SUPPLEMENTARY DATA

Appendix 1. Primers used to sequence the 12 exons of *PGRN*

	Sequence	Product size
Exon 1 Forward	AGGTGTTGAGAAGGCTCAGG	485
Exon 1 Reverse	CGGTAAAGATGCAGGAGTGG	
Exon 2 Forward	GTCCCCTTCTGGTGAGTGC	458
Exon 2 Reverse	GATCTTTGGAAGCAGGATCG	
Exon 3 Forward	ACACTGAGCAGGCATCTGG	512
Exon 3 Reverse	CTGGAGTCTTGCACTTTCTCC	
Exon 4 Forward	AGGGAGGGACTGGATTGTG	550
Exon 4 Reverse	TGCTCTCCCACCTCCTCAC	
Exon 5 Forward	GTTATGGTCGATGGCTCCTG	466
Exon 5 Reverse	CAGCTCACAGCAGGTAGAACC	
Exon 6 Forward	TGCCCAGAGGACTAACAGG	448
Exon 6 Reverse	CAGGCTCAGTAGCACACAGG	
Exon 7 Forward	CTGGCTGATGCAGGGTTC	452
Exon 7 Reverse	CTGTGAGGGAAGCAGAGAGG	
Exon 8 Forward	CCCCTTTCCTCCCTTTTAGG	388
Exon 8 Reverse	CGGGACAGCAGTGTATGTGG	
Exon 9 Forward	GCTGCTGCCCTTTTACCC	498
Exon 9 Reverse	CCGCCTCTCCTGCTTACAG	
Exon 10 Forward	CCTCCGCATAGCCCATAG	498
Exon 10 Reverse	ATCCTCGCAGCACACAGC	
Exon 11 Forward	AGACATCGGCTGTGACCAG	488
Exon 11 Reverse	GCGAGAGGGTTGGACGAG	
Exon 12 Forward	ACCTGCTGCCGAGACAAC	454
Exon 12 Reverse	CCACAACCCCCTTCTGAC	

Appendix 2. *PGRN* sequence variants found in both ALS cases and normal control samples (NM_002087.2)

Variant	Number of ALS/ALS-FTD cases with variant	Control chromosomes (number /total number screened)
R19W (c.274C>T)	1	13/450
D33D (c.318C>T)	1	2/268
IVS2+7 G>A	11	1/478
IVS3-47insAGTC	174*	62/231
V141I (c.640G>A)	1	2/510
IVS7+7 G>A	40†	28/400
A324T (c.1189G>A)	3	3/367
R433W (c.1516C>T)	3	5/184
P458L (c.1592C>T)	1	25/959
R556C (c.1885C>T)	1	1/862

*41 homozygous cases, 133 heterozygous cases

† 2 homozygous cases, 38 heterozygous cases

Clinical description of case ND10418

This non-Hispanic, Caucasian right-handed male patient presented at 67 years of age with leg weakness that progressed to involve all four limbs. He met the criteria for probable ALS by El Escorial criteria. He was not demented and there was no known family history of ALS, dementia or Parkinson Disease. He was 69 years of age at the time of sampling without obvious bulbar involvement.

