

Table 1. Up-regulated synaptic proteins compared EA to CUMS

Name	cellular component	biological process	molecular function
Heat shock cognate 71 kDa protein	dendrite; synaptic vesicle; postsynaptic density ; neuron projection	response to heat; protein import into nucleus; cerebellum development; positive regulation of lysosomal membrane permeability; response to activity; response to odorant; response to estradiol; negative regulation of transcription, DNA-templated; response to drug; positive regulation of gene expression	ADP binding; ATP binding; receptor binding; clathrin-uncoating ATPase activity; prostaglandin binding; RNA binding; ATPase activity, coupled; nucleotide binding; unfolded protein binding; transcription factor binding
Calponin-3	dendrite; postsynaptic density ; neuronal cell body; dendritic spine; focal adhesion; microtubule; actin filament; actin cytoskeleton	epithelial cell differentiation; negative regulation of ATPase activity; actomyosin structure organization	calmodulin binding; microtubule binding; actin binding; protein binding, bridging
Abl interactor 1	postsynaptic density ; neuron projection	lamellipodium morphogenesis; somitogenesis; positive regulation of protein tyrosine kinase activity; peptidyl-tyrosine phosphorylation; cellular process; megakaryocyte development	protein tyrosine kinase activator activity; protein complex binding; transcription factor binding; protein binding
p55 protein	postsynaptic density		
COP9 signalosome complex subunit 4	synaptic vesicle ; synapse	protein deneddylation; cullin deneddylation	NEDD8-specific protease activity; protein binding
Phosphatidylethanolamine-binding protein 1	synaptic vesicle ; neuron projection; axon terminus; neuronal cell body; myelin sheath	hippocampus development; positive regulation of cAMP-mediated signaling; negative regulation of peptidase activity; spermatid development; response to heat; response to corticosterone; response to organic cyclic compound; positive regulation of mitotic nuclear division; MAPK cascade;	ATP binding; serine-type endopeptidase inhibitor activity; receptor binding; protein kinase binding; mitogen-activated protein kinase binding; nucleotide binding; peptidase inhibitor activity; lipid binding; kinase binding

			response to organonitrogen compound	
Platelet glycoprotein Ib beta chain	synaptic vesicle; axon terminus; synapse		positive regulation of exocytosis; regulation of exocytosis	syntaxin binding; nucleotide binding; GTP binding
Alpha-synuclein	synaptic vesicle; axon terminus; cytoskeleton		regulation of dopamine secretion; dopamine biosynthetic process; response to interleukin-1; positive regulation of peptidyl-serine phosphorylation; activation of cysteine-type endopeptidase activity involved in apoptotic process; synaptic vesicle transport; long-term synaptic potentiation; regulation of neuronal synaptic plasticity; negative regulation of platelet-derived growth factor receptor signaling pathway; response to iron(II) ion	dynein binding; beta-tubulin binding; identical protein binding; magnesium ion binding; cysteine-type endopeptidase inhibitor activity involved in apoptotic process; calcium ion binding; phospholipase binding; arachidonic acid binding; alpha-tubulin binding; copper ion binding
Gamma-enolase	synaptic membrane; neuron projection		glycolytic process; gluconeogenesis; response to organic cyclic compound; response to estradiol; response to drug	magnesium ion binding; protein heterodimerization activity; lyase activity; protein homodimerization activity; phosphopyruvate hydratase activity; metal ion binding
NADH dehydrogenase (Ubiquinone) Fe-S protein 7	synaptic membrane; neuron projection; neuronal cell body		mitochondrial respiratory chain complex I assembly; oxidation-reduction process	quinone binding; iron-sulfur cluster binding; NADH dehydrogenase (ubiquinone) activity; NADH dehydrogenase activity; oxidoreductase activity; 4 iron, 4 sulfur cluster binding; protease binding; metal ion binding

