Note: The following information is provided by the authors and has not been reviewed by GeneReviews staff.

Table 3. Hereditary Spastic Paraplegia Loci

SPG	Chrom	MOI	Type	Families[1]	Origin	Gene Product/ Locus Size	Reference
1	Xq28	X	C	>10	W	L1CAM	Jouet et al [1994]
2	Xq22	X	both	>10	W	PLP	Keppen et al [1987]
3	14q11.2-q24.3	D	P	>20	W	Atlastin	Hazan et al [1993] Zhao et al [2001]
4	2p21-p24	D	both	>100	W	Spastin	Hazan et al [1994] Hazan et al [1999]
5	8q12-13	R	P	>10	W	3.8 cM	Hentati et al [1994]
6	15q11.1	D	P	2	W	NIPA1	Fink et al [1995] Rainier et al [2003]
7	16q24.3	R	both	8	Italian/ French	Paraplegin	Casari et al [1998] De Michele et al [1998]
8	8q23-q24	D	P	>5	Caucasian	KIAA0196	Hedera et al [1999] Valdmanis et al [2007]
9	10q23.3-24.2	D	C	2	Italian/ British	4.8 Mb	Seri et al [1999]
10	12q13	D	both	4	Caucasian	KIF5A	Reid et al [1999] Reid et al [2002]
11	15q13-q15	R	both	>20	W	spatacsin	Martinez Murillo et al [1999] Stevanin et

SPG	Chrom	MOI	Type	Families[1]	Origin	Gene Product/ Locus Size	Reference
							al [2007b]
12	19q13.1	D	P	3	W	3.3 cM	Reid et al [2000]
13	2q24-q34	D	P	1	French	HSP60	Fontaine et al [2000] Hansen et al [2002]
14	3q27-q28	R	C	1	Italian	4.5 cM	Vazza et al [2000]
15	14q	R	C	2	Irish	ZFYVE26	Hughes et al [2001]
16	Xq11.2	X	both	2	Japanese/ Caucasian	NOR ins.	Steinmuller et al [1997] Tamagaki et al [2000]
17	11q12-q14	D	C	>10	W	Seipin	Patel et al [2001]
19	9q33-q34	D	P	1	Italian	Not found	Valente et al [2002]
20	13q12.3	R	C	2	Amish	Spartin	Patel et al [2002]
21	15q22.31	R	C	1	Amish	Maspardin	Simpson et al [2003]
22	Xq13.2		C	>10	W	MCT8	Claes et al [2000] Bohan & Azizi [2004] Schwartz et al [2005]
23	1q24-q32	R	C	1	Arab-Israeli	25cM	Blumen et al [2003]
24	13q14	R	P	1	Saudi Arabian	1.8-Mb	Hodgkinson et al [2002]
25	6q23-q24.1	R	C	1	Italian	Not found	Zortea et al [2002]
26	12p11.1-q14	R	C	1	Kuwaiti	22.8 cM	Wilkinson et al [2005]

SPG	Chrom	MOI	Type	Families[1]	Origin	Gene Product/ Locus Size	Reference
27	10q22.1-q24.1	R	P	2	French Canadian	19.6 cM	Meijer et al [2004]
28	14q21.3-q22.3	R	P	1	Moroccan	Not found	Bouslam et al [2005]
29	1p31.1-p21.1	D	C	1	Scottish	22.3cM	Orlacchio et al [2005]
30	2q37.3	R	C	1	Algerian	Not found	Klebe et al [2006]
31	2p12	D	P	6	Caucasian?	REEP1	Zuchner et al [2006a] Zuchner et al [2006b]
32	14q12-21	R			Portuguese	30-cM	Stevanin et al [2007a]
33	10q24.2	D	P	1	?	ZFVE27	Mannan et al [2006]
34	Xq24-25	R	P	1	Brazilian	14cM	Macedo-Souza et al [2008]
35	16q21-q23	R	C	1	Omani	20.4 Mb	Dick et al [2008]
36	12q23-24	D					reserved
37	8p21.1-q13.3	D	P		French	43.5 cM	Hanein et al [2007]
38	4p16-p15	D	C	2	Italian	13.1cM	Orlacchio et al [2008]
unknown	8p12-p11.21	R	C	2	Omani		Al-Yahyaee et al [2006]

