Supplemental table: Genetics and pathology of ALS and FTD. ***Ling et al (2013) Neuron***

Disease	Locus	Gene (protein)	Protein function	Heredity	Onset	fALS %	sALS %	FTD %	Pathology	Other diseases	Ref
				Typical ALS							
ALS1	21q22.1	*SOD1* (Superoxide dismutase)	Detoxification enzyme	AD	Adult	20%	2%	-	SOD1		1
ALS6	16-11.2	*FUS* (Fused in sarcoma)	RNA processing	AD, AR	Adult, juvenile	5%	<1%	<1%	FUS	FTD	2,3
ALS10	1p36.2	*TARDBP* (TDP-43)	RNA processing	AD	Adult	5%	<1%	<1%	TDP-43	FTD	4-6
ALS9	14q11.2	*ANG* (Angiogenin)	Angiogenic activity	AD	Adult				TDP-43	PD	7
ALS11	6q21	*FIG4* (phosphoinositide phosphatase)	Lipid metabolism	AD	Adult					CMT4J	8
ALS12	10p15-p14	*OPTN* (Optineurin)	Multifunction	AD, AR	Adult	4%	<1%	-	TDP-43	POAG, PDB	9
ALS14	9p13.3	*VCP* (Valosin-containing protein)	Protein quality control	AD	Adult	<1%	<1%	<1%	TDP-43	FTD, IBM, PDB	10
	12q24	*DAO* (D-amino acid oxidase)	Amino acid metabolism	AD	Adult						11
	17p13.2	*PFN1* (Profilin)	Cytoskeleton	AD	Adult						12
ALS13	12q24.12	*ATXN2* (Ataxin-2)	RNA processing	Risk factor	Adult				TDP-43	SCA2	13
	5q13.2	*HNRNPA1* (hnRNP-A1)	RNA processing	AD	Adult					MSP	14
	12q22.11	*HNRNPA2B1* (hnRNP-A2/B1)	RNA processing	AD	Adult					MSP	14
PDB	5q35.3	*SQSTM1* (P62/sequestosome 1)	Protein degradation	AD	Adult					PDB	15,16
	21q12.2	*EWSR1* (Ewing sarcoma break region 1)	RNA processing	AD	Adult						17
	17q12	*TAF15* (TBP-associated factor)	RNA processing	AD	Adult						18
ALS3	18q21	Unknown	Unknown	AD	Adult						19
ALS7	20p13	Unknown	Unknown	AD	Adult						20

Abbreviations: **AD**: autosomal dominant, **AR**: autosomal recessive, **XD**: X-linked dominant, **AOA2**: ataxia-ocular apraxia-2, **CMT4J**: Charcot-Marie-Tooth diseae type 4J, **HSP**: hereditary spastic paraplegia, **IBM**: inclusion body myositis, **MSP**: multisystem proteinopathy, **PD**: Parkinson's disease, **PDB**: Paget's disease of the bone, **POAG**: Primary open angle glaucoma, **SCA2**: spinocerebellar ataxia type 2, **SMA**: spinal muscular atrophy

Supplemental table: Genetics and pathology of ALS and FTD (continued). ***Ling et al (2013) Neuron***

Disease	Locus	Gene (protein)	Protein function	Heredity	Onset	fALS %	sALS %	FTD %	Pathology	Other diseases	Ref
Atypical ALS											
Juvenile onset, slow progression											
ALS2	2q33.1	*ALS2* (Alsin)	Vesicle trafficking	AR	Infantile, juvenile					Infantile-onset HSP	21
ALS5	15q15-21	*SPG11* (Spatacsin)	Axonal transport	AR	Juvenile					HSP	22
ALS4	9q34.13	*SETX* (Senataxin)	RNA processing	AD	Juvenile					AOA2	23
Adult onset, slow progression											
ALS8	20q13.3	*VAPB* (VAMP-associated protein)	Vesicle trafficking	AD	Adult					Late- onset SMA	24
ALS with FTD											
ALS-FTD	9q21-22	*C9ORF72* (C9orf72)	Unknown	AD	Adult	25%	5%	10%	TDP-43		25,26
ALS-FTD	9p13.3	*SIGMAR1* (Non-opiod receptor 1)	Signal transduction	AD, AR	Adult, juvenile						27,28
ALS-FTD-X	Xp11.21	*UBQLN2* (Ubiquilin-2)	Protein degradation	XD	Adult	<1%		<1%	TDP-43, FUS		29
FTD											
FTD	17Q21	*MAPT* (Microtubule-associated protein, tau)	cytoskeleton	AD	Adult			10%	Tau		30
FTD-TDP	17q21.31	*PGRN* (Progranulin)	Inflammation	AD	Adult			10%	TDP-43		31,32
FTD-3	3p11.2	*CHMP2B* (Charged multivesicular protein 2B)	Vesicle trafficking	AD	Adult	<1%		<1%	P62		33,34
FTD-TDP	7p21.3	*TMEM106B* (Transmembrane protein 106B)	Lysosome function	Risk factor	Adult						35

