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The proposed new list of hereditary spastic paraplegias

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| --- | --- | --- | --- | --- |
| **New designation**  | **Less common movement phenotype** | **Clinical clues** | **Inheri-tance**  | **Locus Symbol** |
| **Autosomal dominant forms** |
| HSP-*ATL11* |  | Pure or complex; Silver-syndrome, allelic with hereditary sensory neuropathy type 1, cerebral palsy (infantile onset). GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK45978/OMIM 182600 | AD/AR | SPG3A |
| HSP-*SPAST2* |  | Pure or complex; dementia, epilepsy, Peripheral neuropathy, tremor, ataxia, TCC, cerebellar atrophy.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1160/OMIM 182601 | AD | SPG4 |
| HSP-*NIPA13* |  | Pure or complex; Peripheral neuropathy, spinal cord atrophy, spastic dysarthria, facial dystonia, atrophy of the small hand muscles, upper limb spasticity, epilepsy.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 600363 | AD | SPG6 |
| HSP-*KIAA01964* |  | Pure spastic paraplegiaGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1827/OMIM 603563 | AD | SPG8 |
| HSP-*KIF5A5* |  | Pure or complex; allelic to Charcot Marie Tooth Neuropathy Type 2, Silver-syndrome, mental retardation, parkinsonism, deafness, retinitis, dysautonomia, sensory spinal cord-like syndrome.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 604187 | AD | SPG10 |
| HSP-*RTN26* |  | Pure spastic paraplegiaGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 604805 | AD | SPG12 |
| HSP-*HSPD17* |  | Pure or complex; dystonia.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 605280 | AD | SPG13 |
| HSP-*BSCL28* |  | Complex; Silver syndrome, these mutations may also cause distal hereditary neuropathy type 5.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1307/OMIM 270685 | AD | SPG17 |
| HSP-*REEP19* | Ataxia10 | Pure or complex; distal motor neuronopathy, axonal Peripheral neuropathy, Silver-like syndrome, cerebellar ataxia, tremor, dementia.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 610250 | AD | SPG31 |
| HSP-*ZFYV32711* |  | Pure spastic paraplegiaGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 610244 | AD | SPG33 |
| SCA/HSP-*VAMP112* |  | Spastic ataxia, supranuclear upgaze limitationGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1138/OMIM 108600 | AD | SPAX1 |
| HSP-ALDH18A113, 14 |  | Autosomal dominantPure or complex; cognitive impairment, congenital cataract, dysarthria, cerebellar signs, neuropathic pain, epilepsy, infantile psychosis, sensorineural hearing loss, vomiting, biochemical features of delta-1-pyrroline-5-carboxylate synthase deficiency.GeneReviewshttps://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 601162Autosomal recessiveComplex; cognitive impairment.OMIM 616586GeneReviews<https://www.ncbi.nlm.nih.gov/books/NBK1509/>Alternative phenotype: Cutis laxa, autosomal dominant 3 (OMIM 616603) and Cutis laxa, autosomal recessive, type IIIA (OMIM 219150). | AD/AR | SPG9A, autosomal dominantSPG 9B, autosomal recessive |
| **Autosomal Recessive forms** |
| HSP-*CYP7B115* |  | Pure or complex; white matter lesions, optic atrophy, cerebellar ataxia, sensory ataxia.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 270800 | AR | SPG5A |
| HSP-*SPG716* |  | Pure or complex; optic atrophy, cerebellar atrophy, dysarthria, dysphagia, TCC, CPEO-like phenotype, mitochondrial abnormalities on muscle biopsy. GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1107/OMIM 607249 | AR/AD\* | SPG7 |
| HSP-*KIAA184017* | Parkinsonism18 | Pure or complex; May cause Kjellin syndrome; TCC, mental retardation, sensory neuropathy, amyotrophy, dysarthria, nystagmus, ataxia, maculopathy, white matter lesions. Occasional parkinsonism.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1210/OMIM 640360 | AR | SPG11 |
