Charcot Marie Tooth and Sensory Neuropathies

Precision Panel

Overview

Charcot Marie Tooth disease (CMT) belongs to the spectrum motor and sensory neuropathies caused by mutations in genes encoding proteins that code for myelin, gap junctions and axonal structures within the peripheral nerves. It is the most prevalent inherited neuropathy. The association of different mutations within the same gene and various clinical phenotypes is a common finding and causes clinical and genetic heterogeneity. It is characterized by progressive distal weakness, muscle atrophy and sensory loss. The most common inheritance pattern is autosomal dominant, though there also are X-linked and autosomal recessive subtypes. The most important goal for patients with CMT is to maintain movement, muscle strength and flexibility.

The Igenomix Charcot Marie Tooth and Sensory Neuropathies Precision Panel can be used as a tool for an accurate diagnosis and 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, and their high or intermediate penetrance.

Indications

The Igenomix Charcot Marie Tooth and Sensory Neuropathies Precision Panel is used for patients with a clinical suspicion or diagnosis presenting with or without the following symptoms:

- Distal muscle wasting and weakness
- Distal sensory loss
- Muscle atrophy
- Delayed motor development
- Steppage gait
- Ankle injuries
- Foot deformities: pes cavus and thin lower legs
- Family history of CMT or other sensory neuropathies

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.
- Early initiation of treatment involving a multidisciplinary team in the form of orthopaedic care surgical treatment to prevent complications as well as physical therapy and rehabilitation.

- Risk assessment of asymptomatic family members according to the mode of inheritance via genetic counselling.
- Improvement of delineation of genotype-phenotype correlation given the variability of severity and course of disease.

Genes & Diseases

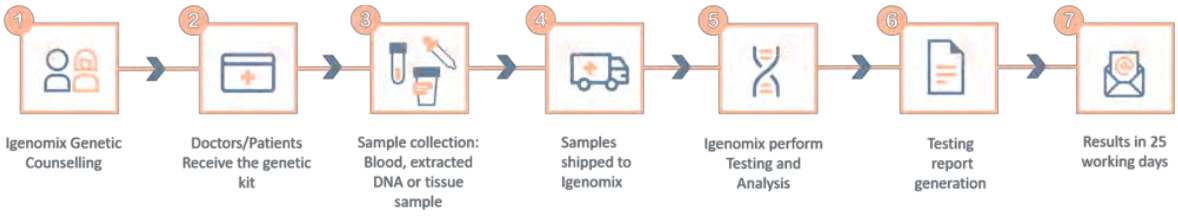
GENE	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
AARS1	Charcot-Marie-Tooth Disease, Epileptic Encephalopathy	AD,AR	99.07	30 of 30
AIFM1	Oxidative Phosphorylation Deficiency, Cowchock Syndrome, Deafness, Spondyloepimetaphyseal Dysplasia, Leukoencephalopathy, Encephalomyopathy , Charcot-Marie-Tooth Disease	X,XR,G	100	-
