LGMD-1D DNAJB6 Foundation
and International Autosomal Dominant Muscular Dystrophy Registry

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The Newsletter 11/20/19

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National LGMD Conference

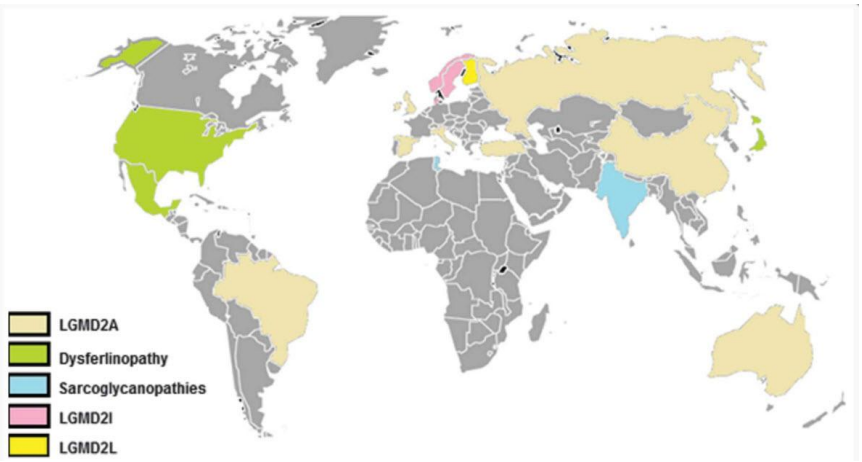
Chicago, August 30-September 1, 2019

THE 2019 NATIONAL LGMD CONFERENCE WAS A HUGE SUCCESS!

Imagine meeting someone who looks just like you or a family member who you haven't seen for years. That was the excitement and energy that permeated the 1st National LGMD conference. Most attendees had never met anyone with similar conditions and the experience was transformative. The positive energy has propelled our foundation to do more: we have extended our registry to include all autosomal dominant muscular dystrophies, an international scope.

Why an international registry for autosomal dominant muscular dystrophies?

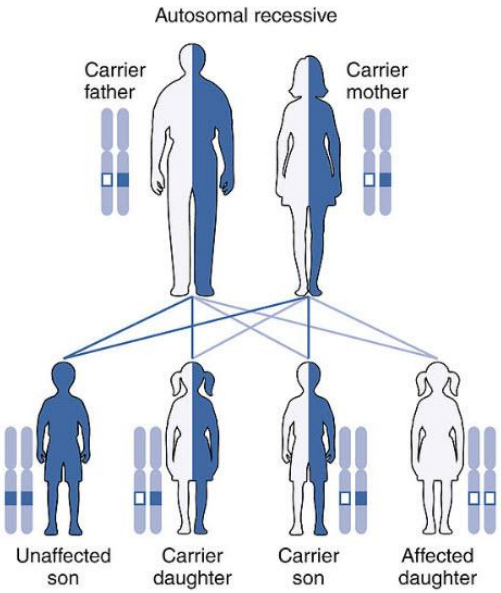
As you can see from this world map of autosomal recessive muscular dystrophies labeled as LGMD"2" , they are worldwide in distribution. The autosomal dominant muscular dystrophies labeled LGMD"1", in addition to others, are less frequent and equally scattered around the world.



There is a pressing need to organize the relatively few autosomal dominant muscular dystrophies since their genetic therapies will be similar. More explanation below. Our foundation has started a registry to achieve this goal and individuals can register at our website: WWW.LGMD1D.ORG

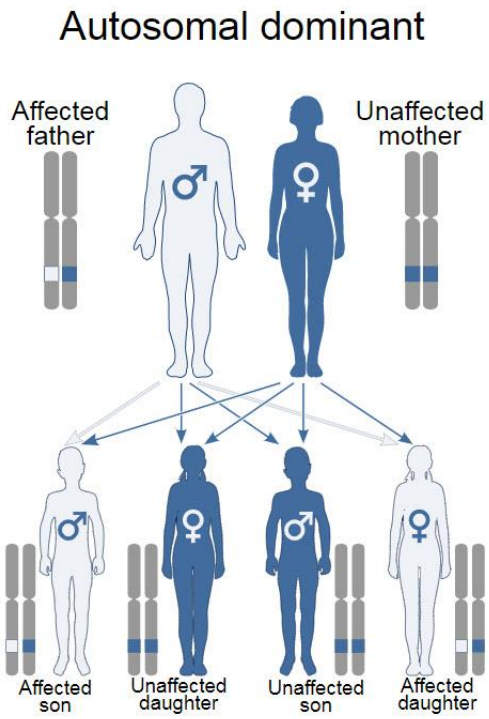
A Basic Primer on Gene Therapy

Autosomal recessive LGMD"2" and others (80% of cases)



Gene therapy for autosomal recessive diseases (very basic): The 2 bad recessive genes produce bad proteins that do not help, analogous to 2 cars in your garage that do not run. If you slip a good gene into the cells (or give you a new car) then you can function again. Diseases such as hemophilia, sickle cell anemia and cystic fibrosis are currently being treated this way.

