) (N-acetylgalactosaminyltransferase 2)	Chpf Css2 D1Bwg1363e
O70302	CIDEA_MOUSE	Cell death activator CIDE-A (Cell death-inducing DFFA-like effector A)	Cidea
Q8BTW8	CK5P1_MOUSE	CDK5 regulatory subunit-associated protein 1 (CDK5 activator-binding protein C42)	Cdk5rap1
Q68FD5	CLH1_MOUSE	Clathrin heavy chain 1	Cltc
Q9Z1Q5	CLIC1_MOUSE	Chloride intracellular channel protein 1 (Nuclear chloride ion channel 27) (NCC27)	Clic1
Q06890	CLUS_MOUSE	Clusterin (Apolipoprotein J) (Apo-J) (Clustrin) (Sulfated glycoprotein 2) (SGP-2) [Cleaved into: Clusterin beta chain; Clusterin alpha chain]	Clu Apoj Msgp-2
Q9JIZ0	CMLO1_MOUSE	Probable N-acetyltransferase CML1 (EC 2.3.1.-) (Camello-like protein 1)	Cml1
Q9JJ93	CN119_MOUSE	Uncharacterized protein C14orf119 homolog	MNCb-2990
P16330	CN37_MOUSE	2',3'-cyclic-nucleotide 3'-phosphodiesterase (CNP) (CNPase) (EC 3.1.4.37)	Cnp Cnp1
P47746	CNR1_MOUSE	Cannabinoid receptor 1 (CB-R) (CB1) (Brain-type cannabinoid receptor)	Cnr1
P00405	COX2_MOUSE	Cytochrome c oxidase subunit 2 (Cytochrome c oxidase polypeptide II)	Mtco2 COII COX2 mt-Co2
P00416	COX3_MOUSE	Cytochrome c oxidase subunit 3 (Cytochrome c oxidase polypeptide III)	mt-Co3 COIII Mtco3
P27786	CP17A_MOUSE	Steroid 17-alpha-hydroxylase/17,20 lyase (EC 1.14.14.19) (EC 1.14.14.32) (17-alpha-hydroxyprogesterone aldolase) (CYPXVII) (Cytochrome P450 17A1) (Cytochrome P450-C17) (Cytochrome P450c17)	Cyp17a1 Cyp17
P00184	CP1A1_MOUSE	Cytochrome P450 1A1 (EC 1.14.14.1) (CYPIA1) (Cytochrome P450-P1)	Cyp1a1 Cyp1a-1
Q64429	CP1B1_MOUSE	Cytochrome P450 1B1 (EC 1.14.14.1) (CYPIB1) (Cytochrome P450CMEF) (Cytochrome P450EF)	Cyp1b1 Cyp1-b1
Q05421	CP2E1_MOUSE	Cytochrome P450 2E1 (EC 1.14.13.-) (4-nitrophenol 2-hydroxylase) (EC 1.14.13.n7) (CYPIIE1) (Cytochrome P450-ALC) (Cytochrome P450-J)	Cyp2e1 Cyp2e Cyp2e-1
Q8BT60	CPNE3_MOUSE	Copine-3 (Copine III)	Cpne3 Kiaa0636
Q9D2A5	CR3L4_MOUSE	Cyclic AMP-responsive element-binding protein 3-like protein 4 (cAMP-responsive element-binding protein 3-like protein 4) (Attaching to CRE-like 1) (ATCE1) (Acre1) (Transcript induced in spermiogenesis protein 40) (Tisp40) (mJAL) [Cleaved into: Processed cyclic AMP-responsive element-binding protein 3-like protein 4]	Creb3l4 Atce1 Jal Tisp40
Q01147	CREB1_MOUSE	Cyclic AMP-responsive element-binding protein 1 (CREB-1) (cAMP-responsive element-binding protein 1)	Creb1 Creb-1
P23927	CRYAB_MOUSE	Alpha-crystallin B chain (Alpha(B)-crystallin) (P23)	Cryab Crya2
O54983	CRYM_MOUSE	Ketimine reductase mu-crystallin (EC 1.5.1.25) (NADP-regulated thyroid-hormone-binding protein)	Crym

Q91W50	CSDE1_MOUSE	Cold shock domain-containing protein E1	Csde1 D3Jfr1
P23242	CXA1_MOUSE	Gap junction alpha-1 protein (Connexin-43) (Cx43) (Gap junction 43 kDa heart protein)	Gja1 Cxn-43
Q61462	CY24A_MOUSE	Cytochrome b-245 light chain (Cytochrome b(558) alpha chain) (Cytochrome b558 subunit alpha) (Neutrophil cytochrome b 22 kDa polypeptide) (Superoxide-generating NADPH oxidase light chain subunit) (p22 phagocyte B-cytochrome) (p22-phox) (p22phox)	Cyba
Q7TN08	DACT2_MOUSE	Dapper homolog 2 (mDpr2) (Dapper antagonist of catenin 2)	Dact2 Dpr2 Frd2
O88487	DC1I2_MOUSE	Cytoplasmic dynein 1 intermediate chain 2 (Cytoplasmic dynein intermediate chain 2) (Dynein intermediate chain 2, cytosolic) (DH IC-2)	Dync1i2 Dnci2 Dncic2
Q80T85	DCAF5_MOUSE	DDB1- and CUL4-associated factor 5 (WD repeat-containing protein 22)	Dcaf5 Kiaa1824 Wdr22
Q8N7N5	DCAF8_MOUSE	DDB1- and CUL4-associated factor 8 (WD repeat-containing protein 42A)	Dcaf8 D1Ucla4 H326 Wdr42a
Q99LD8	DDAH2_MOUSE	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2 (DDAH-2) (Dimethylarginine dimethylaminohydrolase 2) (EC 3.5.3.18) (DDAHII) (Dimethylargininase-2)	Ddah2
Q9D3F7	DDIT4_MOUSE	DNA damage-inducible transcript 4 protein (Dexamethasone-induced gene 2 protein) (HIF-1 responsive protein RTP801) (Protein regulated in development and DNA damage response 1) (REDD-1)	Ddit4 Dig2 Redd1 Rtp801
Q62167	DDX3X_MOUSE	ATP-dependent RNA helicase DDX3X (EC 3.6.4.13) (D1Pas1-related sequence 2) (DEAD box RNA helicase DEAD3) (mDEAD3) (DEAD box protein 3, X-chromosomal) (Embryonic RNA helicase)	Ddx3x D1Pas1-rs2 Ddx3 Dead3 Erh
P54823	DDX6_MOUSE	Probable ATP-dependent RNA helicase DDX6 (EC 3.6.4.13) (ATP-dependent RNA helicase p54) (DEAD box protein 6) (Oncogene RCK homolog)	Ddx6 Hlr2 Rck
O09005	DEGS1_MOUSE	Sphingolipid delta(4)-desaturase DES1 (EC 1.14.19.17) (Degenerative spermatocyte homolog 1)	Degs1 Degs Des1 Mdes
Q64442	DHSO_MOUSE	Sorbitol dehydrogenase (EC 1.1.1.14) (L-iditol 2-dehydrogenase)	Sord Sdh1
Q9D0D4	DIM1_MOUSE	Probable dimethyladenosine transferase (EC 2.1.1.183) (DIM1 dimethyladenosine transferase 1 homolog) (DIM1 dimethyladenosine transferase 1-like) (Probable 18S rRNA (adenine(1779)-N(6)/adenine(1780)-N(6))-dimethyltransferase) (Probable 18S rRNA dimethylase) (Probable S-adenosylmethionine-6-N',N'-adenosyl(rRNA) dimethyltransferase)	Dimt1 Dimt1l
Q811T9	DISC1_MOUSE	Disrupted in schizophrenia 1 homolog	Disc1
Q8CFP6	DJC27_MOUSE	DnaJ homolog subfamily C member 27 (Rab and DnaJ domain-containing protein)	Dnajc27 Rabj Rbj
Q8K4R9	DLGP5_MOUSE	Disks large-associated protein 5 (DAP-5) (Discs large homolog 7) (Disks large-associated protein DLG7) (Hepatoma up-regulated protein homolog) (HURP)	Dlgap5 Dlg7 Kiaa0008
Q9CWP8	DPOD4_MOUSE	DNA polymerase delta subunit 4 (DNA polymerase delta subunit p12)	Pold4
Q9QXB9	DRG2_MOUSE	Developmentally-regulated GTP-binding protein 2 (DRG-2) (Translation factor GTPase DRG2) (TRAFAC GTPase DRG2) (EC 3.6.5.-)	Drg2
Q8VE01	DUS18_MOUSE	Dual specificity protein phosphatase 18 (EC 3.1.3.16) (EC 3.1.3.48)	Dusp18
Q9D9D8	DUS21_MOUSE	Dual specificity phosphatase 21 (EC 3.1.3.16) (EC 3.1.3.48)	Dusp21
P63168	DYL1_MOUSE	Dynein light chain 1, cytoplasmic (8 kDa dynein light chain) (DLC8) (Dynein light chain LC8-type 1) (Protein inhibitor of neuronal nitric oxide synthase) (PIN) (mPIN)	Dynll1 Dlc1 Dncl1 Dnclc1
P39053	DYN1_MOUSE	Dynamin-1 (EC 3.6.5.5)	Dnm1 Dnm Kiaa4093
P39054	DYN2_MOUSE	Dynamin-2 (EC 3.6.5.5) (Dynamin UDNM)	Dnm2 Dyn2

Q8BZ98	DYN3_MOUSE	Dynamin-3 (EC 3.6.5.5)	Dnm3 Kiaa0820
P00375	DYR_MOUSE	Dihydrofolate reductase (EC 1.5.1.3)	Dhfr
P41969	ELK1_MOUSE	ETS domain-containing protein Elk-1	Elk1
P54320	ELN_MOUSE	Elastin (Tropoelastin)	Eln
Q9JIX0	ENY2_MOUSE	Transcription and mRNA export factor ENY2 (Enhancer of yellow 2 transcription factor homolog)	Eny2
Q03137	EPHA4_MOUSE	Ephrin type-A receptor 4 (EC 2.7.10.1) (Tyrosine-protein kinase receptor MPK-3) (Tyrosine-protein kinase receptor SEK-1)	Epha4 Sek Sek1
Q9JIM3	ER6L2_MOUSE	DNA excision repair protein ERCC-6-like 2 (EC 3.6.4.-) (DNA repair and recombination protein RAD26-like)	Ercc6l2 Rad26l
Q9EQY0	ERN1_MOUSE	Serine/threonine-protein kinase/endoribonuclease IRE1 (Endoplasmic reticulum-to-nucleus signaling 1) (Inositol-requiring protein 1) (Ire1-alpha) (IRE1a) [Includes: Serine/threonine-protein kinase (EC 2.7.11.1); Endoribonuclease (EC 3.1.26.-)]	Ern1 Ire1
P19785	ESR1_MOUSE	Estrogen receptor (ER) (ER-alpha) (Estradiol receptor) (Nuclear receptor subfamily 3 group A member 1)	Esr1 Esr Estr Estra Nr3a1
Q8BLQ0	F124B_MOUSE	Protein FAM124B	Fam124b
Q8BFZ8	FA72A_MOUSE	Protein FAM72A	Fam72a
Q920L1	FADS1_MOUSE	Acyl-CoA (8-3)-desaturase (EC 1.14.19.44) (Delta(5) fatty acid desaturase) (D5D) (Delta(5) desaturase) (Delta-5 desaturase) (Fatty acid desaturase 1)	Fads1
P0DJI6	FCOR_MOUSE	Foxo1-corepressor (FCoR) (EC 2.3.1.-) (Foxo1 CoRepressor)	Fcor
B2RXV4	FLVC1_MOUSE	Feline leukemia virus subgroup C receptor-related protein 1 (Feline leukemia virus subgroup C receptor) (Major facilitator superfamily domain containing 7B) (Mfsd7b)	Flvcr1 Mfsd7b
Q9CR13	FMC1_MOUSE	Protein FMC1 homolog (Formation of mitochondrial complex V assembly factor 1)	Fmc1
A2ARZ3	FSIP2_MOUSE	Fibrous sheath-interacting protein 2	Fsip2
P39688	FYN_MOUSE	Tyrosine-protein kinase Fyn (EC 2.7.10.2) (Proto-oncogene c-Fyn) (p59-Fyn)	Fyn
Q61585	G0S2_MOUSE	G0/G1 switch protein 2 (G0S2-like protein)	G0s2
Q8CFX1	G6PE_MOUSE	GDH/6PGL endoplasmic bifunctional protein [Includes: Glucose 1-dehydrogenase (EC 1.1.1.47) (Glucose-6-phosphate dehydrogenase) (EC 1.1.1.363); 6-phosphogluconolactonase (6PGL) (EC 3.1.1.31)]	H6pd
Q9WV18	GABR1_MOUSE	Gamma-aminobutyric acid type B receptor subunit 1 (GABA-B receptor 1) (GABA-B-R1) (GABA-BR1) (GABABR1) (Gb1)	Gabbr1
Q8R3R8	GBRL1_MOUSE	Gamma-aminobutyric acid receptor-associated protein-like 1 (GABA(A) receptor-associated protein-like 1) (Glandular epithelial cell protein 1) (GEC-1)	Gabarapl1 Apg8l Atg8l Gec1 MNCb-0091
Q91X44	GCKR_MOUSE	Glucokinase regulatory protein (Glucokinase regulator)	Gckr
Q8BMP6	GCP60_MOUSE	Golgi resident protein GCP60 (Acyl-CoA-binding domain-containing protein 3) (Golgi complex-associated protein 1) (GOCAP1) (Golgi phosphoprotein 1) (GOLPH1) (PBR- and PKA-associated protein 7) (Peripheral benzodiazepine receptor-associated protein PAP7)	Acbd3 Gcp60 Pap7
P06537	GCR_MOUSE	Glucocorticoid receptor (GR) (Nuclear receptor subfamily 3 group C member 1)	Nr3c1 Grl Grl1
P16882	GHR_MOUSE	Growth hormone receptor (GH receptor) (Somatotropin receptor) [Cleaved into: Growth hormone-binding protein (GH-binding protein) (GHBP) (Serum-binding protein)]	Ghr
Q8BWF2	GIMA5_MOUSE	GTPase IMAP family member 5 (Immunity-associated nucleotide 4-like 1 protein) (Immunity-associated protein 3)	Gimap5 Ian4l1 Imap3
Q8BX05	GLPK5_MOUSE	Putative glycerol kinase 5 (GK 5) (Glycerokinase 5) (EC 2.7.1.30) (ATP:glycerol 3-phosphotransferase 5)	Gk5