Abbreviations: **AD**: autosomal dominant, **AR**: autosomal recessive, **XD**: X-linked dominant, **AOA2**: ataxia-ocular apraxia-2, **CMT4J**: Charcot-Marie-Tooth diseae type 4J, **HSP**: hereditary spastic paraplegia, **IBM**: inclusion body myositis, **MSP**: multisystem proteinopathy, **PD**: Parkinson's disease, **PDB**: Paget's disease of the bone, **POAG**: Primary open angle glaucoma, **SCA2**: spinocerebellar ataxia type 2, **SMA**: spinal muscular atrophy

Supplemental table: Genetics and pathology of ALS and FTD (continued). ***Ling et al (2013) Neuron***

References for Supplemental Table:

1. Rosen, D.R. *et al.* Mutations in Cu/Zn superoxide dismutase gene are associated with familial amyotrophic lateral sclerosis. *Nature* **362**, 59-62 (1993).
2. Vance, C. *et al.* Mutations in FUS, an RNA processing protein, cause familial amyotrophic lateral sclerosis type 6. *Science* **323**, 1208-1211 (2009).
3. Kwiatkowski, T.J. *et al.* Mutations in the FUS/TLS gene on chromosome 16 cause familial amyotrophic lateral sclerosis. *Science* **323**, 1205-1208 (2009).
4. Sreedharan, J. *et al.* TDP-43 mutations in familial and sporadic amyotrophic lateral sclerosis. *Science* **319**, 1668-1672 (2008).
5. Kabashi, E. *et al.* TARDBP mutations in individuals with sporadic and familial amyotrophic lateral sclerosis. *Nat Genet* **40**, 572-574 (2008).
6. Van Deerlin, V.M. *et al.* TARDBP mutations in amyotrophic lateral sclerosis with TDP-43 neuropathology: a genetic and histopathological analysis. *The Lancet Neurology* **7**, 409-416 (2008).
7. Greenway, M.J. *et al.* ANG mutations segregate with familial and sporadic amyotrophic lateral sclerosis. *Nat Genet* **38**, 411-413 (2006).
8. Chow, C.Y. *et al.* Deleterious variants of FIG4, a phosphoinositide phosphatase, in patients with ALS. *Am. J. Hum. Genet.* **84**, 85-88 (2009).
9. Maruyama, H. *et al.* Mutations of optineurin in amyotrophic lateral sclerosis. *Nature* **465**, 223-226 (2010).
10. Johnson, J.O. *et al.* Exome sequencing reveals VCP mutations as a cause of familial ALS. *Neuron* **68**, 857-864 (2010).
11. Mitchell, J. *et al.* Familial amyotrophic lateral sclerosis is associated with a mutation in D-amino acid oxidase. *Proc. Natl. Acad. Sci. U.S.A.* **107**, 7556-7561 (2010).
12. Wu, C.-H. *et al.* Mutations in the profilin 1 gene cause familial amyotrophic lateral sclerosis. *Nature* (2012).
13. Elden, A.C. *et al.* Ataxin-2 intermediate-length polyglutamine expansions are associated with increased risk for ALS. *Nature* **466**, 1069-1075 (2010).
14. Kim, H.J. *et al.* Mutations in prion-like domains in hnRNPA2B1 and hnRNPA1 cause multisystem proteinopathy and ALS. *Nature* (2013).
15. Fecto, F. *et al.* SQSTM1 Mutations in Familial and Sporadic Amyotrophic Lateral Sclerosis. *Arch. Neurol.* **68**, 1440-1446 (2011).
16. Teyssou, E. *et al.* Mutations in SQSTM1 encoding p62 in amyotrophic lateral sclerosis: genetics and neuropathology. *Acta Neuropathol* **125**, 511-522 (2013).
