

Supplementary Table 1 :**Comparison of genes commonly de-regulated at symptomatic ages (90 and 120 day old) in SOD1^{G93A} motoneurons using microarrays**

List of the principal genes whose transcripts were regulated by 1.5- fold or more ($p < 0.05$) in mutant mice at two symptomatic ages. RNA was extracted from 2000 - 2400 microdissected motoneurons issued from one animal. Three chips were analyzed for each condition (control and mutant). Gene expression levels were compared in disease versus control animals. Fold change was calculated as the ratio between the average values of expression in mutant animals relative to the average values of controls; in all comparisons, a positive value indicates a higher level of expression in mutant animals versus negative numbers that show a higher level in controls.

Affymetrix probe set ID	Gene bank	Gene Name	Fold change P 90	Fold change P 120
Genes involved in cell growth and/or maintenance up-regulated at both symptomatic ages				
1449133_at	NM_009264	Small proline-rich protein 1A	14.46	18.09
1449363_at	BC019946	Activating transcription factor 3	10.11	10.46
1419691_at	NM_009921	Cathelicidin antimicrobial peptide	7.95	11.59
1434129_s_at	BG917242	Lipoma HMGIC fusion partner-like 2	4.79	4.05
1426852_x_at	X96585	Nephroblastoma overexpressed gene	4.59	3.73
1423537_at	BB622036	Growth associated protein 43	4.04	3.32
1417381_at	NM_007572	Complement component 1, alpha polypeptide	3.74	8.91
1422557_s_at	NM_013602	Metallothionein 1	3.29	2.87
1437726_x_at	BB111335	Complement component 1, beta polypeptide	3.23	7.16
1416431_at	NM_026473	Tubulin, beta 6	2.93	2.62
1436905_x_at	BB218107	Lsosomal-associated protein transmembrane 5	2.82	5.94
1417256_at	NM_008607	Matrix metalloproteinase 13	2.74	6.17
1428942_at	AA796766	Metallothionein 2	2.65	2.58
1415904_at	BC003305	Lipoprotein lipase	2.63	2.77
1417516_at	NM_007837	DNA-damage inducible transcript 3	2.41	2.33
1438761_a_at	C81193	Ornithine decarboxylase, structural 1	2.39	1.77
1421840_at	BB144704	ATP-binding cassette, sub-family A (ABC1), member 1	2.28	2.04
1417605_s_at	NM_133926	Calcium/calmodulin-dependent protein kinase I	2.24	2.40
1421375_a_at	NM_011313	S100 calcium binding protein A6 (calcyclin)	2.16	3.34
1416318_at	AF426024	Serine (or cysteine) proteinase inhibitor, clade B, member 1a	2.10	2.69
1438606_a_at	BB814844	Chloride intracellular channel 4 (mitochondrial)	2.07	1.66
1420502_at	NM_009121	Spermidine/spermine N1-acetyl transferase 1	2.04	1.84
1422302_s_at	NM_008049	Ferritin light chain 1 and 2, glutamate receptor, ionotropic, kainate 3	2.00	2.81
1419441_at	NM_007475	Acidic ribosomal phosphoprotein P0	1.92	2.09
1438629_x_at	AV166504	Granulin	1.87	2.89
1424635_at	BC018223	Eukaryotic translation elongation factor 1 alpha 1	1.85	2.80
1448232_x_at	NM_009448	Tubulin, alpha 6	1.76	2.55
1450150_a_at	NM_016738	Ribosomal protein L13	1.64	1.77
1415942_at	NM_052835	Ribosomal protein 10	1.64	1.59
1460180_at	NM_010422	Hexosaminidase B	1.50	2.71

