

## Supplementary Materials

### S1. Results

#### S1.1. Differentially Expressed Pathways in HFD-Fed AKO Compared to HFD-fed WT Mice

Using Reactome molecular pathway analysis, we determined the differentially expressed pathways in HFD-fed AKO mice compared to HFD-fed WT mice ( $FDR \leq 0.01$ ). There were 39 pathways in total. 9 of these pathways were unrelated to ribosomal protein subunits and were examined further for transcript function (Supplemental Table S1). These 9 differentially expressed pathways were related to metabolism. Transcripts associated with the electron transport chain [1–8] and citric acid cycle [9–12] were downregulated and upregulated, respectively. Transcripts associated with Golgi transport were upregulated [13–45]. Transcripts relating to mRNA polyadenylation were upregulated [46–51]. Transcripts relating to Wnt/ $\beta$ -Catenin signaling were upregulated [52–57].

**Supplemental Table S1.** Differentially Expressed Pathways in HFD-fed AKO Compared to HFD-fed WT Mice. Pathways with  $FDR \leq 0.01$  are displayed. Pathway name, stable identifier, log fold change ( $\log_2$ ), and false discovery rate for each pathway are displayed. Within each pathway, gene ID, Ensembl ID, gene description, log fold change ( $\log_2$ ),  $\log_{10}$  adjusted  $p$ -value, and relevant known function are displayed.

Reactome Pathway	Gene Symbol	Ensembl ID	Gene Description	Log FC	$p_{adj}$	Known Function
Formation of ATP by chemiosmotic coupling (R-HSA-163210) LFC: -0.13 FDR: $2.40 \times 10^{-4}$	<i>Atp5j2</i> <i>Atp5h</i>	ENSMUST0000161741 ENSMUST0000043931	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit F2 ATP synthase, H+ transporting, mitochondrial F0 complex, subunit D	-0.27 - 0.26	$1.82 \times 10^{-2}$ $3.98 \times 10^{-2}$	Inhibition is neuroprotective in aging and AD [58]
Cristae formation (R-HSA-8949613) LFC: -0.09 FDR: $6.07 \times 10^{-3}$	<i>Atp5j2</i> <i>Atp5h</i>	ENSMUST0000161741 ENSMUST0000043931	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit F2 ATP synthase, H+ transporting, mitochondrial F0 complex, subunit D	-0.27 - 0.26	$1.82 \times 10^{-2}$ $3.98 \times 10^{-2}$	Inhibition is neuroprotective in aging and AD [58]
	<i>Hspa9</i>	ENSMUST0000025217	Heat shock protein 9	0.28	$1.69 \times 10^{-2}$	Oxidative stress sensor [59], Downregulated in AD brain [60]
	<i>Samm50</i>	ENSMUST0000023071	SAMM50 sorting and assembly machinery component	0.37	$1.12 \times 10^{-2}$	Negative regulator of mitochondrial fragmentation [61]