Table 2.. Down-regulated synaptic proteins compared EA to CUMS

Name	cellular component	biological process	molecular function
Potassium voltage-gated channel subfamily D member 2	dendrite; postsynaptic density; neuron projection; voltage-gated potassium channel complex; perikaryon;	protein heterooligomerization; transport; protein homooligomerization; cellular response to hypoxia; transmembrane transport; ion transport; potassium ion transport;	ion channel activity; A-type (transient outward) potassium channel activity; potassium channel activity; protein heterodimerization activity; voltage-gated potassium channel activity;

	cell junction; neuronal cell body membrane	action potential; cardiac muscle cell action potential; potassium ion transmembrane transport	delayed rectifier potassium channel activity; protein binding; voltage-gated ion channel activity; metal ion binding
Protein Neto1	postsynaptic density ; synapse; excitatory synapse; kainate selective glutamate receptor complex	regulation of neuronal synaptic plasticity; regulation of long-term neuronal synaptic plasticity; visual learning; receptor localization to synapse; positive regulation of excitatory postsynaptic potential; memory	ionotropic glutamate receptor binding
Ras-related Rab-8B	protein synaptic vesicle	protein transport; adherens junction organization; protein secretion; vesicle docking involved in exocytosis; positive regulation of cell projection organization; small GTPase mediated signal transduction; transport; cellular response to insulin stimulus; regulation of exocytosis; synaptic vesicle exocytosis	GDP binding; GTPase activity; receptor binding; nucleotide binding; protein binding; TPR domain binding; GTP binding
Protein Sypl1	synaptic vesicle	transport	transporter activity
Protein Syngn3	synaptic vesicle ; synaptic vesicle membrane; synapse	substantia nigra development; positive regulation of transporter activity	SH2 domain binding; protein N-terminus binding
Brefeldin A-inhibited guanine nucleotide- exchange protein 2	dendrite; symmetric synapse; cytoskeleton	positive regulation of tumor necrosis factor production; protein transport; receptor recycling; transport; positive regulation of GTPase activity; regulation of ARF protein signal transduction; exocytosis; endomembrane system organization; Golgi to plasma membrane transport; intracellular signal transduction	guanyl-nucleotide exchange factor activity; GABA receptor binding; myosin binding; protein kinase A regulatory subunit binding; ARF guanyl-nucleotide exchange factor activity; protein binding
Sodium/hydrogen exchanger	dendrite; axon terminus; synapse	neuron projection morphogenesis; sodium ion transport; transport; regulation of pH;	solute:proton antiporter activity; sodium:proton antiporter activity; antiporter activity

regulation of neurotrophin TRK
receptor signaling pathway;
synapse organization;
transmembrane transport;
dendritic spine development;
ion transport;
axon extension

Table 3. Up-regulated mitochondrial proteins compared EA to CUMS

Name	cellular component	biological process	molecular function
NADH dehydrogenase (Ubiquinone) protein 8 (Predicted), isoform CRA a	mitochondrial respiratory chain Fe-S complex I;	mitochondrial respiratory chain complex I;	NADH dehydrogenase (Ubiquinone) Fe-S protein 8 (Predicted), isoform CRA a
NADH dehydrogenase (Ubiquinone) protein 7	mitochondrial respiratory chain Fe-S complex I; synaptic membrane; neuron projection; mitochondrial inner membrane; mitochondrion; neuronal cell body	mitochondrial respiratory chain complex I assembly; oxidation-reduction process	quinone binding; iron-sulfur cluster binding; NADH dehydrogenase (ubiquinone) activity; NADH dehydrogenase activity; oxidoreductase activity; 4 iron, 4 sulfur cluster binding; protease binding; metal ion binding
ATP synthase subunit beta	mitochondrial inner membrane; mitochondrial nucleoid; mitochondrion; plasma membrane; proton-transporting ATP synthase complex, catalytic core F(1); proton-transporting two-sector ATPase complex, catalytic domain; myelin sheath; mitochondrial proton-transporting ATP synthase complex	osteoblast differentiation; angiogenesis; ATP biosynthetic process; transport; ATP synthesis coupled proton transport; regulation of intracellular pH; ion transport; negative regulation of cell adhesion involved in substrate-bound cell migration; lipid metabolic process; ATP hydrolysis coupled proton transport	ATP binding; proton-transporting ATPase activity, rotational mechanism; proton-transporting ATP synthase activity, rotational mechanism; nucleotide binding; MHC class I protein binding; ATPase activity; hydrolase activity, acting on acid anhydrides, catalyzing transmembrane movement of substances
Cytochrome c oxidase subunit 6B1	mitochondrion	hydrogen ion transmembrane transport	cytochrome-c oxidase activity
Pyruvate dehydrogenase component subunit E1	mitochondrion; mitochondrial matrix; pyruvate	glucose metabolic process; metabolic process; carbohydrate metabolic process;	catalytic activity; pyruvate dehydrogenase (acetyl-transferring) activity;

