

# Dynamic interplay between copper toxicity and mitochondrial dysfunction in Alzheimer's Disease

Giusy Tassone<sup>#</sup>, Arian Kola<sup>#</sup>, Daniela Valensin<sup>\*</sup> and Cecilia Pozzi<sup>\*</sup>

Department of Biotechnology, Chemistry and Pharmacy – Department of Excellence 2018-2020, University of Siena, via Aldo Moro 2, Siena, 53100, Italy; [giusy.tassone@unisi.it](mailto:giusy.tassone@unisi.it) (G.T.), [kola2@student.unisi.it](mailto:kola2@student.unisi.it) (A.K.).

<sup>#</sup> These authors contributed equally.

<sup>\*</sup> Correspondence: [daniela.valensin@unisi.it](mailto:daniela.valensin@unisi.it) (D.V.), [pozzi4@unisi.it](mailto:pozzi4@unisi.it) (C.P.); Tel.: +39 0577 232428 (D.V.), +39 0577 232132 (C.P.)

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**Table S1.** Summary of dysregulated mitochondrial proteins (name and acronym, UniProtKB code and gene name) in cortex of copper-exposed mice [1]. Their expression levels are reported as increased (↑) or decreased (↓). Protein alternative names and reference codes are given in Table S2.

Protein name	UniProtKB code ( <i>Mus musculus</i> )	Gene name	Expression level (copper treatment versus control)
NADH dehydrogenase [ubiquinone] flavoprotein 1 (CI-51kD)	Q91YT0	NDUFV1	↑
Cytochrome b-c1 complex subunit 2 (CIII-s2)	Q9DB77	UQCRC2	↑
ATP synthase subunit d (ATPase-d)	Q9DCX2	ATP5PD	↓
75 kDa glucose-regulated protein (GRP75)	P38647	HSPA9	↓
78 kDa glucose-regulated protein (GRP78)	P20029	HSPA5	↓
Aspartate aminotransferase	P05202	Got2	↑
Electron transfer flavoprotein subunit $\alpha$	Q99LC5	ETFA	↑
Dynein light chain	P63168	DYNLL1	↑
Macrophage migration inhibitory factor	P34884	MIF	↑
Dihydropyrimidinase-related protein 2	O08553	DPYSL2	↑
Vesicle-fusing ATPase	P46460	NSF	↓
Isocitrate dehydrogenase [NAD] subunit $\alpha$	Q9D6R2	IDH3A	↓
Myelin basic protein	P04370	MBP	↓

**Table S2.** Summary of protein alternative names and reference codes (UniProtKB and gene name) for the main mitochondrial targets identified by proteomics [1,2] and redox proteomics studies [3–5]. Mouse (*Mus musculus*) and human UniProtKB codes and gene names are given where required.