| HSP-*ZFYVE2619* | Parkinsonism18 | Complex; Kjellin syndrome. TCC, WMLs, mental retardation, dysarthria, pigmentary maculopathy, peripheral neuropathy, distal amyotrophy. Occasional parkinsonism.51GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 270700 | AR | SPG15 |
| HSP-*ERLIN220* |  | Complex; intellectual decline, speech involvement, seizures, congenital hip dislocation.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 611225 | AR | SPG18 |
| HSP-*SPARTIN21* |  | Complex; Troyer-syndrome. Early onset dysarthria, distal muscle wasting with contractures and cerebellar signs in some. Delayed cognition and dysmorphism.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 275900 | AR | SPG20 |
| HSP-*ACP3322* |  | Pure or complex; Mast syndrome, Dementia, cerebellar involvement, dyskinesias, athetoid movements, TCC, white matter lesions.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 248900 | AR | SPG21 |
| HSP-*B4GALNT23* |  | Complex; progressive dysarthria, distal amyotrophy, non-progressive cognitive impairment, cerebellar signs, sensory polyneuropathy, pes cavus, stereotypies, emotional lability, psychiatric illness, seizures.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 609195 | AR | SPG26 |
| HSP-*DDHD124* |  | Pure and complex; cerebellar oculomotor disturbance, Peripheral neuropathy.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 609340 | AR | SPG28 |
| HSP-*KIF1A25* |  | Pure or complex; cerebellar signs, PNP, allelic to hereditary sensory and autonomic neuropathy.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 610347 | AR | SPG30 |
| HSP/NBIA-*FA2H26* | Dystonia, parkinsonism, ataxia27  | Fatty Acid Hydroxylase-associated Neurodegeneration (FAHN) 27:Iron accumulation: GP (more subtle than other NBIAs)Additional clinical features: Spastic tetraparesis, cognitive decline, cerebellar and brainstem atrophy, dysarthria, dysphagia, optic nerve atrophy, seizuresGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 612319 | AR | SPG35 |
| HSP-*PNPLA6/NT28* |  | Complex; axonal peripheral neuropathy, spinal cord atrophy, learning disability, speech impairment, cerebellar signs, allelic with Boucher-Neuhäuser and Gordon Holmes syndromes.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK247161/OMIM 612020 | AR | SPG39 |
| HSP/NBIA-*C19orf1229* | Dystonia, parkinsonism | Mitochondrial membrane protein-associated neurodegeneration (MPAN) 30: Dystonia, parkinsonismIron accumulation: GP - hyperintense streaking of medial medullary lamina between GPi and GPe; SNAdditional clinical features: Progressive spastic paresis, dysarthria, dysphagia, cognitive decline/dementia, motor axonal neuropathy, optic nerve atrophy, psychiatric symptoms, bowel/bladder incontinenceGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK185329/OMIM 614298 | AR | NBIA4/SPG43 |
| HSP-*NT5C231* |  | Complex; mental retardation, ocular signsGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 613162 | AR | SPG45 |
| HSP-*GBA232* |  | Complex; mental impairment, cataract, hypogonadism in males, TCC and cerebellar atrophy on brain imaging.32GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 614409 | AR | SPG46 |
| HSP-*AP4B33* |  | Complex; intellectual disability, seizures, TCC, white matter lesions.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 614066 | AR | SPG47 |
| HSP-*KIAA041534* |  | Pure or complex; cervical cord hyperintensities.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 613647 | AR | SPG48 |
| HSP-*TECPR235* |  | Complex; severe intellectual disability, fluctuating central hypoventilation, gastresophageal reflux disease, awake apnea, areflexia, dysmorphic features.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 615031 | AR | SPG49 |
| HSP-*APAM136* |  | Complex; cerebral palsy, intellectual disability, reduction of cerebral white matter and atrophy of the cerebellum.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 612936 | AR | SPG50 |
| HSP-*AP4E137* |  | Complex; cerebral palsy, intellectual disability and microcephaly.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 613744 | AR | SPG51 |
