

## Supplementary tables

**Table e-1. Primers employed to validate gene expression alterations through qPCR.**

Gene	Forward Primer	Reverse Primer
<i>C4A</i>	CTCAGAGCAATGCCGTGTC	GGTCTGCCATCTCTGCTTTG
<i>NLRC5</i>	CTCACAGGGCCAAAGGTTG	GCAGGTCAGTGGGAAATTG
<i>HCLS1</i>	TGAGGAGAAGAGGAAGCGAG	CATAGCTATCACTGGCTGTGG
<i>ITGB2</i>	GGGATCCTGACTCCATTCG	GGTCGCAGGTAAAGCGTC
<i>ACBD7</i>	TGATTTTGACAGGGCTGC	TTGCTTGTTTGTAAGCCC
<i>CHI3L1</i>	TACCTGAAGGACAGGCAGC	CCTTGATGGCATTGGTGAG
<i>SH3TC1</i>	TTCACTCATCACTGCCTGG	ATGAGGAGGCTCTCGTGG
<i>SH3BP2</i>	GAAGAGATGCATTGGCCTG	GGTACCGCCCTTCTTGTG
<i>CHI3L2</i>	GCTACTTTACCAACTGGTCCC	AACCTTGTTGTTTTCGATGC
<i>PSRC1</i>	GATCCTCGATGAGGCCAAC	TCCGCGTCAAAGAGTTCAC
<i>RPL13</i>	CCTGGAGGAGAAGAGGAAAGAGA	TGAGGACCTCTGTGTATTTGTCAA

Table e-1. Sequence of each pair of primers used to validate differential gene expression between the ALS and HC motor cortex through qPCR.

**Table e-2. List of differentially expressed genes.**

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj
<i>C4A</i>	541.753	2.038	0.278	7.343	2.10E-13	5.89E-09
<i>SH3TC1</i>	541.319	0.986	0.141	6.972	3.13E-12	4.40E-08
<i>CHI3L2</i>	429.052	4.593	0.726	6.323	2.57E-10	2.41E-06
<i>MUC1</i>	29.668	1.736	0.294	5.901	3.60E-09	2.53E-05
<i>CHI3L1</i>	3584.909	2.469	0.425	5.807	6.36E-09	3.57E-05
<i>PSRC1</i>	1853.172	0.519	0.093	5.577	2.45E-08	0.00011
<i>ARHGAP45</i>	312.489	0.617	0.117	5.256	1.47E-07	0.00059
<i>FSTL3</i>	401.142	0.469	0.090	5.186	2.14E-07	0.00075
<i>CCR5</i>	45.636	1.450	0.285	5.092	3.55E-07	0.00111
<i>SFN</i>	25.965	2.835	0.568	4.991	5.99E-07	0.00168
<i>NLRC5</i>	489.559	0.788	0.161	4.886	1.03E-06	0.00262
<i>ALPK1</i>	429.531	0.738	0.154	4.793	1.64E-06	0.00384
<i>TLR2</i>	519.803	1.156	0.246	4.703	2.57E-06	0.00555
<i>C1QC</i>	1379.325	1.227	0.262	4.678	2.89E-06	0.00580
<i>SLC22A8</i>	32.363	-4.112	0.882	-4.661	3.15E-06	0.00591
<i>LIF</i>	43.590	3.256	0.703	4.630	3.65E-06	0.00641
<i>KCNE4</i>	303.524	1.480	0.321	4.610	4.02E-06	0.00664
<i>ACBD7</i>	1967.400	-0.497	0.109	-4.582	4.61E-06	0.00677
<i>SLC11A1</i>	644.920	1.399	0.306	4.579	4.68E-06	0.00677
<i>DSC3</i>	12.617	-3.912	0.856	-4.573	4.81E-06	0.00677
<i>RHBDF2</i>	548.450	0.590	0.130	4.526	6.00E-06	0.00778
<i>VAV1</i>	189.660	0.648	0.143	4.523	6.09E-06	0.00778
<i>HCLS1</i>	736.137	0.838	0.186	4.503	6.70E-06	0.00792
<i>PARVG</i>	297.723	0.911	0.202	4.501	6.77E-06	0.00792
<i>ITPKB-IT1</i>	63.585	1.106	0.247	4.478	7.53E-06	0.00847
<i>AL049839.2</i>	31.315	2.859	0.640	4.469	7.86E-06	0.00850
<i>FLJ16779</i>	160.329	1.232	0.276	4.460	8.21E-06	0.00855
<i>C4B</i>	467.157	2.078	0.468	4.445	8.80E-06	0.00866
<i>SH3BP2</i>	1615.713	0.778	0.175	4.442	8.93E-06	0.00866

