The Genetics of Inherited Peripheral Neuropathies and the Next Frontier: Looking Backwards to Progress Forwards.

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Supplemental Material

Supplementary Table 1. List of 73 genes and two genetic loci associated with IPN that have been published since 2012. Genes and loci were included in the table if they (1) had not previously been associated with any disease, (2) were previously associated with another disease, or (3) were previously reported for IPN, but, since 2012, have been newly associated with a different form of IPN. Genes and loci we consider to be associated with ultra-rare IPN are shaded in light-blue. Adapted from the 2023 gene table of neuromuscular disorders, which includes a full list of IPN-associated genes.(9)

DISEASE NAME	MOI	DISEASE SYMBOL (OMIM)	CHROMOSOME	GENE SYMBOL (OMIM)	PROTEIN	VARIANT TYPE
Autosomal dominant CMT1 (AD-CMT1)						
Charcot-Marie Tooth disease, demyelinating type 1G	AD	CMT1G (618279)	8q21.13	***PMP2*** (170715)	Peripheral myelin protein 2	SNV
Charcot-Marie-Tooth neuropathy	AD/ de novo	CMT1I (619742)	12q23.3	***POLR3B*** (614366)	Polymerase III, RNA, Subunit B	SNV
Charcot-Marie-Tooth neuropathy	AD		6q21.31	***ITPR3*** (147267)	Inositol 1,4,5triphosphate receptor, type 3	SNV
Autosomal recessive CMT1 (AR-CMT1 or CMT4)						
Charcot-Marie Tooth disease, type 4B3	AR	CMT4B3 (615284)	22q13.33	***SBF1*** (603560)	SET-binding factor 1	SNV, indel
Charcot-Marie Tooth disease, type 4K	AR	CMT4K (616684)	9q34.2	***SURF1*** (185620)	Surfeit 1	SNV, indel
Charcot-Marie-Tooth disease	AR		14q32	***AHNAK2*** (608570)	Ahnak nucleoprotein 2	SNV
Charcot-Marie-Tooth disease related to CNTNAP1	AR		17q21.2	***CNTNAP1*** (602346)	Contactin-associated protein 1	SNV

Intermediate CMT (CMTi)						
Charcot-Marie-Tooth disease, dominant intermediate A	AD	CMT2GG (606483)	10q24.1-q25.1	***GBF1*** (603698)	Golgi-specific brefeldin-A resistance factor 1	SNV
Charcot-Marie-Tooth disease, dominant intermediate F	AD	CMTDIF (615185)	3q28.33	***GNB4*** (610863)	Guanine nucleotide-binding protein, beta-4	SNV, indel
Charcot-Marie-Tooth disease, dominant intermediate G	AD	CMTDIG (617882)	8p21.2	***NEFL*** (162280)	Neurofilament, light polypeptide 68kDa	SNV
Charcot-Marie-Tooth disease, intermediate	AD		1p21.2-p13.3	***CFAP276 (C1orf194)*** (618682)	Chromosome 1 open reading frame 194	SNV
Charcot-Marie-Tooth disease, intermediate	AD		1p13.3	***SARS1*** (607529)	Seryl-tRNA synthetase 1	SNV
Autosomal dominant CMT2						
Charcot-Marie-Tooth disease, type 2Q	AD	CMT2Q (615025)	10p14	***DHTKD1*** (614984)	Dehydrogenase E1 and transketolase domain-containing 1	SNV
Charcot-Marie-Tooth disease, type 2U	AD	CMT2U (616280)	12q13.3	***MARS1*** (156560)	Methionyl-tRNA synthetase 1	SNV
Charcot-Marie-Tooth disease, type 2V	AD	CMT2V (616491)	17q21.2	***NAGLU*** (609701)	N-acetyl-alpha-glucosaminidase	SNV
Charcot-Marie-Tooth disease, type 2W	AD	CMT2W (616625)	5q31.3	***HARS1*** (142810)	Histidyl-tRNA synthetase 1	SNV
Charcot-Marie-Tooth disease, type 2Y	AD	CMT2Y (616687)	9p13.3	***VCP*** (601023)	Valosin-containing protein	SNV, splice site
Charcot-Marie-Tooth disease, type 2Z	AD	CMT2Z (616688)	22q12.2	***MORC2*** (616661)	MORC family CW-type zinc finger 2	SNV
Charcot-Marie-Tooth disease, axonal, type 2CC	AD	CMT2CC (616924)	22q12.2	***NEFH*** (162230)	Neurofilament Protein, Heavy Polypeptide	SNV, indel
Charcot-Marie-Tooth disease, axonal, type 2DD	AD	CMT2DD (618036)	1p13.1	***ATP1A1*** (182310)	ATPase, Na^+/K^+ transporting, alpha-1 polypeptide	SNV, indel
Charcot-Marie-Tooth disease, axonal, type 2FF	AD	CMT2FF (619519)	1q23.2	***CADM3*** (609743)	Cell adhesion molecule 3	SNV
CMT2 related to *KIF5A*	AD		12q13.3	***KIF5A*** (602821)	Kinesin family member 5A	SNV, indel, SV
Early onset axonal neuropathy with sensory ataxia	AD	CMT2	1q13.5	***DGAT2*** (606983)	Diacylglycerol O-acyltransferase 2	SNV

