HEREDITARY NEUROPATHY FOUNDATION

cmtupdate

Impact That Matters

Driving CMT Research with the Patient's Voice

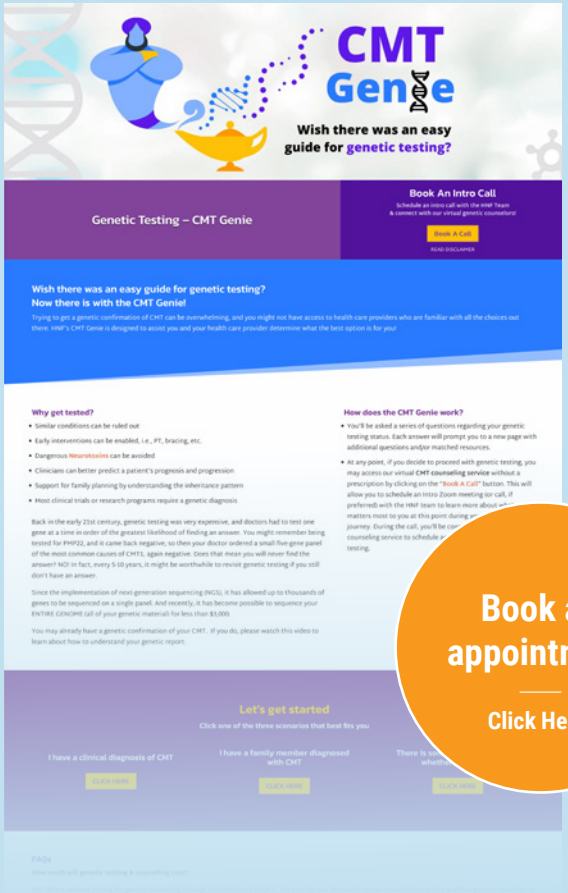
WINTER 2024

Reducing Genetic Testing Barriers

Pg 4

CMT Genie

Despite the best efforts of our CMT community providing resources to obtain genetic testing, there are still barriers that remain challenging in obtaining a definitive diagnosis. HNF has changed that by developing the CMT Genie program. We are here to support and facilitate genetic counseling and provide immediate access to information and support for in-home testing and the translation of genetic reports to patients. Whether you need to learn more about variants identified in your DNA or seek further explanation of inheritance patterns, the CMT Genie is available to all patients and families affected by CMT, and for those that suspect CMT is the cause of their symptoms.



"The process was very easy. I met with a genetic counselor and received the genetic test kit within a few days. The kit was well packaged in a small box and had everything I needed. Shortly after I shipped the kit back, I received an email to register online. Less than two weeks later, I received my test results – CMT1A, just as I suspected. The genetic counselor notified me via text and email about scheduling a follow-up appointment to go over the results."

— Carrie H.

"I got the results which were negative. I am glad I did the testing, so I now know more than I did before about genetic variants I do not have. Kind of like Thomas Edison and his search for a filament for a light bulb."

— Jeff M.

CMT UPDATE
WINTER 2024

Allison T. Moore
Founder and CEO
Hereditary Neuropathy Foundation

Happy New Year!

As we begin 2024, I find myself reflecting on our shared journey and feeling proud of how far we've come as an organization, and as a disease community. We have always been focused on our mission: to increase awareness and accurate diagnosis of Charcot-Marie-Tooth (CMT) and related inherited neuropathies, support patients and families with critical information to improve quality of life, and fund research that will lead to treatments and cures. But, the road map to get us where we are today has been filled with so many more stops along the way, passengers who have helped guide us, and destinations we had not planned on.

I guess that is what sparked our idea to develop and share "The Road to CMT Therapies" (page 7) with you. We want you to join us as we remain steadfast in our journey to heed the guidance of our TRIAD Council, collect and share the voice of the patient from the data collected in the GRIN patient and clinical registry, drive genetic testing for CMT patients by removing barriers and continuing to streamline our CMT Genie Project, and discover the important signs - outcome measures (such as a pain scale) and clinical endpoints - to support successful clinical trials with our CMT Biobank. This is the road map to successful clinical trials.