Complex I biogenesis (R-HSA-6799198) LFC: -0.04 FDR: $3.00 \times 10^{-4}$	<i>Ndufb2</i> <i>Ndufb4</i> <i>Ndufb11</i> <i>Ndufs8</i> <i>Ndufa4</i> <i>Ndufb9</i> <i>Ndufa2</i>	ENSMUST0000119379 ENSMUST0000119379 ENSMUST0000119379 ENSMUST0000023514 ENSMUST0000116621 ENSMUST0000116621 ENSMUST0000237341 ENSMUST0000204978 ENSMUST0000022980 ENSMUST0000014438	NADH:ubiquinone oxidoreductase subunit B2 NADH:ubiquinone oxidoreductase subunit B4 NADH:ubiquinone oxidoreductase subunit B11 NADH:ubiquinone oxidoreductase core subunit S8 Ndufa4, mitochondrial complex associated NADH:ubiquinone oxidoreductase subunit B9 NADH:ubiquinone oxidoreductase subunit A2	-0.32 - 0.29 - 0.28 - 0.27 - 0.25 - 0.23 - 0.20	$2.39 \times 10^{-2}$ $2.89 \times 10^{-2}$ $3.32 \times 10^{-2}$ $4.63 \times 10^{-2}$ $4.69 \times 10^{-2}$ $4.16 \times 10^{-2}$ $4.83 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]

	<i>mt-Nd3</i>	ENSMUST0000082411	Mitochondrially encoded NADH dehydrogenase 3	-0.23	$4.06 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>Acad9</i>	ENSMUST0000011492	Acyl-Coenzyme A dehydrogenase family, member 9	0.29	$2.59 \times 10^{-2}$	Role in fatty acid oxidation, downregulation associated with neurological disease [2]
	<i>Timmdc1</i>	ENSMUST0000002925	Translocase of inner mitochondrial membrane domain containing 1	0.36	$9.17 \times 10^{-3}$	Loss is associated with axonal neuropathy and cognitive decline [3]
Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins (R-HSA-163200) LFC: -0.04 FDR: $8.45 \times 10^{-7}$	<i>Ndufb2</i> <i>Ndufb4</i> <i>Ndufb11</i> <i>Ndufs8</i> <i>Ndufa4</i> <i>Ndufb9</i> <i>Ndufa2</i>	ENSMUST0000119379 ENSMUST0000023514 ENSMUST0000116621 ENSMUST0000237341 ENSMUST0000204978 ENSMUST0000022980 ENSMUST0000014438	NADH:ubiquinone oxidoreductase subunit B2 NADH:ubiquinone oxidoreductase subunit B4 NADH:ubiquinone oxidoreductase subunit B11 NADH:ubiquinone oxidoreductase core subunit S8 Ndufa4, mitochondrial complex associated NADH:ubiquinone oxidoreductase subunit B9 NADH:ubiquinone oxidoreductase subunit A2	-0.32 - 0.29 - 0.28 - 0.27 - 0.25 - 0.23 - 0.20	$2.39 \times 10^{-2}$ $2.89 \times 10^{-2}$ $3.32 \times 10^{-2}$ $4.63 \times 10^{-2}$ $4.69 \times 10^{-2}$ $4.16 \times 10^{-2}$ $4.83 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>Cox7b</i>	ENSMUST0000033582	Cytochrome c oxidase subunit 7B	-0.31	$1.13 \times 10^{-2}$	Loss leads to decrease in oxidative stress and amyloid formation in AD mice [4]
	<i>Uqcrh</i>	ENSMUST0000078676	Ubiquinol-cytochrome c reductase hinge protein	-0.29	$3.04 \times 10^{-2}$	Positive regulator of apoptosis via cytochrome c release [5]
	<i>Atp5j2</i> <i>Atp5h</i>	ENSMUST0000161741 ENSMUST0000043931	ATP synthase, H <sup>+</sup> transporting, mitochondrial F0 complex, subunit F2 ATP synthase, H <sup>+</sup> transporting, mitochondrial F0 complex, subunit D	-0.27 - 0.26	$1.82 \times 10^{-2}$ $3.98 \times 10^{-2}$	Inhibition is neuroprotective in aging and AD [58]
	<i>mt-Nd3</i>	ENSMUST0000082411	Mitochondrially encoded NADH dehydrogenase 3	-0.23	$4.06 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>mt-Co3</i>	ENSMUST0000082409	Mitochondrially encoded cytochrome c oxidase III	-0.21	$3.87 \times 10^{-2}$	Loss leads to decrease in oxidative stress and amyloid formation in AD mice [4]
	<i>mt-Cytb</i>	ENSMUST0000082421	Mitochondrially encoded cytochrome b	0.21	$4.53 \times 10^{-2}$	Decreased in AD brain [6]