beta, mitochondrial	dehydrogenase complex	tricarboxylic acid cycle; oxidation-reduction process; acetyl-CoA biosynthetic process from pyruvate	oxidoreductase activity; pyruvate dehydrogenase activity
Dihydrolipoamide S-succinyltransferase (E2 component of 2-oxoglutarate complex), isoform CRA a	mitochondrion; oxoglutarate dehydrogenase complex; membrane; myelin sheath	metabolic process; tricarboxylic acid cycle; 2-oxoglutarate metabolic process; NADH metabolic process	chaperone binding; transferase activity; heat shock protein binding; transferase activity, transferring acyl groups; dihydrolipoyllysine-residue succinyltransferase activity
GM2 ganglioside activator	mitochondrion; hydrogen:potassium-exchanging ATPase complex	neurological system process; ganglioside catabolic process; lipid transport; ganglioside metabolic process; membrane fusion; oligosaccharide catabolic process; positive regulation of hydrolase activity; neuromuscular process controlling balance; lipid storage; learning or memory	lipid transporter activity; beta-N-acetylhexosaminidase activity; beta-N-acetylgalactosaminidase activity; phospholipase activator activity; enzyme activator activity
Carboxypeptidase	mitochondrion	proteolysis	serine-type carboxypeptidase activity
Thioredoxin	dendrite; mitochondrion; neuronal cell body; axon	cellular response to glucose stimulus; positive regulation of DNA binding; response to activity; cell redox homeostasis; regulation of protein import into nucleus, translocation; response to drug; cellular response to hyperoxia; response to selenium ion; response to axon injury; sulfate assimilation	thioredoxin-disulfide reductase activity; oxidoreductase activity, acting on a sulfur group of donors, disulfide as acceptor; protein disulfide oxidoreductase activity; enzyme binding
Phosphatidylethanolamine-binding protein 1	synaptic vesicle; neuron projection; mitochondrion; axon terminus; mitochondrial outer membrane; membrane; neuronal cell body; myelin sheath	hippocampus development; positive regulation of cAMP-mediated signaling; negative regulation of peptidase activity; spermatid development; response to heat; response to corticosterone; response to organic cyclic compound; positive regulation of mitotic nuclear	ATP binding; serine-type endopeptidase inhibitor activity; receptor binding; protein kinase binding; mitogen-activated protein kinase binding; nucleotide binding; peptidase inhibitor activity; lipid binding; kinase binding

			division; MAPK cascade; response to organonitrogen compound	
Malate dehydrogenase, mitochondrial	mitochondrial inner membrane; mitochondrion; plasma membrane; myelin sheath; mitochondrial matrix		oxaloacetate metabolic process; carbohydrate metabolic process; tricarboxylic acid cycle; oxidation-reduction process; NADH metabolic process; internal protein amino acid acetylation; malate metabolic process; carboxylic acid metabolic process	catalytic activity; poly(A) RNA binding; L-malate dehydrogenase activity; malate dehydrogenase (NADP+) activity; malate dehydrogenase activity; oxidoreductase activity; protein self-association; protein binding; oxidoreductase activity, acting on the CH-OH group of donors, NAD or NADP as acceptor dihydrolipoyllysine-residue acetyltransferase activity; transferase activity; transferase activity, transferring acyl groups; nucleotide binding
Dihydrolipoyllysine- residue acetyltransferase component of pyruvate dehydrogenase complex, mitochondrial	mitochondrion; myelin sheath; mitochondrial matrix; pyruvate dehydrogenase complex		glucose metabolic process; metabolic process; carbohydrate metabolic process; sleep; tricarboxylic acid cycle; pyruvate metabolic process; acetyl-CoA biosynthetic process from pyruvate	
Protein FAM136A Long-chain fatty acid transport protein 1	mitochondrion mitochondrial inner membrane; mitochondrion; plasma membrane; integral component of membrane		metabolic process; lipid transport; transport; long-chain fatty acid metabolic process; lipid metabolic process; fatty acid transport; fatty acid metabolic process	catalytic activity; fatty acid transporter activity; nucleotide binding; ligase activity; protein binding; long-chain fatty acid-CoA ligase activity; very long-chain fatty acid-CoA ligase activity
Protein Dnajc19	mitochondrial inner membrane; mitochondrion		visual perception; protein import into mitochondrial matrix; positive regulation of ATPase activity; genitalia development	protein transporter activity; ATPase activator activity
ADP-ribosylhydrolase like 2	mitochondrion		metabolic process;	hydrolase activity
Hydroxyacyl glutathione hydrolase	mitochondrion		cellular response to superoxide carbohydrate metabolic process; spermatogenesis; glutathione metabolic process; methylglyoxal catabolic process to D-lactate via S-lactoyl-glutathione	hydroxyacylglutathione hydrolase activity; hydrolase activity
Endophilin-B1	mitochondrion; mitochondrial outer		apoptotic process	lipid binding

