Novel *SPG11* mutations in Asian kindreds and disruption of spatacsin function in the zebrafish

Neurogenetics

Laura Southgate; Dimitra Dafou; Jacqueline Hoyle; Nan Li; Esther Kinning; Peter Critchley; Andrea H. Németh; Kevin Talbot; Parayil S. Bindu; Sanjib Sinha; Arun B. Taly; Seetharam Raghavendra; Ferenc Müller; Eamonn R. Maher; Richard C. Trembath

Corresponding Author:

Prof. Richard C. Trembath

King's College London School of Medicine

Email: richard.trembath@kcl.ac.uk

Location(s)	DNA / RNA mutation	Predicted amino acid effect	Class	F / S	Country of origin	Reference
Ex 1	c.118C>T	p.Q40X	n	F	Israel	s1
Ex 2	c.267G>A	p.W89X	n	S	Pakistan	s7
Ex 2 + Int 6	c.[267G>A]+[1457-2A>G]; r.[(267g>a)]+[1457_1602del146]	p.[W89X]+[E486GfsX23]	n, s	S	Germany	s3
Exs 2 + 3	c.[268G>T]+[529_533delATATT]	p.[E90X]+[I177SfsX2]	n, fs	S	Brazil	s18
Exs 2 + 15	c.[349G>T]+[2833A>G]; r.[(349g>u)]+[2834_2835ins2834+1_2834+65][s5]	p.[E117X]+[R945GfsX6]	n, s	S	Italy	s17
Exs 2 + 30	c.[359delT]+[5703delT]	p.[L120X]+[H1902IfsX49]	fs, fs	F	Spain	s10
Ex 2	c.398delG	p.C133LfsX22	fs	F	Iran	s11
Exs 2 + 4	c.[408_428del21]+[733_734delAT]	p.[E136_I142del]+[M245VfsX2]	del, fs	S	Italy	s18
Int 2	c.442+1G>A; r.258_442del185	p.H86QfsX15	s	F	India	s20
Int 2	c.442+1G>C; r.258_442del185[s17]	p.H86QfsX15	s	F	Turkey	s3
Ints 2 + 8	c.[442+1G>C]+[1735+3_+6delAAGT]; r.[258_442del185]+[1603_1735del133]	p.[H86QfsX15]+[A535MfsX5]	s, s	S	Italy	s17

Ex 3	c.529_533delATATT	p.I177SfsX2	fs	F × 3	Portugal	s1, s5
Exs 3 + 22	c.[529_533delATATT]+[3741dupA]	p.[I177SfsX2]+[P1248TfsX17]	fs, fs	F	Brazil	s18
Exs 3 + 33	c.[642delT]+[6206-1G>C]; r.[(642delu)]+[spl?]	p.[F214LfsX3]+[?]	fs, s	F	Sweden	s14
Exs 3 + 22	c.[654_655delTTinsG]+[3719_3720delTA]	p.[S218RfsX2]+[I240RfsX24]	fs, fs	S	China	s12
Ex 4	c.704_705delAT	p.H235RfsX12	fs	F × 2	Turkey	s5, s13
Ex 4	c.733_734delAT	p.M245VfsX2	fs	F × 7	Italy, Tunisia, Brazil	s2, s5, s6, s18
Exs 4 + 14	c.[733_734delAT]+[2471dupT]	p.[M245VfsX2]+[K825QfsX13]	fs, fs	S	Spain	s3
Exs 4 + 31	c.[733_734delAT]+[5974C>T]	p.[M245VfsX2]+[R1992X]	fs, n	F	France	s1
Exs 4 + 32	c.[733_734delAT]+[6157G>A]	p.[M245VfsX2]+[V2053M]	n, m	S	Italy	s17
Exs 4 + 37	c.[733_734delAT]+[6790dupC]	p.[M245VfsX2]+[L2264PfsX76]	fs, fs	F	China	s12
Int 4	c.869+1G>A; r.spl?	p.?	s	F	Argentina	s5
Ex 6	c.1203delA	p.D402IfsX14	fs	S	Italy	s17
Exs 6 + 16	c.[1203delA]+[2842dupG]	p.[D402IfsX14]+[V948GfsX6]	fs, fs	F	Italy	s1
Exs 6 + 21	c.[1203delA]+[3664_3665insT]	p.[D402IfsX14]+[K1222IfsX15]	fs, fs	S	Italy	s18
Exs 6 + 31	c.[1203delA]+[5992dupT]	p.[D402IfsX14]+[Y1998LfsX2]	fs, fs	F	Italy	s18
Ex 6	c.1235C>G	p.S412X	n	F	Portugal	s5
Exs 6 + 32	c.[1235C>G]+[6100C>T]	p.[S412X]+[R2034X]	n, n	S	Spain	s10
Ex 6 + Int 34	c.[1282A>T]+[6477+4A>G]; r.[(1282a>u)]+[(spl?)]	p.[K428X]+[?]	n, s	S	Portugal	s5
Exs 6 + 30	c.[1348dupA]+[5456_5457delAG]	p.[I450NfsX26]+[E1819AfsX10]	fs, fs	F	UK	s7
Int 6 + Ex 9	c.[1457-2A>G]+[1845_1846delGT]; r.[1457_1602del146]+[(1845_1846delgu)]	p.[E486GfsX23]+[S616FfsX3]	s, fs	S	Germany	s3
Exs 7 + 30	c.[1471_1472delCT]+[5532_5533delCA]	p.[L491DfsX66]+[K1845VfsX13]	fs, fs	S	France	s5
Exs 7 + 36	c.[1549_1550delCT]+[6737_6740delTTGA]	p.[C518SfsX39]+[I2246SfsX15]	fs, fs	F	Algeria	s5
Ex 7	c.[1551_1552delTT]+[?]	p.[C518SfsX39]+[?]	fs	S	Spain	s10
Exs 8 + 36	c.[1668delT]+[6739_6742delGAGT]	p.[F556LfsX22]+[E2247LfsX14]	fs, fs	S	France	s5
Exs 8 + 31	c.[1679C>G]+[5870C>G]	p.[S560X]+[S1957X]	n, n	S	Italy	s18
Exs 8 + 31	c.[1697_1712del16insTACTCCCAT] +[5983_5986dupCTCT]	p.[D566VfsX10]+[C1996SfsX5]	fs, fs	F	Italy	s18
Exs 9 + 11	c.[1833dupT]+[2163dupT]	p.[N612X]+[I722YfsX10]	n, fs	F	Korea	s19
Ex 9	c.1837_1838insA	p.L613HfsX7	fs	F	Turkey	s7
Ex 10	c.1951C>T	p.R651X	n	F	Saudi Arabia	s3
Exs 10 + 13	c.[1951C>T]+[2444G>T]; r.[(1951c>u)]+[(spl?)]	p.[R651X]+[R815M]	n, m/s	S	Italy	s18
Exs 10 + 16	c.[1951C>T]+[2849dupT]	p.[R651X]+[L950FfsX4]	n, fs	F	Italy	s18