| HSP-*DDHD238* |  | Complex; mental retardation, dysmorphism, short stature and dysgenesis of the corpus callosum.39GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 615033 | AR | SPG54 |
| HSP-*C12orf6540* |  | Complex; optic atrophy, peripheral neuropathy.GeneReviews http://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 615035 | AR | SPG55 |
| HSP-*KIF1C41*Allelic with autosomal recessive spastic ataxia at the SAX2 locus. | Dystonia, ataxia41 | Pure and complicated, chorea, myoclonus, dysarthria, developmental delay, mild mental retardation, hypodontia, ptosis, short stature, sensorineural deafness, pes planus, white matter lesions.GeneReviews: http://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 611302 | AR | SPG58 |
| HSP-*ERLIN131* |  | Pure and complex; thoracic kyphosis, borderline intelligence.GeneReviews: n/aOMIM 611604 | AR | SPG62 |
| HSP-*NT5C231* |  | Complex; learning disability, optic atrophy, squint, glaucoma, congenital cataract, TCC, white matter lesions, cystic occipital leukomalacia. GeneReviews: http://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 613162 | AR | SPG65 |
| HSP-*ALSIN42*  |  | Complex, generalized dystonia, no speechGeneReviewsOMIM | AR | Alsin |
| HSP-*SACSIN43* |  | Spastic ataxiaGeneReviewsOMIM | AR | SACS |
| HSP- *ALDH3A244* |  | RM, ichtyosis, macular dystrophy, leukoencephalopathyGeneReviewsOMIM | AR | Sjögren-Larsson syndrome |
| HSP-*BICD245* |  | SMA likeGeneReviewsOMIM | AR |  |
| HSP-MAG46Allelic with Pelizaeus-Merzbacher disease.  |  | Complex; infantile-onset Pelizaeus-Merzbacher disease-like phenotype, mental retardation, dysarthria, optic atrophy, peripheral neuropathy, demyelinating leukodystrophyGeneReviewshttps://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM [616680](https://www.omim.org/entry/616680) | AR | SPG75 |
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| **X-linked recessive** |
| HSP-*L1CAM47* |  | Complex; MASA-syndrome, hydrocephalus, TCC.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1182/OMIM 312920 | XR | SPG1 |
| HSP-*PLP148*Allelic with Pelizaeus-Merzbacher disease. |  | Pure or complex; optic atrophy, ataxia, nystagmus, peripheral neuropathy, aphasia, mental retardation.GeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1182/OMIM 312920 | XR | SPG2 |
| HSP-*SLC16A249* |  | Complex; Allan-Herndon-Dudley syndromeGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM 300523 | XR | SPG22 |
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| **Disorders that usually present with other phenotypes but can have predominant spastic paraparesis** |
| SCA-*ATXN1* | HSP50 | Marked non-ataxia features; can have dominant choreapyramidal features, peripheral neuropathy, ophthalmoplegiaGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1184/OMIM 164400 | AD | SCA1 |
| SCA-*ATXN3* | HSP, dystonia51, 41 | Marked non-ataxia features; can have predominant parkinsonism, dystonia, chorea, spasticity, neuropathy, lower motor neuron involvementGeneReviewshttp://www.ncbi.nlm.nih.gov/books/NBK1196/OMIM 109150 | AD | SCA3 |
| DYT\*\*-*TUBB4A52* | HSP53, 54 | Spasmodic dysphonia is most common dystonic presentation. Alternative, phenotype: Hypomyelinating leukodystrophy (see footnote) GeneReviews n/aOMIM: 128101 | AD | TUBB4A |
| HSP/ATX-CAPN155, 56 |  | Hereditary spastic paraplegia: pure or complex; cerebellar dysarthria, cerebellar ataxia, foot deformity, ocular movement abnormalities, peripheral neuropathy, amyotrophy.GeneReviewshttps://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM: [616907](https://www.omim.org/entry/616907) | AR | SPG76 |
| HSP/ATX-KCNA257, 58 |  | Hereditary spastic paraplegia: complex; learning disability, global developmental delay, autism spectrum disorder, sensory-motor peripheral neuropathy, seizures, ataxia.Alternative phenotype: Epileptic encephalopathy, early infantile, 32OMIM: [616366](https://www.omim.org/entry/616366)GeneReviewshttps://www.ncbi.nlm.nih.gov/books/NBK1509/OMIM: not assigned | AD |  |

