Navigating Charcot Marie Tooth Disease Names
For the CMTer and for the Practicing Clinician

CMT-ASSOCIATED GENES and their RELATED SUBTYPES

THE DEFINITIVE GUIDE

FIRST EDITION

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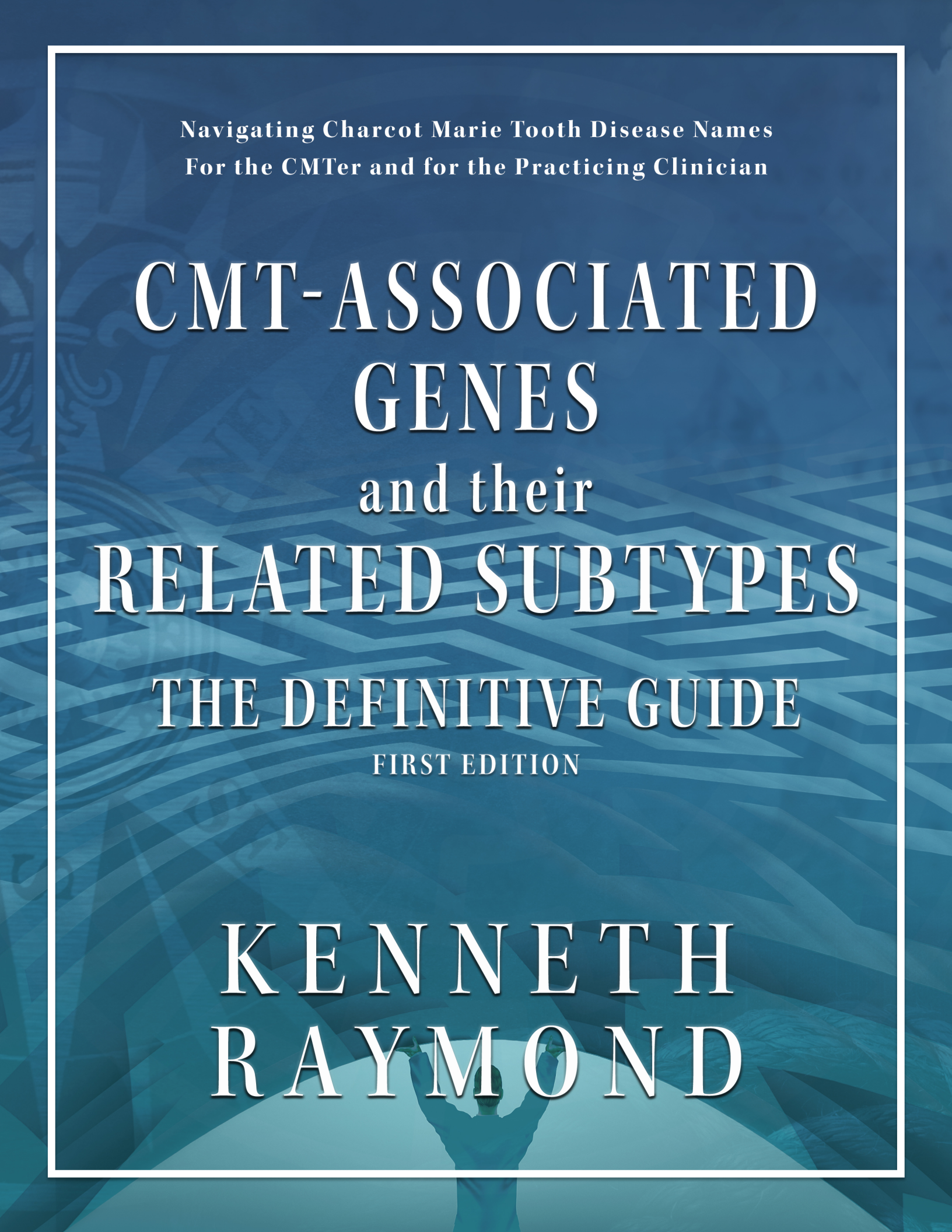

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Foreword

Advances in Charcot Marie Tooth disease (CMT) genetics and associated gene discovery are moving at breakneck speed. Scientists discovered the first CMT-associated gene in 1992. New discoveries have occurred every year since. The number of CMT-associated genes discovered in the last 10 years eclipses the number of genes discovered in the first 20 years. A CMT genetic test result that fails to identify a known CMT cause is far more common than a genetic test that does identify a cause. As new associated genes are discovered, the potential to close the gap increases for CMTers who are unable to obtain a genetic confirmation of their CMT.

With each new discovery representing a new and unique subtype designation, and the overall rate at which new discoveries are occurring, the ability for any one organization or entity to keep up with these changes is severely impaired. This unfortunately leaves everyday CMTers in a vast sea of uncertainty and desperate for answers. At the same time, there is an inherent confusion borne of the everchanging and evolving manner in which new CMT subtype discoveries are named.

A review of all publicly available sources of CMT literature reveals that there isn't a readily available single source that CMTers and clinicians alike can go to for a comprehensive, complete, and up-to-date list of all known CMT subtypes and their respective established associated genes. Information is aggregated across many resources and outlets, and there isn't a great deal of consensus regarding what constitutes a complete and comprehensive list of known CMT subtypes and/or CMT-associated genes. This expansive void of this most basic of CMT information has left everyday CMTers feeling excluded and dejected. The absence of this publicly available information is a byproduct of the speed at which everything moves within CMT genetics and associated gene discoveries.

The purpose of this guide is to provide a complete up-to-date accounting of CMT subtypes and identified CMT-associated genes, current as of this writing, for everyday CMTers and practicing clinicians to reference. The scope of this guide does not discuss symptom and phenotype

descriptions for the many individual CMT subtypes. Rather, this guide represents a comprehensive accounting of the identified subtypes and a comprehensive inclusive listing of all discovered CMT-associated genes, current to this writing. This guide discusses the many non-CMT acronym types and subtypes to clarify for everyday CMTers and for practicing clinicians how each are CMT, as determined by the CMT experts. This guide also discusses the limitations of CMT genetic testing as those limitations relate to everyday CMTers who are yet to obtain a genetic confirmation of their CMT.

CMT by Any Other Name

What is CMT? That's easy. CMT is an inheritable peripheral nervous system disease that bears the names of the 3 doctors who, in the late 19th century, were the first to figure out that several different diseases were actually all the same condition. These 3 doctors, who are also considered the fathers of modern-day neurology, Jean-Martin Charcot [shahr'kō] (1825-1893), Pierre Marie (1853-1940), both from France, and Howard Henry Tooth (1856-1925) from England are the faces behind the CMT name. CMT, however, is much more than this otherwise simple name and acronym.

CMT is an inheritable peripheral nervous system disease, but what does this mean? The peripheral nervous system represents all the nerves of the body that lie outside of the brain and spinal cord. The peripheral nerves are responsible for movement—the motor nerves; touch sensation and sensory signals—the sensory nerves; and some autonomic processes—various organ functions, breathing, etc. CMT is a disease of the nerves that control all these things.

CMT is an inheritable neuromuscular disease—neuro, meaning nerve, and muscular because the disease of the peripheral nerves affects skeletal muscle. CMT is an inheritable polyneuropathy—inheritable because it is caused by one of many different genetic mutations that can be inherited, poly, meaning many, and neuropathy meaning a disease of the peripheral nerves. Of the many things that CMT is, one thing CMT is not, is a syndrome.

Many CMT research papers and publications explain that CMT is a heterogeneous [hedərəˈjēnēəs] group of hereditary disorders. Researchers say hereditary because CMT is inheritable. Researchers sometimes refer to CMT as a group of disorders because the many individual causes of CMT each represent a unique diagnosis. Heterogeneous though? What is heterogeneous?

Heterogeneous is used in medicine to describe something that is diverse and/or dissimilar. As the word use relates to CMT, it is used to explain that CMT has many causes and that CMT can and typically does affect every CMTer differently, regardless of subtype. This is the opposite of a

syndrome. A syndrome, that is, a syndromic condition, is a condition that follows a distinct pattern and everybody who has it is affected in the same manner and to the same degree, with very little variance. Syndrome does not describe CMT at all. Sure, CMTers share some very common symptoms, but the variability of symptom mixes and severity between each CMTer, along with the many different causes, is how and why CMT is non-syndromic. There is a lot of published literature that has syndrome right in the CMT name, as in Charcot Marie Tooth syndrome, but this is based on very old understandings. We now know that CMT is strikingly non-syndromic, that CMT is exceedingly heterogeneous. Now that we know what CMT is and is not, what causes CMT?

CMT has become one of the most complex diseases to understand. People have dedicated their lives to not only figuring out CMT, but to figuring out the cause of CMT. CMT was first described and named c.1886. It wasn't until c.1990 that CMT understandings really started taking off. Everything started launching at that point because of the work of Michael Shy, M.D., and Richard Lewis, M.D., at their original CMT clinic in Detroit. If Drs. Charcot, Marie, and Tooth are the fathers of modern-day neurology, Drs. Shy and Lewis are the fathers of modern-day CMT. Everything we have learned about CMT in the last 30 years is built off of their work, and this includes discovering what are the many causes of CMT.

Prior to the first CMT genetic discovery, scientists knew that CMT was inheritable. Evidence made clear that CMTers could pass it on to their children. Prior to the advent of DNA and individual gene analysis capabilities, however, scientists didn't understand the full mechanisms of that inheritability. Before the emergence of DNA analysis, there were three basic types of CMT: Type 1, Type 2, and Type 3. A CMTer's CMT was determined to be either Type 1 or Type 2 based on nerve conduction characteristics, that is, how well a peripheral nerve transmits a signal.

Type 1 is considered demyelinating CMT. Type 2 is considered axonal CMT. In Type 1, the peripheral nerve myelin is directly affected. In Type 2, the peripheral nerve axon is directly affected. If we think of a peripheral nerve as a lamp cord, the axon is the wire that conducts the electricity, and the myelin is the sheath that protects the wire. Nerve conduction characteristics

rule-of-thumb is such that nerve conduction velocities that are faster than 38 meters per second represent axonal CMT, and nerve conduction velocities that are slower than 38 meters per second represent demyelinating CMT (Stojkovic 2016). Of course, it's much more complex than this, but this is the general rule-of-thumb. Type 3 represented Dejerine-Sottas Syndrome, or DSS, which is essentially demyelinating CMT with clinical symptoms that are present in infancy and early childhood (Parman 2004).

Things went on with these 3 basic types for quite a while. Try as they may, scientists just could not pin down a cause. The ability to analyze DNA, individual chromosomes, and individual genes, however, would change everything.

The Breakthrough

The first CMT-associated gene discovery was published in June 1992. This first CMT-associated gene discovery was a duplication of the PMP22 gene, and this discovery is designated CMT1A (Patel 1992). This discovery was deemed CMT1A because it was a cause for demyelinating CMT—Type 1, and it was the first Type 1 cause scientists discovered. The PMP22 gene is duplicated in CMT1A because the segment of chromosome 17 where the gene lives is duplicated. Shortly before this discovery, scientists had discovered that this segment of chromosome 17 (17p11.2-p12) was duplicated in 128 CMTers from 12 families who each had Type 1 CMT whereas members of these 12 families who did not have CMT did not have this duplication. This chromosome segment duplication was concluded to be the cause of these CMTers' CMT, and scientists referred to this as 1A (Raeymaekers 1991). Patel et al. (1992) discovered the specific gene involved, and therefore get credit for the 1A gene discovery.

The 1990s brought several CMT gene discoveries. January 1993 brought us the discovery that a Type 1 CMT called Hereditary Neuropathy with liability to Pressure Palsies (HNPP) was caused by a deletion of one-copy of the PMP22 gene (Chance 1993). Some consider this as the genetic opposite of CMT1A. The second gene to be discovered as having a CMT causing mutation was the MPZ gene, with having a mutation causing a Type 1 CMT. This was named CMT1B (Hayasaka 1993). The "B" represents that this discovery was the second associated gene

discovery for Type 1 CMT. This discovery was published in September 1993. Three months later, on Christmas Eve no less, the third genetic cause of CMT was published. This discovery was a mutation in the GJB1 gene (formerly called CONNEXIN32), and this was for the first X-Linked CMT-associated gene discovery (Bergoffen 1993). It is called X-Linked because the gene lives on the X-chromosome. This discovery was designated CMT1X to signify a demyelinating CMT and that the cause is with a gene that lives on the X-chromosome.

The first genetic cause for Type 2 CMT came in 1998 when researchers discovered mutations in the MPZ gene caused an axonal CMT. This discovery was designated CMT2I. The decade finished out with researchers discovering an altogether different mutation in MPZ causing a type of CMT called Intermediate CMT (Mastaglia 1999). This discovery, published in August 1999, was designated Dominant Intermediate CMT-D (CMTDID).

I'm confident you can see the emerging pattern of CMT genetic discoveries and the correlation with name designations. Essentially, the discovery is given a CMT name: CMT1A, CMT1B, CMT2A, etc. There are obvious exceptions, but this is the general practice. The first character is the type, and the second character, which denotes the order of gene mutation discovery for that type, is the subtype. The published discovery establishes the subtype and the associated gene. It's a fairly straightforward scheme. As understandings started to evolve, additional Types were designated. Beyond 1, 2, and 3, there was a 4, 5, and 6. However, as CMT genetic cause discoveries took off, scientists started to understand that many of these Type designations were redundant descriptions of the same thing, and genetic mutation discoveries provided the data needed to basically consolidate the several types. CMT Types 3, 5, and 6 were absorbed, so to speak, by Types 1, 2 and 4. Dejerine-Sottas Syndrome, aka CMT3, is still sometimes used as a diagnosis when CMT symptoms are present in infancy (Bird 1998 September 28 (Updated 2021 May 20)), and when there is no established genetic family history of CMT. Once an underlying genetic cause is identified, the DSS diagnosis is transitioned to the CMT subtype that is associated with the identified genetic cause.

The Basic Six

As CMT genetics accelerated into the 21st century, the first twenty years of discoveries (1992 - 2011) brought 55 CMT-associated gene discoveries. With each discovery basically representing a unique subtype of CMT, things were getting complicated and chaotic to keep track of. While there isn't any one organization or entity that determines how CMT subtypes are designated, there is a general framework that is followed. There doesn't seem to be an exact date, but somewhere around c.2010, 6 basic type categories of CMT emerged. These 6 were Type 1, Type 2, Type 4, X-Linked, Dominant Intermediate, and Recessive Intermediate. CMT subtypes were shuffled into these 6 categories according to neuropathy type and inheritance pattern. These 6 categories and their criteria are in use today.

CMT1 is demyelinating and autosomal dominant in inheritance. CMT2 is axonal, and either autosomal dominant or autosomal recessive in inheritance. CMT4 is demyelinating and autosomal recessive in inheritance. X-Linked CMT, or CMTX, represents subtypes caused by mutations in genes that live on the X-chromosome. Intermediate CMT gets its name from nerve conduction characteristics that overlap that which is seen in demyelinating CMT and that which is seen in axonal CMT (Kennerson 2001) and is categorized according to the inheritance pattern of each respective subtype: autosomal dominant or autosomal recessive. "Intermediate" is not used to imply CMT severity. What is all this inheritance pattern garb?

CMT is caused by mutations in genes. These mutations are inheritable. How these mutations are inherited is determined by the underlying genetic mutation, and how the mutation is inherited is known as the inheritance pattern. CMT has four inheritance patterns: autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive. In genetics and inheritance, dominant refers to a gene having one mutation, and recessive refers to a gene having two mutations. Autosomal refers to any gene that lives on any of the numbered chromosomes (1 – 22), also known as the autosomes, and X-Linked refers to any gene that lives on the X-chromosome. Subtypes are sorted according to neuropathy type (demyelinating, axonal, or intermediate) and according to one of these four inheritance patterns. Piece of cake. Time to throw a giant tree trunk into this fine oiled machine though.

Evolution of an Umbrella

CMT is an acronym that represents the three doctors who first described the disease we know as CMT. The keyword here is acronym. Over the years, there have been other acronyms in use to refer to the same disease we know as CMT. This creates a lot of confusion. Published literature pertaining to clinical management of CMT tends to favor HMSN, and published literature pertaining to CMT genetics tends to favor CMT (Reilly 2000). HMSN is the acronym for Hereditary Motor and Sensory Neuropathy. This is an acronym that's been in use to describe CMT for decades. CMT is hereditary (H) and can be a motor (M) and/or sensory (S) neuropathy (N). HMSN, therefore, describes CMT well, and many doctors favor this acronym over one that describes the last names of 3 people. Reilly (2000) concluded that the 2 acronyms are interchangeable with one another insofar as HMSN1 = CMT1 and HMSN2 = CMT2. The two don't interchange beyond this though. HMSN3 is still in use to represent Dejerine-Sottas, but CMT3 is not. HMSN4 and CMT4 are not subtype interchangeable. There is an HMSN5 and HMSN6, but not a CMT5 or CMT6. Fast forward to the late 2010s, and there are now several additional acronyms that refer to CMT.

CMT genetic discoveries skyrocketed in the second decade of the 21st century, and now into the 3rd decade. These last 10 years of CMT-associated gene discovery have eclipsed the first 20 years. Since 2012, there have been 65 CMT-associated genes discovered. The last 5 years have given us almost half of those with 30 discoveries, bringing the total to a whopping 120 identified CMT-associated genes. Appendix B provides a comprehensive master reference list of these 120 genes, including associated subtypes and original publication date for the CMT-associated discovery. This staggering number has forced a change in how new CMT subtype discoveries are designated and named. In 2018, Chiara Pisciotta M.D., Ph.D. and Dr. Michael Shy authored a chapter in the Handbook of Clinical Neuropathy. They conclude that CMT is an "umbrella term that encompasses a wide variety of inherited sensory and/or motor neuropathies" (Pisciotta 2018). This variety is exceptionally wide. Sensory and/or motor neuropathy is an important facet to this exceptionally wide variety, as is the umbrella term evolution.

Today, there are the 6 aforementioned categories that bear the CMT acronym. Beyond these 6 are Distal Hereditary Motor Neuropathy (dHMN), Distal Spinal Muscular Atrophy (dSMA), Giant Axonal Neuropathy (GAN), the previously discussed HMSN, Hereditary Sensory and Autonomic Neuropathy (HSAN), Hereditary Sensory Neuropathy (HSN), Spinal Muscular Atrophy - Lower Extremity Predominant (SMA-LEP), and a category of subtypes known as [Gene Name]-CMT that are expressed as [Gene Name]-associated-CMT, as in Sord-associated-CMT (Cortese 2020) or DST-associated-CMT (Motley 2020), for example. In all, there are 14 categories that CMT is sorted into. How is it that all these other acronyms and names constitute CMT? The details are in the gene discoveries and the authors of the published papers that establish the discovery as a CMT-associated gene.

Name Selection

The general practice with CMT gene discovery and subsequent naming/designation has been that the author of the establishing paper is who gets to name the discovery/subtype. It's an unwritten rule, of sorts. The one who discovers the cause gets to name the subtype. It's a badge of honor, and rightfully so. The scientists tend to follow the naming framework that's been outlined here. Well, they did for quite a while anyway. The evolution of gene discovery, however, has rendered the framework of the six basic categories impractical. That framework, with very few exceptions, is a number that represents the Type (1, 2, 4), followed by a letter that represents the sequential order of gene discovery (A, B, C…). X-Linked CMT is an X followed by a number, Intermediate is DI for Dominant Intermediate, and RI for Recessive Intermediate, and then followed by a letter that denotes subtype, CMTDIB or CMTRIC for example. We say these as, "Dominant (or Recessive) Intermediate CMT D," etc. As easy of a scheme as this is, we can see how unsustainable it becomes when we look at Type 2 CMT.

Type 2 naming/designation criteria are an axonal neuropathy and autosomal dominant or autosomal recessive in inheritance. Following the number-letter format, the scheme tops out at 26 possible subtypes because the English alphabet that is used has 26 letters. However, Type 2 CMT comprises 33 subtypes to date, exceeding the 26 letter threshold. Type 2 CMT includes subtypes with double letters (CC, DD, EE) and [number]-[letter]-[number]-[letter] in various

combinations that gets quickly chaotic (2B4, 2A2B…). While this is the only one of the six basic Type categories to exceed the alphanumeric limitations, the gene discovery explosion brings the potential for the others to also exceed this threshold. In efforts to solve this, CMT experts have proposed several remedies over the years. The most recent proposal found in published literature is from 2018.

CMT experts proposed transitioning to an [Inheritance Pattern]-[Neuropathy Type]-[Gene Name]-CMT based naming schema after polling more than 300 CMT experts in late 2016 (Magy 2018). With this proposed transition, CMT2A, for example, would become AD-Axonal-MFN2-CMT. This translates to Axonal CMT caused by an autosomal dominant mutation in the MFN2 gene. CMT2A2B (Polke 2011) would become AR-Axonal-MFN2-CMT. This translates to Axonal CMT caused by an autosomal recessive mutation in the MFN2 gene. This seems easy enough until we look at CMT2B4 (Nicholson 2008) which is also caused by autosomal recessive mutations in the MFN2 gene. There is also HMSN6A (S. D. Züchner 2006) which is an axonal subtype caused by autosomal dominant mutations in the MFN2 gene. We don't get too deep into the Magy et al. (2018) proposal before we hit limitations. This format doesn't exactly translate well for the average CMTer either.