Up-regulated at both symptomatic ages

1438118_x_at	AV147875	Vimentin	8.96	4.03
1425763_x_at	BC019425	Immunoglobulin heavy chain (J558 family)	8.52	5.26
1449401_at	NM_007574	Complement component 1, gamma polypeptide	8.15	6.86
1436996_x_at	AV066625	P lysozyme structural	6.19	9.78
1448756_at	NM_009114	S100 calcium binding protein A9 (calgranulin B)	5.72	9.18
1419394_s_at	NM_013650	S100 calcium binding protein A8 (calgranulin A)	5.48	13.53
1419764_at	NM_009892	Chitinase 3-like 3	5.04	6.04
1427076_at	L20315	Macrophage expressed gene 1	4.85	8.51
1448591_at	NM_021281	Cathepsin S	4.55	5.38
1418722_at	NM_008694	Neutrophilic granule protein	4.47	5.54
1421799_at	NM_011910	Urotensin 2	3.70	2.38
1437621_x_at	AV216768	Similar to 3-phosphoglycerate dehydrogenase	3.57	2.39
1460227_at	BC008107	Tissue inhibitor of metalloproteinase 1	3.20	6.42
1460351_at	BC021916		3.16	4.06
1434442_at	BB667844	DNA segment, Chr 5, ERATO Doi 593, expressed	2.84	3.56
1456700_x_at	BB100920	Myristoylated alanine rich protein kinase C substrate	2.81	3.34
1428361_x_at	AK011116		2.55	3.65
1429051_s_at	BE825056	RIKEN cDNA 6230403H02 gene	2.39	2.25
1419905_s_at	AV026552		2.41	5.38
1448577_x_at	BC004829	Synaptogyrin 2	2.21	2.46
1434449_at	BB193413	Aquaporin 4	2.08	2.68
1435745_at	BI408317	RIKEN cDNA 5031439G07 gene	1.90	2.17
1433507_a_at	BE553881	High mobility group nucleosomal binding domain 2	1.69	1.96
1417868_a_at	NM_022325	Cathepsin Z	1.62	2.95
1433689_s_at	BI456571	Ribosomal protein S9	1.60	1.94
1424048_a_at	BC024618	NAD(P)H:quinone oxidoreductase type 3, polypeptide A2	1.55	1.79

Genes down-regulated at both symptomatic ages

1427351_s_at	BB22639	Immunoglobulin heavy chain 6 (heavy chain of IgM)	-3.79	-2.25
1451499_at	AF000969	Ca ²⁺ -dependent activator protein for secretion 2	-3.74	-3.03
1441894_s_at	BB071890	GRP1-associated scaffold protein	-3.24	-2.46
1439622_at	AV291679	Ras association (RalGDS/AF-6) domain family 4	-2.41	-1.95
1430776_s_at	AK017778	Ankyrin repeat domain 24	-2.22	-2.21
1455883_a_at	BB269910	Leucine rich repeat transmembrane neuronal 1	-2.17	-2.50
1459903_at	AA144045	Sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A	-1.96	-1.70
1416427_at	NM_017367	Cyclin I	-1.96	-1.81
1423608_at	BI966443	Integral membrane protein 2A	-1.91	-2.89
1435815_at	AW541598	Similar to melanoma antigen, family A, 10	-1.89	-1.97
1424902_at	AF378760	Plexin domain containing 1	-1.86	-2.13
1451440_at	AF311699	chondrolectin	-1.75	-3.44
1450202_at	AI385669	Glutamate receptor, ionotropic, NMDA1 (zeta 1)	-1.75	-2.08
1441049_at	AV328356	Potassium voltage-gated channel, shaker-related, member 6	-1.69	-2.00

Supplementary Table 2 :**Comparison of genes differentially expressed only at early symptomatic stages (90 day old) in SOD1^{G93A} motoneurons using microarrays**

List of the principal genes whose transcripts were regulated by 1.5- fold or more ($p < 0.05$) in mutant mice at an early symptomatic age. RNA was extracted from 2000 - 2400 microdissected motoneurons issued from one animal. Three chips were analyzed for each condition (control and mutant). Gene expression levels were compared in disease versus control animals. Fold change was calculated as the ratio between the average values of expression in mutant animals relative to the average values of controls; in all comparisons, a positive value indicates a higher level of expression in mutant animals versus negative numbers that show a higher level in controls.