	<i>Acad9</i>	ENSMUST0000011492	Acyl-Coenzyme A dehydrogenase family, member 9	0.29	$2.59 \times 10^{-2}$	Role in fatty acid oxidation, downregulation associated with neurological disease [2]
	<i>Sdha</i>	ENSMUST0000022062	Succinate dehydrogenase complex, subunit A, flavoprotein (Fp)	0.29	$1.02 \times 10^{-2}$	Downregulation is associated with oxidative stress and insulin resistance [7]
	<i>Timmdc1</i>	ENSMUST0000002925	Translocase of inner mitochondrial membrane domain containing 1	0.36	$9.17 \times 10^{-3}$	Loss is associated with axonal neuropathy and cognitive decline [3]
	<i>Taco1</i>	ENSMUST0000002048	Translational activator of mitochondrially encoded cytochrome c oxidase I	0.40	$3.68 \times 10^{-2}$	Loss associated with motor dysfunction and mitochondrial disease in mice [8]

Respiratory electron transport (R-HSA-611105) LFC: -0.03 FDR: $2.92 \times 10^{-5}$	<i>Ndufb2</i>	ENSMUST0000119379	NADH:ubiquinone oxidoreductase subunit B2	-0.32 - 0.29 -	$2.39 \times 10^{-2}$ $2.89 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>Ndufb4</i>	ENSMUST0000023514	NADH:ubiquinone oxidoreductase subunit B4	0.28 - 0.27 -	$3.32 \times 10^{-2}$ $4.63 \times 10^{-2}$	
	<i>Ndufb11</i>	ENSMUST0000116621	NADH:ubiquinone oxidoreductase subunit B11	0.25 - 0.23 -	$4.69 \times 10^{-2}$ $4.16 \times 10^{-2}$	
	<i>Ndufs8</i>	ENSMUST0000237341	NADH:ubiquinone oxidoreductase subunit S8	0.20	$4.83 \times 10^{-2}$	
	<i>Ndufa4</i>	ENSMUST0000204978	Ndufa4, mitochondrial complex associated			
	<i>Ndufb9</i>	ENSMUST0000022980	NADH:ubiquinone oxidoreductase subunit B9			
	<i>Ndufa2</i>	ENSMUST0000014438	NADH:ubiquinone oxidoreductase subunit A2			
	<i>Cox7b</i>	ENSMUST0000033582	Cytochrome c oxidase subunit 7B	-0.31	$1.13 \times 10^{-2}$	
	<i>Uqcrrh</i>	ENSMUST0000078676	Ubiquinol-cytochrome c reductase hinge protein	-0.29	$3.04 \times 10^{-2}$	
	<i>mt-Nd3</i>	ENSMUST0000082411	Mitochondrially encoded NADH dehydrogenase 3	-0.23	$4.06 \times 10^{-2}$	
The citric acid (TCA) cycle and respiratory electron transport (R-HSA-1428517) LFC: 0.03 FDR: $2.71 \times 10^{-3}$	<i>mt-Co3</i>	ENSMUST0000082409	Mitochondrially encoded cytochrome c oxidase III	-0.21	$3.87 \times 10^{-2}$	Loss leads to decrease in oxidative stress and amyloid formation in AD mice [4]
	<i>mt-Cytb</i>	ENSMUST0000082421	Mitochondrially encoded cytochrome b	0.21	$4.53 \times 10^{-2}$	Positive regulator of apoptosis via cytochrome c release [5]
	<i>Acad9</i>	ENSMUST0000011492	Acyl-Coenzyme A dehydrogenase family, member 9	0.29	$2.59 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>Sdha</i>	ENSMUST0000022062	Succinate dehydrogenase complex, subunit A, flavoprotein (Fp)	0.29	$1.02 \times 10^{-2}$	Loss leads to decrease in oxidative stress and amyloid formation in AD mice [4]
	<i>Timmdc1</i>	ENSMUST0000002925	Translocase of inner mitochondrial membrane domain containing 1	0.36	$9.17 \times 10^{-3}$	Decreased in AD brain [6]