Alpha-synuclein	membrane; membrane; autophagosome synaptic vesicle; mitochondrion; axon terminus; cytoskeleton	regulation of dopamine secretion; dopamine biosynthetic process; response to interleukin-1; positive regulation of peptidyl-serine phosphorylation; activation of cysteine-type endopeptidase activity involved in apoptotic process; synaptic vesicle transport; long-term synaptic potentiation; regulation of neuronal synaptic plasticity; negative regulation of platelet-derived growth factor receptor signaling pathway; response to iron(II) ion	dynein binding; beta-tubulin binding; identical protein binding; magnesium ion binding; cysteine-type endopeptidase inhibitor activity involved in apoptotic process; calcium ion binding; phospholipase binding; arachidonic acid binding; alpha-tubulin binding; copper ion binding
Mitochondrial fission regulator 1-like	mitochondrion	mitochondrial fission;	Mitochondrial fission regulator 1-like
1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase delta-1	mitochondrial membrane	response to prostaglandin F; regulation of phospholipase C activity; response to organonitrogen compound; response to aluminum ion; positive regulation of cytosolic calcium ion concentration involved in phospholipase C-activating G-protein coupled signaling pathway; response to hyperoxia; lipid catabolic process; G-protein coupled receptor signaling pathway; signal transduction; positive regulation of inositol trisphosphate biosynthetic process	phosphoric diester hydrolase activity; calcium ion binding; signal transducer activity; phosphatidylinositol phospholipase C activity; phospholipid binding; hydrolase activity; protein binding; phosphatidylinositol-4,5-bisphosphate binding; metal ion binding
Mitochondrial ribosomal protein L4 (Predicted), isoform CRA b	mitochondrion	translation	structural constituent of ribosome; poly(A) RNA binding; RNA binding
Peptidylprolyl isomerase	neuron projection; mitochondrion	positive regulation of ubiquitin-protein transferase activity; metabolic process; negative regulation of cell motility; positive regulation of neuron apoptotic process; negative regulation of neuron	mitogen-activated protein kinase kinase binding; phosphoserine binding; phosphothreonine binding; isomerase activity; protein binding; GTPase activating protein binding;

				apoptotic process; negative regulation of ERK1 and ERK2 cascade; positive regulation of cell growth involved in cardiac muscle cell development; positive regulation of GTPase activity; protein peptidyl-prolyl isomerization; regulation of cytokinesis	peptidyl-prolyl cis-trans isomerase activity
Protein Slirp		mitochondrion; intracellular		spermatid development; mitochondrion morphogenesis; negative regulation of mitochondrial RNA catabolic process; sperm motility; single fertilization	poly(A) RNA binding; nucleotide binding; nucleic acid binding
Mitochondrial import inner membrane translocase subunit Tim13		mitochondrial membrane; mitochondrion	inner	protein transport; transport	metal ion binding

