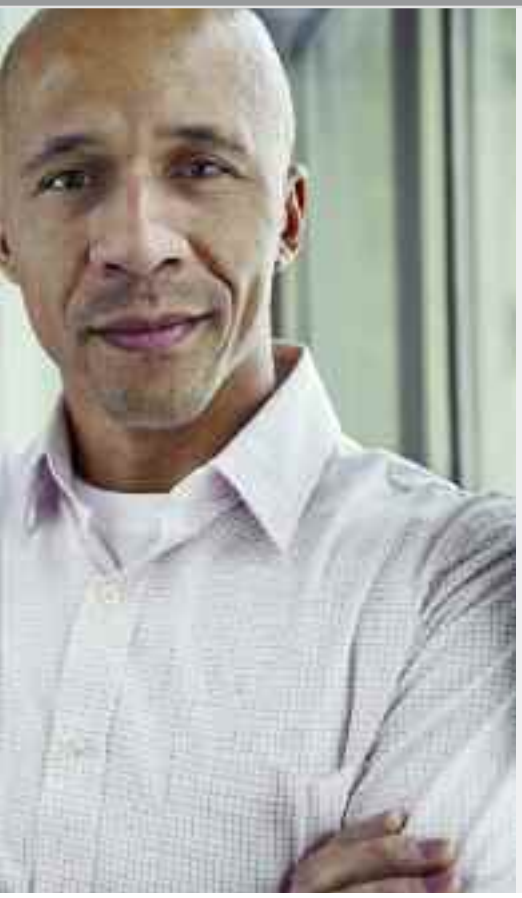
Leading genetic testing for

Charcot-Marie-Tooth (CMT) Disease



Athena Diagnostics introduces a genetic assessment that can identify up to 95% of known genetic causes of CMT.

Diagnosis and genetic counseling for patients with CMT can present a challenge for clinicians. Mutations in a number of genes can cause a similar phenotype. Conversely, mutations within a single gene can cause any number of phenotypes. Clinical trials have started for treating some types of CMT, making an accurate genetic diagnosis essential[1] to understand prognosis and identify underlying drug sensitivities. CMT is the most common inherited neuromuscular disorder, affecting 1 in 2,500 individuals.[2]

Now, a single test of four highly prevalent genes for CMT can provide valuable insight.

Scientists and geneticists at Athena Diagnostics® have recently collaborated with physician thought-leaders and a leading academic institution to confirm the four genes responsible for CMT in 94.9% of cases – *PMP22, GJB1, MPZ,* and *MFN2*.[3] This finding corresponds to earlier publications that reported the same genes accounting for over 90% of CMT.[1,4]

By combining clinical need, the latest scientific insight and leading genetic testing services, physicians can now offer their patients a more efficient path to diagnosis and appropriate management of the disease.

CMT Advanced Evaluations provide a new, streamlined diagnostic approach—one based on gene prevalence—a powerful first step in diagnosing CMT without the pain and expense associated with electromyography (EMG), nerve conduction velocity (NCV), or nerve biopsy.

CMT Advanced Evaluations from Athena Diagnostics: Testing Based on the Frequency of Gene Mutations

Initial Genetic Assessment* (*PMP22* Dup/Del, *GJB1* (Cx32), *MPZ*, *MFN2* Seq)

- **Positive** (90-95% Prevalence)
- **Negative** (5-10% Prevalence)

- EMG/NCV Findings
- Non-Prevalent NGS Evaluation

- **Nonprevalent Axonal**** (*GJB1* (Cx32) Del, *NFL, GDAP1, GARS, RAB7, HSPB1, DNM2, YARS, LMNA, TRPV4, HSPB8* Seq)
- **Nonprevalent Demyelinating**** (*GJB1* (Cx32) Del, *EGR2, LITAF, PMP22, PRX, GDAP1, DNM2, YARS, SH3TC2, MTMR2, NDRG1, FGD4, FIG4, SBF2* Seq)
- **Contraindicated, Refused, or Uninformative**** (*GJB1* (Cx32) Del, *PMP22, EGR2, LITAF, PRX, GDAP1, RAB7, GARS, NFL, HSPB1, LMNA, FIG4, SH3TC2, DNM2, YARS, FGD4, NDRG1, TRPV4, HSPB8, MTMR2, SBF2* Seq)

Notes: *Testing for the first four genes (Initial Assessment) is based on: Murphy et al[1] and DiVincenzo et al.[3]
**The second tier of testing (Nonprevalent CMT) is based on the recommendations of Saporta et al.[5]

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Genetic Testing Expertise that Goes Beyond Results

Only Athena Diagnostics has the power to fuse an unparalleled database of testing history and experience with the latest diagnostic technologies, the newest genetic discoveries, and published clinical algorithms, to provide health care providers with the very best diagnostic information available.

