

Supplementary Information

Investigating neuron degeneration in Huntington's disease using RNA-seq based transcriptome study

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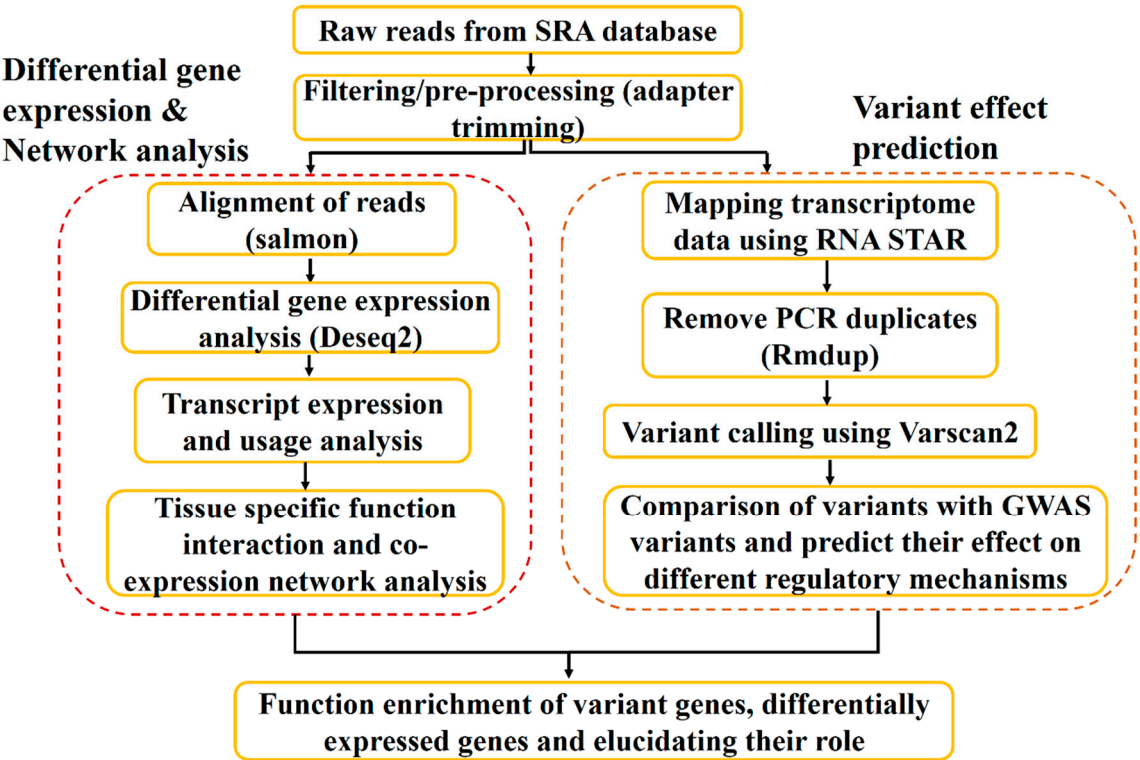
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Supplementary Table S1: Dataset used for meta data analysis

Samples	Count	Age	Post-Mortem Interval (Hours)
Controls	7	42-64	6-24
HD_samples	7	44-69	0-22



Supplementary Figure S1: Workflow for identifying the variants and differentially expressed genes/transcripts