The format of the six basic CMT acronym Type categories is easy for CMTers to follow. It's fairly straightforward, albeit impractical with the current state of CMT genetic discoveries. The Magy et al. (2018) proposal is great for doctors, clinicians, researchers, and scientists. The proposed framework clinically describes the subtype perfectly for scientists, even given its limitations. Not so much for a CMTer though. It's easy to tell somebody you have CMT4C. The vast majority of people will have no idea what that means when you say it, but they can easily remember CMT4C after you tell them what CMT4C is. Imagine instead telling somebody you have "AR-Demyelinating-SH3TC2-CMT." They'll be lost before you even finish "Demyelinating," and they'll never remember a thing. While Magy et al. (2018) makes sense for science, it is impractical, unreasonable, and unsustainable for CMTers. From here, a system that uses acronyms that describe the subtype symptoms and disease presentation have emerged.

The New(er) Players on the Field

The six basic categories of CMT are still used today and are still having subtype designations added to them. December 2020 brought the addition of CMT1H (Safka Brozkova 2020). January 2021 brought us the VWA1 gene discovery that is designated VWA1-dHMN (Pagnamenta 2021). In April 2021, a mutation in the CADM3 gene was discovered to cause an axonal CMT. This discovery was designated as simply CADM3-CMT (Rebelo 2021). While the six basic categories are in use, a [Gene Name]-CMT format appears to be emerging as a favored scheme amongst the scientists, as the scientists who make the discovery get the honor of naming the associated CMT. These 3 recent discoveries though show the diversity amongst the various category placements with the designated names from the discovery authors. What's with this dHMN thing though?

Thomas Bird, M.D., in Charcot-Marie-Tooth (CMT) Hereditary Neuropathy Overview, explains that the two acronyms dHMN and dSMA equal CMT (Bird 1998 September 28 (Updated 2021 May 20)). The two acronyms describe the subtypes they each represent. In dHMN subtypes, the CMT affects primarily the points farthest from the spinal cord, or the distal points (d), and the CMT is primarily a motor (M) neuropathy (N) with little to no sensory involvement. In dSMA, the CMT affects primarily the distal points (d), and the CMT involves the lower motor neurons (S) (the lower motor neurons are the neurons that control movement and are located below the brainstem [hence, "spinal"], whereas upper motor neurons are located in the brainstem or the brain itself), and the CMT causes muscle (M) atrophy (A) of these distal points. Researchers have concluded that because mutations in common genes that are associated with the conventional acronymic CMT subtypes and their corresponding shared symptom profiles, dHMN and dSMA should not be classified as separate diseases from CMT (Bansagi 2017). HMSN, dHMN, dSMA, and CMT all refer to the same thing we know and call CMT. How do these other acronyms fit in?

During the 2020 Charcot-Marie-Tooth Association (CMTA) Patient and Family Conference, Stephan Züchner, M.D., Ph.D., and Steven Scherer, M.D., Ph.D., provided an update on axonal CMT research and CMT gene discovery (Charcot-Marie-Tooth Association (CMTA) 2020). The

presentation included a table of 46 CMT-associated genes that had been discovered since 2012 as the result of CMTA funded initiatives. These genes were listed without their corresponding CMT subtypes. Cataloging these genes reveals that not all of them have the CMT acronym designation. Of the 46 genes presented as CMT genes, 18 are designated as subtypes with the CMT acronym, 4 as dHMN, 1 as dSMA, 1 as GAN, 2 as HMSN, 3 as HSAN, 1 as HSN, 1 as SMA-LEP, and 13 as [Gene Name]-CMT. Three of the 46 genes, DST, IGHMBP2, and PLEKHG5, are established as being associated with both a CMT acronym subtype and another acronym. DST is associated with HSAN6 (Edvardson 2012) and DST-CMT (Motley 2020). IGHMBP2 is associated with CMT2S (Cottenie 2014) and dHMN6 (Grohmann 2001), and PLEKHG5 is associated with CMTRIC (Azzedine 2013) and dSMA4 (Maystadt 2007). HSAN6 predates DST-CMT, dHMN6 predates CMT2S by 13 years (dHMN6 original publication is 2001, and CMT2S publication is 2014), and dSMA4 predates CMTRIC by a few years. For each of the 46 genes that do not have a CMT acronym designation, published literature does not provide a designation other than what has been given by the original establishing publications. This further illustrates how these other acronyms are Type categories of CMT. We've covered how and why dHMN, dSMA, and HMSN are CMT, but what about HSAN, HSN, and SMA-LEP?

One of the 46 genes that were presented as a CMT gene by Drs. Züchner and Scherer in the CMTA 2020 Patient and Family Conference was the BICD2 gene. The BICD2 gene is associated with only two disorders: Spinal Muscular Atrophy-Lower Extremity Predominant (SMA-LEP) 2A & 2B. The SMA-LEP2A publication was June 2013 (Neveling 2013), and the SMA-LEP2B publication was July 2018 (Koboldt 2018). There are no other publications that establish a CMT acronym condition associated with this gene. Given this, and the gene being presented by who are recognized as CMT genetics authorities, provides solid support that SMA-LEP is a type of CMT. As such, SMA-LEP1, associated with the DYNC1H1 gene, is therefore reasonably a type of CMT. Coincidentally, the same gene is associated with CMT2O. The CMT2O publication was August 2011 (Weedon 2011), and the SMA-LEP1 publication was 2012 (Harms 2012). These two discoveries fit the criteria proposed by Bansagi et al. (2017) that the two should not be classified separately. HSAN and HSN are associated with genes also presented as CMT genes by Drs. Züchner and Scherer.

HSAN is the acronym for Hereditary Sensory and Autonomic Neuropathy. HSN is the acronym for Hereditary Sensory Neuropathy. Both describe the corresponding type of CMT. HSAN subtypes of CMT are hereditary (H), and they are primarily a sensory (S) and autonomic (A) neuropathy (N), affecting the sensory and autonomic nerves, with little to no motor nerve involvement. HSN is HSAN but without autonomic involvement. Of the 46 genes given as CMT genes in the 2020 conference, 4 are associated with HSAN/HSN acronyms: ATL3, DST, SCN9A, and SCN11A. The ATL3 gene is associated with HSN1F (Kornak 2014), the aforementioned DST gene is associated with HSAN6, the SCN9A gene is associated with HSAN2D (Yuan 2013), and the SCN11A gene is associated with HSAN7 (Leipold 2013). Each of these discovery publications fall within the presented gene discovery since 2012 timeline, providing further support for these acronyms representing types of CMT. Providing further support for HSAN and HSN as types of CMT, as well as other acronyms as types of CMT, is the Inherited Neuropathies Consortium website.

The Inherited Neuropathies Consortium "is an integrated group of academic medical centers, patient support organizations, and clinical research resources dedicated to conducting clinical research in different forms of CMT and improving the care of patients. Funded by the National Institutes of Health (NIH), the INC is part of the Rare Diseases Clinical Research Network" (Inherited Neuropathies Consortium (INC) 2021). The INC does only CMT, and the INC is spearheaded by none other than Dr. Michael Shy. The INC website explains that CMT "is the eponym for non-syndromic inherited neuropathies that affect motor and sensory axons of the peripheral nervous system," and that "HSAN includes disorders that predominantly affects sensory and autonomic neurons and/or their axons. HMN includes various disorders that affect motor axons in a length-dependent manner"[sic] (Inherited Neuropathis Consortium (INC) 2021). The inclusion of these acronyms by the INC further supports these acronyms as types of CMT, and their inclusion here supports Pisciotta (2018).

The HSAN page on the INC website further explains that "in HSAN, sensory (and variably autonomic) neurons and/or axons are affected. Motor neurons/axons are relatively or completely spared, except in HSAN1" (Inherited Neuropathies Consortium (INC) 2021). The page provides information for several types of HSAN, complete with associated genes and a reference list of

sources. The HMN page on the INC website explains that “the current classification [of HMN] is based on the seven types of “distal hereditary motor neuronopathies” proposed by [Harding, 1993], according to their clinical features and pattern of inheritance. “Distal spinal muscular atrophy” is an alternative name (Inherited Neuropathies Consortium (INC) 2021). The page, like the HSAN page, includes a description of several subtypes and gives their associated genes, complete with a reference list of sources. This further establishes these acronyms as types of CMT. What about the GAN acronym?

GAN is the acronym for Giant Axonal Neuropathy. The INC website includes GAN in the “AR-CMT2” listing. The “AR-CMT2” naming format creates more issues for CMTers than it solves, but the INC website is geared more for healthcare professionals than it is for CMTers, as evidenced by the subtype listings and descriptions being found under the “Healthcare Professionals” site navigation hierarchy. The website has a lot of valuable information for the general public though. The INC website explains that “originally patients with Giant Axonal Neuropathy were described as having a childhood onset of an axonal neuropathy, with associated upper motor neuron and cerebellar findings, and kinky hair. Some patients, however, have a much milder disease, with few clinical CNS findings, so this disorder is discussed here” (Inherited Neuropathies Consortium (INC) 2021). In further support for GAN, and GAN-2 by proxy being subtypes of CMT, the CMTA has recently announced a GAN initiative.

The CMTA website explains that the organization was “founded by patients in 1983,” and that “the vision of the CMTA has always been “A World Without CMT” and we will accomplish this mission by accelerating research and empowering patients” (Charcot-Marie-Tooth Association (CMTA) 2021). The CMTA, like the INC, does only CMT. The CMTA has launched a GAN initiative, and their website details that they are “supporting pilot studies of gene therapy in CMT mouse models following a gene therapy trial for one peripheral neuropathy (GAN) at the National Institutes of Health” (Charcot-Marie-Tooth Association (CMTA) 2021). This further supports GAN as a subtype of CMT.

Categorically Speaking

Predicated by the ever-growing list of CMT-associated gene discoveries, the CMT acronym has fully become an umbrella term that represents many different acronyms. These acronyms, in turn, represent CMT as a whole. The categories of CMT into which the subtypes are sorted has evolved into 14 categories. These categories are CMT1, CMT2, CMT4, CMTX, CMTDI, CMTRI, dHMN, dSMA, GAN, HMSN, HSAN, HSN, SMA-LEP, and [Gene Name]-CMT. These 14 categories encompass a whopping 155 individual subtypes. Appendix A provides the full subtype list, including each subtype's associated gene, inheritance pattern, neuropathy type, and establishing publication date. In short, CMT1 encompasses 9 subtypes, CMT2 encompasses 33 subtypes, CMT4 includes 12 subtypes, CMTX includes 6, CMTDI has 7, CMTRI has 4, dHMN has 18, dSMA has 5, GAN includes 2, HMSN includes 6, HSAN has 12, HSN has 10, SMA-LEP includes 3 subtypes, and the [Gene Name]-CMT category encompasses 28 subtypes. If it has the "CMT" acronym, it's easy to account for the subtypes, but how do we get to the subtype numbers in these non-CMT acronym type categories?

The INC website includes 7 HSAN subtype listings. The Online Mendelian Inheritance in Man (OMIM) website contains 15 subtype listings in their HSAN Phenotype catalog (The Online Mendelian Inheritance in Man (OMIM) 2021). The OMIM listing is a combination of HSAN and HSN subtypes. The 12 subtypes of HSAN included here are an amalgamation of the subtypes given by the INC and the subtypes given by OMIM. The ATL3 gene was specifically given as a CMT gene by Drs. Züchner and Scherer in the CMTA 2020 Patient and Family Conference. As of this writing, HSN1F is the only inherited neuropathy associated with the ATL3 gene in published literature. Considering this, the correlation of HSN subtypes being included in the OMIM Phenotype series listing, and reviewing the published literature that established HSN associated genes reveals that there are 10 HSN subtypes, and they are each included here. GAN1 is a CMT subtype. By proxy, GAN2 is included here as a CMT subtype.

The BICD2 gene was given as a CMT-associated gene in the above conference. Because the SMA-LEP2A & 2B are CMT subtypes due to their association with the BICD2 gene, SMA-LEP1 is included here by proxy, and its inclusion here is supported by Bansagi et al. (2017)

given that SMA-LEP1 and CMT2O share the same associated gene and have similar lower-limb symptom profiles. We know that dHMN and dSMA are not only interchangeable with one another (Inherited Neuropathies Consortium (INC) 2021), but that they are both clearly CMT type categories (Bird 1998 September 28 (Updated 2021 May 20)). Published literature reveals that there are 18 subtypes of dHMN, and there are 5 separate subtypes of dSMA. As such, each are included here. The category that is referred to as [Gene Name]-CMT encompasses the many subtypes of CMT in which the establishing publications did not conclude or propose a subtype designation, or the authors proposed the straightforward [Gene Name]-associated-CMT designation. From that, there are 28 subtypes that are known simply as [Gene Name]-associated-CMT, and they are each included here. This brings us to the oldest non-CMT acronym of HMSN.

The Hereditary Motor and Sensory Neuropathy name has been around for a very long time. HMSN has long been synonymous with CMT. It is so synonymous with CMT that the ICD10 diagnostic code manual used for medical billing directs diagnostic code G60.0: Hereditary Motor and Sensory Neuropathy to be used for CMT (eORIF 2021). As Reilly (2000) concluded, HMSN1=CMT1 and HMSN2=CMT2. This association went to Types 6 at one point. As gene discoveries prompted a reshuffling of CMT subtype categories and sorting, the subtype association now breaks down after Types 1 and 2. HMSN6A is caused by mutations in the MFN2 gene just as is CMT2A, and the 2 have nearly identical symptom profiles, but CMT2A still equals HMSN2A. If we are to equally apply Bansagi (2017), which we should, HMSN6A is its own subtype of CMT, and is included here as such. From here, we capture as CMT subtypes (but without the HMSN/CMT acronym direct synonym) HMSN4 (Mihalik 1997), HMSN5 (Muglia 2008), HMSN6B (Abrams 2915), HMSN6C (Chelban 2019), and HMSN-Okinawa Type (Ishiura 2012) whose associated gene, the TFG gene, was given as a CMT gene in the aforementioned CMTA conference, and each are included here. There are no other HMSN subtypes found in published literature that do not directly associate and correlate with the CMT1 or the CMT2 category.

As Science Evolves, CMT Genetics Evolves

Science is an ever-evolving endeavor. Science never sits still. When it comes to CMT, and especially CMT genetics, the science is approaching warp speed. In December 1990, there wasn't a single known cause of CMT. By Christmas Eve 1993, there were 3 discovered associated genes. By May 1, 1998, there were 6 identified CMT-associated genes. By the end of 2011, marking the end of the first 20 years of CMT gene discovery, there were 55 identified CMT-associated genes. As of this writing, scientists have discovered 120 CMT-associated genes. Sometimes, a discovery is a correction to a previously published discovery. Thus far, a review of published literature reveals 2 such occurrences.

The cause of CMT2A was discovered and published in 2001. Scientists had found that mutations in the KIF1B gene were responsible for causing an axonal CMT (Zhao 2001). In 2004, scientists discovered that the actual cause for CMT2A was a mutation in the MFN2 gene (S. M.-T.-V. Züchner 2004). Although published literature doesn't specifically say, this initial confusion might have been from the 2 genes sharing the same chromosomal location – they are literal roommates. Both the KIF1B gene and the MFN2 gene live at chromosome 1. Specifically, they both live at 1p36.22. This is equivalent to the two genes' house number, street, city, and postal code. The same chromosomal situation is shared by the CMT2B2 gene discovery.

An autosomal recessive Type 2 CMT was discovered to be caused by mutations in the MED25 gene. This finding was published in March 2009 (A. H. Leal 2009), and was designated CMT2B2. The same lead author of this published discovery later discovered in 2018 that the actual cause of CMT2B2 was with the PNKP gene (A. B.-L. Leal 2018). Like the KIF1B gene and the MFN2 gene being genetic roommates, so are the MED25 gene and the PNKP gene, with both living at chromosome 19q13.33. And, again, while published literature might not specifically conclude, the confusion might stem from this genetic roommate arrangement. To date, these are the only two CMT-associated gene corrections found in a review of published literature. The MED25/PNKP correction is straightforward. Nothing changed except for the associated gene. KIF1B/MFN2 is a completely different story.

The Confusion Sets In

The CMT2A genetic correction, while it was a seemingly smooth transition for scientists, it was a completely different story for CMTers who had CMT2A at the time, and who have since been diagnosed with CMT2A. Published literature doesn't reveal an exact date to cite, but after Züchner et al. (2004) discovered that the actual cause of CMT2A was associated with the MFN2 gene, 2 designations emerged for CMT2A. CMT2A1 emerged to represent the Zhao et al. (2001) KIF1B subtype, and CMT2A2 emerged to represent the Züchner et al. (2004) MFN2 subtype. CMT2A1 represented that it was discovered first, and CMT2A2 represented that it was second. As confusing as this was for CMTers, this wasn't too bad once everybody was used to it. But, then, came another MFN2 CMT discovery.

Polke et al. (2011) discovered a recessive mutation in the MFN2 gene causing a Type 2 CMT. This discovery was designated CMT2A2B, and this represents that it is an MFN2 discovery that followed Züchner et al. (2004) discovery, hence the "B" at the end. Published literature, again, does not provide a date to cite, but a CMT2A2A designation emerged to represent the Züchner et al. (2004) MFN2 subtype in favor of the CMT2A2 designation. This was likely an effort to clear up CMTer confusion over these several CMT2A designations. We had CMT2A1, CMT2A2, and CMT2A2A all at the same time and referring to the same thing; and then CMT2A2B just to keep things interesting. CMTers were as confused as ever, but a viable solution emerged over time.

As of this writing, but, again, and unfortunately, without published literature revealing an exact date to cite, the several CMT2A subtypes have been reduced to just 2. Today, CMT2A represents the Züchner et al. (2004) MFN2 discovery and CMT2A2B represents the Polke et al. (2011) recessive MFN2 discovery. CMT2A1 no longer applies and is not in use because of its KIF1B association. Any finding of CMT2A1, CMT2A2, and CMT2A2A in internet and literature searches should be considered synonymous with MFN2 associated CMT2A. Any finding of KIF1B associated CMT2A should be considered synonymous with MFN2 associated CMT2A, but only after disregarding the KIF1B gene association. Symptom descriptions are the same, but the KIF1B association to CMT is incorrect. In further support, Clinical Genome Resource, who is a genome curation authority and whose Charcot-Marie-Tooth Disease Gene Curation expert

panel is chaired by Dr. Züchner, retracted the KIF1B association to CMT in October 2020 (Clinical Genome Resource 2020). Therefore, it is concluded here that the KIF1B association to CMT should be abandoned and should be disregarded. Then, there's the X-linked confusion.

X-Linked CMT refers to the category of CMT in which the underlying genetic cause is in a gene that lives on the X-chromosome. X-Linked CMT (CMTX) encompasses 6 subtypes to date. There are 3 additional X-Linked subtypes of CMT that are not included in the CMTX category: dSMAX2, dSMAX3, and DRP2-CMT. Pertaining to CMTX and its 6 subtypes, the first X-Linked CMT discovery was the aforementioned GJB1 gene discovery by Bergoffen et al. (1993). This discovery was designated CMT1X and categorized as a Type 1 CMT. This made sense because the subtype is considered demyelinating. The X, of course, represented that the subtype was X-Linked. This worked fine until additional X-Linked causes of CMT were discovered. Published literature does not reveal a date to cite, but CMTX emerged as its own category by around c.2016. As this category emerged, CMT1X transitioned to CMTX1. Today, CMT1X and X1 are synonymous with one another, but the current designation is CMTX1. There is a CMT2X which is associated with the SPG11 gene (Montecchiani 2015), but this is a different subtype than CMTX2 (Ionasescu 1992). CMTX2 and CMT2X are not synonymous with one another.

The Limitations of CMT Genetic Testing

Overall knowledge and understandings of CMT have grown exponentially year-over-year for the last 30 years, and especially regarding the genetics of CMT. With each new associated gene discovery comes new hope for many CMTers who have yet to obtain a genetic confirmation for their CMT clinical diagnosis. To date, scientists have published discoveries for 120 CMT-associated genes, and an additional 5 discoveries that do not yet have an identified gene, but suspect locations within a chromosome have been identified. These 120 genes and 5 chromosomal suspect locations account for 155 individual CMT subtypes that are sorted into 14 Type categories, and each category is represented by a different acronym. Despite the enormity of these numbers, a CMT genetic test is not guaranteed to genetically confirm a CMTer's clinical CMT diagnosis.