SIPA1	546.039	0.504	0.114	4.433	9.29E-06	0.00871
C3	7906.239	1.165	0.265	4.391	1.13E-05	0.00974
RGL3	222.279	0.699	0.159	4.389	1.14E-05	0.00974
PLAUR	163.552	0.846	0.193	4.382	1.18E-05	0.00974
CMTM7	74.478	0.642	0.146	4.382	1.18E-05	0.00974
SPATA20	2193.417	0.448	0.103	4.348	1.37E-05	0.01079
CHST6	1135.575	1.258	0.290	4.342	1.41E-05	0.01079
ANKRD22	20.569	1.868	0.431	4.338	1.44E-05	0.01079
ABI3	189.658	0.841	0.194	4.335	1.46E-05	0.01079
AC008760.2	35.139	1.543	0.357	4.326	1.52E-05	0.01088
VWA5A	1358.062	0.633	0.146	4.318	1.58E-05	0.01088
TMC8	160.640	0.632	0.146	4.314	1.60E-05	0.01088
SERPINA5	70.031	3.486	0.810	4.303	1.68E-05	0.01088
LTF	364.640	4.076	0.948	4.302	1.70E-05	0.01088
SLA	540.550	0.953	0.222	4.301	1.70E-05	0.01088
ITGB4	2901.485	1.142	0.267	4.274	1.92E-05	0.01199
MAFF	406.748	1.243	0.292	4.259	2.05E-05	0.01253
MSR1	364.378	1.345	0.318	4.229	2.35E-05	0.01374
PDPN	401.179	0.826	0.195	4.229	2.35E-05	0.01374
EPHX2	615.468	-0.344	0.082	-4.217	2.48E-05	0.01420
SLC16A3	395.164	0.939	0.224	4.200	2.67E-05	0.01503
CARD9	164.533	0.569	0.136	4.183	2.87E-05	0.01583
P2RY6	73.458	1.445	0.346	4.172	3.02E-05	0.01627
CD44	1900.235	2.037	0.489	4.168	3.07E-05	0.01627
HSD3B7	179.229	0.947	0.228	4.158	3.21E-05	0.01659
BRS3	6.209	2.433	0.586	4.155	3.25E-05	0.01659
PLEKHA4	136.731	0.954	0.230	4.149	3.34E-05	0.01677
LRRC75A	439.528	-0.559	0.135	-4.140	3.48E-05	0.01679
ABCC9	2070.042	0.788	0.190	4.137	3.53E-05	0.01679
WAS	107.596	0.700	0.169	4.133	3.58E-05	0.01679
TNFRSF10D	192.015	1.097	0.266	4.130	3.63E-05	0.01679
TRIM56	921.828	0.591	0.143	4.128	3.66E-05	0.01679
AL133330.1	12.996	2.411	0.584	4.125	3.70E-05	0.01679
PGGHG	344.405	0.770	0.187	4.111	3.95E-05	0.01734
ADGRE2	148.190	0.927	0.225	4.111	3.95E-05	0.01734
TKTL1	12.824	1.983	0.485	4.090	4.31E-05	0.01834
AQP1	2214.068	2.194	0.537	4.087	4.38E-05	0.01834
C1QB	1956.506	1.307	0.320	4.081	4.49E-05	0.01834
ITGB2	844.816	0.816	0.200	4.080	4.50E-05	0.01834
S100A3	7.314	2.478	0.607	4.080	4.50E-05	0.01834
EML3	788.709	0.495	0.122	4.074	4.62E-05	0.01856
WDFY3-AS2	627.814	-0.410	0.101	-4.065	4.79E-05	0.01867
AC020904.2	57.488	0.874	0.215	4.065	4.81E-05	0.01867
PPIAP70	20.241	0.839	0.207	4.062	4.87E-05	0.01867
LNCAROD	17.022	1.119	0.276	4.060	4.92E-05	0.01867
C1R	809.188	1.117	0.276	4.050	5.13E-05	0.01902
MYBPH	11.528	2.086	0.515	4.049	5.14E-05	0.01902
POM121L9P	29.404	1.896	0.469	4.040	5.35E-05	0.01954
NRL	99.629	-0.432	0.107	-4.035	5.47E-05	0.01970
ADCY7	962.007	0.518	0.129	4.021	5.80E-05	0.02065
GRAMD2A	190.740	0.927	0.232	3.998	6.39E-05	0.02247
ARHGAP4	328.965	0.557	0.140	3.981	6.86E-05	0.02368
AL355974.2	154.789	1.526	0.384	3.975	7.03E-05	0.02368
CIITA	484.640	0.757	0.191	3.974	7.07E-05	0.02368
HSD17B7P2	180.736	0.779	0.196	3.971	7.15E-05	0.02368
IRF9	164.054	0.517	0.130	3.971	7.16E-05	0.02368
NAPSB	165.675	2.114	0.537	3.933	8.41E-05	0.02747

