LGMD-1D DNAJB6 Foundation

and

MYOSYND™

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6/9/2022

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MDA Conference Summary

March 13-16, 2022

The 2022 MDA conference was a hybrid virtual event which was fortunate for most of us who find it hard to travel. The organizers listed their post event statistics:

- **1028 in-person attendees from 15 countries**
- **675 virtual live-stream attendees (and counting) from 16 countries**
- **32 sessions with one full day of clinical trial updates**
- **Over 120 Speakers**
- **Over 150 Posters**
- **Over 30 Exhibitors**
- **10 Industry Forums**
- **Over 100 Virtual Posters**
- **Over 40 Virtual Exhibits**

There was so much material on all varieties of muscular dystrophy that I became saturated but the 10,000 foot view was what I took away as most important. First the most common forms of muscular dystrophy are receiving the most research in genetic therapy which is not surprising. CRISPR editing, anti -sense oligonucleotides and small molecule therapies are exploding in all forms of muscular dystrophy and let me emphasize that this includes autosomal dominant, autosomal recessive and X linked disorders. Eventually no one will be left out. Second, on a micro level, an exciting area of research is gene delivery to muscle tissue which is becoming more targeted and efficient so less payload is needed to achieve clinical improvement (and less side effects).

MDA Conference Summary

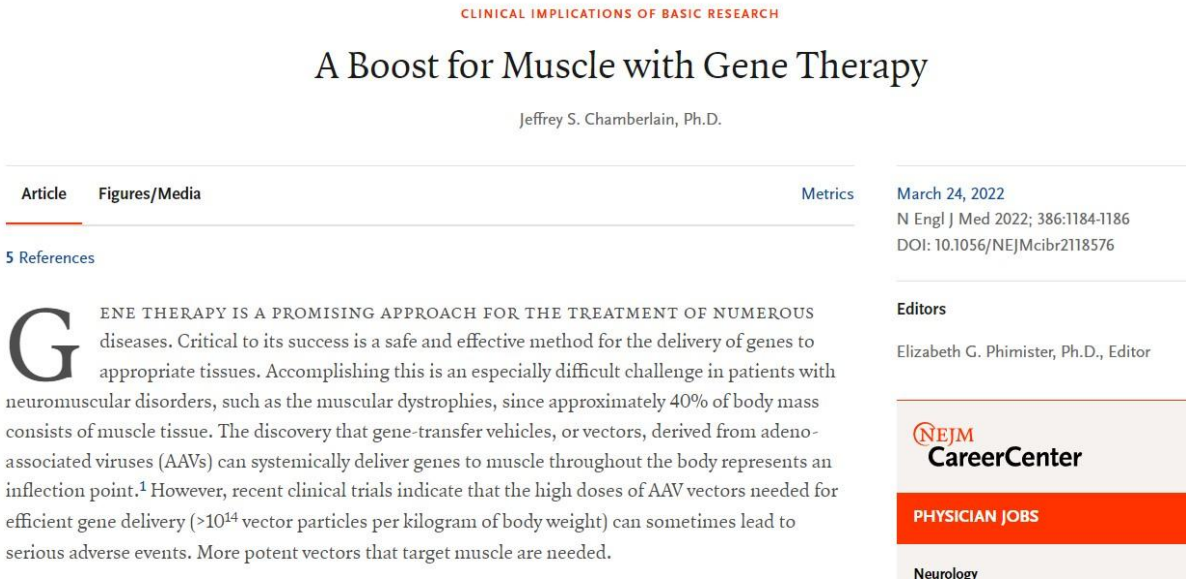
Finally, there were earnest sessions on "variants of uncertain significance" (VUS) and their resolution to a genetic diagnosis. There are currently large groups of scientists working through a collaboration to resolve each genetic variant not only in LGMD but multiple genetic disorders. These efforts are under the ClinGen working groups (see the neuromuscular group HERE) . They provide a patient portal called GenomeConnect.

