STAR 101

By Elizabeth Ouellette, Vice Chair, CMTA Board of Directors

At the end of 2007, the CMTA's Board of Directors met in Palo Alto, California, to discuss methods of advancing CMT research. At the time, medical research grants were awarded to the scientists whose proposals had the most potential to break open new territory in the field of CMT, hopefully paving the road to a cure. We were not satisfied with this model, however: It was costly, time-consuming and ineffective. We only had the capital to fund one or two projects a year, most of which took two to three years to complete. In retrospect, discovering a major breakthrough using this traditional method would have been like finding a needle in a haystack. We had nothing but the best intentions, but discovering a major breakthrough in the world of CMT research would have been a long shot.

Discussions in Palo Alto focused on how to change the face of CMT research by adopting a more proactive and strategic approach, loosely modeled after a few key organizations that had started to apply a business strategy approach to medical research. Key elements of this new approach included:

- Clearly articulating the strategy to achieve our vision and goals.
- Identifying the best researchers in the world to implement plans in support of this strategy.
- Defining metrics to measure progress and linking future funding to achieving success.
- Encouraging and facilitating active collaboration and sharing among our researchers.
- Developing intellectual property to encourage partnerships with pharmaceutical companies and potentially help fund future research.

We called this new model our "Strategy to Accelerate Research," or STAR. STAR promised to speed up the pace of CMT research by capitalizing on advances in scientific knowledge and technology to find a treatment to stop the progression of CMT.

Our new drug discovery initiative requires the collaboration of the world's best CMT scientists, working together, sharing and communicating ideas, discoveries and research findings in real time. These teams of top scientists work hand in hand with the CMTA's STAR Advisory Board to advance CMT research using a translational approach (applying discoveries generated in the laboratory to human beings).

<u>Our STAR strategy comprises six different elements</u>:

1. **Creation of Cell lines/Assays (tests)**

Our scientists replicate the effects of CMT-causing mutations in cells grown in laboratory dishes.

2. **High Throughput Screening (HTS)**

We then robotically test large collections of 10,000 to 2 million compounds on these cells to see if any of these potential drugs inhibit the CMT-causing mutations without causing unwanted side effects.

3. **Laboratory Models**

In parallel with the creation of cell-based assays and the HTS process, the CMTA supports the creation and utilization of laboratory models with each disease type so that promising compounds can be tested immediately.

4. **Pharmaceutical Partnerships**

The CMTA works in collaboration with top pharmaceutical, biotech and governmental organizations like Sanofi-Genzyme, Addex, Pfizer and the National Institutes of Health. In fact, between the NIH and Sanofi-Genzyme, we've screened well over 2.4 million compounds to date. In the coming months, this 2.4 million will be narrowed down to the most promising one or two leading drug candidates, with the goal of beginning clinical trials in the next couple of years.

5. **The Human Element: Skin Cells to Stem Cells**

Realizing that testing on animal models does not always translate into cures for humans, the CMTA has partnered with the New York Stem Cell Foundation (NYSCF), an organization that transforms blood and tissue samples of people with CMT into human stem cells, which are further differentiated into nerve cells and Schwann cells. Once differentiated, promising medications are tested on human cells.

6. **Clinical Trials**

Human clinical trials for candidate therapies will take place at the CMTA-sponsored Centers of Excellence (www.cmtausa.org/coe). Envisioning clinical trials in the very near future, it is critical that everyone in the CMT community join the CMT Patient Contact Registry (www.rarediseasesnetwork.org/INC/register/index.htm). By joining the Registry, you will be informed of current and new research studies and upcoming clinical trials.

STAR's multipronged efforts are paying off on a number of different fronts, as we are currently working on CMT1A, CMT1B, CMT2A, CMT2E, CMTX and CMT4, which constitute 90 percent of all types of CMT. For more information on the work being completed on each type, please visit our website: www.cmtausa.org.

Why give to STAR? There is more hope and promise for a world without CMT than ever before. The CMTA does not receive governmental grants or external money and is 100 percent funded by our Board of Directors, community members, friends and families. As we near the end of 2015, please consider donating to the CMTA's drug discovery program. By supporting the CMTA, you are investing in the future of millions throughout the world. To donate today, please visit www.cmtausa.org/donate.