According to Dr. Shy, approximately 95% of CMTers with a demyelinating type of CMT are able to obtain a genetic confirmation of their CMT. In sharp contrast, only about 30% of CMTers with an axonal type of CMT are able to obtain a genetic confirmation (Michael Shy 2020). Dr. Züchner estimates that the statistic for axonal CMT might be as high as 50% (Charcot-Marie-Tooth Association (CMTA) 2020). To put this disparage into contextual perspective, there are 112 axonal subtypes of CMT, but only 27 demyelinating subtypes of CMT, and these numbers are continually growing. Dr. Shy also advises that researchers feel there will likely be more than 200 CMT-associated genes by the time all are discovered, leaving us at only about halfway there (Michael Shy 2020). Adding to CMTers' and practicing clinicians' frustrations are the limitations inherent in CMT genetic test panels.

Lab A's Complete CMT panel (labs call a genetic test a "panel") might analyze 43 genes. Lab B's Complete CMT panel might analyze 72 genes. Both panels might include genes that the other does not. Appendix C provides a panel comparison for reference. A review of publicly available CMT panel included gene lists from the various commercial labs who offer CMT genetic testing reveals that there isn't any one lab that analyzes all known CMT-associated genes. Labs design their own panels and decide what to include based on their own criteria, and understandably so. This is perhaps the single most significant variable with the potential genetic confirmation for a CMTer. When a CMT genetic test does not identify an underlying responsible genetic cause that is consistent with a known cause of CMT, the first variable that must be considered is the included genes.

Invitae Corp. is arguably one of the most frequently used commercial labs for CMT genetic testing. A review of their website reveals that their Comprehensive Neuropathies Panel, test 03200 is one of the most comprehensive CMT genetic tests in a single panel. This panel includes 102 genes, and there is an option for the ordering doctor to add up to an additional 9 genes, for a total of 111 genes (Invitae Comprehensive Neuropathies Panel 2021). This number is comparatively huge. For all of this panel's inclusion, it's easy to see the panel's limitations right up front though. The panel analyzes a maximum of 111 genes, but there are 120 CMT-associated genes to date. Of these 111 genes, only 89 are associated with CMT. These 89 genes, however, can potentially identify up to 118 different CMT subtypes. That's a fairly hefty feat. The

numbers reveal that the panel is limited in overall CMT scope though, despite its level of CMT-associated gene inclusion. Appendix C provides an accounting of this panel's publicly available included genes, current as of this writing, and indicates the genes that are associated with CMT, together with the respective subtypes.

A genetic test that does not genetically confirm the CMTer's CMT is not only a common result, but it does not mean that CMT is ruled out by the result. The consensus of the CMT experts is that when symptoms and nerve conduction characteristics are consistent with CMT, that when there is a clinical diagnosis of CMT and a genetic test either does not genetically confirm CMT or does not identify a non-CMT genetic cause for the clinical presentation, CMT is not ruled out. The consensus is that a CMT genetic test result like this, and under the given clinical circumstances, the result means only that the underlying genetic cause of the CMT has not yet been tested for, and the results mean only this. This further clarifies, when a CMT genetic test result does not confirm the clinical diagnosis, the importance of first knowing the genes that were analyzed so that they can be compared against the discovered CMT-associated genes. It is through this that it becomes apparent that the result means only that the underlying cause was not tested for.

Conclusion

CMT genetics and associated gene discovery continues to grow at an incredibly fast rate. Naming and designating new subtypes as their respective causes are discovered is an ever-evolving dynamic process. If the CMT naming history has taught us anything, it's taught us that there will have to be additional modifications to subtype naming and designation formats, especially since scientists believe they are only about halfway to discovering all CMT-associated genes.

Every effort has been made to ensure that all information presented and discussed is accurate and current as of this writing. The subtype master list provided in Appendix A represents an exhaustive and fully inclusive list of all CMT subtypes, current to this writing. The CMT-associated genes master list provided in Appendix B represents an exhaustive and fully inclusive

list of all discovered CMT-associated genes current to this writing. The CMT genetic test panels comparison provided in Appendix C is provided for informational purposes only and is intended to be used only as a reference. Appendix D provides an exhaustive and fully inclusive bibliographic listing of the original establishing publication for each individual CMT subtype, arranged in alphabetical order. While every effort has been made to ensure accuracy and completeness throughout, things change rapidly in the CMT world, and updates to this guide will undoubtedly be required.

The information provided is provided for reference only and is not intended to serve as medical advice and nor is it intended to be a means by which to diagnose any condition. The information provided and discussed should not be considered a replacement for the advice and opinion of your doctor and should not be used in place of sound medical advice from a qualified healthcare professional.

About The Author

Kenneth Raymond is a CMTer who was first diagnosed with Type 1 CMT in late 2002, at the age of 29. He was genetically confirmed to have CMT1A a year later. He has devoted his life since diagnosis to studying, researching, and learning all things CMT, with an emphasis on the genetics of CMT as they relate to everyday CMTers. As a member of the CMTA Advisory Board, he is a CMT advocate who is committed to raising CMT awareness through fact-based information rooted in the latest understandings of CMT.

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Appendix A
CMT Subtypes Master List

This CMT subtypes master list is intended to be used as a reference for CMTers and clinicians alike. This master list is organized alphanumerically according to Type category, and then according to subtype. This subtype master list includes a glossary of abbreviations that appear in the list and each subtype entry includes the respective associated gene, the inheritance pattern, the neuropathy type, and the original date of discovery publication that established the subtype.

Glossary of Abbreviations	
AD	Autosomal Dominant Inheritance Pattern
AR	Autosomal Recessive Inheritance Pattern
CMT	Charcot Marie Tooth disease
dHMN	distal Hereditary Motor Neuronopathy
dSMA	distal Spinal Muscular Atrophy
GAN	Giant Axon Neuropathy
HMSN	Hereditary Motor and Sensory Neuropathy
HNPP	Hereditary Neuropathy with liability to Pressure Palsies
HSAN	Hereditary Sensory and Autonomic Neuropathy
HSN	Hereditary Sensory Neuropathy
mtDNA	Mitochondrial DNA
PHARC	Polyneuropathy, Hearing Loss, Ataxia, Retinitis Pigmentosa, and Cataract
SCAN	Spinocerebellar Ataxia with Axonal Neuropathy
SMA	Spinal Muscular Atrophy
SMA-LEP	Spinal Muscular Atrophy - Lower Extremity- Predominant
SPG	Spastic Paraplegia
XLD	X-Linked Dominant Inheritance Pattern
XLR	X-Linked Recessive Inheritance Pattern

CMT1				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMT1A	PMP22	AD	Demyelinating	June 1, 1992
CMT1B	MPZ	AD	Demyelinating	September 1, 1993
CMT1C	LITAF	AD	Demyelinating	January 14, 2003
CMT1D	EGR2	AD	Demyelinating	April 1, 1998
CMT1E	PMP22	AD	Demyelinating	June 1, 1999
CMT1F	NEFL	AD	Demyelinating	March 3, 2003
CMT1G	PMP2	AD	Demyelinating	June 6, 2016
CMT1H	FBLN5	AD	Demyelinating	August 5, 2020
HNPP	PMP22	AD	Demyelinating	January 15, 1993

CMT2				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMT2A	MFN2	AD	Axonal	4/4/2004
CMT2A1-Archaic	*KIF1B*	*N/A*	*NA*	*6/1/2001*
CMT2A2B	MFN2	AR	Axonal	6/29/2011
CMT2B	RAB7A	AD	Axonal	3/1/2003
CMT2B1	LMNA	AR	Axonal	3/1/2002
CMT2B2	PNKP	AR	Axonal	7/24/2018
CMT2B2 - Archaic	*MED25*	*N/A*	*NA*	*3/17/2009*
CMT2B3	GDAP1	AR	Axonal	3/8/2007
CMT2B4	MFN2	AR	Axonal	5/5/2008
CMT2B5	NEFL	AR	Axonal	4/13/2009
CMT2C	TRPV4	AD	Axonal	2/1/2010
CMT2CC	NEFH	AD	Axonal	4/7/2016
CMT2D	GARS1	AD	Axonal	5/1/2003
CMT2DD	ATP1A1	AD	Axonal	3/1/2018
CMT2E	NEFL	AD	Axonal	7/1/2000
CMT2EE	MPV17	AR	Axonal	1/3/2019
CMT2F	HSPB1	AD	Axonal	5/2/2004
CMT2I	MPZ	AD	Axonal	5/1/1998
CMT2J	MPZ	AD	Axonal	12/1/2000
CMT2K	GDAP1	AD, AR	Axonal	8/13/2008

CMT2 (Cont.)				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMT2L	HSPB8	AD	Axonal	February 1, 2005
CMT2M	DNM2	AD	Axonal	July 16, 2007
CMT2N	AARS1	AD	Axonal	January 8, 2010
CMT2O	DYNC1H1	AD	Axonal	August 4, 2011
CMT2P	LRSAM1	AD, AR	Axonal	April 1, 1998
CMT2Q	DHTKD1	AD	Axonal	December 7, 2012
CMT2R	TRIM2	AR	Axonal	August 1, 2013
CMT2S	IGHMBP2	AR	Axonal	November 6, 2014
CMT2T	MME	AD, AR	Axonal	April 8, 2016
CMT2U	MARS1	AD	Axonal	June 1, 2013
CMT2V	NAGLU	AD	Axonal	March 27, 2015
CMT2W	HARS1	AD	Axonal	June 13, 2015
CMT2X	SPG11	AR	Axonal	November 10, 2015
CMT2Y	VCP	AD	Axonal	August 14, 2014
CMT2Z	MORC2	AD	Axonal	March 10, 2016

Note: KIF1B associated CMT2A1 and MED25 associated CMT2B2 are not included in the overall subtype total as these two genes are no longer associated with CMT.

CMT4				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMT4A	GDAP1	AR	Demyelinating	January 3, 2002
CMT4B1	MTMR2	AR	Demyelinating	May 1, 2000
CMT4B2	SBF2	AR	Demyelinating	February 1, 2003
CMT4B3	SBF1	AR	Demyelinating	June 7, 2013
CMT4C	SH3TC2	AR	Demyelinating	November 1, 2003
CMT4D	NDRG1	AR	Demyelinating	July 1, 2000
CMT4E	EGR2	AR	Demyelinating	April 1, 1998
CMT4F	PRX	AR	Demyelinating	February 15, 2001
CMT4G	HK1	AR	Demyelinating	June 17, 2009
CMT4H	FGD4	AR	Demyelinating	July 1, 2007
CMT4J	FIG4	AR	Demyelinating	June 17, 2007
CMT4K	SURF1	AR	Demyelinating	October 22, 2013

X-Linked CMT (CMTX)				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMTX1	GJB1	XLD	Intermediate	December 24, 1993
CMTX2	Unknown, but mapped to Xp22.2	XLR	Intermediate	March 15, 1992
CMTX3	Genomic Rearrangement Between 8q24.3 and Xq27.1	XLR	Demyelinating	July 20, 2016
CMTX4	AIFM1	XLR	Axonal	December 7, 2012
CMTX5	PRPS1	XLR	Intermediate	September 1, 2007
CMTX6	PDK3	XLD	Axonal	April 1, 2013

Dominant Intermediate CMT (CMT-DI)				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMTDIA	Unknown, but mapped to 10q24.1 - 10q25.1	AD	Intermediate	October 1, 2001
CMTDIB	DNM2	AD	Intermediate	January 30, 2005
CMTDIC	YARS1	AD	Intermediate	January 22, 2006
CMTDID	MPZ	AD	Intermediate	August 1, 1999
CMTDIE	INF2	AD	Intermediate	December 22, 2011
CMTDIF	GNB4	AD	Intermediate	March 7, 2013
CMTDIG	NEFL	AD	Intermediate	February 1, 2004
Recessive Intermediate CMT (CMT-RI)				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
CMTRIA	GDAP1	AR	Intermediate	March 1, 2003
CMTRIB	KARS1	AR	Intermediate	October 8, 2010
CMTRIC	PLEKHG5	AR	Intermediate	June 17, 2013
CMTRID	COX6A1	AR	Intermediate	September 4, 2014

dHMN				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
AARS1-dHMN	AARS1	AD	Axonal	May 9, 2012
dHMN-1	Unknown, but Mapped to 7q34-q36	AD	Axonal	March 13, 2007
dHMN-2A	HSPB8	AD	Axonal	May 2, 2004
dHMN-2B	HSPB1	AD	Axonal	May 2, 2004
dHMN-2C	HSPB3	AD	Axonal	February 9, 2010
dHMN-2D	FBXO38	AD	Axonal	October 24, 2013
dHMN-5A	GARS1	AD	Axonal	May 1, 2003
dHMN-5B	REEP1	AD	Axonal	July 13, 2012
dHMN-5C	BSCL2	AD	Axonal	February 22, 2004
dHMN-6	IGHMBP2	AR	Axonal	August 13, 2001
dHMN-7A	SLC5A7	AD	Axonal	November 8, 2012
dHMN-7B	DCTN1	AD	Axonal	March 10, 2003
dHMN-8	TRPV4	AD	Axonal	February 1, 2010
dHMN-9	WARS1	AD	Axonal	May 1, 2017
MYH14-dHMN	MYH14	AD	Axonal	July 16, 2017
SIGMAR1-dHMN2	SIGMAR1	AR	Axonal	June 16, 2015
SLC12A6-dHMN2	SLC12A6	AD	Axonal	August 2, 2016
VWA1-dHMN	VWA1	AR	Axonal	January 18, 2021

dSMA				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
dSMA	VRK1	AR	Axonal	July 5, 2016
dSMA4	PLEKHG5	AR	Intermediate	July 1, 2007
dSMA-5	DNAJB2	AR	Axonal	April 20, 2012
dSMAX-2	UBA1	XLR	Axonal	January 10, 2008
dSMAX-3	ATP7A	XLR	Axonal	March 12, 2010
GAN				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
GAN-1	GAN	AR	Axonal	November 1, 2000
GAN-2	DCAF8	AD	Axonal	March 11, 2014
HMSN				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
HMSN-4	PYHY	AR	Axonal	October 1, 1997
HMSN-5	Unknown, but mapped to 4q34.3-q35.2	AD	Axonal	April 7, 2008
HMSN-6A	MFN2	AD	Axonal	January 25, 2006
HMSN-6B	SLC25A46	AR	Axonal	July 13, 2015
HMSN-6C	PDXK	AR	Axonal	July 11, 2019
HMSN-Okinawa Type	TFG	AD	Axonal	August 10, 2012

HSAN				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
HSAN-1A	SPTLC1	AD	Axonal	March 27, 2001
HSAN-1B	Unknown, but mapped to 3p22-p24	AD	Axonal	September 1, 2003
HSAN-1C	SPTLC2	AD	Axonal	October 8, 2010
HSAN-2A	WNK1	AR	Axonal	June 2, 2008
HSAN-2B	RETREG1	AR	Axonal	October 18, 2009
HSAN-2D	SCN9A	AR	Axonal	April 17, 2013
HSAN-3	ELP1	AR	Axonal	March 1, 2001
HSAN-4	NTRK1	AR	Axonal	August 1, 1996
HSAN-5	NGF	AR	Axonal	February 4, 2004
HSAN-6	DST	AR	Axonal	January 9, 2012
HSAN-7	SCN11A	AD	Axonal	September 15, 2013
HSAN-8	PRDM12	AR	Axonal	May 25, 2015

HSN				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
FLVCR1-HSN	FLVCR1	AR	Axonal	December 1, 2019
HSN w/SPG	CCT5	AR	Axonal	February 1, 2006
HSN-1A	SPTLC1	AD	Axonal	March 27, 2001
HSN-1B	Unknown, but mapped to 3p22-p24	AD	Axonal	September 1, 2003
HSN-1C	SPTLC2	AD	Axonal	October 8, 2010
HSN-1D	ATL1	AD	Axonal	January 7, 2011
HSN-1E	DNMT1	AD	Axonal	May 1, 2011
HSN-1F	ATL3	AD	Axonal	January 22, 2014
HSN-2A	WNK1	AR	Axonal	June 2, 2008
HSN-2C	KIF1A	AR	Axonal	August 4, 2011
SMA-LEP				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
SMA-LEP-1	DYNC1H1	AD	Axonal	March 28, 2012
SMA-LEP-2A	BICD2	AD	Axonal	June 6, 2013
SMA-LEP-2B	BICD2	AD	Axonal	July 27, 2018

[Gene Name]-CMT				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
ABHD12-CMT/PHARC	ABHD12	AR	Demyelinating	August 26, 2010
ARHGEF10-CMT	ARHGEF10	AD	Demyelinating	October 1, 2003
ATP6-CMT	ATP6	mtDNA	Axonal	September 3, 2019
BAG3-CMT	BAG3	AD	Axonal	February 19, 2018
C12ORF65-CMT	C12ORF65	AR	Axonal	April 10, 2014
C19ORF12-CMT	C19ORF12	AR	Axonal	July 15, 2013
C1ORF194-CMT	C1ORF194	AD	Demyelinating	June 14, 2019
CADM3-CMT	CADM3	AD	Axonal	April 23, 2021
CHCHD10-CMT	CHCHD10	AD	Axonal	April 14, 2015
CNTNAP1-CMT	CNTNAP1	AR	Axonal	August 9, 2019
COA7-CMT/SCAN3	COA7	AR	Axonal	April 27, 2018
CTDP1-CMT	CTDP1	AR	Demyelinating	March 1, 2006
DGAT-CMT	DGAT2	AD	Axonal	January 20, 2016
DRP2-CMT	DRP2	XLD	Intermediate	July 7, 2015
DST-CMT	DST	AR	Axonal	July 31, 2020
HADHB-CMT	HADHB	AR	Axonal	December 5, 2013
HINT1-CMT	HINT1	AR	Axonal	September 9, 2012
KIF5A-CMT	KIF5A	AD	Axonal	October 10, 2018
MCM3AP-CMT	MCM3AP	AR	Axonal	June 19, 2017
POLG-CMT	POLG	AR	Axonal	March 6, 2019

[Gene Name]-CMT (Cont.)				
Subtype	**Gene**	**Inheritance Pattern**	**Neuropathy Type**	**Date of Discovery**
SCO2-CMT	SCO2	AR	Axonal	January 16, 2018
SCYL1-CMT/SCAR21	SCYL1	AR	Axonal	December 3, 2015
SEPT9-CMT	SEPTIN9	AD	Demyelinating	March 2, 2020
SETX-dHMN	SETX	AR	Axonal	June 1, 2004
SGPL1-CMT	SGPL1	AR	Axonal	February 7, 2017
SORD-CMT	SORD1	AR	Axonal	May 4, 2020
SYT2-dHMN	SYT2	AD	Axonal	September 4, 2014
TUBB3-CMT	TUBB3	AD	Axonal	January 8, 2010

Appendix B
CMT-Associated Genes Master List

This CMT-associated genes master list is intended to be used as a reference for CMTers and clinicians alike. This master list is organized alphabetically, includes the subtypes that are associated with each gene, includes the inheritance pattern(s) associated with each gene, and includes the original date of discovery publication that established the gene as a CMT-associated gene CMT.