Ten years ago, we were advocating for genetic testing panels to facilitate identification of more patients with CMT for future clinical trials. Today, we not only have a whole host of genetic testing panels to choose from, but we have inked an important partnership with InformedDNA® which adds more value to our CMT Genie Project and provides a patient-initiated at-home genetic testing program, providing faster and more equitable access to critical genetic care for the CMT community and their health care providers. If you don't have a genetic confirmation of CMT, please read more about the CMT Genie (page 4) and why it has never been more critical (page 10) and book an appointment today!

All of this adds to our shared journey to bring us to where we stand today - a Phase III clinical trial wrapped up and struggling to get across the finish line, several more biotech and pharma companies announcing promising pipelines to CMT therapies, the exciting acquisition of two CMT assets by the $250 billion innovative medicine company, Novartis, and HNF's book launch, the "ABCs of CMT Pain Management Guide" (page 12). Together, we are making a difference in advancing the development of therapeutics through CMT patient community engagement and putting issues like pain on the map.

There is still so much to do to cure ALL TYPES of CMT! I hope you will value the information in this *CMT Update*, and I look forward to hearing from you with any feedback, questions, or ideas. With all of the current advancements, there is no better time to support HNF! Please consider supporting our efforts by making a donation today, contacting us to help you plan a community fundraiser, and including HNF in your estate planning. HNF is BBB Accredited and 95% of all donations directly fund CMT Research & Programs.

Warm regards,

Allison T. Moore

GLOBAL REGISTRY FOR INHERITED NEUROPATHIES

REDUCING GENETIC TESTING BARRIERS FOR THE CHARCOT-MARIE-TOOTH COMMUNITY

Hereditary Neuropathy Foundation Partners with InformedDNA® on CMT Genie Project

In partnership with InformedDNA®, the Hereditary Neuropathy Foundation (HNF) has added more value to their Charcot-Marie-Tooth (CMT) Genie Project — a patient-initiated at-home genetic testing program, providing faster and more equitable access to critical genetic care for the CMT community and their health care providers. CMT is an inherited, progressive condition that occurs when gene mutations affect all the nerves outside the brain and spinal column. Scientists have now discovered 131 CMT-related genes. Mutations in these genes cause 165 individual subtypes. The most common is CMT1A.

Since its launch in August 2022, over 300 patients have been connected to genetic testing through the CMT Genie. This new partnership is a more comprehensive approach allowing us to more efficiently connect patients with genetic counseling and genetic testing options for an increased diagnosis rate.

*"Knowing what to test for, which panel to order, and from which lab to order the test requires a level of expertise previously not widely available to the CMT community. Many commercial labs offer genetic testing for CMT, but they each test for different genes, and many have several different panels, each with different genes. No commercial lab offers testing for **all known CMT genes**. Unless a patient is within proximity to a CMT Center of Excellence, access to this expertise isn't an option. With telehealth visits with InformedDNA's genetic counselors, licensed in all 50 states, HNF now has the solution."*

–Joy Aldrich, HNF Global Registry for Inherited Neuropathies Coordinator.

"Since our inception in 2007 as the first telehealth genetic counseling company in the nation, we have remained focused on one vision: to revolutionize the application of genomic insights to enhance patient care and improve outcomes for all. With the largest team of independent genetics experts and board-certified genetic counselors on staff, we specialize in connecting rare disease patients to the information and testing they need to navigate a challenging diagnosis. We are thrilled to add HNF and their CMT patients to our genetics community."

– Megan Czarniecki, MS, MS, CGC | Chief Operating Officer, InformedDNA

The CMT community has endured a historical absence of patient education and self-advocacy resources around the importance and availability of genetic counseling, genetic testing, clinical trials, and research participation opportunities. These combine to form a significant healthcare barrier that often prevents many community members from receiving a definitive genetic diagnosis.

Additionally, due to cost-prohibitive genetic testing options, providers are hesitant to order testing for many reasons, including a perceived lack of available treatments and a shortfall of CMT genetic testing expertise, worsening the barrier to a definitive genetic diagnosis. By connecting CMT patients to proper CMT genetic testing, HNF's new partnership with InformedDNA® strengthens our commitment to eliminating barriers to genetic testing and adequate CMT care.

