Supplementary Table 1: Haplotype analysis in family 2 by using short tandem repeat loci.

Short tandem repeat loci	II-1		I-1		I-2	
	Allele 1	Allele 2	Allele 1	Allele 2	Allele 1	Allele 2
AMEL	X	X	X	Y	X	X
D3S1358	17	15	17	17	17	15
D13S317	11	11	11	10	11	11
D7S820	10	8	10	12	11	8
D16S539	11	12	12	9	9	11
SE33	19	25.2	19	26.2	30.2	25.2
D10S1248	18	13	18	14	15	13
D5S818	10	12	10	10	10	12
D21S11	29	30	29	30.2	30	30
TPOX	8	11	8	8	8	11

D1S1656	15	16	15	14	16	16
D6S1043	19	13	19	12	13	13
D22S1045	11	15	11	16	11	15
D8S1179	13	10	13	11	16	10
Penta E	14	19	14	11	19	19
DYS391	11	11	11	11	11	11
D2S441	10	12	10	12	11	12
D12S391	20	19	20	17	17	19
D2S1338	23	17	23	25	22	17
vWA	14	16	14	16	14	16
Penta D	9	9	9	8	12	9
TH01	9	9	9	9	9	9
D18S51	15	16	15	18	14	16

CSF1PO	12	12	12	12	10	12
FGA	21	18	21	22	23	18

The figures in table present short tandem repeat number detected after polymerase chain reaction.

Supplementary Table 2: Nerve conduction study of patient 1 and 2 reported in this study.

Patient	Patient 1								Patient 2							
Nerve	Median		Ulnar		Peroneal		Tibial		Median		Ulnar		Peroneal		Tibial	
	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R
MNCV (m/s)	ND	50.0	ND	64.8	ND	42.6	ND	47.5	ND	38.9↓	ND	59.1	ND	45.1	ND	48.0
CMAP (mV)	ND	2.8↓	ND	5.6	ND	0.8↓	ND	14.0	ND	2.1↓	ND	7.5	ND	6.7	ND	13.5
SNCV (m/s)	ND	56.2	ND	49.5	ND	53.1	ND	ND	ND	57.9	ND	53.7	ND	48.2	ND	ND
SNAP (uV)	ND	46.0	ND	24.0	ND	41.0	ND	ND	ND	22.0	ND	21.1	ND	12.0	ND	ND

CMAP: Compound muscle action potential (normal range: median nerve ≥ 5.0 mV; ulnar nerve ≥5.0 mV; peroneal nerve ≥ 2.0 mV; tibial nerve ≥4.8 mV); L: Left; MNCV: Motor nerve conduction velocity (normal range: median nerve ≥ 50.0 m/s; ulnar nerve ≥ 50.0 m/s; peroneal nerve ≥37.0 m/s; tibial nerve ≥37.0 m/s); ND: Not detected; R: Right; SNAP: Sensory nerve action potential (normal range: median nerve ≥ 20.0 μV; ulnar nerve ≥ 17.0 μV; peroneus superficial nerve ≥ 6.0 μV); SNCV: Sensory nerve conduction velocity (normal range: median nerve ≥ 44.0 m/s; ulnar nerve ≥ 44.0 m/s; peroneus superficial nerve ≥ 41.0 m/s); ↓: lower than normal range.

Supplementary Table 3: Clinical features of 43 JALS patients with *FUS* mutations including one patient reported in this study and 42 patients collected from 29 articles met our inclusion criteria.

Patient	Country	*FUS* mutation	Exon	Inheritance pattern	Gender	AAO (years)	Onset site	Respiratory failure	Cognitive impairment	Disease duration (months)	Other features	EMG (Motor)	EMG (Sensory)	Cranial MRI	Spinal MRI	Reference
P1	China	p.P525L	15	*de novo*	F	18	Spinal	+	–	13	–	Axonal loss, denervation	Normal	Normal	NA	Our study
P2	China	p.R498Afs*32	14	NA	F	20	Spinal	+	NA	12	–	Lower motor neuron lesion	Normal	Normal	Normal	Liu *et al*[11]
P3	China	p.G486Pf	14	*de novo*	M	15	Spinal	NA	NA	>73	Mental retardation	Denervation	NA	Normal	Normal	Liu *et al*[11]

		s*30														
P4	China	p.G515Vfs*14	15	NA	F	22	Spinal	+	NA	84	–	Axonal loss, denervation	Normal	NA	NA	Liu *et al*[11]
P5	China	p.Q519Ifs*9	15	*de novo*	M	11	Spinal	+	NA	76	Consanguineous family	Axonal loss, denervation	Normal	NA	NA	Liu *et al*[11]
P6	China	p.P525L	15	NA	F	13	Spinal	+	–	>40	–	Axonal loss, denervation	Normal	Normal	Normal	Liu *et al*[12]
P7	China	p.P525L	15	NA	M	24	Bulbar and spinal	+	–	>27	–	Axonal loss, denervation	Normal	NA	Normal	Liu *et al*[12]
P8	China	p.G505Wfs*12	14	NA	M	14	Bulbar and spinal	+	+	11	Mental retardation	Denervation	NA	Normal	NA	Yu *et al*[19]