<i>MSLN</i>	35.923	1.407	0.358	3.930	8.51E-05	0.02749
<i>EMILIN1</i>	347.423	0.828	0.212	3.913	9.10E-05	0.02882
<i>DGKK</i>	26.247	-1.434	0.367	-3.913	9.13E-05	0.02882
<i>BMP4</i>	138.095	-0.876	0.224	-3.908	9.33E-05	0.02885
<i>BCO1</i>	53.009	1.574	0.403	3.905	9.44E-05	0.02885
<i>MRO</i>	23186.863	-0.502	0.129	-3.904	9.44E-05	0.02885
<i>PRICKLE3</i>	57.197	0.561	0.145	3.882	0.00010	0.03134
<i>LINC00663</i>	277.129	0.331	0.086	3.874	0.00011	0.03200
<i>ADAMTS9</i>	1813.640	1.732	0.449	3.856	0.00012	0.03357
<i>AC104574.2</i>	14.432	1.956	0.507	3.854	0.00012	0.03357
<i>AL158151.4</i>	11.057	1.609	0.417	3.854	0.00012	0.03357
<i>GFAP</i>	233090.111	1.371	0.356	3.851	0.00012	0.03357
<i>GBP1</i>	403.518	1.159	0.301	3.850	0.00012	0.03357
<i>RARRES3</i>	400.207	1.188	0.309	3.842	0.00012	0.03436
<i>PLD2</i>	904.232	0.550	0.143	3.838	0.00012	0.03450
<i>FGFRL1</i>	1574.018	0.717	0.187	3.828	0.00013	0.03557
<i>C1QA</i>	1058.728	1.113	0.291	3.826	0.00013	0.03557
<i>PDLIM4</i>	338.412	0.781	0.205	3.814	0.00014	0.03701
<i>SLC44A3-AS1</i>	265.272	0.868	0.229	3.793	0.00015	0.03956
<i>GPR4</i>	127.593	1.229	0.324	3.792	0.00015	0.03956
<i>LSP1</i>	101.088	1.033	0.273	3.786	0.00015	0.04021
<i>AC093390.1</i>	6.405	-1.262	0.334	-3.781	0.00016	0.04057
<i>CYBA</i>	357.933	0.685	0.182	3.769	0.00016	0.04233
<i>FAM189A2</i>	1355.360	0.968	0.257	3.765	0.00017	0.04251
<i>SERPINA1</i>	492.707	1.331	0.355	3.755	0.00017	0.04375
<i>SPOCD1</i>	51.919	1.446	0.385	3.754	0.00017	0.04375
<i>FLVCR1-DT</i>	58.581	-0.844	0.225	-3.748	0.00018	0.04423
<i>PPP1R3D</i>	497.104	-0.301	0.080	-3.746	0.00018	0.04423
<i>RREB1</i>	614.871	0.411	0.110	3.743	0.00018	0.04449
<i>ADAMTS9-AS1</i>	44.297	1.222	0.327	3.734	0.00019	0.04533
<i>STEAP3</i>	313.437	0.777	0.208	3.734	0.00019	0.04533
<i>PRPH</i>	19.470	1.989	0.533	3.730	0.00019	0.04561
<i>MIR128-2</i>	14.640	-0.894	0.240	-3.726	0.00019	0.04576
<i>HAMP</i>	186.942	1.915	0.514	3.725	0.00020	0.04576
<i>PLCD3</i>	1498.742	0.616	0.166	3.716	0.00020	0.04709
<i>NODAL</i>	5.222	-1.974	0.532	-3.713	0.00020	0.04716
<i>FAM153C</i>	702.447	-0.627	0.169	-3.703	0.00021	0.04865
<i>ROM1</i>	685.598	0.699	0.189	3.697	0.00022	0.04948

Table e-2. List of the genes showing a significant differential expression in the ALS motor cortex as compared to HC provided by DESeq2.

**Table e-3.** Concordance between RNAseq expression and qPCR expression data.

Gene	R	P-value
<i>CHI3L1</i>	0.87	2,2x10 <sup>-6</sup>
<i>CHI3L2</i>	0.84	2,2x10 <sup>-6</sup>
<i>C4A</i>	0.79	8,3x10 <sup>-5</sup>
<i>SH3BP2</i>	0.78	0.00014
<i>NLRC5</i>	0.65	0.003
<i>SH3TC1</i>	0.61	0.007
<i>PSRC1</i>	0.55	0.016
<i>ACBD7</i>	0.53	0.021
<i>ITGB2</i>	0.52	0.023
<i>HCLS1</i>	0.5	0.031

Table e-3. Correlation analyses between gene expression counts obtained through RNAseq and RNA relative expression values derived from qPCR. We calculated relative expression values using the  $2^{-\Delta\Delta Ct}$  method and *RPL13* for normalization and correlated them with the DESeq2 normalized RNAseq counts for each gene and individual.

**Table e-4. List of differentially expressed isoforms.**

Transcript ID	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj
ENST00000582911	16.704	-23.659	2.623	-9.021	1.87E-19	9.79E-15
ENST00000536159	17.537	-23.722	2.630	-9.018	1.91E-19	9.79E-15
ENST00000322269	16.679	-23.653	2.634	-8.979	2.74E-19	9.79E-15
ENST00000402434	73.330	-25.675	2.908	-8.831	1.04E-18	2.79E-14
ENST00000414778	54.052	23.559	2.685	8.774	1.72E-18	3.69E-14
ENST00000413393	385.316	26.296	3.010	8.737	2.40E-18	4.28E-14
ENST00000620924	73.808	23.993	2.760	8.693	3.53E-18	5.29E-14
ENST00000379089	59.334	23.684	2.729	8.680	3.95E-18	5.29E-14
ENST00000409346	45.296	23.309	2.701	8.629	6.18E-18	7.35E-14
ENST00000320254	59.296	23.687	2.754	8.601	7.93E-18	7.86E-14
ENST00000603639	52.433	23.513	2.735	8.599	8.07E-18	7.86E-14
ENST00000641317	86.766	-25.124	2.986	-8.413	3.99E-17	3.56E-13
ENST00000394537	241.450	25.128	3.010	8.349	6.91E-17	5.69E-13
ENST00000433529	38.552	-24.797	2.987	-8.303	1.02E-16	7.79E-13
ENST00000611648	120.809	24.680	3.010	8.200	2.41E-16	1.72E-12
ENST00000629725	28.829	-24.396	2.987	-8.168	3.13E-16	2.00E-12
ENST00000382892	28.605	-24.391	2.987	-8.166	3.18E-16	2.00E-12
ENST00000639952	27.012	-24.294	2.987	-8.134	4.16E-16	2.48E-12
ENST00000510372	24.727	-24.161	2.987	-8.089	6.01E-16	3.39E-12
ENST00000309502	76.417	24.016	3.010	7.979	1.48E-15	7.90E-12
ENST00000402788	69.437	23.905	3.010	7.942	1.99E-15	1.02E-11
ENST00000512982	52.071	23.506	3.010	7.809	5.76E-15	2.72E-11
ENST00000517903	51.880	23.501	3.010	7.808	5.83E-15	2.72E-11
ENST00000614999	49.214	23.427	3.010	7.783	7.09E-15	3.17E-11

