Vol 3 / Issue 2

# LGMD News

Uniting the Limb-Girdle Muscular Dystrophy Community

## PARENTING WITH LGMD
Having a Family Is Not "Off Limits" Simply Due to a Diagnosis of LGMD

## GENETICS OF LGMD AND FAMILY PLANNING
Understanding the Genetics and Inheritance of LGMD Can Be an Important Part of Making Informed Family Planning Decisions

## ML BIO SOLUTIONS
Substrate Supplementation Therapy as a Potential Treatment for LGMD R9/2I

## GENE THERAPY 101
Part Two of Sarepta Therapeutics' Educational Series

## ADOPTION & SURROGACY
More Than One Way to Grow a Family

## Parenting Children with Muscular Dystrophy

Three Parents Share Their Children's Journeys to Diagnosis and Beyond as They Continue to Live Life to the Fullest

**ML Bio Solutions is developing an oral therapy for Limb-Girdle Muscular Dystrophy Type 2I (LGMD2I/LGMDR9).**

Information about our Phase 3 study will soon be available on **www.clinicaltrials.gov** and at **www.mlbiosolutions.com** and will be shared with LGMD patient advocacy organizations.

Scan to visit our website.

ML Bio Solutions (ML Bio) is a biotechnology company founded by a family whose child was diagnosed with LGMD2I. ML Bio Solutions is a member of the BridgeBio family — a team of experienced drug discoverers, developers, and innovators working to create life-altering medicines that target genetic diseases.

mlbiosolutions.com
info@mlbiosolutions.com

ML BioSolutions
a bridgebio company

LGMD News

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## How To Donate

Visit **TheSpeakFoundation.com** and select "Donate" to support our mission and programs. The Speak Foundation is a 501(c)(3) nonprofit charity. All donations are secure and tax deductible.

*Thank you for your support!*

**The Speak Foundation**
Uniting the entire LGMD community to make a difference together in future treatments for this rare disease.

The origin of The Speak Foundation's name comes from Proverbs 31:8. It is, "Speak up for those who have no voice." Living with a rare disease means many of us wait years to have a voice in areas that impact our daily lives. The Speak Foundation helps our voices to be heard.



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## Departments



## Feature Articles









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# Education is Key

*It is our aim at the Speak Foundation to continue to share with you the latest information on this type of progress so that you remain informed.*

**This is an incredibly exciting time** for the LGMD community as there are multiple companies announcing plans for current or future clinical trials.

The following companies either currently have or are planning future clinical trials for LGMD: Ask Bio, Atamyo, Edgewise Therapeutics, ML Bio Solutions, Myogenica, Sarepta Therapeutics, and Vita Therapeutics. It is our aim at the Speak Foundation to continue to share with you the latest information on this type of progress so that you remain informed.

One related topic that we want to share is the importance of lead-in studies for clinical trials. A lead-in study typically identifies individuals living with a particular subtype and follows the natural history of the disease. At the Speak Foundation, we want to reiterate the value of participation in such studies, as they can provide you with access to world-class oversight from experienced clinicians. Additionally, the centers that house these natural history studies are often the sites of future clinical trials. While participation in a lead-in study does not guarantee that you will go on to receive an investigational drug, you may be more likely to be considered for a clinical trial if the progression of your condition has been monitored in a lead-in study.

Remaining informed is critical. That is why you will hear some very important updates at the 2023 International LGMD Conference, which will be held in person in Washington, D.C., October 27–29, 2023. Through this event, we will highlight the work of top researchers in the field of LGMD. Attendees will also hear from industry and clinicians on the trials that we hope will help bring treatments to patients. Registration opens April 5 so be sure to save the date!

Thank you all for your support. If you are interested in donating to our efforts so that we can continue to provide events like the International LGMD Conference and resources such as *LGMD News* magazine, please reach out to one of our coordinators at ***ContactUs@TheSpeakFoundation.com***. Your help is vital for us to continue our work. ▪

Kat Bryant Knudson

**Kathryn Bryant Knudson**
Editor In Chief
Founder & CEO, The Speak Foundation

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## Our Mission

**The Speak Foundation** was based on the principle of "Speak up for those who have no voice." *Speak up for those who cannot speak for themselves.* —Proverbs 31:8

***LGMD News*** is a program of the Speak Foundation. In order to help individuals and families living with limb-girdle muscular dystrophy receive critical and life-saving information, the Speak Foundation began publishing this resource in 2021.

# International Consortium of LGMD Organizations

## United States

**The Speak Foundation**
*Uniting the entire LGMD community*
TheSpeakFoundation.com

**Beyond Labels & Limitations**
*Funding research for LGMD R1/2A and educating on its disease course*
BeyondLabelsLimitations.com

**Breathe with MD**
*Educating and raising awareness about breathing muscle weakness in neuromuscular disease*
BreatheWithMD.org