D = Dominant
R = Recessive
P = Pure
C = Complicated
MR = Mental retardation
TCC = Thin corpus callosum
W = worldwide
Modified from Soderblom & Blackstone [2006] and Tallaksen et al [2001]
[1] According to OMIM

References

Al-Yahyaee S, Al-Gazali LI, De Jonghe P, Al-Barwany H, Al-Kindi M, De Vriendt E, Chand P, Koul R, Jacob PC, Gururaj A, Sztriha L, Parrado A, Van Broeckhoven C, Bayoumi RA (2006) A novel locus for hereditary spastic paraplegia with thin corpus callosum and epilepsy. *Neurology* 66:1230-4

Blumen SC, Bevan S, Abu-Mouch S, Negus D, Kahana M, Inzelberg R, Mazarib A, Mahamid A, Carasso RL, Slor H, Withers D, Nisipeanu P, Navon R, Reid E (2003) A locus for complicated hereditary spastic paraplegia maps to chromosome 1q24-q32. *Ann Neurol* 54:796-803

Bohan TP, Azizi P (2004) Allan-Herndon-Dudley syndrome: should the locus for this hereditary spastic paraplegia be designated SPG 22? *Arch Neurol* 61:1470-1; author reply 1471

Bouslam N, Benomar A, Azzedine H, Bouhouche A, Namekawa M, Klebe S, Charon C, Durr A, Ruberg M, Brice A, Yahyaoui M, Stevanin G (2005) Mapping of a new form of pure autosomal recessive spastic paraplegia (SPG28). *Ann Neurol* 57:567-71

Casari G, De Fusco M, Ciarmatori S, Zeviani M, Mora M, Fernandez P, De Michele G, Filla A, Cocozza S, Marconi R, Durr A, Fontaine B, Ballabio A (1998) Spastic paraplegia and OXPHOS impairment caused by mutations in paraplegin, a nuclear encoded mitochondrial metalloprotease. *Cell* 93:973-83

Claes S, Devriendt K, Van Goethem G, Roelen L, Meireleire J, Raeymaekers P, Cassiman JJ, Fryns JP (2000) Novel syndromic form of X-linked complicated spastic paraplegia. *Am J Med Genet* 94:1-4

De Michele G, De Fusco M, Cavalcanti F, Filla A, Marconi R, Volpe G, Monticelli A, Ballabio A, Casari G, Cocozza S (1998) A new locus for autosomal recessive hereditary spastic paraplegia maps to chromosome 16q24.3. *Am J Hum Genet* 63:135-9

Dick KJ, Al-Mjeni R, Baskir W, Koul R, Simpson MA, Patton MA, Raeburn S, Crosby AH (2008) A novel locus for an autosomal recessive hereditary spastic paraplegia (SPG35) maps to 16q21-q23. *Neurology* 71:248-52

Fink JK, Wu CT, Jones SM, Sharp GB, Lange BM, Lesicki A, Reinglass T, Varvil T, Otterud B, Leppert M (1995) Autosomal dominant familial spastic paraplegia: tight linkage to chromosome15q. *Am J Hum Genet* 56:188-92

Fontaine B, Davoine CS, Durr A, Paternotte C, Feki I, Weissenbach J, Hazan J, Brice A (2000) A new locus for autosomal dominant pure spastic paraplegia on chromosome 2q24-q34. *Am J Hum Genet* 66:702-7

Hanein S, Durr A, Ribai P, Forlani S, Leutenegger AL, Nelson I, Babron MC, Elleuch N, Depienne C, Charon C, Brice A, Stevanin G (2007) A novel locus for autosomal dominant "uncomplicated" hereditary spastic paraplegia maps to chromosome 8p21.1-q13.3. *Hum Genet* 122:261-73