TCC=thinning of the corpus callosum, SACS=Spastic Ataxia of Charlevoix-Saguenay, SMA=Spinal Muscular Atrophy

Silver syndrome: Complex HSP involving amyotrophy of the hand muscles

Kjellin syndrome: Complex HSP including thinning of the corpus callosum and central retinal degeneration

**\*** Note that some studies have suggested that some SPG7 mutations may have an autosomal dominant effect, particularly autosomal dominant optic atrophy.

\*\* Mutations in this gene more commonly cause a hypomyelinating leukodystrophy

 with developmental delay, dystonia,choreoathetosis, rigidity, opisthotonus, andoculogyric crises, progressive spastic tetraplegia, ataxia, and, more rarely, seizures.

1. Zhao X, Alvarado D, Rainier S, et al. Mutations in a newly identified GTPase gene cause autosomal dominant hereditary spastic paraplegia. Nat Genet 2001;29(3):326-331.

2. Nielsen JE, Koefoed P, Abell K, et al. CAG repeat expansion in autosomal dominant pure spastic paraplegia linked to chromosome 2p21-p24. Hum Mol Genet 1997;6(11):1811-1816.

3. Rainier S, Chai JH, Tokarz D, Nicholls RD, Fink JK. NIPA1 gene mutations cause autosomal dominant hereditary spastic paraplegia (SPG6). Am J Hum Genet 2003;73(4):967-971.

4. Valdmanis PN, Meijer IA, Reynolds A, et al. Mutations in the KIAA0196 gene at the SPG8 locus cause hereditary spastic paraplegia. Am J Hum Genet 2007;80(1):152-161.

5. Reid E, Kloos M, Ashley-Koch A, et al. A kinesin heavy chain (KIF5A) mutation in hereditary spastic paraplegia (SPG10). Am J Hum Genet 2002;71(5):1189-1194.

6. Montenegro G, Rebelo AP, Connell J, et al. Mutations in the ER-shaping protein reticulon 2 cause the axon-degenerative disorder hereditary spastic paraplegia type 12. J Clin Invest 2012;122(2):538-544.

7. Hansen JJ, Durr A, Cournu-Rebeix I, et al. Hereditary spastic paraplegia SPG13 is associated with a mutation in the gene encoding the mitochondrial chaperonin Hsp60. Am J Hum Genet 2002;70(5):1328-1332.

8. Windpassinger C, Auer-Grumbach M, Irobi J, et al. Heterozygous missense mutations in BSCL2 are associated with distal hereditary motor neuropathy and Silver syndrome. Nat Genet 2004;36(3):271-276.

9. Zuchner S, Wang G, Tran-Viet KN, et al. Mutations in the novel mitochondrial protein REEP1 cause hereditary spastic paraplegia type 31. Am J Hum Genet 2006;79(2):365-369.

10. Goizet C, Depienne C, Benard G, et al. REEP1 mutations in SPG31: frequency, mutational spectrum, and potential association with mitochondrial morpho-functional dysfunction. Hum Mutat 2011;32(10):1118-1127.

11. Mannan AU, Krawen P, Sauter SM, et al. ZFYVE27 (SPG33), a novel spastin-binding protein, is mutated in hereditary spastic paraplegia. Am J Hum Genet 2006;79(2):351-357.

12. Bourassa CV, Meijer IA, Merner ND, et al. VAMP1 mutation causes dominant hereditary spastic ataxia in Newfoundland families. Am J Hum Genet 2012;91(3):548-552.

13. Coutelier M, Goizet C, Durr A, et al. Alteration of ornithine metabolism leads to dominant and recessive hereditary spastic paraplegia. Brain : a journal of neurology 2015;138(Pt 8):2191-2205.

14. Panza E, Escamilla-Honrubia JM, Marco-Marin C, et al. ALDH18A1 gene mutations cause dominant spastic paraplegia SPG9: loss of function effect and plausibility of a dominant negative mechanism. Brain : a journal of neurology 2016;139(Pt 1):e3.

15. Tsaousidou MK, Ouahchi K, Warner TT, et al. Sequence alterations within CYP7B1 implicate defective cholesterol homeostasis in motor-neuron degeneration. Am J Hum Genet 2008;82(2):510-515.

16. Casari G, De Fusco M, Ciarmatori S, et al. Spastic paraplegia and OXPHOS impairment caused by mutations in paraplegin, a nuclear-encoded mitochondrial metalloprotease. Cell 1998;93(6):973-983.

17. Stevanin G, Santorelli FM, Azzedine H, et al. Mutations in SPG11, encoding spatacsin, are a major cause of spastic paraplegia with thin corpus callosum. Nat Genet 2007;39(3):366-372.

18. Renvoise B, Chang J, Singh R, et al. Lysosomal abnormalities in hereditary spastic paraplegia types SPG15 and SPG11. Annals of clinical and translational neurology 2014;1(6):379-389.

19. Hanein S, Martin E, Boukhris A, et al. Identification of the SPG15 gene, encoding spastizin, as a frequent cause of complicated autosomal-recessive spastic paraplegia, including Kjellin syndrome. Am J Hum Genet 2008;82(4):992-1002.

20. Yildirim Y, Orhan EK, Iseri SA, et al. A frameshift mutation of ERLIN2 in recessive intellectual disability, motor dysfunction and multiple joint contractures. Hum Mol Genet 2011;20(10):1886-1892.