**CamronsCure**
*Funding research for LGMD R19/2S*
CamronsCure.com

**Coalition to Cure Calpain 3**
*Funding research for LGMD R1/2A*
CureCalpain3.org

**Cure LGMD2I**
*Funding research for LGMD R9/2I*
CureLGMD2I.org

**Kurt + Peter Foundation**
*Funding research for LGMD R5/2C*
KurtPeterFoundation.org

**LGMD Awareness Foundation**
*Join us for LGMD Awareness Day*
LGMD-Info.org

**LGMD-1D DNAJB6 Foundation**
*Representing LGMD D1/1D and DNAJB6 subgroup*
LGMD1D.org

**LGMD2D Foundation**
*Funding research for LGMD R3/2D and educating patients and physicians*
LGMD2D.org

**LGMD2I Research Fund**
*Funding research for LGMD R9/2I and educating the patient community*
LGMD2IFund.org

**LGMD2L Foundation**
*Representing the LGMD R12/2L Anoctamin5-related community*
LGMD2L-Foundation.org

**Team Titin**
*A consortium of scientists and affected community members for LGMD R10/2J Titin-related*
TitinMyopathy.com

**The Jain Foundation**
*Funding research for LGMD R2/2B and educating the patient community*
Jain-Foundation.org

## Argentina

**ADM Argentina Muscular Dystrophy LGMD Group**
*Funding research for neuromuscular diseases*
ADM.org.ar

## Australia

**Daniel Ferguson LGMD2A Foundation**
*Funding research for LGMD R1/2A and educating the patient community*
DFFoundation.com.au

## France

**"GI LGMD"/LGMD Patient Group of AFM-Telethon**
*Focusing on all subtypes of LGMD, supporting research and educating the patient community*
LGMD.AFM-Telethon.fr

## Italy

**Conquistando Escalones Association**
*Funding research for LGMD D2/1F*
ConquistandoEscalones.org

**"GFB ONLUS"/ Family Group of Beta-Sarcoglycanopathy**
*Representing the LGMD R5/2C Gamma Sarcoglycan-related, LGMD R3/2D Alpha Sarcoglycan-related, LGMD R4/2E Bèta-Sarcoglycan-related, and LGMD R6/2F Delta-Sarcoglycan-related communities*
Beta-Sarcoglicanopathy.org

**Gruppo Cingoli of UILDM – Unione Italiana Lotta alla Distrofia Muscolare**
*Focusing on all subtypes of LGMD, raising awareness and providing support for the entire Italian community*
UILDM.org

**Italian Association Calpain 3**
*Funding research for the LGMD R1/2A Calpain 3-related community*
AICA3.org

## Japan

**Patients' Association for Dysferlinopathy Japan**
*Representing the Japanese and International LGMD R2/2B Dysferlin-related and Miyoshi Muscular Dystrophy 1 (MMD) communities*
PADJ.jp/index.html

## Netherlands

**Stichting Spierkracht**
*Raising awareness and supporting the LGMD R3/2D Alpha Sarcoglycan-related community*
StichtingSpierkracht.com

## Spain

**Conquistando Escalones Association**
*Funding research for LGMD D2/1F*
ConquistandoEscalones.org

**Proyecto Alpha**
*Funding research for LGMD R5/2C Gamma Sarcoglycan-related, LGMD R3/2D Alpha Sarcoglycan-related, LGMD R4/2E Bèta-Sarcoglycan-related, and LGMD R6/2F Delta-Sarcoglycan-related*
ProyectoAlpha.org


# Jerry R. Mendell, MD

*Nationwide Children's Hospital*


## Meet the Expert

**Jerry R. Mendell, MD** is a clinician-scientist with decades of experience studying and treating limb-girdles. Currently, Dr. Mendell is an attending neurologist at Nationwide Children's Hospital, the Dwight E. Peters and Juanita R. Curran Endowed Chair in Pediatric Research at the Abigail Wexner Research Institute at Nationwide Children's Hospital, and Professor of Pediatrics and Neurology at Nationwide Children's and The Ohio State University. He was the PI on the first gene therapy trials for DMD and LGMD and was the PI on the SMA gene therapy trial that was FDA-approved for systemic delivery for infants with SMA Type 1 in 2017. His life's work has emphasized clinical translation. Dr. Mendell has published more than 400 articles with a focus on neuromuscular disease and authored books on muscle disease, peripheral nerve disorders, and most recently, gene therapy for muscle disease.



## Q

**My daughter has LGMD R1/2A. She is self-conscious about her feet being purple and cold. She has tried compression socks, but they are very hard for her to get on. Is there anything else you can recommend to help?**

## A

The color change of purple accompanied by cold temperature usually means blood supply is compromised. There are many possibilities. It is not usually expected in LGMD R1/2A, although an unrelated cause could be made worse by muscular dystrophy. For example, there could be muscle atrophy of front lower leg muscles (tibiales) that reduce blood flow to the extremity. I would also be concerned about unrelated vascular insufficiency. A well-known condition called Raynaud's disease or syndrome causes vasoconstriction of the blood vessels in the hands and feet leading to decreased blood supply, low oxygen levels, and the blue/purple/white discoloration. There are other conditions like diabetes and peripheral arterial disease that restrict blood flow. For this type of change, it is best to consult your doctor or a rheumatologist. The condition can be treated by medications that increase extremity blood flow including calcium channel blockers and angiotensin-receptor blockers.