Supplementary Table S2: Genes identified using DTE/ DTU analysis

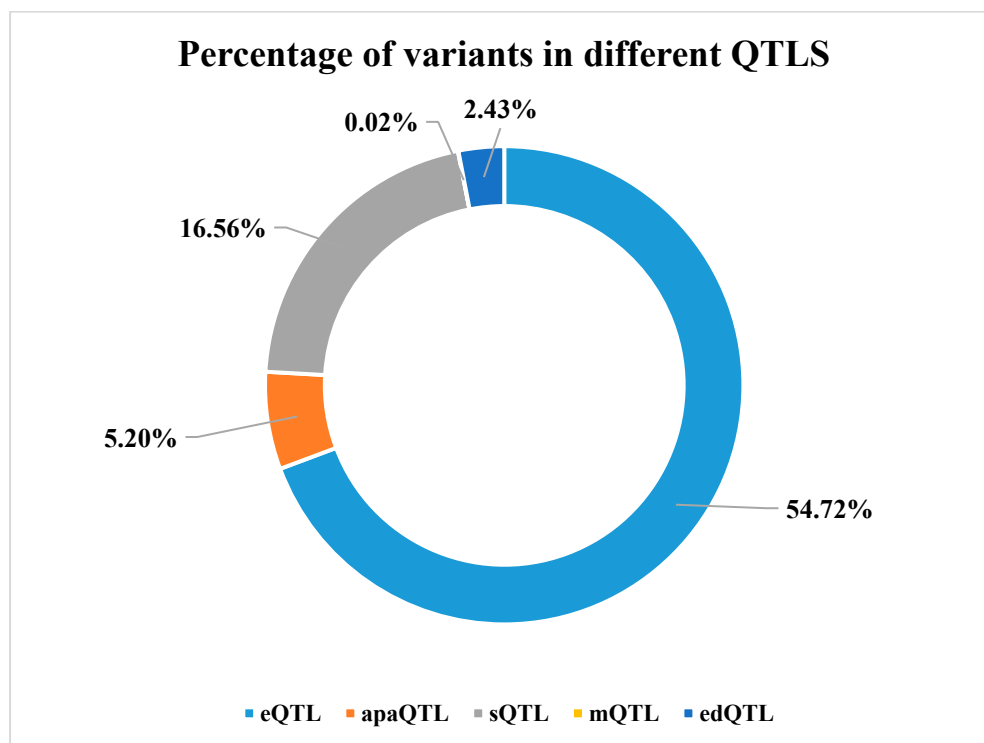
Gene ID	Gene Name	Gene q-value	Number of transcripts	Number of significant transcripts
ENSG00000175287	<i>PHYHDI</i>	0.014434	10	1
ENSG00000120833	<i>SOCS2</i>	0.03452	8	1
ENSG00000100722	<i>ZC3H14</i>	0.020912	8	1
ENSG00000100519	<i>PSMC6</i>	1.11E-10	7	1
ENSG00000088836	<i>SLC4A11</i>	0.007169	7	1
ENSG00000167196	<i>FBXO22</i>	9.54E-06	7	1
ENSG00000144857	<i>BOC</i>	0.002836	7	1
ENSG00000169220	<i>RGS14</i>	0.020116	7	1
ENSG00000111203	<i>ITFG2</i>	0.024131	7	1
ENSG00000110077	<i>MS4A6A</i>	4.09E-11	6	2
ENSG00000104953	<i>TLE6</i>	0.00146	6	1
ENSG00000114857	<i>NKTR</i>	0.001498	6	1
ENSG00000235220	<i>HLA-F</i>	0.00554	6	1
ENSG00000100600	<i>LGMN</i>	3.88E-05	6	1
ENSG00000141076	<i>UTP4</i>	0.000273	6	1
ENSG00000128274	<i>A4GALT</i>	0.017088	6	1
ENSG00000166526	<i>ZNF3</i>	0.031697	6	1
ENSG00000267060	<i>PTGES3L</i>	0.000787	6	1
ENSG00000140153	<i>WDR20</i>	0.000649	6	1
ENSG00000164597	<i>COG5</i>	0.017088	5	1
ENSG00000136826	<i>KLF4</i>	4.04E-05	5	1
ENSG00000149781	<i>FERMT3</i>	0.000455	5	1
ENSG00000215126	<i>ZNGIF</i>	2.03E-05	5	1
ENSG00000183484	<i>GPRI32</i>	0.007169	5	1
ENSG00000234651	<i>BAG6</i>	0.043997	5	1
ENSG00000130649	<i>CYP2E1</i>	0.003332	5	1
ENSG00000114062	<i>UBE3A</i>	0.000665	5	1
ENSG00000160218	<i>TRAPPC10</i>	2.99E-05	5	1
ENSG00000087303	<i>NID2</i>	0.049472	5	1
ENSG00000132141	<i>CCT6B</i>	0.033065	5	1
ENSG00000104870	<i>FCGRT</i>	0.004871	5	1
ENSG00000111452	<i>ADGRD1</i>	0.000799	5	1
ENSG00000104129	<i>DNAJC17</i>	8.03E-05	5	2
ENSG00000161526	<i>SAP30BP</i>	0.01653	5	1
ENSG00000150687	<i>PRSS23</i>	0.001452	5	1
ENSG00000168824	<i>NSG1</i>	1.50E-10	5	1
ENSG00000138442	<i>WDR12</i>	0.000891	5	1
ENSG00000185988	<i>PLK5</i>	0.028369	5	1

ENSG00000060138	<i>YBX3</i>	0.025774	5	1
ENSG00000009830	<i>POMT2</i>	0.00024	5	1
ENSG00000078487	<i>ZCWPW1</i>	0.029922	5	1
ENSG00000108231	<i>LGII</i>	0.01283	5	1
ENSG00000115556	<i>PLCD4</i>	0.004436	5	1
ENSG00000129646	<i>QRICH2</i>	0.024131	5	1
ENSG00000088876	<i>ZNF343</i>	0.019295	5	1
ENSG00000106070	<i>GRB10</i>	0.034105	5	1
ENSG00000079459	<i>FDFT1</i>	0.007753	5	1
ENSG00000167699	<i>GLOD4</i>	0.008841	5	1
ENSG00000122687	<i>MRM2</i>	0.031947	5	1
ENSG00000143373	<i>ZNF687</i>	0.042807	5	1
ENSG00000133067	<i>LGR6</i>	0.010462	4	1
ENSG00000173085	<i>COQ2</i>	5.20E-05	4	1
ENSG00000153551	<i>CMTM7</i>	0.000511	4	1
ENSG00000196684	<i>HSH2D</i>	0.004314	4	1
ENSG00000100526	<i>CDKN3</i>	0.003846	4	1
ENSG00000206376	<i>EHMT2</i>	0.001657	4	2
ENSG00000106123	<i>EPHB6</i>	4.71E-05	4	1
ENSG00000276887	<i>TTYH1</i>	0.039631	4	2
ENSG00000109171	<i>SLAIN2</i>	2.21E-05	4	1
ENSG00000157303	<i>SUSD3</i>	0.029384	4	1
ENSG00000182378	<i>PLCXDI</i>	0.012999	4	1
ENSG00000023228	<i>NDUFS1</i>	0.00219	4	1
ENSG00000150459	<i>SAP18</i>	0.008408	4	1
ENSG00000151789	<i>ZNF385D</i>	0.018551	4	1
ENSG00000187243	<i>MAGED4B</i>	0.02358	4	1
ENSG00000101146	<i>RAE1</i>	0.039398	4	1
ENSG00000177000	<i>MTHFR</i>	0.028369	4	1
ENSG00000131778	<i>CHDIL</i>	0.03092	4	1
ENSG00000156097	<i>GPR61</i>	0.007957	4	1
ENSG00000172551	<i>MUCL1</i>	0.038699	4	1
ENSG00000112280	<i>COL9A1</i>	0.000344	4	1
ENSG00000156531	<i>PHF6</i>	0.013047	4	1
ENSG00000147364	<i>FBXO25</i>	0.024465	4	1
ENSG00000136560	<i>TANK</i>	0.025721	4	1
ENSG00000148339	<i>SLC25A25</i>	0.001416	4	1
ENSG00000262860	<i>LSMI4A</i>	0.000283	4	1
ENSG00000143106	<i>PSMA5</i>	0.011914	4	1
ENSG00000128253	<i>RFPL2</i>	0.047869	4	1
ENSG00000106853	<i>PTGRI</i>	0.001342	4	1
ENSG00000157837	<i>SPPL3</i>	0.005656	4	1
ENSG00000170035	<i>UBE2E3</i>	0.026186	4	1