Charcot-Marie-Tooth disease, axonal, related to *BAG3*	AD		10q26.11	***BAG3*** (603883)	BCL2-associated athanogene 3	SNV
Charcot-Marie-Tooth disease, axonal, related to *JAG1*	AD	CMT2	20p12.2	***JAG1*** (601920)	Jagged 1	SNV
Charcot-Marie-Tooth disease, axonal, related to *NOTCH2NLC*	AD	CMT2	1q21.2	***NOTCH2NLC*** (618025)	Notch2 N-terminal-like protein	STR expansion
Autosomal recessive CMT2						
Charcot-Marie-Tooth disease, axonal, type 2B2	AR	CMT2B2 (605589)	19q13.33	***PNKP*** (605610)	Polynucleotide kinase 3-prime phosphatase	SNV, indel
Charcot-Marie-Tooth disease, axonal, type 2EE	AR	CMT2EE (618400)	2p23.3	***MPV17*** (137960)	MPV17, mouse, homolog of	SNV, splice region
Charcot-Marie-Tooth disease, axonal, related to *DNAJB2*	AR		2q35	***DNAJB2*** (604139)	DnaJ/Hsp40 homolog, subfamily B, member 2	SNV, indel, splice site, CNV
Neuromyotonia and axonal neuropathy, autosomal recessive	AR	NMAN	5q23.3	***HINT1*** (601314)	histidine triad nucleotide binding protein 1	SNV
Charcot-Marie-Tooth disease, recessive intermediate, C	AR	CMTRIC (615376)	1p36.31	***PLEKHG5*** (611101)	Pleckstrin homology domain- and RhoGEF domain containing, family G5	SNV, indel
Charcot-Marie-Tooth disease, recessive intermediate, D	AR	CMTRID (616039)	12q24.31	***COX6A1*** (602072)	Cytochrome c oxidase subunit 6a1	Indel, splice region
Charcot-Marie-Tooth disease, type 2R	AR	CMT2R (615490)	4q31.3	***TRIM2*** (614141)	Tripartite motif-containing protein 2	SNV, indel
Charcot-Marie-Tooth disease, type 2S	AR	CMT2S (616155)	11q13.3	***IGHMBP2*** (600502)	Immunoglobulin mu-binding protein 2	SNV, indel, splice site
Charcot-Marie-Tooth disease, type 2T	AR, AD	CMT2T (617017)	3q25.2	***MME*** (120520)	Membrane metalloendopeptidase	SNV, indel, splice region
Charcot-Marie-Tooth disease, type 2X	AR	CMT2X (616668)	15q21.1	***SPG11*** (610844)	SPG11 vesicle trafficking associated Spatacsin	SNV, indel
Early-onset axonal Charcot-Marie-Tooth with ataxia	AR	AOA4 (616267)	19q13.33	***PNKP*** (605610)	Polynucleotide kinase 3'-phosphatase	SNV, indel
Charcot-Marie-Tooth disease, axonal	AR		10q22.1	***SGPL1*** (603729)	Sphingosine-1 phosphate lyase 1	SNV
Charcot-Marie-Tooth disease, axonal; related to SCO2	AR		22q13.33	***SCO2*** (604272)	Cytochrome c oxidase assembly protein 2	SNV
Charcot-Marie-Tooth	AR		13q12.12	***SACS***	Sacsin	SNV, indel, SV