## Q

**How does exercise impact muscle loss and damage? I feel little or no exercise would cause atrophy, but I understand exercising can damage existing muscle. How much/what type of exercise is good, yet not damaging?**

## A

This is always a challenging question. You are right that too much exercise can cause a condition of significant muscle breakdown called rhabdomyolysis. This happens most often in the muscular dystrophies where the membrane of the muscle, as the surrounding (protective) coat, is damaged and lets in fluids and cells that will damage the muscle fiber. The forms of muscular dystrophy most vulnerable include Duchenne and many of the limb-girdles, especially the sarcoglycans (LGMD R3/2D, R4/2E, R5/2C, R6/2F). In some cases, the first sign of the disease is brown-colored urine caused by the breakdown of muscle myoglobin that escapes from the muscle fiber through the blood stream to the kidney. Appropriate, not too stressful forms of exercise include stretching, yoga or yoga-like positions, range of motion, and even gentle bike riding. Keep your muscles limber. You can use the swimming pool to passively exercise by treading water or holding onto the edge and gently kicking the legs. Weightlifting, contact sports, and efforts to win a physical competition should be avoided.

## Q

**Do you think there will be further advancements for trials or treatments of LGMD R3/2D in 2023?**

## A

The way our clinical trials are moving forward, I am very optimistic that LGMD R3/2D will respond to gene therapy. There have been very good results in the LGMD R4/2E trial (beta-sarcoglycan gene replacement), making it likely that other sarcoglycans, like alpha-sarcoglycan (deficient in LGMD R3/2D), will respond to gene replacement. The path has been established, and I suspect that we are looking down the road a year or so. I think we are in good shape to have this move from the bench to the clinic. The exact time-frame depends on a collaborative effort between the Nationwide Children's Hospital (NCH) or other Gene Therapy Centers and Sarepta, our industry partners. Further advancements on the horizon will happen reasonably soon. I hope that we can help all patients with this, and subsequently all forms of LGMD soon.

## Q

**If a treatment, such as gene therapy, is developed for a particular LGMD subtype, do you anticipate that it will pave the way for finding treatments for other subtypes? Can advancements in therapy within one subtype also apply to other subtypes?**

## A

The entire field of gene therapy is very young, so efficacy in any type of muscular dystrophy will affect the entire field. The closer one form of LGMD is biologically related to another form, the more it will influence the related variety. The best example is the sarcoglycan complex (alpha, LGMD R3/2D; beta, LGMD R4/2E; gamma, LGMD R5/2C; and delta, LGMD R6/2F). These four proteins are all part of the same complex. The current success in gene transfer of beta will apply to the other sarcoglycans because of considerations such as the similar size of the gene involved, the delivery, and dosing. Having said that, the safety and dosing of even unrelated LGMD-related proteins like calpain (CAPN3) are more likely to be considered for clinical trials because of LGMD R4/2E successes.

## Q

**What advice do you have for patients regarding day-to-day self-care that will most likely support muscle maintenance while awaiting medical treatments such as gene therapy?**

## A

As your question suggests, we are optimistic that gene therapy will be successful for LGMDs. The LGMD R4/2E clinical trials demonstrate a favorable response. The best thing to do to maintain muscles while waiting for treatments is to remain active. Not to overdo activities, but maintain muscle tone and prevent muscle atrophy by stretching and range of motion exercises. A gentle swimming or yoga program is an excellent choice. I also recommend a well-balanced diet, not overloaded with carbohydrates or fatty foods, but balanced with high protein foods like poultry, beans, dairy products, eggs, and nuts. ■

*The entire field of gene therapy is very young, so efficacy in any type of muscular dystrophy will affect the entire field. The closer one form of LGMD is biologically related to another form, the more it will influence the related variety.*

**Have a Question for Our Experts?**

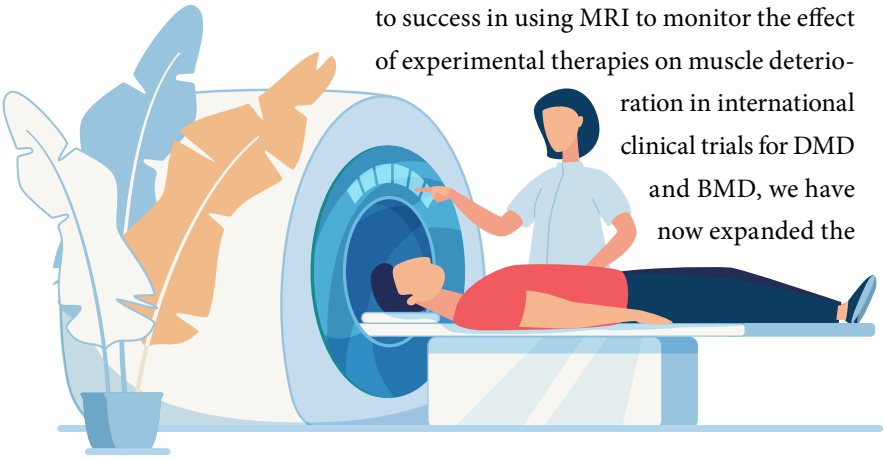
Send Questions To:
ContactUs@TheSpeakFoundation.com

# Seeing Muscle Changes from Within

*One of the proudest achievements of my career has been to see research that we started in mice progress to its implementation in individuals living with muscular dystrophy, and ultimately help accelerate therapeutic development in muscular dystrophies.*

**More than 25 years ago,** Krista Vandenborne and I set out to determine if MRI could be used to assess muscle damage and regeneration. Clearly there was then, and there is still today, an unmet clinical need to find noninvasive biomarkers for the muscular dystrophies. We have made it our life's passion to develop these measures so that they can be used in clinical trials. In our initial work with Lee Sweeney at the University of Pennsylvania, we found that MRI could be used to detect muscle improvement and correction in preclinical animal models of LGMD and Duchenne muscular dystrophy (DMD). Others were able to later build upon this work for treatment of LGMD in preclinical models and for evaluating microdystrophin gene therapy in mouse models of DMD.