ENSG00000072518	<i>MARK2</i>	0.017807	4	1
ENSG00000144744	<i>UBA3</i>	0.026984	4	1
ENSG00000185104	<i>FAF1</i>	0.013047	4	1
ENSG00000232045	<i>EHMT2</i>	0.000455	3	3
ENSG00000124256	<i>ZBP1</i>	0.004675	3	1
ENSG00000164744	<i>SUN3</i>	0.027889	3	1
ENSG00000228299	<i>HLA-C</i>	0.000795	3	1
ENSG00000273622	<i>CDC42EP5</i>	0.007582	3	2
ENSG00000281385	<i>AP2A2</i>	0.008295	3	1
ENSG00000276725	<i>CEP170</i>	0.012527	3	1
ENSG00000240230	<i>COX19</i>	5.01E-10	3	2
ENSG00000150054	<i>MPP7</i>	0.000107	3	2
ENSG00000125850	<i>OVOL2</i>	0.000625	3	1
ENSG00000145220	<i>LYAR</i>	3.50E-07	3	2
ENSG00000134940	<i>ACRV1</i>	0.003478	3	1
ENSG00000181856	<i>SLC2A4</i>	0.014434	3	1
ENSG00000236014	<i>VPS52</i>	0.003712	3	2
ENSG00000231129	<i>ABCF1</i>	0.007183	3	2
ENSG00000132792	<i>CTNBL1</i>	0.001312	3	1
ENSG00000151131	<i>NOPCHAP1</i>	0.000283	3	1
ENSG00000278229	<i>RPS17</i>	0.033215	3	2
ENSG00000130699	<i>TAF4</i>	0.047869	3	1
ENSG00000186174	<i>BCL9L</i>	0.001099	3	1
ENSG00000102144	<i>PGK1</i>	0.000787	3	1
ENSG00000274081	<i>PUF60</i>	0.000595	3	1
ENSG00000103707	<i>MTFMT</i>	9.54E-06	3	1
ENSG00000181450	<i>ZNF678</i>	0.047908	3	1
ENSG00000165731	<i>RET</i>	0.029181	3	1
ENSG00000277273	<i>CDK7</i>	0.030087	3	1
ENSG00000167680	<i>SEMA6B</i>	0.03039	3	1
ENSG00000198168	<i>SVIP</i>	0.02941	3	1
ENSG00000120158	<i>RCL1</i>	0.037738	3	1
ENSG00000065665	<i>SEC61A2</i>	0.007487	3	1
ENSG00000278318	<i>ZNF229</i>	0.024131	3	1
ENSG00000115561	<i>CHMP3</i>	0.04319	3	1
ENSG00000170043	<i>TRAPPC1</i>	0.000283	3	1
ENSG00000169181	<i>GSG1L</i>	0.035077	3	1
ENSG00000137996	<i>RTCA</i>	0.031947	3	2
ENSG00000168495	<i>POLR3D</i>	0.000787	3	1
ENSG00000129083	<i>COPB1</i>	0.006458	3	1
ENSG00000173409	<i>ARV1</i>	0.000795	3	1
ENSG00000162735	<i>PEX19</i>	0.028196	3	1
ENSG00000239961	<i>LILRA4</i>	0.013484	2	2

ENSG00000213931	<i>HBE1</i>	0.00037	2	2
ENSG00000230475	<i>ABHD16A</i>	0.004137	2	2
ENSG00000237071	<i>TRIM27</i>	0.01394	2	2
ENSG00000228570	<i>NUTM2E</i>	0.038699	2	2
ENSG00000212866	<i>HSPA1B</i>	0.00554	2	2
ENSG00000162843	<i>WDR64</i>	0.038869	2	2
ENSG00000226882	<i>GNL1</i>	0.007774	2	2
ENSG00000196993	<i>NPIP9</i>	0.008408	2	2
ENSG00000230596	<i>GPAAIP2</i>	0.012904	2	2
ENSG00000223532	<i>HLA-B</i>	0.028369	2	2
ENSG00000213648	<i>SULT1A4</i>	0.025579	2	2
ENSG00000290457	NA	0.017969	2	2
ENSG00000214274	<i>ANG</i>	0.028938	2	2
ENSG00000129757	<i>CDKN1C</i>	0.047367	2	2
ENSG00000278728	<i>CNTNAP2</i>	3.78E-07	2	2
ENSG00000149089	<i>APIP</i>	0.007228	2	2
ENSG00000214026	<i>MRPL23</i>	0.008408	2	2
ENSG00000170915	<i>PAQR8</i>	0.012809	2	2
ENSG00000274332	<i>LRRC37A2</i>	0.023126	2	2
ENSG00000169635	<i>HIC2</i>	0.018651	2	2
ENSG00000273673	NA	0.028369	2	2
ENSG00000078237	<i>TIGAR</i>	0.013047	2	2
ENSG00000170893	<i>TRH</i>	0.038802	2	2
ENSG00000188916	<i>INSYN2A</i>	0.038747	2	2
ENSG00000224740	<i>FLOT1</i>	0.038699	2	2
ENSG00000128285	<i>MCHR1</i>	0.000103	2	2
ENSG00000076003	<i>MCM6</i>	0.003846	2	2
ENSG00000276802	<i>HERC2</i>	0.002292	2	2
ENSG00000155962	<i>CLIC2</i>	0.028369	2	2
ENSG00000130720	<i>FIBCD1</i>	0.033065	2	2
ENSG00000213753	<i>CENPBD2P</i>	0.000663	2	2
ENSG00000205423	<i>CNEPIR1</i>	0.007487	2	2
ENSG00000130703	<i>OSBPL2</i>	0.023126	2	2
ENSG00000139291	<i>TMEM19</i>	0.042593	2	2
ENSG00000112852	<i>PCDHB2</i>	0.010462	2	2
ENSG00000198783	<i>ZNF830</i>	0.033863	2	2
ENSG00000125851	<i>PCSK2</i>	0.03092	2	2
ENSG00000265681	<i>RPL17</i>	0.001342	2	2
ENSG00000160214	<i>RRP1</i>	0.032229	2	2
ENSG00000004059	<i>ARF5</i>	0.018977	2	2
ENSG00000134153	<i>EMC7</i>	7.89E-05	2	2
ENSG00000131016	<i>AKAP12</i>	0.01056	2	2
ENSG00000163655	<i>GMPS</i>	0.002232	2	2