ENST00000648339	110.924	23.083	3.010	7.669	1.73E-14	7.28E-11
ENST00000395857	9.615	-22.908	2.988	-7.667	1.77E-14	7.28E-11
ENST00000361642	37.233	23.038	3.010	7.653	1.96E-14	7.77E-11
ENST00000610831	35.222	22.957	3.010	7.626	2.41E-14	9.24E-11
ENST00000407925	34.683	22.936	3.010	7.619	2.55E-14	9.41E-11
ENST00000441328	34.139	22.911	3.010	7.611	2.72E-14	9.71E-11
ENST00000626691	32.731	22.854	3.010	7.592	3.15E-14	1.09E-10
ENST00000538576	8.089	-22.647	2.988	-7.578	3.50E-14	1.17E-10
ENST00000513391	7.691	-22.603	2.989	-7.563	3.94E-14	1.28E-10
ENST00000646390	70.771	22.730	3.010	7.551	4.31E-14	1.36E-10
ENST00000620040	7.577	-22.553	2.989	-7.546	4.47E-14	1.37E-10
ENST00000482202	27.688	22.619	3.010	7.514	5.74E-14	1.69E-10
ENST00000464964	27.458	22.613	3.010	7.512	5.84E-14	1.69E-10
ENST00000423351	29.895	22.591	3.010	7.504	6.17E-14	1.74E-10
ENST00000357055	26.577	22.568	3.010	7.497	6.55E-14	1.78E-10
ENST00000552588	41.833	22.560	3.010	7.495	6.65E-14	1.78E-10
ENST00000295571	25.162	22.491	3.010	7.471	7.96E-14	2.06E-10
ENST00000275080	6.259	-22.325	2.989	-7.469	8.09E-14	2.06E-10
ENST00000334286	6.152	-22.303	2.989	-7.461	8.56E-14	2.13E-10
ENST00000460540	22.647	22.344	3.011	7.422	1.15E-13	2.81E-10
ENST00000424608	22.004	22.301	3.011	7.407	1.29E-13	3.06E-10
ENST00000642395	21.168	22.251	3.011	7.391	1.46E-13	3.40E-10
ENST00000367731	48.636	22.215	3.010	7.380	1.58E-13	3.60E-10
ENST00000614223	17.616	21.992	2.982	7.376	1.64E-13	3.65E-10
ENST00000436978	20.359	22.193	3.011	7.372	1.68E-13	3.68E-10
ENST00000646590	19.588	22.142	3.011	7.355	1.91E-13	4.10E-10
ENST00000352187	16.542	21.909	2.982	7.347	2.03E-13	4.27E-10
ENST00000409001	35.967	22.089	3.010	7.338	2.17E-13	4.46E-10
ENST00000602871	17.613	21.989	2.999	7.333	2.25E-13	4.54E-10
ENST00000545294	18.568	22.067	3.011	7.330	2.31E-13	4.58E-10
ENST00000448695	27.681	22.053	3.010	7.326	2.38E-13	4.63E-10
ENST00000634560	15.701	21.835	2.989	7.305	2.78E-13	5.31E-10
ENST00000645539	13.859	21.656	2.985	7.255	4.01E-13	7.53E-10
ENST00000445503	15.637	21.830	3.011	7.250	4.16E-13	7.68E-10
ENST00000486839	15.363	21.793	3.010	7.241	4.45E-13	8.08E-10
ENST00000319217	14.358	21.711	3.011	7.211	5.56E-13	9.94E-10
ENST00000457361	31.327	21.672	3.010	7.199	6.05E-13	1.06E-09
ENST00000391874	12.428	21.508	2.992	7.189	6.51E-13	1.11E-09
ENST00000536827	13.665	21.642	3.011	7.187	6.60E-13	1.11E-09
ENST00000482287	13.092	21.576	3.002	7.187	6.62E-13	1.11E-09
ENST00000393349	32.868	21.575	3.010	7.167	7.65E-13	1.26E-09
ENST00000379344	12.380	21.485	3.005	7.150	8.67E-13	1.41E-09
ENST00000569055	12.404	21.508	3.011	7.143	9.16E-13	1.46E-09
ENST00000541972	11.289	21.374	3.011	7.098	1.27E-12	1.99E-09
ENST00000393304	11.132	21.356	3.011	7.092	1.32E-12	2.05E-09
ENST00000428931	10.964	21.336	3.011	7.085	1.39E-12	2.11E-09
ENST00000414543	10.978	21.333	3.011	7.084	1.40E-12	2.11E-09
ENST00000369699	10.781	21.311	3.011	7.077	1.47E-12	2.19E-09