Through generous support from the National Institutes of Health, Parent Project Muscular Dystrophy, and the Muscular Dystrophy Association, these preclinical findings were translated to and implemented in people living with DMD, Becker Muscular Dystrophy (BMD), Congenital Muscular Dystrophy, and LGMD through the ImagingDMD consortium and Senator Paul D. Wellstone Muscular Dystrophy Specialized Research Center. Due to success in using MRI to monitor the effect of experimental therapies on muscle deterioration in international clinical trials for DMD and BMD, we have now expanded the use of these MRI biomarkers to other forms of muscular dystrophies.



As in DMD and BMD, the muscles in people living with LGMD are progressively replaced by fatty tissue. However, the pattern of muscle involvement, rate of progression, and cause of pathology is different in LGMD, and our team is developing the most optimal biomarker for LGMD. In collaboration with the GRASP-LGMD Consortium, we are tracking a number of MRI biomarkers in combination with measures of muscle function to examine how MRI measurements relate to and predict changes in strength and mobility in patients with BMD, LGMD R9/2I, and LGMD R1/2A.

My research program has been shaped and positively impacted by discussions with people living with LGMD R1/2A. One patient with LGMD R1/2A reported he is able to walk well, until the muscles on the front of his lower legs (the dorsiflexors) get tired, which is when he trips and falls. This opened our eyes to consider the importance of muscle fatigue and not just muscle mass.

In building upon this concept as part of our Wellstone Center, we are investigating whether muscle bioenergetics/mitochondrial function in the dorsiflexor muscles of people living with LGMD R1/2A is also impacted by the disease and how to best quantify this. One of the proudest achievements of my career has been to see research that we started in mice progress to its implementation in individuals living with muscular dystrophy, and ultimately help accelerate therapeutic development in muscular dystrophies. ■

**Written by** Glenn Walter, PhD
*College of Medicine at the University of Florida*

UPDATED: APRIL 1, 2023

# GRASP-LGMD Natural History Studies

## Recruiting Defining Clinical Endpoints in Limb-Girdle Muscular Dystrophy (LGMD) (GRASP-01-001)

### Inclusion Criteria

- Ages 4–65
- Clinically affected (defined as weakness on bedside evaluation in either a limb-girdle pattern or in a distal extremity)
- Genetic confirmation of one of the LGMD subtypes listed below

### Exclusion Criteria

- Any other illness that interferes with subject safety or data integrity
- Positive pregnancy test at any timepoint of the study

**Note:** Each subtype will enroll 80% of subjects who are able to walk 10m independently in 12 second or less. Twenty percent will be subjects who ambulate more slowly or not at all.

### Subtypes

- CAPN3 (LGMD R1/2A)
- DYSF (LGMD R2/2B)
- DNAJB6 (LGMD D1/1D)
- Sarcoglycan (LGMD R3/2D, LGMD R4/2E, LGMD R5/2C, LGMD R6/2F)

## Recruiting Defining Endpoints in Becker Muscular Dystrophy (GRASP-01-002)

### Inclusion Criteria

- Ages 8 and older
- Clinically affected (defined as weakness on bedside evaluation consistent with BMD)
- Genetic confirmation of a dystrophin mutation

### Exclusion Criteria

- >16 hours of ventilatory support
- Any other illness that interferes with subject safety or data integrity

**Note:** Subjects ages 8-16 must be ambulatory and their dystrophin mutation must be in-frame.

**Note:** Subjects 17 and older may be non-ambulatory, but must not have lost ambulation prior to the age of 16.

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# GRASP-LGMD Consortium Members

- **Urvi Desai**, MD | Atrium Health
- **Jordi Diaz-Manera**, MD, PhD | Newcastle University
- **Vijay Ganesh**, MD, PhD | Brigham and Women's Hospital
- **Meredith James** | Newcastle University
- **Nicholas Johnson**, MD, MSci, FAAN | Virginia Commonwealth University
- **Peter B. Kang**, MD | University of Minnesota Medical School
- **Monkol Lek**, PhD | Yale University, Non-Clinical Site
- **Doris Leung**, MD, PhD | Hugo W. Moser Research Institute at Kennedy Krieger
- **Linda P. Lowes**, PT, PhD | The Research Institute at Nationwide Children's Hospital
- **Katherine Mathews**, MD | University of Iowa
- **Tahseen Mozaffar**, MD, FAAN | University of California Irvine
- **Jeffrey M. Statland**, MD | University of Kansas Medical Center Research Institute, Inc.
- **Volker Straub**, MD, PhD | Newcastle University
- **John Vissing**, MD | University of Copenhagen
- **Glenn Walter**, PhD | University of Florida
- **Conrad "Chris" Weihl**, MD, PhD | Washington University in St. Louis
- **Matthew Wicklund**, MD | University of Colorado Denver

## Spotlight: Dr. Glenn Walter

College of Medicine at the University of Florida

**Dr. Glenn Walter** is the Vice Chair and Professor in the department of Physiology and Aging in the College of Medicine at the University of Florida. Dr. Walter's research expertise is in the area of noninvasive measurement of muscle plasticity and viral modification of gene expression in adult skeletal muscle. His research focus is on the development of both optical and magnetic resonance methods to monitor changes in both cardiac and skeletal muscle gene expression during disease progression in neuromuscular diseases and the potential of gene therapy to prevent myopathy and muscle wasting. Dr. Walter has developed noninvasive techniques to measure blood flow, muscle damage, mitochondrial function, and foreign gene expression in muscle. Dr. Walter's research is funded by NIH (NIAMS).