ENSG00000198242	<i>RPL23A</i>	0.026173	2	2
ENSG00000137198	<i>GMPR</i>	0.02223	2	2
ENSG00000169217	<i>CD2BP2</i>	0.028092	2	2
ENSG00000146006	<i>LRRTM2</i>	0.02223	2	2
ENSG00000134508	<i>CABLES1</i>	0.008408	2	2
ENSG00000100902	<i>PSMA6</i>	0.025213	2	2
ENSG00000165704	<i>HPRT1</i>	0.013047	2	2
ENSG00000213463	<i>SYNJ2BP</i>	0.020489	2	2



Supplementary Figure S2: Percentage of variants involved in different Quantitative Trait Loci

Supplementary Table S3: Variants that affect miRNA binding and its expression in HD.

Chromosome	Alt/Ref	Gene	SNP	GWAS/novel SNP	Affected miRNA	miRNA expression	miRNA target gene/s	Expression of gene
Chr16	G/C	<i>SMPD3</i>	rs12927738	Novel	miR-29-3p	UP	<i>COL4A2</i> , <i>KLF4</i> , <i>ITGB1</i> , <i>COL1A2</i>	DOWN
Chr5	T/C	<i>EFNA5</i>	rs252682	AD, PD	miR-29-3p	UP	<i>COL4A2</i> , <i>KLF4</i> , <i>ITGB1</i> , <i>COL1A2</i>	DOWN
Chr1	C/T	<i>KLC1</i>	rs4652791	AMD	miR-34a-5p	UP	<i>ERBB2</i> , <i>SRC</i> , <i>GAS1</i> , <i>PDGFR</i>	DOWN
Chr5	G/T	<i>SEMA6A</i>	rs258012	Novel	miR-124	UP	<i>ITGB1</i> , <i>PTBP1</i> , <i>MTDH</i> , <i>GNAI3</i>	DOWN
Chr7	G/T	<i>HDAC9</i>	rs2520362	PD,AMD	miR-196a-5p	UP	<i>RANBP9</i> , <i>NOTCH2</i> , <i>SRRT</i> , <i>TRAP1</i>	DOWN
Chr2	C/T	<i>IGFBP5</i>	rs11575134	PD,AMD	miR-146a-5p	DOWN	<i>SOX2</i> , <i>ERBB4</i> , <i>BCLAF1</i> , <i>RAC1</i>	UP
Chr6	T/G	<i>BCLAF1</i>	rs180998508	Novel	miR-146a-5p	DOWN	<i>SOX2</i> , <i>ERBB4</i> , <i>BCLAF1</i> , <i>RAC1</i>	UP



Supplementary Figure S3: Identification of essential genes through single gene deletion analysis