Athena Insight™ Variant Investigation

This powerful bioinformatic service is included with every genetic test ordered. Our variant science group collaborates to accumulate, integrate and weigh the value of information from scientific and medical literature, our own extensive database and bioinformatics experience, and *in silico* predictive algorithms to determine the likelihood of variants being benign or pathogenic. The result report is clear and concise, with a pathogenicity assessment and complete sourced synopsis that clinicians can review with patients.

A Team of Genetic Counselors

Our genetic counselors are readily available to provide in-depth information on the nature, inheritance, and implication of genetic mutations. Genetic counseling can help physicians guide their patient in making informed medical and personal decisions for themselves and their family.

Care360® EHR

The power and flexibility of this cloud-based, electronic health record system developed by Quest Diagnostics enables 24/7 access and greater efficiencies in managing lab orders and results. Care360 lets you place test orders, analyze results, save time and access to critical patient information.

Test Ordering Information for Charcot-Marie-Tooth (CMT) Advanced Evaluations

Test Code	Test Name	Specimen Volume Tube Type	Turnaround Time
4010	**CMT Advanced Evaluation – Initial Genetic Assessment** *(PMP22 Dup/Del, GJB1 (Cx32), MPZ, MFN2 Seq)*	7-10 mL whole blood Lavender (EDTA) top tube	6 weeks
4011	**CMT Advanced Evaluation – Nonprevalent Axonal** *(GJB1 (Cx32) Del, NFL, GDAP1, GARS, RAB7, HSPB1, DNM2, YARS, LMNA, TRPV4, HSPB8 Seq)*	7-10 mL whole blood Lavender (EDTA) top tube	6 weeks
4012	**CMT Advanced Evaluation – Nonprevalent Demyelinating** *(GJB1 (Cx32) Del, EGR2, LITAF, PMP22, PRX, GDAP1, DNM2, YARS SH3TC2, MTMR2, NDRG1, FGD4, FIG4, SBF2 Seq)*	7-10 mL whole blood Lavender (EDTA) top tube	6 weeks
4013	**CMT Advanced Evaluation – Nonprevalent** *(GJB1 (Cx32) Del, PMP22, EGR2, LITAF, PRX, GDAP1, RAB7, GARS NFL, HSPB1, LMNA, FIG4, SH3TC2, DNM2, YARS, FGD4, NDRG1, TRPV4, HSPB8, MTMR2, SBF2 Seq)*	7-10 mL whole blood Lavender (EDTA) top tube	6 weeks

To receive Athena Diagnostics lab updates, test launch announcements, news and information via E-Mail, please visit AthenaDiagnostics.com/update or scan this QR Code with your smartphone.

Client Services Representatives are available from 8:30am to 6:30pm Eastern Time (U.S.). Customers in the U.S. and Canada please call toll free **800-394-4493** or visit us on our website at **AthenaDiagnostics.com.**

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References: 1. Murphy SM, Laura M, Fawcett K, et al. Charcot-Marie-Tooth disease: frequency of genetic subtypes and guidelines for genetic testing. *J Neurol Neurosurg Psychiatry* 2012; 83(7): 706–710. 2. Wiszniewski W, Szigeti K, Lupski JR. Chapter 126 - Hereditary Motor and Sensory Neuropathies. In: David LR, Reed EP, Bruce KorfA2 - David L. Rimoin REP, Bruce K, eds. Emery and Rimoin's Principles and Practice of Medical Genetics (Sixth Edition). Oxford: Academic Press; 2013:1-24. 3. DiVincenzo C, Elzinga CD, Medeiros AC, et al. The Allelic Spectrum of Charcot-Marie-Tooth Disease in Over 17,000 Individuals with Neuropathy. *Molecular Genetics & Genomic Medicine* 2014; doi: 10.1002/mgg3.106. 4. Siskind CE, Panchal S, Smith CO, et al. A Review of Genetic Counseling for Charcot Marie Tooth Disease (CMT). *J Genetic Counseling* 2013;22:422-36. 5. Saporta ASD, Sottile SL, Miller LJ, Feely SME, Siskind CE, Shy ME. Charcot-Marie-Tooth (CMT) Subtypes and Genetic Testing Strategies. *Ann Neurol* 2011;69(1):22-33.

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