	<i>Taco1</i>	ENSMUST0000002048	Translational activator of mitochondrially encoded cytochrome c oxidase I	0.40	$3.68 \times 10^{-2}$	Role in fatty acid oxidation, downregulation associated with neurological disease [2]
						Downregulation is associated with oxidative stress and insulin resistance [7]
						Loss is associated with axonal neuropathy and cognitive decline [3]
						Loss associated with motor dysfunction and mitochondrial disease in mice [8]
The citric acid (TCA) cycle and respiratory electron transport (R-HSA-1428517) LFC: 0.03 FDR: $2.71 \times 10^{-3}$	<i>Ndufb2</i>	ENSMUST0000119379	NADH:ubiquinone oxidoreductase subunit B2	-0.32 - 0.29 -	$2.39 \times 10^{-2}$ $2.89 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>Ndufb4</i>	ENSMUST0000023514	NADH:ubiquinone oxidoreductase subunit B4	0.28 - 0.27 -	$3.32 \times 10^{-2}$ $4.63 \times 10^{-2}$	
	<i>Ndufb11</i>	ENSMUST0000116621	NADH:ubiquinone oxidoreductase subunit B11	0.25 - 0.23 -	$4.69 \times 10^{-2}$ $4.16 \times 10^{-2}$	
	<i>Ndufs8</i>	ENSMUST0000237341	NADH:ubiquinone oxidoreductase subunit S8	0.20	$4.83 \times 10^{-2}$	
	<i>Ndufa4</i>	ENSMUST0000204978	Ndufa4, mitochondrial complex associated			
	<i>Ndufb9</i>	ENSMUST0000022980	NADH:ubiquinone oxidoreductase subunit B9			
	<i>Ndufa2</i>	ENSMUST0000014438	NADH:ubiquinone oxidoreductase subunit A2			
	<i>Cox7b</i>	ENSMUST0000033582	Cytochrome c oxidase subunit 7B	-0.31	$1.13 \times 10^{-2}$	

	<i>Uqcrrh</i>	ENSMUST0000078676	Ubiquinol-cytochrome c reductase hinge protein	-0.29	$3.04 \times 10^{-2}$	Positive regulator of apoptosis via cytochrome c release [5]
	<i>Atp5j2</i> <i>Atp5h</i>	ENSMUST0000161741 ENSMUST0000043931	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit F2 ATP synthase, H+ transporting, mitochondrial F0 complex, subunit D	-0.27 - 0.26	$1.82 \times 10^{-2}$ $3.98 \times 10^{-2}$	Inhibition is neuroprotective in aging and AD [58]
	<i>mt-Nd3</i>	ENSMUST0000082411	Mitochondrially encoded NADH dehydrogenase 3	-0.23	$4.06 \times 10^{-2}$	Partial inhibition of Complex I leads to reduced oxidative stress and increased long-term potentiation in AD mice [1]
	<i>mt-Co3</i>	ENSMUST0000082409	Mitochondrially encoded cytochrome c oxidase III	-0.21	$3.87 \times 10^{-2}$	Loss leads to decrease in oxidative stress and amyloid formation in AD mice [4]
	<i>mt-Cytb</i>	ENSMUST0000082421	Mitochondrially encoded cytochrome b	0.21	$4.53 \times 10^{-2}$	Decreased in AD brain [6]
	<i>Acad9</i>	ENSMUST0000011492	Acyl-Coenzyme A dehydrogenase family, member 9	0.29	$2.59 \times 10^{-2}$	Role in fatty acid oxidation, downregulation associated with neurological disease [2]
	<i>Aco2</i>	ENSMUST0000023116	Aconitase 2, mitochondrial	0.29	$1.42 \times 10^{-2}$	Suppressed by nitric oxide (Palmieri et al., 2020), Decreased in AD patient lymphocytes [9]
