Hereditary Spastic Paraplegia

Precision Panel

Overview

Hereditary Spastic Paraplegia (HSP) includes a group of familial diseases that are characterized by progressive degeneration of the corticospinal tracts responsible for movement and sensation. HSPs are differentiated into “pure” forms if there is bladder involvement and “complicated” if there are additional neurologic or systemic abnormalities. The genetic classification of HSP is based upon the mode of inheritance, chromosomal locus, and causative mutation. Modes of inheritance include autosomal dominant, autosomal recessive and X-linked forms. The correlation of clinical classification with genetic classification is not yet defined as some genetic types of HSP are associated with both pure and complex phenotypes.

The Igenomix Hereditary Spastic Paraplegia Precision Panel can serve as an accurate and directed diagnostic tool as well as a differential diagnosis of muscle weakness ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Indications

The Igenomix Hereditary Spastic Paraplegia Precision Panel is indicated in patients with a clinical suspicion or diagnosis presenting with or without the following manifestations:

- Leg weakness
- Leg spasticity
- Brisk tendon reflexes
- Extensor plantar reflex
- Bladder dysfunction (urinary urgency)
- Visual loss
- Hearing loss
- Difficulty speaking
- Peripheral neuropathy

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular diagnosis for an accurate clinical diagnosis of a symptomatic patient.

- Early initiation of treatment with a multidisciplinary team for symptomatic treatment to improve mobility, increase range of motion and relieve discomfort using pharmacologic treatment as well as physical medicine and rehabilitation.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

Genes & Diseases

GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
ABCD1	Adrenoleukodystrophy	X,XR,G	100	-
ACO2	Cerebellar-Retinal Degeneration, Optic Atrophy	AR	100	33 of 33
ACOX1	Mitchell Syndrome, Peroxisomal Acyl-Coa Oxidase Deficiency	AD,AR	96.95	22 of 22
ADAR	Aicardi-Goutieres Syndrome, Dyschromatosis Symmetrica, Bilateral Striatal Necrosis	AD,AR	99.93	252 of 252
AFG3L2	Optic Atrophy, Spinocerebellar And Spastic Ataxia, Myoclonic Epilepsy, Neuropathy	AD,AR	99.74	42 of 42
AIMP1	Leukodystrophy, Intellectual Disability	AR	100	10 of 10
ALDH18A1	Cutis Laxa, Corneal Clouding, Mental Retardation, Spastic Paraplegia, De Barsy Syndrome	AD,AR	100	39 of 40
ALS2	Amyotrophic Lateral Sclerosis, Primary Lateral Sclerosis, Spastic Paralysis	AR	99.09	83 of 83
AMPD2	Pontocerebellar Hypoplasia, Spastic Paraplegia	AR	99.99	24 of 24
AP4B1	Spastic Paraplegia, Intellectual Disability	AR	99.64	22 of 22
AP4E1	Spastic Paraplegia, Stuttering, Intellectual Disability	AD,AR	99.94	17 of 17
AP4M1	Spastic Paraplegia, Severe Intellectual Disability	AR	100	18 of 18
AP4S1	Spastic Paraplegia, Intellectual Disability	AR	99.95	8 of 8
AP5Z1	Spastic Paraplegia	AR	99.97	18 of 18
ARG1	Argininemia	AR	100	66 of 68
ARL6IP1	Spastic Paraplegia	AR	99.96	5 of 5
ARSI	Spastic Paraplegia	-	99.23	2 of 2
ATAD3A	Harel-Yoon Syndrome, Pontocerebellar Hypoplasia, Hypotonia, Respiratory Insufficiency, Ocular Anomalies, Neuropathy, Developmental Delay	AD,AR	90.98	6 of 8
ATL1	Neuropathy, Spastic Paraplegia	AD	100	93 of 93
ATL3	Neuropathy	AD	99.91	5 of 5
ATP13A2	Kufor-Rakeb Syndrome, Spastic Paraplegia, Ceroid Lipofuscinosis	AR	99.97	53 of 53
ATP2B4	Cerebellar Ataxia, Malaria, Schnyder Corneal Dystrophy, Spastic Paraplegia	-	100	6 of 6
ATRX	Alpha-Thalassemia, Myelodysplasia, Mental Retardation, Carpenter-Waziri Syndrome, Chudley-Lowry-Hoar Syndrome, Holmes-Gang Syndrome, Juberg-Marsidi Syndrome, Neuroendocrine Tumor Of Stomach, Smith-Fineman-Myers Syndrome	X,XR,XD,G	98.5	-
B4GALNT1	Spastic Paraplegia	AR	98.69	13 of 13
BICD2	Spinal Muscular Atrophy	AD	99.94	39 of 39
BSCL2	Encephalopathy, Lipodystrophy, Neuronopathy, Spastic Paraplegia	AD,AR	99.83	60 of 61
BTD	Biotinidase Deficiency	AR	100	261 of 262
C12ORF65	Spastic Paraplegia, Oxidative Phosphorylation Defect	AR	-	-
C19ORF12	Neurodegeneration, Brain Iron Accumulation, Spastic Paraplegia	AD,AR	-	-
CACNA1G	Spinocerebellar Ataxia, Neurodevelopmental Deficits	AD	99.52	16 of 16