Q9QUH0	GLRX1_MOUSE	Glutaredoxin-1 (Thioltransferase-1) (TTase-1)	Glrx Glrx1 Grx Grx1
P98192	GNPAT_MOUSE	Dihydroxyacetone phosphate acyltransferase (DAP-AT) (DHAP-AT) (EC 2.3.1.42) (Acyl-CoA:dihydroxyacetonephosphateacyltransferase) (Glycerone-phosphate O-acyltransferase)	Gnpat Dhapat
Q14DK4	GPAT2_MOUSE	Glycerol-3-phosphate acyltransferase 2, mitochondrial (GPAT-2) (EC 2.3.1.15) (xGPAT1)	Gpat2
P13707	GPDA_MOUSE	Glycerol-3-phosphate dehydrogenase [NAD(+)], cytoplasmic (GPD-C) (GPDH-C) (EC 1.1.1.8)	Gpd1 Gdc-1 Gdc1 Kiaa4010
Q8VCE2	GPN1_MOUSE	GPN-loop GTPase 1 (EC 3.6.5.-) (MBD2-interacting protein) (MBDin) (XPA-binding protein 1)	Gpn1 Mbdin Xab1
Q8CB12	GSDC3_MOUSE	Gasdermin-C3	Gsdmc3
Q99NB5	GSDMC_MOUSE	Gasdermin-C (Gasdermin-C1) (Melanoma-derived leucine zipper-containing extranuclear factor) (mMLZE)	Gsdmc Gsdmc1 Mlze
Q9WV60	GSK3B_MOUSE	Glycogen synthase kinase-3 beta (GSK-3 beta) (EC 2.7.11.26) (Serine/threonine-protein kinase GSK3B) (EC 2.7.11.1)	Gsk3b
P19157	GSTP1_MOUSE	Glutathione S-transferase P 1 (Gst P1) (EC 2.5.1.18) (GST YF-YF) (GST class-pi) (GST-piB) (Preadipocyte growth factor)	Gstp1 Gstpib
P46425	GSTP2_MOUSE	Glutathione S-transferase P 2 (Gst P2) (EC 2.5.1.18) (GST YF-YF) (GST class-pi) (GST-piA)	Gstp2 Gstpia
Q3TC93	H1BP3_MOUSE	HCLS1-binding protein 3 (HS1-binding protein 3) (HSP1BP-3)	Hs1bp3
Q8K2C9	HACD3_MOUSE	Very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3 (EC 4.2.1.134) (3-hydroxyacyl-CoA dehydratase 3) (HACD3) (Butyrate-induced protein 1) (B-ind1) (Protein-tyrosine phosphatase-like A domain-containing protein 1)	Hacd3 Ptplad1
Q8QZX2	HAUS3_MOUSE	HAUS augmin-like complex subunit 3	Haus3
O35387	HAX1_MOUSE	HCLS1-associated protein X-1 (HS1-associating protein X-1) (HAX-1) (HS1-binding protein 1) (HSP1BP-1)	Hax1 Hs1bp1
P49710	HCLS1_MOUSE	Hematopoietic lineage cell-specific protein (Hematopoietic cell-specific LYN substrate 1) (LckBP1)	Hcls1 Hs1
Q3SXD3	HDDC2_MOUSE	HD domain-containing protein 2	Hddc2
Q9WU63	HEBP2_MOUSE	Heme-binding protein 2 (Protein SOUL)	Hebp2 Soul
P51163	HEM4_MOUSE	Uroporphyrinogen-III synthase (UROIIIS) (UROS) (EC 4.2.1.75) (Hydroxymethylbilane hydrolyase [cyclizing]) (Uroporphyrinogen-III cosynthase)	Uros Uros3
Q4U2R1	HERC2_MOUSE	E3 ubiquitin-protein ligase HERC2 (EC 2.3.2.26) (HECT domain and RCC1-like domain-containing protein 2) (HECT-type E3 ubiquitin transferase HERC2)	Herc2 Jdf2 Kiaa0393 Rjs
Q0VBL6	HIF3A_MOUSE	Hypoxia-inducible factor 3-alpha (HIF-3-alpha) (HIF3-alpha) (Basic-helix-loop-helix-PAS protein MOP7) (HIF3-alpha-1) (Inhibitory PAS domain protein) (IPAS) (Member of PAS protein 7) (Neonatal and embryonic PAS protein)	Hif3a Mop7 Nepas
Q9CRB3	HIUH_MOUSE	5-hydroxyisourate hydrolase (HIU hydrolase) (HIUHase) (EC 3.5.2.17) (Transthyretin-related protein)	Urah
Q91W97	HKDC1_MOUSE	Putative hexokinase HKDC1 (EC 2.7.1.1) (Hexokinase domain-containing protein 1)	Hkdc1
P61979	HNRPK_MOUSE	Heterogeneous nuclear ribonucleoprotein K (hnRNP K)	Hnrnpk Hnrpk
P62816	HRK_MOUSE	Activator of apoptosis harakiri (BH3-interacting domain-containing protein 3) (Neuronal death protein DP5)	Hrk Bid3 Dp5
Q61696	HS71A_MOUSE	Heat shock 70 kDa protein 1A (Heat shock 70 kDa protein 3) (HSP70.3) (Hsp68)	Hspa1a Hsp70-3 Hsp70A1
Q6VYH9	HSH2D_MOUSE	Hematopoietic SH2 domain-containing protein (Hematopoietic SH2 protein) (Adaptor in lymphocytes of unknown function X)	Hsh2d Alx
P17156	HSP72_MOUSE	Heat shock-related 70 kDa protein 2 (Heat shock protein 70.2)	Hspa2 Hcp70.2 Hsp70-2
Q3TRM8	HXK3_MOUSE	Hexokinase-3 (EC 2.7.1.1) (Hexokinase type III) (HK III)	Hk3
P52792	HXK4_MOUSE	Glucokinase (EC 2.7.1.2) (Hexokinase type IV) (HK IV) (Hexokinase-4) (HK4) (Hexokinase-D)	Gck Gk

P58044	IDI1_MOUSE	Isopentenyl-diphosphate Delta-isomerase 1 (EC 5.3.3.2) (Isopentenyl pyrophosphate isomerase 1) (IPP isomerase 1) (IPPI1)	Idi1
Q64345	IFIT3_MOUSE	Interferon-induced protein with tetratricopeptide repeats 3 (IFIT-3) (Glucocorticoid-attenuated response gene 49 protein) (GARG-49) (P49) (IRG2)	Ifit3 Garg49 Ifi49 Isg49
Q9Z1X4	ILF3_MOUSE	Interleukin enhancer-binding factor 3	Ilf3
Q6PCQ0	IQCE_MOUSE	IQ domain-containing protein E	Iqce
Q9DCC7	ISC2B_MOUSE	Isochorismatase domain-containing protein 2B	Isoc2b Isoc2
Q62315	JARD2_MOUSE	Protein Jumonji (Jumonji/ARID domain-containing protein 2)	Jarid2 Jmj
O88824	JTB_MOUSE	Protein JTB	Jtb Gm622
Q8BTY1	KAT1_MOUSE	Kynurenine--oxoglutarate transaminase 1 (EC 2.6.1.7) (Cysteine-S-conjugate beta-lyase) (EC 4.4.1.13) (Glutamine transaminase K) (GTK) (Glutamine--phenylpyruvate transaminase) (EC 2.6.1.64) (Kynurenine aminotransferase 1) (Kynurenine aminotransferase I) (KATI) (Kynurenine--oxoglutarate transaminase I)	Kyat1 Ccbl1 Kat
Q6ZPU9	KBP_MOUSE	KIF1-binding protein	Kif1bp Kbp Kiaa1279
Q08460	KCMA1_MOUSE	Calcium-activated potassium channel subunit alpha-1 (BK channel) (BKCA alpha) (Calcium-activated potassium channel, subfamily M subunit alpha-1) (K(VCA)alpha) (KCa1.1) (Maxi K channel) (MaxiK) (Slo-alpha) (Slo1) (mSlo1) (Slowpoke homolog) (Slo homolog) (mSlo)	Kcnma1 Kcnma
P97794	KCNJ8_MOUSE	ATP-sensitive inward rectifier potassium channel 8 (Inward rectifier K(+) channel Kir6.1) (Potassium channel, inwardly rectifying subfamily J member 8) (uKATP-1)	Kcnj8
Q04447	KCRB_MOUSE	Creatine kinase B-type (EC 2.7.3.2) (B-CK) (Creatine kinase B chain) (Creatine phosphokinase B-type) (CPK-B)	Ckb Ckbb
P20444	KPCA_MOUSE	Protein kinase C alpha type (PKC-A) (PKC-alpha) (EC 2.7.11.13)	Prkca Pkca
P28867	KPCD_MOUSE	Protein kinase C delta type (EC 2.7.11.13) (Tyrosine-protein kinase PRKCD) (EC 2.7.10.2) (nPKC-delta) [Cleaved into: Protein kinase C delta type regulatory subunit; Protein kinase C delta type catalytic subunit (Sphingosine-dependent protein kinase-1) (SDK1)]	Prkcd Pkcd
P52480	KPYM_MOUSE	Pyruvate kinase PKM (EC 2.7.1.40) (Pyruvate kinase muscle isozyme)	Pkm Pk3 Pkm2 Pykm
Q7TPS0	KS6A6_MOUSE	Ribosomal protein S6 kinase alpha-6 (S6K-alpha-6) (EC 2.7.11.1)	Rps6ka6
Q9CXF0	KYNU_MOUSE	Kynureninase (EC 3.7.1.3) (L-kynurenine hydrolase)	Kynu
P06151	LDHA_MOUSE	L-lactate dehydrogenase A chain (LDH-A) (EC 1.1.1.27) (LDH muscle subunit) (LDH-M)	Ldha Ldh-1 Ldh1
Q91VD1	LEG12_MOUSE	Galectin-12 (Gal-12)	Lgals12
P54310	LIPS_MOUSE	Hormone-sensitive lipase (HSL) (EC 3.1.1.79)	Lipe
Q8K3W2	LRC10_MOUSE	Leucine-rich repeat-containing protein 10 (Heart-restricted leucine-rich repeat protein)	Lrrc10 Hrlrrp
O54791	MAFF_MOUSE	Transcription factor MafF (V-maf musculoaponeurotic fibrosarcoma oncogene homolog F)	Maff
Q8BHE8	MAIP1_MOUSE	m-AAA protease-interacting protein 1, mitochondrial (Matrix AAA peptidase-interacting protein 1)	Maip1
Q9CW42	MARC1_MOUSE	Mitochondrial amidoxime-reducing component 1 (mARC1) (EC 1.-.-.-) (Molybdenum cofactor sulfurase C-terminal domain-containing protein 1) (MOSC domain-containing protein 1) (Moco sulfurase C-terminal domain-containing protein 1)	Marc1 Mosc1
Q99LB6	MAT2B_MOUSE	Methionine adenosyltransferase 2 subunit beta (Methionine adenosyltransferase II beta) (MAT II beta)	Mat2b
P97287	MCL1_MOUSE	Induced myeloid leukemia cell differentiation protein Mcl-1 homolog (Bcl-2-related protein EAT/mcl1)	Mcl1

P15265	MCSP_MOUSE	Sperm mitochondrial-associated cysteine-rich protein	Smcp Mcs Mcsp
P06795	MDR1B_MOUSE	Multidrug resistance protein 1B (EC 7.6.2.2) (ATP-binding cassette sub-family B member 1B) (P-glycoprotein 1) (CD antigen CD243)	Abcb1b Abcb1 Mdr1 Mdr1b Pgy1 Pgy1-1
Q4QQM5	MIGA1_MOUSE	Mitoguardin 1 (Protein FAM73A)	Miga1 Fam73a
P63085	MK01_MOUSE	Mitogen-activated protein kinase 1 (MAP kinase 1) (MAPK 1) (EC 2.7.11.24) (ERT1) (Extracellular signal-regulated kinase 2) (ERK-2) (MAP kinase isoform p42) (p42-MAPK) (Mitogen-activated protein kinase 2) (MAP kinase 2) (MAPK 2)	Mapk1 Erk2 Mapk Prkm1
Q63844	MK03_MOUSE	Mitogen-activated protein kinase 3 (MAP kinase 3) (MAPK 3) (EC 2.7.11.24) (ERT2) (Extracellular signal-regulated kinase 1) (ERK-1) (Insulin-stimulated MAP2 kinase) (MAP kinase isoform p44) (p44-MAPK) (MNK1) (Microtubule-associated protein 2 kinase) (p44-ERK1)	Mapk3 Erk1 Prkm3
O08911	MK12_MOUSE	Mitogen-activated protein kinase 12 (MAP kinase 12) (MAPK 12) (EC 2.7.11.24) (Extracellular signal-regulated kinase 6) (ERK-6) (Mitogen-activated protein kinase p38 gamma) (MAP kinase p38 gamma) (Stress-activated protein kinase 3)	Mapk12 Sapk3
Q2VPU4	MLXIP_MOUSE	MLX-interacting protein (Transcriptional activator MondoA)	Mlxip Mir
Q8C7H1	MMAA_MOUSE	Methylmalonic aciduria type A homolog, mitochondrial (EC 3.6.-.-)	Mmaa
Q80WJ6	MRP9_MOUSE	Multidrug resistance-associated protein 9 (ATP-binding cassette sub-family C member 12)	Abcc12 Mrp9
Q8JZY4	MRPP3_MOUSE	Mitochondrial ribonuclease P catalytic subunit (EC 3.1.26.5) (Mitochondrial ribonuclease P protein 3) (Mitochondrial RNase P protein 3)	Kiaa0391 Mrpp3
Q2YDW2	MSTO1_MOUSE	Protein misato homolog 1	Msto1
Q5HZI1	MTUS1_MOUSE	Microtubule-associated tumor suppressor 1 homolog (AT2 receptor-binding protein) (Angiotensin-II type 2 receptor-interacting protein) (Coiled-coiled tumor suppressor gene 1 protein) (Mitochondrial tumor suppressor 1 homolog)	Mtus1 Atbp Atip Cctsg1 Kiaa1288 Mtsg1
Q9EQS3	MYCBP_MOUSE	c-Myc-binding protein (Associate of Myc 1) (AMY-1)	Mycbp Amy1
P70414	NAC1_MOUSE	Sodium/calcium exchanger 1 (Na(+)/Ca(2+)-exchange protein 1) (Solute carrier family 8 member 1)	Slc8a1 Ncx
Q8K596	NAC2_MOUSE	Sodium/calcium exchanger 2 (Na(+)/Ca(2+)-exchange protein 2) (Solute carrier family 8 member 2)	Slc8a2 Ncx2
Q9DCM7	NACC2_MOUSE	Nucleus accumbens-associated protein 2 (NAC-2) (BTB/POZ domain-containing protein 14A)	Nacc2 Btbd14a
Q6PFD7	NAIF1_MOUSE	Nuclear apoptosis-inducing factor 1	Naif1
Q3UGX3	NAT8L_MOUSE	N-acetylaspartate synthetase (NAA synthetase) (EC 2.3.1.17) (N-acetyltransferase 8-like protein) (Protein Shati)	Nat8l
Q3UYV9	NCBP1_MOUSE	Nuclear cap-binding protein subunit 1 (80 kDa nuclear cap-binding protein) (CBP80) (NCBP 80 kDa subunit)	Ncbp1 Cbp80
Q925Q3	NCLX_MOUSE	Mitochondrial sodium/calcium exchanger protein (Na(+)/K(+)/Ca(2+)-exchange protein 6) (Sodium/calcium exchanger protein, mitochondrial) (Sodium/potassium/calcium exchanger 6) (Solute carrier family 24 member 6) (Solute carrier family 8 member B1)	Slc8b1 Nckx6 Nclx Slc24a6
Q01768	NDKB_MOUSE	Nucleoside diphosphate kinase B (NDK B) (NDP kinase B) (EC 2.7.4.6) (Histidine protein kinase NDKB) (EC 2.7.13.3) (P18) (nm23-M2)	Nme2
P19246	NFH_MOUSE	Neurofilament heavy polypeptide (NF-H) (200 kDa neurofilament protein) (Neurofilament triplet H protein)	Nefh Kiaa0845 Nfh
P25799	NFKB1_MOUSE	Nuclear factor NF-kappa-B p105 subunit (DNA-binding factor KBF1) (EBP-1) (NF-kappa-B1 p84/NF-kappa-B1 p98) (Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1) [Cleaved into: Nuclear factor NF-kappa-B p50 subunit]	Nfkb1
Q9ER97	NGB_MOUSE	Neuroglobin	Ngb
Q9DB96	NGDN_MOUSE	Neuroguidin (EIF4E-binding protein)	Ngdn Ngd

