

# Demyelinating CMT: Type 1, Type X and Type 4 Research Developments

In a multipronged approach to identifying novel treatments for demyelinating CMT, the CMTA is pursuing several therapeutic opportunities in collaboration with more than a dozen key partners:

## GENETIC THERAPIES FOR CMT:

- In collaboration with **Ionis Pharmaceuticals**, we are developing antisense oligonucleotides (ASOs), which have shown dramatic results in two rodent models of CMT1A.
- CMTA-funded studies by **Dr. Kleopas Kleopa** have shown that gene therapy is feasible in rodent models of **CMT1X** and **CMT4C**. This approach is being adapted to use **RNA interference** to decrease the **PMP22** levels found in **CMT1A** and to optimize delivery to the affected Schwann cells in demyelinating **CMT**.
- We are currently collaborating with one company for application of **CRISPR** technology (genome editing) to demyelinating **CMT** and additional collaborations with leading labs are underway for development of this exciting technology for **CMT**.

## DRUG DEVELOPMENT FOR CMT

- We are supporting Acceleron Pharmaceuticals' efforts, which are already in clinical trials, to strengthen affected muscles in individuals with demyelinating CMT.
- In partnership with InFlectis BioScience, we are developing agents to modulate aberrant protein synthesis for CMT1A and CMT1B. Phase 1 clinical trials are currently underway.
- The progression of all types of CMT occurs as the longest axons are compromised in a process called axon degeneration. We are working with partners to develop chemical inhibitors of the triggers of axon degeneration. We are currently testing the applicability of this approach to multiple models of CMT, and collaborating with several companies with candidate drugs to promote axon survival and preserve nerve function.

## CLINICAL TRIAL PREPARATION

- Because CMT typically progresses very slowly, we need sensitive methods to measure the effect of a given treatment and make CMT an appealing target for therapeutic development by companies/partners.
- We are supporting the efforts of the Inherited Neuropathies Consortium to conduct natural history studies for CMT to be able to show how treatments will affect its natural progression.
- In partnership with Genzyme, a Sanofi Company, we are sponsoring identification of novel biomarkers in skin and plasma that reflect the status of demyelinating CMT, which can be used as early indicators of success in a clinical trial.
- We support the development and validation of novel MRI assessments, functional outcome measures, and wearable sensors that can remotely assess patient strength and balance so that progress can be measured at the patient's home.

*We've deliberately kept our descriptions simple, but if you'd like to go deeper on any project or type, email Jeana Sweeney at [jeana@cmtausa.org](mailto:jeana@cmtausa.org).*

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