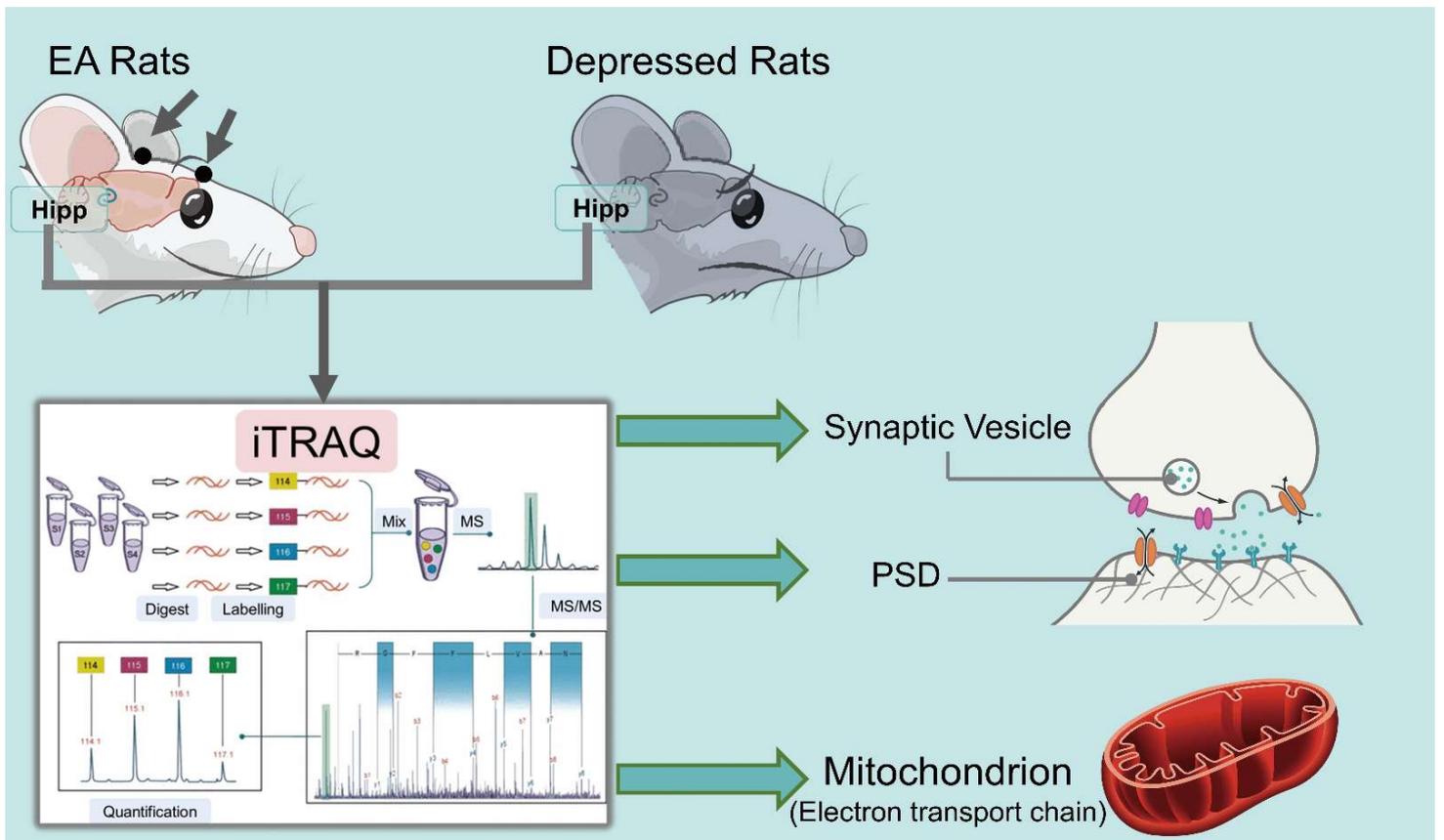
Table 4. Down-regulated mitochondrial proteins compared EA to CUMS

Name	cellular component	biological process	molecular function
NADH-ubiquinone oxidoreductase chain 1	mitochondrial inner membrane; mitochondrion	oxidation-reduction process	NADH dehydrogenase (ubiquinone) activity; oxidoreductase activity
NADH-ubiquinone oxidoreductase chain 4	mitochondrion	oxidation-reduction process; mitochondrial electron transport, NADH to ubiquinone; ATP synthesis coupled electron transport	NADH dehydrogenase (ubiquinone) activity; oxidoreductase activity
NADH-ubiquinone oxidoreductase chain 5	mitochondrial inner membrane; mitochondrion; respiratory chain	oxidation-reduction process; ATP synthesis coupled electron transport	NADH dehydrogenase (ubiquinone) activity; oxidoreductase activity
NADH dehydrogenase [ubiquinone] flavoprotein 3, mitochondrial	mitochondrial respiratory chain complex I; mitochondrial inner membrane; mitochondrion; respiratory chain	oxidation-reduction process	NADH dehydrogenase [ubiquinone] flavoprotein 3, mitochondrial OS=Rattus norvegicus GN=Ndufv3 PE=3 SV=1 - [NDUV3_RAT]
NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9,	mitochondrial respiratory chain complex I;	response to glucose; ubiquinone-6 biosynthetic process; oxidation-reduction process	NADH dehydrogenase activity