ENST00000442986	10.154	21.228	3.011	7.049	1.80E-12	2.65E-09
ENST00000401393	9.669	21.161	3.012	7.027	2.12E-12	3.07E-09
ENST00000617051	9.400	21.122	3.012	7.013	2.33E-12	3.32E-09
ENST00000324330	9.188	21.085	3.012	7.001	2.54E-12	3.58E-09
ENST00000498133	9.409	-20.888	2.988	-6.990	2.74E-12	3.82E-09
ENST00000622668	8.431	20.971	3.012	6.963	3.34E-12	4.58E-09
ENST00000611443	18.928	20.669	3.011	6.865	6.63E-12	9.00E-09
ENST00000646224	20.478	20.431	3.011	6.786	1.15E-11	1.54E-08
ENST00000428956	3171.962	2.006	0.300	6.686	2.30E-11	3.04E-08
ENST00000601237	100.837	0.751	0.130	5.772	7.82E-09	1.02E-05
ENST00000369748	309.908	5.453	0.954	5.716	1.09E-08	1.41E-05
ENST00000375481	32.823	2.137	0.378	5.658	1.53E-08	1.95E-05
ENST00000538532	22.051	7.638	1.351	5.652	1.58E-08	2.00E-05
ENST00000255409	2509.971	2.454	0.441	5.559	2.71E-08	3.38E-05
ENST00000468936	62.498	1.971	0.358	5.501	3.78E-08	4.66E-05
ENST00000393078	3706.541	3.434	0.657	5.228	1.72E-07	0.00021
ENST00000648821	268.245	1.490	0.288	5.172	2.32E-07	0.00028
ENST00000453791	305.115	-0.649	0.128	-5.085	3.67E-07	0.00044
ENST00000418236	87.222	9.622	1.911	5.035	4.79E-07	0.00056
ENST00000586793	4825.503	1.510	0.301	5.025	5.04E-07	0.00059
ENST00000589701	1215.245	1.810	0.362	4.993	5.94E-07	0.00068
ENST00000511819	169.879	-0.774	0.155	-4.986	6.17E-07	0.00070
ENST00000473704	7.312	3.066	0.621	4.934	8.05E-07	0.00091
ENST00000393080	1484.236	3.447	0.703	4.903	9.42E-07	0.00105
ENST00000510204	80.075	0.958	0.198	4.834	1.34E-06	0.00148
ENST00000356189	1509.833	-0.507	0.105	-4.818	1.45E-06	0.00159
ENST00000502559	50.223	1.026	0.214	4.802	1.57E-06	0.00170
ENST00000472064	169.808	2.553	0.537	4.758	1.96E-06	0.00210
ENST00000490872	7.789	2.760	0.582	4.739	2.15E-06	0.00228
ENST00000459981	16.190	1.573	0.335	4.694	2.68E-06	0.00281
ENST00000377653	46.794	0.898	0.191	4.691	2.72E-06	0.00282
ENST00000292303	43.928	1.483	0.317	4.673	2.97E-06	0.00306
ENST00000491786	8.382	6.244	1.341	4.655	3.23E-06	0.00330
ENST00000468221	145.099	1.504	0.326	4.615	3.93E-06	0.00398
ENST00000379775	2442.701	1.619	0.352	4.599	4.25E-06	0.00425
ENST00000409349	8.357	6.238	1.378	4.528	5.96E-06	0.00591
ENST00000460846	31.064	1.260	0.280	4.508	6.56E-06	0.00645
ENST00000245105	212.197	1.126	0.250	4.504	6.66E-06	0.00649
ENST00000232014	1056.712	0.961	0.214	4.500	6.81E-06	0.00657
ENST00000576820	6.091	5.781	1.287	4.492	7.07E-06	0.00676
ENST00000249075	38.051	3.324	0.742	4.482	7.40E-06	0.00699
ENST00000552773	68.403	1.020	0.228	4.481	7.44E-06	0.00699
ENST00000261201	821.044	0.876	0.196	4.476	7.60E-06	0.00708
ENST00000460934	70.693	1.365	0.306	4.462	8.14E-06	0.00752
ENST00000545466	23.207	2.516	0.565	4.455	8.37E-06	0.00767
ENST00000543082	116.882	-1.140	0.257	-4.445	8.81E-06	0.00800
ENST00000648089	15.562	-7.690	1.732	-4.441	8.94E-06	0.00805
ENST00000478742	163.475	2.490	0.564	4.414	1.01E-05	0.00905

ENST00000350792	841.611	-1.082	0.245	-4.410	1.03E-05	0.00914
ENST00000377414	156.871	0.974	0.221	4.399	1.09E-05	0.00954
ENST00000380529	200.717	1.029	0.235	4.375	1.21E-05	0.01057
ENST00000295685	266.215	0.658	0.151	4.354	1.34E-05	0.01151
ENST00000359172	1970.574	1.450	0.333	4.353	1.34E-05	0.01151
ENST00000311813	3023.650	2.201	0.507	4.343	1.41E-05	0.01197
ENST00000498330	14.311	2.628	0.606	4.338	1.44E-05	0.01215
ENST00000553947	57.036	3.032	0.699	4.335	1.46E-05	0.01219
ENST00000382164	938.925	0.436	0.101	4.317	1.58E-05	0.01312
ENST00000435363	2560.226	2.170	0.503	4.315	1.60E-05	0.01312
ENST00000435494	84.255	-1.035	0.240	-4.312	1.62E-05	0.01312
ENST00000475485	85.038	1.104	0.256	4.309	1.64E-05	0.01312
ENST00000473185	150.786	2.535	0.588	4.309	1.64E-05	0.01312
ENST00000511663	59.330	0.861	0.200	4.309	1.64E-05	0.01312
ENST00000586127	395.572	1.580	0.369	4.288	1.81E-05	0.01433
ENST00000446583	16.506	1.466	0.343	4.277	1.89E-05	0.01489
ENST00000374640	1103.087	1.140	0.267	4.268	1.97E-05	0.01542
ENST00000281830	278.405	1.468	0.344	4.260	2.04E-05	0.01586
ENST00000460658	70.357	1.014	0.238	4.258	2.07E-05	0.01593
ENST00000591598	11.204	-7.217	1.696	-4.255	2.09E-05	0.01599
ENST00000593460	240.221	0.919	0.216	4.249	2.15E-05	0.01635
ENST00000530597	3.888	5.133	1.210	4.241	2.23E-05	0.01679
ENST00000406058	5.918	5.737	1.357	4.226	2.38E-05	0.01780
ENST00000421751	23.432	-0.996	0.236	-4.224	2.40E-05	0.01786
ENST00000263398	1206.741	2.031	0.482	4.217	2.48E-05	0.01829
ENST00000650254	793.923	1.235	0.293	4.210	2.55E-05	0.01871
ENST00000456291	10.748	1.307	0.311	4.202	2.65E-05	0.01932
ENST00000503868	22.421	7.663	1.825	4.199	2.69E-05	0.01943
ENST00000588455	15.734	1.921	0.458	4.197	2.70E-05	0.01943
ENST00000339276	22.843	2.682	0.640	4.192	2.77E-05	0.01954
ENST00000531840	323.606	0.684	0.163	4.191	2.78E-05	0.01954
ENST00000336967	632.142	-0.508	0.121	-4.190	2.79E-05	0.01954
ENST00000614781	18.516	1.596	0.381	4.189	2.80E-05	0.01954
ENST00000591327	2112.509	1.513	0.361	4.189	2.81E-05	0.01954
ENST00000550482	393.318	0.450	0.108	4.170	3.05E-05	0.02100
ENST00000586704	91.871	0.839	0.201	4.169	3.06E-05	0.02100
ENST00000482507	335.344	0.570	0.137	4.157	3.23E-05	0.02201
ENST00000424415	22.174	7.646	1.841	4.152	3.29E-05	0.02231
ENST00000484021	579.565	0.484	0.117	4.150	3.32E-05	0.02231
ENST00000476846	409.716	0.832	0.200	4.150	3.33E-05	0.02231
ENST00000254942	1641.453	-0.201	0.048	-4.147	3.36E-05	0.02237
ENST00000528922	29.310	2.586	0.624	4.145	3.40E-05	0.02237
ENST00000598805	30.499	1.291	0.311	4.145	3.40E-05	0.02237
ENST00000495447	369.248	-1.363	0.330	-4.127	3.67E-05	0.02398
ENST00000324849	637.232	-0.428	0.104	-4.126	3.70E-05	0.02400
ENST00000438120	1262.454	0.441	0.107	4.123	3.73E-05	0.02411
ENST00000613509	111.571	-0.713	0.173	-4.114	3.89E-05	0.02495
ENST00000325658	1231.513	-0.222	0.054	-4.110	3.95E-05	0.02518