Exs 10 + 31	c.[1951C>T]+[5989_5992delCTGT]	p.[R651X]+[L1997MfsX60]	n, fs	S	Romania	s5
Ex 11	c.2146C>T	p.Q716X	n	F	India	s20
Exs 11 + 39	c.[2163dupT]+[7101dupT]	p.[I722YfsX10]+[K2368X]	fs, fs	F	China	s12
Ex 11	c.2198T>G	p.L733X	n	F	Italy	s1
Int 12	c.2316+1G>A; r.spl?	p.?	s	S	Norway	s5
Int 12	c.[2316+1G>A]+[?]; r.[spl?]+[?]	p.?	s	S	Norway	s4
Ex 13	c.2357_2358delAG	p.K787LfsX10	fs	F	Italy	s18
Int 13 + Ex 25	c.[2444+1G>C]+[4307_4308delAA]; r.[spl?]+[(4307_4308delaa)]	p.[?]+[Q1436RfsX7]	s, fs	S	Brazil	s18
Ex 14	c.2608A>G; r.2608_2620del13	p.I870NfsX21	s	F × 2	Italy	s16, s17
Ex 15	c.2697G>A	p.W899X	n	F × 2	Turkey	s18
Ex 15	c.2716delC	p.Q906SfsX15	fs	F	Brazil	s18
Ex 15	c.2833A>G; r.2834_2835ins2834+1_2834+65	p.R945GfsX6	s	F × 2	Israelian-Arab, Italy	s5, s17
Exs 15 + 38	c.[2833A>G]+[6856C>T]; r.[2834_2835ins2834+1_2834+65][s5]+[(6856c>u)]	p.[R945GfsX6]+[R2286X]	s, n	S	Italy	s18
Ints 15 + 36	c.[2834+1G>T]+[6754+2_6754+3dupTG]; r.[spl?]+[(spl?)]	p.[?]+[?]	s, s	F	England	s11
Ex 17	c.3075dupA	p.E1026RfsX4	fs	F × 2	Turkey, Iran	s3, s14
Exs 17 + 24	c.[3075dupA]+[4045T>A]	p.[E1026RfsX4]+[F1349I]	fs, m	S	Italy	s18
Exs 17 + 30	c.[3075dupA]+[5470C>T]	p.[E1026RfsX4]+[R1824X]	fs, n	S	Germany	s18
Ex 17	c.3145_3146insCA	p.D1049QfsX5	fs	F	Turkey	s3
Int 18 + Ex 30	c.[3291+1G>T]+[5410_5411delTG]; r.[spl?]+[(5410_5411delug)]	p.[?]+[C1804PfsX25]	s, fs	F	Korea	s19
Ex 21	c.3602_3603delAT	p.Y1201LfsX4	fs	F	India	s20
Ex 25	c.4307_4308delAA	p.Q1436RfsX7	fs	F	China	s8
Exs 25 + 31	c.[4307_4308delAA]+[5986dupT]	p.[Q1436RfsX7]+[C1996LfsX4]	fs, fs	F	Poland-Israel	s5
Ex 26	c.4462_4463delGT	p.V1488LfsX13	fs	F	Taiwan	s9
Exs 26 + 32	c.[4462_4463delGT]+[6091C>T]	p.[V1488LfsX13]+[R2031X]	fs, n	F	Taiwan	s9
Ex 27	c.4668T>A	p.Y1556X	n	S	China	s12
Ex 28	c.4846C>T	p.Q1616X	n	F	Pakistan	s20
Ex 30	c.[5255delT]+[?]	p.[F1752SfsX86]+[?]	fs	S	Germany	s3
Exs 30 + 31	c.[5255delT]+[5986dupT]	p.[F1752SfsX86]+[C1996LfsX4]	fs, fs	F	Italy	s18
Ex 30	c.5399_5402delAGATinsTGGAGGAG	p.Q1800LfsX31	fs	F	Pakistan	s7
Ex 30 + Int 39	c.[5623C>T]+[7152-1G>T]; r.[(5623c>u)]+[spl?]	p.[Q1875X]+[?]	n, s	F	Sweden	s14
Exs 30 + 40	c.[5623C>T]+[7158_7161dupACAA]	p.[Q1875X]+[H2388TfsX6]	n, fs	F	England	s11