ATL1	Neuropathy, Spastic Paraplegia	AD	100	93 of 93
ATP1A1	Charcot-Marie-Tooth Disease, Hypomagnesemia, Seizures, Mental Retardation	AD	100	16 of 16
ATP7A	Cutis Laxa, Menkes Disease, Spinal Muscular Atrophy, Occipital Horn Syndrome	X,XR,G	99.83	-
BSCL2	Encephalopathy, Lipodystrophy, Neuronopathy, Spastic Paraplegia, Berardinelli-Seip Lipodystrophy, Neurodegenerative Syndrome	AD,AR	99.83	60 of 61
COX6A1	Charcot-Marie-Tooth Disease	AR	100	1 of 1
DHTKD1	2-Aminoadipic 2-Oxoadipic Aciduria, Charcot-Marie-Tooth Disease	AD,AR	99.94	25 of 25
DNAJB2	Spinal Muscular Atrophy	AR	99.97	4 of 5
DNM2	Charcot-Marie-Tooth Disease, Contracture Syndrome, Myopathy	AD,AR	99	57 of 57
DNMT1	Cerebellar Ataxia, Deafness, Narcolepsy, Neuropathy	AD	97.87	30 of 30
DYNC1H1	Charcot-Marie-Tooth Disease, Mental Retardation, Spinal Muscular Atrophy	AD	100	104 of 104
EGR2	Charcot-Marie-Tooth Disease, Hypertrophic Neuropathy Of Dejerine-Sottas	AD,AR	100	23 of 23
ELP1	Neuropathy, Dysautonomia	AR	100	-
FGD4	Charcot-Marie-Tooth Disease	AR	99.95	30 of 30
FIG4	Amyotrophic Lateral Sclerosis, Charcot-Marie-Tooth Disease, Cleidocranial Dysplasia, Micrognathia, Polymicrogyria, Yunis-Varon Syndrome	AD,AR	99.92	72 of 72
GAN	Giant Axonal Neuropathy	AR	100	75 of 75
GARS1	Charcot-Marie-Tooth Disease, Neuronopathy	AD	100	46 of 46
GDAP1	Charcot-Marie-Tooth Disease	AD,AR	100	106 of 106
GJB1	Charcot-Marie-Tooth Disease, Cerebellar Ataxia	X,XR,XD,G	100	-
GNB4	Charcot-Marie-Tooth Disease	AD	100	5 of 5
HARS1	Charcot-Marie-Tooth Disease, Usher Syndrome	AD,AR	100	-
HINT1	Neuromyotonia, Axonal Neuropathy	AR	99.94	19 of 19
HK1	Hemolytic Anemia, Neurodevelopmental Disorder, Visual Defects, Brain Anomalies, Neuropathy, Retinitis Pigmentosa, Charcot-Marie-Tooth Disease	AD,AR	100	14 of 17
HSPB1	Charcot-Marie-Tooth Disease, Neuronopathy	AD	99.96	45 of 46
HSPB8	Charcot-Marie-Tooth Disease, Neuronopathy	AD	97.59	9 of 9
IGHMBP2	Charcot-Marie-Tooth Disease, Spinal Muscular Atrophy	AR	99.94	141 of 142
INF2	Charcot-Marie-Tooth Disease, Glomerulosclerosis	AD	99.91	79 of 79
JPH1	Charcot-Marie-Tooth Disease	AD,AR	99.59	1 of 1
KARS1	Charcot-Marie-Tooth Disease, Deafness	AR	100	34 of 34
KIF1A	Mental Retardation, Neuropathy, Spastic Paraplegia, Peho Syndrome	AD,AR	100	76 of 76