Q8R5K4	NOL6_MOUSE	Nucleolar protein 6 (Nucleolar RNA-associated protein) (Nrap)	Nol6
Q9Z0J4	NOS1_MOUSE	Nitric oxide synthase, brain (EC 1.14.13.39) (Constitutive NOS) (NC-NOS) (NOS type I) (Neuronal NOS) (N-NOS) (nNOS) (Peptidyl-cysteine S-nitrosylase NOS1) (bNOS)	Nos1
Q9JHI8	NOX4_MOUSE	NADPH oxidase 4 (EC 1.6.3.-) (Kidney oxidase-1) (KOX-1) (Kidney superoxide-producing NADPH oxidase) (Renal NAD(P)H-oxidase) (Superoxide-generating NADPH oxidase 4)	Nox4 Renox
Q62443	NPTX1_MOUSE	Neuronal pentraxin-1 (NP1) (Neuronal pentraxin I) (NP-I)	Nptx1
P49282	NRAM2_MOUSE	Natural resistance-associated macrophage protein 2 (NRAMP 2) (Divalent cation transporter 1) (Divalent metal transporter 1) (DMT-1) (Solute carrier family 11 member 2)	Slc11a2 Dct1 Dmt1 Nramp2
Q8VC33	NXNL1_MOUSE	Nucleoredoxin-like protein 1 (Rod-derived cone viability factor) (RdCVF) (Thioredoxin-like protein 6)	Nxnl1 Rdcvf Txnl6
E9Q9A9	OAS2_MOUSE	2'-5'-oligoadenylate synthase 2 ((2-5')oligo(A) synthase 2) (2-5A synthase 2) (EC 2.7.7.84) (2',5'-oligoadenylate synthetase-like 11)	Oas2 oasl11
Q9EQQ9	OGA_MOUSE	Protein O-GlcNAcase (OGA) (EC 3.2.1.169) (Beta-N-acetylhexosaminidase) (Beta-hexosaminidase) (Bifunctional protein NCOAT) (Meningioma-expressed antigen 5) (N-acetyl-beta-D-glucosaminidase) (N-acetyl-beta-glucosaminidase)	Oga Hexc Kiaa0679 Mgea5
Q8CGY8	OGT1_MOUSE	UDP-N-acetylglucosamine--peptide N-acetylglucosaminyltransferase 110 kDa subunit (EC 2.4.1.255) (O-GlcNAc transferase subunit p110) (O-linked N-acetylglucosamine transferase 110 kDa subunit) (OGT)	Ogt
P49650	P2RY1_MOUSE	P2Y purinoceptor 1 (P2Y1) (ADP receptor) (Purinergic receptor)	P2ry1
Q9CPV9	P2Y12_MOUSE	P2Y purinoceptor 12 (P2Y12)	P2ry12
Q60715	P4HA1_MOUSE	Prolyl 4-hydroxylase subunit alpha-1 (4-PH alpha-1) (EC 1.14.11.2) (Procollagen-proline,2-oxoglutarate-4-dioxygenase subunit alpha-1)	P4ha1
Q3V3Q7	PACS2_MOUSE	Phosphofurin acidic cluster sorting protein 2 (PACS-2) (PACS1-like protein)	Pacs2 Kiaa0602 Pacs1l
P11103	PARP1_MOUSE	Poly [ADP-ribose] polymerase 1 (PARP-1) (EC 2.4.2.30) (ADP-ribosyltransferase diphtheria toxin-like 1) (ARTD1) (DNA ADP-ribosyltransferase PARP1) (EC 2.4.2.-) (NAD(+) ADP-ribosyltransferase 1) (ADPRT 1) (Poly[ADP-ribose] synthase 1) (msPARP) (Protein poly-ADP-ribosyltransferase PARP1) (EC 2.4.2.-)	Parp1 Adprp Adprt Adprt1
Q8CAS9	PARP9_MOUSE	Protein mono-ADP-ribosyltransferase PARP9 (EC 2.4.2.-) (ADP-ribosyltransferase diphtheria toxin-like 9) (ARTD9) (B aggressive lymphoma protein homolog) (Poly [ADP-ribose] polymerase 9) (PARP-9)	Parp9 Bal
O88689	PCDA4_MOUSE	Protocadherin alpha-4 (PCDH-alpha-4)	Pcdha4 Cnr1
P27773	PDIA3_MOUSE	Protein disulfide-isomerase A3 (EC 5.3.4.1) (58 kDa glucose-regulated protein) (58 kDa microsomal protein) (p58) (Disulfide isomerase ER-60) (Endoplasmic reticulum resident protein 57) (ER protein 57) (ERp57) (Endoplasmic reticulum resident protein 60) (ER protein 60) (ERp60)	Pdia3 Erp Erp60 Grp58
Q9QY39	PDZD4_MOUSE	PDZ domain-containing protein 4 (PDZ domain-containing RING finger protein 4-like protein)	Pdzd4 Pdzk4 Pdzrn4l Xlu
P70296	PEBP1_MOUSE	Phosphatidylethanolamine-binding protein 1 (PEBP-1) (HCNPpp) [Cleaved into: Hippocampal cholinergic neurostimulating peptide (HCNP)]	Pebp1 Pbp Pebp
Q99MZ7	PECR_MOUSE	Peroxisomal trans-2-enoyl-CoA reductase (TERP) (EC 1.3.1.38)	Pecr
Q61907	PEMT_MOUSE	Phosphatidylethanolamine N-methyltransferase (PEAMT) (PEMT) (EC 2.1.1.17) (EC 2.1.1.71) (Phospholipid methyltransferase) (PLMT)	Pemt Pempt Pemt2
Q9R269	PEPL_MOUSE	Periplakin	Ppl
Q8BWM0	PGES2_MOUSE	Prostaglandin E synthase 2 (EC 5.3.99.3) (GATE-binding factor 1) (GBF-1) (Microsomal prostaglandin E synthase 2) (mPGES-2) [Cleaved into: Prostaglandin E synthase 2 truncated form]	Ptges2 Gbf1 Pges2

Q8BKC8	PI4KB_MOUSE	Phosphatidylinositol 4-kinase beta (PI4K-beta) (PI4Kbeta) (PtdIns 4-kinase beta) (EC 2.7.1.67)	Pi4kb Pik4cb
Q9CWW6	PIN4_MOUSE	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 4 (EC 5.2.1.8) (Parvulin-14) (Par14) (Peptidyl-prolyl cis-trans isomerase Pin4) (PPIase Pin4) (Rotamase Pin4)	Pin4
Q8K4X7	PLCD_MOUSE	1-acyl-sn-glycerol-3-phosphate acyltransferase delta (EC 2.3.1.51) (1-acylglycerol-3-phosphate O-acyltransferase 4) (1-AGP acyltransferase 4) (1-AGPAT 4) (Lysophosphatidic acid acyltransferase delta) (LPAAT-delta)	Agpat4
Q5SWZ9	PLD6_MOUSE	Mitochondrial cardiolipin hydrolase (EC 3.1.-.-) (Choline phosphatase 6) (Mitochondrial phospholipase) (MitoPLD) (Phosphatidylcholine-hydrolyzing phospholipase D6) (Phospholipase D6) (PLD 6) (Protein zucchini homolog) (mZuc)	Pld6
P97819	PLPL9_MOUSE	85/88 kDa calcium-independent phospholipase A2 (CaI-PLA2) (EC 3.1.1.4) (Group VI phospholipase A2) (GVI PLA2) (Intracellular membrane-associated calcium-independent phospholipase A2 beta) (iPLA2-beta) (Patatin-like phospholipase domain-containing protein 9) (PNPLA9)	Pla2g6 Pnpla9
Q9JLV6	PNKP_MOUSE	Bifunctional polynucleotide phosphatase/kinase (DNA 5'-kinase/3'-phosphatase) (Polynucleotide kinase-3'-phosphatase) [Includes: Polynucleotide 3'-phosphatase (EC 3.1.3.32) (2'(3')-polynucleotidase); Polynucleotide 5'-hydroxyl-kinase (EC 2.7.1.78)]	Pnkp
P20263	PO5F1_MOUSE	POU domain, class 5, transcription factor 1 (NF-A3) (Octamer-binding protein 3) (Oct-3) (Octamer-binding protein 4) (Oct-4) (Octamer-binding transcription factor 3) (OTF-3)	Pou5f1 Oct-3 Oct-4 Otf-3 Otf3
Q9ES83	POPD1_MOUSE	Blood vessel epicardial substance (mBVES) (Popeye domain-containing protein 1) (Popeye protein 1)	Bves Pop1 Popdc1
P63328	PP2BA_MOUSE	Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform (EC 3.1.3.16) (CAM-PRP catalytic subunit) (Calmodulin-dependent calcineurin A subunit alpha isoform) (CNA alpha)	Ppp3ca Calna
Q9CR16	PPID_MOUSE	Peptidyl-prolyl cis-trans isomerase D (PPIase D) (EC 5.2.1.8) (40 kDa peptidyl-prolyl cis-trans isomerase) (Cyclophilin-40) (CYP-40) (Rotamase D)	Ppid
P61014	PPLA_MOUSE	Cardiac phospholamban (PLB)	Pln
Q80TL0	PPM1E_MOUSE	Protein phosphatase 1E (EC 3.1.3.16) (Ca(2+)/calmodulin-dependent protein kinase phosphatase N) (CaMKP-N) (CaMKP-nucleus) (CaMKN) (Partner of PIX 1) (Partner of PIX-alpha) (Partner of PIXA)	Ppm1e Camkn Kiaa1072
Q8BU27	PPM1M_MOUSE	Protein phosphatase 1M (EC 3.1.3.16) (Protein phosphatase 2C isoform eta) (PP2C-eta) (PP2CE)	Ppm1m Ppm1e
P17564	PR15A_MOUSE	Protein phosphatase 1 regulatory subunit 15A (Growth arrest and DNA damage-inducible protein GADD34) (Myeloid differentiation primary response protein MyD116)	Ppp1r15a Gadd34 Myd116
P35700	PRDX1_MOUSE	Peroxiredoxin-1 (EC 1.11.1.15) (Macrophage 23 kDa stress protein) (Osteoblast-specific factor 3) (OSF-3) (Thioredoxin peroxidase 2) (Thioredoxin-dependent peroxide reductase 2)	Prdx1 Msp23 Paga Tdpx2
O70343	PRGC1_MOUSE	Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1-alpha) (PPAR-gamma coactivator 1-alpha) (PPARGC-1-alpha)	Ppargc1a Pgc1 Pgc1a Ppargc1
P04925	PRIO_MOUSE	Major prion protein (PrP) (PrP27-30) (PrP33-35C) (CD antigen CD230)	Prnp Prn-p Prp
Q6P1E7	PRIPO_MOUSE	DNA-directed primase/polymerase protein (EC 2.7.7.-) (Coiled-coil domain-containing protein 111)	Primpol Ccdc111
A2AVJ5	PRR5L_MOUSE	Proline-rich protein 5-like (Protein observed with Rictor-2) (Protor-2)	Prr5l Protor2
P49769	PSN1_MOUSE	Presenilin-1 (PS-1) (EC 3.4.23.-) (Protein S182) [Cleaved into: Presenilin-1 NTF subunit; Presenilin-1 CTF subunit; Presenilin-1 CTF12 (PS1-CTF12)]	Psen1 Ad3h Psnl1
O08586	PTEN_MOUSE	Phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase and dual-specificity protein phosphatase PTEN (EC 3.1.3.16) (EC 3.1.3.48) (EC 3.1.3.67) (Mutated in multiple advanced cancers 1) (Phosphatase and tensin homolog)	Pten Mmac1