21. Patel H, Cross H, Proukakis C, et al. SPG20 is mutated in Troyer syndrome, an hereditary spastic paraplegia. Nat Genet 2002;31(4):347-348.

22. Simpson MA, Cross H, Proukakis C, et al. Maspardin is mutated in mast syndrome, a complicated form of hereditary spastic paraplegia associated with dementia. Am J Hum Genet 2003;73(5):1147-1156.

23. Boukhris A, Schule R, Loureiro JL, et al. Alteration of ganglioside biosynthesis responsible for complex hereditary spastic paraplegia. Am J Hum Genet 2013;93(1):118-123.

24. Tesson C, Nawara M, Salih MA, et al. Alteration of fatty-acid-metabolizing enzymes affects mitochondrial form and function in hereditary spastic paraplegia. Am J Hum Genet 2012;91(6):1051-1064.

25. Erlich Y, Edvardson S, Hodges E, et al. Exome sequencing and disease-network analysis of a single family implicate a mutation in KIF1A in hereditary spastic paraparesis. Genome Res 2011;21(5):658-664.

26. Edvardson S, Hama H, Shaag A, et al. Mutations in the fatty acid 2-hydroxylase gene are associated with leukodystrophy with spastic paraparesis and dystonia. Am J Hum Genet 2008;83(5):643-648.

27. Kruer MC, Paisán-Ruiz C, Boddaert N, et al. Defective FA2H leads to a novel form of neurodegeneration with brain iron accumulation (NBIA). Annals of Neurology 2010;68(5):611-618.

28. Rainier S, Bui M, Mark E, et al. Neuropathy target esterase gene mutations cause motor neuron disease. Am J Hum Genet 2008;82(3):780-785.

29. Hartig MB, Iuso A, Haack T, et al. Absence of an orphan mitochondrial protein, c19orf12, causes a distinct clinical subtype of neurodegeneration with brain iron accumulation. Am J Hum Genet 2011;89(4):543-550.

30. Hogarth P, Gregory A, Kruer MC, et al. New NBIA subtype: genetic, clinical, pathologic, and radiographic features of MPAN. Neurology 2013;80(3):268-275.

31. Novarino G, Fenstermaker AG, Zaki MS, et al. Exome sequencing links corticospinal motor neuron disease to common neurodegenerative disorders. Science 2014;343(6170):506-511.

32. Martin E, Schule R, Smets K, et al. Loss of function of glucocerebrosidase GBA2 is responsible for motor neuron defects in hereditary spastic paraplegia. American Journal of Human Genetics 2013;92(2):238-244.

33. Abou Jamra R, Philippe O, Raas-Rothschild A, et al. Adaptor protein complex 4 deficiency causes severe autosomal-recessive intellectual disability, progressive spastic paraplegia, shy character, and short stature. Am J Hum Genet 2011;88(6):788-795.

34. Slabicki M, Theis M, Krastev DB, et al. A genome-scale DNA repair RNAi screen identifies SPG48 as a novel gene associated with hereditary spastic paraplegia. PLoS Biol 2010;8(6):e1000408.

35. Oz-Levi D, Ben-Zeev B, Ruzzo EK, et al. Mutation in TECPR2 reveals a role for autophagy in hereditary spastic paraparesis. Am J Hum Genet 2012;91(6):1065-1072.

36. Verkerk AJ, Schot R, Dumee B, et al. Mutation in the AP4M1 gene provides a model for neuroaxonal injury in cerebral palsy. Am J Hum Genet 2009;85(1):40-52.

37. Moreno-De-Luca A, Helmers SL, Mao H, et al. Adaptor protein complex-4 (AP-4) deficiency causes a novel autosomal recessive cerebral palsy syndrome with microcephaly and intellectual disability. Journal of medical genetics 2011;48(2):141-144.

38. Schuurs-Hoeijmakers JH, Geraghty MT, Kamsteeg EJ, et al. Mutations in DDHD2, encoding an intracellular phospholipase A(1), cause a recessive form of complex hereditary spastic paraplegia. Am J Hum Genet 2012;91(6):1073-1081.

39. Gonzalez M, Nampoothiri S, Kornblum C, et al. Mutations in phospholipase DDHD2 cause autosomal recessive hereditary spastic paraplegia (SPG54). European Journal of Human Genetics 2013;21(11):1214-1218.