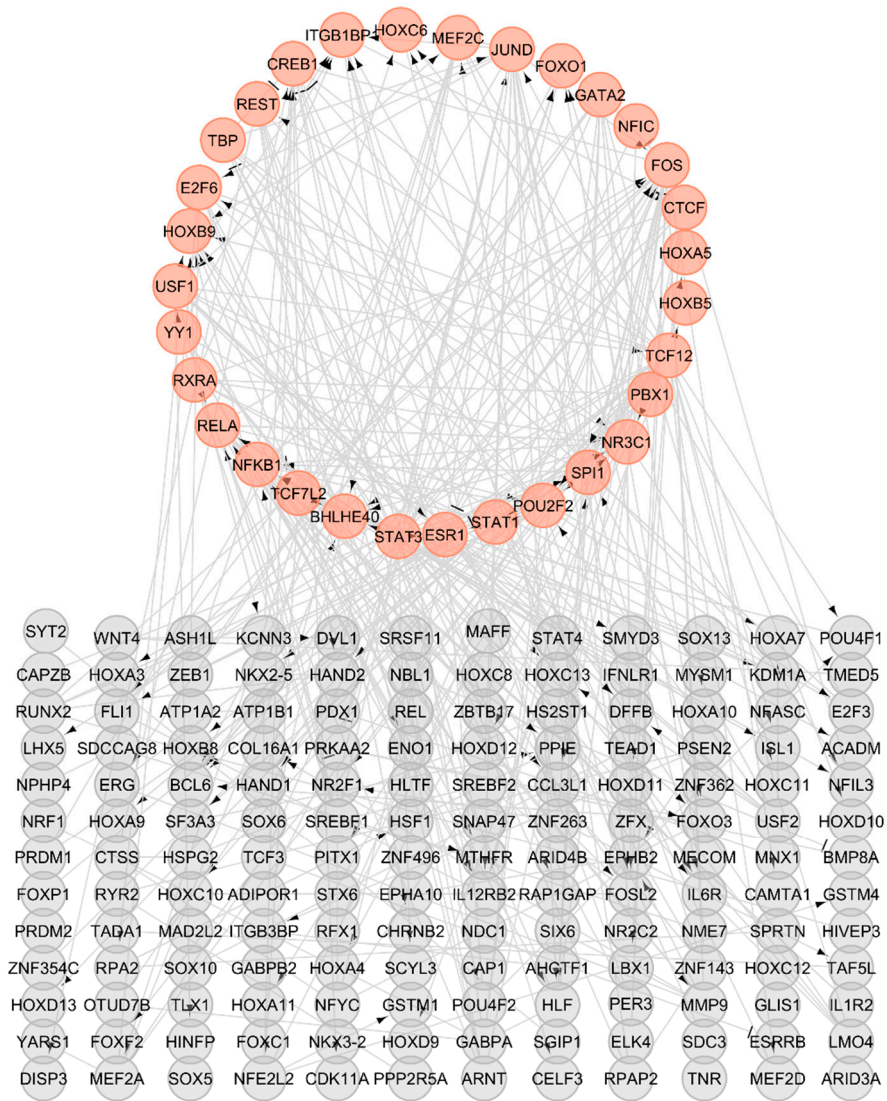
Supplementary Table S4: Importance of essential genes and the their metabolic flux

GENE	Number of reactions deleted through gene deletion	Metabolic flux	Importance of the gene
<i>SLC25A10</i>	20	789.3583	Knockdown of this gene causes defects in mitochondrial respiration[108]
<i>CMPK1</i>	40	826.2042	Eliminating this gene will inhibit proliferation and increase apoptosis [109]
<i>RRM1</i>	6	879.9701	Knockout of this gene will trigger apoptosis and inhibit growth significantly [110]
<i>GBE1</i>	1	880.7468	Knockdown of <i>GBE1</i> makes it more susceptible in neuron degeneration [111]
<i>PYGL</i>	1	904.0637	Removal of this gene from the system effects the metabolic pathways and cause glycogen storage disease [112]

<i>ACSL1</i>	21	916.7597	Knockout of this gene causes major metabolic defects like mitochondria based long chain FA degradation [113]
<i>GPI</i>	3	919.3579	Removal of GPI gene induces cell proliferation inhibition [114]
<i>DERA</i>	1	925.6295	Knockdown of this gene causes stress within mitochondria which starts a cascade of events for energy crisis in brain [115]
<i>TALDO1</i>	1	932.2939	<i>TALDO1</i> is a crucial gene involving in metabolic pathways and its removal can cause major impact on the metabolic system [116]
<i>MCCC2</i>	1	943.0063	Knockout study on <i>MCCC2</i> showed that it induces cell proliferation [117]
<i>PGLS</i>	2	945.7904	<i>PGLS</i> is crucial and a knockdown study in glioblastoma is performed on PGLS and it is found that NADPH and GSH neurotransmitter are reduced [118]
<i>DMAC2L</i>	1	947.3364	Removal of <i>DMAC2L</i> results in reduced carbohydrate metabolism and in turn restricts motility/ movement. [119]
<i>GUK1</i>	3	951.0216	<i>GUK1</i> is a major participant of GTP and dGTP metabolism and its removal can impact majorly on metabolic pathways that aid in energy supply for brain [120][121]
<i>PGD</i>	3	951.9599	Knockout of this gene will cause increased cell stress and expansion of endoplasmic reticulum volume leading to energy catastrophe [122]
<i>PFKL</i>	5	956.2257	<i>PFKL</i> gene inhibits glycolysis , a crucial mechanism in energy pumping when it is knocked down.[123]
<i>DBI</i>	21	958.2383	<i>DBI</i> is mostly found to be expressed in astrocytes and its removal will cause

			alterations in GABA signalling that is crucial in brain [124]
<i>HMGCR</i>	4	959.3648	Removal of <i>HMGCR</i> will cause ER stress in the cell which is a sign for energy insufficiency[125]
<i>BCAT2</i>	3	963.2047	<i>BCAT2</i> gene removal will effect mitochondrial respiration, oxygen consumption rate of cells [126]
<i>CPT2</i>	46	964.122	Knockout study on <i>BCAT2</i> effects the beta oxidation [127]
<i>SDHB</i>	2	965.545	<i>CPT2</i> is a crucial metabolic gene and reduced complex 2 activity is observed when removed in zebrafish [128]
<i>CTH</i>	2	970.6769	<i>CTH</i> is top gene producing H ₂ S in blood vessels and its knockdown results in brain vasculature development [129]
<i>CPT1A</i>	12	970.9974	Knockdown of <i>CPT1A</i> caused metabolic disturbances in the cell [130]
<i>NADSYN1</i>	3	976.0198	<i>NADSYN1</i> is an essential gene due to its role in neovascularization and its impairment can cause major loss of function in blood vessel morphogenesis [131]
<i>COX8A</i>	2	976.4597	Loss of <i>COX8A</i> gene will result in epilepsy and leigh like syndrome – movement related disorders [132]
<i>COX7A2</i>	2	976.4597	Knock down of <i>COX7A2</i> will lead to locomotor defect [133]
<i>COX4II</i>	2	976.4597	<i>COX4II</i> is a crucial gene and reduced neuronal network activity is observed [134]
<i>COX7B</i>	2	976.4597	Altered CNS activity is observed when <i>COX7B</i> is knocked out [135]

