Table 1 Variants in previously described and presently reported ALS genes

Gene	Reported inheritance model‡	Reported FALS explained‡	Reported SALS explained‡	Best model with case enrichment in present study (p-value)†	Cases with variant in best model†	Controls with variant in best model†	Potential ALS cases explained††
TBK1	N/A	N/A	N/A	Dom no benign (D=1.13x10-5; R=5.78x10-7; C=3.63x10-11)	D=23 (0.8%); R=23 (1.745%); C=46 (1.097%)	D=12 (0.187%); R=5 (0.211%); C=17 (0.194%)	0.904%
NEK1	N/A	N/A	N/A	Dom LoF (D=1.08x10-6; R=0.001; C=3.20x10-9)	D=25 (0.870%); R=10 (0.759%); C=35 (0.835%)	D=6 (0.094%); R=2 (0.084%); C=8 (0.091%)	0.744%
SOD1	AR/AD	12%	1.50%	Dom coding (7.23x10-8)	25 (0.870%)	5 (0.078%)	0.792%
TARDBP	AD	4%	1%	Dom coding	19 (0.661%)	6 (0.094%)	0.567%

				(2.97x10-6)			
OPTN	AR/AD	<1%	<1%	Dom no benign (D=0.023; R=0.002; C=0.002)	D=18 (0.626%); R=8 (0.607%); C=26 (0.620%)	D=16 (0.25%); R=4 (0.169%); C=20 (0.228%)	0.392%
SPG11	AR	<1%	<1%	Dom LoF (D=0.015; R=0.183; C=0.017)	D=21 (0.731%); R=5 (0.379%); C=26 (0.620%)	D=20 (0.312%); R=7 (0.295%); C=27 (0.308%)	0.313%
VCP	AD	1%	1%	Dom coding (0.022)	8 (0.278%)	4 (0.062%)	0.216%
HNRNPA1	AD	<1%	<1%	Dom coding (0.103)	6 (0.209%)	5 (0.078%)	0.131%
*ATXN2***	AD	<1%	<1%	Rec coding (0.206)	4 (0.139%)	2 (0.031%)	0.108%
ANG	AD	<1%	<1%	Dom LoF (0.217)	2 (0.070%)	1 (0.016%)	0.054%
CHCHD10	AD	<1%	<1%	Dom coding (0.226)	2 (0.070%)	0 (0%)	0.070%
SIGMAR1	AR	<1%	<1%	Dom LoF (0.226)	1 (0.035%)	0 (0%)	0.035%
FIG4	AR/AD	<1%	<1%	Dom LoF (0.233)	9 (0.313%)	12 (0.187%)	0.126%

SS18L1	AD	<1%	<1%	Dom LoF (0.241)	1 (0.035%)	0 (0%)	0.035%
GRN	AD	<1%	<1%	Dom no benign (0.357)	14 (0.487%)	24 (0.375%)	0.112%
SETX	AD	<1%	<1%	Rec no benign (0.380)	3 (0.104%)	4 (0.062%)	0.042%
HNRNPA2B1	AD	<1%	<1%	Dom no benign (0.423)	3 (0.104%)	4 (0.062%)	0.042%
SQSTM1	AD	1%	<1%	Dom LoF (0.546)	1 (0.035%)	2 (0.031%)	0.004%
TAF15	AR/AD	<1%	<1%	Rec no benign (0.555)	2 (0.070%)	1 (0.016%)	0.054%
FUS	AR/AD	4%	1%	Dom LoF (0.612)	2 (0.070%)	3 (0.047%)	0.023%
ALS2	AR	<1%	<1%	Rec coding (0.655)	2 (0.070%)	4 (0.062%)	0.007%
VAPB	AD	<1%	<1%	Dom no benign (0.688)	3 (0.104%)	5 (0.078%)	0.026%

NEFH	AD	<1%	<1%	Dom coding (0.777)	22 (0.765%)	37 (0.578%)	0.188%
*C9orf72***	AD	40%	7%	Dom no benign (1.000)	4 (0.139%)	7 (0.109%)	0.030%
CHMP2B	AD	<1%	<1%	Rec coding (1.000)	1 (0.035%)	1 (0.016%)	0.019%
MATR3	AD	<1%	<1%	Dom coding (1.000)	19 (0.661%)	35 (0.546%)	0.115%
PFN1	AD	<1%	<1%	Rec coding (1.000)	9 (0.313%)	15 (0.234%)	0.079%
PRPH	AD	<1%	<1%	Dom LoF (1.000)	1 (0.035%)	2 (0.031%)	0.004%
SPAST	AD	<1%	<1%	Dom coding (1.000)	6 (0.209%)	12 (0.187%)	0.021%
*TUBA4A**	AD	1%	<1%	Dom coding (0.743)	3 (0.104%)	7 (0.109%)	0%
*ELP3**	Allelic	<1%	<1%	Rec coding (1.000)	0 (0%)	0 (0%)	0%
*DAO**	AD	<1%	<1%	Rec coding (1.000)	0 (0%)	0 (0%)	0%
*DCTN1**	AD	<1%	<1%	Dom coding (0.668)	32 (1.113%)	76 (1.187%)	0%
*EWSR1**	AD	<1%	<1%	Dom coding (0.375)	10 (0.348%)	28 (0.437%)	0%

*GLE1**	AD	<1%	<1%	Rec LoF (1.000)	0 (0%)	0 (0%)	0%
*UBQLN2**	XD	<1%	<1%	Dom LoF (1.000)	0 (0%)	0 (0%)	0%

* No model showed case enrichment. **Because the known causal variants are repeat expansions that are not generally captured by next generation sequencing, no case enrichment is expected. †Based on discovery dataset for genes not included in the replication dataset, and otherwise D=discovery, R=replication, and C=combined. ††Calculated as Cases with variant in best model - Controls with variant in best model; as case variants are risk factors for disease and may not be causal, this represents the potential percentage of cases for which this gene plays a role in disease. ‡Adapted from (*3, 4, 42*) with additional information from *(13-17, 43-45)*).