Affymetrix probe set ID	Gene bank	Gene Name	Fold change
Genes involved in cell growth and/or maintenance up-regulated at early symptomatic age			
1416067_at	NM_013562	Interferon-related developmental regulator 1	2.10
1415897_a_at	BI150149	Microsomal glutathione S-transferase 1	1.96
1451803_a_at	U48800	Vascular endothelial growth factor B	1.90
1451064_a_at	BC004827	Phosphoserine aminotransferase 1	1.86
1423080_at	AK002902	Translocase of outer mitochondrial membrane 20 homolog	1.81
1417492_at	M14222	Cathepsin B	1.75
1425364_a_at	U25708	Solute carrier family 3 (activators of dibasic and neutral amino acid transport), member 2	1.67
1425964_x_at	U03561	Heat shock protein 1	1.62
1448430_a_at	NM_013608	Nascent polypeptide-associated complex alpha polypeptide	1.60
1450815_s_at	NM_024166	Coiled-coil-helix-coiled-coil-helix domain containing 2	1.59
1436760_a_at	BQ127746	Ribosomal protein S8	1.54
Up-regulated at early symptomatic ages			
1417928_at	NM_019417	PDZ and LIM domain 4	6.58
1419127_at	NM_023456	Neuropeptide Y	5.92
1415845_at	AV336547	Synaptotagmin 4	2.48
1448392_at	NM_009242	Secreted acidic cysteine rich glycoprotein	2.11
1452428_a_at	AI099111	Beta-2 microglobulin	1.96
1451310_a_at	J02583	Cathepsin L	1.74
1455002_at	AV331223	Protein tyrosine phosphatase 4a1	1.58
Down-regulated at early symptomatic age			
1429316_at	AK018120	RasGEF domain family, member 1A	-3.03
1447771_at	AW050081		-2.48
1449571_at	M59811	Thyrotropin releasing hormone receptor	-2.37
1449899_at	NM_130455	Glutamate receptor, ionotropic, NMDA3B	-2.25
1457587_at	BB196645	Adult male spinal cord cDNA, RIKEN, clone:A330095G09	-2.04
1435125_at	BB303627	Transcribed locus	-2.01
1458396_at	BB452660	15 days embryo head cDNA, RIKEN, clone:D930017N16	-1.92
1437724_x_at	BB206460	Phosphatidylinositol membrane-associated 1	-1.91
1428642_at	AK018094	Solute carrier family 35, member D3	-1.88
1457248_x_at	BB554029	Hydroxysteroid (17-beta) dehydrogenase 7	-1.85
1457829_at	BM199355	Calmegin	-1.78
1457979_at	BM938335	Adult male hypothalamus cDNA, RIKEN A230017C18	-1.76

Supplementary Table 3 :**Comparison of genes differentially expressed only at the end stage of the disease (120 day old) in SOD1^{G93A} motoneurons using microarrays**

List of the principal genes whose transcripts were regulated by 1.5- fold or more ($p < 0.05$) in mutant mice at the end stage of the disease. RNA was extracted from 2000 - 2400 microdissected motoneurons issued from one animal. Three chips were analyzed for each condition (control and mutant). Gene expression levels were compared in disease versus control animals. Fold change was calculated as the ratio between the average values of expression in mutant animals relative to the average values of controls; in all comparisons, a positive value indicates a higher level of expression in mutant animals versus negative numbers that show a higher level in controls.