	<i>Sdha</i>	ENSMUST0000022062	Succinate dehydrogenase complex, subunit A, flavoprotein (Fp)	0.29	$1.02 \times 10^{-2}$	Downregulation is associated with oxidative stress and insulin resistance [7]
	<i>Ogdh</i>	ENSMUST0000003461	Oxoglutarate (alpha-ketoglutarate) dehydrogenase (lipoamide)	0.30	$3.73 \times 10^{-2}$	Inhibited by lipopolysaccharide and IFN- $\gamma$ stimulation in macrophages [10]
	<i>Cs</i>	ENSMUST0000005826	Citrate synthase	0.32	$1.53 \times 10^{-2}$	Downregulated in AD patient platelets [11]
	<i>Pdk2</i>	ENSMUST0000038431	Pyruvate dehydrogenase kinase, isoenzyme 2	0.35	$4.52 \times 10^{-2}$	mRNA levels modulated during aging in brain [12]
	<i>Timmdc1</i>	ENSMUST0000002925	Translocase of inner mitochondrial membrane domain containing 1	0.36	$9.17 \times 10^{-3}$	Loss is associated with axonal neuropathy and cognitive decline [3]
	<i>Taco1</i>	ENSMUST0000002048	Translational activator of mitochondrially encoded cytochrome c oxidase I	0.40	$3.68 \times 10^{-2}$	Loss associated with motor dysfunction and mitochondrial disease in mice [8]
Transport to the Golgi and subsequent modification (R-HSA-948021) LFC: 0.27 FDR: $5.71 \times 10^{-3}$	<i>Arcn1</i>	ENSMUST0000034607	Archain 1	0.24	$2.71 \times 10^{-2}$	Loss is associated with increased ER stress [13]
	<i>Dctn4</i> <i>Dctn5</i> <i>Dctn1</i>	ENSMUST0000025505 ENSMUST0000033156 ENSMUST0000113919	Dynactin 4 Dynactin 5 Dynactin 1	0.25 0.30 0.56	$4.42 \times 10^{-2}$ $2.38 \times 10^{-2}$ $2.10 \times 10^{-2}$	Positive regulators of retrograde axonal transport, decreased activity associated with neurodegeneration [14]
	<i>Ykt6</i>	ENSMUST0000002818	YKT6 v-SNARE homolog (S. cerevisiae)	0.26	$1.97 \times 10^{-2}$	Negative regulator of $\alpha$ -synuclein, downregulated in PD brain [15]
	<i>Kdelr2</i>	ENSMUST0000110731	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 2	0.27	$4.30 \times 10^{-2}$	Regulator of ER proteome homeostasis in response to ER stress [16]

<i>Man1a2</i> <i>Man2a2</i>	ENSMUST0 0000008907 ENSMUST0 0000098346	Mannosidase, alpha, class 1A, member 2 Mannosidase 2, alpha 2	0.28 0.65	$3.16 \times 10^{-2}$ $1.70 \times 10^{-2}$	Regulators of N- glycosylation [17]
<i>Copz1</i> <i>Copg1</i>	ENSMUST0 0000100162 ENSMUST0 0000113607	Coatomer protein complex, subunit zeta 1 Coatomer protein complex, subunit gamma 1	0.30 0.46	$1.59 \times 10^{-2}$ $4.97 \times 10^{-3}$	Positive regulators of neurite outgrowth [18]
<i>Tbc1d20</i>	ENSMUST0 0000028963	TBC1 domain family, member 20	0.32	$4.24 \times 10^{-2}$	Downregulation leads to disrupted neuronal autophagic flux and motor dysfunction [19]
<i>Cog4</i> <i>Cog1</i>	ENSMUST0 0000034203 ENSMUST0 0000018805	Component of oligomeric golgi complex 4 Component of oligomeric golgi complex 1	0.34 0.44	$1.62 \times 10^{-2}$ $8.60 \times 10^{-3}$	Regulator of Golgi vesicle trafficking, defects are associated with neurological disorders [20]