# Gene Therapy 101

Produced by
Sarepta Therapeutics

Sarepta Therapeutics is a biotech company headquartered in Cambridge, Massachusetts. We have over 20 gene therapy programs in development, including for limb-girdle muscular dystrophy types 2E/R4, 2D/R3, 2C/R5, 2B/R2, 2L/R12, and 2A/R1.

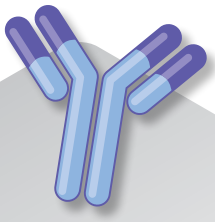
## Due to its potential to treat serious diseases, gene therapy is the focus of much scientific research.

Learning more about gene therapy science will help individuals have informed discussions with their doctors.

Gene therapies have unique features which may affect who is eligible for treatment.

**Certain tests may help clarify eligibility for gene therapy clinical trials or treatment. Tests that may be required include:**

**Genetic testing**
that confirms the disease diagnosis



**Antibody testing**
to confirm that the body doesn't have elevated antibodies that recognize the gene therapy vector


**Sarepta is committed to providing educational resources to rare disease communities to improve understanding of this investigational treatment approach.**

In case you missed it, in Chapter 1, we explored the goal of gene therapy and how it's intended to work. Check out the January 2023 issue of the *LGMD News Magazine* or contact us at Advocacy@Sarepta.com

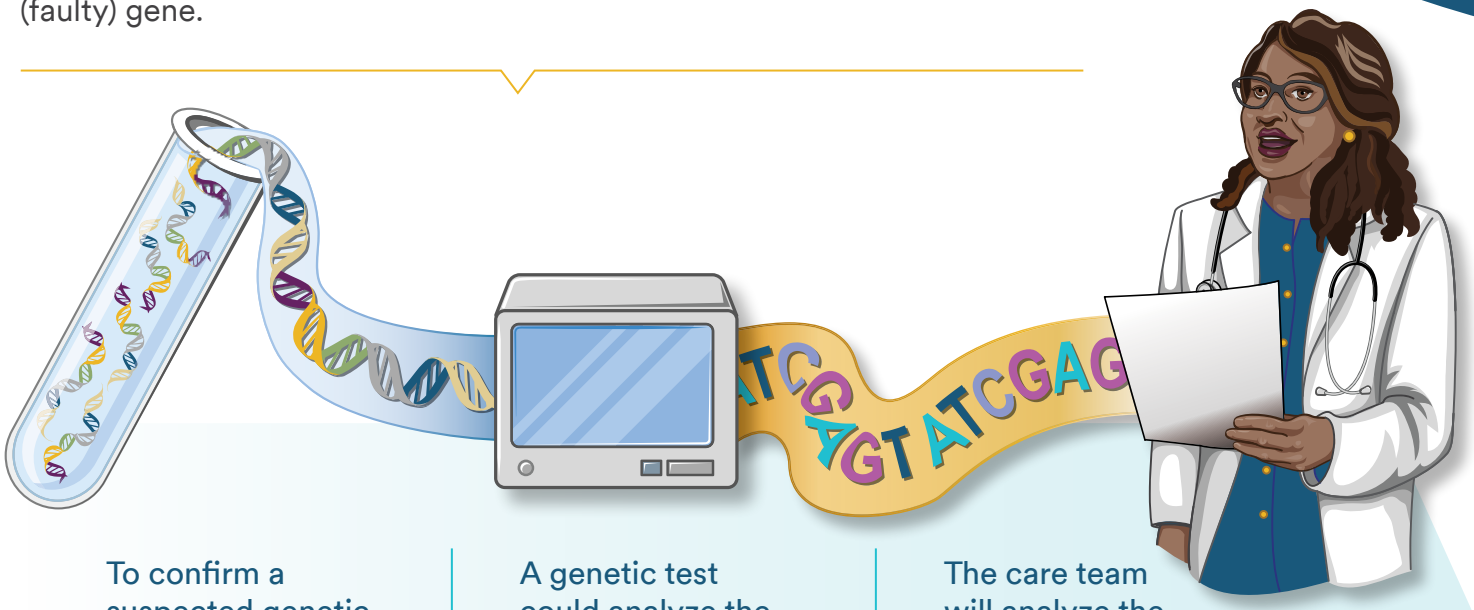
Intended for US audiences

# Why is genetic testing important for gene therapy?

CHAPTER 2

OF A FOUR-PART SERIES

There are different ways that a doctor may diagnose a disease. However, genetic testing is required to determine if a disease is caused by a mutated (faulty) gene.




To confirm a suspected genetic muscle disease, a person may have to give a DNA sample, usually via blood or saliva.

A genetic test could analyze the sequences of dozens of muscle-related genes (DNA).

The care team will analyze the sequencing results and will determine if the person has a genetic diagnosis.