For more information on the CMT Genie Project (http://tinyurl.com/tpm8r74e), contact Estela Lugo at (212) 860-5405 or estela@hnf-cure.org.

About InformedDNA

Established in 2007 as the nation's pioneer telehealth Genetic Counseling company, InformedDNA has evolved into a leading tech-enabled genomic solutions provider. With a team of experienced board-certified genetics experts and proprietary logic technologies, InformedDNA offers cost and clinical management solutions including Genetic Testing Utilization Management, Genetic Counseling, Payment Integrity, and Clinical Trial support. InformedDNA partners with clients across commercial and government health plans, health systems, biopharma, and other risk-bearing organizations to optimize clinical decision-making, reduce risk and downstream costs, and ensure compliance with safety and quality standards. InformedDNA is headquartered in St. Petersburg, FL. For more information, visit www.InformedDNA.com.

2024 CMT ROAD MAP TO CLINICAL TRIALS

As we look ahead to emerging CMT clinical trials, the road map has never been clearer. At the Hereditary Neuropathy Foundation, **we understand the importance of approaching each critical step with the utmost efficiency, competency and urgency**. For any medical treatment to reach human clinical trials, there is a precise formula and path we all must follow. **This is the 4 step pathway HNF's vital initiatives are designed around…**

And this is why HNF's TRIAD, GRIN, CMT Genie, and CMT Biobank are pivotal to each and every step.

But what exactly are the 4 steps on the road to human trials?

HNF has created a new downloadable map to help simplify & visualize all 4 important steps!

(See opposite page)

VIEW, DOWNLOAD & PRINT HERE!

http://tinyurl.com/mv8yxcw3

VIEW VIDEOS HERE

www.hnf-cure.org/our-impact/clinical-trials

Support CMT impact that matters!

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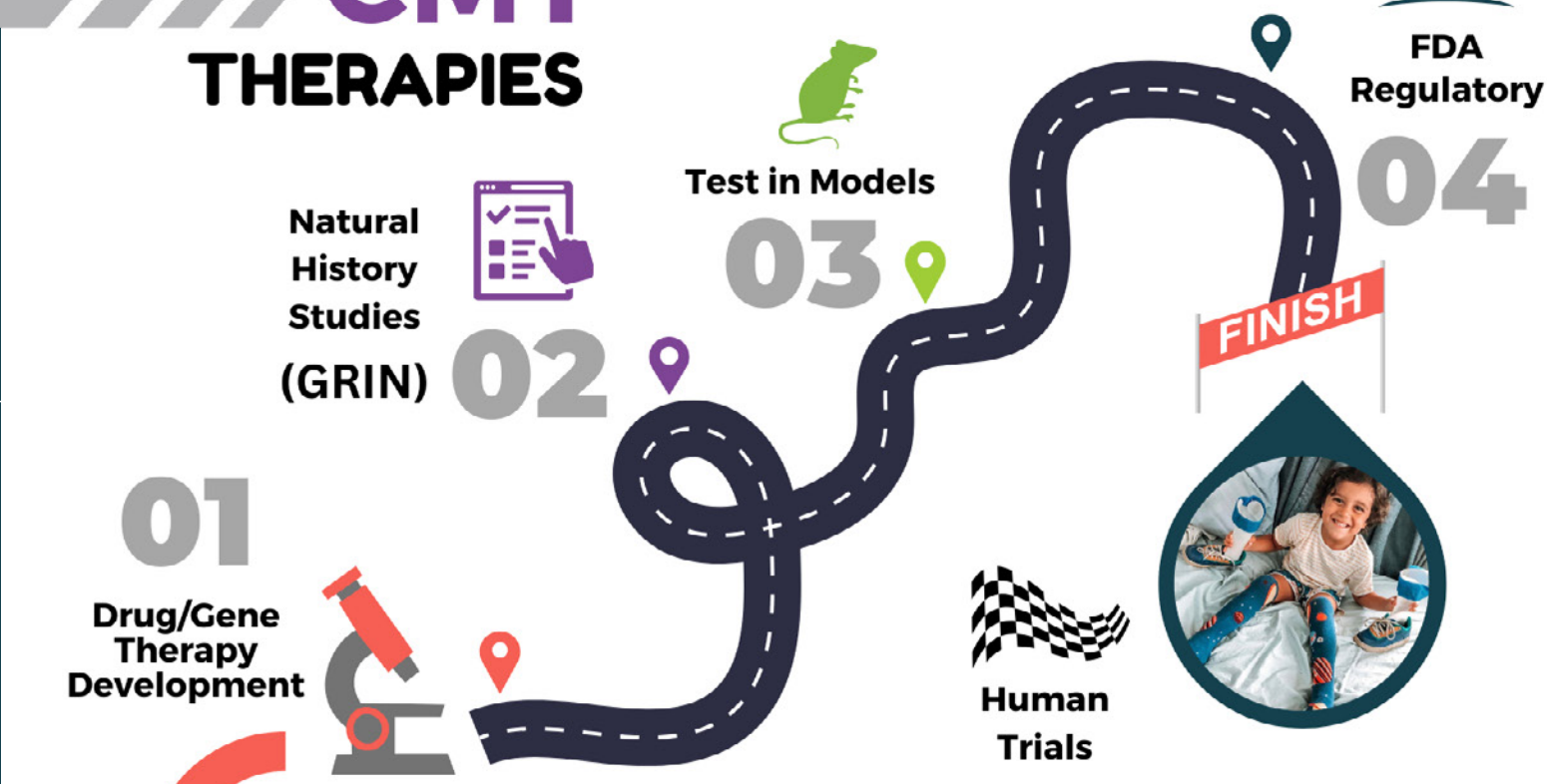
THE ROAD TO CMT THERAPIES