Glossary of Abbreviations	
AD	Autosomal Dominant Inheritance Pattern
AR	Autosomal Recessive Inheritance Pattern
CMT	Charcot Marie Tooth disease
dHMN	distal Hereditary Motor Neuronopathy
dSMA	distal Spinal Muscular Atrophy
GAN	Giant Axon Neuropathy
HMSN	Hereditary Motor and Sensory Neuropathy
HNPP	Hereditary Neuropathy with liability to Pressure Palsies
HSAN	Hereditary Sensory and Autonomic Neuropathy
HSN	Hereditary Sensory Neuropathy
mtDNA	Mitochondrial DNA
PHARC	Polyneuropathy, Hearing Loss, Ataxia, Retinitis Pigmentosa, and Cataract
SCAN	Spinocerebellar Ataxia with Axonal Neuropathy
SMA	Spinal Muscular Atrophy
SMA-LEP	Spinal Muscular Atrophy - Lower Extremity- Predominant
SPG	Spastic Paraplegia
XLD	X-Linked Dominant Inheritance Pattern
XLR	X-Linked Recessive Inheritance Pattern

CMT-Associated Genes Master List

Gene	Subtype	Inheritance Pattern	Date of Discovery
AARS1	CMT2N, AARS1-dHMN	AD	January 8, 2010
ABHD12	ABHD12-CMT/PHARC	AR	August 26, 2010
AIFM1	CMTX4	XLR	December 7, 2012
ARHGEF10	ARHGEF10-CMT	AD	October 1, 2003
ATL1	HSN-1D	AD	January 7, 2011
ATL3	HSN-1F	AD	January 22, 2014
ATP1A1	CMT2DD	AD	March 1, 2018
ATP6	ATP6-CMT	mtDNA	September 3, 2019
ATP7A	dSMAX-3	XLR	March 12, 2010
BAG3	BAG3-CMT	AD	February 19, 2018
BICD2	SMA-LEP-2A, SMA-LEP-2B	AD	June 6, 2013
BSCL2	dHMN-5C	AD	February 22, 2004
C12ORF65	C12ORF65-CMT	AR	April 10, 2014
C19ORF12	C19ORF12-CMT	AR	July 15, 2013
C1ORF194	C1ORF194-CMT	AD	June 14, 2019
CADM3	CADM3-CMT	AD	April 23, 2021
CCT5	HSN w/SPG	AR	February 1, 2006
CHCHD10	CHCHD10-CMT	AD	April 14, 2015
CNTNAP1	CNTNAP1-CMT	AR	August 9, 2019
COA7	COA7-CMT/SCAN3	AR	April 27, 2018
COX6A1	CMTRID	AR	September 4, 2014
CTDP1	CTDP1-CMT	AR	March 1, 2006

Gene	Subtype	Inheritance Pattern	Date of Discovery
DCAF8	GAN-2	AD	March 11, 2014
DCTN1	dHMN-7B	AD	March 10, 2003
DGAT2	DGAT-CMT	AD	January 20, 2016
DHTKD1	CMT2Q	AD	December 7, 2012
DNAJB2	dSMA-5	AR	April 20, 2012
DNM2	CMT2M, CMTDIB	AD	January 30, 2005
DNMT1	HSN-1E	AD	May 1, 2011
DRP2	DRP2-CMT	XLD	July 7, 2015
DST	HSAN-6, DST-CMT	AR	January 9, 2012
DYNC1H1	CMT2O, SMA-LEP-1	AD	August 4, 2011
EGR2	CMT1D, CMT4E	AD, AR	April 1, 1998
ELP1	HSAN-3	AR	March 1, 2001
FBLN5	CMT1H	AD	August 5, 2020
FBXO38	dHMN-2D	AD	October 24, 2013
FGD4	CMT4H	AR	July 1, 2007
FIG4	CMT4J	AR	June 17, 2007
FLVCR1	FLVCR1-HSN	AR	December 1, 2019
GAN	GAN-1	AR	November 1, 2000
GARS1	CMT2D, dHMN-5A	AD	May 1, 2003
GDAP1	CMT2B3, CMT2K, CMT4A, CMTRIA	AD, AR	January 3, 2002
Genomic Rearrangement Between 8q24.3 and Xq27.1	CMTX3	XLR	July 20, 2016
GJB1	CMTX1	XLD	December 24, 1993

Gene	Subtype	Inheritance Pattern	Date of Discovery
GNB4	CMTDIF	AD	March 7, 2013
HADHB	HADHB-CMT	AR	December 5, 2013
HARS1	CMT2W	AD	June 13, 2015
HINT1	HINT1-CMT	AR	September 9, 2012
HK1	CMT4G	AR	June 17, 2009
HSPB1	CMT2F, dHMN-2B	AD	May 2, 2004
HSPB3	dHMN-2C	AD	February 9, 2010
HSPB8	CMT2L, dHMN-2A	AD	May 2, 2004
IGHMBP2	CMT2S, dHMN-6	AR	August 13, 2001
INF2	CMTDIE	AD	December 22, 2011
KARS1	CMTRIB	AR	October 8, 2010
KIF1A	HSN-2C	AR	August 4, 2011
KIF1B	*CMT2A1-Archaic*	*N/A*	*June 1, 2001*
KIF5A	KIF5A-CMT	AD	October 10, 2018
LITAF	CMT1C	AD	January 14, 2003
LMNA	CMT2B1	AR	March 1, 2002
LRSAM1	CMT2P	AD, AR	August 26, 2010
MARS1	CMT2U	AD	June 1, 2013
MCM3AP	MCM3AP-CMT	AR	June 19, 2017
MED25	*CMT2B2 - Archaic*	*N/A*	*March 17, 2009*
MFN2	CMT2A, CMT2B4, CMT2A2B, HMSN-6A	AD, AR	April 4, 2004
MME	CMT2T	AD, AR	April 8, 2016

Gene	Subtype	Inheritance Pattern	Date of Discovery
MORC2	CMT2Z	AD	March 10, 2016
MPV17	CMT2EE	AR	January 3, 2019
MPZ	CMT1B, CMT2I, CMT2J, CMTDID	AD	September 1, 1993
MTMR2	CMT4B1	AR	May 1, 2000
MYH14	MYH14-dHMN	AD	July 16, 2017
NAGLU	CMT2V	AD	March 27, 2015
NDRG1	CMT4D	AR	July 1, 2000
NEFH	CMT2CC	AD	April 7, 2016
NEFL	CMT1F, CMT2E, CMT2B5, CMTDIG	AD, AR	July 1, 2000
NGF	HSAN-5	AR	February 4, 2004
NTRK1	HSAN-4	AR	August 1, 1996
PDK3	CMTX6	XLD	April 1, 2013
PDXK	HMSN-6C	AR	July 11, 2019
PLEKHG5	CMTRIC, dSMA4	AR	July 1, 2007
PMP2	CMT1G	AD	June 6, 2016
PMP22	CMT1A, HNPP, CMT1E	AD	June 1, 1992
PNKP	CMT2B2	AR	July 24, 2018
POLG	POLG-CMT	AR	March 6, 2019
PRDM12	HSAN-8	AR	May 25, 2015
PRPS1	CMTX5	XLR	September 1, 2007
PRX	CMT4F	AR	February 15, 2001
PYHY	HMSN-4	AR	October 1, 1997

Gene	Subtype	Inheritance Pattern	Date of Discovery
RAB7A	CMT2B	AD	March 1, 2003
REEP1	dHMN-5B	AD	July 13, 2012
RETREG1	HSAN-2B	AR	October 18, 2009
SBF1	CMT4B3	AR	June 7, 2013
SBF2	CMT4B2	AR	February 1, 2003
SCN11A	HSAN-7	AD	September 15, 2013
SCN9A	HSAN-2D	AR	April 17, 2013
SCO2	SCO2-CMT	AR	January 16, 2018
SCYL1	SCYL1-CMT/SCAR21	AR	December 3, 2015
SEPTIN9	SEPT9-CMT	AD	March 2, 2020
SETX	SETX-dHMN	AR	June 1, 2004
SGPL1	SGPL1-CMT	AR	February 7, 2017
SH3TC2	CMT4C	AR	November 1, 2003
SIGMAR1	SIGMAR1-dHMN2	AR	June 16, 2015
SLC12A6	SLC12A6-dHMN2	AD	August 2, 2016
SLC25A46	HMSN-6B	AR	July 13, 2015
SLC5A7	dHMN-7A	AD	November 8, 2012
SORD1	SORD-CMT	AR	May 4, 2020
SPG11	CMT2X	AR	November 10, 2015
SPTLC1	HSAN-1A, HSN-1A	AD	March 27, 2001
SPTLC2	HSAN-1C, HSN-1C	AD	October 8, 2010
SURF1	CMT4K	AR	October 22, 2013

Gene	Subtype	Inheritance Pattern	Date of Discovery
SYT2	SYT2-dHMN	AD	September 4, 2014
TFG	HMSN-Okinawa Type	AD	August 10, 2012
TRIM2	CMT2R	AR	August 1, 2013
TRPV4	CMT2C, dHMN-8	AD	February 24, 2010
TUBB3	TUBB3-CMT	AD	January 8, 2010
UBA1	dSMAX-2	XLR	January 10, 2008
Unknown, but mapped to 10q24.1 - 10q25.1	CMTDIA	AD	October 1, 2001
Unknown, but mapped to 3p22-p24	HSAN-1B	AD	September 1, 2003
Unknown, but mapped to 4q34.3-q35.2	HMSN-5	AD	April 7, 2008
Unknown, but Mapped to 7q34-q36	dHMN-1	AD	March 13, 2007
Unknown, but mapped to Xp22.2	CMTX2	XLR	March 15, 1992
VCP	CMT2Y	AD	August 14, 2014
VRK1	dSMA	AR	July 5, 2016
VWA1	VWA1-dHMN	AR	January 18, 2021
WARS1	dHMN-9	AD	May 1, 2017
WNK1	HSAN-2A, HSN-2A	AR	June 2, 2008
YARS1	CMTDIC	AD	January 22, 2006

Note: KIF1B and MED25 are not included in the overall associated gene total as these two genes are no longer associated with CMT.

Appendix C
CMT Gene Panel Comparison

Appendix C provides a side-by-side comparison of 2 CMT genetic test panels, with each being from a different independent commercial laboratory that offers CMT genetic testing services. This appendix compares the aforementioned Invitae Corp. Comprehensive Neuropathies Panel test 03200 with the Blueprint Genetics Charcot-Marie-Tooth Neuropathies Panel test NE1301. The two panels are directly comparable. The comparison is provided for informational and reference purposes only as an example of the variations between panels as those variations relate to potential CMT genetic confirmation outcomes for CMTers. The comparison of these 2 panels does not infer an endorsement for, of, or by either of the 2 independent laboratories.

Blueprint NE1301 vs Invitae 03200 Comparison Overview

Total Combined Genes Analyzed	135	**Blueprint NE1301**	**Invitae 03200**
Genes Analyzed by Each		105	111
CMT-Associated Genes Unique to Each Panel (One Includes, but Not the Other)		10	10
CMT-Associated Genes Analyzed		89	89
CMT Subtypes Potentially Identifiable		118	118
Subtypes with CMT Acronym (Includes HNPP)		64	62
Subtypes with Non-CMT Acronym (HNPP not Included)		39	45
Subtypes with [Gene Name]-CMT Formatted Name		15	11
Genes with Multiple Associated Subtypes		20	20
Autosomal Dominant Inheritance Subtypes		61	63
Autosomal Recessive Inheritance Subtypes		49	45
Subtypes that Can Be Either Autosomal Dominant or Autosomal Recessive		3	3
X-Linked Dominant Subtypes		2	3
X-Linked Recessive Subtypes		3	4
Mitochondrial DNA Subtypes		0	0
Known Subtypes Not Included		37	37

Overall Autosomal Dominant	78	Overall Autosomal Recessive	64
Overall X-Linked Dominant	3	Overall X-Linked Recessive	6
Overall Mitochondrial DNA	1	Overall Known CMT Subtypes	155
CMT-Associated Genes Both Panels Exclude	21	Subtypes Both Panels Excluded	27

Glossary of Abbreviations	
AD	Autosomal Dominant Inheritance Pattern
AR	Autosomal Recessive Inheritance Pattern
CMT	Charcot Marie Tooth disease
dHMN	distal Hereditary Motor Neuronopathy
dSMA	distal Spinal Muscular Atrophy
GAN	Giant Axon Neuropathy
HMSN	Hereditary Motor and Sensory Neuropathy
HNPP	Hereditary Neuropathy with liability to Pressure Palsies
HSAN	Hereditary Sensory Neuropathy
HSN	Hereditary Sensory and Autonomic Neuropathy
mtDNA	Mitochondrial DNA
PHARC	Polyneuropathy, Hearing Loss, Ataxia, Retinitis Pigmentosa, and Cataract
SCAN	Spinocerebellar Ataxia with Axonal Neuropathy
SMA	Spinal Muscular Atrophy
SMA-LEP	Spinal Muscular Atrophy - Lower Extremity- Predominant
SPG	Spastic Paraplegia
XLD	X-Linked Dominant Inheritance Pattern
XLR	X-Linked Recessive Inheritance Pattern

Subtypes Included in Both Blueprint NE1301 and Invitae 03200 Panels	
CMT1	CMT1A CMT1B CMT1C CMT1D CMT1E CMT1F CMT1H HNPP
CMT2	CMT2A CMT2A2B CMT2B CMT2B1 CMT2B3 CMT2B4 CMT2B5 CMT2C CMT2CC CMT2D CMT2DD CMT2E CMT2F CMT2I CMT2J CMT2K CMT2L CMT2M CMT2N CMT2O CMT2P CMT2Q CMT2R CMT2S CMT2T CMT2U CMT2W CMT2X CMT2Z
CMT4	CMT4A CMT4B1 CMT4B2 CMT4B3 CMT4C CMT4D CMT4E CMT4F CMT4H CMT4J CMT4K
X-Linked CMT (CMTX)	CMTX1 CMTX4 CMTX5 CMTX6
Dominant Intermediate CMT	CMTDIB CMTDIC CMTDID CMTDIE CMTDIF CMTDIG
Recessive Intermediate CMT	CMTRIA CMTRIC CMTRID
dHMN	AARS1-dHMN dHMN-2A dHMN-2B dHMN-5A dHMN-5B dHMN-5C dHMN-6 dHMN-7B dHMN-8 SLC12A6-dHMN2
dSMA	dSMA4 dSMAX-3
GAN	GAN-1
HMSN	HMSN-6A HMSN-6B HMSN-Okinawa Type
HSAN	HSAN-1A HSAN-1C HSAN-2A HSAN-2B HSAN-2D HSAN-3 HSAN-4 HSAN-5 HSAN-6 HSAN-7
HSN	HSN w/SPG HSN-1A HSN-1C HSN-1D HSN-1E HSN-1F HSN-2A HSN-2C
SMA-LEP	SMA-LEP-1 SMA-LEP-2A SMA-LEP-2B
[Gene Name]-CMT	ARHGEF10-CMT BAG3-CMT CHCHD10-CMT DST-CMT HINT1-CMT KIF5A-CMT MCM3AP-CMT POLG-CMT SEPT9-CMT

Subtypes Excluded in Both Blueprint NE1301 and Invitae 03200 Panels				
CMT2	CMT2B2	CMT2EE	CMT2V	
X-Linked CMT (CMTX)	CMTX2	CMTX3		
Dominant Intermediate CMT	CMTDIA			
dHMN	dHMN-1	dHMN-9	MYH14-dHMN	VWA1-dHMN
HMSN	HMSN-4	HMSN-5	HMSN-6C	
HSAN	HSAN-1B			
HSN	FLVCR1-HSN	HSN-1B		
[Gene Name]-CMT	ABHD12-CMT/PHARC	ATP6-CMT	C19ORF12-CMT	C1ORF194-CMT
	CADM3-CMT	CNTNAP1-CMT	DGAT-CMT	SCO2-CMT
	SORD-CMT	SYT2-dHMN	TUBB3-CMT	

Subtypes Unique to Blueprint NE1301				
CMT2	CMT2Y			
CMT4	CMT4G			
Recessive Intermediate CMT	CMTRIB			
GAN	GAN-2			
[Gene Name]-CMT	C12ORF65-CMT	COA7-CMT/SCAN3	CTDP1-CMT	HADHB-CMT
	SCYL1-CMT/SCAR21	SETX-dHMN		
Subtypes Unique to Invitae 03200				
CMT1	CMT1G			
dHMN	dHMN-2C	dHMN-2D	dHMN-7A	SIGMAR1-dHMN2
dSMA	dSMA	dSMA-5	dSMAX-2	
[Gene Name]-CMT	DRP2-CMT	SGPL1-CMT		

Genes with Multiple Subtypes			
Gene	**Associated Subtypes**	**Blueprint NE1301**	**Invitae 03200**
AARS1	CMT2N, AARS1-dHMN	Y	Y
BICD2	SMA-LEP-2A, SMA-LEP-2B	Y	Y
DNM2	CMT2M, CMTDIB	Y	Y
DST	HSAN-6, DST-CMT	Y	Y
DYNC1H1	CMT2O, SMA-LEP-1	Y	Y
EGR2	CMT1D, CMT4E	Y	Y
GARS1	CMT2D, dHMN-5A	Y	Y
GDAP1	CMT2B3, CMT2K, CMT4A, CMTRIA	Y	Y
HSPB1	CMT2F, dHMN-2B	Y	Y
HSPB8	CMT2L, dHMN-2A	Y	Y
IGHMBP2	CMT2S, dHMN-6	Y	Y
MFN2	CMT2A, CMT2B4, CMT2A2B, HMSN-6A	Y	Y
MPZ	CMT1B, CMT2I, CMT2J, CMTDID	Y	Y
NEFL	CMT1F, CMT2E, CMT2B5, CMTDIG	Y	Y
PLEKHG5	CMTRIC, dSMA4	Y	Y
PMP22	CMT1A, HNPP, CMT1E	Y	Y
SPTLC1	HSAN-1A, HSN-1A	Y	Y
SPTLC2	HSAN-1C, HSN-1C	Y	Y
TRPV4	CMT2C, dHMN-8	Y	Y
WNK1	HSAN-2A, HSN-2A	Y	Y

CMT-Associated Genes Included in Both Blueprint NE1301 and Invitae 03200 Panels				
AARS1	AIFM1	ARHGEF10	ATL1	ATL3
ATP1A1	ATP7A	BAG3	BICD2	BSCL2
CCT5	CHCHD10	COX6A1	DCTN1	DHTKD1
DNM2	DNMT1	DST	DYNC1H1	EGR2
ELP1	FBLN5	FGD4	FIG4	GAN
GARS1	GDAP1	GJB1	GNB4	HARS1
HINT1	HSPB1	HSPB8	IGHMBP2	INF2
KIF1A	KIF5A	LITAF	LMNA	LRSAM1
MARS1	MCM3AP	MFN2	MME	MORC2
MPZ	MTMR2	NDRG1	NEFH	NEFL
NGF	NTRK1	PDK3	PLEKHG5	PMP22
POLG	PRDM12	PRPS1	PRX	RAB7A
REEP1	RETREG1	SBF1	SBF2	SCN11A
SCN9A	SEPTIN9	SH3TC2	SLC12A6	SLC25A46
SPG11	SPTLC1	SPTLC2	SURF1	TFG
TRIM2	TRPV4	WNK1	YARS1	

CMT-Associated Genes Excluded in Both Blueprint NE1301 and Invitae 03200 Panels				
ABHD12	ATP6	C19ORF12	C1ORF194	CADM3
CNTNAP1	DGAT2	FLVCR1	Genomic Rearrangement Between 8q24.3 and Xq27.1	
MPV17	MYH14	NAGLU	PDXK	PNKP
PYHY	SCO2	SORD1	SYT2	TUBB3
Unknown, but mapped to 10q24.1 - 10q25.1	Unknown, but mapped to 3p22-p24	Unknown, but mapped to 4q34.3-q35.2	Unknown, but Mapped to 7q34-q36	Unknown, but mapped to Xp22.2
VWA1	WARS1			
CMT-Associated Genes Unique to Blueprint NE1301				
C12ORF65	COA7	CTDP1	DCAF8	HADHB
HK1	KARS1	SCYL1	SETX	VCP
CMT-Associated Genes Unique to Invitae 03200				
DNAJB2	DRP2	FBXO38	HSPB3	PMP2
SGPL1	SIGMAR1	SLC5A7	UBA1	VRK1

CMT-Associated Genes Excluded in Blueprint NE1301				
ABHD12	ATP6	C19ORF12	C1ORF194	CADM3
CNTNAP1	DGAT2	DNAJB2	DRP2	FBXO38
FLVCR1	Genomic Rearrangement Between 8q24.3 and Xq27.1		HSPB3	MPV17
MYH14	NAGLU	PDXK	PMP2	PNKP
PYHY	SCO2	SGPL1	SIGMAR1	SLC5A7
SORD1	SYT2	TUBB3	UBA1	Unknown, but mapped to 10q24.1 - 10q25.1
Unknown, but mapped to 3p22-p24	Unknown, but mapped to 4q34.3-q35.2	Unknown, but Mapped to 7q34-q36	Unknown, but mapped to Xp22.2	VRK1
VWA1	WARS1			

CMT-Associated Genes Excluded in Invitae 03200				
ABHD12	ATP6	C12ORF65	C19ORF12	C1ORF194
CADM3	CNTNAP1	COA7	CTDP1	DCAF8
DGAT2	FLVCR1	Genomic Rearrangement Between 8q24.3 and Xq27.1		HADHB
HK1	KARS1	MPV17	MYH14	NAGLU
PDXK	PNKP	PYHY	SCO2	SCYL1
SETX	SORD1	SYT2	TUBB3	Unknown, but mapped to 10q24.1 - 10q25.1
Unknown, but mapped to 3p22-p24	Unknown, but mapped to 4q34.3-q35.2	Unknown, but Mapped to 7q34-q36	Unknown, but mapped to Xp22.2	VCP
VWA1	WARS1			

CMT1				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMT1A	PMP22	AD	Y	Y
CMT1B	MPZ	AD	Y	Y
CMT1C	LITAF	AD	Y	Y
CMT1D	EGR2	AD	Y	Y
CMT1E	PMP22	AD	Y	Y
CMT1F	NEFL	AD	Y	Y
CMT1G	PMP2	AD	N	Y
CMT1H	FBLN5	AD	Y	Y
HNPP	PMP22	AD	Y	Y

CMT2				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMT2A	MFN2	AD	Y	Y
CMT2A1-Archaic	*KIF1B*	*N/A*	*Y*	*N*
CMT2A2B	MFN2	AR	Y	Y
CMT2B	RAB7A	AD	Y	Y
CMT2B1	LMNA	AR	Y	Y
CMT2B2	PNKP	AR	N	N
CMT2B2 - Archaic	*MED25*	*N/A*	*Y*	*Y*
CMT2B3	GDAP1	AR	Y	Y
CMT2B4	MFN2	AR	Y	Y
CMT2B5	NEFL	AR	Y	Y
CMT2C	TRPV4	AD	Y	Y
CMT2CC	NEFH	AD	Y	Y
CMT2D	GARS1	AD	Y	Y
CMT2DD	ATP1A1	AD	Y	Y
CMT2E	NEFL	AD	Y	Y
CMT2EE	MPV17	AR	N	N
CMT2F	HSPB1	AD	Y	Y
CMT2I	MPZ	AD	Y	Y
CMT2J	MPZ	AD	Y	Y
CMT2K	GDAP1	AD, AR	Y	Y

CMT2 (Cont.)				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMT2L	HSPB8	AD	Y	Y
CMT2M	DNM2	AD	Y	Y
CMT2N	AARS1	AD	Y	Y
CMT2O	DYNC1H1	AD	Y	Y
CMT2P	LRSAM1	AD, AR	Y	Y
CMT2Q	DHTKD1	AD	Y	Y
CMT2R	TRIM2	AR	Y	Y
CMT2S	IGHMBP2	AR	Y	Y
CMT2T	MME	AD, AR	Y	Y
CMT2U	MARS1	AD	Y	Y
CMT2V	NAGLU	AD	N	N
CMT2W	HARS1	AD	Y	Y
CMT2X	SPG11	AR	Y	Y
CMT2Y	VCP	AD	Y	N
CMT2Z	MORC2	AD	Y	Y

Note: KIF1B associated CMT2A1 and MED25 associated CMT2B2 are not included in the overall subtype total as these two genes are no longer associated with CMT.