<i>COX6C</i>	2	976.4597	Removal of <i>COX6C</i> will lead to developmental death in cells which makes it crucial [136]
<i>COX5A</i>	2	976.4597	Knock down of this gene induces STRESS and lead to autophagy [137]
<i>SLC37A4</i>	3	981.487	<i>SLC37A4</i> is a key activator of autophagy so, its absence will create major impact on metabolic pathways of brain [138]
<i>DPYD</i>	2	982.7158	<i>DPYD</i> produces inhibitory neurotransmitters which are crucial for functioning of neuronal population and knockdown will have a great impact on them [139]
<i>PTDSSI</i>	1	986.7217	Removal of gene <i>PTDSSI</i> may lead to reduced neuron growth/ axon extension [140]



Supplementary Figure S4: Function interaction network of variant genes, differentially expressed genes and transcription factors. Orange color nodes represent hub genes based on network properties like degree, betweenness centrality. Grey nodes represent non-hub genes of FI network.

Supplementary Table S5: Gene interactions between DEGs, variant genes and transcription factors of hub genes

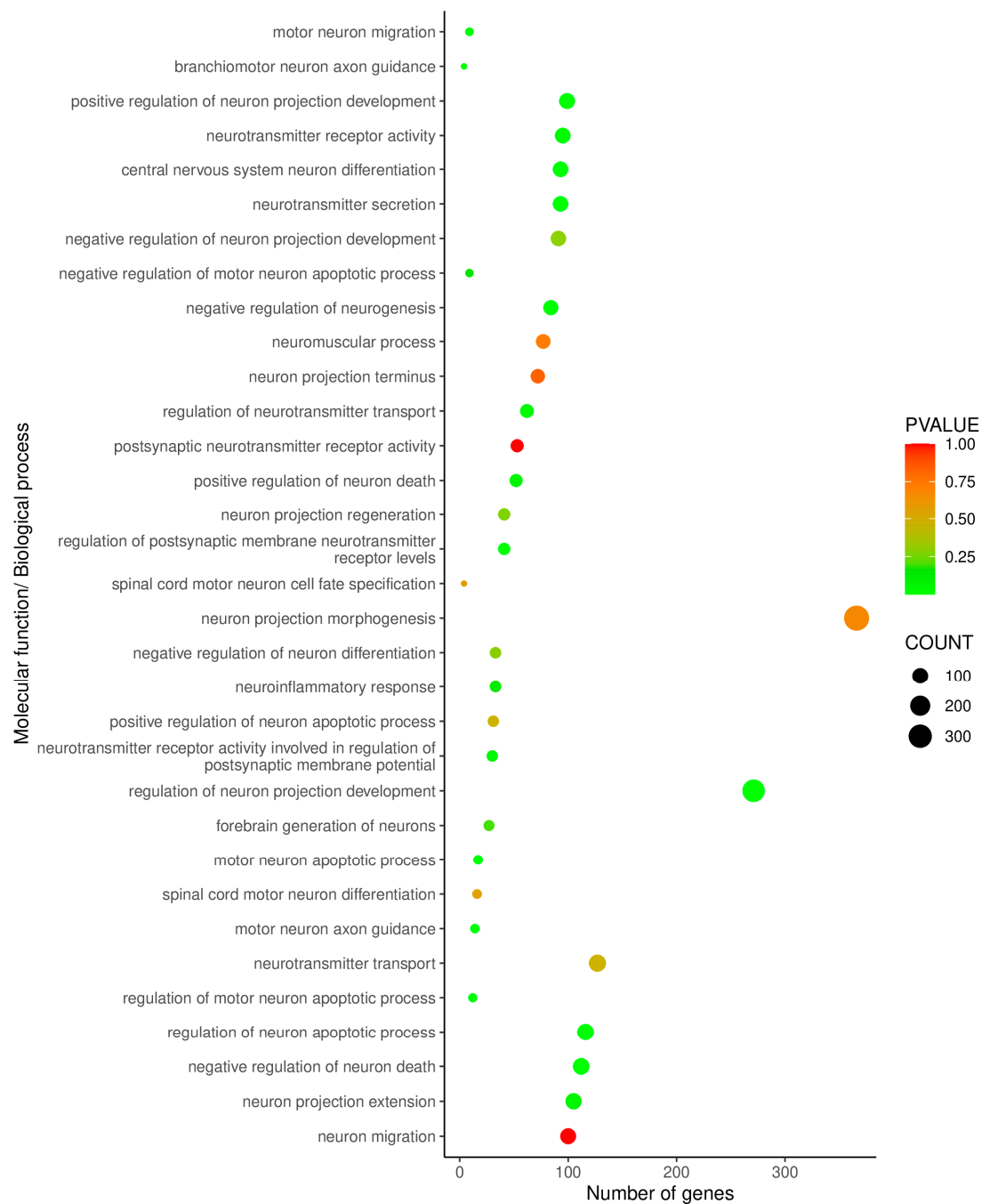
GENE1	FI Direction	GENE2	FI Score	FI Annotation
<i>HOXA5</i>	←	<i>TCF12</i>	1	expression regulated by
<i>NR3C1</i>	←	<i>SPI1</i>	1	expression regulated by; reaction
<i>NR3C1</i>	←	<i>PBX1</i>	1	activated by; inhibit
<i>NR3C1</i>	←	<i>RXRA</i>	1	activated by
<i>NR3C1</i>	←	<i>RELA</i>	1	activate; activated by; complex; inhibit
<i>NR3C1</i>	←	<i>TBP</i>	1	activated by; inhibit
<i>NR3C1</i>	←	<i>RUNX2</i>	1	activated by; inhibit
<i>HOXC6</i>	←	<i>SPI1</i>	1	expression regulated by
<i>HOXC6</i>	←	<i>ZEB1</i>	1	expression regulated by
<i>HOXC6</i>	←	<i>TCF12</i>	1	expression regulated by
<i>ESR1</i>	-	<i>LMO4</i>	1	complex
<i>ESR1</i>	-	<i>POU4F2</i>	1	complex; inhibit
<i>ESR1</i>	-	<i>USF2</i>	1	complex
<i>ESR1</i>	-	<i>KDM1A</i>	1	complex
<i>ESR1</i>	→	<i>POU4F1</i>	1	activate; complex
<i>ESR1</i>	→	<i>HOXA10</i>	1	expression regulates
<i>ESR1</i>	→	<i>NR3C1</i>	1	activate; inhibited by
<i>ESR1</i>	→	<i>OTUD7B</i>	1	expression regulates
<i>ESR1</i>	→	<i>NFIC</i>	1	activate; inhibited by
<i>ESR1</i>	-	<i>TBP</i>	1	complex
<i>ESR1</i>	←	<i>USF1</i>	1	complex; expression regulated by
<i>ESR1</i>	→	<i>JUND</i>	1	complex; expression regulates; reaction
<i>JUND</i>	→	<i>TEAD1</i>	1	expression regulates
<i>JUND</i>	→	<i>NR2F1</i>	1	expression regulates
<i>JUND</i>	→	<i>SPI1</i>	1	expression regulates
<i>JUND</i>	→	<i>POU2F2</i>	1	expression regulates
<i>JUND</i>	→	<i>PRDM1</i>	1	expression regulates
<i>JUND</i>	←	<i>TCF12</i>	1	expression regulated by; expression regulates
<i>JUND</i>	→	<i>MEF2C</i>	1	expression regulates
<i>JUND</i>	←	<i>TBP</i>	1	expression regulated by
<i>JUND</i>	→	<i>STAT3</i>	1	expression regulates
<i>JUND</i>	→	<i>STAT1</i>	1	expression regulates
<i>JUND</i>	←	<i>SREBF1</i>	1	expression regulated by
<i>JUND</i>	→	<i>SREBF2</i>	1	expression regulates
<i>GATA2</i>	→	<i>SPI1</i>	1	complex; expression regulates
<i>GATA2</i>	→	<i>ZEB1</i>	1	expression regulates
<i>GATA2</i>	-	<i>TCF3</i>	1	complex
<i>GATA2</i>	→	<i>HLF</i>	1	expression regulates
<i>GATA2</i>	→	<i>NR3C1</i>	1	expression regulates

