

DEMYELINATING FORMS OF CMT: STAR's AGENDA

The CMTA's Strategy to Accelerate Research, or STAR, has been a beacon of light and hope for the CMT community since 2008. Its unique approach is built on collaboration: It connects our world-renowned STAR Advisory Board to pharmaceutical, biotechnology and research service companies that are pursuing therapy development.

These STAR alliance members, along with the CMT patients who are the real experts, complement a network of sponsored university laboratories and biotech companies positioned to deliver therapies to the market in the near future. The CMTA's funding and operations focus is on translational research that will lead as directly as possible to therapeutic treatments for CMT.

Demyelinating forms of CMT affect the protective coating, or myelin, that insulates the "electrical wire" that is the nerve. Research specific to demyelinating forms of CMT—Types 1A, 1B, 1X and 4—includes some two dozen projects:

GENE THERAPY AND GENE EDITING PROJECTS

- 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 of the Cyprus Institute of Neurology and Genetics have shown that gene therapy is feasible in rodent models of CMT1X and CMT4C and the CMTA is actively supporting the efforts of several gene therapy companies to develop new CMT gene therapies. Pioneering CMTA-sponsored preclinical gene therapy studies have shown great promise in models of demyelinating CMT. This approach is now being extended 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 to use CRISPR (genome editing) to treat demyelinating CMT, and additional collaborations with leading labs are underway.

SMALL MOLECULE AND BIOLOGICAL THERAPY PROJECTS

- In partnership with InFlectis BioScience, we are developing agents to restore myelin protein balance for CMT1A and CMT1B. Phase 1 clinical trials have concluded and InFlectis is gearing up for Phase 2 trials.
- 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 molecules that regulate of the triggers of axon degeneration. We are currently testing the applicability of this approach in multiple models of CMT, collaborating with a number of companies to show that candidate drugs can promote axon survival, preserve nerve function and prolong patient mobility in demyelinating Type 1 CMT disorders.
- We are supporting work done by Dr. Maurizio D'Antonio of the San Raffaele Scientific Institute to test new drug classes for CMT1B, which are being developed for stress-related disorders such as stroke, Alzheimer's and retinal degeneration.
- The CMTA has just approved two new projects to test small molecule therapies in preclinical models of CMT1A.

PREPARING FOR CLINICAL TRIALS

In partnership with the Inherited Neuropathy Consortium, we are building on their recent successes in development of novel biomarkers and outcome measures in CMT1A and supporting major efforts to extend development and testing of critical biomarkers for CMT1B and CMT1X to support upcoming clinical trials.

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.

Donate at cmtausa.org/inspire