CMT4				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMT4A	GDAP1	AR	Y	Y
CMT4B1	MTMR2	AR	Y	Y
CMT4B2	SBF2	AR	Y	Y
CMT4B3	SBF1	AR	Y	Y
CMT4C	SH3TC2	AR	Y	Y
CMT4D	NDRG1	AR	Y	Y
CMT4E	EGR2	AR	Y	Y
CMT4F	PRX	AR	Y	Y
CMT4G	HK1	AR	Y	N
CMT4H	FGD4	AR	Y	Y
CMT4J	FIG4	AR	Y	Y
CMT4K	SURF1	AR	Y	Y

X-Linked CMT (CMTX)				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMTX1	GJB1	XLD	Y	Y
CMTX2	Unknown, but mapped to Xp22.2	XLR	N	N
CMTX3	Genomic Rearrangement Between 8q24.3 and Xq27.1	XLR	N	N
CMTX4	AIFM1	XLR	Y	Y
CMTX5	PRPS1	XLR	Y	Y
CMTX6	PDK3	XLD	Y	Y

Dominant Intermediate CMT (CMT-DI)				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMTDIA	Unknown, but mapped to 10q24.1 - 10q25.1	AD	N	N
CMTDIB	DNM2	AD	Y	Y
CMTDIC	YARS1	AD	Y	Y
CMTDID	MPZ	AD	Y	Y
CMTDIE	INF2	AD	Y	Y
CMTDIF	GNB4	AD	Y	Y
CMTDIG	NEFL	AD	Y	Y
Recessive Intermediate CMT (CMT-RI)				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
CMTRIA	GDAP1	AR	Y	Y
CMTRIB	KARS1	AR	Y	N
CMTRIC	PLEKHG5	AR	Y	Y
CMTRID	COX6A1	AR	Y	Y

dHMN				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
AARS1-dHMN	AARS1	AD	Y	Y
dHMN-1	Unknown, but Mapped to 7q34-q36	AD	N	N
dHMN-2A	HSPB8	AD	Y	Y
dHMN-2B	HSPB1	AD	Y	Y
dHMN-2C	HSPB3	AD	N	Y
dHMN-2D	FBXO38	AD	N	Y
dHMN-5A	GARS1	AD	Y	Y
dHMN-5B	REEP1	AD	Y	Y
dHMN-5C	BSCL2	AD	Y	Y
dHMN-6	IGHMBP2	AR	Y	Y
dHMN-7A	SLC5A7	AD	N	Y
dHMN-7B	DCTN1	AD	Y	Y
dHMN-8	TRPV4	AD	Y	Y
dHMN-9	WARS1	AD	N	N
MYH14-dHMN	MYH14	AD	N	N
SIGMAR1-dHMN2	SIGMAR1	AR	N	Y
SLC12A6-dHMN2	SLC12A6	AD	Y	Y
VWA1-dHMN	VWA1	AR	N	N

dSMA				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
dSMA	VRK1	AR	N	Y
dSMA4	PLEKHG5	AR	Y	Y
dSMA-5	DNAJB2	AR	N	Y
dSMAX-2	UBA1	XLR	N	Y
dSMAX-3	ATP7A	XLR	Y	Y
GAN				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
GAN-1	GAN	AR	Y	Y
GAN-2	DCAF8	AD	Y	N
HMSN				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
HMSN-4	PYHY	AR	N	N
HMSN-5	Unknown, but mapped to 4q34.3-q35.2	AD	N	N
HMSN-6A	MFN2	AD	Y	Y
HMSN-6B	SLC25A46	AR	Y	Y
HMSN-6C	PDXK	AR	N	N
HMSN-Okinawa Type	TFG	AD	Y	Y

HSAN				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
HSAN-1A	SPTLC1	AD	Y	Y
HSAN-1B	Unknown, but mapped to 3p22-p24	AD	N	N
HSAN-1C	SPTLC2	AD	Y	Y
HSAN-2A	WNK1	AR	Y	Y
HSAN-2B	RETREG1	AR	Y	Y
HSAN-2D	SCN9A	AR	Y	Y
HSAN-3	ELP1	AR	Y	Y
HSAN-4	NTRK1	AR	Y	Y
HSAN-5	NGF	AR	Y	Y
HSAN-6	DST	AR	Y	Y
HSAN-7	SCN11A	AD	Y	Y
HSAN-8	PRDM12	AR	Y	Y

HSN				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
FLVCR1-HSN	FLVCR1	AR	N	N
HSN w/SPG	CCT5	AR	Y	Y
HSN-1A	SPTLC1	AD	Y	Y
HSN-1B	Unknown, but mapped to 3p22-p24	AD	N	N
HSN-1C	SPTLC2	AD	Y	Y
HSN-1D	ATL1	AD	Y	Y
HSN-1E	DNMT1	AD	Y	Y
HSN-1F	ATL3	AD	Y	Y
HSN-2A	WNK1	AR	Y	Y
HSN-2C	KIF1A	AR	Y	Y
SMA-LEP				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
SMA-LEP-1	DYNC1H1	AD	Y	Y
SMA-LEP-2A	BICD2	AD	Y	Y
SMA-LEP-2B	BICD2	AD	Y	Y

[Gene Name]-CMT				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
ABHD12-CMT/PHARC	ABHD12	AR	N	N
ARHGEF10-CMT	ARHGEF10	AD	Y	Y
ATP6-CMT	ATP6	mtDNA	N	N
BAG3-CMT	BAG3	AD	Y	Y
C12ORF65-CMT	C12ORF65	AR	Y	N
C19ORF12-CMT	C19ORF12	AR	N	N
C1ORF194-CMT	C1ORF194	AD	N	N
CADM3-CMT	CADM3	AD	N	N
CHCHD10-CMT	CHCHD10	AD	Y	Y
CNTNAP1-CMT	CNTNAP1	AR	N	N
COA7-CMT/SCAN3	COA7	AR	Y	N
CTDP1-CMT	CTDP1	AR	Y	N
DGAT-CMT	DGAT2	AD	N	N
DRP2-CMT	DRP2	XLD	N	Y
DST-CMT	DST	AR	Y	Y
HADHB-CMT	HADHB	AR	Y	N
HINT1-CMT	HINT1	AR	Y	Y
KIF5A-CMT	KIF5A	AD	Y	Y
MCM3AP-CMT	MCM3AP	AR	Y	Y
POLG-CMT	POLG	AR	Y	Y

[Gene Name]-CMT (Cont.)				
Subtype	**Gene**	**Inheritance Pattern**	**Blueprint NE1301**	**Invitae 03200**
SCO2-CMT	SCO2	AR	N	N
SCYL1-CMT/SCAR21	SCYL1	AR	Y	N
SEPT9-CMT	SEPTIN9	AD	Y	Y
SETX-dHMN	SETX	AR	Y	N
SGPL1-CMT	SGPL1	AR	N	Y
SORD-CMT	SORD1	AR	N	N
SYT2-dHMN	SYT2	AD	N	N
TUBB3-CMT	TUBB3	AD	N	N

Blueprint NE1301 - Invitae 03200 Included Genes Side-by-Side Comparison							
Gene	**CMT Gene**	**Blueprint NE1301**	**Invitae 03200**	**Gene**	**CMT Gene**	**Blueprint NE1301**	**Invitae 03200**
AARS1	Y	Y	Y	COX6A1	Y	Y	Y
AGTPBP1	N	Y	N	CTDP1	Y	Y	N
AIFM1	Y	Y	Y	CYP27A1	N	N	Y
AMACR	N	Y	N	CYP7B1	N	N	Y
APOA1	N	N	Y	DCAF8	Y	Y	N
ARHGEF10	Y	Y	Y	DCTN1	Y	Y	Y
ASAH1	N	N	Y	DHTKD1	Y	Y	Y
ATAD3A	N	Y	N	DNAJB2	Y	N	Y
ATL1	Y	Y	Y	DNM2	Y	Y	Y
ATL3	Y	Y	Y	DNMT1	Y	Y	Y
ATP1A1	Y	Y	Y	DRP2	Y	N	Y
ATP7A	Y	Y	Y	DST	Y	Y	Y
BAG3	Y	Y	Y	DYNC1H1	Y	Y	Y
BICD2	Y	Y	Y	EGR2	Y	Y	Y
BSCL2	Y	Y	Y	ELP1	Y	Y	Y
C12ORF65	Y	Y	N	EXOSC9	N	N	Y
CCT5	Y	Y	Y	FBLN5	Y	Y	Y
CHCHD10	Y	Y	Y	FBXO38	Y	N	Y
COA7	Y	Y	N	FGD4	Y	Y	Y
COX10	N	Y	N	FIG4	Y	Y	Y

Blueprint NE1301 - Invitae 03200 Included Genes Side-by-Side Comparison (Cont.)							
Gene	**CMT Gene**	**Blueprint NE1301**	**Invitae 03200**	**Gene**	**CMT Gene**	**Blueprint NE1301**	**Invitae 03200**
FXN	N	Y	N	KARS1	Y	Y	N
GAN	Y	Y	Y	KIF1A	Y	Y	Y
GARS1	Y	Y	Y	KIF1B	N	Y	N
GDAP1	Y	Y	Y	KIF5A	Y	Y	Y
GJB1	Y	Y	Y	LAS1L	N	N	Y
GLA	N	N	Y	LDB3	N	Y	N
GNB4	Y	Y	Y	LITAF	Y	Y	Y
GNE	N	Y	N	LMNA	Y	Y	Y
GSN	N	N	Y	LRSAM1	Y	Y	Y
HADHB	Y	Y	N	MARS1	Y	Y	Y
HARS1	Y	Y	Y	MCM3AP	Y	Y	Y
HEXA	N	N	Y	MED25	N	Y	Y
HINT1	Y	Y	Y	MFN2	Y	Y	Y
HK1	Y	Y	N	MICAL1	N	N	Y
HMBS	N	N	Y	MME	Y	Y	Y
HSPB1	Y	Y	Y	MORC2	Y	Y	Y
HSPB3	Y	N	Y	MPZ	Y	Y	Y
HSPB8	Y	Y	Y	MTMR2	Y	Y	Y
IGHMBP2	Y	Y	Y	MYOT	N	Y	N
INF2	Y	Y	Y	NDRG1	Y	Y	Y

Blueprint NE1301 - Invitae 03200 Included Genes Side-by-Side Comparison (Cont.)

Gene	CMT Gene	Blueprint NE1301	Invitae 03200	Gene	CMT Gene	Blueprint NE1301	Invitae 03200
NEFH	Y	Y	Y	SCN11A	Y	Y	Y
NEFL	Y	Y	Y	SCN9A	Y	Y	Y
NGF	Y	Y	Y	SCYL1	Y	Y	N
NTRK1	Y	Y	Y	SEPTIN9	Y	Y	Y
PDK3	Y	Y	Y	SETX	Y	Y	N
PLEKHG5	Y	Y	Y	SGPL1	Y	N	Y
PMP2	Y	N	Y	SH3TC2	Y	Y	Y
PMP22	Y	Y	Y	SIGMAR1	Y	N	Y
POLG	Y	Y	Y	SLC12A6	Y	Y	Y
POLG2	N	N	Y	SLC25A21	N	N	Y
PRDM12	Y	Y	Y	SLC25A46	Y	Y	Y
PRPS1	Y	Y	Y	SLC52A1	N	N	Y
PRX	Y	Y	Y	SLC52A2	N	N	Y
RAB7A	Y	Y	Y	SLC52A3	N	N	Y
REEP1	Y	Y	Y	SLC5A7	Y	N	Y
RETREG1	Y	Y	Y	SMAD3	N	Y	N
SACS	N	Y	N	SMN1	N	N	Y
SBF1	Y	Y	Y	SMN2	N	N	Y
SBF2	Y	Y	Y	SPG11	Y	Y	Y
SCN10A	N	N	Y	SPTBN4	N	Y	N

Blueprint NE1301 - Invitae 03200 Included Genes Side-by-Side Comparison (Cont.)							
Gene	**CMT Gene**	**Blueprint NE1301**	**Invitae 03200**	**Gene**	**CMT Gene**	**Blueprint NE1301**	**Invitae 03200**
SPTLC1	Y	Y	Y	UBA1	Y	N	Y
SPTLC2	Y	Y	Y	VAPB	N	N	Y
SURF1	Y	Y	Y	VCP	Y	Y	N
TFG	Y	Y	Y	VRK1	Y	N	Y
TRIM2	Y	Y	Y	WNK1	Y	Y	Y
TRPV4	Y	Y	Y	YARS1	Y	Y	Y
TTR	N	Y	Y	ZFYVE26	N	Y	N
TYMP	N	Y	N				

Appendix D

CMT-Associated Genes and Related Subtypes

Complete Bibliographic Original Source Publications Master List

Appendix D provides an exhaustive and fully inclusive bibliographic mater list of the original establishing publication for each CMT-associated gene. This master list is organized alphabetically, each entry includes the subtype(s) associated with each gene, and the publication date for each subtype.

Table of Contents

AARS1 – ARHGEF10

AARS1 – CMT2N (January 8, 2010)
Latour, P., Thauvin-Robinet, C., Baudelet-Méry, C., Soichot, P., Cusin, V., Faivre, L., Locatelli, M. C., Mayençon, M., Sarcey, A., Broussolle, E., Camu, W., David, A., & Rousson, R. (2010). A major determinant for binding and aminoacylation of tRNA(Ala) in cytoplasmic Alanyl-tRNA synthetase is mutated in dominant axonal Charcot-Marie-Tooth disease. American journal of human genetics, 86(1), 77–82. https://doi.org/10.1016/j.ajhg.2009.12.005

AARS1 – AARS1-dHMN (No OMIM Entry) (May 9, 2012)
Zhao, Z., Hashiguchi, A., Hu, J., Sakiyama, Y., Okamoto, Y., Tokunaga, S., Zhu, L., Shen, H., & Takashima, H. (2012). Alanyl-tRNA synthetase mutation in a family with dominant distal hereditary motor neuropathy. Neurology, 78(21), 1644–1649. https://doi.org/10.1212/WNL.0b013e3182574f8f

ABHD12 – ABHD12-CMT/ Polyneuropathy, Hearing Loss, Ataxia, Retinitis Pigmentosa, and Cataract (PHARC) (August 26, 2010)
Fiskerstrand, T., H'mida-Ben Brahim, D., Johansson, S., M'zahem, A., Haukanes, B. I., Drouot, N., Zimmermann, J., Cole, A. J., Vedeler, C., Bredrup, C., Assoum, M., Tazir, M., Klockgether, T., Hamri, A., Steen, V. M., Boman, H., Bindoff, L. A., Koenig, M., & Knappskog, P. M. (2010). Mutations in ABHD12 cause the neurodegenerative disease PHARC: An inborn error of endocannabinoid metabolism. *American journal of human genetics*, *87*(3), 410–417. https://doi.org/10.1016/j.ajhg.2010.08.002

AIFM1 – CMTX4 (December 7, 2012)
Rinaldi, C., Grunseich, C., Sevrioukova, I. F., Schindler, A., Horkayne-Szakaly, I., Lamperti, C., Landouré, G., Kennerson, M. L., Burnett, B. G., Bönnemann, C., Biesecker, L. G., Ghezzi, D., Zeviani, M., & Fischbeck, K. H. (2012). Cowchock syndrome is associated with a mutation in apoptosis-inducing factor. American journal of human genetics, 91(6), 1095–1102. https://doi.org/10.1016/j.ajhg.2012.10.008

ARHGEF10 - ARHGEF10-CMT (OMIM Entry 608236 – Slowed Nerve Conduction Velocity) (October 1, 2003)
Verhoeven, K., De Jonghe, P., Van de Putte, T., Nelis, E., Zwijsen, A., Verpoorten, N., De Vriendt, E., Jacobs, A., Van Gerwen, V., Francis, A., Ceuterick, C., Huylebroeck, D., & Timmerman, V. (2003). Slowed conduction and thin myelination of peripheral nerves associated with mutant rho Guanine-nucleotide exchange factor 10. American journal of human genetics, 73(4), 926–932. https://doi.org/10.1086/378159

ATL1 – HSN1D (January 7, 2011)
Guelly, C., Zhu, P. P., Leonardis, L., Papić, L., Zidar, J., Schabhüttl, M., Strohmaier, H., Weis, J., Strom, T. M., Baets, J., Willems, J., De Jonghe, P., Reilly, M. M., Fröhlich, E., Hatz, M., Trajanoski, S., Pieber, T. R., Janecke, A. R., Blackstone, C., & Auer-Grumbach, M. (2011). Targeted high-throughput sequencing identifies mutations in atlastin-1 as a cause of hereditary sensory neuropathy type I. American journal of human genetics, 88(1), 99–105. https://doi.org/10.1016/j.ajhg.2010.12.003

ATL3 – HSN1F (January 22, 2014)
Kornak, U., Mademan, I., Schinke, M., Voigt, M., Krawitz, P., Hecht, J., Barvencik, F., Schinke, T., Gießelmann, S., Beil, F. T., Pou-Serradell, A., Vílchez, J. J., Beetz, C., Deconinck, T., Timmerman, V., Kaether, C., De Jonghe, P., Hübner, C. A., Gal, A., Amling, M., … Kurth, I. (2014). Sensory neuropathy with bone destruction due to a mutation in the membrane-shaping atlastin GTPase 3. Brain : a journal of neurology, 137(Pt 3), 683–692. https://doi.org/10.1093/brain/awt357

ATP1A1 – CMT2DD (March 1, 2018)
Lassuthova, P., Rebelo, A. P., Ravenscroft, G., Lamont, P. J., Davis, M. R., Manganelli, F., Feely, S. M., Bacon, C., Brožková, D. Š., Haberlova, J., Mazanec, R., Tao, F., Saghira, C., Abreu, L., Courel, S., Powell, E., Buglo, E., Bis, D. M., Baxter, M. F., Ong, R. W., … Züchner, S. (2018). Mutations in ATP1A1 Cause Dominant Charcot-Marie-Tooth Type 2. American journal of human genetics, 102(3), 505–514. https://doi.org/10.1016/j.ajhg.2018.01.023

ATP6 – ATP6-CMT (September 3, 2019)
Bardakjian, T., & Scherer, S. S. (2019). A MT-ATP6 Mutation Causes a Slowly Progressive Myeloneuropathy. Journal of neuromuscular diseases, 6(3), 385–387. https://doi.org/10.3233/JND-190400

ATP7A – dSMAX3 (March 12, 2010)
Kennerson, M. L., Nicholson, G. A., Kaler, S. G., Kowalski, B., Mercer, J. F., Tang, J., Llanos, R. M., Chu, S., Takata, R. I., Speck-Martins, C. E., Baets, J., Almeida-Souza, L., Fischer, D., Timmerman, V., Taylor, P. E., Scherer, S. S., Ferguson, T. A., Bird, T. D., De Jonghe, P., Feely, S. M., … Garbern, J. Y. (2010). Missense mutations in the copper transporter gene ATP7A cause X-linked distal hereditary motor neuropathy. American journal of human genetics, 86(3), 343–352. https://doi.org/10.1016/j.ajhg.2010.01.027

