Supplementary table 1. Genes implicated in ALS between 1993 and February 2019.

Year of discovery	Gene	Loci	Accession number	Principal reference*
2018	*KIF5A*	12q13.3	NM_004984	[1]
2017	*GPX3-TNIP1*	5q33.1	NM_002084	[4]
2017	*TIA1*	2p13.3	NM_022173	[5]
2016	*C21orf2*	21q22.3	NM_004928	[9]
2016	*CCNF*	16p13.3	NM_001761	[10]
2016	*NEK1*	4q33	NM_001199397	[15]
2015	*TBK1*	12q14.2	NM_013254	[20]
2014	*CHCHD10*	22q11.23	NM_213720, NM_001301339	[39]
2014	*MATR3*	5q31.2	NM_199189, NM_001194956	[49]
2014	*TUBA4A*	2q35	NM_006000	[53]
2013	*HNRNPA1*	12q13	NM_031157	[55]
2016	*HNRNPA2B1*	7p15	NM_031243	[55]
2012	*PFN1*	17p13	NM_005022	[59]
2011	*C9orf72*	9p21	NM_018325, NM_145005, NM_001256054	[63, 64]
2011	*SQSTM1*	5q35	NM_003900	[66]
2011	*UBQLN2*	Xp11	NM_013444	[88]
2010	*ATXN2*	12q24	NM_002973	[91]
2010	*OPTN*	10p13	NM_021980, NM_001008211, NM_001008213	[105]
2010	*SPG11*	15q14	NM_025137, NM_001160227	[116]
2010	*VCP*	9p13	NM_007126	[121]
2006	*ANG*	14q11	NM_001145	[135]
2009	*ELP3*	8p21	NM_018091, NC_000008	[147]
2009	*FUS*	16p11	NM_004960	[153, 180]
2008	*TARDBP*	1p36	NM_007375	[212]
2006	*CHMP2B*	3p11	NM_014043	[246]
2004	*VAPB*	20q13	NM_004738	[249]
2003	*DCTN1*	2p13	NM_004082	[258]
2001	*ALS2*	2q33	NM_020919	[264]
1994	*NEFH*	22q12	NM_021076	[267]
2004	*SETX*	9q34	NM_015046	[272]
1993	*SOD1*	21q22	NM_000454	[336]

* According to reference list provided in Supplementary file 2

Supplementary table 2. ALS-implicated variants identified among 616 Australian sporadic ALS patients.