Protein name	UniProtKB code	Gene name	Alternative protein names
Cytochrome b-c1 complex subunit 2 (CIII-s2)	Q9DB77 ( <i>Mus musculus</i> ) P22695 (human)	UQCRC2 ( <i>Mus musculus</i> , human)	Complex III subunit 2, Core protein II, Ubiquinol-cytochrome-c reductase complex core protein 2
NADH dehydrogenase [ubiquinone] flavoprotein 1 (CI-51kD)	Q91YT0 ( <i>Mus musculus</i> ) P49821 (human)	NDUFV1 ( <i>Mus musculus</i> , human)	Complex I-51kD, NADH-ubiquinone oxidoreductase 51 kDa subunit
ATP synthase subunit d (ATPase-d)	Q9DCX2 ( <i>Mus musculus</i> ) O75947 (human)	ATP5PD ( <i>Mus musculus</i> , human)	ATPase subunit d, ATP synthase peripheral stalk subunit d
75 kDa glucose-regulated protein (GRP75)	P38647 ( <i>Mus musculus</i> ) P38646 (human)	HSPA9 ( <i>Mus musculus</i> , human)	75 kDa glucose-regulated protein, GRP-75, Heat shock 70 kDa protein 9, Mortalin, Peptide-binding protein 74, PBP74, p66 MOT
78 kDa glucose-regulated protein (GRP78)	P20029 ( <i>Mus musculus</i> ) P11021 (human)	HSPA5 ( <i>Mus musculus</i> , human)	78 kDa glucose-regulated protein1, GRP-78, Binding-immunoglobulin protein1, BiP, Heat shock protein 70 family protein 5, HSP70 family protein 5C, Heat shock protein family A member 5, Immunoglobulin heavy chain-binding protein
NADH dehydrogenase [ubiquinone] 1 $\alpha$ subcomplex subunit 1 (CI- $\alpha$ 1)	O35683 ( <i>Mus musculus</i> ) O15239 (human)	NDUFA1 ( <i>Mus musculus</i> , human)	Complex I-MWFE, CI-MWFE, NADH-ubiquinone oxidoreductase MWFE subunit
NADH dehydrogenase [ubiquinone] iron-sulfur protein 2 (CI-49kD)	O75306 ( <i>Mus musculus</i> ) O15239 (human)	NDUFS2 ( <i>Mus musculus</i> , human)	Complex I-49kD, CI-49kD, NADH-ubiquinone oxidoreductase 49 kDa subunit
NADH dehydrogenase [ubiquinone] iron-sulfur protein 8 (CI-23kD)	Q8K3J1 ( <i>Mus musculus</i> ) O00217 (human)	NDUFS8 ( <i>Mus musculus</i> , human)	Complex I-23kD, CI-23kD, NADH-ubiquinone oxidoreductase 23 kDa subunit
Cytochrome b-c1 complex subunit Rieske (CIII-RISP)	Q9CR68 ( <i>Mus musculus</i> ) P47985 (human)	UQCRRF1 ( <i>Mus musculus</i> , human)	Complex III subunit 5, Cytochrome b-c1 complex subunit 5, Rieske iron-sulfur protein, RISP, Rieske protein UQCRRF1, Ubiquinol-cytochrome c reductase iron-sulfur subunit
Cytochrome c oxidase subunit 5A (CIV-COX5A)	P12787 ( <i>Mus musculus</i> ) P47985 (human)	COX5A ( <i>Mus musculus</i> , human)	Cytochrome c oxidase polypeptide Va
Cytochrome c oxidase subunit 5B (CIV-COX5B)	P19536 ( <i>Mus musculus</i> ) P10606 (human)	COX5B ( <i>Mus musculus</i> , human)	Cytochrome c oxidase polypeptide Vb
ATP-Citrate synthase (ATP-CS)	Q91V92 ( <i>Mus musculus</i> ) P53396 (human)	ACLY ( <i>Mus musculus</i> , human)	ATP-citrate (pro-S)-lyase, Citrate cleavage enzyme
Malate dehydrogenase (MDH)	P08249 ( <i>Mus musculus</i> ) P40926 (human)	MDH2 ( <i>Mus musculus</i> , human)	Cytosolic malate dehydrogenase
Pyruvate dehydrogenase E1 component subunit $\alpha$ (PDHE1-A1)	P35486 ( <i>Mus musculus</i> ) P08559 (human)	PDHA1 ( <i>Mus musculus</i> , human)	PDHE1-A type I
Pyruvate dehydrogenase (acetyl-transferring) kinase isoform 2 (PDKII)	Q9JK42 ( <i>Mus musculus</i> ) Q15119 (human)	PDK2 ( <i>Mus musculus</i> , human)	Pyruvate dehydrogenase kinase isoform 2, PDH kinase 2