<i>GATA2</i>	→	<i>TCF12</i>	1	complex; expression regulates
<i>CREB1</i>	-	<i>TCF12</i>	1	complex
<i>CREB1</i>	→	<i>NR3C1</i>	1	activate; expression regulates; inhibited by
<i>CREB1</i>	→	<i>ZBTB17</i>	1	activate; inhibited by
<i>CREB1</i>	→	<i>KCNN3</i>	1	expression regulates
<i>CREB1</i>	→	<i>REST</i>	1	activate; inhibited by
<i>CREB1</i>	→	<i>TBP</i>	1	expression regulates; reaction
<i>CREB1</i>	-	<i>NFE2L2</i>	1	complex
<i>CREB1</i>	→	<i>STAT3</i>	1	expression regulates; reaction
<i>CREB1</i>	-	<i>MEF2D</i>	1	complex; reaction
<i>CREB1</i>	←	<i>NFKB1</i>	1	expression regulated by; reaction
<i>TCF12</i>	←	<i>USF1</i>	1	expression regulated by
<i>SPI1</i>	←	<i>ZNF263</i>	1	expression regulated by
<i>SPI1</i>	←	<i>STAT3</i>	1	expression regulated by
<i>SPI1</i>	→	<i>ZEB1</i>	1	expression regulates
<i>SPI1</i>	-	<i>TBP</i>	1	complex
<i>SPI1</i>	→	<i>USF1</i>	1	expression regulates
<i>SPI1</i>	←	<i>USF2</i>	1	expression regulated by
<i>TBP</i>	-	<i>ZNF143</i>	1	complex
<i>TBP</i>	→	<i>ZBTB17</i>	1	activate; inhibited by
<i>MEF2C</i>	←	<i>ZNF263</i>	1	expression regulated by
<i>MEF2C</i>	-	<i>TCF3</i>	1	complex
<i>MEF2C</i>	←	<i>USF1</i>	1	expression regulated by
<i>MEF2C</i>	-	<i>NKX2-5</i>	1	complex; reaction
<i>RELA</i>	←	<i>SREBF1</i>	1	activated by; inhibited
<i>RELA</i>	←	<i>SREBF2</i>	1	activated by; inhibit
<i>RELA</i>	←	<i>STAT4</i>	1	activated by
<i>RELA</i>	←	<i>RXRA</i>	1	activated by; inhibited
<i>YY1</i>	→	<i>ZNF143</i>	1	expression regulates
<i>YY1</i>	→	<i>ZBTB17</i>	1	expression regulates
<i>HOXB9</i>	←	<i>MAFF</i>	1	expression regulated by
<i>HOXB9</i>	←	<i>USF1</i>	1	expression regulated by
<i>HOXB9</i>	←	<i>JUND</i>	1	expression regulated by
<i>HOXB9</i>	←	<i>SREBF1</i>	1	expression regulated by
<i>HOXB9</i>	←	<i>TCF7L2</i>	1	expression regulated by
<i>HOXB9</i>	←	<i>TCF12</i>	1	expression regulated by
<i>HOXB9</i>	←	<i>RXRA</i>	1	expression regulated by
<i>CTCF</i>	→	<i>NFIL3</i>	1	expression regulates
<i>CTCF</i>	-	<i>RXRA</i>	1	complex
<i>CTCF</i>	→	<i>ITGB1BP1</i>	1	expression regulates
<i>CTCF</i>	-	<i>PBX1</i>	1	complex
<i>CTCF</i>	→	<i>TCF12</i>	1	expression regulates
<i>CTCF</i>	→	<i>SPI1</i>	1	expression regulates
<i>CTCF</i>	→	<i>FLI1</i>	1	expression regulates
<i>CTCF</i>	→	<i>STAT3</i>	1	expression regulates