Hansen JJ, Durr A, Cournu-Rebeix I, Georgopoulos C, Ang D, Nielsen MN, Davoine CS, Brice A, Fontaine B, Gregersen N, Bross P (2002) Hereditary spastic paraplegia SPG13 is associated with a mutation in the gene encoding the mitochondrial chaperonin Hsp60. *Am J Hum Genet* 70:1328-32

Hazan J, Fonknechten N, Mavel D, Paternotte C, Samson D, Artiguenave F, Davoine CS, Cruaud C, Durr A, Wincker P, Brottier P, Cattolico L, Barbe V, Burgunder JM, Prud'homme JF, Brice A, Fontaine B, Heilig B, Weissenbach J (1999) Spastin, a new AAA protein, is altered in the most frequent form of autosomal dominant spastic paraplegia. *Nature Genetics* 23:296-303

Hazan J, Fontaine B, Bruyn RP, Lamy C, van Deutekom JC, Rime CS, Dürr A, Melki J, Lyon-Caen O, Agid Y, et al (1994) Linkage of a new locus for autosomal dominant familial spastic paraplegia to chromosome 2p. *Hum Mol Genet* 3:1569-73

Hazan J, Lamy C, Melki J, Munnich A, de Recondo J, Weissenbach J (1993) Autosomal dominant familial spastic paraplegia is genetically heterogeneous and one locus maps to chromosome 14q. *Nature Genetics* 5:163-7

Hedera P, Rainier S, Alvarado D, Zhao X, Williamson J, Otterud B, Leppert M, Fink JK (1999) Novel locus for autosomal dominant hereditary spastic paraplegia, on chromosome 8q. *Am J Hum Genet* 64:563-9

Hentati A, Pericak-Vance MA, Hung WY, Belal S, Laing N, Boustany RM, Hentati F, Ben Hamida M, SIddique T (1994) Linkage of 'pure' autosomal recessive familial spastic paraplegia to chromosome 8 markers and evidence of genetic locus heterogeneity. *Hum Mol Genet* 3:1263-7

Hodgkinson CA, Bohlega S, Abu-Amero SN, Cupler E, Kambouris M, Meyer BF, Bharucha VA (2002) A novel form of autosomal recessive pure hereditary spastic paraplegia maps to chromosome 13q14. *Neurology* 59:1905-9

Hughes CA, Byrne PC, Webb S, McMonagle P, Patterson V, Hutchinson M, Parfrey NA (2001) SPG15, a new locus for autosomal recessive complicated HSP on chromosome 14q. *Neurology* 56:1230-3

Jouet M, Rosenthal A, Armstrong G, MacFarlane J, Stevenson R, Paterson J, Metzenberg A, Ionasescu V, Temple K, Kenwrick S (1994) X-linked spastic paraplegia (SPG1), MASA syndrome and X-linked hydrocephalus result from mutations in the L1 gene. *Nat Genet* 7:402-7

Keppen L, Leppert M, O'Connell P, Nakamura Y, Stauffer D, Lathrop M, Lalouel J, White R (1987) Etiological heterogeneity in X-linked spastic paraplegia. *Am J Hum Genet* 41:933-43

Klebe S, Azzedine H, Durr A, Bastien P, Bouslam N, Elleuch N, Forlani S, Charon C, Koenig M, Melki J, Brice A, Stevanin G (2006) Autosomal recessive spastic paraplegia (SPG30) with mild ataxia and sensory neuropathy maps to chromosome 2q37.3. *Brain* 129:1456-62

Macedo-Souza LI, Kok F, Santos S, Licinio L, Lezirovitz K, Nascimento RM, Bueno C, Martyn M, Leao EK, Zatz M (2008) Reevaluation of a large family defines a new locus

for X-linked recessive pure spastic paraplegia (SPG34) on chromosome Xq25. *Neurogenetics* 9:225-6

Mannan AU, Krawen P, Sauter SM, Boehm J, Chronowska A, Paulus W, Neesen J, Engel W (2006) ZFYVE27 (SPG33), a Novel Spastin-Binding Protein, Is Mutated in Hereditary Spastic Paraplegia. *Am J Hum Genet* 79:351-7