To reflect on the progress being made I have to feel optimistic although all this takes time. The early trials are not without problems, setbacks and side effects. For a lot of autosomal dominant and rare forms of LGMD, which will eventually have some form of gene therapy, these issues will have been worked out and like some of the current gene therapies it will be a 30 minute infusion and off we'll go. Let's look on the bright side, do you really want version 1.0?

See the New England Journal of Medicine excerpt below (please use your enlarge function in the right upper corner of your browser to be able to read the small print, the tiny 3 dots)

New England Journal of Medicine

March 2022



CLINICAL IMPLICATIONS OF BASIC RESEARCH

A Boost for Muscle with Gene Therapy

Jeffrey S. Chamberlain, Ph.D.

Article Figures/Media Metrics

5 References

GENE THERAPY IS A PROMISING APPROACH FOR THE TREATMENT OF NUMEROUS diseases. Critical to its success is a safe and effective method for the delivery of genes to appropriate tissues. Accomplishing this is an especially difficult challenge in patients with neuromuscular disorders, such as the muscular dystrophies, since approximately 40% of body mass consists of muscle tissue. The discovery that gene-transfer vehicles, or vectors, derived from adeno-associated viruses (AAVs) can systemically deliver genes to muscle throughout the body represents an inflection point.[1] However, recent clinical trials indicate that the high doses of AAV vectors needed for efficient gene delivery (>10^{14} vector particles per kilogram of body weight) can sometimes lead to serious adverse events. More potent vectors that target muscle are needed.

March 24, 2022
N Engl J Med 2022; 386:1184-1186
DOI: 10.1056/NEJMcibr2118576

Editors

Elizabeth G. Phimister, Ph.D., Editor

NEJM CareerCenter

PHYSICIAN JOBS

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Conclusion:

Dose-escalation studies of the new vectors have not revealed any clear toxic or immune-related side effects. Consequently, it is likely they will be advanced into clinical trials. If the delivery profile of the new vectors in humans is similar to that in macaques, this approach could transform current genetic therapies involving muscle by enabling the use of lower doses or perhaps by allowing increased gene delivery and efficacy at currently used doses.

Links Update

Since our inception in 2018 I have collected links to help everyone's journey. Due to the onboarding of new members and new links I am adding this as a recurrent list to our newsletter.

LGMD1D DNAJB6 Foundation

LGMD1D Foundation YouTube Archive

LGMD1D Foundation assisted sponsored genetic testing

LGMD1D Foundation Autosomal Dominant Registry

LGMD1D Foundation VUS tips

Sponsored Whole Genome Sequencing: (next step for VUS resolution)

NIH

Harvard

Are You Having a Muscle Biopsy?

Tissue referral to University of Iowa

University of Iowa Muscle Biopsy Requisition

Do I really have a genetic muscle disorder or is it something else!?

See HERE

Links Update

LGMD nomenclature

Gene matching sites:

MyGene2

GenomeConnect

Rare-X

Upcoming Events

LGMD Awareness Foundation Calendar 2022

Speak Foundation FaceBook 2022

Giving

1. **OUR WEBSITE** **(a secure site with all the listings below)**
2. **AMAZON SMILE** **(list the LGMD-1D DNAJB6 Foundation for donation with each purchase at no cost to you.)**
3. **PAYPAL** **(Our foundation's secure site)**
4. **CREDIT CARD** **(Network For Good credit card portal)**
5. **VENMO** **(@lgmd1d) Foundation Account**
6. **EVERY.ORG** **(ALL CRYPTO CURRENCIES)**
7. **SQUARE**
8. **If you are over 72 consider a Qualified Charitable Distribution (QCD) from a traditional IRA and lower that dreadful RMD and avoid that higher tax bracket. Also available to Roth IRA participants.**

   RMD calculator HERE, medicare income bracket HERE.
   tax bracket for SS HERE.

Thank you for your support and all the best from us!

William Lowery MD