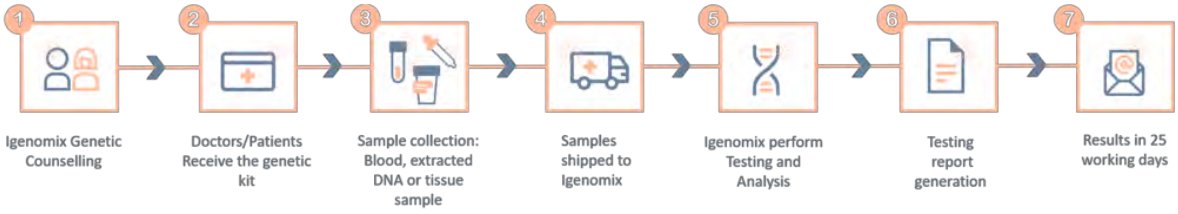
CAPN1	Spastic Paraplegia	AR	99.96	31 of 31
CCT5	Neuropathy, Spastic Paraplegia	AR	100	1 of 1
CDK16	Microcephaly	-	99.86	-
COASY	Neurodegeneration, Brain Iron Accumulation, Pontocerebellar Hypoplasia	AR	99.5	5 of 5
CPT1C	Spastic Paraplegia	AD	95.66	4 of 4
CTNNB1	Exudative Vitreoretinopathy, Medulloblastoma, Mental Retardation, Pilomatrixoma, Craniopharyngioma, Desmoid Tumor, Hepatocellular Carcinoma, Spastic Diplegia	AD,AR	100	63 of 63
CYP27A1	Cerebrotendinous Xanthomatosis	AR	100	118 of 118
CYP2U1	Spastic Paraplegia	AR	95.36	18 of 21
CYP7B1	Bile Acid Synthesis Defect, Spastic Paraplegia	AR	99.95	70 of 70
DARS1	Hypomyelination	AR	99.99	18 of 18
DDHD1	Spastic Paraplegia	AR	99.92	15 of 16
DDHD2	Spastic Paraplegia	AR	99.96	27 of 27
DNM2	Charcot-Marie-Tooth Disease, Contracture Syndrome, Myopathy	AD,AR	99	57 of 57
DSTYK	Congenital Anomalies Of Kidney And Urinary Tract, Spastic Paraplegia	AD,AR	99.89	10 of 10
ENTPD1	Spastic Paraplegia	AR	100	5 of 5
ERLIN1	Spastic Paraplegia	AR	100	4 of 4
ERLIN2	Spastic Paraplegia, Primary Lateral Sclerosis	AR	99.98	17 of 17
EXOSC3	Pontocerebellar Hypoplasia	AR	100	19 of 20
FA2H	Spastic Paraplegia, Fatty Acid Hydroxylase-Associated Neurodegeneration	AR	88.77	60 of 62
FARS2	Oxidative Phosphorylation Deficiency, Spastic Paraplegia	AR	99.98	23 of 23
FLRT1	Spastic Paraplegia, Optic Atrophy, Neuropathy	-	100	2 of 2
FXN	Friedreich Ataxia	AR	99.93	52 of 52
GAD1	Cerebral Palsy	AR	100	6 of 6
GALC	Krabbe Disease	AR	99.38	252 of 254
GBA2	Spastic Paraplegia, Cerebellar Ataxia	AR	99.96	25 of 25
GBE1	Glycogen Storage Disease, Polyglucosan Body Disease	AR	99.95	71 of 74
GCH1	Dystonia, GTP Cyclohydrolase I Deficiency	AD,AR	99.41	225 of 244
GJC2	Leukodystrophy, Lymphedema, Spastic Paraplegia, Milroy Disease	AD,AR	95.37	52 of 63
GPT2	Mental Retardation, Postnatal Microcephaly, Hypotonia, Spastic Diplegia, Dysarthria	AR	97.54	16 of 16
HACE1	Spastic Paraplegia, Seizures, Neuroblastoma, Developmental Delay, Epilepsy	AR	100	15 of 15
HEXA	Tay-Sachs Disease	AR	100	205 of 206
HSPD1	Leukodystrophy, Spastic Paraplegia	AD,AR	100	7 of 7
IBA57	Mitochondrial Dysfunctions Syndrome, Spastic Paraplegia	AR	93.35	25 of 27
IFIH1	Aicardi-Goutieres Syndrome, Singleton-Merten Syndrome	AD	99.62	26 of 27
IRF2BPL	Neurodevelopmental Disorder, Abnormal Movements, Loss Of Speech, Seizures	AD	95.01	24 of 25
ITPR1	Aniridia, Spinocerebellar And Cerebellar Ataxia, Intellectual Disability	AD,AR	99.87	93 of 97
KDM5C	Mental Retardation	X,XR,G	100	-
KIDINS220	Spastic Paraplegia, Intellectual Disability, Nystagmus, Obesity	AD	99.83	17 of 17
KIF1A	Mental Retardation, Neuropathy, Spastic Paraplegia, Neuropathy, Peho Syndrome	AD,AR	100	76 of 76
KIF1C	Ataxia, Autosomal Spastic Paraplegia	AR	99.74	18 of 19
KIF5A	Amyotrophic Lateral Sclerosis, Myoclonus, Spastic Paraplegia	AD	100	85 of 85