P54822	PUR8_MOUSE	Adenylosuccinate lyase (ASL) (EC 4.3.2.2) (Adenylosuccinase) (ASase)	Adsl Adl
P70303	PYRG2_MOUSE	CTP synthase 2 (EC 6.3.4.2) (CTP synthetase 2) (CTPsH) (UTP--ammonia ligase 2)	Ctps2
Q924H5	RA51C_MOUSE	DNA repair protein RAD51 homolog 3 (R51H3) (RAD51 homolog C) (RAD51-like protein 2)	Rad51c Rad51l2
Q8QZZ8	RAB38_MOUSE	Ras-related protein Rab-38	Rab38
P35276	RAB3D_MOUSE	Ras-related protein Rab-3D	Rab3d
Q91YQ1	RAB7L_MOUSE	Ras-related protein Rab-7L1 (Rab-7-like protein 1)	Rab29 Rab7l1
P61028	RAB8B_MOUSE	Ras-related protein Rab-8B	Rab8b
P68040	RACK1_MOUSE	Receptor of activated protein C kinase 1 (12-3) (Guanine nucleotide-binding protein subunit beta-2-like 1) (Receptor for activated C kinase) (Receptor of activated protein kinase C 1) (p205) [Cleaved into: Receptor of activated protein C kinase 1, N-terminally processed (Guanine nucleotide-binding protein subunit beta-2-like 1, N-terminally processed)]	Rack1 Gnb2-rs1 Gnb2l1
Q61818	RAI1_MOUSE	Retinoic acid-induced protein 1	Rai1 Kiaa1820
Q9EP71	RAI14_MOUSE	Ankycorbin (Ankyrin repeat and coiled-coil structure-containing protein) (Novel retinal pigment epithelial cell protein) (Retinoic acid-induced protein 14) (p125)	Rai14 Kiaa1334 Norpeg
P62492	RB11A_MOUSE	Ras-related protein Rab-11A (Rab-11)	Rab11a Rab11
P46638	RB11B_MOUSE	Ras-related protein Rab-11B	Rab11b
Q9ERU9	RBP2_MOUSE	E3 SUMO-protein ligase RanBP2 (EC 2.3.2.-) (Ran-binding protein 2) (RanBP2)	Ranbp2
Q8BHC7	RHBL4_MOUSE	Rhomboid-related protein 4 (RRP4) (EC 3.4.21.105) (Rhomboid domain-containing protein 1) (mRHBDD1) (Rhomboid-like protein 4)	Rhbdd1 Rhbdl4 MSD-50 MSD50
Q9QUI0	RHOA_MOUSE	Transforming protein RhoA	Rhoa Arha Arha2
Q5ND29	RILP_MOUSE	Rab-interacting lysosomal protein	Rilp
Q60855	RIPK1_MOUSE	Receptor-interacting serine/threonine-protein kinase 1 (EC 2.7.11.1) (Cell death protein RIP) (Receptor-interacting protein 1) (RIP-1)	Ripk1 Rinp Rip
Q6PEE3	RIR2B_MOUSE	Ribonucleoside-diphosphate reductase subunit M2 B (EC 1.17.4.1) (TP53-inducible ribonucleotide reductase M2 B) (p53-inducible ribonucleotide reductase small subunit 2-like protein) (p53R2)	Rrm2b P53r2
Q3TLD5	RMP_MOUSE	Unconventional prefoldin RPB5 interactor (Protein NNX3) (Protein phosphatase 1 regulatory subunit 19) (RNA polymerase II subunit 5-mediating protein) (RPB5-mediating protein)	Uri1 Nnx3 Ppp1r19 Rmp Uri
Q05921	RN5A_MOUSE	2-5A-dependent ribonuclease (2-5A-dependent RNase) (EC 3.1.26.-) (Ribonuclease 4) (Ribonuclease L) (RNase L)	Rnasel Rns4
O35445	RNF5_MOUSE	E3 ubiquitin-protein ligase RNF5 (EC 2.3.2.27) (RING finger protein 5) (RING-type E3 ubiquitin transferase RNF5)	Rnf5 Ng2
O88561	S27A3_MOUSE	Solute carrier family 27 member 3 (EC 6.2.1.-) (Long-chain fatty acid transport protein 3) (FATP-3) (Fatty acid transport protein 3) (Very long-chain acyl-CoA synthetase homolog 3) (VLCS-3)	Slc27a3 Acsvl3 Fatp3
Q922Q5	S35B3_MOUSE	Adenosine 3'-phospho 5'-phosphosulfate transporter 2 (PAPS transporter 2) (Solute carrier family 35 member B3)	Slc35b3
Q8VE96	S35F6_MOUSE	Solute carrier family 35 member F6 (ANT2-binding protein) (ANT2BP) (Transport and Golgi organization 9 homolog)	Slc35f6
Q61207	SAP_MOUSE	Prosaposin (Sulfated glycoprotein 1) (SGP-1) [Cleaved into: Saposin-A; Saposin-B-Val; Saposin-B; Saposin-C; Saposin-D]	Psap Sgp1
Q60648	SAP3_MOUSE	Ganglioside GM2 activator (Cerebroside sulfate activator protein) (GM2-AP) (Sphingolipid activator protein 3) (SAP-3)	Gm2a
Q9ESL0	SCO2B_MOUSE	Succinyl-CoA:3-ketoacid coenzyme A transferase 2B, mitochondrial (EC 2.8.3.5) (3-oxoacid CoA-transferase 2B) (Testis-specific succinyl-CoA:3-oxoacid CoA-transferase 2) (SCOT-t2)	Oxct2b

Q8BTE0	SDHF4_MOUSE	Succinate dehydrogenase assembly factor 4, mitochondrial (SDH assembly factor 4) (SDHAF4)	Sdhaf4
Q8VBT2	SDHL_MOUSE	L-serine dehydratase/L-threonine deaminase (SDH) (EC 4.3.1.17) (L-serine deaminase) (L-threonine dehydratase) (TDH) (EC 4.3.1.19)	Sds
Q8R238	SDSL_MOUSE	Serine dehydratase-like (EC 4.3.1.17) (L-serine deaminase) (L-serine dehydratase/L-threonine deaminase) (L-threonine dehydratase) (TDH) (EC 4.3.1.19) (SDH)	Sdsl Sds
Q6QD59	SEC20_MOUSE	Vesicle transport protein SEC20	Bnip1 Sec20 Sec20l
Q9EPB5	SERHL_MOUSE	Serine hydrolase-like protein (SHL) (EC 3.1.-.-)	Serhl
Q9JK48	SHLB1_MOUSE	Endophilin-B1 (SH3 domain-containing GRB2-like protein B1)	Sh3glb1 Kiaa0491
Q8VDQ8	SIR2_MOUSE	NAD-dependent protein deacetylase sirtuin-2 (EC 3.5.1.-) (Regulatory protein SIR2 homolog 2) (SIR2-like protein 2) (mSIR2L2)	Sirt2 Sir2l2
O54926	SIVA_MOUSE	Apoptosis regulatory protein Siva (CD27-binding protein) (CD27BP)	Siva1 Siva
Q61165	SL9A1_MOUSE	Sodium/hydrogen exchanger 1 (Na(+)/H(+) exchanger 1) (NHE-1) (Solute carrier family 9 member 1)	Slc9a1 Nhe1
Q91WV7	SLC31_MOUSE	Neutral and basic amino acid transport protein rBAT (Solute carrier family 3 member 1) (b(0,+)-type amino acid transport protein) (NBAT)	Slc3a1 Nbat
Q9WVB4	SLIT3_MOUSE	Slit homolog 3 protein (Slit-3) (Slit3)	Slit3
Q8C1Q6	SMIM4_MOUSE	Small integral membrane protein 4 (Small nucleolar RNA host gene 8)	Smim4
Q9CUN6	SMUF1_MOUSE	E3 ubiquitin-protein ligase SMURF1 (EC 2.3.2.26) (HECT-type E3 ubiquitin transferase SMURF1) (SMAD ubiquitination regulatory factor 1) (SMAD-specific E3 ubiquitin-protein ligase 1)	Smurf1
Q9CWZ7	SNAG_MOUSE	Gamma-soluble NSF attachment protein (SNAP-gamma) (N-ethylmaleimide-sensitive factor attachment protein gamma)	Napg Snapg
P61807	SNN_MOUSE	Stannin	Snn
Q80U23	SNPH_MOUSE	Syntaphilin	Snph Kiaa0374
O88908	SOAT2_MOUSE	Sterol O-acyltransferase 2 (EC 2.3.1.26) (Acyl-coenzyme A:cholesterol acyltransferase 2) (ACAT-2) (Cholesterol acyltransferase 2)	Soat2 Acact-2 Acat2
P06880	SOMA_MOUSE	Somatotropin (Growth hormone)	Gh1 Gh
Q6P069	SORCN_MOUSE	Sorcin	Sri
Q04888	SOX10_MOUSE	Transcription factor SOX-10 (Protein SOX-21) (Transcription factor SOX-M)	Sox10 Sox-10 Sox21
Q06831	SOX4_MOUSE	Transcription factor SOX-4	Sox4 Sox-4
Q8R1X6	SPART_MOUSE	Spartin	Spart Kiaa0610 Spg20
Q6NSW3	SPKAP_MOUSE	A-kinase anchor protein SPHKAP (SPHK1-interactor and AKAP domain-containing protein)	Sphkap Kiaa1678
Q8R0G7	SPNS1_MOUSE	Protein spinster homolog 1	Spns1
Q3U1N2	SRBP2_MOUSE	Sterol regulatory element-binding protein 2 (SREBP-2) (Sterol regulatory element-binding transcription factor 2) [Cleaved into: Processed sterol regulatory element-binding protein 2]	Srebf2 Srebp2
Q9JM90	STAP1_MOUSE	Signal-transducing adaptor protein 1 (STAP-1) (Stem cell adaptor protein 1)	Stap1
Q61542	STAR3_MOUSE	StAR-related lipid transfer protein 3 (Protein ES 64) (Protein MLN 64) (START domain-containing protein 3) (StARD3)	Stard3 Es64 Mln64
Q99JV5	STAR4_MOUSE	StAR-related lipid transfer protein 4 (START domain-containing protein 4) (StARD4)	Stard4
O08599	STXB1_MOUSE	Syntaxin-binding protein 1 (Protein unc-18 homolog 1) (Unc18-1) (Protein unc-18 homolog A) (Unc-18A)	Stxbp1
Q68FL6	SYMC_MOUSE	Methionine--tRNA ligase, cytoplasmic (EC 6.1.1.10) (Methionyl-tRNA synthetase) (MetRS)	Mars

Q8BP47	SYNC_MOUSE	Asparagine--tRNA ligase, cytoplasmic (EC 6.1.1.22) (Asparaginyl-tRNA synthetase) (AsnRS)	Nars
Q6ZWQ0	SYNE2_MOUSE	Nesprin-2 (KASH domain-containing protein 2) (KASH2) (Nuclear envelope spectrin repeat protein 2) (Nucleus and actin connecting element protein) (Protein NUANCE) (Synaptic nuclear envelope protein 2) (Syne-2)	Syne2
Q9D2G5	SYNJ2_MOUSE	Synaptojanin-2 (EC 3.1.3.36) (Synaptic inositol 1,4,5-trisphosphate 5-phosphatase 2)	Synj2 Kiaa0348
P26638	SYSC_MOUSE	Serine--tRNA ligase, cytoplasmic (EC 6.1.1.11) (Seryl-tRNA synthetase) (SerRS) (Seryl-tRNA(Ser/Sec) synthetase)	Sars Sars1 Sers
O55042	SYUA_MOUSE	Alpha-synuclein (Non-A beta component of AD amyloid) (Non-A4 component of amyloid precursor) (NACP)	Snca Syn
Q9D1R1	T126B_MOUSE	Complex I assembly factor TMEM126B, mitochondrial (Transmembrane protein 126B)	Tmem126b
Q8K3F7	TDH_MOUSE	L-threonine 3-dehydrogenase, mitochondrial (EC 1.1.1.103)	Tdh
Q14BI7	TDRD9_MOUSE	ATP-dependent RNA helicase TDRD9 (EC 3.6.4.13) (Tudor domain-containing protein 9)	Tdrd9
O70372	TERT_MOUSE	Telomerase reverse transcriptase (EC 2.7.7.49) (Telomerase catalytic subunit)	Tert
Q3UNW5	TF2L1_MOUSE	Transcription factor CP2-like protein 1 (CP2-related transcriptional repressor 1) (CRTR-1)	Tfcp2l1 Crtr1 Tcfcp2l1
P63058	THA_MOUSE	Thyroid hormone receptor alpha (Nuclear receptor subfamily 1 group A member 1) (c-erbA-1) (c-erbA-alpha)	Thra C-erba-alpha Nr1a1
Q8CAY6	THIC_MOUSE	Acetyl-CoA acetyltransferase, cytosolic (EC 2.3.1.9) (Cytosolic acetoacetyl-CoA thiolase)	Acat2
Q8BZA9	TIGAR_MOUSE	Fructose-2,6-bisphosphatase TIGAR (EC 3.1.3.46) (TP53-induced glycolysis and apoptosis regulator) (TP53-induced glycolysis regulatory phosphatase)	Tigar
Q99JR5	TINAL_MOUSE	Tubulointerstitial nephritis antigen-like (Adrenocortical zonation factor 1) (AZ-1) (Androgen-regulated gene 1 protein) (Tubulointerstitial nephritis antigen-related protein) (TARP)	Tinagl1 Arg1 Lcn7 Tinagl
Q9CYV5	TM135_MOUSE	Transmembrane protein 135 (Peroxisomal membrane protein 52) (PMP52)	Tmem135
P56983	TM14A_MOUSE	Transmembrane protein 14A	Tmem14a
Q149F5	TMM71_MOUSE	Transmembrane protein 71	Tmem71
P54797	TNG2_MOUSE	Transport and Golgi organization 2 homolog (Ser/Thr-rich protein T10 in DGCR region)	Tango2 D16H22S680E T10
P25118	TNR1A_MOUSE	Tumor necrosis factor receptor superfamily member 1A (Tumor necrosis factor receptor 1) (TNF-R1) (Tumor necrosis factor receptor type I) (TNF-RI) (TNFR-I) (p55) (p60) (CD antigen CD120a)	Tnfrsf1a Tnfr-1 Tnfr1
P25446	TNR6_MOUSE	Tumor necrosis factor receptor superfamily member 6 (Apo-1 antigen) (Apoptosis-mediating surface antigen FAS) (FASLG receptor) (CD antigen CD95)	Fas Apt1 Tnfrsf6
Q9D4V6	TO20L_MOUSE	TOMM20-like protein 1	Tomm20l
Q6PD31	TRAK1_MOUSE	Trafficking kinesin-binding protein 1 (Protein Milton)	Trak1
Q8R0K2	TRI31_MOUSE	E3 ubiquitin-protein ligase TRIM31 (EC 2.3.2.27) (RING-type E3 ubiquitin transferase TRIM31) (Tripartite motif-containing protein 31)	Trim31
Q9ESN2	TRI39_MOUSE	E3 ubiquitin-protein ligase TRIM39 (EC 2.3.2.27) (RING finger protein 23) (RING-type E3 ubiquitin transferase TRIM39) (Testis-abundant finger protein) (Tripartite motif-containing protein 39)	Trim39 Rnf23 Tfp
Q9D0C4	TRM5_MOUSE	tRNA (guanine(37)-N1)-methyltransferase (EC 2.1.1.228) (M1G-methyltransferase) (tRNA [GM37] methyltransferase) (tRNA methyltransferase 5 homolog)	Trmt5 Kiaa1393 Trm5
Q99MD6	TRXR3_MOUSE	Thioredoxin reductase 3 (EC 1.8.1.9) (Thioredoxin and glutathione reductase) (Thioredoxin reductase TR2)	Txnrd3 Tgr Trxr3