BAG3 – BAG3-CMT (February 19, 2018)
Shy, M., Rebelo, A. P., Feely, S. M., Abreu, L. A., Tao, F., Swenson, A., Bacon, C., & Züchner, S. (2018). Mutations in BAG3 cause adult-onset Charcot-Marie-Tooth disease. Journal of neurology, neurosurgery, and psychiatry, 89(3), 313–315. https://doi.org/10.1136/jnnp-2017-315929

BICD2 – SMA-LEP2A (June 6, 2013)
Neveling, K., Martinez-Carrera, L. A., Hölker, I., Heister, A., Verrips, A., Hosseini-Barkooie, S. M., Gilissen, C., Vermeer, S., Pennings, M., Meijer, R., te Riele, M., Frijns, C. J., Suchowersky, O., MacLaren, L., Rudnik-Schöneborn, S., Sinke, R. J., Zerres, K., Lowry, R. B., Lemmink, H. H., Garbes, L., … Wirth, B. (2013). Mutations in BICD2, which encodes a golgin and important motor adaptor, cause congenital autosomal-dominant spinal muscular atrophy. American journal of human genetics, 92(6), 946–954. https://doi.org/10.1016/j.ajhg.2013.04.011

BICD2-SMA-LEP2B – CCT5

BICD2 – SMA-LEP2B (July 27, 2018)
Koboldt, D. C., Kastury, R. D., Waldrop, M. A., Kelly, B. J., Mosher, T. M., McLaughlin, H., Corsmeier, D., Slaughter, J. L., Flanigan, K. M., McBride, K. L., Mehta, L., Wilson, R. K., & White, P. (2018). In-frame de novo mutation in BICD2 in two patients with muscular atrophy and arthrogryposis. Cold Spring Harbor molecular case studies, 4(5), a003160. https://doi.org/10.1101/mcs.a003160

BSCL2 – dHMN5C (February 22, 2004)
Windpassinger, C., Auer-Grumbach, M., Irobi, J., Patel, H., Petek, E., Hörl, G., Malli, R., Reed, J. A., Dierick, I., Verpoorten, N., Warner, T. T., Proukakis, C., Van den Bergh, P., Verellen, C., Van Maldergem, L., Merlini, L., De Jonghe, P., Timmerman, V., Crosby, A. H., & Wagner, K. (2004). Heterozygous missense mutations in BSCL2 are associated with distal hereditary motor neuropathy and Silver syndrome. Nature genetics, 36(3), 271–276. https://doi.org/10.1038/ng1313

C12ORF65 – C12ORF65-CMT (April 10, 2014)
Tucci, A., Liu, Y. T., Preza, E., Pitceathly, R. D., Chalasani, A., Plagnol, V., Land, J. M., Trabzuni, D., Ryten, M., UKBEC, Jaunmuktane, Z., Reilly, M. M., Brandner, S., Hargreaves, I., Hardy, J., Singleton, A. B., Abramov, A. Y., & Houlden, H. (2014). Novel C12orf65 mutations in patients with axonal neuropathy and optic atrophy. Journal of neurology, neurosurgery, and psychiatry, 85(5), 486–492. https://doi.org/10.1136/jnnp-2013-306387

C19ORF12 – C19ORF12-CMT/SPG43 (July 15, 2013)
Landouré, G., Zhu, P. P., Lourenço, C. M., Johnson, J. O., Toro, C., Bricceno, K. V., Rinaldi, C., Meilleur, K. G., Sangaré, M., Diallo, O., Pierson, T. M., Ishiura, H., Tsuji, S., Hein, N., Fink, J. K., Stoll, M., Nicholson, G., Gonzalez, M. A., Speziani, F., Dürr, A., … Burnett, B. G. (2013). Hereditary spastic paraplegia type 43 (SPG43) is caused by mutation in C19orf12. Human mutation, 34(10), 1357–1360. https://doi.org/10.1002/humu.22378

C1ORF194 – C1ORF194-CMT (June 14, 2019)
Sun, S. C., Ma, D., Li, M. Y., Zhang, R. X., Huang, C., Huang, H. J., Xie, Y. Z., Wang, Z. J., Liu, J., Cai, D. C., Liu, C. X., Yang, Q., Bao, F. X., Gong, X. L., Li, J. R., Hui, Z., Wei, X. F., Zhong, J. M., Zhou, W. J., Shang, X., … Xu, X. M. (2019). Mutations in C1orf194, encoding a calcium regulator, cause dominant Charcot-Marie-Tooth disease. Brain : a journal of neurology, 142(8), 2215–2229. https://doi.org/10.1093/brain/awz151

CADM3 – CADM3-CMT (April 23, 2021)
Rebelo, A. P., Cortese, A., Abraham, A., Eshed-Eisenbach, Y., Shner, G., Vainshtein, A., Buglo, E., Camarena, V., Gaidosh, G., Shiekhattar, R., Abreu, L., Courel, S., Burns, D. K., Bai, Y., Bacon, C., Feely, S., Castro, D., Peles, E., Reilly, M. M., Shy, M. E., … Züchner, S. (2021). A CADM3 variant causes Charcot-Marie-Tooth disease with marked upper limb involvement. Brain : a journal of neurology, 144(4), 1197–1213. https://doi.org/10.1093/brain/awab019

CCT5 – CCT5-CMT (February 1, 2006)
Bouhouche, A., Benomar, A., Bouslam, N., Ouazzani, R., Chkili, T., & Yahyaoui, M. (2006). Autosomal recessive mutilating sensory neuropathy with spastic paraplegia maps to chromosome 5p15.31-14.1. European journal of human genetics : EJHG, 14(2), 249–252. https://doi.org/10.1038/sj.ejhg.5201537

CHCHD10 – DGAT2

CHCHD10 – CHCHD10-CMT (April 14, 2015)
Auranen, M., Ylikallio, E., Shcherbii, M., Paetau, A., Kiuru-Enari, S., Toppila, J. P., & Tyynismaa, H. (2015). CHCHD10 variant p.(Gly66Val) causes axonal Charcot-Marie-Tooth disease. Neurology. Genetics, 1(1), e1. https://doi.org/10.1212/NXG.0000000000000003

CNTNAP1 – CNTNAP1-CMT (August 9, 2019)
Freed, A. S., Weiss, M. D., Malouf, E. A., & Hisama, F. M. (2019). CNTNAP1 mutations in an adult with Charcot Marie Tooth disease. Muscle & nerve, 60(5), E28–E30. https://doi.org/10.1002/mus.26658

COA7 - Spinocerebellar Ataxia with Axonal Neuropathy 3 (SCAN3) (April 27, 2018)
Higuchi, Y., Okunushi, R., Hara, T., Hashiguchi, A., Yuan, J., Yoshimura, A., Murayama, K., Ohtake, A., Ando, M., Hiramatsu, Y., Ishihara, S., Tanabe, H., Okamoto, Y., Matsuura, E., Ueda, T., Toda, T., Yamashita, S., Yamada, K., Koide, T., Yaguchi, H., … Takashima, H. (2018). Mutations in COA7 cause spinocerebellar ataxia with axonal neuropathy. *Brain : a journal of neurology*, *141*(6), 1622–1636. https://doi.org/10.1093/brain/awy104

COX6A1- CMTRID (September 4, 2014)
Tamiya, G., Makino, S., Hayashi, M., Abe, A., Numakura, C., Ueki, M., Tanaka, A., Ito, C., Toshimori, K., Ogawa, N., Terashima, T., Maegawa, H., Yanagisawa, D., Tooyama, I., Tada, M., Onodera, O., & Hayasaka, K. (2014). A mutation of COX6A1 causes a recessive axonal or mixed form of Charcot-Marie-Tooth disease. American journal of human genetics, 95(3), 294–300. https://doi.org/10.1016/j.ajhg.2014.07.013

CTDP1 – CTDP1-CMT (March 1, 2006)
Dubourg, O., Azzedine, H., Verny, C., Durosier, G., Birouk, N., Gouider, R., Salih, M., Bouhouche, A., Thiam, A., Grid, D., Mayer, M., Ruberg, M., Tazir, M., Brice, A., & LeGuern, E. (2006). Autosomal-recessive forms of demyelinating Charcot-Marie-Tooth disease. Neuromolecular medicine, 8(1-2), 75–86. https://link.springer.com/article/10.1385/NMM:8:1-2:75

DCAF8 – GAN2 (March 11, 2014)
Klein, C. J., Wu, Y., Vogel, P., Goebel, H. H., Bönnemann, C., Zukosky, K., Botuyan, M. V., Duan, X., Middha, S., Atkinson, E. J., Mer, G., & Dyck, P. J. (2014). Ubiquitin ligase defect by DCAF8 mutation causes HMSN2 with giant axons. Neurology, 82(10), 873–878. https://doi.org/10.1212/WNL.0000000000000206

DCTN1 – dHMN7B (March 10, 2003)
Puls, I., Jonnakuty, C., LaMonte, B. H., Holzbaur, E. L., Tokito, M., Mann, E., Floeter, M. K., Bidus, K., Drayna, D., Oh, S. J., Brown, R. H., Jr, Ludlow, C. L., & Fischbeck, K. H. (2003). Mutant dynactin in motor neuron disease. Nature genetics, 33(4), 455–456. https://doi.org/10.1038/ng1123

DGAT2 – DGAT2-CMT (January 20, 2012)
Hong, Y. B., Kang, J., Kim, J. H., Lee, J., Kwak, G., Hyun, Y. S., Nam, S. H., Hong, H. D., Choi, Y. R., Jung, S. C., Koo, H., Lee, J. E., Choi, B. O., & Chung, K. W. (2016). DGAT2 Mutation in a Family with Autosomal-Dominant Early-Onset Axonal Charcot-Marie-Tooth Disease. Human mutation, 37(5), 473–480. https://doi.org/10.1002/humu.22959

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Xu, W. Y., Gu, M. M., Sun, L. H., Guo, W. T., Zhu, H. B., Ma, J. F., Yuan, W. T., Kuang, Y., Ji, B. J., Wu, X. L., Chen, Y., Zhang, H. X., Sun, F. T., Huang, W., Huang, L., Chen, S. D., & Wang, Z. G. (2012). A nonsense mutation in DHTKD1 causes Charcot-Marie-Tooth disease type 2 in a large Chinese pedigree. American journal of human genetics, 91(6), 1088–1094. https://doi.org/10.1016/j.ajhg.2012.09.018

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Blumen, S. C., Astord, S., Robin, V., Vignaud, L., Toumi, N., Cieslik, A., Achiron, A., Carasso, R. L., Gurevich, M., Braverman, I., Blumen, N., Munich, A., Barkats, M., & Viollet, L. (2012). A rare recessive distal hereditary motor neuropathy with HSJ1 chaperone mutation. Annals of neurology, 71(4), 509–519. https://doi.org/10.1002/ana.22684

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Züchner, S., Noureddine, M., Kennerson, M., Verhoeven, K., Claeys, K., De Jonghe, P., Merory, J., Oliveira, S. A., Speer, M. C., Stenger, J. E., Walizada, G., Zhu, D., Pericak-Vance, M. A., Nicholson, G., Timmerman, V., & Vance, J. M. (2005). Mutations in the pleckstrin homology domain of dynamin 2 cause dominant intermediate Charcot-Marie-Tooth disease. Nature genetics, 37(3), 289–294. https://doi.org/10.1038/ng1514

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Klein, C. J., Botuyan, M. V., Wu, Y., Ward, C. J., Nicholson, G. A., Hammans, S., Hojo, K., Yamanishi, H., Karpf, A. R., Wallace, D. C., Simon, M., Lander, C., Boardman, L. A., Cunningham, J. M., Smith, G. E., Litchy, W. J., Boes, B., Atkinson, E. J., Middha, S., B Dyck, P. J., … Dyck, P. J. (2011). Mutations in DNMT1 cause hereditary sensory neuropathy with dementia and hearing loss. Nature genetics, 43(6), 595–600. https://doi.org/10.1038/ng.830

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Sumner, C. J., d'Ydewalle, C., Wooley, J., Fawcett, K. A., Hernandez, D., Gardiner, A. R., Kalmar, B., Baloh, R. H., Gonzalez, M., Züchner, S., Stanescu, H. C., Kleta, R., Mankodi, A., Cornblath, D. R., Boylan, K. B., Reilly, M. M., Greensmith, L., Singleton, A. B., Harms, M. B., Rossor, A. M., … Houlden, H. (2013). A dominant mutation in FBXO38 causes distal spinal muscular atrophy with calf predominance. American journal of human genetics, 93(5), 976–983. https://doi.org/10.1016/j.ajhg.2013.10.006

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Bertino, F., Firestone, K., Bellacchio, E., Jackson, K. E., Asamoah, A., Hersh, J., Fiorito, V., Destefanis, F., Gonser, R., Tucker, M. E., Altruda, F., Tolosano, E., & Chiabrando, D. (2019). Heme and sensory neuropathy: insights from novel mutations in the heme exporter feline leukemia virus subgroup C receptor 1. Pain, 160(12), 2766–2775. https://doi.org/10.1097/j.pain.0000000000001675

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Bomont, P., Cavalier, L., Blondeau, F., Ben Hamida, C., Belal, S., Tazir, M., Demir, E., Topaloglu, H., Korinthenberg, R., Tüysüz, B., Landrieu, P., Hentati, F., & Koenig, M. (2000). The gene encoding gigaxonin, a new member of the cytoskeletal BTB/kelch repeat family, is mutated in giant axonal neuropathy. Nature genetics, 26(3), 370–374. https://doi.org/10.1038/81701

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Antonellis, A., Ellsworth, R. E., Sambuughin, N., Puls, I., Abel, A., Lee-Lin, S. Q., Jordanova, A., Kremensky, I., Christodoulou, K., Middleton, L. T., Sivakumar, K., Ionasescu, V., Funalot, B., Vance, J. M., Goldfarb, L. G., Fischbeck, K. H., & Green, E. D. (2003). Glycyl tRNA synthetase mutations in Charcot-Marie-Tooth disease type 2D and distal spinal muscular atrophy type V. American journal of human genetics, 72(5), 1293–1299. https://doi.org/10.1086/375039

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Baxter, R. V., Ben Othmane, K., Rochelle, J. M., Stajich, J. E., Hulette, C., Dew-Knight, S., Hentati, F., Ben Hamida, M., Bel, S., Stenger, J. E., Gilbert, J. R., Pericak-Vance, M. A., & Vance, J. M. (2002). Ganglioside-induced differentiation-associated protein-1 is mutant in Charcot-Marie-Tooth disease type 4A/8q21. Nature genetics, 30(1), 21–22. https://doi.org/10.1038/ng796

GDAP1-CMTRIA – GNB4

GDAP1 – CMTRIA (March 1, 2003)
Senderek, J., Bergmann, C., Ramaekers, V. T., Nelis, E., Bernert, G., Makowski, A., Züchner, S., De Jonghe, P., Rudnik-Schöneborn, S., Zerres, K., & Schröder, J. M. (2003). Mutations in the ganglioside-induced differentiation-associated protein-1 (GDAP1) gene in intermediate type autosomal recessive Charcot-Marie-Tooth neuropathy. Brain : a journal of neurology, 126(Pt 3), 642–649. https://doi.org/10.1093/brain/awg068

GDAP1 – CMT2B3 (March 8, 2007)
Bouhouche, A., Birouk, N., Azzedine, H., Benomar, A., Durosier, G., Ente, D., Muriel, M. P., Ruberg, M., Slassi, I., Yahyaoui, M., Dubourg, O., Ouazzani, R., & LeGuern, E. (2007). Autosomal recessive axonal Charcot-Marie-Tooth disease (ARCMT2): phenotype-genotype correlations in 13 Moroccan families. Brain : a journal of neurology, 130(Pt 4), 1062–1075. https://doi.org/10.1093/brain/awm014
"Recessive mutations in GDAP1 cause AR-CMT2C/CMT2B3, although this has yet to be officially recognized in OMIM (and given a number)." (Inherited Neuropathies Consortium, CMT In-Depth, AR-CMT2: Autosomal Recessive 2021).

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Xin, B., Puffenberger, E., Nye, L., Wiznitzer, M., & Wang, H. (2008). A novel mutation in the GDAP1 gene is associated with autosomal recessive Charcot-Marie-Tooth disease in an Amish family. Clinical genetics, 74(3), 274–278. https://doi.org/10.1111/j.1399-0004.2008.01018.x

GDAP1 – CMT2K (Dominant) (August 3, 2010)
Crimella, C., Tonelli, A., Airoldi, G., Baschirotto, C., D'Angelo, M. G., Bonato, S., Losito, L., Trabacca, A., Bresolin, N., & Bassi, M. T. (2010). The GST domain of GDAP1 is a frequent target of mutations in the dominant form of axonal Charcot Marie Tooth type 2K. *Journal of medical genetics*, *47*(10), 712–716. https://doi.org/10.1136/jmg.2010.077909

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Brewer, M. H., Chaudhry, R., Qi, J., Kidambi, A., Drew, A. P., Menezes, M. P., Ryan, M. M., Farrar, M. A., Mowat, D., Subramanian, G. M., Young, H. K., Züchner, S., Reddel, S. W., Nicholson, G. A., & Kennerson, M. L. (2016). Whole Genome Sequencing Identifies a 78 kb Insertion from Chromosome 8 as the Cause of Charcot-Marie-Tooth Neuropathy CMTX3. PLoS genetics, 12(7), e1006177. https://doi.org/10.1371/journal.pgen.1006177

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GNB4 – CMTDIF (March 7, 2013)
Soong, B. W., Huang, Y. H., Tsai, P. C., Huang, C. C., Pan, H. C., Lu, Y. C., Chien, H. J., Liu, T. T., Chang, M. H., Lin, K. P., Tu, P. H., Kao, L. S., & Lee, Y. C. (2013). Exome sequencing identifies GNB4 mutations as a cause of dominant intermediate Charcot-Marie-Tooth disease. American journal of human genetics, 92(3), 422–430. https://doi.org/10.1016/j.ajhg.2013.01.014

HADHB – HSPB1

HADHB – HANDHB-CMT (Dec 5, 2013)
Hong, Y. B., Lee, J. H., Park, J. M., Choi, Y. R., Hyun, Y. S., Yoon, B. R., Yoo, J. H., Koo, H., Jung, S. C., Chung, K. W., & Choi, B. O. (2013). A compound heterozygous mutation in HADHB gene causes an axonal Charcot-Marie-tooth disease. BMC medical genetics, 14, 125. https://doi.org/10.1186/1471-2350-14-125

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Safka Brozkova, D., Deconinck, T., Griffin, L. B., Ferbert, A., Haberlova, J., Mazanec, R., Lassuthova, P., Roth, C., Pilunthanakul, T., Rautenstrauss, B., Janecke, A. R., Zavadakova, P., Chrast, R., Rivolta, C., Züchner, S., Antonellis, A., Beg, A. A., De Jonghe, P., Senderek, J., Seeman, P., … Baets, J. (2015). Loss of function mutations in HARS cause a spectrum of inherited peripheral neuropathies. Brain : a journal of neurology, 138(Pt 8), 2161–2172. https://doi.org/10.1093/brain/awv158

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Zimoń, M., Baets, J., Almeida-Souza, L., De Vriendt, E., Nikodinovic, J., Parman, Y., Battaloğlu, E., Matur, Z., Guergueltcheva, V., Tournev, I., Auer-Grumbach, M., De Rijk, P., Petersen, B. S., Müller, T., Fransen, E., Van Damme, P., Löscher, W. N., Barišić, N., Mitrovic, Z., Previtali, S. C., … Jordanova, A. (2012). Loss-of-function mutations in HINT1 cause axonal neuropathy with neuromyotonia. Nature genetics, 44(10), 1080–1083. https://doi.org/10.1038/ng.2406

HK1 – CMT4G (June 17, 2009)
Hantke, J., Chandler, D., King, R., Wanders, R. J., Angelicheva, D., Tournev, I., McNamara, E., Kwa, M., Guergueltcheva, V., Kaneva, R., Baas, F., & Kalaydjieva, L. (2009). A mutation in an alternative untranslated exon of hexokinase 1 associated with hereditary motor and sensory neuropathy -- Russe (HMSNR). European journal of human genetics : EJHG, 17(12), 1606–1614. https://doi.org/10.1038/ejhg.2009.99

HSPB1 – CMT2F (May 2, 2004)
Evgrafov, O. V., Mersiyanova, I., Irobi, J., Van Den Bosch, L., Dierick, I., Leung, C. L., Schagina, O., Verpoorten, N., Van Impe, K., Fedotov, V., Dadali, E., Auer-Grumbach, M., Windpassinger, C., Wagner, K., Mitrovic, Z., Hilton-Jones, D., Talbot, K., Martin, J. J., Vasserman, N., Tverskaya, S., … Timmerman, V. (2004). Mutant small heat-shock protein 27 causes axonal Charcot-Marie-Tooth disease and distal hereditary motor neuropathy. Nature genetics, 36(6), 602–606. https://doi.org/10.1038/ng1354