Affymetrix probe set ID	Gene bank	Gene Name	Fold change
Genes involved in cell growth and/or maintenance up-regulated at the disease end stage			
1424638_at	AK007630	Cyclin-dependent kinase inhibitor 1A (P21)	30.27
1415927_at	NM_009608	Actin, alpha, cardiac	8.08
1452114_s_at	BF225802	Insulin-like growth factor binding protein 5	7.57
1443702_at	BE197560	Microtubule-associated protein 4	6.60
1427306_at	X83932	Ryanodine receptor 1, skeletal muscle	6.17
1438175_x_at	BB288010	Myomesin 2	5.66
1423427_at	AI323434	Adenylate cyclase activating polypeptide 1	5.58
1449519_at	NM_007836	Growth arrest and DNA-damage-inducible 45 alpha	5.29
1417023_a_at	NM_024406	Fatty acid binding protein 4, adipocyte	4.87
1437313_x_at	C85885	High mobility group box 2	4.17
1416889_at	NM_009405	Troponin I, skeletal, fast 2	4.14
1449434_at	NM_007606	Carbonic anhydrase 3	3.55
1427445_a_at	BC025840	Similar to titin isoform N2-A; connectin; CMH9, included; cardiomyopathy, dilated 1G (autosomal dominant)	3.44
1421027_a_at	AI595932	Myocyte enhancer factor 2C	3.44
1450118_a_at	NM_011620	Troponin T3, skeletal, fast	3.43
1425028_a_at	BC024358	Tropomyosin 2, beta	3.21
1427735_a_at	M12233	Actin, alpha 1, skeletal muscle	3.21
1418773_at	BE652876	Fatty acid desaturase 3	3.11
1417409_at	NM_010591	Jun oncogene	2.99
1423049_a_at	AK002271	Tropomyosin 1, alpha	2.97
1444083_at	BM122177	Titin	2.69
1435751_at	BG791642	ATP-binding cassette, sub-family C, member 9	2.44
1423233_at	BB831146	CCAAT/enhancer binding protein (C/EBP), delta	2.42
1428936_at	BI080417	RIKEN cDNA 2810442I22 gene	2.26
1417013_at	AF250139	Heat shock 27kDa protein 8	2.23
1423223_a_at	BB796358	Peroxiredoxin 6	2.22
1427868_x_at	AJ002522	Myosin, heavy polypeptide 1, skeletal muscle, adult	2.21
1450779_at	NM_021272	Fatty acid binding protein 7, brain	2.21
1420375_at	NM_008443	Kinesin family member 3A	2.10
1426805_at	AW701251	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4	2.06

1453851_a_at	AK007410	Growth arrest and DNA-damage-inducible 45 gamma	2.03
1433508_at	AV025472	Core promoter element binding protein	1.95
1417533_a_at	NM_010580	Integrin beta 5	1.95
1424143_a_at	AF477481	Retroviral integration site 2	1.91
1416344_at	NM_010685	Lysosomal membrane glycoprotein 2	1.80
1455168_a_at	BM210111	Guanine nucleotide binding protein, beta 2	1.70
1422459_a_at	NM_011875	Proteasome 26S subunit, non-ATPase, 13	1.67
1416947_s_at	NM_130864	Acetyl-Coenzyme A acyltransferase 1, 3-ketoacyl-CoA thiolase B	1.67
1452158_at	BM238943	Glutamyl-prolyl-tRNA synthetase	1.66
1426083_a_at	L16846	B-cell translocation gene 1, anti-proliferative	1.63
1448128_at	NM_008906	Protective protein for beta-galactosidase	1.62
1448118_a_at	NM_009983	Cathepsin D	1.61
1419091_a_at	NM_007585	Annexin A2	1.56
1422475_a_at	NM_016959	Ribosomal protein S3a	1.55
Genes up-regulated at the disease end stage			
1420884_at	AK008863	Sarcolipin	85.82
1437324_x_at	BB504826	Fibromodulin	15.75
1418199_at	NM_053149	Hemogen	12.98
1444494_at	W09692	Kelch repeat and BTB (POZ) domain containing 10	11.89
1456014_s_at	BB113173	cDNA sequence BC032204	10.46
1426808_at	X16834	Lectin, galactose binding, soluble 3	10.09
1450857_a_at	BF227507	Procollagen, type I, alpha 2	9.10
1455494_at	BI794771	Transcribed locus	8.50
1458368_at	BG794681	Myosin, heavy polypeptide 4, skeletal muscle	7.34
1426144_x_at	AF223417	Triadin	7.22
1448021_at	AA266723	Transcribed locus	6.18
1431609_a_at	AK008391	Acid phosphatase 5, tartrate resistant	5.85
1423760_at	M27130	CD44 antigen	5.67
1420699_at	NM_020008	C-type lectin domain family 7, member a	5.63
1449164_at	BC021637	CD68 antigen	5.08
1456586_x_at	BB139464	Major vault protein	4.83
1418021_at	NM_009780	Complement component 4 (within H-2S)	4.43
1450652_at	NM_007802	Cathepsin K	4.23
1422903_at	NM_010745	Lymphocyte antigen 86	4.22
1419872_at	AI323359		4.09
1434437_x_at	AV301324	Ribonucleotide reductase M2	3.90
1417464_at	NM_009394	Troponin C2, fast	3.75
1433428_x_at	AW321975	Transglutaminase 2, C polypeptide	3.43
1448891_at	BC016551	Macrophage scavenger receptor 2	3.37
1419873_s_at	AI323359	Colony stimulating factor 1 receptor	3.37
1417081_a_at	BC004829	Synaptogyrin 2	3.21
1422860_at	NM_024435	Neurotensin	3.20
1453125_at	BM508495	RIKEN cDNA 6230403H02 gene	3.15
1420664_s_at	NM_011171	Protein C receptor, endothelial	3.04
1454137_s_at	AK009636	Hemochromatosis type 2 (juvenile) (human homolog)	2.96
1418365_at	NM_007801	Cathepsin H	2.95
1457633_x_at	AV005759	Cytochrome c oxidase, subunit VI a, polypeptide 2	2.87
1452679_at	AA986082	RIKEN cDNA 2410129E14 gene	2.84
1441811_x_at	AU040201	RIKEN cDNA 0610011I04 gene	2.83