40. Shimazaki H, Takiyama Y, Ishiura H, et al. A homozygous mutation of C12orf65 causes spastic paraplegia with optic atrophy and neuropathy (SPG55). Journal of medical genetics 2012;49(12):777-784.

41. Dor T, Cinnamon Y, Raymond L, et al. KIF1C mutations in two families with hereditary spastic paraparesis and cerebellar dysfunction. Journal of medical genetics 2014;51(2):137-142.

42. Eymard-Pierre E, Lesca G, Dollet S, et al. Infantile-onset ascending hereditary spastic paralysis is associated with mutations in the alsin gene. Am J Hum Genet 2002;71(3):518-527.

43. Bouchard JP, Barbeau A, Bouchard R, Bouchard RW. Autosomal recessive spastic ataxia of Charlevoix-Saguenay. The Canadian journal of neurological sciences Le journal canadien des sciences neurologiques 1978;5(1):61-69.

44. Sillen A, Jagell S, Wadelius C. A missense mutation in the FALDH gene identified in Sjogren-Larsson syndrome patients originating from the northern part of Sweden. Human genetics 1997;100(2):201-203.

45. Oates E  C, Rossor A  M, Hafezparast M, et al. Mutations in BICD2 Cause Dominant Congenital Spinal Muscular Atrophy and Hereditary Spastic Paraplegia. Am J Hum Genet 2013;92(6):965-973.

46. Lossos A, Elazar N, Lerer I, et al. Myelin-associated glycoprotein gene mutation causes Pelizaeus-Merzbacher disease-like disorder. Brain : a journal of neurology 2015;138(Pt 9):2521-2536.

47. Jouet M, Rosenthal A, Armstrong G, et al. X-linked spastic paraplegia (SPG1), MASA syndrome and X-linked hydrocephalus result from mutations in the L1 gene. Nat Genet 1994;7(3):402-407.

48. Saugier-Veber P, Munnich A, Bonneau D, et al. X-linked spastic paraplegia and Pelizaeus-Merzbacher disease are allelic disorders at the proteolipid protein locus. Nat Genet 1994;6(3):257-262.

49. Dumitrescu AM, Liao XH, Best TB, Brockmann K, Refetoff S. A novel syndrome combining thyroid and neurological abnormalities is associated with mutations in a monocarboxylate transporter gene. Am J Hum Genet 2004;74(1):168-175.

50. Pedroso JL, de Souza PV, Pinto WB, et al. SCA1 patients may present as hereditary spastic paraplegia and must be included in spastic-ataxias group. Parkinsonism & related disorders 2015;21(10):1243-1246.

51. Song Y, Liu Y, Zhang N, Long L. Spinocerebellar ataxia type 3/Machado-Joseph disease manifested as spastic paraplegia: A clinical and genetic study. Experimental and therapeutic medicine 2015;9(2):417-420.

52. Hersheson J, Mencacci NE, Davis M, et al. Mutations in the autoregulatory domain of beta-tubulin 4a cause hereditary dystonia. Annals of neurology 2013;73(4):546-553.

53. Blumkin L, Halevy A, Ben-Ami-Raichman D, et al. Expansion of the spectrum of TUBB4A-related disorders: a new phenotype associated with a novel mutation in the TUBB4A gene. Neurogenetics 2014;15(2):107-113.

54. Kancheva D, Chamova T, Guergueltcheva V, et al. Mosaic dominant TUBB4A mutation in an inbred family with complicated hereditary spastic paraplegia. Movement disorders : official journal of the Movement Disorder Society 2015;30(6):854-858.

55. Gan-Or Z, Bouslam N, Birouk N, et al. Mutations in CAPN1 Cause Autosomal-Recessive Hereditary Spastic Paraplegia. Am J Hum Genet 2016;98(5):1038-1046.

56. Wang Y, Hersheson J, Lopez D, et al. Defects in the CAPN1 Gene Result in Alterations in Cerebellar Development and Cerebellar Ataxia in Mice and Humans. Cell reports 2016;16(1):79-91.

57. Helbig KL, Hedrich UB, Shinde DN, et al. A recurrent mutation in KCNA2 as a novel cause of hereditary spastic paraplegia and ataxia. Annals of neurology 2016;80(4).

58. Manole A, Mannikko R, Hanna MG, Kullmann DM, Houlden H. De novo KCNA2 mutations cause hereditary spastic paraplegia. Annals of neurology 2017;81(2):326-328.