17. Couthouis, J. *et al.* Evaluating the role of the FUS/TLS-related gene EWSR1 in amyotrophic lateral sclerosis. *Hum Mol Genet* **21**, 2899-2911 (2012).
18. Couthouis, J. *et al.* Feature Article: A yeast functional screen predicts new candidate ALS disease genes. *Proc. Natl. Acad. Sci. U.S.A.* **108**, 20881-20890 (2011).
19. Hand, C.K. *et al.* A novel locus for familial amyotrophic lateral sclerosis, on chromosome 18q. *Am. J. Hum. Genet.* **70**, 251-256 (2002).
20. Sapp, P.C. *et al.* Identification of two novel loci for dominantly inherited familial amyotrophic lateral sclerosis. *Am. J. Hum. Genet.* **73**, 397-403 (2003).
21. Hadano, S. *et al.* A gene encoding a putative GTPase regulator is mutated in familial amyotrophic lateral sclerosis 2. *Nat Genet* **29**, 166-173 (2001).
22. Daoud, H. *et al.* Exome sequencing reveals SPG11 mutations causing juvenile ALS. *Neurobiol. Aging* **33**, 839.e5-9 (2012).
23. Chen, Y.-Z. *et al.* DNA/RNA helicase gene mutations in a form of juvenile amyotrophic lateral sclerosis (ALS4). *Am. J. Hum. Genet.* **74**, 1128-1135 (2004).
24. Nishimura, A.L. *et al.* A mutation in the vesicle-trafficking protein VAPB causes late-onset spinal muscular atrophy and amyotrophic lateral sclerosis. *Am. J. Hum. Genet.* **75**, 822-831 (2004).
25. Renton, A.E. *et al.* A Hexanucleotide Repeat Expansion in C9ORF72 Is the Cause of Chromosome 9p21-Linked ALS-FTD. *Neuron 72*, 257-268 (2011).
26. Dejesus-Hernandez, M. *et al.* Expanded GGGGCC Hexanucleotide Repeat in Noncoding Region of C9ORF72 Causes Chromosome 9p-Linked FTD and ALS. *Neuron* **72**, 245-256 (2011).
27. Luty, A.A. *et al.* Sigma nonopioid intracellular receptor 1 mutations cause frontotemporal lobar degeneration-motor neuron disease. *Ann Neurol.* **68**, 639-649 (2010).
28. Al-Saif, A., Al-Mohanna, F. & Bohlega, S. A mutation in sigma-1 receptor causes juvenile amyotrophic lateral sclerosis. *Ann Neurol.* **70**, 913-919 (2011).
29. Deng, H.-X. *et al.* Mutations in UBQLN2 cause dominant X-linked juvenile and adult-onset ALS and ALS/dementia. *Nature* **477**, 211-215 (2011).
30. Hutton, M. *et al.* Association of missense and 5'-splice-site mutations in tau with the inherited dementia FTDP-17. *Nature* **393**, 702-705 (1998).
31. Cruts, M. *et al.* Null mutations in progranulin cause ubiquitin-positive frontotemporal dementia linked to chromosome 17q21. *Nature* **442**, 920-924 (2006).
32. Barker, M. *et al.* Mutations in progranulin cause tau-negative frontotemporal dementia linked to chromosome 17. *Nature* **442**, 916-919 (2006).
33. Parkinson, N. *et al.* ALS phenotypes with mutations in CHMP2B (charged multivesicular body protein 2B). *Neurology* **67**, 1074-1077 (2006).
34. Skibinski, G. *et al.* Mutations in the endosomal ESCRTIII-complex subunit CHMP2B in frontotemporal dementia. *Nat Genet* **37**, 806-808 (2005).
35. Van Deerlin, V.M. *et al.* Common variants at 7p21 are associated with frontotemporal lobar degeneration with TDP-43 inclusions. *Nat Genet* **42**, 234-239 (2010).