Q8CGV9	TSH3_MOUSE	Teashirt homolog 3 (Zinc finger protein 537)	Tshz3 Kiaa1474 Tsh3 Zfp537 Znf537
Q8BTV1	TUSC3_MOUSE	Tumor suppressor candidate 3 (Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit TUSC3) (Oligosaccharyl transferase subunit TUSC3) (Magnesium uptake/transporter TUSC3) (Protein N33)	Tusc3 N33
P24529	TY3H_MOUSE	Tyrosine 3-monooxygenase (EC 1.14.16.2) (Tyrosine 3-hydroxylase) (TH)	Th
P07607	TYSY_MOUSE	Thymidylate synthase (TS) (TSase) (EC 2.1.1.45)	Tyms
P0CG49	UBB_MOUSE	Polyubiquitin-B [Cleaved into: Ubiquitin]	Ubb
Q9DC60	UBIA1_MOUSE	UbiA prenyltransferase domain-containing protein 1 (EC 2.5.1.-)	Ubiad1
Q8R5H1	UBP15_MOUSE	Ubiquitin carboxyl-terminal hydrolase 15 (EC 3.4.19.12) (Deubiquitinating enzyme 15) (Ubiquitin thioesterase 15) (Ubiquitin-specific-processing protease 15)	Usp15 Kiaa0529
Q3UN04	UBP30_MOUSE	Ubiquitin carboxyl-terminal hydrolase 30 (EC 3.4.19.12) (Deubiquitinating enzyme 30) (Ubiquitin thioesterase 30) (Ubiquitin-specific-processing protease 30) (Ub-specific protease 30)	Usp30
Q64435	UD16_MOUSE	UDP-glucuronosyltransferase 1-6 (UDPGT 1-6) (UGT1*6) (UGT1-06) (UGT1.6) (EC 2.4.1.17) (Phenol UDP-glucuronosyltransferase) (UDP-glucuronosyltransferase 1A6) (UGT1A6) (UGP1A1) (UGT1A7)	Ugt1a6 Ugt1 Ugt1a6a Ugt1a7
Q9CZT5	VASN_MOUSE	Vasorin (Protein slit-like 2)	Vasn Slitl2
P50516	VATA_MOUSE	V-type proton ATPase catalytic subunit A (V-ATPase subunit A) (EC 7.1.2.2) (V-ATPase 69 kDa subunit) (Vacuolar proton pump subunit alpha)	Atp6v1a Atp6a1 Atp6a2 Atp6v1a1
P40338	VHL_MOUSE	von Hippel-Lindau disease tumor suppressor (pVHL)	Vhl Vhlh
Q8R5H6	WASF1_MOUSE	Wiskott-Aldrich syndrome protein family member 1 (WASP family protein member 1) (Protein WAVE-1)	Wasf1 Wave1
Q5ND34	WDR81_MOUSE	WD repeat-containing protein 81	Wdr81
Q91WL8	WWOX_MOUSE	WW domain-containing oxidoreductase (EC 1.1.1.-)	Wwox Wox1
Q9EPK5	WWTR1_MOUSE	WW domain-containing transcription regulator protein 1 (Transcriptional coactivator with PDZ-binding motif)	Wwtr1 Taz
Q5NBU8	XAF1_MOUSE	XIAP-associated factor 1 (BIRC4-binding protein)	Xaf1 Birc4bp Xiapaf1
Q9CXE6	XRCC3_MOUSE	DNA repair protein XRCC3 (X-ray repair cross-complementing protein 3)	Xrcc3
Q3U5F4	YRDC_MOUSE	YrdC domain-containing protein, mitochondrial (Ischemia/reperfusion-inducible protein) (mIRIP)	Yrdc Irip
Q5Y5T5	ZDHC8_MOUSE	Probable palmitoyltransferase ZDHHC8 (EC 2.3.1.225) (Zinc finger DHHC domain-containing protein 8) (DHHC-8)	Zdhhc8
Q03172	ZEP1_MOUSE	Zinc finger protein 40 (Alpha A-crystallin-binding protein 1) (Alpha A-CRYBP1) (Alpha A-crystallin-binding protein I) (Transcription factor alphaA-CRYBP1)	Hivep1 Cryabp1 Znf40
P10754	ZFP13_MOUSE	Zinc finger protein 13 (Zfp-13) (Zinc finger protein Krox-8)	Zfp13 Krox-8 Zfp-13

Table A.3. Proteins enriched by dAKAP1 KHT 2.5-fold over background.

Proteins whose enrichment score (KHT/MBP z-score normalized intensity) was > 2.5, irrespective of statistical significance, are listed below. Entry name, protein names, and gene names were retrieved from UniProt.[81] These proteins comprise the "KHT associated proteins" represented in **Figure 5.3.1.**

UniProt ID	Entry name	Protein names	Gene names
Q6P542	ABCF1_MOUSE	ATP-binding cassette sub-family F member 1	Abcf1
P05064	ALDOA_MOUSE	Fructose-bisphosphate aldolase A (EC 4.1.2.13) (Aldolase 1) (Muscle-type aldolase)	Aldoa Aldo1
Q925I1	ATAD3_MOUSE	ATPase family AAA domain-containing protein 3 (AAA-ATPase TOB3)	Atad3 Atad3a Kiaa1273
Q7TQH0	ATX2L_MOUSE	Ataxin-2-like protein	Atxn2l A2lp
P80318	TCPG_MOUSE	T-complex protein 1 subunit gamma (TCP-1-gamma) (CCT-gamma) (Matricin) (mTRiC-P5)	Cct3 Cctg
Q8BI72	CARF_MOUSE	CDKN2A-interacting protein (Collaborator of ARF)	Cdkn2aip Carf
Q8BMK4	CKAP4_MOUSE	Cytoskeleton-associated protein 4 (63-kDa cytoskeleton-linking membrane protein) (Climp-63) (p63)	Ckap4
P70698	PYRG1_MOUSE	CTP synthase 1 (EC 6.3.4.2) (CTP synthetase 1) (UTP--ammonia ligase 1)	Ctps1 Ctps
Q922B2	SYDC_MOUSE	Aspartate--tRNA ligase, cytoplasmic (EC 6.1.1.12) (Aspartyl-tRNA synthetase) (AspRS)	Dars
Q91VR5	DDX1_MOUSE	ATP-dependent RNA helicase DDX1 (EC 3.6.4.13) (DEAD box protein 1)	Ddx1
Q501J6	DDX17_MOUSE	Probable ATP-dependent RNA helicase DDX17 (EC 3.6.4.13) (DEAD box protein 17)	Ddx17
Q9JIK5	DDX21_MOUSE	Nucleolar RNA helicase 2 (EC 3.6.4.13) (DEAD box protein 21) (Gu-alpha) (Nucleolar RNA helicase Gu) (Nucleolar RNA helicase II) (RH II/Gu)	Ddx21
O35286	DHX15_MOUSE	Pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15 (EC 3.6.4.13) (DEAH box protein 15)	Dhx15 Ddx15 Deah9
Q91WN1	DNJC9_MOUSE	DnaJ homolog subfamily C member 9	Dnajc9
P32233	DRG1_MOUSE	Developmentally-regulated GTP-binding protein 1 (DRG-1) (Neural precursor cell expressed developmentally down-regulated protein 3) (NEDD-3) (Translation factor GTPase DRG1) (TRAFAC GTPase DRG1) (EC 3.6.5.-)	Drg1 Drg Nedd-3 Nedd3
P10126	EF1A1_MOUSE	Elongation factor 1-alpha 1 (EF-1-alpha-1) (Elongation factor Tu) (EF-Tu) (Eukaryotic elongation factor 1 A-1) (eEF1A-1)	Eef1a1 Eef1a
Q9D8N0	EF1G_MOUSE	Elongation factor 1-gamma (EF-1-gamma) (eEF-1B gamma)	Eef1g
Q9Z0N1	IF2G_MOUSE	Eukaryotic translation initiation factor 2 subunit 3, X-linked (Eukaryotic translation initiation factor 2 subunit gamma, X-linked) (eIF-2-gamma X)	Eif2s3x
Q6NZJ6	IF4G1_MOUSE	Eukaryotic translation initiation factor 4 gamma 1 (eIF-4-gamma 1) (eIF-4G 1) (eIF-4G1)	Eif4g1
P70372	ELAV1_MOUSE	ELAV-like protein 1 (Elav-like generic protein) (Hu-antigen R) (HuR) (MelG)	Elavl1 Elra Hua
P17182	ENOA_MOUSE	Alpha-enolase (EC 4.2.1.11) (2-phospho-D-glycerate hydro-lyase) (Enolase 1) (Non-neural enolase) (NNE)	Eno1 Eno-1
Q6A0A9	F120A_MOUSE	Constitutive coactivator of PPAR-gamma-like protein 1 (Oxidative stress-associated Src activator) (Protein FAM120A)	FAM120A Kiaa0183 Ossa
Q8C3F2	F120C_MOUSE	Constitutive coactivator of PPAR-gamma-like protein 2 (Protein FAM120C)	Fam120c ORF34
Q922J9	FACR1_MOUSE	Fatty acyl-CoA reductase 1 (EC 1.2.1.84)	Far1

Q8C0C7	SYFA_MOUSE	Phenylalanine--tRNA ligase alpha subunit (EC 6.1.1.20) (Phenylalanyl-tRNA synthetase alpha subunit) (PheRS)	Farsa Farsla
P97855	G3BP1_MOUSE	Ras GTPase-activating protein-binding protein 1 (G3BP-1) (EC 3.6.4.12) (EC 3.6.4.13) (ATP-dependent DNA helicase VIII) (GAP SH3 domain-binding protein 1) (HDH-VIII)	G3bp1 G3bp
E9PVA8	GCN1_MOUSE	eIF-2-alpha kinase activator GCN1 (GCN1 eIF-2-alpha kinase activator homolog) (GCN1-like protein 1) (General control of amino-acid synthesis 1-like protein 1) (Translational activator GCN1)	Gcn1 Gcn1l1
Q6Y7W8	GGYF2_MOUSE	GRB10-interacting GYF protein 2 (PERQ amino acid-rich with GYF domain-containing protein 2) (Trinucleotide repeat-containing gene 15 protein)	Gigyf2 Kiaa0642 Perq2 Tnrc15
Q9EST1	GSDMA_MOUSE	Gasdermin-A (Gasdermin-1) (Gasdermin-A1)	Gsdma Gsdm Gsdm1 Gsdma1
Q9JLZ6	HIC2_MOUSE	Hypermethylated in cancer 2 protein (Hic-2)	Hic2 Kiaa1020
P43275	H11_MOUSE	Histone H1.1 (H1 VAR.3) (Histone H1a) (H1a)	Hist1h1a H1a H1f1
P43277	H13_MOUSE	Histone H1.3 (H1 VAR.4) (H1d)	Hist1h1d H1f3
O88569	ROA2_MOUSE	Heterogeneous nuclear ribonucleoproteins A2/B1 (hnRNP A2/B1)	Hnrnpa2b1 Hnrpa2b1
Q8BG05	ROA3_MOUSE	Heterogeneous nuclear ribonucleoprotein A3 (hnRNP A3)	Hnrnpa3 Hnrpa3
Q9Z130	HNRDL_MOUSE	Heterogeneous nuclear ribonucleoprotein D-like (hnRNP D-like) (hnRNP DL) (JKT41-binding protein)	Hnrnpdl Hnrpdl Jktbp
Q9Z2X1	HNRPF_MOUSE	Heterogeneous nuclear ribonucleoprotein F (hnRNP F) [Cleaved into: Heterogeneous nuclear ribonucleoprotein F, N-terminally processed]	Hnrnpf Hnrpf
O35737	HNRH1_MOUSE	Heterogeneous nuclear ribonucleoprotein H (hnRNP H) [Cleaved into: Heterogeneous nuclear ribonucleoprotein H, N-terminally processed]	Hnrnph1 Hnrph Hnrph1
Q8R081	HNRPL_MOUSE	Heterogeneous nuclear ribonucleoprotein L (hnRNP L)	Hnrnpl Hnrpl
Q9D0E1	HNRPM_MOUSE	Heterogeneous nuclear ribonucleoprotein M (hnRNP M)	Hnrnpm Hnrpm
Q8VEK3	HNRPU_MOUSE	Heterogeneous nuclear ribonucleoprotein U (hnRNP U) (Scaffold-attachment factor A) (SAF-A)	Hnrnpu Hnrpu
Q00PI9	HNRL2_MOUSE	Heterogeneous nuclear ribonucleoprotein U-like protein 2 (MLF1-associated nuclear protein)	Hnrnpul2 Hnrpul2 Manp
Q3TEA8	HP1B3_MOUSE	Heterochromatin protein 1-binding protein 3	Hp1bp3
P17879	HS71B_MOUSE	Heat shock 70 kDa protein 1B (Heat shock 70 kDa protein 1) (HSP70.1)	Hspa1b Hcp70.1 Hsp70-1 Hsp70a1 Hspa1
Q02257	PLAK_MOUSE	Junction plakoglobin (Desmoplakin III) (Desmoplakin-3)	Jup
Q8BX02	KANK2_MOUSE	KN motif and ankyrin repeat domain-containing protein 2 (Ankyrin repeat domain-containing protein 25)	Kank2 Ankrd25
Q60749	KHDR1_MOUSE	KH domain-containing, RNA-binding, signal transduction-associated protein 1 (GAP-associated tyrosine phosphoprotein p62) (Src-associated in mitosis 68 kDa protein) (Sam68) (p21 Ras GTPase-activating protein-associated p62) (p68)	Khdrbs1
Q6ZQ58	LARP1_MOUSE	La-related protein 1 (La ribonucleoprotein domain family member 1)	Larp1 Kiaa0731 Larp
Q8BWW4	LARP4_MOUSE	La-related protein 4 (La ribonucleoprotein domain family member 4)	Larp4
Q6A0A2	LAR4B_MOUSE	La-related protein 4B (La ribonucleoprotein domain family member 4B) (La ribonucleoprotein domain family member 5) (La-related protein 5)	Larp4b D13Wsu64e Kiaa0217 Larp5