P9	China	p.R495Ter	14	AD	M	17	Bulbar and spinal	+	–	21	–	Denervation	NA	Normal	NA	Yu *et al*[19]
P10	China	p.G504Wfs*12	14	*de novo*	F	18	Spinal	NA	–	>7	Learning difficulties	Denervation	NA	NA	NA	Zou *et al*[20]
P11	China	p.P525L	15	*de novo*	F	19	Spinal	NA	–	>7	–	Denervation	NA	NA	NA	Zou *et al*[20]
P12	China	p.R495Ter	14	NA	M	22	Spinal	NA	–	>5	–	Denervation	NA	NA	NA	Zou *et al*[20]
P13	China	p.P525L	15	*de novo*	M	19	Bulbar and spinal	+	NA	7	Ophthalmoplegia, tremor, developmental delay, learning	Denervation	NA	Normal	Normal	Zhou *et al*[21]

											difficulties, adventitious movements					
P14	China	p.G504Wfs*12	14	*de novo*	F	18	Spinal	NA	–	25	Learning difficulties	NA	NA	NA	NA	Zou *et al*[16]
P15	China	p.P525L	15	*de novo*	F	19	Spinal	NA	–	25	–	NA	NA	NA	NA	Zou *et al*[16]
P16	China	p.P525L	15	NA	M	13	Spinal	NA	–	23	–	NA	NA	NA	NA	Zou *et al*[16]
P17	China	p.R495Ter	14	NA	M	22	Spinal	NA	–	17	–	NA	NA	NA	NA	Zou *et al*[16]
P18	China	p.G507Af	14	*de novo*	M	15	Bulbar and	+	NA	5	Atypical bilateral abducens	Lower motor neuron lesion	Normal	Normal	Normal	Wu *et al*[22]

		s*22					spinal				palsy					
P19	China	p.P525L	15	NA	M	22	Spinal	NA	NA	>8	–	NA	NA	NA	NA	Deng *et al*[23]
P20	China	p.G504Rfs*13	14	*de novo*	F	17	Spinal	+	NA	15	–	NA	NA	NA	NA	Chen *et al*[24]
P21	Japan	p.P525L	15	NA	F	19	Bulbar	+	NA	>8	Autism spectrum disorder, learning difficulties, postural tremor	No denervation	NA	Normal	Normal	Eura *et al*[25]
P22	Japan	p.P525L	15	NA	F	15	Spinal	+	–	14	After receiving the human	Denervation	NA	NA	NA	Hikiami *et al*[26]

											papilloma virus vaccine					
P23	Japan	p.G504W fs*12	14	NA	F	24	Spinal	NA	+	>7	–	Denervation	NA	High signal intensities along the bilateral pyramidal tracts on T2WI FLAIR and mild frontal lobe atrophy on DWI	NA	Hirayanagi *et al*[27]

P24	Japan	p.R514S	15	NA	F	24	Spinal	–	NA	>9	–	Denervation, central conducting times in MEP	NA	Normal	Normal	Yamashita *et al*[28]
P25	Japan	p.G492Efs*37	14	NA	M	17	Bulbar	+	+	>7	Mental retardation	Denervation, central conducting times in MEP	NA	Normal	NA	Yamashita *et al*[28]
P26	Canada	p.P525L	15	*de novo*	F	21	Bulbar	+	–	>18	Diplopia	Denervation	Normal	Normal	Normal	Leblond *et al*[29]
P27	Canada	p.R495Qfs*34	14	NA	M	19	Spinal	+	–	>8	Incomplete penetrance	Denervation	NA	Normal	Normal	Belzil *et al*[30]
P28	Canada	p.Q519Ifs*9	15	NA	M	9	Spinal	NA	–	9	Developmental delay, postural	Axonal loss, denervation	NA	Normal	Normal	Picher-Martel *et al*[31]

											tremor					
P29	German	p.D502Tfs*27	14	NA	M	19	Spinal	NA	NA	>15	–	NA	NA	NA	NA	Hübers *et al*[10]
P30	German	p.P525L	15	*de novo*	F	18	Bulbar	NA	NA	>9	–	NA	NA	NA	NA	Hübers *et al*[10]
P31	German	p.P525L	15	*de novo*	F	20	Bulbar	NA	NA	>15	–	NA	NA	NA	NA	Hübers *et al*[10]
P32	German	p.P525L	15	*de novo*	F	24	Bulbar	NA	NA	7	–	NA	NA	NA	NA	Hübers *et al*[10]
P33	German	p.G478Lfs*23	14	AD	M	21	Bulbar	+	–	24	–	Denervation	NA	NA	NA	Waibel *et al*[32]
P34	Italy	p.P525L	15	*de novo*	F	11	Spinal	+	–	>99	–	Denervation, central	NA	Normal	Normal	Conte *et al*[33]