ENST00000439368	349.375	-0.546	0.133	-4.106	4.02E-05	0.02542
ENST00000458657	17.633	1.981	0.482	4.106	4.03E-05	0.02542
ENST00000496823	194.960	1.331	0.325	4.096	4.21E-05	0.02638
ENST00000441885	182.504	-1.315	0.321	-4.092	4.27E-05	0.02660
ENST00000445506	92.158	1.250	0.306	4.089	4.33E-05	0.02682
ENST00000290200	71.794	1.021	0.250	4.087	4.37E-05	0.02690
ENST00000369568	7.341	6.053	1.483	4.083	4.45E-05	0.02722
ENST00000574453	192.350	1.597	0.392	4.077	4.55E-05	0.02767
ENST00000612722	149.657	1.220	0.299	4.075	4.59E-05	0.02767
ENST00000587188	67.608	0.531	0.130	4.075	4.60E-05	0.02767
ENST00000373302	4944.456	-0.685	0.168	-4.074	4.62E-05	0.02768
ENST00000300006	725.137	-0.639	0.157	-4.062	4.87E-05	0.02900
ENST00000252490	261.037	1.254	0.309	4.058	4.95E-05	0.02933
ENST00000586125	3128.723	1.547	0.382	4.048	5.17E-05	0.03046
ENST00000425427	62.386	0.636	0.158	4.037	5.41E-05	0.03164
ENST00000409138	310.992	0.628	0.156	4.031	5.57E-05	0.03241
ENST00000245907	6617.961	1.148	0.285	4.028	5.62E-05	0.03243
ENST00000314583	420.365	0.942	0.234	4.028	5.63E-05	0.03243
ENST00000532315	51.657	0.676	0.168	4.024	5.71E-05	0.03274
ENST00000464203	49.433	-0.589	0.147	-4.014	5.96E-05	0.03399
ENST00000369912	10.862	2.285	0.571	4.005	6.19E-05	0.03510
ENST00000588750	114.131	1.800	0.450	4.002	6.28E-05	0.03540
ENST00000361203	18961.292	0.530	0.133	3.996	6.45E-05	0.03621
ENST00000482740	198.210	3.384	0.847	3.994	6.50E-05	0.03629
ENST00000265195	6.956	5.977	1.500	3.984	6.78E-05	0.03765
ENST00000534313	370.169	0.506	0.127	3.975	7.04E-05	0.03889
ENST00000579572	7.148	2.023	0.510	3.966	7.30E-05	0.04009
ENST00000580977	3.304	-3.812	0.962	-3.961	7.45E-05	0.04074
ENST00000590168	107.222	0.764	0.193	3.958	7.55E-05	0.04105
ENST00000306085	848.186	0.578	0.147	3.947	7.92E-05	0.04286
ENST00000340552	105.634	1.329	0.337	3.945	7.99E-05	0.04301
ENST00000381998	79.767	1.505	0.382	3.940	8.14E-05	0.04360
ENST00000353334	2312.162	0.752	0.191	3.938	8.22E-05	0.04380
ENST00000524067	15.913	-0.892	0.227	-3.931	8.47E-05	0.04494
ENST00000583444	47.668	0.935	0.238	3.924	8.72E-05	0.04602
ENST00000340093	102.630	0.792	0.202	3.917	8.97E-05	0.04712
ENST00000634504	602.763	1.029	0.263	3.912	9.17E-05	0.04790
ENST00000578776	426.621	1.278	0.327	3.905	9.44E-05	0.04908
ENST00000370996	463.124	-0.306	0.078	-3.902	9.53E-05	0.04933

Table e-4. List of the isoforms showing a significant differential usage in the ALS motor cortex as compared to HC provided by DESeq2.



