



In "Under the Microscope," CMTA Chief Research Officer Katherine Forsey, PhD, takes a closer look at issues related to the CMTA's Strategy to Accelerate Research. Katherine is a research biologist by training and holds a doctorate in biology from the University of York in the area of expression, activity and localization of metabolic enzymes during preimplantation embryo development. She and members of her family have CMT1A. She lives in Yorkshire, England with her husband and two children.

More than **\$23.5 Million** has been invested in CMTA-STAR research since 2008.



Patients as Partners IN RESEARCH

The CMTA launched the "Patients as Partners in Research" (PPR) initiative in 2018 with the goal of engaging the patient community to participate in its Strategy to Accelerate Research (STAR).

PPR works to:

- **Support access** to surveys, natural history studies and clinical trial opportunities.
- **Educate patients** about research progress in their own subtype and relevant cross-type initiatives.
- **Collect patient-informed data** to improve our support provision.
- **Collate, analyze and present anonymized data** to inform current research partners, the wider CMT research community and the PPR community.

More than 6,200 PPR participants have created profiles via a secure online form as of January 2023, a hugely powerful collection to inform and advance CMT research.

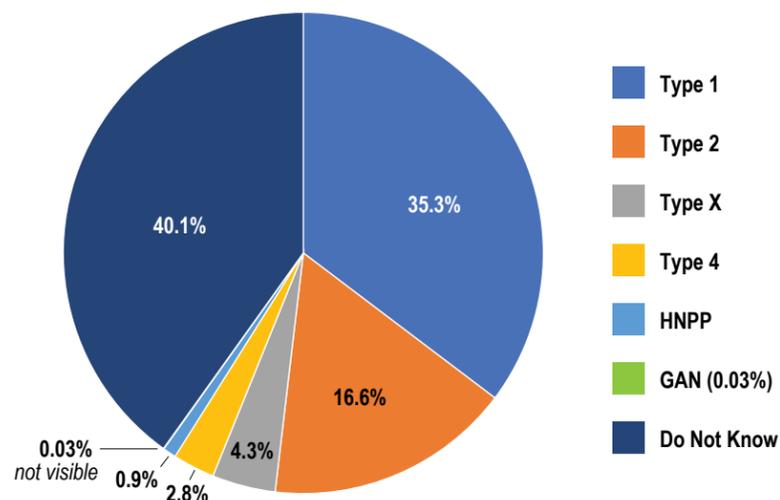
The profile currently asks 22 questions on topics that include CMT type and subtype, age, location, age of symptom

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onset, age of diagnosis, genetic testing and Center of Excellence attendance. The CMTA uses the information to share updates with participants personalized to their CMT type and subtype, as well as opportunities to enroll in upcoming clinical trials, natural history studies and researcher-created surveys. Participation in these activities helps researchers and clinicians learn more about how CMT progresses.

The data has been fully anonymized and statistically analyzed to help increase knowledge around, for example, CMT patient type and subtype distribution, the size of the diagnostic gap (number of participants who don't know their CMT type or subtype) and the percentage of people accessing genetic testing.

Patients as Partners in Research — CMT Type Data



Of the 97 percent of patients who responded to the question about their CMT type, just over 40 percent said they don't know their type, proof of a significant diagnostic gap.

More than 4,000 participants have also provided subtype data, representing 47 different CMT subtypes ranging from the most common to the very rare. Some 98 percent of people with Type 1 know their subtype, compared to the 80 percent of Type 4 patients. And just 60 percent of people with Type 2 CMT know their subtypes.

The last finding highlights the importance of the CMTA's Type 2 gene discovery efforts and demonstrates the need for advanced research diagnostic capabilities. Stephan Zuchner, MD, PhD, at the University of Miami is leading the charge to identify new CMT causative genes in addition to the more than 120 already identified. Commercially available genetic testing panels are regularly updated to include the new subtypes. Patients can speak to their neurologists or family doctors for a referral to a genetics counselor for testing, which usually involves taking a family history and a simple blood draw.

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new treatments for CMT. For example, the gene therapy approaches currently in development through CMTA-sponsored research projects will only work on the specific CMT subtypes they are designed to treat, like the CMT4C project underway with Kleopas Kleopa, MD, at the Cyprus Institute, and the CMT2A and CMT2E CRISPR projects with Bruce Conklin, MD, and Luke Judge, MD, PhD, at the Gladstone Institutes USA. The takeaways from these projects will also benefit all other subtypes.

The CMTA is also working closely with STAR Alliance partners like ToolGen, which created a potential therapy for CMT1A using CRISPR gene editing technology.

The CMTA plans to expand PPR even further, adding more questions to help researchers understand the CMT patient population better and including essential diversity-capturing questions that are important for future clinical trials and natural history studies. Work is also needed to ensure that traditionally underrepresented groups, which have huge potential to strengthen our knowledge and understanding of CMT, are supported to participate.

When members of the community ask what they can do to help CMT research, one of the things I always suggest is signing up to be a PPR participant. Filling out a profile for oneself or one's child takes less than 10 minutes—asking affected family members to do it takes even less.

To view the current surveys, natural history studies and clinical trial opportunities for Patients as Partners in Research, visit bit.ly/3XSyshQ.