**Gene therapy is intended to address the underlying cause of a genetic disease. Therefore, it is necessary to confirm a diagnosis through genetic testing to determine if a gene therapy may be appropriate.**

**Several programs in the US offer free genetic testing for LGMD and other muscle diseases.**
**Learn more at limbgirdle.com/genetic-testing**

SAREPTA THERAPEUTICS

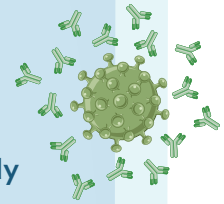
SPONSORED CONTENT

# What are antibodies and why do they matter to gene therapy?

## First, some background about antibodies:

Antibody

- Antibodies are an important part of the immune system, which aim to protect the body from foreign invaders, like viruses
- When a person has a virus, the immune system may help them recover, in part by developing antibodies that specifically try to fight it

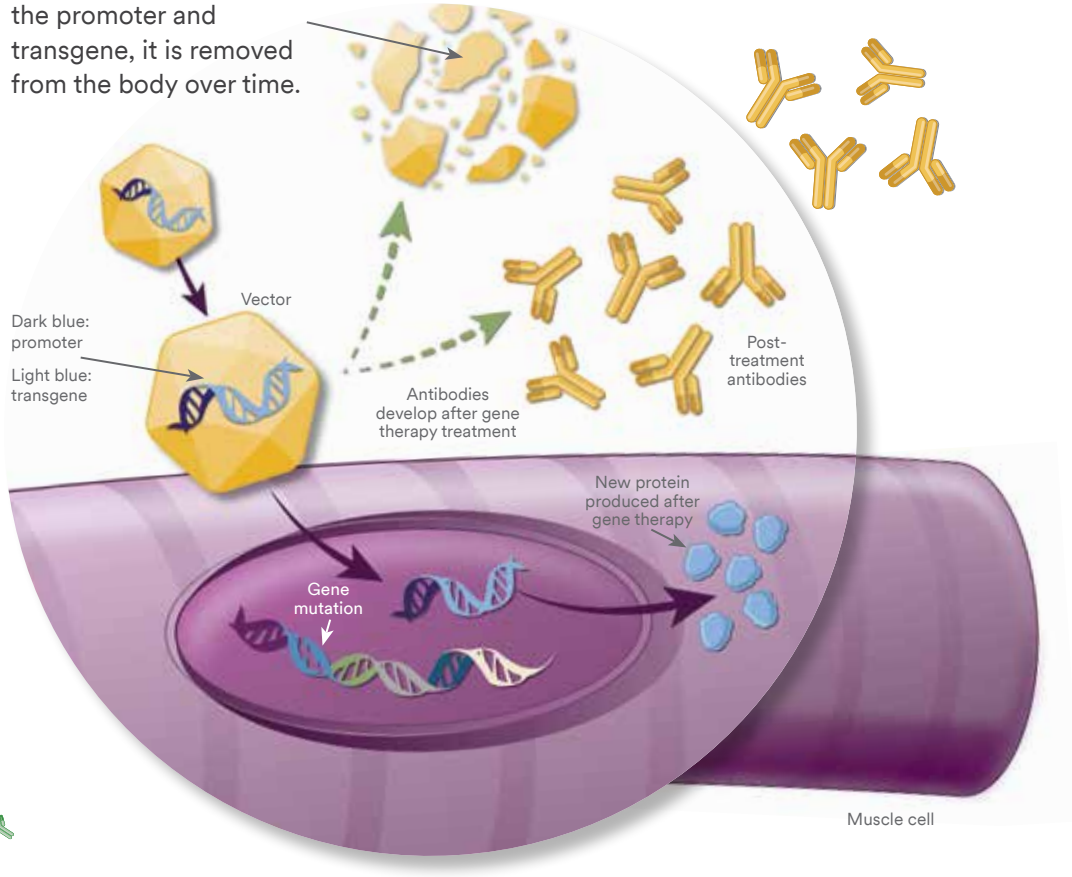


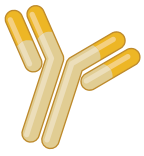
- Antibodies can exist in the body for a long time. This could help the body fight the same or similar virus if it is infected again

## Antibodies form after vector exposure

The vector aims to deliver the promoter and transgene to the target cell, with the goal of producing a new protein that may slow the disease progression.

After the vector delivers the promoter and transgene, it is removed from the body over time.



**After gene therapy, the body will produce antibodies that recognize the vector. For this reason, gene therapy is currently a one-time treatment.**