<i>CTCF</i>	→	<i>HOXA5</i>	1	expression regulates
<i>ITGB1BP1</i>	←	<i>USF1</i>	1	expression regulated by
<i>ITGB1BP1</i>	←	<i>ZNF263</i>	1	expression regulated by
<i>ITGB1BP1</i>	←	<i>MAFF</i>	1	expression regulated by
<i>ITGB1BP1</i>	←	<i>RXRA</i>	1	expression regulated by
<i>ITGB1BP1</i>	←	<i>SPI1</i>	1	expression regulated by
<i>ITGB1BP1</i>	←	<i>YY1</i>	1	expression regulated by
<i>ITGB1BP1</i>	←	<i>JUND</i>	1	expression regulated by
<i>NFKB1</i>	→	<i>REL</i>	1	complex; expression regulates
<i>NFKB1</i>	←	<i>SREBF2</i>	1	activated by; inhibit
<i>NFKB1</i>	←	<i>SREBF1</i>	1	activated by; inhibit
<i>NFKB1</i>	←	<i>SPI1</i>	1	expression regulated by
<i>NFKB1</i>	→	<i>STAT1</i>	1	expression regulates
<i>NFKB1</i>	←	<i>STAT4</i>	1	activated by
<i>NFKB1</i>	→	<i>NR3C1</i>	1	activate; complex; expression regulates; inhibited by; input
<i>NFKB1</i>	→	<i>POU2F2</i>	1	activate; expression regulates
<i>NFIC</i>	→	<i>NR3C1</i>	1	expression regulates
<i>BHLHE40</i>	→	<i>HOXB9</i>	1	expression regulates
<i>BHLHE40</i>	←	<i>TCF7L2</i>	1	expression regulated by
<i>BHLHE40</i>	←	<i>STAT3</i>	1	expression regulated by
<i>BHLHE40</i>	←	<i>NR3C1</i>	1	expression regulated by
<i>BHLHE40</i>	←	<i>TCF12</i>	1	expression regulated by
<i>BHLHE40</i>	←	<i>MEF2C</i>	1	expression regulated by
<i>BHLHE40</i>	←	<i>MEF2A</i>	1	expression regulated by
<i>USF1</i>	←	<i>YY1</i>	1	expression regulated by
<i>USF1</i>	-	<i>USF2</i>	1	complex; input
<i>REST</i>	←	<i>TCF12</i>	1	activated by; expression regulates; inhibit
<i>FOS</i>	→	<i>HLF</i>	1	expression regulates
<i>FOS</i>	-	<i>TCF7L2</i>	1	complex; input
<i>FOS</i>	-	<i>GATA2</i>	1	complex; input; reaction
<i>FOS</i>	→	<i>NFIC</i>	1	activate; inhibited by
<i>FOS</i>	→	<i>STAT4</i>	1	activate; inhibited by; reaction
<i>FOS</i>	→	<i>HLTF</i>	1	expression regulates
<i>FOS</i>	→	<i>ZNF143</i>	1	expression regulates
<i>FOS</i>	→	<i>RFX1</i>	1	expression regulates
<i>FOS</i>	→	<i>NR3C1</i>	1	activate; complex; inhibited by; input; reaction
<i>FOS</i>	→	<i>FOSL2</i>	1	expression regulates
<i>FOS</i>	←	<i>JUND</i>	1	complex; expression regulated by
<i>FOXO1</i>	←	<i>LMO4</i>	1	activated by
<i>FOXO1</i>	-	<i>NFYC</i>	1	complex
<i>FOXO1</i>	←	<i>IL6R</i>	1	activated by
<i>FOXO1</i>	-	<i>NR3C1</i>	1	complex; reaction
<i>E2F6</i>	→	<i>TCF12</i>	1	expression regulates

E2F6	→	<i>HLF</i>	1	expression regulates
E2F6	→	<i>ZEB1</i>	1	expression regulates
E2F6	←	<i>NR3C1</i>	1	expression regulated by
E2F6	←	<i>JUND</i>	1	expression regulated by
E2F6	→	<i>ENO1</i>	1	expression regulates
E2F6	→	<i>MEF2A</i>	1	expression regulates
E2F6	→	<i>POU2F2</i>	1	expression regulates
E2F6	→	<i>PER3</i>	1	expression regulates
HOXB5	←	<i>TCF12</i>	1	expression regulated by
POU4F2	←	<i>REST</i>	1	expression regulated by

FI: Functional Interaction



Supplementary Figure S5: Number of differentially expressed genes and variant genes in different biological processes