

CMD Tissue Repository

Accelerating Research for Congenital Muscle Disease

Congenital Muscular Dystrophy • Congenital Myopathy • Congenital Myasthenic Syndrome

Annual Newsletter

Dec 2018

A Look At 2018

The Invited Speaker Series continued this year. The first web talk featured Kimberly Trant, RN, MBA, Director of Patient Advocacy, and Dr. Sal Rico, MD, PhD, VP of Clinical Development, from Audentes Therapeutics, Inc. as they provided a general overview of the company, gene therapy as a potential treatment for congenital muscle disease, and the XLMTM development program as an example of what can be done. The second web talk featured Sandra Donkervoort, a board certified genetic counselor at the Neuromuscular and Neurogenetic Disorders of Childhood Section of the NIH National Institutes of Health, entitled Obtaining a Genetic Diagnosis in Congenital Muscle Disease.

Tissue distributions of ten individual samples were provided to prominent research laboratories conducting approved studies of protein, transcript, and functional analysis.

Program participation increased and we coordinated tissue transfers from 10 medical centers across the United States to the biorepository. Our honored donors have contributed over 383 tissue samples in total for research use. In the past year we also assisted 31 new families interested in donation of blood and/or skin samples for cell line development.

December '18 Issue

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The CMD-TR is accepting tissue donations. Visit our website at mcw.edu/CMDTR to learn more.



Dr. Sal Rico and Kimberly Trant of Audentes



Sandra Donkervoort

National Institutes
of Health

Stronger Together 2019 Scientific & Family Conference July 25-28 • Chicago USA

Please join all of us this summer-2019 for the first-ever collaboration of three neuromuscular disease communities all working toward the same goal: to find treatments for these rare congenital muscle disorders.

Watch for updates in your inbox as the planning team finalizes the details. The scientific portion of the conference will be July 25 and 26, while the family portion will be held on July 27 and 28, 2018.

Having recognized significant overlap in symptomatology, care management, and research strategies, we can reach our goals sooner working together. We look forward to learning from one another and collectively improving our efforts in research, care practices, and advocacy.

Join the fun to see old friends and make new ones, while we learn from each other.



Scientific Engagement

We have been involved in scientific presentations, seminars, publications, and press releases nationally and internationally. Some examples include:

1. Development and Translation of Treatments for Congenital Myopathy seminar given at three events to faculty, staff, residents, medical students, and graduate students associated with the Pathology or Physiology Department at the Medical College of Wisconsin, plus to those associated with the Clinical and Translational Science Institute of Southeastern Wisconsin.
2. Proteomic profiling in nemaline myopathy to identify disease subclass biomarkers poster presentation, 2018 World Muscle Society Meeting in Mendoza, Argentina.
3. Use of abnormal protein expression to identify subclasses of nemaline myopathy for the improvement of treatment study design, 2018 American Society for Gene and Cell Therapy (ASGCT) Meeting on May 18th in Chicago, IL.
4. Proteomic profiling in nemaline myopathy to identify disease subclass biomarkers, 2018 Harmony 4 Hope meeting in Milwaukee, WI.
5. Dowling JJ, Lawlor MW, Das S. X-linked myotubular myopathy. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. 2002 Feb 25 [updated 2018 Aug 23].
6. Fox MD, Carson VJ, Feng HZ, Lawlor MW, Gray JT, Brigatti KW, Jin JP, Strauss KA. TNNT1 nemaline myopathy: Natural history and therapeutic frontier. *Human Molecular Genetics*. 2018;27(18):3272-3282.
7. Froedtert/MCW Press Release. "Neuroscience Researcher with a Passion for Muscular Dystrophy Therapies Honored at Imagine More Dinner." June 26, 2018.
8. MCW "Knowledge Changing Life" Video, "The Whistons' Story." This video featured a family living with X-linked myotubular myopathy, and described our efforts to develop treatments for this disease. <https://knowledge.mcw.edu/whistons>.
9. CTSI Discovery Radio Episode #51- XLMTM: Exploring Gene Therapy In Battling Muscular Disease. This was a radio interview focused on our work in the gene therapy field and in developing treatments for X-linked myotubular myopathy. <https://ctsi.mcw.edu/blog/news-events/news/discovery-radio/discovery-radio-episode-51-xlmtm-exploring-gene-therapy-in-battling-muscular-disease/>.