HSPB1 – dHMN2B (May 2, 2004)
Evgrafov, O. V., Mersiyanova, I., Irobi, J., Van Den Bosch, L., Dierick, I., Leung, C. L., Schagina, O., Verpoorten, N., Van Impe, K., Fedotov, V., Dadali, E., Auer-Grumbach, M., Windpassinger, C., Wagner, K., Mitrovic, Z., Hilton-Jones, D., Talbot, K., Martin, J. J., Vasserman, N., Tverskaya, S., … Timmerman, V. (2004). Mutant small heat-shock protein 27 causes axonal Charcot-Marie-Tooth disease and distal hereditary motor neuropathy. Nature genetics, 36(6), 602–606. https://doi.org/10.1038/ng1354

HSPB3 – INF2

HSPB3 – dHMN2C (February 9, 2010)
Kolb, S. J., Snyder, P. J., Poi, E. J., Renard, E. A., Bartlett, A., Gu, S., Sutton, S., Arnold, W. D., Freimer, M. L., Lawson, V. H., Kissel, J. T., & Prior, T. W. (2010). Mutant small heat shock protein B3 causes motor neuropathy: utility of a candidate gene approach. Neurology, 74(6), 502–506. https://doi.org/10.1212/WNL.0b013e3181cef84a

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Irobi, J., Van Impe, K., Seeman, P., Jordanova, A., Dierick, I., Verpoorten, N., Michalik, A., De Vriendt, E., Jacobs, A., Van Gerwen, V., Vennekens, K., Mazanec, R., Tournev, I., Hilton-Jones, D., Talbot, K., Kremensky, I., Van Den Bosch, L., Robberecht, W., Van Vandekerckhove, J., Van Broeckhoven, C., … Timmerman, V. (2004). Hot-spot residue in small heat-shock protein 22 causes distal motor neuropathy. Nature genetics, 36(6), 597–601. https://doi.org/10.1038/ng1328

HSPB8 – CMT2L (February 1, 2005)
Tang, B. S., Zhao, G. H., Luo, W., Xia, K., Cai, F., Pan, Q., Zhang, R. X., Zhang, F. F., Liu, X. M., Chen, B., Zhang, C., Shen, L., Jiang, H., Long, Z. G., & Dai, H. P. (2005). Small heat-shock protein 22 mutated in autosomal dominant Charcot-Marie-Tooth disease type 2L. Human genetics, 116(3), 222–224. https://doi.org/10.1007/s00439-004-1218-3

IGHMBP2 – dHMN6 (August 13, 2001)
Grohmann, K., Schuelke, M., Diers, A., Hoffmann, K., Lucke, B., Adams, C., Bertini, E., Leonhardt-Horti, H., Muntoni, F., Ouvrier, R., Pfeufer, A., Rossi, R., Van Maldergem, L., Wilmshurst, J. M., Wienker, T. F., Sendtner, M., Rudnik-Schöneborn, S., Zerres, K., & Hübner, C. (2001). Mutations in the gene encoding immunoglobulin mu-binding protein 2 cause spinal muscular atrophy with respiratory distress type 1. Nature genetics, 29(1), 75–77. https://doi.org/10.1038/ng703

IGHMBP2 – CMT2S (November 6, 2014)
Cottenie, E., Kochanski, A., Jordanova, A., Bansagi, B., Zimon, M., Horga, A., Jaunmuktane, Z., Saveri, P., Rasic, V. M., Baets, J., Bartsakoulia, M., Ploski, R., Teterycz, P., Nikolic, M., Quinlivan, R., Laura, M., Sweeney, M. G., Taroni, F., Lunn, M. P., Moroni, I., … Houlden, H. (2014). Truncating and missense mutations in IGHMBP2 cause Charcot-Marie Tooth disease type 2. American journal of human genetics, 95(5), 590–601. https://doi.org/10.1016/j.ajhg.2014.10.002

INF2 – CMTDIE (December 22, 2011)
Boyer, O., Nevo, F., Plaisier, E., Funalot, B., Gribouval, O., Benoit, G., Huynh Cong, E., Arrondel, C., Tête, M. J., Montjean, R., Richard, L., Karras, A., Pouteil-Noble, C., Balafrej, L., Bonnardeaux, A., Canaud, G., Charasse, C., Dantal, J., Deschenes, G., Deteix, P., … Mollet, G. (2011). INF2 mutations in Charcot-Marie-Tooth disease with glomerulopathy. The New England journal of medicine, 365(25), 2377–2388. https://doi.org/10.1056/NEJMoa1109122

KARS1 – LRSAM1-CMT2P (Recessive)

KARS1 – CMTRIB (October 8, 2010)
McLaughlin, H. M., Sakaguchi, R., Liu, C., Igarashi, T., Pehlivan, D., Chu, K., Iyer, R., Cruz, P., Cherukuri, P. F., Hansen, N. F., Mullikin, J. C., NISC Comparative Sequencing Program, Biesecker, L. G., Wilson, T. E., Ionasescu, V., Nicholson, G., Searby, C., Talbot, K., Vance, J. M., Züchner, S., … Antonellis, A. (2010). Compound heterozygosity for loss-of-function lysyl-tRNA synthetase mutations in a patient with peripheral neuropathy. American journal of human genetics, 87(4), 560–566. https://doi.org/10.1016/j.ajhg.2010.09.008

KIF1A – HSN2C (August 4, 2011)
Rivière, J. B., Ramalingam, S., Lavastre, V., Shekarabi, M., Holbert, S., Lafontaine, J., Srour, M., Merner, N., Rochefort, D., Hince, P., Gaudet, R., Mes-Masson, A. M., Baets, J., Houlden, H., Brais, B., Nicholson, G. A., Van Esch, H., Nafissi, S., De Jonghe, P., Reilly, M. M., … Rouleau, G. A. (2011). KIF1A, an axonal transporter of synaptic vesicles, is mutated in hereditary sensory and autonomic neuropathy type 2. American journal of human genetics, 89(2), 219–230. https://doi.org/10.1016/j.ajhg.2011.06.013

KIF1B – CMT2A/CMT2A1 (June 1, 2001)
Zhao, C., Takita, J., Tanaka, Y., Setou, M., Nakagawa, T., Takeda, S., Yang, H. W., Terada, S., Nakata, T., Takei, Y., Saito, M., Tsuji, S., Hayashi, Y., & Hirokawa, N. (2001). Charcot-Marie-Tooth disease type 2A caused by mutation in a microtubule motor KIF1Bbeta. *Cell*, *105*(5), 587–597. https://doi.org/10.1016/s0092-8674(01)00363-4 [*Archaic for CMT2A. See: Mutations in the mitochondrial GTPase mitofusin 2 cause Charcot-Marie-Tooth neuropathy type 2A.* (Züchner 2004)]

KIF5A – KIF5A-CMT (October 10, 2018)
Nam, D. E., Yoo, D. H., Choi, S. S., Choi, B. O., & Chung, K. W. (2018). Wide phenotypic spectrum in axonal Charcot-Marie-Tooth neuropathy type 2 patients with KIF5A mutations. Genes & genomics, 40(1), 77–84. https://doi.org/10.1007/s13258-017-0612-x

LITAF – CMT1C (January 14, 2003)
Street, V. A., Bennett, C. L., Goldy, J. D., Shirk, A. J., Kleopa, K. A., Tempel, B. L., Lipe, H. P., Scherer, S. S., Bird, T. D., & Chance, P. F. (2003). Mutation of a putative protein degradation gene LITAF/SIMPLE in Charcot-Marie-Tooth disease 1C. Neurology, 60(1), 22–26. https://doi.org/10.1212/wnl.60.1.22

LMNA – CMT2B1 (March 1, 2002)
De Sandre-Giovannoli, A., Chaouch, M., Kozlov, S., Vallat, J. M., Tazir, M., Kassouri, N., Szepetowski, P., Hammadouche, T., Vandenberghe, A., Stewart, C. L., Grid, D., & Lévy, N. (2002). Homozygous defects in LMNA, encoding lamin A/C nuclear-envelope proteins, cause autosomal recessive axonal neuropathy in human (Charcot-Marie-Tooth disorder type 2) and mouse. American journal of human genetics, 70(3), 726–736. https://doi.org/10.1086/339274

LRSAM1 – CMT2P (Recessive) (August 26, 2010)
Guernsey, D. L., Jiang, H., Bedard, K., Evans, S. C., Ferguson, M., Matsuoka, M., Macgillivray, C., Nightingale, M., Perry, S., Rideout, A. L., Orr, A., Ludman, M., Skidmore, D. L., Benstead, T., & Samuels, M. E. (2010). Mutation in the gene encoding ubiquitin ligase LRSAM1 in patients with Charcot-Marie-Tooth disease. PLoS genetics, 6(8), e1001081. https://doi.org/10.1371/journal.pgen.1001081

LRSAM1-CMT2P (Dominant) – MFN2-HMSN6A

LRSAM1 – CMT2P (Dominant) (January 15, 2012)
Weterman, M. A., Sorrentino, V., Kasher, P. R., Jakobs, M. E., van Engelen, B. G., Fluiter, K., de Wissel, M. B., Sizarov, A., Nürnberg, G., Nürnberg, P., Zelcer, N., Schelhaas, H. J., & Baas, F. (2012). A frameshift mutation in LRSAM1 is responsible for a dominant hereditary polyneuropathy. Human molecular genetics, 21(2), 358–370. https://doi.org/10.1093/hmg/ddr471

MARS1 – CMT2U (June 1, 2013)
Gonzalez, M., McLaughlin, H., Houlden, H., Guo, M., Yo-Tsen, L., Hadjivassilious, M., Speziani, F., Yang, X. L., Antonellis, A., Reilly, M. M., Züchner, S., & Inherited Neuropathy Consortium (2013). Exome sequencing identifies a significant variant in methionyl-tRNA synthetase (MARS) in a family with late-onset CMT2. Journal of neurology, neurosurgery, and psychiatry, 84(11), 1247–1249. https://doi.org/10.1136/jnnp-2013-305049

MCM3AP – MCM3AP-CMT (June 19, 2017)
Ylikallio, E., Woldegebriel, R., Tumiati, M., Isohanni, P., Ryan, M. M., Stark, Z., Walsh, M., Sawyer, S. L., Bell, K. M., Oshlack, A., Lockhart, P. J., Shcherbii, M., Estrada-Cuzcano, A., Atkinson, D., Hartley, T., Tetreault, M., Cuppen, I., van der Pol, W. L., Candayan, A., Battaloglu, E., … Tyynismaa, H. (2017). MCM3AP in recessive Charcot-Marie-Tooth neuropathy and mild intellectual disability. Brain : a journal of neurology, 140(8), 2093–2103. https://doi.org/10.1093/brain/awx138

MED25 – CMT2B2 (March 17, 2009)
Leal, A., Huehne, K., Bauer, F., Sticht, H., Berger, P., Suter, U., Morera, B., Del Valle, G., Lupski, J. R., Ekici, A., Pasutto, F., Endele, S., Barrantes, R., Berghoff, C., Berghoff, M., Neundörfer, B., Heuss, D., Dorn, T., Young, P., Santolin, L., … Rautenstrauss, B. (2009). Identification of the variant Ala335Val of MED25 as responsible for CMT2B2: molecular data, functional studies of the SH3 recognition motif and correlation between wild-type MED25 and PMP22 RNA levels in CMT1A animal models. *Neurogenetics*, *10*(4), 375–376. https://doi.org/10.1007/s10048-009-0213-1 [*Archaic for CMT2B2. See: The polynucleotide kinase 3'-phosphatase gene (PNKP) is involved in Charcot-Marie-Tooth disease (CMT2B2) previously related to MED25.* (A. B.-L. Leal 2018)]

MFN2 – CMT2A (April 4, 2004) [*Archaic CMT2A2A*] [*Archaic KIF1B associated cause (Züchner et al. 2004*)] Züchner, S., Mersiyanova, I. V., Muglia, M., Bissar-Tadmouri, N., Rochelle, J., Dadali, E. L., Zappia, M., Nelis, E., Patitucci, A., Senderek, J., Parman, Y., Evgrafov, O., Jonghe, P. D., Takahashi, Y., Tsuji, S., Pericak-Vance, M. A., Quattrone, A., Battaloglu, E., Polyakov, A. V., Timmerman, V., … Vance, J. M. (2004). Mutations in the mitochondrial GTPase mitofusin 2 cause Charcot-Marie-Tooth neuropathy type 2A. Nature genetics, 36(5), 449–451. https://doi.org/10.1038/ng1341 [*Correction of* (Zhao 2001) *KIF1B associated CMT2A*]

MFN2 – HMSN6A (January 25, 2006)
Züchner, S., De Jonghe, P., Jordanova, A., Claeys, K. G., Guergueltcheva, V., Cherninkova, S., Hamilton, S. R., Van Stavern, G., Krajewski, K. M., Stajich, J., Tournev, I., Verhoeven, K., Langerhorst, C. T., de Visser, M., Baas, F., Bird, T., Timmerman, V., Shy, M., & Vance, J. M. (2006). Axonal neuropathy with optic atrophy is caused by mutations in mitofusin 2. Annals of neurology, 59(2), 276–281. https://doi.org/10.1002/ana.20797

MFN2-CMT2B4 – MPZ-CMT1B

MFN2 – CMT2B4 (May 5, 2008)
Nicholson, G. A., Magdelaine, C., Zhu, D., Grew, S., Ryan, M. M., Sturtz, F., Vallat, J. M., & Ouvrier, R. A. (2008). Severe early-onset axonal neuropathy with homozygous and compound heterozygous MFN2 mutations. Neurology, 70(19), 1678–1681. https://doi.org/10.1212/01.wnl.0000311275.89032.22

MFN2 – CMT2A2B (June 29, 2011)
Polke, J. M., Laurá, M., Pareyson, D., Taroni, F., Milani, M., Bergamin, G., Gibbons, V. S., Houlden, H., Chamley, S. C., Blake, J., Devile, C., Sandford, R., Sweeney, M. G., Davis, M. B., & Reilly, M. M. (2011). Recessive axonal Charcot-Marie-Tooth disease due to compound heterozygous mitofusin 2 mutations. Neurology, 77(2), 168–173. https://doi.org/10.1212/WNL.0b013e3182242d4d

MME – CMT2T (Autosomal Recessive) (April 8,2016)
Higuchi, Y., Hashiguchi, A., Yuan, J., Yoshimura, A., Mitsui, J., Ishiura, H., Tanaka, M., Ishihara, S., Tanabe, H., Nozuma, S., Okamoto, Y., Matsuura, E., Ohkubo, R., Inamizu, S., Shiraishi, W., Yamasaki, R., Ohyagi, Y., Kira, J., Oya, Y., Yabe, H., … Takashima, H. (2016). Mutations in MME cause an autosomal-recessive Charcot-Marie-Tooth disease type 2. Annals of neurology, 79(4), 659–672. https://doi.org/10.1002/ana.24612

MME – CMT2T (Autosomal Dominant) (September 1, 2016)
Auer-Grumbach, M., Toegel, S., Schabhüttl, M., Weinmann, D., Chiari, C., Bennett, D., Beetz, C., Klein, D., Andersen, P. M., Böhme, I., Fink-Puches, R., Gonzalez, M., Harms, M. B., Motley, W., Reilly, M. M., Renner, W., Rudnik-Schöneborn, S., Schlotter-Weigel, B., Themistocleous, A. C., Weishaupt, J. H., … Senderek, J. (2016). Rare Variants in MME, Encoding Metalloprotease Neprilysin, Are Linked to Late-Onset Autosomal-Dominant Axonal Polyneuropathies. American journal of human genetics, 99(3), 607–623. https://doi.org/10.1016/j.ajhg.2016.07.008

MORC2 – CMT2Z (March 10, 2016)
Albulym, O. M., Kennerson, M. L., Harms, M. B., Drew, A. P., Siddell, A. H., Auer-Grumbach, M., Pestronk, A., Connolly, A., Baloh, R. H., Züchner, S., Reddel, S. W., & Nicholson, G. A. (2016). MORC2 mutations cause axonal Charcot-Marie-Tooth disease with pyramidal signs. Annals of neurology, 79(3), 419–427. https://doi.org/10.1002/ana.24575

MPV17-CMT2EE (January 3, 2019)
Baumann, M., Schreiber, H., Schlotter-Weigel, B., Löscher, W. N., Stucka, R., Karall, D., Strom, T. M., Bauer, P., Krabichler, B., Fauth, C., Glaeser, D., & Senderek, J. (2019). MPV17 mutations in juvenile- and adult-onset axonal sensorimotor polyneuropathy. Clinical genetics, 95(1), 182–186. https://doi.org/10.1111/cge.13462

MPZ – CMT1B (September 1, 1993)
Hayasaka, K., Himoro, M., Sato, W., Takada, G., Uyemura, K., Shimizu, N., Bird, T.D., Conneally, P.M., and Chance, P.F. (1993). Charcot-Marie-Tooth neuropathy type 1B is associated with mutations of the myelin P0 gene. Nat Genet 5, 31-34. https://doi.org/10.1038/ng0993-31

MPZ-CMT2I – NDRG1

MPZ – CMT2I (May 1, 1998)
Marrosu, M. G., Vaccargiu, S., Marrosu, G., Vannelli, A., Cianchetti, C., & Muntoni, F. (1998). Charcot-Marie-Tooth disease type 2 associated with mutation of the myelin protein zero gene. Neurology, 50(5), 1397–1401. https://doi.org/10.1212/wnl.50.5.1397

MPZ – CMTDID (August 1, 1999)
Mastaglia, F. L., Nowak, K. J., Stell, R., Phillips, B. A., Edmondston, J. E., Dorosz, S. M., Wilton, S. D., Hallmayer, J., Kakulas, B. A., & Laing, N. G. (1999). Novel mutation in the myelin protein zero gene in a family with intermediate hereditary motor and sensory neuropathy. Journal of neurology, neurosurgery, and psychiatry, 67(2), 174–179. https://doi.org/10.1136/jnnp.67.2.174

MPZ – CMT2J (December 1, 2000)
Misu, K., Yoshihara, T., Shikama, Y., Awaki, E., Yamamoto, M., Hattori, N., Hirayama, M., Takegami, T., Nakashima, K., & Sobue, G. (2000). An axonal form of Charcot-Marie-Tooth disease showing distinctive features in association with mutations in the peripheral myelin protein zero gene (Thr124Met or Asp75Val). Journal of neurology, neurosurgery, and psychiatry, 69(6), 806–811. https://doi.org/10.1136/jnnp.69.6.806

MTMR2 – CMT4B1 (May 1, 2000)
Bolino, A., Muglia, M., Conforti, F. L., LeGuern, E., Salih, M. A., Georgiou, D. M., Christodoulou, K., Hausmanowa-Petrusewicz, I., Mandich, P., Schenone, A., Gambardella, A., Bono, F., Quattrone, A., Devoto, M., & Monaco, A. P. (2000). Charcot-Marie-Tooth type 4B is caused by mutations in the gene encoding myotubularin-related protein-2. Nature genetics, 25(1), 17–19. https://doi.org/10.1038/75542

MYH14 – MYH14-dHMN (July 16, 2017)
Iyadurai, S., Arnold, W. D., Kissel, J. T., Ruhno, C., Mcgovern, V. L., Snyder, P. J., Prior, T. W., Roggenbuck, J., Burghes, A. H., & Kolb, S. J. (2017). Variable phenotypic expression and onset in MYH14 distal hereditary motor neuropathy phenotype in a large, multigenerational North American family. Muscle & nerve, 56(2), 341–345. https://doi.org/10.1002/mus.25491

NAGLU – CMT2V (March 27, 2015)
Tétreault, M., Gonzalez, M., Dicaire, M. J., Allard, P., Gehring, K., Leblanc, D., Leclerc, N., Schondorf, R., Mathieu, J., Züchner, S., & Brais, B. (2015). Adult-onset painful axonal polyneuropathy caused by a dominant NAGLU mutation. Brain : a journal of neurology, 138(Pt 6), 1477–1483. https://doi.org/10.1093/brain/awv074

NDRG1 – CMT4D (July 1, 2000)
Kalaydjieva, L., Gresham, D., Gooding, R., Heather, L., Baas, F., de Jonge, R., Blechschmidt, K., Angelicheva, D., Chandler, D., Worsley, P., Rosenthal, A., King, R. H., & Thomas, P. K. (2000). N-myc downstream-regulated gene 1 is mutated in hereditary motor and sensory neuropathy-Lom. American journal of human genetics, 67(1), 47–58. https://doi.org/10.1086/302978