Ex 30	c.5769delT	p.S1923RfsX28	fs	S, F	Saudi-Arabia, India	s5, s7
Ex 30	c.[5798delC]+[?]	p.[A1933VfsX18]+[?]	fs	F	Germany	s3
Exs 31-34	c.5867-3237_6478-451del8323; r.(5867_6477del611)	p.T1956SfsX18	fs	F	Netherlands	s18
Exs 31-34 + Int 36	c.[5867-3237_6478-451del8323]+[6754+2_ 6754+3dupTG]; r.[(5867_6477del611)]+[(spl?)]	p.[T1956SfsX18]+[?]	fs, s	F	Germany	s15
Ex 31	c.5970C>G	p.Y1990X	n	F	Italy	s18
Ex 31	c.5977C>T	p.Q1993X	n	F, S	China	s8, s12
Ex 31	c.5989_5992delCTGT	p.L1997MfsX60	fs	F	Turkey	s7
Ex 32	c.6091C>T	p.R2031X	n	F	Turkish-German	s18
Ex 32	c.6100C>T	p.R2034X	n	F × 9, S	Algeria, Morocco, Tunisia, Brazil	s1, s5, s6, s18
Ex 34	c.6451delG	p.A2151PfsX22	fs	F	France	s1
Ex 36	c.6737_6740delTTGA	p.I2246SfsX15	fs	F	Japan	s5
Exs 37-39 + Int 38	[g.96677_99386del2710]+[c.7000-3_-2insGGA]; r.[6755_7151del397]+[6999_7000insgaag]	p.[E2252DfsX15]+[A2334EfsX7]	fs, s	F	Italy	s17
Ex 37	c.6832_6833delAG	p.S2278LfsX61	fs	F	Portugal	s5
Ex 38	c.6898_6899delCT	p.L2300AfsX39	fs	S	China	s12
Ex 39	c.7023C>A	p.Y2341X	n	F	Brazil	s18
Ex 39	c.7029dupT	p.V2344CfsX6	fs	F	Tunisia	s1
Ex 39	c.7085_7088dupATTA	p.Y2363X	fs	F	China	s12
Int 39	c.7151+4_7151+7delAGTA; r.7151_7152ins46	p.K2386X	s	S	China	s12
Int 39	c.7152-1G>C; r.spl?	p.?	s	S	Sweden	s14

Supplementary Table 1 Collated list of all *SPG11* mutations reported to date.

Variants are described according to the recommendations of the Human Genome Variation Society (HGVS; http://www.hgvs.org/mutnomen). Mutations in square brackets denote heterozygous variants, with separate alleles described in adjacent brackets. All other variants have been observed in the homozygous state. Experimentally verified mutations are described at both the DNA and RNA level. Where RNA has not been analysed, expected changes are listed in parentheses. **Key:** Ex(s) = Exon(s); Int(s) = Intron(s); c. = cDNA variant; g. = genomic DNA; r. = RNA; p. = protein; [?] = variant unknown; spl? = variant is expected to affect splicing, but has not been experimentally verified; (spl?) = variant might affect splicing; del = in-frame deletion; fs = frameshift; m = missense; n = nonsense; s = splicing variant; F = Familial; S = Sporadic

Supplementary References

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s20. This study