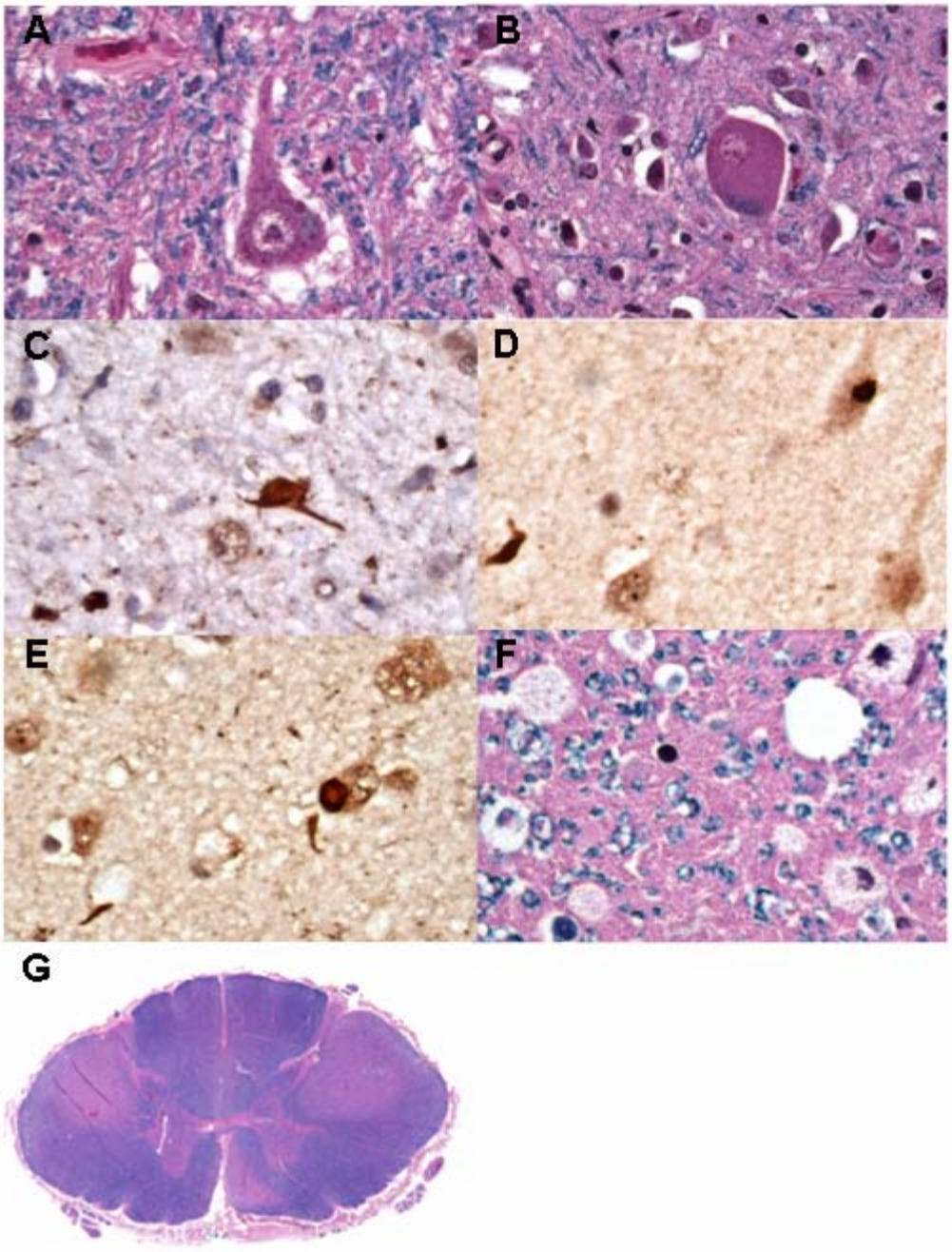

Figure 1. Histology of case T-51 carrying S120Y mutation. (A) Luxol fast blue counterstained with hematoxylin and eosin (LHE) stain of hypoglossal nucleus showing a neuron containing a cytoplasmic, eosinophilic inclusion (Bunina body). In addition, neuronal density is decreased and neuropil is traversed by glial fibrillary processes (Original magnification 630X); (B) LHE stain of motor cortex (Brodmann area 4) showing

an atrophic, centrally located Betz cells with scattered, shrunken neurons (400X); (C) Sixth cortical layer of motor cortex (BA4) with neuropil ubiquitinated aggregates (630X); (D) Fifth cortical layer of cingulate gyrus (BA24) showing two neurons with ubiquitinated nuclear inclusions (round compact on the upper right, two punctate on the bottom/center) and comma-shaped cytoplasmic aggregates on the lower left (630X); (E) Fifth cortical layer of superior frontal gyrus (BA 9) showing a neuron with a large, globular ubiquitinated, cytoplasmic inclusion (630X); (F) LHE stain of the cervical cord showing marked myelin loss of the corticospinal tract; (G) LHE stain of cervical corticospinal tract showing marked myelin loss with scattered macrophages (630X).