Gene name	Nucleotide alteration	Consequence	rs ID	Frequency in SALS (n=616)				MAF in gnomAD non-neuro NFE	MAF in Project MiNE cases (n=4366)	MAF in Project MiNE controls (n=1832)	Fisher's Exact p-values		Previous implication in ALS	
				No. WT patients	No. het patients	No. hom patients	MAF				SALS vs gnomad non-neuro NFE	Project MiNE cases vs controls	Aggregate of evidence of	Population(s)
ANG	c.A122T	p.K41I	rs121909536	614	2	0	0.001623	0.001745	0.00126	0.0005459	1	0.36844968	FALS and SALS (often oligogenic)	Ireland/Scotland, Caucasian/Australia/ Netherlands/USA, India, France, USA, Serbia
ANG	c.A208G	p.I70V	rs121909541	615	1	0	0.000812	0.000950	0.0006871	0.0002729	1	0.681691849	FALS and SALS (often oligogenic)	Scotland/Australia/France, Italy, Serbia
ATXN2	CAG repeat expansion (~29-30 repeats)			605	11	0	0.008929	unknown	unknown	unknown	.	.	Risk allele	Caucasian
C21orf2	c.G172T	p.V58L	rs75087725	593	22	1	0.019481	0.011330	0.0205	0.01174	0.01401241	0.000610774	Risk allele	Caucasian
C9orf72	GGGGCC repeat expansion (>30 repeats)			600	16	0	0.01299	unknown	unknown	unknown	.	.	FALS and SALS	Predominately European/Caucasian
CCNF	c.T1810A	p.F604I	rs118131564	615	1	0	0.000812	0.001238	0.0002291	0.0002729	1	1	FALS proband	Japan
CCNF	c.G2140A	p.V714M	rs61755288	598	17	1	0.015422	0.014690	0.01844	0.01992	0.811119094	0.612706525	FALS and SALS probands	Australia and Canada
CHCHD10	c.C100T	p.P34S	rs551521196	609	6	0	0.004878	0.004014	0.004237	0.004094	0.642725608	1	SALS probands	France, Italy, Europe, Caucasian
CHCHD10	c.C239T	p.P80L	rs775332895	613	2	0	0.001626	0.000291	0.0002291	0	0.037786242	1	SALS probands	Belgium, Italy, Europe, Caucasian
CHCHD10	c.T403C	p.Y135H	rs145649831	614	1	0	0.000813	0.000293	0.0003436	0.0002729	0.309427643	1	SALS probands	Europe
DCTN1	c.C3746T	p.T1249I	rs72466496	610	6	0	0.004870	0.004954	0.005039	0.006277	1	0.420642917	SALS probands	Germany, USA
ELP3	g.28086088G>A	unknown	rs6985069	44	227	345	0.744318	0.717100	no data	no data	0.04338141	1	SALS risk allele	USA
ELP3	g.28136109T>C	unknown	rs2614046	10	104	502	0.899351	0.874600	no data	no data	0.5108734	1	SALS risk allele	UK, Belgium and USA
FUS	c.*41G>A	unknown	rs80301724	604	12	0	0.009740	0.007952	0.00836	0.01037	0.421110732	0.296120456	FALS proband	USA
FUS	c.833-29C>T	unknown	rs72550862	600	15	1	0.013799	0.013460	0.01306	0.01228	0.90061586	0.793160078	FALS proband	Italy
GPX3-TNIP1	c.*3144C>T	unknown	rs10463311	315	248	53	0.287338	0.245900	.	.	0.001547101	.	Risk allele	China and Australia
NEFH	c.2230_2247del	unknown	rs59890097	614	1	0	0.000813	0.000357	0.0009221	0.001103	0.361798434	0.756756096	SALS proband	Scandinavia
NEK1	c.G782A	p.R261H	rs200161705	613	3	0	0.002435	0.003831	0.007787	0.003548	0.638711211	0.006844789	Risk allele	Belgium, Caucasian
NEK1	c.C3107G	p.S1036X	rs199947197	611	5	0	0.004058	0.000195	0.001775	0.002519	1.02038E-05	0.000647562	FALS proband	Europe
OPTN	c.T293A	p.M98K	rs11258194	588	26	2	0.024351	0.028150	0.02943	0.02593	0.487386764	0.313724819	Risk allele, oligogenic FALS	UK, Germany, Turkey
OPTN	c.G403T	p.E135X	rs140599944	614	2	0	0.001623	0.000155	0.0001145	0	0.01880108	1	FALS proband (homozygous)	Germany
OPTN	c.G476T	p.G159V	rs563413263	615	1	0	0.000812	0.000022	0	0.0002729	0.040159848	0.295579219	SALS proband	Denmark
SETX	c.A431G	p.N144S	rs767453182	615	1	0	0.000812	0.000192	0	0	0.023465067	1	SALS proband	China
SETX	c.G2755C	p.V919L	rs561190371	615	1	0	0.000812	0.000117	0.0006871	0.0002729	0.143251904	0.681691849	SALS proband	Ireland
SETX	c.A2975G	p.K992R	rs61742937	606	10	0	0.008117	0.018080	0.015	0.01556	0.006545908	0.80944997	FALS proband	Ireland
SETX	c.C4433A	p.A1478E	rs143661911	615	1	0	0.000812	0.000543	0.0006871	0.0005459	0.491779417	1	FALS proband	German
SETX	c.T4660G	p.C1554G	rs112089123	615	1	0	0.000812	0.003423	0.003207	0.002183	0.138824442	0.464086666	SALS probands	USA, Japan
SETX	c.T7640C	p.I2547T	rs151117904	608	8	0	0.006494	0.005854	0.006528	0.004094	0.705495943	0.11989856	SALS probands	USA

SOD1	c.A272C	p.D91A	rs80265967	615	1	0	0.000812	0.000611	0.002061	0.001092	0.532313329	0.349457171	FALS and SALS (homozygous in Scandinavian families)	USA, Scandinavia, Italy, Hungary, Iran, Portugal, Sweden, Canada, Spain, Belgium, Switzerland, Russia, Germany, Turkey, China, Australia, Serbia, North America
SOD1	c.T341C	p.I114T	rs121912441	613	3	0	0.002435	0.000011	0.0006871	0	9.87096E-06	0.189084762	FALS and SALS	USA, UK, Italy, Caucasian, China, Sweden, Canada, Scotland, Japan, Germany, Australia
SPG11	c.C491T	p.S164L	rs148175530	615	0	1	0.001623	0.000087	0	0	0.007139184	1	SALS proband	Korea
SPG11	c.A6224G	p.N2075S	rs140824939	611	5	0	0.004058	0.004207	0.005497	0.006277	1	0.602975628	FALS (homozygous)	Turkey
SQSTM1	c.C98T	p.A33V	rs200396166	615	1	0	0.000812	0.001154	0.001718	0.0008188	1	0.305637284	FALS and SALS probands	USA, Spain, France
SQSTM1	c.A712G	p.K238E	rs11548633	609	7	0	0.005682	0.003558	0.006184	0.005186	0.220728053	0.60700484	SALS probands	Italy
SQSTM1	c.G822C	p.E274D	rs55793208	586	30	0	0.024351	0.022680	0	0	0.69959601	1	Compound heterozygote (juvenile FALS), SALS risk allele	Turkey, Italy
SQSTM1	c.C1175T	p.P392L	rs104893941	613	3	0	0.002435	0.001382	0.0009162	0.001092	0.247160389	0.757283059	FALS and SALS	USA, Spain, France, China
TARDBP	c.543+112C>A	unknown	rs538912451	614	2	0	0.001623	0.001762	0.002634	0.001638	1	0.41480668	SALS proband	UK
TARDBP	c.G859A	p.G287S	rs80356719	615	1	0	0.000812	0.000022	0.000229	0	0.040161593	1	SALS probands	UK, France, Italy, Ireland, USA
TARDBP	c.G883A	p.G295S	rs80356723	615	1	0	0.000812	0.000000	0.0001145	0	0.01357112	1	FALS and SALS	France, Italy, Sardinia
TARDBP	c.G1144A	p.A382T	rs367543041	615	1	0	0.000812	0.000012	0.000229	0	0.029255294	1	FALS and SALS	France, Italy, USA, Sardinia
TARDBP	c.A1147G	p.I383V	rs80356740	614	2	0	0.001623	0.000000	0.000229	0	0.000216008	1	FALS and SALS	Italy, Netherlands, USA, Turkey, China, Japan
TBK1	c.A871G	p.K291E	rs34774243	615	1	0	0.000812	0.000244	0.00126	0.0008188	0.267066192	0.770019893	SALS proband	Italy
TBK1	c.G1073A	p.R358H	rs374208742	615	1	0	0.000812	0.000019	0.0001145	0	0.035011685	1	FALS proband	Europe
UBQLN2	c.G1019T	p.S340I	rs201549050	614	1	0	0.000813	0.000031	no data	no data	0.05575814	1	FALS family	Turkey