1427633_a_at	AF439513	Pregnancy-associated plasma protein A	2.74
1416382_at	NM_009982	Cathepsin C	2.62
1425545_x_at	M86502	Histocompatibility 2, D region	2.56
1428409_at	AK013287	Mak3 homolog (S. cerevisiae)	2.45
1438948_x_at	AV101079	Benzodiazepine receptor, peripheral	2.39
1455033_at	BB325849	RIKEN cDNA B430201A12 gene	2.34
1422650_a_at	NM_024182	RIO kinase 3 (yeast)	2.34
1418393_a_at	NM_008398	Integrin alpha 7	2.29
1433465_a_at	BB234337	Expressed sequence AI467606	2.28
1448748_at	AF181829	Pleckstrin	2.24
1420760_s_at	NM_008681	N-myc downstream regulated-like	2.18
1448154_at	NM_013864	N-myc downstream regulated gene 2	2.06
1454714_x_at	AA561726	Similar to 3-phosphoglycerate dehydrogenase	2.05
1460436_at	BI652065	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 1	2.00
1451201_s_at	BC010331	Ribonuclease/angiogenin inhibitor 1	1.97
1422555_s_at	BI662324	Guanine nucleotide binding protein, alpha 13	1.97
1447676_x_at	AV074236	S100 calcium binding protein A16	1.97
1416028_a_at	NM_008258	Hematological and neurological expressed sequence 1	1.96
1449556_at	NM_010398	Histocompatibility 2, T region locus 23	1.95
1452203_at	AV313559	RIKEN cDNA 5830411E10 gene	1.94
1438377_x_at	BB497312	Solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3	1.92
1420895_at	BM248342	Transforming growth factor, beta receptor I	1.88
1452110_at	BB757908	5-methyltetrahydrofolate-homocysteine methyltransferase reductase	1.88
1439399_a_at	BB493265	RNA, U22 small nucleolar	1.85
1419100_at	NM_009252	Serine (cysteine) proteinase inhibitor, clade A, member 3N	1.84
1435910_at	BM235658		1.82
1423985_at	BC002316	Guanine nucleotide binding protein, gamma 5 subunit	1.78
1417676_a_at	NM_011216	Protein tyrosine phosphatase, receptor type, O	1.78
1439740_s_at	AU018180	Expressed sequence AI481316	1.76
1426724_at	AI314104	Calponin 3, acidic	1.75
1435190_at	BB378591	Cell adhesion molecule with homology to L1CAM	1.73
1422156_a_at	NM_008503	Ribosomal protein S2	1.71
1420376_a_at	NM_008211	H3 histone, family 3B	1.64
1426195_a_at	AF483486	Cystatin C	1.54
1416901_at	BC007190	Niemann Pick type C2	1.51
Genes down-regulated at the disease end stage			
1459717_at	AW045505		-2.19
1436087_at	BQ176414	Dipeptidylpeptidase 10	-2.10
1426871_at	BM939903	F-box only protein 33	-2.02
1456862_at	AI893638		-1.89
1428662_a_at	AK009007	Homeobox only domain	-1.81
1423294_at	AW555393	Mesoderm specific transcript	-1.78
1433868_at	AV028445		-1.72
1422638_s_at	NM_018750	Ras association (RalGDS/AF-6) domain family 5	-1.62