Creatine kinase U-type (Mia-CK)	P30275 ( <i>Mus musculus</i> ) C9JT96 (human)	CKMT1 ( <i>Mus musculus</i> ) CKMT1A (human)	Acidic-type mitochondrial creatine kinase, Mia-CK, Ubiquitous mitochondrial creatine kinase, U-MtCK
Voltage-dependent anion-selective channel protein 1 (VDAC1)	Q60932 ( <i>Mus musculus</i> ) P21796 (human)	VDAC1 ( <i>Mus musculus</i> , human)	VDAC-1, VDAC1, Outer mitochondrial membrane protein porin 1, Plasmalemmal porin, Porin 31HL, Porin 31HM
Voltage-dependent anion-selective channel protein 2 (VDAC2)	Q60930 ( <i>Mus musculus</i> ) P45880 (human)	VDAC2 ( <i>Mus musculus</i> , human)	VDAC-2, VDAC2, Outer mitochondrial membrane protein porin 2
ADT/ATP translocase 1 (ANT1)	P48962 ( <i>Mus musculus</i> ) P12235 (human)	Slc25a4 ( <i>Mus musculus</i> , human)	ADP,ATP carrier protein 1, ADP,ATP carrier protein, heart/skeletal muscle isoform T1 Adenine nucleotide translocator 1, ANT 1, Solute carrier family 25 member 4
ATP synthase subunit $\alpha$ (ATPase- $\alpha$ )	P25705 (human)	ATP5F1A (human)	ATP synthase F1 subunit $\alpha$
Aconitate hydratase (Aconitase)	Q99798 (human)	ACO2 (human)	Aconitase, Citrate hydro-lyase
Superoxide dismutase [Mn] (MnSOD)	P04179 (human)	SOD2 (human)	

**Table S3.** Summary of dysregulated mitochondrial proteins (protein name, UniProtKB code and gene name) in the hippocampus of copper-exposed 3xTg-AD mice [2]. Their expression levels are reported as increased (↑) or decreased (↓). Protein alternative names and reference codes are given in Table S2.

Protein name	UniProtKB code ( <i>Mus musculus</i> )	Gene name	Expression level (copper treatment versus control)
NADH dehydrogenase [ubiquinone] 1 $\alpha$ subcomplex subunit 1 (CI- $\alpha$ 1)	O35683	NDUFA1	↓
NADH dehydrogenase [ubiquinone] iron-sulfur protein 2 (CI-49kD)	Q91WD5	NDUFS2	↑
NADH dehydrogenase [ubiquinone] iron-sulfur protein 8 (CI-23kD)	Q8K3J1	NDUFS8	↓
Creatine kinase U-type (Mia-CK)	P30275	CKMT1	↑
ATP-Citrate synthase (ATP-CS)	Q91V92	ACLY	↑
Malate dehydrogenase (MDH)	P08249	MDH2	↑
Pyruvate dehydrogenase E1 component subunit $\alpha$ (PDHE1-A1)	P35486	PDHA1	↓
Pyruvate dehydrogenase (acetyl-transferring) kinase isozyme 2 (PDKII)	Q9JK42	PDK2	↑
Cytochrome b-c1 complex subunit Rieske (CIII-RISP)	Q9CR68	UQCRCF1	↓
Cytochrome c oxidase subunit 5A (CIV-COX5A)	P12787	COX5A	↓
Cytochrome c oxidase subunit 5B (CIV-COX5B)	P19536	COX5B	↓
ATP synthase subunit d (ATPase-d)	Q9DCX2	ATP5PD	↓
Voltage-dependent anion-selective channel protein 1 (VDAC1)	Q60932	VDAC1	↓
Voltage-dependent anion-selective channel protein 2 (VDAC2)	Q60930	VDAC2	↓
Elongation factor 1- $\alpha$ 1	P10126	EEF1A1	↑
Vesicle-fusing ATPase	P46460	NSF	↑
Actin, aortic smooth muscle	P62737	ACTA2	↑
Actin, cytoplasmatic 1	P60710	ACTB	↑
Dihydropyrimidinase-related protein 2	O08553	DPYSL2	↑
Mitogen-activated protein kinase 1	P63085	MAPK1	↑
Flotillin-1	O08917	FLOT1	↑
$\alpha$ -enolase	P17182	ENO1	↑
LIM and SH3 domain protein 1	Q61792	LASP1	↑
Septin-6	Q9R1T4	SEPTIN6	↓

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