<i>Gosr2</i> <i>Gosr1</i>	ENSMUST0 0000021329 ENSMUST0 0000010536	Golgi SNAP receptor complex member 2 Golgi SNAP receptor complex member 1	0.35 0.38	$9.17 \times 10^{-3}$ $6.24 \times 10^{-3}$	Regulator of ER to Golgi trafficking, dysregulation associated with neurological disorders [21]
<i>Dynll2</i> <i>Dync1li1</i> <i>Dync1h1</i>	ENSMUST0 0000020775 ENSMUST0 0000047404 ENSMUST0 0000018851	Dynein light chain LC8-type 2 Dynein cytoplasmic 1 light intermediate chain 1 Dynein cytoplasmic 1 heavy chain 1	0.36 0.38 0.50	$5.25 \times 10^{-3}$ $7.11 \times 10^{-3}$ $1.28 \times 10^{-2}$	Positive regulators of retrograde axonal transport [22], Downregulated in AD hippocampus [23]
<i>Sec22b</i> <i>Sec24b</i> <i>Sec31a</i> <i>Sec24c</i> <i>Sec22c</i>	ENSMUST0 0000029476 ENSMUST0 0000001079 ENSMUST0 0000094578 ENSMUST0 0000048657 ENSMUST0 0000078547	SEC22 homolog B, vesicle trafficking protein Sec24 related gene family, member B (S. cerevisiae) Sec31 homolog A (S. cerevisiae) Sec24 related gene family, member C (S. cerevisiae) SEC22 homolog C, vesicle trafficking protein	0.36 0.40 0.46 0.49 0.82	$3.74 \times 10^{-2}$ $9.12 \times 10^{-3}$ $7.12 \times 10^{-3}$ $1.35 \times 10^{-2}$ $3.28 \times 10^{-3}$	Regulators of vesicle trafficking, downregulated in aging and AD brains [24], Loss leads to neuronal apoptotic cell death [25]
<i>Tmed9</i>	ENSMUST0 0000109905	Transmembrane p24 trafficking protein 9	0.38	$1.50 \times 10^{-2}$	Positive regulator of autophagosome biogenesis [26]
<i>Napa</i>	ENSMUST0 0000006181	N-ethylmaleimide sensitive fusion protein attachment protein alpha	0.41	$2.59 \times 10^{-2}$	Loss leads to impairment of Golgi to ER trafficking and apoptosis [27]
<i>Actr1a</i>	ENSMUST0 0000040270	ARP1 actin-related protein 1A, centractin alpha	0.41	$4.56 \times 10^{-3}$	Positive regulator of retrograde axonal transport [28]
<i>Trappc5</i> <i>Trappc9</i>	ENSMUST0 0000044857 ENSMUST0 0000089770	Trafficking protein particle complex 5 Trafficking protein particle complex 9	0.42 0.43	$6.44 \times 10^{-3}$ $3.92 \times 10^{-2}$	Loss leads to decreased social memory and obesity in mice [29]
<i>Tubb6</i> <i>Tuba4a</i>	ENSMUST0 0000001513 ENSMUST0 0000186213	Tubulin, beta 6 class V Tubulin, alpha 4A	0.45 0.52	$4.40 \times 10^{-2}$ $8.60 \times 10^{-3}$	Downregulation leads to motor axon defects [30]
<i>Tmem115</i>	ENSMUST0 0000010189	Transmembrane protein 115	0.45	$7.28 \times 10^{-3}$	Regulator of Golgi to ER retrograde transport [31]
<i>Arfgap1</i>	ENSMUST0 0000029092	ADP-ribosylation factor GTPase activating protein 1	0.46	$1.28 \times 10^{-2}$	Regulator of targeting of GABA transporter 1 in axon terminals [32]

	<i>Mgat4b</i> <i>Mgat5</i>	ENSMUST0 0000041725 ENSMUST0 0000038361	Mannoside acetylglucosaminyltransferase 4, isoenzyme B Mannoside acetylglucosaminyltransferase 5	0.47 0.70	$1.50 \times 10^{-2}$ $3.81 \times 10^{-3}$	Negative regulators of spontaneous inflammatory demyelination and neurodegeneration [33]