Q9D0R8	LSM12_MOUSE	Protein LSM12 homolog	Lsm12
Q7TNC4	LC7L2_MOUSE	Putative RNA-binding protein Luc7-like 2 (CGI-74 homolog)	Luc7l2
Q5SUF2	LC7L3_MOUSE	Luc7-like protein 3 (Cisplatin resistance-associated-overexpressed protein)	Luc7l3 Crop
Q8K310	MATR3_MOUSE	Matrin-3	Matr3
Q6ZQI3	MLEC_MOUSE	Malectin	Mlec Kiaa0152
Q9D2P8	MOBP_MOUSE	Myelin-associated oligodendrocyte basic protein	Mobp
Q80UM7	MOGS_MOUSE	Mannosyl-oligosaccharide glucosidase (EC 3.2.1.106) (Glucosidase 1) (Glycoprotein-processing glucosidase I)	Mogs Gcs1
P23249	MOV10_MOUSE	Putative helicase MOV-10 (EC 3.6.4.13) (Moloney leukemia virus 10 protein)	Mov10 Gb110
Q7TPV4	MBB1A_MOUSE	Myb-binding protein 1A (Myb-binding protein of 160 kDa)	Mybbp1a P160
Q9WU42	NCOR2_MOUSE	Nuclear receptor corepressor 2 (N-CoR2) (Silencing mediator of retinoic acid and thyroid hormone receptor) (SMRT) (SMRTe) (T3 receptor-associating factor) (TRAC) (Thyroid-, retinoic-acid-receptor-associated corepressor)	Ncor2 Smrt
P70255	NFIC_MOUSE	Nuclear factor 1 C-type (NF1-C) (Nuclear factor 1/C) (CCAAT-box-binding transcription factor) (CTF) (Nuclear factor I/C) (NF-I/C) (NFI-C) (TGGCA-binding protein)	Nfic
Q61753	SERA_MOUSE	D-3-phosphoglycerate dehydrogenase (3-PGDH) (EC 1.1.1.95) (A10)	Phgdh
Q8BG81	PDIP3_MOUSE	Polymerase delta-interacting protein 3 (S6K1 Aly/REF-like target) (SKAR)	Poldip3
Q8CFI7	RPB2_MOUSE	DNA-directed RNA polymerase II subunit RPB2 (EC 2.7.7.6) (DNA-directed RNA polymerase II 140 kDa polypeptide) (DNA-directed RNA polymerase II subunit B) (RNA polymerase II subunit 2) (RNA polymerase II subunit B2)	Polr2b
Q5EG47	AAPK1_MOUSE	5'-AMP-activated protein kinase catalytic subunit alpha-1 (AMPK subunit alpha-1) (EC 2.7.11.1) (Acetyl-CoA carboxylase kinase) (ACACA kinase) (EC 2.7.11.27) (Hydroxymethylglutaryl-CoA reductase kinase) (HMGCR kinase) (EC 2.7.11.31) (Tau-protein kinase PRKAA1) (EC 2.7.11.26)	Prkaa1
Q7TPM1	PRC2B_MOUSE	Protein PRRC2B (HLA-B-associated transcript 2-like 1) (Proline-rich coiled-coil protein 2B)	Prrc2b Bat2l Bat2l1 Kiaa0515
Q3TLH4	PRC2C_MOUSE	Protein PRRC2C (BAT2 domain-containing protein 1) (HLA-B-associated transcript 2-like 2) (Proline-rich and coiled-coil-containing protein 2C)	Prrc2c Bat2d Bat2d1 Bat2l2 Kiaa1096
P17225	PTBP1_MOUSE	Polypyrimidine tract-binding protein 1 (PTB) (Heterogeneous nuclear ribonucleoprotein I) (hnRNP I)	Ptbp1 Ptb
Q3UEB3	PUF60_MOUSE	Poly(U)-binding-splicing factor PUF60 (60 kDa poly(U)-binding-splicing factor)	Puf60
P42669	PURA_MOUSE	Transcriptional activator protein Pur-alpha (Purine-rich single-stranded DNA-binding protein alpha)	Pura
O35295	PURB_MOUSE	Transcriptional activator protein Pur-beta (Purine-rich element-binding protein B) (Vascular actin single-stranded DNA-binding factor 2 p44 component)	Purb
Q8BML9	SYQ_MOUSE	Glutamine--tRNA ligase (EC 6.1.1.18) (Glutaminyl-tRNA synthetase) (GlnRS)	Qars
Q9QYS9	QKI_MOUSE	Protein quaking (MqkI) (qkI)	Qki Qk Qk1 Qka1
Q60972	RBBP4_MOUSE	Histone-binding protein RBBP4 (Chromatin assembly factor 1 subunit C) (CAF-1 subunit C) (Chromatin assembly factor I p48 subunit) (CAF-I 48 kDa subunit) (CAF-I p48) (Nucleosome-remodeling factor subunit RBAP48) (Retinoblastoma-binding protein 4) (RBBP-4) (Retinoblastoma-binding protein p48)	Rbbp4 Rbap48
Q8BP71	RFOX2_MOUSE	RNA binding protein fox-1 homolog 2 (Fox-1 homolog B) (Fox-1 homolog Fxh) (Hexaribonucleotide-binding protein 2) (RNA-binding motif protein 9) (RNA-binding protein 9)	Rbfox2 Fox2 Fxh Hrnbp2 Rbm9
Q8C2Q3	RBM14_MOUSE	RNA-binding protein 14 (RNA-binding motif protein 14)	Rbm14
Q91WT8	RBM47_MOUSE	RNA-binding protein 47 (RNA-binding motif protein 47)	Rbm47
Q8VC70	RBMS2_MOUSE	RNA-binding motif, single-stranded-interacting protein 2	Rbms2

P19253	RL13A_MOUSE	60S ribosomal protein L13a (Transplantation antigen P198) (Tum-P198 antigen)	Rpl13a P198 Tstap198-7
P67984	RL22_MOUSE	60S ribosomal protein L22 (Heparin-binding protein HBp15)	Rpl22
P62830	RL23_MOUSE	60S ribosomal protein L23	Rpl23
P62751	RL23A_MOUSE	60S ribosomal protein L23a	Rpl23a
Q8BP67	RL24_MOUSE	60S ribosomal protein L24	Rpl24
P61255	RL26_MOUSE	60S ribosomal protein L26 (Silica-induced gene 20 protein) (SIG-20)	Rpl26
Q6ZWV7	RL35_MOUSE	60S ribosomal protein L35	Rpl35
Q9D8E6	RL4_MOUSE	60S ribosomal protein L4	Rpl4
P47962	RL5_MOUSE	60S ribosomal protein L5	Rpl5
P47955	RLA1_MOUSE	60S acidic ribosomal protein P1	Rplp1
Q91YQ5	RPN1_MOUSE	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1 (Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 67 kDa subunit) (Ribophorin I) (RPN-I) (Ribophorin-1)	Rpn1
P63325	RS10_MOUSE	40S ribosomal protein S10	Rps10
P62281	RS11_MOUSE	40S ribosomal protein S11	Rps11
P62301	RS13_MOUSE	40S ribosomal protein S13	Rps13
Q9CZX8	RS19_MOUSE	40S ribosomal protein S19	Rps19
P25444	RS2_MOUSE	40S ribosomal protein S2 (40S ribosomal protein S4) (Protein LLRep3)	Rps2 Llrep3 Rps4
P62852	RS25_MOUSE	40S ribosomal protein S25	Rps25
P62908	RS3_MOUSE	40S ribosomal protein S3 (EC 4.2.99.18)	Rps3
P97351	RS3A_MOUSE	40S ribosomal protein S3a (Protein TU-11)	Rps3a Rps3a1
P62702	RS4X_MOUSE	40S ribosomal protein S4, X isoform	Rps4x Rps4
P97461	RS5_MOUSE	40S ribosomal protein S5 [Cleaved into: 40S ribosomal protein S5, N-terminally processed]	Rps5
P62242	RS8_MOUSE	40S ribosomal protein S8	Rps8
Q6ZWN5	RS9_MOUSE	40S ribosomal protein S9	Rps9
Q99LF4	RTCB_MOUSE	tRNA-splicing ligase RtcB homolog (EC 6.5.1.3) (Focal adhesion-associated protein) (FAAP)	Rtcb D10Wsu52e
Q9JLI8	SART3_MOUSE	Squamous cell carcinoma antigen recognized by T-cells 3 (SART-3) (mSART-3) (Tumor-rejection antigen SART3)	Sart3 Kiaa0156
Q8R0X7	SGPL1_MOUSE	Sphingosine-1-phosphate lyase 1 (S1PL) (SP-lyase 1) (SPL 1) (mSPL) (EC 4.1.2.27) (Sphingosine-1-phosphate aldolase)	Sgpl1
Q9CZU3	MTREX_MOUSE	Exosome RNA helicase MTR4 (EC 3.6.4.13) (ATP-dependent helicase SKIV2L2) (Superkiller viralicidic activity 2-like 2) (TRAMP-like complex helicase)	Mtrex Skiv2l2
Q64HY3	SP9_MOUSE	Transcription factor Sp9	Sp9
P32067	LA_MOUSE	Lupus La protein homolog (La autoantigen homolog) (La ribonucleoprotein)	Ssb Ss-b
Q9Z108	STAU1_MOUSE	Double-stranded RNA-binding protein Staufen homolog 1	Stau1 Stau
Q7TMK9	HNRPQ_MOUSE	Heterogeneous nuclear ribonucleoprotein Q (hnRNP Q) (Glycine- and tyrosine-rich RNA-binding protein) (GRY-RBP) (NS1-associated protein 1) (Synaptotagmin-binding, cytoplasmic RNA-interacting protein) (pp68)	Syncrip Hnrpq Nsap1 Nsap1l
P11983	TCPA_MOUSE	T-complex protein 1 subunit alpha (TCP-1-alpha) (CCT-alpha) (Tailless complex polypeptide 1A) (TCP-1-A) (Tailless complex polypeptide 1B) (TCP-1-B)	Tcp1 Cct1 Ccta
Q7TSK7	ATL2_MOUSE	ADAMTS-like protein 2 (ADAMTSL-2) (TSP1-repeat-containing protein 1) (TCP-1)	Adamtsl2 Kiaa0605 Tcp1
Q8BKI2	TNR6B_MOUSE	Trinucleotide repeat-containing gene 6B protein	Tnrc6b Kiaa1093

Q62318	TIF1B_MOUSE	Transcription intermediary factor 1-beta (TIF1-beta) (E3 SUMO-protein ligase TRIM28) (EC 2.3.2.27) (KRAB-A-interacting protein) (KRIP-1) (RING-type E3 ubiquitin transferase TIF1-beta) (Tripartite motif-containing protein 28)	Trim28 Kap1 Krip1 Tif1b
P68372	TBB4B_MOUSE	Tubulin beta-4B chain (Tubulin beta-2C chain)	Tubb4b Tubb2c
P99024	TBB5_MOUSE	Tubulin beta-5 chain	Tubb5
Q922F4	TBB6_MOUSE	Tubulin beta-6 chain	Tubb6
P26369	U2AF2_MOUSE	Splicing factor U2AF 65 kDa subunit (U2 auxiliary factor 65 kDa subunit) (U2 snRNP auxiliary factor large subunit)	U2af2 U2af65
Q91VX2	UBAP2_MOUSE	Ubiquitin-associated protein 2 (UBAP-2) (Protein lingerer homolog 1) (mLig-1)	Ubap2 Lig1
Q80X50	UBP2L_MOUSE	Ubiquitin-associated protein 2-like	Ubap2l
Q9EPU0	RENT1_MOUSE	Regulator of nonsense transcripts 1 (EC 3.6.4.-) (ATP-dependent helicase RENT1) (Nonsense mRNA reducing factor 1) (NORF1) (Up-frameshift suppressor 1 homolog) (mUpf1)	Upf1 Rent1
Q9DBR1	XRN2_MOUSE	5'-3' exoribonuclease 2 (EC 3.1.13.-) (Protein Dhm1)	Xrn2 Dhm1
P62960	YBOX1_MOUSE	Nuclease-sensitive element-binding protein 1 (CCAAT-binding transcription factor I subunit A) (CBF-A) (DNA-binding protein B) (DBPB) (Enhancer factor I subunit A) (EFI-A) (Y-box transcription factor) (Y-box-binding protein 1) (YB-1)	Ybx1 Msy-1 Msy1 Nsep1 Yb1
Q9JKB3	YBOX3_MOUSE	Y-box-binding protein 3 (Cold shock domain-containing protein A) (DNA-binding protein A) (Y-box protein 3)	Ybx3 Csda Msy4
Q91YT7	YTHD2_MOUSE	YTH domain-containing family protein 2	Ythdf2
P61982	1433G_MOUSE	14-3-3 protein gamma [Cleaved into: 14-3-3 protein gamma, N-terminally processed]	Ywhag
Q3UPF5	ZCCHV_MOUSE	Zinc finger CCCH-type antiviral protein 1 (ADP-ribosyltransferase diphtheria toxin-like 13) (ARTD13) (Inactive Poly [ADP-ribose] polymerase 13) (PARP13)	Zc3hav1

References

1. Friedman, J. R. & Nunnari, J. Mitochondrial form and function. *Nature* **505,** 335–343 (2014).

2. Smith, D. F., Samelson, B. K. & Scott, J. D. Discovery of cellular substrates for protein kinase A using a peptide array screening protocol. *Biochem J* **438,** 103–110 (2011).