**Table e-5. Synaptic enrichment of differentially expressed isoforms.**

Ontology term	Gene count	P-value	Q-value
postsynapse	16	3.64e-4	8.49e-4
postsynaptic specialization	11	2.89e-4	8.49e-4
postsynaptic density	10	2.26e-4	8.49e-4
postsynaptic density membrane	6	6.98e-4	1.22e-3
synapse	20	1.96e-3	2.29e-3
integral component of postsynaptic density membrane	5	1.75e-3	2.29e-3
process in the synapse	16	6.60e-3	0.0396

Table e-5. Enrichment of synaptic ontology terms within the list of differently expressed isoforms using SynGO. The number of genes belonging to each term and the p-value and associated q-value for each term are shown.

**Table e-6. List of deregulated genes in the Transcript and Gene models.**

Transcript Model (n=149)	Overlapping genes (n=32)	Gene model (n=92)
<i>TMUB1</i>	<i>CD44</i>	<i>MYBPH</i>
<i>ASPH</i>	<i>C4B</i>	<i>LNCAROD</i>
<i>FAM219A</i>	<i>PARVG</i>	<i>BCO1</i>
<i>CARHSP1</i>	<i>C1R</i>	<i>PDPN</i>
<i>MPDZ</i>	<i>C1QC</i>	<i>SLC22A8</i>
<i>TMEM130</i>	<i>SH3BP2</i>	<i>CYBA</i>
<i>ARPC2</i>	<i>CCR5</i>	<i>ROM1</i>
<i>PFKP</i>	<i>ACBD7</i>	<i>S100A3</i>
<i>GAB3</i>	<i>TRIM56</i>	<i>ADCY7</i>
<i>RTN4</i>	<i>AC008760.2</i>	<i>CARD9</i>
<i>SLC43A3</i>	<i>CHI3L2</i>	<i>ADAMTS9-AS1</i>
<i>CD163</i>	<i>MSR1</i>	<i>AL133330.1</i>
<i>DNM3</i>	<i>C3</i>	<i>MSLN</i>
<i>NBPF12</i>	<i>PPP1R3D</i>	<i>SLA</i>
<i>CITED2</i>	<i>SIPA1</i>	<i>DSC3</i>
<i>ADGRD1</i>	<i>SFN</i>	<i>PLD2</i>
<i>NDRG2</i>	<i>SH3TC1</i>	<i>PLCD3</i>
<i>ZNF438</i>	<i>SLC16A3</i>	<i>LSP1</i>
<i>SLC2A5</i>	<i>LIF</i>	<i>TMC8</i>
<i>RGS6</i>	<i>PLAUR</i>	<i>ANKRD22</i>
<i>ZEB1</i>	<i>SLC11A1</i>	<i>RGL3</i>
<i>TIA1</i>	<i>AL049839.2</i>	<i>NAPSB</i>
<i>TSPAN15</i>	<i>TKTL1</i>	<i>FSTL3</i>
<i>ARRDC2</i>	<i>C4A</i>	<i>AC104574.2</i>

IKZF2  
SLC45A3  
ANK2  
DYRK1A  
AC087651.1  
MIR100HG  
SGK1  
SHISA6  
NSD2  
ZNF48  
DGKG  
HIST1H4H  
PHF19  
ANTXR1  
STXBP1  
TERF2  
DMD  
STAT3  
RPGR  
FYB1  
AC006504.5  
C19orf47  
NMT1  
ZNF83  
C1orf61  
ANKRD10  
SORBS1  
TRIM27  
PTPRF  
CD164  
INCA1  
NCK2  
ITPRID2  
MAGI2  
SNX2  
MINK1  
ADORA1  
MSH6  
PCDH15  
IP6K1  
TBC1D3G  
NIN  
PLEKHG4  
RFX4  
PFKFB3  
MGST3  
MYT1L  
BX890604.2  
NDFIP2  
AL121827.2

CHI3L1  
PSRC1  
KCNE4  
RHBDF2  
HCLS1  
AQP1  
ABCC9  
GFAP

PLEKHA4  
AC093390.1  
POM121L9P  
PRICKLE3  
P2RY6  
FLJ16779  
NLRC5  
RREB1  
ITGB4  
VWA5A  
NRL  
NODAL  
GPR4  
BRS3  
AL158151.4  
WAS  
BMP4  
PDLIM4  
MIR128-2  
STEAP3  
RARRES3  
C1QA  
HAMP  
AL355974.2  
MUC1  
GBP1  
LRRC75A  
ADGRE2  
PGGHG  
FAM153C  
EMILIN1  
ITPKB-IT1  
ITGB2  
AC020904.2  
LINC00663  
TLR2  
ADAMTS9  
ARHGAP45  
IRF9  
CHST6  
ALPK1  
ARHGAP4  
EML3  
LTF  
SPATA20  
SERPINA5  
MAFF  
CIITA  
WDFY3-AS2  
TNFRSF10D

SORCS3  
SERPINB6  
GAS2L1  
VPS37A  
PPM1A  
FEZ2  
ARHGAP26  
NBPF14

RCAN3  
CNTNAP3  
FAM131B  
HSD17B4  
BCL6  
CD74  
ARHGEF4  
TTC7A  
SIL1  
DOCK4  
OCIAD1  
INO80  
SERPINA3  
LRRC37A  
NUCB1  
EOGT  
TMEM259  
NCOR1  
LTBP1  
BCL2L13  
IL10RB  
PICK1  
MAPK10  
DDX3X  
STRIP2  
FAM153CP  
UBAP2L  
RPL18  
ATG4B  
RAB43  
AQP4  
PTPN13  
VPS35L  
HNRNPA1  
ZNF292  
CD81  
SLC30A6  
ABTB1  
CNKSR2  
KPNA1  
SLC16A1