	<i>B4gal13</i> <i>B4gal16</i> <i>B4gal15</i>	ENSMUST0 0000064272 ENSMUST0 0000070080 ENSMUST0 0000109221	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 3 UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 6 UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 5	0.48 0.57 0.62	$3.60 \times 10^{-2}$ $4.56 \times 10^{-3}$ $3.27 \times 10^{-3}$	Regulators of inflammatory cytokine response in LPS- treated microglia [34]
	<i>Uso1</i>	ENSMUST0 0000031355	USO1 vesicle docking factor	0.50	$9.05 \times 10^{-3}$	Positive regulator of ER to Golgi transport [35]
	<i>St8sia3</i>	ENSMUST0 0000025477	ST8 alpha-N-acetyl- neuraminide alpha-2,8- sialyltransferase 3	0.52	$5.84 \times 10^{-3}$	Regulator of dopamine D1R and D2R receptors, downregulated in neurodegenerative disease [36]
	<i>Cnih3</i>	ENSMUST0 0000027795	Cornichon family AMPA receptor auxiliary protein 3	0.54	$2.00 \times 10^{-2}$	Positive regulator of hippocampal AMPAR synaptic transmission [37]
	<i>Arf3</i>	ENSMUST0 0000053183	ADP-ribosylation factor 3	0.56	$7.12 \times 10^{-2}$	Paralog ARF6 mediates BACE1 and APP processing [38]
	<i>Ppp6r1</i>	ENSMUST0 0000064099	Protein phosphatase 6, regulatory subunit 1	0.56	$4.91 \times 10^{-3}$	Negative regulator of NF- $\kappa$ B signaling [39]
	<i>Nsf</i>	ENSMUST0 0000103075	N-ethylmaleimide sensitive fusion protein	0.59	$2.66 \times 10^{-2}$	Positive regulator of synaptic AMPA receptor function [40]
	<i>Sptbn2</i> <i>Sptbn1</i>	ENSMUST0 0000008991 ENSMUST0 0000011877	Spectrin beta, non- erythrocytic 2 Spectrin beta, non- erythrocytic 1	0.62 0.85	$7.88 \times 10^{-3}$ $4.89 \times 10^{-3}$	Loss leads to decrease in dendritic spine density and neurodegeneration [41]
	<i>Csnk1d</i>	ENSMUST0 0000070575	Casein kinase 1, delta	0.65	$5.83 \times 10^{-3}$	Positive regulator of Wnt/ $\beta$ - catenin signaling [42]
	<i>Lman2</i> <i>Lman2l</i>	ENSMUST0 0000021940 ENSMUST0 0000125304	Lectin, mannose-binding 2 Lectin, mannose-binding 2- like	0.69 0.86	$5.30 \times 10^{-3}$ $5.07 \times 10^{-3}$	Regulator of glycoprotein transport and sorting, dysregulation associated with neurodegenerative disease [43]
	<i>Gbf1</i>	ENSMUST0 0000026254	Golgi-specific brefeldin A- resistance factor 1	0.69	$7.23 \times 10^{-3}$	Dysregulation associated with Golgi fragmentation [44]
	<i>Fut8</i>	ENSMUST0 0000062804	Fucosyltransferase 8	0.84	$3.62 \times 10^{-3}$	Loss leads to increased microgliosis under LPS stimulation [45]
Processing of Intronless Pre- mRNAs (R-HSA-77595) LFC: 0.29 FDR: $7.79 \times 10^{-3}$	<i>Cstf2</i> <i>Cstf1</i> <i>Cstf2t</i>	ENSMUST0 0000113286 ENSMUST0 0000116375 ENSMUST0 0000066039	Cleavage stimulation factor, 3' pre-RNA subunit 2 Cleavage stimulation factor, 3' pre-RNA, subunit Cleavage stimulation factor, 3' pre- RNA subunit 2, tau	-0.70 0.33 0.34	$3.86 \times 10^{-2}$ $1.41 \times 10^{-2}$ $1.29 \times 10^{-2}$	Positive regulators of 3' cleavage and polyadenylation [46]