NEFH – CMT2CC (April 7, 2016)
Rebelo, A. P., Abrams, A. J., Cottenie, E., Horga, A., Gonzalez, M., Bis, D. M., Sanchez-Mejias, A., Pinto, M., Buglo, E., Markel, K., Prince, J., Laura, M., Houlden, H., Blake, J., Woodward, C., Sweeney, M. G., Holton, J. L., Hanna, M., Dallman, J. E., Auer-Grumbach, M., … Züchner, S. (2016). Cryptic Amyloidogenic Elements in the 3' UTRs of Neurofilament Genes Trigger Axonal Neuropathy. American journal of human genetics, 98(4), 597–614. https://doi.org/10.1016/j.ajhg.2016.02.022

NEFL – CMT2E (July 1, 2000)
Mersiyanova, I. V., Perepelov, A. V., Polyakov, A. V., Sitnikov, V. F., Dadali, E. L., Oparin, R. B., Petrin, A. N., & Evgrafov, O. V. (2000). A new variant of Charcot-Marie-Tooth disease type 2 is probably the result of a mutation in the neurofilament-light gene. American journal of human genetics, 67(1), 37–46. https://doi.org/10.1086/302962

NEFL – CMT1F (March 3, 2003)
Jordanova, A., De Jonghe, P., Boerkoel, C. F., Takashima, H., De Vriendt, E., Ceuterick, C., Martin, J. J., Butler, I. J., Mancias, P., Papasozomenos, S., Terespolsky, D., Potocki, L., Brown, C. W., Shy, M., Rita, D. A., Tournev, I., Kremensky, I., Lupski, J. R., & Timmerman, V. (2003). Mutations in the neurofilament light chain gene (NEFL) cause early onset severe Charcot-Marie-Tooth disease. Brain : a journal of neurology, 126(Pt 3), 590–597. https://doi.org/10.1093/brain/awg059

NEFL – CMTDIG (February 1, 2004)
Züchner, S., Vorgerd, M., Sindern, E., & Schröder, J. M. (2004). The novel neurofilament light (NEFL) mutation Glu397Lys is associated with a clinically and morphologically heterogeneous type of Charcot-Marie-Tooth neuropathy. Neuromuscular disorders : NMD, 14(2), 147–157. https://doi.org/10.1016/j.nmd.2003.10.003

NEFL – CMT2B5 (April 13, 2009)
Yum, S. W., Zhang, J., Mo, K., Li, J., & Scherer, S. S. (2009). A novel recessive Nefl mutation causes a severe, early-onset axonal neuropathy. Annals of neurology, 66(6), 759–770. https://doi.org/10.1002/ana.21728

NGF – HSAN5 (February 4, 2004)
Einarsdottir, E., Carlsson, A., Minde, J., Toolanen, G., Svensson, O., Solders, G., Holmgren, G., Holmberg, D., & Holmberg, M. (2004). A mutation in the nerve growth factor beta gene (NGFB) causes loss of pain perception. Human molecular genetics, 13(8), 799–805. https://doi.org/10.1093/hmg/ddh096

NTRK1 – HSAN4 (August 1, 1996)
Indo, Y., Tsuruta, M., Hayashida, Y., Karim, M. A., Ohta, K., Kawano, T., Mitsubuchi, H., Tonoki, H., Awaya, Y., & Matsuda, I. (1996). Mutations in the TRKA/NGF receptor gene in patients with congenital insensitivity to pain with anhidrosis. Nature genetics, 13(4), 485–488. https://doi.org/10.1038/ng0896-485

PDK3 – PMP22-HNPP

PDK3 – CMTX6 (April 1, 2013)
Kennerson, M. L., Yiu, E. M., Chuang, D. T., Kidambi, A., Tso, S. C., Ly, C., Chaudhry, R., Drew, A. P., Rance, G., Delatycki, M. B., Züchner, S., Ryan, M. M., & Nicholson, G. A. (2013). A new locus for X-linked dominant Charcot-Marie-Tooth disease (CMTX6) is caused by mutations in the pyruvate dehydrogenase kinase isoenzyme 3 (PDK3) gene. Human molecular genetics, 22(7), 1404–1416. https://doi.org/10.1093/hmg/dds557

PDXK – HMSN-6C (July 11, 2019)
Chelban, V., Wilson, M. P., Warman Chardon, J., Vandrovcova, J., Zanetti, M. N., Zamba-Papanicolaou, E., Efthymiou, S., Pope, S., Conte, M. R., Abis, G., Liu, Y. T., Tribollet, E., Haridy, N. A., Botía, J. A., Ryten, M., Nicolaou, P., Minaidou, A., Christodoulou, K., Kernohan, K. D., Eaton, A., … Care4Rare Canada Consortium and the SYNaPS Study Group (2019). PDXK mutations cause polyneuropathy responsive to pyridoxal 5'-phosphate supplementation. *Annals of neurology*, *86*(2), 225–240. https://doi.org/10.1002/ana.25524

PLEKHG5 – dSMA4 (July 1, 2007)
Maystadt, I., Rezsöhazy, R., Barkats, M., Duque, S., Vannuffel, P., Remacle, S., Lambert, B., Najimi, M., Sokal, E., Munnich, A., Viollet, L., & Verellen-Dumoulin, C. (2007). The nuclear factor kappaB-activator gene PLEKHG5 is mutated in a form of autosomal recessive lower motor neuron disease with childhood onset. American journal of human genetics, 81(1), 67–76. https://doi.org/10.1086/518900

PLEKHG5 – CMTRIC (June 17, 2013)
Azzedine, H., Zavadakova, P., Planté-Bordeneuve, V., Vaz Pato, M., Pinto, N., Bartesaghi, L., Zenker, J., Poirot, O., Bernard-Marissal, N., Arnaud Gouttenoire, E., Cartoni, R., Title, A., Venturini, G., Médard, J. J., Makowski, E., Schöls, L., Claeys, K. G., Stendel, C., Roos, A., Weis, J., … Chrast, R. (2013). PLEKHG5 deficiency leads to an intermediate form of autosomal-recessive Charcot-Marie-Tooth disease. Human molecular genetics, 22(20), 4224–4232. https://doi.org/10.1093/hmg/ddt274

PMP2 – CMT1G (June 6, 2016)
Motley, W. W., Palaima, P., Yum, S. W., Gonzalez, M. A., Tao, F., Wanschitz, J. V., Strickland, A. V., Löscher, W. N., De Vriendt, E., Koppi, S., Medne, L., Janecke, A. R., Jordanova, A., Züchner, S., & Scherer, S. S. (2016). De novo PMP2 mutations in families with type 1 Charcot-Marie-Tooth disease. Brain : a journal of neurology, 139(Pt 6), 1649–1656. https://doi.org/10.1093/brain/aww055

PMP22 – CMT1A (June 1, 1992)
Patel, P. I., Roa, B. B., Welcher, A. A., Schoener-Scott, R., Trask, B. J., Pentao, L., Snipes, G. J., Garcia, C. A., Francke, U., Shooter, E. M., Lupski, J. R., & Suter, U. (1992). The gene for the peripheral myelin protein PMP-22 is a candidate for Charcot-Marie-Tooth disease type 1A. Nature genetics, 1(3), 159–165. https://doi.org/10.1038/ng0692-159

PMP22 – HNPP (Deletion) (January 15, 1993)
Chance, P. F., Alderson, M. K., Leppig, K. A., Lensch, M. W., Matsunami, N., Smith, B., Swanson, P. D., Odelberg, S. J., Disteche, C. M., & Bird, T. D. (1993). DNA deletion associated with hereditary neuropathy with liability to pressure palsies. Cell, 72(1), 143–151. https://doi.org/10.1016/0092-8674(93)90058-x

PMP22-CMT1E – PRX

PMP22 – CMT1E (June 1, 1999)
Kovach, M. J., Lin, J. P., Boyadjiev, S., Campbell, K., Mazzeo, L., Herman, K., Rimer, L. A., Frank, W., Llewellyn, B., Jabs, E. W., Gelber, D., & Kimonis, V. E. (1999). A unique point mutation in the PMP22 gene is associated with Charcot-Marie-Tooth disease and deafness. American journal of human genetics, 64(6), 1580–1593. https://doi.org/10.1086/302420

PMP22 – HNPP (Point Mutation) (June 17, 2004)
Kleopa, K. A., Georgiou, D. M., Nicolaou, P., Koutsou, P., Papathanasiou, E., Kyriakides, T., & Christodoulou, K. (2004). A novel PMP22 mutation Ser22Phe in a family with hereditary neuropathy with liability to pressure palsies and CMT1A phenotypes. *Neurogenetics*, *5*(3), 171–175. https://doi.org/10.1007/s10048-004-0184-1

PNKP – CMT2B2 (July 24, 2018)
Leal, A., Bogantes-Ledezma, S., Ekici, A. B., Uebe, S., Thiel, C. T., Sticht, H., Berghoff, M., Berghoff, C., Morera, B., Meisterernst, M., & Reis, A. (2018). The polynucleotide kinase 3'-phosphatase gene (PNKP) is involved in Charcot-Marie-Tooth disease (CMT2B2) previously related to MED25. Neurogenetics, 19(4), 215–225. https://doi.org/10.1007/s10048-018-0555-7 [*Correction of* (A. H. Leal 2009) *MED25 associated CMT2B2.*]

POLG – POLG-CMT (March 6, 2019)
Phillips, J., Courel, S., Rebelo, A. P., Bis-Brewer, D. M., Bardakjian, T., Dankwa, L., Hamedani, A. G., Züchner, S., & Scherer, S. S. (2019). POLG mutations presenting as Charcot-Marie-Tooth disease. Journal of the peripheral nervous system : JPNS, 24(2), 213–218. https://doi.org/10.1111/jns.12313

PRDM12 – HSAN8 (May 25, 2015)
Chen, Y. C., Auer-Grumbach, M., Matsukawa, S., Zitzelsberger, M., Themistocleous, A. C., Strom, T. M., Samara, C., Moore, A. W., Cho, L. T., Young, G. T., Weiss, C., Schabhüttl, M., Stucka, R., Schmid, A. B., Parman, Y., Graul-Neumann, L., Heinritz, W., Passarge, E., Watson, R. M., Hertz, J. M., … Senderek, J. (2015). Transcriptional regulator PRDM12 is essential for human pain perception. Nature genetics, 47(7), 803–808. https://doi.org/10.1038/ng.3308

PRPS1 – CMTX5 (September 1, 2007)
Kim, H. J., Sohn, K. M., Shy, M. E., Krajewski, K. M., Hwang, M., Park, J. H., Jang, S. Y., Won, H. H., Choi, B. O., Hong, S. H., Kim, B. J., Suh, Y. L., Ki, C. S., Lee, S. Y., Kim, S. H., & Kim, J. W. (2007). Mutations in PRPS1, which encodes the phosphoribosyl pyrophosphate synthetase enzyme critical for nucleotide biosynthesis, cause hereditary peripheral neuropathy with hearing loss and optic neuropathy (cmtx5). American journal of human genetics, 81(3), 552–558. https://doi.org/10.1086/519529

PRX – CMT4F (February 15, 2001)
Guilbot, A., Williams, A., Ravisé, N., Verny, C., Brice, A., Sherman, D. L., Brophy, P. J., LeGuern, E., Delague, V., Bareil, C., Mégarbané, A., & Claustres, M. (2001). A mutation in periaxin is responsible for CMT4F, an autosomal recessive form of Charcot-Marie-Tooth disease. Human molecular genetics, 10(4), 415–421. https://doi.org/10.1093/hmg/10.4.415

PYHY – HMSN-4 Refsum Disease) [*Formerly PAHX gene OMIM Entry 602026*] (October 1, 1997)
Mihalik, S. J., Morrell, J. C., Kim, D., Sacksteder, K. A., Watkins, P. A., & Gould, S. J. (1997). Identification of PAHX, a Refsum disease gene. *Nature genetics*, *17*(2), 185–189. https://doi.org/10.1038/ng1097-185

RAB7A – CMT2B (March 1, 2003)
Verhoeven, K., De Jonghe, P., Coen, K., Verpoorten, N., Auer-Grumbach, M., Kwon, J. M., FitzPatrick, D., Schmedding, E., De Vriendt, E., Jacobs, A., Van Gerwen, V., Wagner, K., Hartung, H. P., & Timmerman, V. (2003). Mutations in the small GTP-ase late endosomal protein RAB7 cause Charcot-Marie-Tooth type 2B neuropathy. American journal of human genetics, 72(3), 722–727. https://doi.org/10.1086/367847

REEP1 – dHMN5B (July 13, 2012)
Beetz, C., Pieber, T. R., Hertel, N., Schabhüttl, M., Fischer, C., Trajanoski, S., Graf, E., Keiner, S., Kurth, I., Wieland, T., Varga, R. E., Timmerman, V., Reilly, M. M., Strom, T. M., & Auer-Grumbach, M. (2012). Exome sequencing identifies a REEP1 mutation involved in distal hereditary motor neuropathy type V. American journal of human genetics, 91(1), 139–145. https://doi.org/10.1016/j.ajhg.2012.05.007

RETREG1 – HSAN2B [*Formerly FAM134B gene OMIM Entry 613114*]
(October 18, 2009)
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Appendix E

General CMT-Associated Genes and Subtypes

By the Numbers Statistical Overview

Appendix E provides a general statistical overview of the numerical data associated with CMT-associated genes and related subtypes, including a subtype breakdown, inheritance pattern breakdown, and other relevant and useful data for CMTers and clinicians alike.

CMT-Associated Genes and Subtypes Overview	
Total CMT Associated Genes (CMTX3 is associated with a genomic rearrangement between 8q24.3 and Xq27.1, and is included in this total)	120
Additional Unknown Associated Gene, But Mapped to a Chromosomal Location	5
Genes Associated with Multiple Subtypes	20
Total Identified Subtypes	155
Autosomal Dominant Inheritance Pattern	78
Autosomal Recessive Inheritance Pattern	64
Can be Autosomal Dominant or Autosomal Recessive in Inheritance	3
X-Linked Dominant Inheritance Pattern	3
X-Linked Recessive Inheritance Pattern	6
Mitochondria DNA Inheritance	1
Subtypes Represented by the "CMT" Acronym (Includes HNPP, as HNPP is Categorized with CMT1)	71
Subtypes Represented by Other Acronyms	56
Subtypes Represented by [Gene Name]-CMT, and referred to as "[Gene Name] associated CMT"	28
Demyelinating Subtypes	27
Axonal Subtypes	112
Intermediate Subtypes	16

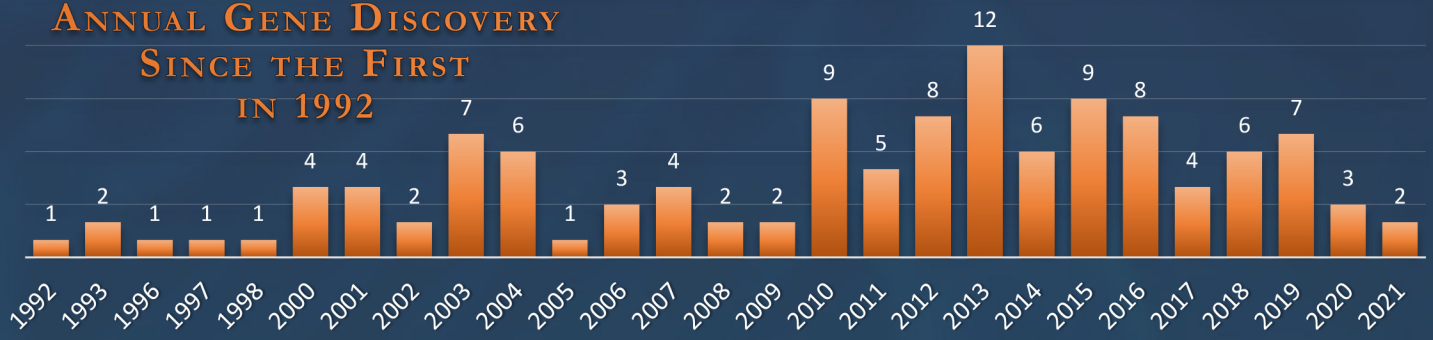
Glossary of Abbreviations	
AD	Autosomal Dominant Inheritance Pattern
AR	Autosomal Recessive Inheritance Pattern
CMT	Charcot Marie Tooth disease
dHMN	distal Hereditary Motor Neuronopathy
dSMA	distal Spinal Muscular Atrophy
GAN	Giant Axon Neuropathy
HMSN	Hereditary Motor and Sensory Neuropathy
HNPP	Hereditary Neuropathy with liability to Pressure Palsies
HSAN	Hereditary Sensory and Autonomic Neuropathy
HSN	Hereditary Sensory Neuropathy
mtDNA	Mitochondrial DNA
PHARC	Polyneuropathy, Hearing Loss, Ataxia, Retinitis Pigmentosa, and Cataracts
SCAN	Spinocerebellar Ataxia with Axonal Neuropathy
SMA	Spinal Muscular Atrophy
SMA-LEP	Spinal Muscular Atrophy - Lower Extremity- Predominant
SPG	Spastic Paraplegia
XLD	X-Linked Dominant Inheritance Pattern
XLR	X-Linked Recessive Inheritance Pattern

Genes Associated with Multiple Subtypes		
Gene	**Subtypes**	**Inheritance Pattern**
AARS1	CMT2N, AARS1-dHMN	AD
BICD2	SMA-LEP-2A, SMA-LEP-2B	AD
DNM2	CMT2M, CMTDIB	AD
DST	HSAN-6, DST-CMT	AR
DYNC1H1	CMT2O, SMA-LEP-1	AD
EGR2	CMT1D, CMT4E	AD, AR
GARS1	CMT2D, dHMN-5A	AD
GDAP1	CMT2B3, CMT2K, CMT4A, CMTRIA	AD, AR
HSPB1	CMT2F, dHMN-2B	AD
HSPB8	CMT2L, dHMN-2A	AD
IGHMBP2	CMT2S, dHMN-6	AR
MFN2	CMT2A, CMT2B4, CMT2A2B, HMSN-6A	AD, AR
MPZ	CMT1B, CMT2I, CMT2J, CMTDID	AD
NEFL	CMT1F, CMT2E, CMT2B5, CMTDIG	AD, AR
PLEKHG5	CMTRIC, dSMA4	AR
PMP22	CMT1A, HNPP, CMT1E	AD
SPTLC1	HSAN-1A, HSN-1A	AD
SPTLC2	HSAN-1C, HSN-1C	AD
TRPV4	CMT2C, dHMN-8	AD
WNK1	HSAN-2A, HSN-2A	AR

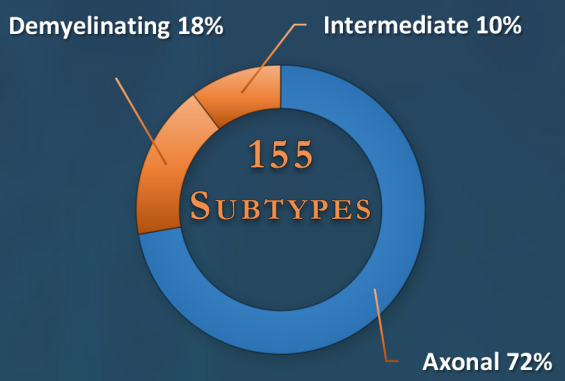
Type Categories	
Category	**Subtypes**
CMT1 (Includes HNPP)	9
CMT2	33
CMT4	12
X-Linked CMT (CMTX)	6
Dominant Intermediate (CMTDI)	7
Recessive Intermediate (CMTRI)	4
Distal Hereditary Motor Neuropathy (dHMN)	18
Distal Spinal Muscular Atrophy (dSMA)	5
Giant Axon Neuropathy (GAN)	2
Hereditary Motor and Sensory Neuropathy (HMSN)	6
Hereditary Sensory and Autonomic Neuropathy (HSAN)	12
Hereditary Sensory Neuropathy (HSN)	10
Spinal Muscular Atrophy - Lower Extremity-Predominant (SMA-LEP)	3
[Gene Name]-CMT	28
Total Subtypes	155

CMT Genes & Subtypes

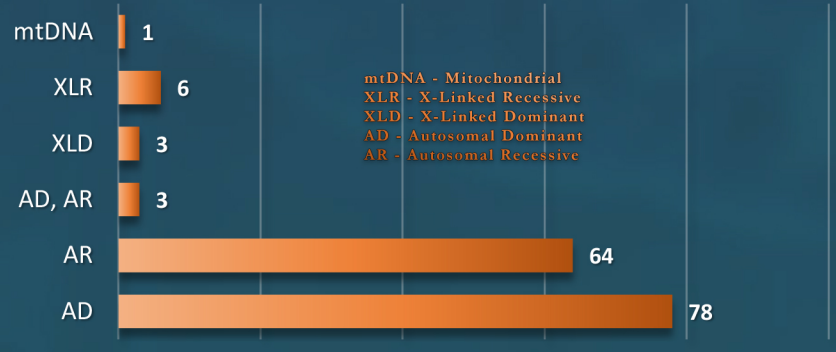
Annual Gene Discovery Since the First in 1992



14 Type Classifications



Subtypes by Inheritance



120 Associated Genes