disease, axonal; related to SACS				(604490)		
Sorbitol dehydrogenase deficiency with peripheral neuropathy (CMT2 AR)	AR	SORDD (619912)	15q21.1	***SORD*** (182500)	Sorbitol dehydrogenase	SNV, indel
Charcot-Marie-Tooth disease, axonal	AR		21q22.3	***MCM3AP*** (603294)	Minichromosome maintenance 3-associated protein	SNV, indel
Charcot-Marie-Tooth disease, axonal	AR		12q13.3	***B4GALNT1*** (601823)	Beta-1,4-N-Acetyl-galactosaminyl transferase 1	SNV, indel
Charcot-Marie-Tooth disease, axonal	AR		19p13.11	***MYO9B*** (602129)	Myosin IXB	SNV, indel
Charcot-Marie-Tooth disease, axonal	AD/ de novo		1q25.3	***DHX9*** (603115)	DExH-Box helicase 9	SNV, indel
X-linked CMT (CMTX)						
Charcot-Marie-Tooth neuropathy, X-linked recessive, 3	XR	CMTX3 (302802)	Xq27.1	78kb insertion of Chr8 8q24.3	78kb inter-chromosomal insertion	SV
Charcot-Marie-Tooth neuropathy, X-linked 4 (Cowchock syndrome)	XR	COWCK (310490)	Xq26.1	***AIFM1*** (300169)	Apoptosis-inducing factor, mitochondria-associated, 1	SNV
Charcot-Marie-Tooth disease, X-linked dominant, 6	XD	CMTX6 (300905)	Xp22.11	***PDK3*** (300906)	Pyruvate dehydrogenase kinase, isoenzyme 3	SNV
Distal hereditary motor neuropathy (dHMN)						
Distal hereditary motor neuronopathy	AR		5q23.3	***HINT1*** (601314)	Histidine triad nucleotide-binding protein	SNV
Neuronopathy, distal hereditary motor, type IID	AD	HMN2D (615575)	7p14.3	***FBXO38*** (608533)	F-box only protein 38	SNV
Distal spinal muscular atrophy, type VB	AD, AR	HMNS5B (614751)	2p11.2	***REEP1*** (609139)	Receptor expression-enhancing protein 1	SNV, splice site
Dominant distal hereditary motor neuropathy	AD	dHMN	16q22.1	***AARS1*** (601065)	Alanyl-tRNA sythetase 1	SNV
Neuronopathy, distal hereditary motor, type IX	AD	HMN9 (61772)	14q32.2	***WARS1*** (191050)	Tryptophanyl-tRNA synthetase 1	SNV
Spinal motor neuropathy			11q23.2	***RBM7*** (612413)	RNA-binding motif protein 7	SNV
Distal motor neuropathy related to *SYT2*	AD		1q32.1	***SYT2*** (600104)	Synaptotagmin 2	SNV
Distal hereditary motor neuropathy		DHMN1	7q34–q36.2	1.35 Mb insertion of Chr7 7q36.3	1.35 Mb intra-chromosomal insertion (inverted)	SV