mitochondrial	mitochondrion; respiratory chain; mitochondrial matrix					
Cytochrome c oxidase subunit 7B, mitochondrial	mitochondrial membrane; mitochondrion; integral component of membrane; respiratory chain complex IV; mitochondrial respiratory chain	inner	central nervous system development; hydrogen ion transport	transmembrane		cytochrome-c oxidase activity
Cytochrome c oxidase subunit 7C, mitochondrial	mitochondrial membrane; mitochondrion; integral component of membrane	inner	hydrogen ion transport	transmembrane		cytochrome-c oxidase activity
Cytochrome c oxidase subunit 6A1, mitochondrial	mitochondrial membrane; mitochondrion; mitochondrial respiratory chain complex IV	inner	hydrogen ion transport	transmembrane		cytochrome-c oxidase activity
Cytochrome c oxidase subunit 7A2, mitochondrial	mitochondrial membrane; mitochondrion; mitochondrial respiratory chain	inner	hydrogen ion transport	transmembrane		cytochrome-c oxidase activity; electron carrier activity
Phospholipid scramblase 3	mitochondrion; mitochondrial membrane		glucose homeostasis; apoptotic process; phospholipid scrambling; cellular response to lipopolysaccharide; cholesterol homeostasis			phospholipid scramblase activity; SH3 domain binding; calcium-dependent protein binding
Nucleoside diphosphate kinase	mitochondrion		nucleoside phosphorylation; UTP biosynthetic process; phosphorylation; GTP biosynthetic process; CTP biosynthetic process	diphosphate		ATP binding; nucleoside diphosphate kinase activity; kinase activity; transferase activity; nucleotide binding
Protein Tomm7	mitochondrion; integral component of mitochondrial membrane; mitochondrial membrane translocase complex	outer	positive regulation of protein targeting to mitochondrion; protein import into mitochondrial matrix; mitophagy in response to mitochondrial depolarization; protein import into mitochondrial outer membrane;			protein channel activity

Mitochondrial pyruvate carrier 2	mitochondrial membrane; mitochondrion	inner	regulation of protein stability transport; pyruvate transmembrane transport; pyruvate metabolic process; mitochondrial pyruvate transport	pyruvate transmembrane transporter activity
Ras-related protein Rab-8B	synaptic vesicle; mitochondrion		protein transport; adherens junction organization; protein secretion; vesicle docking involved in exocytosis; positive regulation of cell projection organization; small GTPase mediated signal transduction; transport; cellular response to insulin stimulus; regulation of exocytosis; synaptic vesicle exocytosis	GDP binding; GTPase activity; receptor binding; nucleotide binding; protein binding; TPR domain binding; GTP binding
Solute carrier family 25 member 51 Serine/threonine-protein kinase A-Raf	mitochondrial membrane; mitochondrion; cytosol	inner	mitochondrial inner membrane; MAPK cascade; phosphorylation; regulation of proteasomal ubiquitin-dependent protein catabolic process; activation of MAPKK activity; signal transduction; regulation of TOR signaling; protein phosphorylation; intracellular signal transduction	Solute carrier family 25 member 51 protein kinase activity; ATP binding; MAP kinase kinase kinase activity; protein serine/threonine kinase activity; kinase activity; transferase activity; nucleotide binding; receptor signaling protein activity; metal ion binding
Myelin-associated oligodendrocyte basic protein Protein Nars	mitochondrion; myelin sheath mitochondrion		nervous system development asparaginyl-tRNA aminoacylation; tRNA aminoacylation for protein translation; translation	structural constituent of myelin sheath aminoacyl-tRNA ligase activity; ATP binding; asparagine-tRNA ligase activity; nucleotide binding; nucleic acid binding; ligase activity
Mitochondrial fission 1 protein	mitochondrion; integral component of mitochondrial membrane; peroxisome; mitochondrial membrane	outer outer	regulation of mitochondrion organization; positive regulation of protein targeting to membrane; peroxisome fission; positive regulation of mitochondrial calcium ion concentration; positive regulation of cysteine-type endopeptidase activity involved in apoptotic process;	receptor binding

				positive regulation of intrinsic apoptotic signaling pathway; protein homooligomerization; mitochondrion morphogenesis; negative regulation of endoplasmic reticulum calcium ion concentration; protein targeting to mitochondrion
Growth hormone-inducible transmembrane protein	Sodium/hydrogen exchanger	mitochondrial membrane; mitochondrion	inner apoptotic process	
		dendrite; mitochondrion; axon terminus; synapse	neuron projection morphogenesis; sodium ion transport; transport; regulation of pH; regulation of neurotrophin TRK receptor signaling pathway; synapse organization; transmembrane transport; dendritic spine development; ion transport; axon extension	solute:proton antiporter activity; sodium:proton antiporter activity; antiporter activity



Graphic abstract

EA: EA. Hipp, hippocampus. PSD: postsynaptic density.