KLC2	Spastic Paraplegia, Optic Atrophy, Neuropathy	AR	100	4 of 4
L1CAM	Corpus Callosum Dysgenesis, Hydrocephalus, Stenosis Of Aqueduct Of Sylvius, Masa Syndrome	X,XR,G	100	-
L2HGDH	L-2-Hydroxyglutaric Aciduria	AR	100	72 of 73
LYST	Chediak-Higashi Syndrome	AR	99.98	117 of 117
MAG	Spastic Paraplegia	AR	99.97	7 of 7
MARS1	Charcot-Marie-Tooth Disease, Interstitial Lung And Liver Disease, Spastic Paraplegia	AD,AR	99.98	19 of 19
MARS2	Oxidative Phosphorylation Deficiency, Spastic Ataxia, Leukoencephalopathy	AR	99.94	3 of 3
MFN2	Charcot-Marie-Tooth Disease, Motor And Sensory Neuropathy, Symmetric Lipomatosis	AD,AR	100	233 of 233
MTPAP	Spastic Ataxia, Optic Atrophy, Dysarthria	AR	99.99	2 of 2
NARS2	Oxidative Phosphorylation Deficiency, Deafness	AR	99.63	13 of 13
NIPA1	Spastic Paraplegia	AD	95.02	13 of 13
NKX6-2	Spastic Ataxia, Hypomyelinating Leukodystrophy	AR	82.95	8 of 9
NT5C2	Spastic Paraplegia	AR	97.89	6 of 7
OPA3	3-Methylglutaconic Aciduria, Optic Atrophy, Cataract	AD,AR	100	18 of 18
PAH	Phenylketonuria	AR	100	964 of 969
PCYT2	Spastic Paraplegia	AR	92.59	-
PGAP1	Mental Retardation, Spastic Paraplegia	AR	99.94	13 of 13
PLA2G6	Neuroaxonal Dystrophy, Neurodegeneration, Brain Iron Accumulation, Parkinson Disease	AR	99.94	190 of 191
PLP1	Pelizaeus-Merzbacher Disease, Spastic Paraplegia	X,XR,G	100	-
PNPLA6	Boucher-Neuhauser Syndrome, Laurence-Moon Syndrome, Oliver-Mcfarlane Syndrome, Spastic Paraplegia, Ataxia, Hypogonadism, Choroidal Dystrophy	AR	100	65 of 65
POLR3A	Leukodystrophy, Oligodontia, Hypogonadotropic Hypogonadism, Progeroid Syndrome, Hypomyelination, Hypodontia, Tremor, Ataxia, Wiedemann-Rautenstrauch Syndrome	AR	100	122 of 122
RAB3GAP2	Martsolf Syndrome, Warburg Micro Syndrome, Spastic Paraplegia, Cataract, Intellectual Disability, Hypogonadism, Micro Syndrome	AR	100	17 of 17
RARS1	Leukodystrophy, Hypomyelinating Leukodystrophy	AR	99.64	28 of 28
REEP1	Neuronopathy, Spastic Paraplegia	AD	100	62 of 62
REEP2	Spastic Paraplegia	AD,AR	99.98	5 of 5
RNASEH2B	Aicardi-Goutieres Syndrome	AR	99.95	41 of 41
RNF170	Ataxia	AD	99.03	2 of 3
RTN2	Spastic Paraplegia	AD	99.99	4 of 4
SACS	Spastic Ataxia	AR	99.91	291 of 292
SARS2	Hyperuricemia, Pulmonary Hypertension, Renal Failure, Alkalosis	AR	97.5	6 of 6
SERAC1	3-Methylglutaconic Aciduria, Deafness, Encephalopathy, Leigh Syndrome	AR	99.93	53 of 53
SETX	Amyotrophic Lateral Sclerosis, Spinocerebellar Ataxia, Neuropathy	AD,AR	99.71	219 of 227
SLC16A2	Allan-Herndon-Dudley Syndrome	X,XR,G	99.94	-
SLC1A4	Spastic Tetraplegia, Thin Corpus Callosum, Microcephaly	AR	99.76	8 of 9
SLC25A15	Hyperornithinemia, Hyperammonemia, Homocitrullinuria	AR	100	41 of 41
SLC25A46	Neuropathy	AR	99.79	16 of 17
SLC2A1	Choreoathetosis, Spasticity, Epilepsy, Glut1 Deficiency Syndrome, Cryohydrocytosis, Dyskinesia	AD,AR	99.99	301 of 304
SLC33A1	Congenital Cataracts, Hearing Loss, Neurodegeneration, Spastic Paraplegia	AD,AR	99.44	9 of 9
SOD1	Amyotrophic Lateral Sclerosis, Spastic Tetraplegia, Axial Hypotonia	AD,AR	100	217 of 221