Supplementary table 3. SALS patient pairs identified as sharing a genomic locus as identical by descent, over their common ALS-implicated variant.

Sample ID one	Sample ID two	ALS-implicated variant			IBD locus				
		Gene	Consequence	Genomic location	Start genomic location	End genomic location	Length (bp)	Length (cM)	Estimated degree
MN201418	SALS1354	*FUS*	c.*41G>A	16:31202800	16:27102070	16:50404393	23302323	7.002	9
SALS0260	SALS1536	*FUS*	c.833-29C>T	16:31200415	16:28291553	16:50341952	22050399	4.786	9
SALS0312	SALS1895	*FUS*	c.833-29C>T	16:31200415	16:27000142	16:31635220	4635078	4.602	9
MN201517	SALS2258	*SOD1*	p.I114T	21:33039672	21:31208259	21:45727098	14518839	28.331	6
MQ130077	SALS0307	*SQSTM1*	p.K238E	5:179252184	5:177383301	5:180713115	3329814	7.892	9
MQ130077	SALS0621	*SQSTM1*	p.K238E	5:179252184	5:177383301	5:180713115	3329814	7.892	10
SALS0307	SALS0621	*SQSTM1*	p.K238E	5:179252184	5:174996473	5:180713115	5716642	11.442	8
MQ160055	SALS0859	*OPTN*	p.M98K	10:13152400	10:12769364	10:13811686	1042322	3.032	10
SALS0541	SALS2285	*OPTN*	p.M98K	10:13152400	10:12591939	10:13859897	1267958	3.602	9
MQ140145	SALS1910	*CHCHD10*	p.P34S	22:24109722	22:23222208	22:24633894	1411686	3.553	9
MN201529	SALS1003	*DCTN1*	p.T1249I	2:74588717	2:74445035	2:77387034	2941999	3.733	9
MN201529	SALS1119	*DCTN1*	p.T1249I	2:74588717	2:74480659	2:76946613	2465954	3.238	9
SALS1003	SALS1119	*DCTN1*	p.T1249I	2:74588717	2:74120961	2:76756549	2635588	3.49	9
SALS0066	SALS0320	*CCNF*	p.V714M	16:2506800	16:808061	16:4275176	3467115	7.335	9
SALS0066	SALS2407	*CCNF*	p.V714M	16:2506800	16:1532880	16:3300975	1768095	3.183	10
SALS0195	SALS0705	*CCNF*	p.V714M	16:2506800	16:1192542	16:2923879	1731337	3.387	11
SALS0320	SALS2407	*CCNF*	p.V714M	16:2506800	16:1504702	16:3281499	1776797	3.186	10
SALS1209	SALS2293	*CCNF*	p.V714M	16:2506800	16:2026442	16:3710097	1683655	3.107	9

Supplementary table 4. Multinomial logistic regression results of association testing between the clinical variables having either zero, one or more than one ALS-implicated variant.

	Variable	Odds Ratio	z-statistic	p-value
No ALS-implicated variants	Intercept	0.842	-0.15	0.881
	Site of onset: Spinal	0.532	-1.278	0.201
	Sex: Male	2.096	1.871	0.061
	Age at onset	1.036	2.241	0.025*
	Duration^^	1.009	1.117	0.264
One ALS-implicated variant	Intercept	0.555	-0.483	0.629
	Site of onset: Spinal	0.582	-1.044	0.297
	Sex: Male	1.639	1.179	0.238
	Age at onset	1.03	1.797	0.072
	Duration^^	1.008	0.934	0.35

^The baseline variable is more than one ALS-implicated variant.

^^Disease duration is included for both patients who are deceased and those who are alive.