Martinez Murillo F, Kobayashi H, Pegoraro E, Galluzzi G, Creel G, Mariani C, Farina E, Ricci E, Alfonso G, Pauli RM, Hoffman EP (1999) Genetic localization of a new locus for recessive familial spastic paraparesis to 15q13-15. *Neurology* 53:50-6

Meijer IA, Cossette P, Roussel J, Benard M, Toupin S, Rouleau GA (2004) A novel locus for pure recessive hereditary spastic paraplegia maps to 10q22.1-10q24.1. *Ann Neurol* 56:579-82

Orlacchio A, Kawarai T, Gaudiello F, St George-Hyslop PH, Floris R, Bernardi G (2005) New locus for hereditary spastic paraplegia maps to chromosome 1p31.1-1p21.1. *Ann Neurol* 58:423-9

Orlacchio A, Patrono C, Gaudiello F, Rocchi C, Moschella V, Floris R, Bernardi G, Kawarai T (2008) Silver syndrome variant of hereditary spastic paraplegia: A locus to 4p and allelism with SPG4. *Neurology* 70:1959-66

Patel H, Cross H, Proukakis C, Hershberger R, Bork P, Ciccarelli FD, Patton MA, McKusick VA, Crosby AH (2002) SPG20 is mutated in Troyer syndrome, an hereditary spastic paraplegia. *Nat Genet* 31:347-8

Patel H, Hart PE, Warner TT, Houlston RS, Patton MA, Jeffrey S, Crosby AH (2001) The Silver syndrom variant of Hereditary Spastic Paraplegia maps to chromosome11q12-q14, with evidence for genetic heterogeneity within this subtype. *Am J Hum Gen* 69:209-15

Rainier S, Chai JH, Tokarz D, Nicholls RD, Fink JK (2003) NIPA1 gene mutations cause autosomal dominant hereditary spastic paraplegia (SPG6). *Am J Hum Genet* 73:967-71

Reid E, Dearlove AM, Osborn O, Rogers MT, Rubinsztein DC (2000) A locus for autosomal dominant "pure" hereditary paraplegia maps to chromosome 19q13. *Am J Hum Genet* 66:728-32

Reid E, Dearlove AM, Rhodes M, Rubinsztein DC (1999) A new locus for autosomal dominant "pure" hereditary spastic paraplegia mapping to chromosome 12q13, and evidence for further genetic heterogeneity. *Am J Hum Genet* 65:757-63

Reid E, Kloos M, Ashley-Koch A, Hughes L, Bevan S, Svenson IK, Graham FL, Gaskell PC, Dearlove A, Pericak-Vance MA, Rubinsztein DC, Marchuk DA (2002) A kinesin heavy chain (KIF5A) mutation in hereditary spastic paraplegia (SPG10). *Am J Hum Genet* 71:1189-94

Schwartz CE, May MM, Carpenter NJ, Rogers RC, Martin J, Bialer MG, Ward J, Sanabria J, Marsa S, Lewis JA, Echeverri R, Lubs HA, Voeller K, Simensen RJ,

Stevenson RE (2005) Allan-Herndon-Dudley syndrome and the monocarboxylate transporter 8 (MCT8) gene. *Am J Hum Genet* 77:41-53

Seri M, Cusano R, Forabosco P, Cinti R, Caroli F, Picco P, Bini R, Morra VB, De Michele G, Lerone M, Silengo M, Pela I, Borrone C, Romeo G, Devoto M (1999) Genetic mapping to 10q23.3-q24.2, in a large Italian pedigree, of a new syndrome showing bilateral cataracts, gastroesophageal reflux, and spastic paraparesis with amyotrophy. *Am J Hum Genet* 64:586-93

Simpson MA, Cross H, Proukakis C, Pryde A, Hershberger R, Chatonnet A, Patton MA, Crosby AH (2003) Maspardin is mutated in mast syndrome, a complicated form of hereditary spastic paraplegia associated with dementia. *Am J Hum Genet* 73:1147-56

Soderblom C, Blackstone C (2006) Traffic accidents: Molecular genetic insights into the pathogenesis of the hereditary spastic paraplegias. *Pharmacol Ther* 109:42-56