	<i>Nudt21</i>	ENSMUST0 0000034204	Nudix (nucleoside diphosphate linked moiety X)-type motif 21	0.23	$2.59 \times 10^{-2}$	Loss leads to dysregulated hippocampal alternative polyadenylation and learning deficits [47]

	<i>Ncbp1</i> <i>Ncbp2</i>	ENSMUST0 0000030014 ENSMUST0 0000023460	Nuclear cap binding protein subunit 1 Nuclear cap binding protein subunit 2	0.25 0.28	$3.87 \times 10^{-2}$ $1.48 \times 10^{-2}$	Positive regulator of mRNA export from the nucleus [48]
	<i>Cpsf7</i> <i>Cpsf2</i>	ENSMUST0 0000038379 ENSMUST0 0000047357	Cleavage and polyadenylation specific factor 7 Cleavage and polyadenylation specific factor 2	0.28 0.34	$2.41 \times 10^{-2}$ $1.26 \times 10^{-2}$	Positive regulators of 3' cleavage and polyadenylation [46]
	<i>Wdr33</i>	ENSMUST0 0000025264	WD repeat domain 33	0.29	$2.75 \times 10^{-2}$	Positive regulator of polyadenylation signal recognition [49]
	<i>Papola</i>	ENSMUST0 0000109901	Poly (A) polymerase alpha	0.39	$3.72 \times 10^{-2}$	Positive regulator of polyadenylation [46]
	<i>Sympk</i>	ENSMUST0 0000023882	Symplekin	0.48	$7.15 \times 10^{-3}$	Positive regulator of polyadenylation [50], Downregulated in AD brain [51]
Disassembly of the destruction complex and recruitment of AXIN to the membrane (R-HSA-4641262) LFC: 0.38 FDR: $7.21 \times 10^{-3}$	<i>Ppp2cb</i> <i>Ppp2r5a</i> <i>Ppp2r5e</i> <i>Ppp2r1a</i>	ENSMUST0 0000009774 ENSMUST0 0000067976 ENSMUST0 0000021447 ENSMUST0 0000007708	Protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform Protein phosphatase 2, regulatory subunit B', alpha Protein phosphatase 2, regulatory subunit B', epsilon Protein phosphatase 2, regulatory subunit A, alpha	0.25 0.26 0.31 0.37	$1.94 \times 10^{-2}$ $4.25 \times 10^{-2}$ $2.85 \times 10^{-2}$ $3.87 \times 10^{-2}$	Positive regulator of Wnt/ $\beta$ - catenin signaling [52], Inhibition leads to spatial memory impairment [53]
	<i>Csnk1a1</i> <i>Csnk1g2</i>	ENSMUST0 0000165123 ENSMUST0 0000085435	Casein kinase 1, alpha 1 Casein kinase 1, gamma 2	0.26 0.33	$3.90 \times 10^{-2}$ $4.73 \times 10^{-2}$	Negative regulators of SMAD3 and TGF- $\beta$ signaling [54]
	<i>Ctnnb1</i>	ENSMUST0 0000007130	Catenin (cadherin associated protein), beta 1	0.37	$1.38 \times 10^{-2}$	Positive regulator of Wnt/ $\beta$ - catenin signaling, neuronal survival and synaptic plasticity, negative regulator of A $\beta$ production [55]
	<i>Gsk3b</i>	ENSMUST0 0000023507	Glycogen synthase kinase 3 beta	0.52	$3.62 \times 10^{-3}$	Regulator of Wnt/ $\beta$ -catenin signaling, loss leads to synaptic and social defects in mice [56]
	<i>Dvl3</i>	ENSMUST0 0000003318	Dishevelled segment polarity protein 3	0.72	$2.23 \times 10^{-2}$	Positive regulator of Wnt/ $\beta$ - catenin signaling, downregulated in AD brain [55]
	<i>Fzd1</i>	ENSMUST0 0000054294	Frizzled class receptor 1	0.73	$3.81 \times 10^{-3}$	Positive regulator of Wnt/ $\beta$ - catenin signaling, loss leads to impairment of neuronal differentiation [57]

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