												conducting times in MEP					
P35	Italy	pG504Wfs*12	14	*de novo*	F	11	Spinal	+	+	>23	–	Axonal loss, denervation	Normal	Normal	Normal	Lanteri *et al*[34]
P36	Turkey	p.P525L	15	*de novo*	M	17	Bulbar	+	NA	11	–	Axonal loss, denervation	NA	High signal intensity along bilateral internal capsule hind legs to mesencephalon on T2WI	Normal	Bodur *et al*[35]

														and slight diffusion restriction on DWI		
P37	UK	p.R495Ter	14	NA	M	17	Bulbar and spinal	+	NA	10	Myoclonic jerks	Denervation	NA	Normal	Normal	Dodd *et al*[36]
P38	UK	p.P525L	15	NA	F	22	Spinal	+	–	10	–	Denervation	NA	NA	NA	Bäumer *et al*[37]
P39	UK	p.P525L	15	NA	F	18	Spinal	NA	–	11	–	NA	NA	NA	NA	Bäumer *et al*[37]
P40	UK	p.Q519Ifs*9	15	NA	M	18	Spinal	–	NA	6	Congenital deformities of both feet,	NA	NA	NA	NA	Bäumer *et al*[37]

											learning difficulties					
P41	UK	p.G174del	5	NA	F	23	Bulbar	+	–	26	Multiple sclerosis	Anterior horn involvement	NA	Demyelination consistent with the earlier diagnosis of multiple sclerosis	Demyelination consistent with the earlier diagnosis of multiple sclerosis	Hewitt *et al*[38]
P42	USA	p.G466Vfs*14	14	*de novo*	F	20	Bulbar	+	–	22	–	NA	NA	NA	NA	DeJesus-Hernandez *et al*[39]
P43	USA	p.P5	15	*de novo*	F	13	Spinal	+	–	20	–	Demyelinatin	NA	NA	NA	Huang *et*

25L					g polyneuropathy, Denervation	*al*[40]

–: Absent; +: Present; AAO: Age at onset; AD: Autosomal dominant inheritance; DWI: Diffusion-weighted imaging; EMG: Electromyography; F: Female; FLAIR: Fluid attenuated inversion recovery; JALS: Juvenile amyotrophic lateral sclerosis; M: Male; MEP: Motor-evoked potentials; MRI: Magnetic resonance imaging; NA: Not available; T2WI: T2-weighted imaging; UK: United Kingdom; US: United States.

Supplementary Table 4: Clinical features differ among different populations of JALS patients with *SPTLC1* and *FUS* mutations.

Variable	Caucasian JALS patients with *SPTLC1* mutations (*n* = 15)	Caucasian JALS patients with *FUS* mutations (*n* = 18)	Asian JALS patients with *FUS* mutations (*n* = 25)	Statistics	*P*-values
Gender ratio (male/female)	0.5 (5/10)	0.6 (7/11)	0.9 (12/13)	0.90*	0.67
AAO (years, mean ± SD)	7.9 ± 4.9	17.8 ± 4.3	18.3 ± 3.7	32.52†	<0.01
Onset site *n*, (%)				15.60*	<0.01
Bulbar	0	8 (44.4)	2 (8.0)		
Bulbar and spinal	0	1 (5.6)	5 (20.0)		
Spinal	15 (100.0)	9 (50.0)	18 (72.0)		
Disease duration (months, mean [95% CI])	NA	27.0 (9.0–44.9)	35.8 (20.9–50.6)	25.14‡	<0.01

*$\chi 2$ test.

†One-way analysis of variance.

‡Kaplan–Meier analysis. AAO: Age at onset; CI: Confidence interval; JALS: Juvenile amyotrophic lateral sclerosis; NA: Not available; SD: Standard deviation.

Supplementary Table 5: Clinical features differ between JALS patients with *de novo SPTLC1* and *FUS* mutations.

Variable	JALS patients with *de novo SPTLC1* mutations (*n* = 11)	JALS patients with *de novo FUS* mutations (*n* = 19)	Statistics	*P*-values
Gender ratio (male/female)	0.6 (4/7)	0.4 (5/14)	0.33*	0.69
AAO (years, mean ± SD)	5.4 ± 2.4	17.1 ± 3.6	-9.60†	<0.01
Onset site (*n*)			5.77*	<0.05
Bulbar	0	6 (31.6)		
Bulbar and spinal	0	2 (10.5)		
Spinal	11 (100.0)	11 (57.9)		
Disease duration (months, mean [95% CI])	260.0 (210.9–309.1)	37.3 (18.6–56.0)	13.50‡	0.01

*$\chi 2$ test.

†Student's *t* test.

‡Kaplan–Meier analysis.. AAO: Age at onset; CI: Confidence interval; JALS: Juvenile amyotrophic lateral sclerosis; SD: Standard deviation