HEREDITARY NEUROPATHY FOUNDATION



Drug/Gene Therapy Development

HNF works with our **TRIAD** partners including innovative biotech, pharma and award-winning researchers to fund and support the most promising scientific approaches to potential treatments.

01 WATCH VIDEO

Natural History Studies

GRIN's Natural History Studies are critical in identifying more patients to understand impact of disease and to support clinical trial design and patient recruitment. The **CMT Genie** supports patients to confirm the genetic mutation of their CMT.

02 WATCH VIDEO

Test in Models

HNF develops and validates CMT cell and animal models to test the efficacy of viable treatment approaches. This includes toxicology and dosing studies. Our **CMT Biobank** collects patients' biospecimens to accelerate crucial biomarker development.

03 WATCH VIDEO

FDA Regulatory

HNF engages with FDA regulators to incorporate innovative and digital technologies to enhance the precision of sensitive data capture. HNF pilot studies serve to accelerate, develop, and validate CMT functional outcome measures for clinical trials.

04 WATCH VIDEO

hnf-cure.org Watch videos: www.hnf-cure.org/our-impact/clinical-trials

Two CMT1A Therapeutics Updates

1. Pharnext announces the evaluation of the Phase III results is on-going into Q1 of 2024

Pharnext announces a drastic cost-cutting plan and focus on the evaluation of the Phase III results which is on-going into Q1 of 2024. "To focus financial resources on issues directly related to this new development phase, Pharnext has decided to stop all other operating expenses." They have also previously stated, "From all these new results, results of the Phase II study, first Phase III study and extension studies, one of which is over 6 years, the product's remarkable safety profile, and the absence of any approved treatment or in advanced clinical stage for CMT1A, Pharnext believes there may be a chance to agree on a registration pathway for PXT3003 in CMT1A, with the FDA and the EMA."

Read more **here:** http://tinyurl.com/2248fcrx and **here:** http://tinyurl.com/yfw3vne7.

If you were in the trial and have not completed the **PXT3003 Patient Survey:** http://tinyurl.com/2s3h27t7, yet, please take a few minutes to do it now. Your voice is important!

Update:

HNF is excited to announce that the PXT3003 Trial Patient Survey will now be available in eight additional languages to better understand the patient perspective of PXT3003 and their participation in clinical trials.