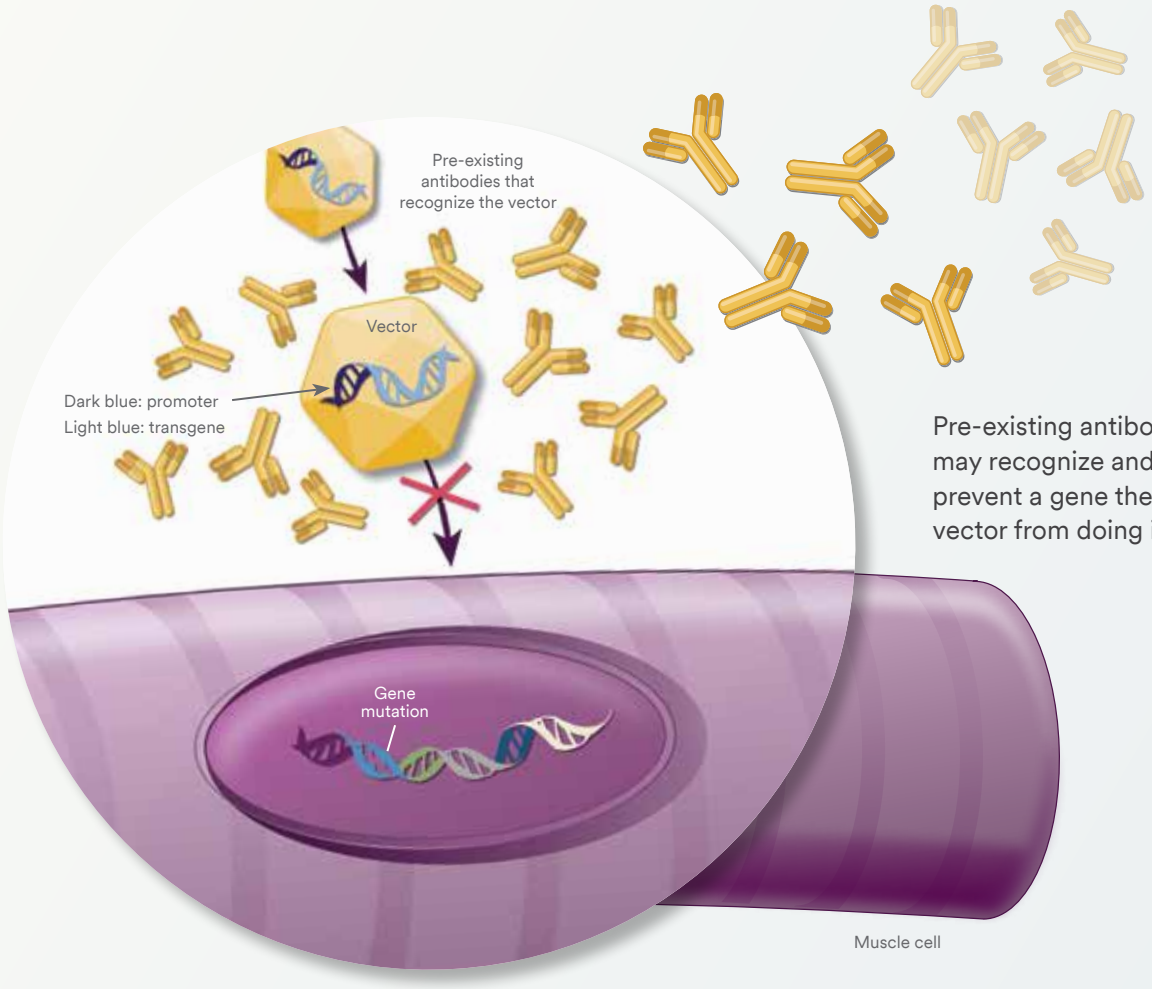
Intended for US audiences

SAREPTA THERAPEUTICS

## Even if a person has never received a gene therapy before, they might have pre-existing antibodies that recognize the vector.

This could happen if they were exposed naturally to viruses similar to the gene therapy vector. Some viruses naturally present in the environment are similar to vectors used in gene therapy.

## Pre-existing antibodies could prevent gene therapy from working as intended




Pre-existing antibodies may recognize and prevent a gene therapy vector from doing its job.

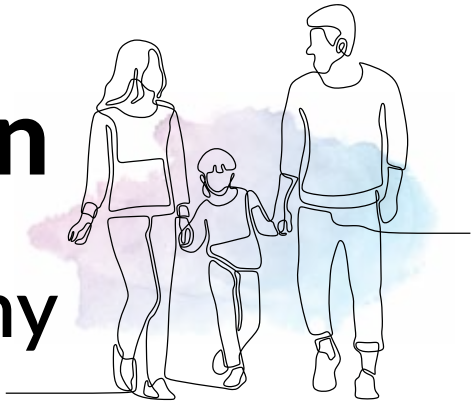
**Pre-existing antibodies that recognize the vector may prevent a gene therapy from working as intended. Therefore, antibody testing is an important part of determining eligibility.**

### Want to test your knowledge?

**Scan the QR code to take a short gene therapy quiz on limbgirdle.com**
**If you have questions or comments for us, email us at Advocacy@Sarepta.com**

By Rachel DeConti • Brooke Saalman • Oriol Fuster

# Parenting Children with Muscular Dystrophy



When a child in your family is diagnosed with muscular dystrophy, it can feel like the world stops as you come to grips with a new normal. Three parents share their children's journeys to diagnosis and beyond, as they continue to live life to the fullest despite the many challenges of being affected by muscle-wasting conditions.

## Rachel DeConti

**Mother of Son, Jacob (6), LGMD R3/2D**

In July of 2021, our son Jacob was riding his scooter with friends. He fell off and was crying at one point, but then started playing again. When we took him inside and got him ready for his bath, we noticed his urine was a dark brown color. Of course, we were alarmed thinking he was hurt internally from the fall. My husband took him to Connecticut Children's Medical Center (CCMC) for scans, x-rays, and tests. Fortunately, all his scans came back normal. But what was uncovered through a blood test was that his creatine kinase (CK) was over 75,000! We were told he had a case of rhabdomyolysis, so he remained at the hospital for three nights to receive IV hydration to bring the levels down. After more tests, and another short hospital stay, the doctors recommended we do genetic testing that included muscular dystrophy. In late August, we received a call from the doctor that his results confirmed limb-girdle muscular dystrophy type R3/2D.