6,000 PROFILES

32 ACTIVE SPONSORED RESEARCH PROJECTS

18 preclinical studies worth over \$2 million

JOIN THE PROJECT!
To create your own PPR profile and be part of this important initiative to advance CMT research, visit bit.ly/3x3euW1.
OR SCAN THIS QR CODE



CMTA Co-Sponsors Tour of Conklin Lab And Its ‘Life-Changing’ Gene Editing Work

Members of the CMTA community toured Dr. Bruce Conklin’s lab at Gladstone Institutes in San Francisco during “CMT/Peripheral Neuropathy Day” on Jan. 18. Conklin, a renowned geneticist, is a member of the CMTA’s STAR Advisory Board. His lab focuses on biomedical applications of CRISPR gene editing technology, emphasizing motor neuron diseases including CMT.

Co-sponsored by the CMTA, the event also included educational sessions about the future of gene therapy to treat CMT. Gladstone Institutes President Deepak Srivastava, MD, gave an overview of the organization, whose mission is to drive a new era of discovery in disease-oriented science and to mentor tomorrow’s leaders in an inspiring and diverse environment.

Luke Judge, MD, PhD, and graduate student Gokul Ramadoss gave a patient-centric presentation on the lab’s work and discussed the evolution of gene therapy for neurological diseases. According to them:

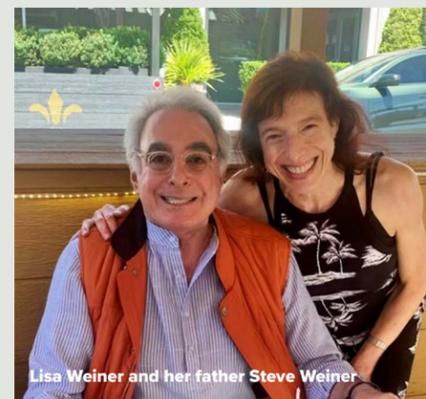
- CRISPR-Cas9 gene editing has the potential to treat many forms of CMT by correcting the root cause of the problem at the genetic level.
- Induced pluripotent stem cells (iPSCs) generated from blood draws allow researchers to test these therapies on nerve cells grown from actual CMT patients.
- The lab has already demonstrated that cells from CMT2E patients are healthier after gene editing, and it is now developing new approaches to treat the largest number of patients.
- Safe and effective methods to deliver CRISPR-Cas9 to the spinal cord without causing long-term side effects will be critical to translating this approach into clinical development.

After the presentation, four panelists took questions from the audience—Judge; UCSF Center of Excellence director Alexander Fay, MD, PhD; CMTA Board Chair Gilles Bouchard; and Zach Nevin, PhD. Conklin moderated the Q&A.



Dr. Bruce Conklin moderated a Q&A session.

It was a memorable afternoon of CMT education and community, and an amazing opportunity to tour a CRISPR lab and meet the brilliant researchers working tirelessly to find a treatment for CMT.



Lisa Weiner and her father Steve Weiner

THE CONKLIN LAB TOUR:

A Patient’s Perspective

Entering the spacious Gladstone Institutes building, my dad, his partner and I mingled with many other CMT warriors, family and friends during a momentous afternoon. The smart, talented and ambitious scientists in Dr. Bruce Conklin’s lab opened their doors to explain how their research could help treat CMT and other debilitating neurodegenerative diseases.

Our tour guide, a young PhD graduate and full-time scientist, showed us where they run cells and neurons created from iPSC cells through expensive high-tech machines, then examine them under a microscope at extremely high magnification. We actually saw live pulsing neuron cells, created right there in their lab.

The Conklin Lab is working on several different CMT variants, including the most common, CMT1A. After viewing the lab equipment, the live neuron cells and the numerous refrigerators safeguarding the research, we headed to the building’s theater for an hour-long presentation.

Dr. Fay, a pediatric neurologist, explained how spinal muscular atrophy (SMA), which previously ended an infant’s life at age 1 or 2, can be eliminated when gene therapy is applied at birth, ideally before symptoms ensue.

It was a remarkable, life-changing afternoon as Gladstone helped us connect the dots.

— Lisa Weiner



APPLICATION PERIOD FOR \$5,000 SCHOLARSHIPS FOR STUDENTS WITH RARE DISEASES OPENS

The Everylife Foundation for Rare Diseases—with the support of Horizon Therapeutics—will award \$5,000 scholarships to 35 recipients with rare diseases in 2023. The application period opens March 8 and runs through April 13. Recipients will be notified in the summer, and funds will be paid directly to their schools in early August 2023.

Anyone 17 or older who is a U.S. resident and who has been diagnosed by a physician with any form of rare disease can apply for a #RAREis Scholarship. Applicants will be asked to provide a Diagnosis Verification Form. Applicants must plan to enroll full-time or part-time in undergraduate or graduate study at an accredited two- or four-year college, university or vocational-technical/trade school for the fall 2023 semester. There is no minimum credit-hour requirement to be part-time and students do not need to be pursuing an undergraduate or graduate degree.

As the foundation’s website explains, a disease is defined as rare when it affects fewer than 200,000 people in the United States. CMT meets that definition.

Applicants must provide their latest official transcripts and answer an essay question. In 2022, the question was “How will your education and career goals help you become an advocate for the rare disease community?” Recipients will be selected based on their essay responses, leadership and participation in school and community activities, work experience, academic performance and financial need.

The Everylife Foundation is a 501 (c)(3) nonprofit dedicated to empowering the rare disease patient community to advocate for impactful, science-driven legislation and policy that advances the equitable development of and access to lifesaving diagnoses, treatments and cures. As the foundation website states: “We do not speak for patients. We provide the training, education, resources and opportunities to make their voices heard. By activating the patient advocate, we can change public policy and save lives.”

FOR MORE INFORMATION, visit everylifefoundation.org/rare-scholarship/.



The CMTA and Conklin Lab teams