***The survey results will be shared in a de-identified manner with the sponsor and the clinical sites and will support TRIAD partnerships to further improve clinical trial design and participation amongst stakeholders.*

2. FDA awards orphan drug designation for South Korean biotechnology company ToolGen Inc.'s gene therapy, TGT-001

"TGT-001 corrects genes within the body directly, using the CRISPR gene-editing tool to regulate the expression of PMP22 to normal levels. The treatment strategy was validated via animal testing", according to ToolGen. Read more here: http://tinyurl.com/mryx2kzj

Orphan drug status gives a company exclusive marketing rights for a seven-year period, along with other benefits such as tax credits on clinical trials, to recoup the costs of researching and developing drugs to treat rare diseases. The Orphan Drug Act was designed to encourage companies to develop drugs for rare diseases.

Stay tuned to HNF for more research updates for all types of CMT. Join HNF's Global Registry for Inherited Neuropathies (GRIN: http://tinyurl.com/56kwjjjb) and upload your genetic report to help advance CMT research and be pre-screened for upcoming human clinical trials. Make an appointment with HNF's CMT Genie (http://tinyurl.com/tpm8r74e) to be connected to genetic counseling and testing.

HNF's CMT Genie: Because genetic testing for CMT has never been more critical

Collaborative efforts between researchers, healthcare providers, and patients, facilitated by the Hereditary Neuropathy Foundation, has created a synergy that has accelerated the pace of discovery. Genetic testing not only benefits individual patients but also contributes to the collective knowledge that can improve the understanding and management of CMT on a broader scale.

1. Clinical Trials are on the Horizon

The landscape of CMT research is evolving quickly - particularly for the most common type, CMT1A. Advances in genetic testing technologies and our understanding of genetic contributions to diseases are influencing the design of clinical trials to target specific patient subgroups for more personalized and effective treatments. Clinical trials are essential for evaluating the safety and efficacy of new treatments, drugs, or interventions. However, the success of a clinical trial depends on recruiting participants who are not only willing but also suitable candidates based on their CMT subtype.

2. Avoid Neurotoxic Drugs

Without genetic confirmation, patients may unknowingly be prescribed neurotoxic drugs (some as common as antibiotics, vitamins, and antidepressants), which can lead to loss of muscle strength, sensation, mobility, and additional symptoms including pain, numbness, and unpredictable complications. It may take years before the permanent and accelerated decline is associated with a neurotoxic drug.

3. Early Interventions Can Help

Due to the progressive nature of CMT, early interventions such as bracing, physical and occupational therapy, proper nutrition, and mental health and community support can have a positive impact and, in some cases, slow the progression of comorbidities and loss of function.

4. Family Planning

Genetic testing plays a crucial role in family planning and genetic counseling. Genetic testing allows for informed family planning decisions, enabling individuals to make choices that align with their values and preferences. Moreover, genetic counseling provides emotional support and guidance for individuals and families navigating the complexities of rare diseases. Genetic counselors help interpret test results, discuss potential implications, and address psychosocial concerns.

ARE YOU READY FOR CMT CLINICAL TRIALS?

- Make an appointment with CMT Genie for genetic counseling and testing
- Join HNF's patient registry, GRIN and consent to be contacted if you are a match for a clinical trial
- Upload your genetic report to GRIN
- Complete all GRIN surveys

HNF's CMT Genie Update:
New CMT gene discovery, CRYAB

Do you have late onset autosomal dominant CMT2 - subtype unknown, with breathing involvement, unexplained cardiac complications, and/or congenital cataracts?

A recent publication (http://tinyurl.com/mr3yp472) detailed a patient in the UK who presented in his 40s with progressive foot drop and falls. He had a normal birth and milestones, was very good at sports and had no symptoms earlier in life. His past medical history was uneventful except for bilateral congenital cataracts, which did not need surgery. Neurological examination in his early 50s showed a high stepping gait. He could not stand on either heels or toes. Muscle strength was mildly reduced in the distal upper limb muscles, and markedly reduced in the distal lower limb muscles. There was paradoxical breathing due to diaphragm weakness. Reflexes were present in the upper limbs, but absent in the lower limbs. Vibration was reduced distally in the lower limbs.

His initial diagnosis: Late onset autosomal dominant CMT2 - subtype unknown.