FLVCR1-DT  
SERPINA1  
C1QB  
GRAMD2A  
PPIAP70  
ABI3  
VAV1  
EPHX2  
SLC44A3-  
AS1  
CMTM7  
HSD17B7P2  
MRO  
PRPH  
SPOCD1  
FAM189A2  
DGKK  
FGFRL1  
HSD3B7

*NEB*  
*APOC1*  
*EGLN2*  
*TARDBP*  
*ENAH*  
*TCF4*  
*CTDP1*  
*APOC2*  
*PADI2*  
*SNHG29*  
*GALNT10*  
*DST*  
*BMERB1*  
*HDAC9*  
*AHCYL1*  
*LIMK2*  
*CCDC144NL*  
*PBRM1*  
*UHMK1*  
*MAPRE2*  
*MYADM*  
*FAM3A*  
*PTCD2*  
*ARMH1*  
*SMTN*  
*KCNH1*

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Table e-6. List of genes uniquely identified using the Transcript (n=149) and the Gene (n=92) model approaches and those overlapping between both approaches (n=32).

**Table e-7. Mic1 cluster marker genes differentially expressed in the motor cortex of ALS patients.**

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue
<i>SH3TC1</i>	541.88177	0.98702	0.14128	6.98651	2.82E-12
<i>C1QC</i>	1380.45342	1.22834	0.26160	4.69551	2.66E-06
<i>SLC11A1</i>	645.58614	1.39994	0.30514	4.58786	4.48E-06
<i>HCLS1</i>	736.79959	0.83873	0.18552	4.52089	6.16E-06
<i>C1QB</i>	1958.01574	1.30791	0.31948	4.09389	4.24E-05
<i>C1QA</i>	1059.47395	1.11390	0.29014	3.83920	0.00012
<i>CYBA</i>	358.21168	0.68657	0.18133	3.78620	0.00015
<i>CD74</i>	5374.47042	0.74826	0.20555	3.64033	0.00027
<i>CD14</i>	792.78544	0.93826	0.26432	3.54969	0.00039
<i>SPP1</i>	15331.58619	1.14054	0.32440	3.51581	0.00044
<i>SLC2A5</i>	752.71310	0.75229	0.23907	3.14677	0.00165
<i>TYROBP</i>	236.54198	0.65957	0.21291	3.09791	0.00195
<i>MS4A6A</i>	417.69742	0.98211	0.31739	3.09432	0.00197
<i>ADGRG1</i>	4295.69194	0.37460	0.12199	3.07075	0.00214
<i>LPTM5</i>	1659.65625	0.62069	0.20221	3.06947	0.00214
<i>HCK</i>	294.05885	0.73629	0.24095	3.05575	0.00224
<i>HLA-DRA</i>	1943.49867	0.78919	0.26925	2.93101	0.00338
<i>VSIG4</i>	781.52898	0.82604	0.28744	2.87376	0.00406
<i>HLA-DRB1</i>	1122.17116	0.74079	0.25798	2.87154	0.00408
<i>PLEKHA7</i>	563.81928	0.29028	0.10382	2.79602	0.00517
<i>DPYD</i>	2095.44922	0.32946	0.12349	2.66799	0.00763
<i>FTH1</i>	32588.30554	-0.22656	0.11183	-2.02600	0.04276

Table e-7. List of genes differentially expressed (unadjusted p-value<0.05) in the ALS motor cortex provided by DESeq2 which overlap with Mic1 marker genes.

**Table e-8. Gene co-expression modules significantly associated with ALS.**

	P value	R	Number of genes	Most significant GO term	Log <sub>10</sub> P enrichment
Meblack	0.003	0.637	439	myeloid leukocyte activation	-33.41
				activation of immune response	-28.84
				cytokine production	-25.89
MEpink	0.011	-0.512	851	postsynaptic membrane	-13.54
				potassium channel activity	-8.59
				neuron projection morphogenesis	-6.06
Meyellow	0.025	0.572	1145	cytokine-mediated signaling pathway	-19.94
				adherens junction	-18.18
				blood vessel development	-17.16

Table e-8. This table includes the three modules significantly associated with ALS. For each module, *p*-value, correlation coefficient (R), numbers of genes, the three most significant Gene Ontology terms and their associated log<sub>10</sub> p-value are shown.

**Table e-9. Synaptic enrichment of the MEpink module.**

Ontology term	Gene count	P-value	Q-value
postsynaptic process involved in chemical synaptic transmission	7	3.01e-4	6.93e-3
postsynaptic modulation of chemical synaptic transmission	6	1.32e-3	0.0152
synapse	63	8.37e-3	0.0269
postsynaptic specialization	25	6.69e-3	0.0269
postsynaptic density	23	2.20e-3	0.0269
postsynaptic density membrane	12	4.94e-3	0.0269
integral component of postsynaptic density membrane	10	8.39e-3	0.0269
integral component of presynaptic membrane	12	0.0108	0.0289
process in the synapse	54	5.91e-3	0.0359
synaptic vesicle fusion to presynaptic active zone membrane	3	6.24e-3	0.0359
postsynapse	40	0.0181	0.0415
chemical synaptic transmission	14	9.88e-3	0.0454

Table e-9. Enrichment of synaptic markers within the MEpink gene expression module using SynGO ontology terms. The number of genes belonging to each term and the *p*-value and associated *q*-value for each term are shown.