3. Zhang, F., Zhang, L., Qi, Y. & Xu, H. Mitochondrial cAMP signaling. *Cell Mol Life Sci* **73,** 4577–4590 (2016).

4. Nunnari, J. & Suomalainen, A. Mitochondria: In Sickness and in Health. *Cell* **148,** 1145–1159 (2012).

5. Mishra, P. & Chan, D. C. Mitochondrial dynamics and inheritance during cell division, development and disease. *Nat Rev Mol Cell Bio* **15,** nrm3877 (2014).

6. Wong, W. & Scott, J. D. AKAP signalling complexes: focal points in space and time. *Nat Rev Mol Cell Bio* **5,** 959–970 (2004).

7. Welch, E. J., Jones, B. W. & Scott, J. D. Networking with AKAPs: context-dependent regulation of anchored enzymes. *Mol Interv* **10,** 86–97 (2010).

8. Huang, L., Durick, K., Weiner, J. A., Chun, J. & Taylor, S. S. Identification of a Novel Protein Kinase A Anchoring Protein That Binds Both Type I and Type II Regulatory Subunits. *J Biol Chem* **272,** 8057–8064 (1997).

9. Means, C. K. *et al.* An entirely specific type I A-kinase anchoring protein that can sequester two molecules of protein kinase A at mitochondria. *Proc National Acad Sci* **108,** E1227–E1235 (2011).

10. Ma, Y. & Taylor, S. A 15-Residue Bifunctional Element in d-AKAP1 Is Required for Both Endoplasmic Reticulum and Mitochondrial Targeting. *J Biol Chem* **277,** 27328–27336 (2002).

11. Newhall, K. J. *et al.* Dynamic Anchoring of PKA Is Essential during Oocyte Maturation. *Curr Biology Cb* **16,** 321–7 (2006).

12. Abrenica, B., AlShaaban, M. & Czubryt, M. P. The A-kinase anchor protein AKAP121 is a negative regulator of cardiomyocyte hypertrophy. *J Mol Cell Cardiol* **46,** 674–681 (2009).

13. Merrill, R. A. *et al.* Mechanism of Neuroprotective Mitochondrial Remodeling by

PKA/AKAP1. *Plos Biol* **9,** e1000612 (2011).

14. Zhang, J. *et al.* Neuroprotective Mitochondrial Remodeling by AKAP121/PKA Protects HT22 Cell from Glutamate-Induced Oxidative Stress. *Mol Neurobiol* 1–22 (2019). doi:10.1007/s12035-018-1464-3

15. Huang, L. *et al.* NH2-Terminal Targeting Motifs Direct Dual Specificity A-Kinase–anchoring Protein 1 (D-AKAP1) to Either Mitochondria or Endoplasmic Reticulum. *J Cell Biology* **145,** 951–959 (1999).

16. Jun, Y. *et al.* D-AKAP1a is a signal-anchored protein in the mitochondrial outer membrane. *Febs Lett* **590,** 954–961 (2016).

17. Valverde, R., Edwards, L. & Regan, L. Structure and function of KH domains. *Febs J* **275,** 2712–2726 (2008).

18. Chen, C., Nott, T. J., Jin, J. & Pawson, T. Deciphering arginine methylation: Tudor tells the tale. *Nat Rev Mol Cell Bio* **12,** 629 (2011).

19. Chojnacki, S., Cowley, A., Lee, J., Foix, A. & Lopez, R. Programmatic access to bioinformatics tools from EMBL-EBI update: 2017. *Nucleic Acids Res* **45,** W550–W553 (2017).

20. Waterhouse, A. M., Procter, J. B., Martin, D. M., Clamp, M. & Barton, G. J. Jalview Version 2—a multiple sequence alignment editor and analysis workbench. *Bioinformatics* **25,** 1189–1191 (2009).

21. Küntziger, T., Rogne, M., Folstad, R. L. & Collas, P. Association of PP1 with Its Regulatory Subunit AKAP149 Is Regulated by Serine Phosphorylation Flanking the RVXF Motif of AKAP149†. *Biochemistry-us* **45,** 5868–5877 (2006).

22. Rogne, M., Stokka, A., Taskén, K., Collas, P. & Küntziger, T. Mutually exclusive binding of PP1 and RNA to AKAP149 affects the mitochondrial network. *Hum Mol Genet* **18,** 978–987 (2009).

23. Oughtred, R. *et al.* The BioGRID interaction database: 2019 update. *Nucleic Acids Res* doi:10.1093/nar/gky1079

24. Orchard, S. *et al.* The MIntAct project—IntAct as a common curation platform for 11 molecular interaction databases. *Nucleic Acids Res* **42,** D358–D363 (2014).

25. Ginsberg, M. D., Feliciello, A., Jones, J. K., Avvedimento, E. V. & Gottesman, M. E. PKA-dependent Binding of mRNA to the Mitochondrial AKAP121 Protein. *J Mol Biol* **327,** 885–897 (2003).

26. Ranganathan, G. *et al.* The Translational Regulation of Lipoprotein Lipase by Epinephrine Involves an RNA Binding Complex Including the Catalytic Subunit of Protein Kinase A. *J Biol Chem* **277,** 43281–43287 (2002).

27. Grozdanov, P. N. & occo, D. Short RNA Molecules with High Binding Affinity to the KH Motif of A-Kinase Anchoring Protein 1 (AKAP1): Implications for the Regulation of Steroidogenesis. *Mol Endocrinol* **26,** 2104–2117 (2012).

28. Hentze, M. W., Castello, A., Schwarzl, T. & Preiss, T. A brave new world of RNA-binding proteins. *Nat Rev Mol Cell Bio* **19,** 327 (2018).

29. Pereira, B., Billaud, M. & Almeida, R. RNA-Binding Proteins in Cancer: Old Players and New Actors. *Trends Cancer* **3,** 506–528 (2017).

30. Tome, J. M. *et al.* Comprehensive analysis of RNA-protein interactions by high-throughput sequencing–RNA affinity profiling. *Nat Methods* **11,** nmeth.2970 (2014).

31. Queiroz, R. M. *et al.* Comprehensive identification of RNA–protein interactions in any organism using orthogonal organic phase separation (OOPS). *Nat Biotechnol* **37,** 169–178 (2019).

32. Wang, Z.-L. *et al.* Comprehensive Genomic Characterization of RNA-Binding Proteins across Human Cancers. *Cell Reports* **22,** 286–298 (2018).

33. Castello, A. *et al.* Comprehensive Identification of RNA-Binding Domains in Human Cells. *Mol Cell* **63,** 696–710 (2016).

34. Lunde, B. M., Moore, C. & Varani, G. RNA-binding proteins: modular design for efficient function. *Nat Rev Mol Cell Bio* **8,** 479–490 (2007).

35. Auweter, S. D., Oberstrass, F. C. & Allain, F. Sequence-specific binding of single-stranded RNA: is there a code for recognition? *Nucleic Acids Res* **34,** 4943–4959 (2006).

36. Wang, X., McLachlan, J., Zamore, P. D. & Hall, T. Modular Recognition of RNA by a Human Pumilio-Homology Domain. *Cell* **110,** 501–512 (2002).

37. Dyson, M. T. *et al.* Mitochondrial A-Kinase Anchoring Protein 121 Binds Type II Protein Kinase A and Enhances Steroidogenic Acute Regulatory Protein-Mediated Steroidogenesis in MA-10 Mouse Leydig Tumor Cells. *Biol Reprod* **78,** 267–277 (2008).

38. Stocco, D. M. & Clark, B. J. Role of the steroidogenic acute regulatory protein (StAR) in steroidogenesis. *Biochem Pharmacol* **51,** 197–205 (1996).

39. Tait, S. W. & Green, D. R. Mitochondria and cell signalling. *J Cell Sci* **125,** 807–815 (2012).

40. Quirós, P. M., Mottis, A. & Auwerx, J. Mitonuclear communication in homeostasis and stress. *Nat Rev Mol Cell Bio* **17,** 213–226 (2016).

41. Youle, R. J. & van der Bliek, A. M. Mitochondrial Fission, Fusion, and Stress. *Science* **337,** 1062–1065 (2012).

42. Wang, C. & Youle, R. J. The Role of Mitochondria in Apoptosis*. *Genetics* **43,** 95–118 (2009).

43. Patron, M. *et al.* The Mitochondrial Calcium Uniporter (MCU): Molecular Identity and Physiological Roles. *J Biol Chem* **288,** 10750–10758 (2013).

44. Wellen, K. E. & Thompson, C. B. A two-way street: reciprocal regulation of metabolism and signalling. *Nat Rev Mol Cell Bio* **13,** 270 (2012).

45. Sena, L. A. & Chandel, N. S. Physiological Roles of Mitochondrial Reactive Oxygen Species. *Mol Cell* **48,** 158–167 (2012).

46. Herzig, S. & Shaw, R. J. AMPK: guardian of metabolism and mitochondrial homeostasis. *Nat Rev Mol Cell Bio* **19,** 121 (2017).

47. Garrido, C. *et al.* Mechanisms of cytochrome c release from mitochondria. *Cell Death Differ* **13,** 4401950 (2006).

48. Kanneganti, T.-D., Kundu, M. & Green, D. R. Innate Immune Recognition of mtDNA—An Undercover Signal? *Cell Metab* **21,** 793–794 (2015).

49. Chandel, N. S. Evolution of Mitochondria as Signaling Organelles. *Cell Metab* **22,** 204–206 (2015).

50. Eisner, V., Picard, M. & Hajnóczky, G. Mitochondrial dynamics in adaptive and maladaptive cellular stress responses. *Nat Cell Biol* **20,** 755–765 (2018).

51. Westermann, B. Mitochondrial fusion and fission in cell life and death. *Nat Rev Mol Cell Bio* **11,** 872 (2010).

52. Lee, J. E., Westrate, L. M., Wu, H., Page, C. & Voeltz, G. K. Multiple dynamin family members collaborate to drive mitochondrial division. *Nature* **540,** 139 (2016).

53. Merrill, R. A. & Strack, S. Mitochondria: A kinase anchoring protein 1, a signaling

platform for mitochondrial form and function. *Int J Biochem Cell Biology* **48,** 92–96 (2014).

54. Dickey, A. S. & Strack, S. PKA/AKAP1 and PP2A/Bβ2 Regulate Neuronal Morphogenesis via Drp1 Phosphorylation and Mitochondrial Bioenergetics. *J Neurosci* **31,** 15716–15726 (2011).

55. Feliciello, A., Gottesman, M. E. & Avvedimento, E. V. cAMP-PKA signaling to the mitochondria: protein scaffolds, mRNA and phosphatases. *Cell Signal* **17,** 279–287 (2005).

56. Calvo, S. E. & Mootha, V. K. The Mitochondrial Proteome and Human Disease. *Annu Rev Genom Hum G* **11,** 25–44 (2010).

57. Pagliarini, D. J. *et al.* A Mitochondrial Protein Compendium Elucidates Complex I Disease Biology. *Cell* **134,** 112–123 (2008).

58. Zemanovic, S. *et al.* Dynamic Phosphorylation of the C Terminus of Hsp70 Regulates the Mitochondrial Import of SOD2 and Redox Balance. *Cell Reports* **25,** 2605-2616.e7 (2018).

59. Gerbeth, C. *et al.* Glucose-Induced Regulation of Protein Import Receptor Tom22 by Cytosolic and Mitochondria-Bound Kinases. *Cell Metab* **18,** 578–587 (2013).

60. Rao, S. *et al.* Biogenesis of the preprotein translocase of the outer mitochondrial membrane: protein kinase A phosphorylates the precursor of Tom40 and impairs its import. *Mol Biol Cell* **23,** 1618–1627 (2012).

61. Harada, H. *et al.* Phosphorylation and Inactivation of BAD by Mitochondria-Anchored Protein Kinase A. *Mol Cell* **3,** 413–422 (1999).

62. Smith, D. F. *et al.* Local protein kinase A action proceeds through intact holoenzymes. *Science* **356,** 1288–1293 (2017).

63. Kumar, S., Kostin, S., Flacke, J.-P., Reusch, P. H. & Ladilov, Y. Soluble Adenylyl Cyclase Controls Mitochondria-dependent Apoptosis in Coronary Endothelial Cells. *J Biol Chem* **284,** 14760–14768 (2009).

64. Prilusky, J. *et al.* FoldIndex©: a simple tool to predict whether a given protein sequence is intrinsically unfolded. *Bioinformatics* **21,** 3435–3438 (2005).

65. Kelley, L. A., Mezulis, S., Yates, C. M., Wass, M. N. & Sternberg, M. J. The Phyre2 web portal for protein modeling, prediction and analysis. *Nat Protoc* **10,** 845–858 (2015).

66. Hollingworth, D. *et al.* KH domains with impaired nucleic acid binding as a tool for functional analysis. *Nucleic Acids Res* **40,** 6873–6886 (2012).

67. Nygren, P. J. *et al.* Intrinsic disorder within AKAP79 fine-tunes anchored phosphatase activity toward substrates and drug sensitivity. *Elife* **6,** e30872 (2017).

68. Whiting, J. L. *et al.* Protein Kinase A Opposes the Phosphorylation-dependent Recruitment of Glycogen Synthase Kinase 3β to A-kinase Anchoring Protein 220. *J Biol Chem* **290,** 19445–19457 (2015).

69. Durkin, M. E., Qian, X., Popescu, N. C. & Lowy, D. R. Isolation of Mouse Embryo Fibroblasts. *Bio-protocol* **3,** (2013).

70. Mi, H. *et al.* PANTHER version 11: expanded annotation data from Gene Ontology and Reactome pathways, and data analysis tool enhancements. *Nucleic Acids Res* **45,** D183–D189 (2017).