Ten years later, the neuropathy had moderately progressed and he needed two crutches to walk. He was also noticed to have developed mild parkinsonism with right-sided predominant tremor and rigidity. The persistent testing (whole exome) led to the identification of a previously unidentified cause of CMT - the CRYAB gene. Read the entire paper here: http://tinyurl.com/mr3yp472

A very important finding with this new subtype is that for the first time, scientists have made a distinct connection between CMT and possible cardiac complications, and between CMT and breathing involvement. Because of these potential complications with this new subtype, researchers recommend regular cardiac and respiratory monitoring for any patient who has this CMT subtype in order to identify, and possibly prevent, life-threatening cardiac complications. This CMT discovery is also the first direct connection to the possibility of cataracts, which may or may not need surgical intervention.

Researchers have identified several others who have this new CMT subtype. It is known presently as "CRYAB-CMT", but a more conventional CMT name may emerge in the future. If any of this sounds like what you experience with your CMT, and despite all efforts testing has not revealed your gene, this might be your subtype.

Testing for this gene is now available. Get genetic counseling and request at-home testing via HNF's CMT Genie initiative by setting up an appointment with a genetic counselor today: http://www.cmtgenie.org/

Book an Appointment
Click Here!

JOIN GRIN
Click Here!

CMT'S FIRST PAIN MANAGEMENT GUIDE IS LIVE!

HNF LAUNCHES THE "ABCs OF CMT PAIN MANAGEMENT GUIDE"

In the world of Charcot-Marie-Tooth disease, patients often hide one of their toughest challenges: pain. But this pain isn't imaginary—it's very real for those living with this condition.

Recognizing this, the Hereditary Neuropathy Foundation (HNF) resourced its ever-growing GRIN patient registry data, Inspire™ CMT online patient community and top CMT specialists to create the **"ABCs of CMT Pain Management guide"**. This 90-page guide comes free as a PDF or can be purchased on Amazon in paperback or Kindle. It is the first comprehensive resource of its kind and provides an accessible support system designed to help individuals find personalized ways to manage their pain effectively.

Categories range from topical creams to nutrients, from prescription medications to holistic treatments, and more, providing patients with as many options for relief as possible. Each item links to a supporting paper so patients can feel empowered to explore the science behind potential approaches and weigh the benefits and risks with listed "WARNING" content.

The guide is in no way intended to serve as medical advice or replace healthcare providers. Instead, we encourage users of the guide to discuss resources of interest with their doctors before making decisions. It's important for all users to note that even with seemingly harmless dietary changes or holistic approaches, side effects and risks can be dangerous and trigger unexpected interactions.

VIEW THE GUIDE:

http://tinyurl.com/9zp7dtns

PURCHASE ON AMAZON

http://tinyurl.com/yucmhkab

HNF would like to sincerely thank the over 5000 CMT patients worldwide who have helped make this guide possible by sharing their CMT journey through HNF's Global Registry for Inherited Neuropathy, GRIN (http://tinyurl.com/4834srfd). Not only does GRIN provide vital information to CMT researchers and industry for treatment and clinical trial design, but it is also a patient registry that gives back to the CMT Community. We encourage anyone not yet enrolled to participate in CMT research and join TODAY!

"We are thrilled to finally have a resource to share with the many individuals living in debilitating pain whom we speak with each week and for those who continue to suffer in silence, feeling as if they do not have a path to a pain-free life. As always, we believe in bringing power back to our CMT family… and knowledge is power."

– Estela Lugo, HNF Program Development Manager, CMT4A (GDAP1)

HNF's Experience with CMT Pain:

Our quest to understand and address CMT-related pain started with a simple yet powerful realization: not enough people knew how much pain CMT patients experience. To change that, HNF started the Inspire™ online CMT patient community in 2009, now named CMT Safe Space (http://tinyurl.com/mr3z924m). Through these conversations, it became clear just how challenging CMT-related pain could be.

A significant turning point came in 2013 with the launch of HNF's Global Registry for Inherited Neuropathies (GRIN). The data collected confirmed what patients had been saying all along: pain is a significant part of CMT. Over the past 14 years, HNF has been working tirelessly to unravel and address pain in CMT, gaining global recognition along the way.