Supplementary Table 4 : Sequences of oligonucleotide primer pairs used for real time quantitative PCR

Gene name	Description	Forward primer (5' - 3') Reverse primer (5' - 3')
Rps9	Mitochondrial ribosomal protein S9	GACCAGGAGCTAAAGTTGATTGGA TCTTGGCCAGGGTAAACTTGA
Gapdh	Glyceraldehyde-3-phosphate dehydrogenase	TCCATGACAACCTTTGGCATTG CAGTCTTCTGGGTGGCAGTGA
Gja1	Gap junction membrane channel protein alpha 1	CTTGATTCTGAGTTTAACAGTCTTTTAGATTG CCTTCACCCCCTCTAGTATCTCAA
Grin1	Glutamate receptor, ionotropic, NMDA1 (zeta1)	CTAGGGCTCCAGACTCCAAGAG CCAGCGTCTGAGGAAGCCTAT
Nov	Nephroblastoma overexpressed gene	GCCTCTCAGCTCATGGTTTGT GAGTCCCTGTTTAATTTTGAAGAAGTG
Hexb	Hexosaminidase B	TCACTGACCTAGAAAATGCCTACAA CTATTCCACGGCTGACCATTC
Mmp13	Matrix metalloproteinase 13	TGGTCAGTCGCCCTTTTGAG GCTAAGGAAAGCAGAGAGGGATT
Gap43	Growth associated protein 43	TGGCGAGTTTTTGGTAATGATG CACGCACCAGATCAAAAAACC
Vim	Vimentin	CCTCTGGTTGACACCCACTCA GTCTCATTGATCACCTGTCCATCT
Rex3	Reduced expression 3	TCACTATAGATGGGACCTGATGCA ACCCCCAAACCTCTGTACGTT
XIAP	X-linked inhibitor of apoptosis protein	ITTGGGCCGGAACGTTAAT TTGTTGAATTTGGGAAATTCCTAT
TNF α	Tumor necrosis factor alpha	GACCCTCACACTCAGATCATCTTCT CCACTTGGTGGTTTGCTACGA
Bax	Bcl2-associated X protein	TGGAGCTGCAGAGGATGATTG AGCTGCCACCCGGAAGA
Casp-1	Caspase-1	CATGCCGTGGAGAGAAACAA CATCCGTAAAGAAATCCTCTTCAG
Casp-3	Caspase-3	CTGGACTGTGGCATTGAGACA GCCTCCACCGGTATCTTCTG
Casp-7	Caspase-7	AAAATGGTTGGTTATTACTCATGGA GCAGAGGGCCTGCACAAA
Casp-9	Caspase-9	GAGCTCATGATGTCTGTGTTC GAATCCAGGGTGTATGCCATATC
ChAT	Choline acetyltransferase	ACCCAGTGGTGCACATGGTA GGGCCCATAGCATGTGATG
NF-H	Neurofilament, heavy polypeptide	GGATGACAAGAGCCTTTCCAAA GAGGATTTTTCAGCCTTTTCTGTCT
CGRP	Calcitonin gene-related peptide	ACTCCTGGTTCCGGTCCAA CCTGGGTACTCTGGCAACAAG