71. Ashburner, M. *et al.* Gene Ontology: tool for the unification of biology. *Nat Genet* **25,** 25–29 (2000).

72. Carbon, S. *et al.* The Gene Ontology Resource: 20 years and still GOing strong. *Nucleic Acids Res* doi:10.1093/nar/gky1055

73. Szklarczyk, D. *et al.* STRING v11: protein–protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Res* doi:10.1093/nar/gky1131

74. Szklarczyk, D. *et al.* The STRING database in 2017: quality-controlled protein–protein association networks, made broadly accessible. *Nucleic Acids Res* **45,** D362–D368 (2017).

75. Hornbeck, P. V. *et al.* PhosphoSitePlus: a comprehensive resource for investigating the structure and function of experimentally determined post-translational modifications in man and mouse. *Nucleic Acids Res* **40,** D261–D270 (2012).

76. Blom, N., Gammeltoft, S. & Brunak, S. Sequence and structure-based prediction of eukaryotic protein phosphorylation sites1 1Edited by F. E. Cohen. *J Mol Biol* **294,** 1351–1362 (1999).

77. Blom, N., Sicheritz-Pontén, T., Gupta, R., Gammeltoft, S. & Brunak, S. Prediction of post-translational glycosylation and phosphorylation of proteins from the amino acid sequence. *Proteomics* **4,** 1633–1649 (2004).

78. Obenauer, J. C., Cantley, L. C. & Yaffe, M. B. Scansite 2.0: proteome-wide prediction of cell signaling interactions using short sequence motifs. *Nucleic Acids Res* **31,** 3635–3641 (2003).

79. Desiere, F. *et al.* The PeptideAtlas project. *Nucleic Acids Res* **34,** D655–D658 (2006).

80. Bateman, A. *et al.* UniProt: a worldwide hub of protein knowledge. *Nucleic Acids Res* doi:10.1093/nar/gky1049

81. Maraia, R. J., Mattijssen, S., Cruz-Gallardo, I. & Conte, M. R. The La and related RNA-binding proteins (LARPs): structures, functions, and evolving perspectives. *Wiley Interdiscip Rev Rna* **8,** e1430 (2017).

82. Bayfield, M. A., Kaiser, T. E., Intine, R. V. & Maraia, R. J. Conservation of a Masked Nuclear Export Activity of La Proteins and Its Effects on tRNA Maturation ▿ . *Mol Cell Biol* **27,** 3303–3312 (2007).

83. Yang, R. *et al.* La-Related Protein 4 Binds Poly(A), Interacts with the Poly(A)-Binding Protein MLLE Domain via a Variant PAM2w Motif, and Can Promote mRNA Stability†. *Mol Cell Biol* **31,** 542–556 (2011).

84. Blagden, S. P. *et al.* Drosophila Larp associates with poly(A)-binding protein and is required for male fertility and syncytial embryo development. *Dev Biol* **334,** 186–197 (2009).

85. Yi, H. *et al.* PABP Cooperates with the CCR4-NOT Complex to Promote mRNA Deadenylation and Block Precocious Decay. *Mol Cell* **70,** 1081-1088.e5 (2018).

86. Nicholson, A. L. & Pasquinelli, A. E. Tales of Detailed Poly(A) Tails. *Trends Cell Biol* (2018). doi:10.1016/j.tcb.2018.11.002

87. Goss, D. J. & Kleiman, F. Poly(A) binding proteins: are they all created equal? *Wiley Interdiscip Rev Rna* **4,** 167–179 (2013).

88. Lahr, R. M. *et al.* La-related protein 1 (LARP1) binds the mRNA cap, blocking eIF4F assembly on TOP mRNAs. *Elife* **6,** e24146 (2017).

89. Philippe, L., Vasseur, J.-J., Debart, F. & Thoreen, C. C. La-related protein 1 (LARP1) repression of TOP mRNA translation is mediated through its cap-binding domain and controlled by an adjacent regulatory region. *Nucleic Acids Res* gkx1237-doi:10.1093/nar/gkx1237

90. Küspert, M. *et al.* LARP4B is an AU-rich sequence associated factor that promotes

mRNA accumulation and translation. *Rna* **21,** 1294–1305 (2015).

91. Schäffler, K. *et al.* A stimulatory role for the La-related protein 4B in translation. *Rna* **16,** 1488–1499 (2010).

92. Markmiller, S. *et al.* Context-Dependent and Disease-Specific Diversity in Protein Interactions within Stress Granules. *Cell* **172,** 590-604.e13 (2018).

93. Namkoong, S., Ho, A., Woo, Y., Kwak, H. & Lee, J. Systematic Characterization of Stress-Induced RNA Granulation. *Mol Cell* **70,** (2018).

94. Jain, S. *et al.* ATPase-Modulated Stress Granules Contain a Diverse Proteome and Substructure. *Cell* **164,** 487–498 (2016).

95. Wang, Z., Gerstein, M. & Snyder, M. RNA-Seq: a revolutionary tool for transcriptomics. *Nat Rev Genet* **10,** nrg2484 (2009).

96. Kim, D. *et al.* TopHat2: accurate alignment of transcriptomes in the presence of insertions, deletions and gene fusions. *Genome Biol* **14,** R36 (2013).

97. Bray, N. L., Pimentel, H., Melsted, P. & Pachter, L. Near-optimal probabilistic RNA-seq quantification. *Nat Biotechnol* **34,** 525–527 (2016).

98. Calvo, S. E., Clauser, K. R. & Mootha, V. K. MitoCarta2.0: an updated inventory of mammalian mitochondrial proteins. *Nucleic Acids Res* **44,** D1251–D1257 (2016).

99. Holley, A. K., Bakthavatchalu, V., Velez-Roman, J. M. & Clair, D. K. Manganese Superoxide Dismutase: Guardian of the Powerhouse. *Int J Mol Sci* **12,** 7114–7162 (2011).

100. Schmidt, E. K., Clavarino, G., Ceppi, M. & Pierre, P. SUnSET, a nonradioactive method to monitor protein synthesis. *Nat Methods* **6,** nmeth.1314 (2009).

101. Schneider-Poetsch, T. *et al.* Inhibition of eukaryotic translation elongation by cycloheximide and lactimidomycin. *Nat Chem Biol* **6,** 209 (2010).

102. Chaban, Y., Boekema, E. J. & Dudkina, N. V. Structures of mitochondrial oxidative phosphorylation supercomplexes and mechanisms for their stabilisation. *Biochimica Et Biophysica Acta Bba - Bioenergetics* **1837,** 418–426 (2014).

103. Mot, A. I., Liddell, J. R., White, A. R. & Crouch, P. J. Circumventing the Crabtree Effect: A method to induce lactate consumption and increase oxidative phosphorylation in cell culture. *Int J Biochem Cell Biology* **79,** 128–138 (2016).

104. Aft, R., Zhang, F. & Gius, D. Evaluation of 2-deoxy-D-glucose as a chemotherapeutic agent: mechanism of cell death. *Brit J Cancer* **87,** 805 (2002).

105. EAGLE, H., RBAN, S., LEVY, M. & SCHULZE, H. The utilization of carbohydrates by human cell cultures. *J Biological Chem* **233,** 551–8 (1958).

106. Aggarwal, S. *et al.* Depletion of dAKAP1-protein kinase A signaling islands from the outer mitochondrial membrane alters breast cancer cell metabolism and motility. *J Biol Chem* jbc.RA118.006741 (2018). doi:10.1074/jbc.ra118.006741

107. Mertins, P. *et al.* Proteogenomics connects somatic mutations to signalling in breast cancer. *Nature* **534,** 55 (2016).

108. Bardella, C., Pollard, P. J. & Tomlinson, I. SDH mutations in cancer. *Biochimica Et Biophysica Acta Bba - Bioenergetics* **1807,** 1432–1443 (2011).

109. Hendrickson, D. G., Kelley, D. R., Tenen, D., Bernstein, B. & Rinn, J. L. Widespread RNA binding by chromatin-associated proteins. *Genome Biol* **17,** 28 (2016).

110. Kaewsapsak, P., Shechner, D., Mallard, W., Rinn, J. L. & Ting, A. Y. Live-cell mapping of organelle-associated RNAs via proximity biotinylation combined with protein-RNA crosslinking. *Elife* **6,** e29224 (2017).

111. Fazal, F. M. *et al.* Atlas of Subcellular RNA Localization Revealed by APEX-seq. *Biorxiv* 454470 (2018). doi:10.1101/454470

112. Burke, K. S., Antilla, K. A. & Tirrell, D. A. A Fluorescence in Situ Hybridization Method To Quantify mRNA Translation by Visualizing Ribosome–mRNA Interactions in Single Cells. *Acs Central Sci* (2017). doi:10.1021/acscentsci.7b00048

113. Chen, F. *et al.* Nanoscale imaging of RNA with expansion microscopy. *Nat Methods* **13,** nmeth.3899 (2016).

114. Moon, S. L. *et al.* Multicolour single-molecule tracking of mRNA interactions with RNP granules. *Nat Cell Biol* 1–7 (2019). doi:10.1038/s41556-018-0263-4

115. Lee, C.-Y. & Seydoux, G. Dynamics of mRNA entry into stress granules. *Nat Cell Biol* 1–2 (2019). doi:10.1038/s41556-019-0278-5

116. Treeck, B. *et al.* RNA self-assembly contributes to stress granule formation and defining the stress granule transcriptome. *Proc National Acad Sci* **115,** 201800038 (2018).

117. Protter, D. & Parker, R. Principles and Properties of Stress Granules. *Trends Cell Biol* **26,** 668–679 (2016).

118. Schisa, J. A. Effects of stress and aging on ribonucleoprotein assembly and function in the germ line. *Wiley Interdiscip Rev Rna* **5,** 231–246 (2014).

119. Wang, C. *et al.* Context-dependent deposition and regulation of mRNAs in P-bodies. *Elife* **7,** e29815 (2018).

120. Kershaw, C. J. & Ashe, M. P. Untangling P-Bodies: Dissecting the Complex Web of Interactions that Enable Tiered Control of Gene Expression. *Mol Cell* **68,** 3–4 (2017).

121. Hubstenberger, A. *et al.* P-Body Purification Reveals the Condensation of Repressed mRNA Regulons. *Mol Cell* **68,** (2017).

122. D'Lima, N. G. *et al.* A human microprotein that interacts with the mRNA decapping complex. *Nat Chem Biol* **13,** 174–180 (2016).

123. Ernoult-Lange, M., Bénard, M., Kress, M. & Weil, D. P-bodies and mitochondria: Which place in RNA interference? *Biochimie* **94,** 1572–1577 (2012).

124. Huang, L. *et al.* Mitochondria Associate with P-bodies and Modulate MicroRNA-mediated RNA Interference. *J Biol Chem* **286,** 24219–24230 (2011).

125. Kozlov, G., Safaee, N., Rosenauer, A. & Gehring, K. Structural Basis of Binding of P-body-associated Proteins GW182 and Ataxin-2 by the Mlle Domain of Poly(A)-binding Protein. *J Biol Chem* **285,** 13599–13606 (2010).

126. Eulalio, A., Behm-Ansmant, I. & Izaurralde, E. P bodies: at the crossroads of post-transcriptional pathways. *Nat Rev Mol Cell Bio* **8,** 9–22 (2007).

127. TEIXEIRA, D., SHETH, U., VALENCIA-SANCHEZ, M. A., BRENGUES, M. & PARKER, R. Processing bodies require RNA for assembly and contain nontranslating mRNAs. *Rna* **11,** 371–382 (2005).

128. Jin, M. *et al.* Glycolytic Enzymes Coalesce in G Bodies under Hypoxic Stress. *Cell Reports* **20,** 895–908 (2017).

129. Putnam, A., Cassani, M., Smith, J. & Seydoux, G. A gel phase promotes condensation of liquid P granules in Caenorhabditis elegans embryos. *Nat Struct Mol Biol* **26,** 220–226 (2019).

130. Boeynaems, S. *et al.* Protein Phase Separation: A New Phase in Cell Biology. *Trends Cell Biol* (2018). doi:10.1016/j.tcb.2018.02.004

131. Mittag, T. & Fawzi, N. L. Protein quality and miRNA slicing get into phase. *Nat Cell Biol* **20,** 635–637 (2018).

132. Mugridge, J. S., Coller, J. & Gross, J. D. Structural and molecular mechanisms for the control of eukaryotic 5′–3′ mRNA decay. *Nat Struct Mol Biol* **25,** 1077 (2018).

133. Cioni, J.-M. *et al.* Late Endosomes Act as mRNA Translation Platforms and Sustain Mitochondria in Axons. *Cell* (2019). doi:10.1016/j.cell.2018.11.030

134. Rangaraju, V., Lauterbach, M. & Schuman, E. M. Spatially Stable Mitochondrial Compartments Fuel Local Translation during Plasticity. *Cell* (2019). doi:10.1016/j.cell.2018.12.013

135. Glock, C., Heumüller, M. & human, E. mRNA transport & local translation in neurons. *Curr Opin Neurobiol* **45,** 169–177 (2017).

136. Chekulaeva, M. & Landthaler, M. Eyes on Translation. *Mol Cell* **63,** 918–925 (2016).

137. Cox, J. & Mann, M. MaxQuant enables high peptide identification rates, individualized p.p.b.-range mass accuracies and proteome-wide protein quantification. *Nat Biotechnol* **26,** nbt.1511 (2008).

138. Tyanova, S., Temu, T. & Cox, J. The MaxQuant computational platform for mass spectrometry-based shotgun proteomics. *Nat Protoc* **11,** nprot.2016.136 (2016).

139. Tyanova, S. *et al.* The Perseus computational platform for comprehensive analysis of (prote)omics data. *Nat Methods* **13,** 731–740 (2016).

140. Carnegie, G. K. *et al.* AKAP-Lbc Mobilizes a Cardiac Hypertrophy Signaling Pathway. *Mol Cell* **32,** 169–179 (2008).

141. Carnegie, G. K., Smith, F. D., McConnachie, G., Langeberg, L. K. & Scott, J. D. AKAP-Lbc Nucleates a Protein Kinase D Activation Scaffold. *Mol Cell* **15,** 889–899 (2004).

142. Clayton, D. A. & Shadel, G. S. Isolation of Mitochondria from Tissue Culture Cells. *Cold Spring Harb Protoc* **2014,** pdb.prot080002 (2014).