HNF's Latest CMT Pain Research:

In 2020, our fundraising efforts led to a vital collaboration with Dr. Florian Thomas, MD, PhD, Director, Hereditary Neuropathy Foundation Center of Excellence, and Chair & Professor, Department of Neurology, Hackensack Meridian School of Medicine & Hackensack University Medical Center. Together, we delved deep into GRIN data. This collaboration resulted in the groundbreaking 2023 study: "Patient-Reported Psychosocial Outcomes in Charcot-Marie-Tooth Disease."

Key Findings:

Our study, based on data collected through GRIN, uncovered something significant: most CMT patients experience mild to moderate pain at least once a week. This pain doesn't just affect physical health—it also leads to increased social isolation and reduced life satisfaction. These findings were shared at the 2023 meeting of the American Academy of Neurology in Boston, marking a significant milestone in CMT research.

What This Means and What's Next:

Dr. Florian Thomas emphasized the importance of addressing neuropathic pain, saying, "These findings suggest addressing neuropathic pain will go a long way in improving the quality of life & community participation in people with CMT" Dr. Thomas said. "We can make a difference in CMT patients' lives if we find ways to address their pain." This sentiment echoes HNF's core mission: to shine a light on the hidden challenges of CMT and show a way forward to improved well-being and empowerment.

CMT Biobank: *We Need Your HELP!*

Complete the form:
Click Here!

HNF is excited to continue collecting samples for researchers and industry to help develop treatments for CMT. CMT impacts the quality of life starting in childhood and is progressively debilitating. Currently, there are no treatments, but there are many potential therapies in the pipeline. There are still gaps in understanding the natural history of the disease correlation of genotype/phenotype, the availability of patient biospecimens for translational research, and the validation of drug candidates and biomarkers for CMT.

HNF is the only CMT advocacy group that gives access to these patient samples at minimal cost.

The locations for specimen collection are currently being discussed. Please give us feedback if you would like us to come to a city near you!

NEW BOARD MEMBER: DENNIS SULLIVAN

Dennis has spent his 36-year career in medical devices, with significant experience in research and development, operations, quality, and sales/marketing. Having worked at start-up and Fortune 500 companies (such as Johnson & Johnson and Medtronic), he has gained invaluable experience, such as developing relationships with the medical community, regulatory strategies, and medical device design and product launch that can support HNF within the medical industry.

Dennis comes to the team with direct experience of CMT, a member of his family has the disease. His goal with HNF is to create awareness of hereditary peripheral neuropathies, work on therapies with industry leaders for today, and an eventual cure for future generations.

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LEARN MORE: http://tinyurl.com/5n92v4sz

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BBB

95% of donations

Fund CMT Research & Programs

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Turn CMT Symptoms into Science

60
Countries Represented

4160
Participants

41
Types of CMT Represented

Willingness to Participate in a Clinical Trial

2% NO
8% UNSURE
90%YES

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- Patient Resources

Global Registry for Inherited Neuropathies (GRIN):

A Patient-Powered Registry Boosts the Study of Charcot-Marie-Tooth (CMT) Disease

CMT is a genetic, degenerative neuromuscular disease that affects 1:2500 in the US and 2.5 million worldwide—many are still undiagnosed—and currently, there is no cure. CMT is progressive, and over time, muscles in the feet, legs, and hands lose strength. Muscles waste away and cause atrophy leading to mobility issues. It can have a serious impact on vision, hearing, breathing, speech, and swallowing in extreme cases. Some patients experience hip dysplasia, scoliosis, and/or blindness.

MISSION:
As part of TRIAD, the Global Registry for Inherited Neuropathies (GRIN) was established as a patient registry and research consortium to advance knowledge of patient records, analyze patient-reported data, collect genetic reports and clinical CMT validated scales (CMTPeds, CMTInfS). The data has been instrumental in identifying the burden, diagnostic journey and prevalence of CMT.

The Hereditary Neuropathy Foundation mission is to increase awareness and accurate diagnosis of Charcot-Marie-Tooth (CMT) and related inherited neuropathies, support people living with CMT and their families with critical information to improve quality of life, and fund research that will lead to treatments and cures.

www.hnf-cure.org