SPART	Spastic Paraplegia	AR	99.9	-
SPAST	Spastic Paraplegia	AD	99.98	616 of 655
SPG11	Amyotrophic Lateral Sclerosis, Charcot-Marie-Tooth Disease, Spastic Paraplegia	AR	99.93	289 of 297
SPG21	Mast Syndrome, Spastic Paraplegia	AR	100	3 of 3
SPG7	Spastic Paraplegia, Primary Lateral Sclerosis	AD,AR	99.94	125 of 126
SPR	Dystonia, Sepiapterin Reductase Deficiency	AD,AR	99.89	27 of 27
SPTAN1	Epileptic Encephalopathy, West Syndrome	AD	100	52 of 53
TECPR2	Spastic Paraplegia, Neuropathy	AR	95.5	9 of 9
TFG	Neuropathy, Spastic Paraplegia	AD,AR	99.67	9 of 9
TH	Segawa Syndrome, Dystonia	AR	100	71 of 71
TRPV4	Avascular Necrosis Of Femoral Head, Brachyrachia, Digital Arthropathy, Neuropathy, Metatropic Dysplasia, Parastremmatic Dwarfism, Spondyloepiphyseal Dysplasia, Spinal Muscular Atrophy	AD	100	88 of 88
TUBB4A	Dystonia Musculorum Deformans, Leukodystrophy	AD	89.81	44 of 44
UBAP1	Spastic Paraplegia	AD	88.64	5 of 14
UCHL1	Neurodegeneration, Optic Atrophy, Parkinson Disease	AD,AR	100	5 of 5
UNC80	Hypotonia, Hypotonia, Speech Impairment, Cognitive Delay	AR	99.95	39 of 39
USP8	Pituitary Adenoma, Spastic Paraplegia, Cushing Disease	AD,AR	98.19	3 of 3
VAMP1	Myasthenic Syndrome, Spastic Ataxia, Myasthenic Syndromes	AD,AR	99.51	8 of 8
VCP	Amyotrophic Lateral Sclerosis, Frontotemporal Dementia, Charcot-Marie-Tooth Disease, Myopathy, Paget Disease, Aphasia, Spastic Paraplegia	AD	100	68 of 69
VPS37A	Spastic Paraplegia	AR	99.95	2 of 2
WASHC5	Dandy-Walker-Like Malformation, Atrioventricular Septal Defect, Spastic Paraplegia, 3C Syndrome	AD,AR	99.99	-
WDR45B	Neurodevelopmental Disorder, Spastic Quadriplegia, Brain Abnormalities, Seizures	AR	99	4 of 4
WDR48	Spastic Paraplegia	-	99.89	2 of 2
ZFR	Spastic Paraplegia	-	99.47	2 of 2
ZFYVE26	Spastic Paraplegia	AR	99.95	48 of 48
ZFYVE27	Spastic Paraplegia	AD	100	5 of 5

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



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Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

References

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