Distal motor neuropathy	AD		9q34.11	***SPTAN1*** (182810)	Spectrin, alpha, nonerythrocytic 1	SNV
Distal hereditary motor neuropathies	AD		10q24.32	***GBF1*** (603698)	Golgi-specific brefeldin-A resistance factor 1	SNV
Peripheral neuropathy, autosomal recessive, with or without impaired intellectual development	AR	PNRIID (618124)	21q22.3	***MCM3AP*** (603294)	Minichromosome maintenance 3-associated protein	SNV, indel
Neuropathy, hereditary motor, with myopathic features	AR	HMNMYO (619216)	1p36.33	***VWA1*** (611901)	Von Willebrand factor A domain-containing protein 1	SNV, indel, STR expansion
Progressive neuropathy (with ichthyosis, contractures)	AR		9q21.2	***PSAT1*** (610936)	Phosphoserine Aminotransferase 1	SNV
Neuronopathy, distal hereditary motor, autosomal recessive 2	AR	HMNR2 (605726)	9p13.3	***SIGMAR1*** (601978)	Sigma non-opioid intracellular receptor 1	SNV, splice site
Neuronopathy, distal hereditary motor, autosomal recessive 9	AR	HMNR9 (620402)	16p12.3	***COQ7*** **(601683)**	Coenzyme Q7 hydroxylase	SNV, splice site
Hereditary sensory and autonomic neuropathy (HSAN)						
Hereditary sensory and autonomic neuropathy, type IID	AR	CIP (24300)	2q24.3	***SCN9A*** (603415)	Sodium channel, voltage-gated alpha subunit	SNV, indel
Hereditary sensory and autonomic neuropathy type VI	AR	HSAN6 (614653)	6p12.1	***DST*** (113810)	Dystonin	SNV, indel
Neuropathy, hereditary sensory and autonomic, type VII	AD	HSAN7 (615548)	3p22.2	***SCN11A*** (604385)	Sodium channel, voltage-gated alpha subunit	SNV, splice site
Neuropathy, hereditary sensory and autonomic, type VIII	AR	HSAN8 (616488)	9q34.12	***PRDM12*** (616458)	PR Domain-containing protein 12	SNV, indel, splice site, STR expansion
Neuropathy, hereditary sensory, type IF	AD	HSN1F (615632)	11q13.1	***ATL3*** (609369)	Atlastin GTPase 3	SNV
Absence of pain, Congenital	AR		22q11.21	***CLTCL1*** (601273)	Clathrin, heavy polypeptide-like 1	SNV
Marsili syndrome (insensitivity to pain, congenital, AD)	AD	MARSIS (147430)	14q11.2	***ZFHX2*** (617828)	Zinc finger homeobox 2	SNV
Episodic pain syndrome, familial 3	AD	FEPS3 (615552)	3p22.2	***SCN11A*** (604385)	Sodium channel, voltage-gated alpha subunit	SNV
Polyneuropathy with erythromelalgia	AR		1q25.3	***NMNAT2*** (608701)	Nicotinamide nucleoside adenyltransferase 2	SNV

Sensory neuronopathy	AR		1q44	***COX20*** (614698)	Cytochrome c Oxidase Assembly Factor COX20	SNV, splice site
Cerebellar ataxia, neuropathy, and vestibular areflexia syndrome	AR	CANVAS (614575)	4p14	***RFC1*** (102579)	Replication factor C Subunit 1	SNV, STR expansion
Other complex neuropathy syndromes						
Giant axonal neuropathy-2	AD	GAN2 (610100)	1q23.2	***DCAF8*** (615820)	DDB1- and CUL4-associated factor 8	SNV
Complex motor and sensory axonal neuropathy plus microcephaly and cerebral dysgenesis	AR		14q32.2	***VRK1*** (602168)	Vaccinia related kinase 1	SNV
Neuronal intranuclear inclusion diseases	AD	603472	1q21.2	***NOTCH2NLC*** (618025)	Notch2 N-terminal-like protein	STR expansion
Hereditary peripheral neuropathy (CMT?)	AD		17q25.1	***NHERF1 (SLC9A3R1)*** (604990)	NHERF family PDZ scaffold protein 1	SNV
Neurodevelopmental disorder with microcephaly, impaired language and gait abnormalities	AR, AD	NEDMILG (619091)	18q21.31	***NARS1*** (108410)	Asparaginyl-tRNA Synthetase 1	SNV, indel
Axonal neuropathy and motor dysfunction, with speech delay and intellectual disability	AR, de novo		14q21.3	***NEMF*** (608378)	Nuclear export mediator factor	SNV, indel, slice site
Neurodegeneration, childhood-onset, stress-induced, with variable ataxia and seizures	AR	CONDSIAS (618170)	1p34.3	***ADPRS (ADPRHL2)*** (610624)	ADP-riboslyserine hydrolase	SNV, indel, splice site

AD, autosomal dominant; AR, autosomal recessive; CMT1, demyelinating Charcot-Marie-Tooth neuropathy; CMT2, axonal Charcot-Marie-Tooth neuropathy; indel, insertion/deletion; MOI, mode of inheritance; SNV, single nucleotide variants; STR, short tandem repeat; SV, structural variant; XR, X-linked recessive