Steinmuller R, Lantigua-Cruz A, Garcia-Garcia R, Kostrzewa M, Steinberger D, Muller U (1997) Evidence of a third locus in X-linked recessive spastic paraplegia. *Hum Genet* 100:287-9

Stevanin G, Paternotte C, Coutinho P, Klebe S, Elleuch N, Loureiro JL, Denis E, Cruz VT, Durr A, Prud'homme JF, Weissenbach J, Brice A, Hazan J (2007a) A new locus for autosomal recessive spastic paraplegia (SPG32) on chromosome 14q12-q21. *Neurology* 68:1837-40

Stevanin G, Santorelli FM, Azzedine H, Coutinho P, Chomilier J, Denora PS, Martin E, Ouvrard-Hernandez AM, Tessa A, Bouslam N, Lossos A, Charles P, Loureiro JL, Elleuch N, Confavreux C, Cruz VT, Ruberg M, Leguern E, Grid D, Tazir M, Fontaine B, Filla A, Bertini E, Durr A, Brice A (2007b) Mutations in SPG11, encoding spatacsin, are a major cause of spastic paraplegia with thin corpus callosum. *Nat Genet* 39:366-72

Tallaksen CM, Durr A, Brice A (2001) Recent advances in hereditary spastic paraplegia. *Curr Opin Neurol* 14:457-63

Tamagaki A, Shima M, Tomita R, Okumura M, Shibata M, Morichika S, Kurahashi H, Giddings J, Yoshioka A, Yokobayashi Y (2000) Segregation of a pure form of spastic paraplegia and NOR insertion into Xq11.2. *Am J Med Genet* 94:5-8

Valdmanis PN, Meijer IA, Reynolds A, Lei A, MacLeod P, Schlesinger D, Zatz M, Reid E, Dion PA, Drapeau P, Rouleau GA (2007) Mutations in the KIAA0196 gene at the SPG8 locus cause hereditary spastic paraplegia. *Am J Hum Genet* 80:152-61

Valente EM, Brancati F, Caputo V, Bertini E, Patrono C, Costanti D, Dallapiccola B (2002) Novel locus for autosomal dominant pure hereditary spastic paraplegia (SPG19) maps to chromosome 9q33-q34. *Ann Neurol* 51:681-5

Vazza G, Zortea M, Boaretto F, Micaglio GF, Sartori V, Mostacciuolo ML (2000) A new locus for autosomal recessive spastic paraplegia associated with mental retardation and distal motor neuropathu, SPG14, maps to chromosome 3q27-q28. *Am J Hum Genet* 67:504-9

Wilkinson PA, Simpson MA, Bastaki L, Patel H, Reed JA, Kalidas K, Samilchuk E, Khan R, Warner TT, Crosby AH (2005) A new locus for autosomal recessive complicated hereditary spastic paraplegia (SPG26) maps to chromosome 12p11.1-12q14. *J Med Genet* 42:80-2

Zhao X, Alvarado D, Rainier S, Lemons R, Hedera P, Weber C, Tukel T, Apak M, Heiman-Patterson T, Ming L, Bui M, Fink J (2001) Mutations in a newly identified GTPase gene cause autosomal dominant hereditary spastic paraplegia. *Nat Genet* 29:326-31

Zortea M, Vettori A, Trevisan CP, Bellini S, Vazza G, Armani M, Simonati A, Mostacciuolo ML (2002) Genetic mapping of a susceptibility locus for disc herniation and spastic paraplegia on 6q23.3-q24.1. *J Med Genet* 39:387-90

Zuchner S, Kail ME, Nance MA, Gaskell PC, Svenson IK, Marchuk DA, Pericak-Vance MA, Ashley-Koch AE (2006a) A new locus for dominant hereditary spastic paraplegia maps to chromosome 2p12. *Neurogenetics* 7:127-9

Zuchner S, Wang G, Tran-Viet KN, Nance MA, Gaskell PC, Vance JM, Ashley-Koch AE, Pericak-Vance MA (2006b) Mutations in the Novel Mitochondrial Protein REEP1 Cause Hereditary Spastic Paraplegia Type 31. *Am J Hum Genet* 79:365-9