Autosomal dominant LGMD"1" and others (20% of cases)



Gene therapy for autosomal dominant diseases (very very basic): Unlike a recessive gene, a dominant gene produces a bad protein that overshadows the good protein being produced concurrently by the good gene. Providing an additional good gene will not work for work for dominantly inherited disorders. Treatment strategies will require the correction of the existing bad gene. This may be achieved with CRISPR/Cas9 technology, a gene editor. Another strategy is to delete or block the bad gene, while leaving the good gene intact such as blocking oligonucleotides, small DNA molecules. The article below illustrates the exciting progress that is being made with these techniques.

What has gene therapy done for me lately:

The New England Journal of Medicine

ORIGINAL ARTICLE BRIEF REPORT

Patient-Customized Oligonucleotide Therapy for a Rare Genetic Disease

Jinkuk Kim, Ph.D., Chunguang Hu, M.D., Ph.D., Christelle Moufawad El Achkar, M.D., Lauren E. Black, Ph.D., Julie Douville, Ph.D., Austin Larson, M.D., Mary K. Pendergast, J.D., Sara F. Goldkind, M.D., Eunjung A. Lee, Ph.D., Ashley Kuniholm, B.S., Aubrie Soucy, B.A., Jai Vaze, B.A., et al.

Article Figures/Media Metrics

October 9, 2019
DOI: 10.1056/NEJMoa1813279

Summary

Genome sequencing is often pivotal in the diagnosis of rare diseases, but many of these conditions lack specific treatments. We describe how molecular diagnosis of a rare, fatal neurodegenerative condition led to the rational design, testing, and manufacture of milasen, a splice-modulating antisense oligonucleotide drug tailored to a particular patient. Proof-of-concept experiments in cell lines from the patient served as the basis for launching an "N-of-1" study of milasen within 1 year after first contact with the patient. There were no serious adverse events, and treatment was associated with objective reduction in seizures (determined by electroencephalography and parental reporting). This study offers a possible template for the rapid development of patient-customized treatments. (Funded by Mila's Miracle Foundation and others.)

Although very technical, this article illustrates how one genetic disease was significantly improved from bench research to clinical usefulness in one year! Unheard of until now. Hope is on the horizon!

Join Natasha Lowery, President

LGMD-1D DNAJB6 Foundation and Registry

for the

TREAT-NMD Conference

Amsterdam December 9-11, 2019

An International Conference for Neuro-Muscular Disease

New Links

International registry links for our foundation:

1. https://rarediseases.org/organizations/lgmd-1d-dnajb6-foundation-and-international-registry/
2. https://lgmd-info.org/organizations/

Find us on these sites if you have membership:

1. **Research Gate:** https://www.researchgate.net
2. **LinkedIn:** https://www.linkedin.com
3. **FaceBook:** https://www.facebook.com/LGMD.1D
4. **Our website:** www.lgmd1d.org **(a registered Facebook Giving Tuesday Affiliate, YOUR DONATIONS ARE MATCHED ON FACEBOOK but only on 12/3/19 starting at 8 am EST)**

Stay Involved!

How do my donations help?

Patients suffering from LGMD1 and all autosomal dominant muscular dystrophies require special needs to travel for research and therapy. In addition, organizing the relatively small numbers of autosomal dominant muscular dystrophies worldwide requires financial support to maintain a registry that will connect the urgent needs of patients with the exploding pace of genetic research and cures. Your donations help, not only defray the cost to the most needy of persons in the LGMD1 and autosomal dominant community, but also to propel our international registry to help even more who languish in underserved areas. We represent the tip of the iceberg for many more people with other orphan genetic diseases who will benefit from the explosion in genetic research.

There are many ways to donate:

1. **Use Amazon Smile and list the LGMD-1D DNAJB6 Foundation for donation with each purchase at no cost to you.**
2. **Please help us on "Giving Tuesday"**
   Tuesday December 3rd, starting 8 an EST.
   EACH DONATION IS MATCHED!!
   See our donation site on: FACEBOOK.
3. **Or donate by our secure site on:**
   PAYPAL or CREDIT CARD!!
4. **Contact me for foundation or registry interests:**
   wslowery.57@lgmd1d.org , WWW.LGMD1D.ORG

Together we will make a difference! Again thank you for for time and generosity.

William S Lowery M.D.