KIF1B	Charcot-Marie-Tooth Disease, Neuroblastoma, Pheochromocytoma	AD	99.89	17 of 17
KIF5A	Amyotrophic Lateral Sclerosis, Myoclonus, Spastic Paraplegia	AD	100	85 of 85
LITAF	Charcot-Marie-Tooth Disease	AD	90.74	18 of 18
LMNA	Cardiomyopathy, Charcot-Marie-Tooth Disease, Emery-Dreifuss Muscular Dystrophy, Heart-Hand Syndrome, Hutchinson-Gilford Progeria Syndrome, Lipodystrophy, Malouf Syndrome, Mandibuloacral Dysplasia, Restrictive Dermopathy, Werner Syndrome, Hypergonadotropic Hypogonadism	AD,AR	100	619 of 620
LRSAM1	Charcot-Marie-Tooth Disease	AD,AR	100	18 of 18
MARS1	Charcot-Marie-Tooth Disease, Lung And Liver Disease, Spastic Paraplegia	AD,AR	99.98	19 of 19
MED25	Basel-Vanagaite-Smirin-Yosef Syndrome, Charcot-Marie-Tooth Disease, Intellectual Disability, Cataract, Microcephaly, Nevus Flammeus Simplex	AR	100	5 of 5
MFN2	Charcot-Marie-Tooth Disease, Motor And Sensory Neuropathy, Symmetric Lipomatosis	AD,AR	100	233 of 233
MME	Charcot-Marie-Tooth Disease, Spinocerebellar Ataxia, Membranous Nephropathy	AD,AR	100	33 of 33
MORC2	Charcot-Marie-Tooth Disease	AD	100	20 of 20
MPV17	Charcot-Marie-Tooth Disease, Mitochondrial Dna Depletion Syndrome	AR	100	48 of 49
MPZ	Charcot-Marie-Tooth Disease, Neuropathy Of Dejerine-Sottas, Roussy-Levy Areflexic Dystasia	AD,AR	99.98	245 of 245
MTMR2	Charcot-Marie-Tooth Disease	AR	100	34 of 34
NAGLU	Charcot-Marie-Tooth Disease, Mucopolysaccharidosis	AD,AR	93.23	194 of 222
NDRG1	Charcot-Marie-Tooth Disease	AR	100	11 of 11
NEFH	Amyotrophic Lateral Sclerosis, Charcot-Marie-Tooth Disease	AD,AR	97.5	28 of 31
NEFL	Charcot-Marie-Tooth Disease	AD,AR	-	-
NGF	Neuropathy	AR	100	5 of 5
NTRK1	Insensitivity To Pain, Anhidrosis, Sensory And Autonomic Neuropathy	AR	100	128 of 130
PDK3	Charcot-Marie-Tooth Disease	X,XD,G	99.7	-
PLEKHG5	Charcot-Marie-Tooth Disease, Spinal Muscular Atrophy	AR	99.98	14 of 14
PMP2	Charcot-Marie-Tooth Disease	AD	99.74	5 of 5
PMP22	Charcot-Marie-Tooth Disease, Deafness, Hypertrophic Neuropathy Of Dejerine-Sottas, Roussy-Levy Areflexic Dystasia, Demyelinating Polyradiculoneuropathy	AD,AR	97.82	110 of 110
PNKP	Ataxia, Oculomotor Apraxia, Charcot-Marie-Tooth Disease, Epileptic Encephalopathy	AR	100	36 of 36
PRPS1	Arts Syndrome, Charcot-Marie-Tooth Disease, Deafness, Phosphoribosylpyrophosphate Synthetase Superactivity, Lethal Ataxia, Optic Atrophy, Limb Spasticity, Retinal Dystrophy, Diabetes Insipidus	X,XR,G	100	-
PRX	Charcot-Marie-Tooth Disease, Hypertrophic Neuropathy Of Dejerine-Sottas	AD,AR	100	59 of 59
RAB7A	Charcot-Marie-Tooth Disease	AD	100	7 of 7
REEP1	Neuronopathy, Spastic Paraplegia	AD	100	62 of 62
RETREG1	Neuropathy	AR	99.94	-
SBF1	Charcot-Marie-Tooth Disease	AR	99.94	19 of 19
SBF2	Charcot-Marie-Tooth Disease	AR	99.98	44 of 44
SCO2	Cardioencephalomyopathy, Myopia, Charcot-Marie-Tooth Disease, Leigh Syndrome	AD,AR	100	38 of 38
SH3TC2	Charcot-Marie-Tooth Disease, Mononeuropathy Of The Median Nerve	AD,AR	99.95	114 of 114
SLC12A6	Agenesis Of The Corpus Callosum, Peripheral Neuropathy	AR	100	21 of 21
SPG11	Amyotrophic Lateral Sclerosis, Charcot-Marie-Tooth Disease, Spastic Paraplegia	AR	99.93	289 of 297
SPTLC1	Neuropathy	AD	99.81	12 of 12
SPTLC2	Neuropathy	AD	100	18 of 18

SURF1	Charcot-Marie-Tooth Disease, Leigh Syndrome, Cardiomyopathy, Leukodystrophy	AR,MI	98.59	117 of 124
TRIM2	Charcot-Marie-Tooth Disease	AR	97.87	8 of 8
TRPV4	Avascular Necrosis Of Femoral Head, Brachyrachia, Digital Arthropathy, Neuropathy, Metatropic Dysplasia, Parastremmatic Dwarfism, Scapuloperoneal Spinal Muscular Atrophy, Spondyloepiphyseal Dysplasia, Brachyolmia	AD	100	88 of 88
TTR	Amyloidosis, Carpal Tunnel Syndrome	AD	100	195 of 196
VCP	Amyotrophic Lateral Sclerosis, Charcot-Marie-Tooth Disease, Myopathy, Paget Disease, Frontotemporal Dementia, Aphasia, Spastic Paraplegia	AD	100	68 of 69
WNK1	Neuropathy, Pseudohypoaldosteronism	AD,AR	99.45	44 of 50
YARS1	Charcot-Marie-Tooth Disease	AD	100	15 of 15

*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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