The CMD-TR Preserves Your Tissue Specimens

The Congenital Muscle Disease Tissue Repository (CMD-TR) at The Medical College of Wisconsin is a place to store specimens that are donated after diagnostic testing is complete, through routine surgery. Centralizing tissue access will make it easier for scientists to obtain appropriate numbers of samples for their research studies, which can accelerate results.

There are a number of potential research uses for preserved tissue, but they may not be well-known to patients, clinicians, and families, so this article will review some of them.

Genetic studies allow for evaluation of gene and protein expression in the context of a person's disease, which may identify additional modifiers of disease severity or treatment response.

Single fiber functional studies require tissue samples. Some laboratories can study the process of contraction in frozen tissue samples, allowing for the study of weakness mechanisms in human muscle disease.

Tissue samples are useful for the review and evaluation of pathological findings in these rare diseases. This is a big deal for clinical trials, since having a clear understanding of how disease severity varies from one person to another is important.

Scientists are able to identify which disease models most accurately reflect the muscle diseases of interest through comparisons of findings and markers expressed in each animal model and comparing those to human samples. This applies to cell culture models as well as animal models, since it is important to understand whether the abnormalities seen in these models are actually relevant to the human muscle disease state.

Understanding how biopsy findings or protein expression might predict disease progression or treatment responsiveness is another potential use of specimens. A muscle disease subtype may be highly variable when people are grouped based on their genetic mutations, but there may be certain markers found through tissue sample studies that can more easily predict clinical symptoms and treatment outcomes.

For a list of all muscle disorder subtypes centralized at the CMD-TR, please visit our website mcw.edu/cmdtr.



With the implementation of the General Data Protection Regulation (GDPR) this year, the ability to engage citizens of EU countries is changing. Although it is meant to increase data privacy protection for consumers, there may be ramifications affecting medical research participants who are citizens of EU countries. Updates will be available on how this may impact our biobanking activities going forward.

Early Consent

The CMD Tissue Repository (CMD-TR) is a centralization point for tissue samples from those with congenital muscle disease. The samples are transferred to our biorepository, preserved, and then shared with top scientists doing meaningful research on the very muscle disorders of our community members. The CMD-TR's purpose is two-fold: serving families that want to contribute to the science that can find a treatment, and serving the scientists that can make that treatment a reality. As a participant, Stacy Cossette can look for left-over samples from a previous muscle biopsy you had, or coordinate with your surgical team to save tissue during a surgery you must have per your doctor's orders. You can learn more about the program at mcw.edu/cmdtr.



Photo Credit: Stacia Creative Photography

Signing-up now means that when a surgery or medical emergency happens, our staff can contact you and your medical team sooner to make arrangements. Time runs out quickly and unexpectedly, so please have the consent paperwork done before the stress of surgery or a medical crisis occurs.

If you or your family member has already consented for tissue donation with Stacy Cossette at the CMD-TR, thank you.

In the Community: Imagine More

At this year's Imagine More Dinner event, we were wowed by an excellent presentation from keynote speaker Dr. Michael Lawlor, Associate Professor of Pathology, Director of the Pediatric Pathology Clinical Neuromuscular Laboratory, and Director of the Congenital Muscular Disease Tissue Repository at the Medical College of Wisconsin. Since his research is focused on the development of novel therapies for pediatric muscle disease, and his laboratory participates in a number of preclinical and clinical trials occurring around the world, we were fortunate to hear updates on treatment trials aimed at childhood neuromuscular diseases, like myotubular myopathy and Duchenne muscular dystrophy.

The CMD Tissue Repository is made possible through the generous contributions of Cure CMD, A Foundation Building Strength for Nemaline Myopathy (AFBS), Where There's a Will There's a Cure, Joshua Frase Foundation (JFF), Team Titin, SC Research Services, Solid Bioscience, and Audentes Therapeutics.