During Jacob's second stay, the doctors referred us to neurology. Dr. Gyula Ascadi, head of neurology, has been one of his core doctors since, and a wonderful support for us locally. There are many times we've reached out with questions or concerns and his quick response has been so helpful to us.

Once Jacob was diagnosed, we became aware of the current *Journey* natural history study. We ultimately joined and chose Nationwide Children's Hospital in Columbus, OH, as our site location after learning of their amazing doctors, many with years of experience and focus on LGMDs. Through this study, Jacob is now followed twice a year by an incredible team, which includes

Jacob DeConti

Jacob with Dr. Jerry Mendell

> ***Don't give up! We can't. We are our children's main advocates, and they need us to push the progress of treatment for them.***
> *–Rachel DeConti*

Dr. Jerry Mendell. This gives us reassurance and peace of mind that Jacob is receiving the best care possible.

Jacob, being six years old, is very active and always on the go. He runs instead of walks, climbs on whatever he can, and never sits still. We have him drink about 48 oz of water a day, given his previous cases of rhabdomyolysis. We have noticed a difference in his physical activity depending on his hydration. When he is going too hard, you can see his legs start to hurt after a while, especially if he isn't well-hydrated; he will walk differently and have a hard time bending his legs. In these instances, we immediately have him rest and hydrate. Jacob knows the risks of dehydration and understands proper hydration will help his muscles. Currently, his main restriction is from playing team impact sports because of the potential strain on his muscles if he is pushed too much. He does all the standard activity at school and does not need physical therapy at this time.

It is heartbreaking for us to have our son go through this. We are optimistic, however, about future treatments for LGMD R3/2D. We know Jacob's current enrollment in natural history studies is an important step for treatment trials. And they can't come soon enough! Our prayer is that someday soon there will be multiple treatment options for LGMDs. A treatment like gene therapy could drastically change Jacob's future. We hope for a treatment that would significantly slow down or stop the progression of this disease to maintain or even improve the muscle strength he has now. Fully understanding the treatment process, how it will affect him, and potential side effects and risks would be critically important for us as a family.

My advice for other parents — whether days or years into this journey — is **don't give up!** We can't. We are our children's main advocates, and they need us to push the progress of treatment for them. All patients living with LGMD deserve the best life, and we know effective treatments are possible. I know it is scary, and hopefully, the wait won't be much longer. We are all in this together.

## Brooke Saalman

**Mother of Sons, Jacob (10) and Hudson (6), Duchenne Muscular Dystrophy**

In the summer of 2017, my oldest son Jacob (10), who was 5 years old at the time, began taking a gymnastics class with a friend. By the end of his first class, he was complaining of leg pain. After brushing this off for a few days, my worry got the best of me, and I decided to have him checked out. We ultimately began seeing a physical therapist who would find warning signs for muscular dystrophy. While waiting for further testing with a neurologist, Jacob had an episode of rhabdomyolysis following a soccer game, which landed him in the ICU at Scottish Rite Children's Hospital in Atlanta, Georgia. Genetic testing was done during his hospital stay, and a month later, we found out that Jacob and his younger brother Hudson (6), who was 1 year old at the time, both have Duchenne muscular dystrophy.

***Live in the moment as much as possible, find the right care team and support system, and continue to have high expectations for your child because they can still accomplish so much despite this disease.***

*–Brooke Saalman*

Jacob Saalman

Our first encounter with a neurologist was during Jacob's hospital stay for rhabdomyolysis. We continued to see this doctor after the diagnosis. After much research, I found out that one of the top research hospitals in the country for DMD is Nationwide Children's Hospital in Columbus, OH. We made an appointment as quickly as we could to begin talking about clinical trials and getting our sons on their radar. Over the last five years, both of my sons have been fortunate enough to participate in clinical trials that we feel have slowed their disease progression. Being in a trial takes a lot of dedication and commitment, but we feel it has been well worth it for our boys.

At this time, our boys are still ambulatory, and we are hopeful that the treatments they have received through clinical trials will allow them to stay that way for the foreseeable future. Our boys love sports and have both been able to participate in little league baseball up to a certain level. This has really helped them and our family forge friendships and a support network that has been such a blessing to all of us. Now that Jacob is unable to play sports at a higher level, there have been times he has felt discouraged. We take time to address his feelings and talk about what he can do now instead of dwelling on what he can't. He still enjoys going to watch his friends play, and it feels good for him to be included in that way. There are other times when he physically can't do activities with his friends, but we try to find ways for him to be included. His friends understand his limitations and love and accept him nevertheless. It's amazing how inclusive children can be if they are educated about a condition.

My advice for other parents would be to live in the moment as much as possible, find the right care team and support system, and continue to have high expectations for your child because they can still accomplish so much despite this disease. I think these things have helped our whole family thrive despite this diagnosis. Find things your child can do. My children love playing video games, playing in the yard, riding electric bikes, building legos and model cars and planes, solving Rubik's Cubes, collecting sports cards and Pokemon, drawing, and much more. The bottom line is we must live for today and savor each moment. None of us know the future for ourselves or our children, whether we have a diagnosis or not. No one is guaranteed tomorrow. We all have the gift of today, and we must take hold of it and LIVE.

## Oriol Fuster

**Father of Son, Gerard (10) and Daughter, Claudia (7), LGMD R3/2D**

My son Gerard started walking when he was around 18 months old. Everything was difficult, from crawling to standing up. As time went by, we noticed that his gait was unstable; he used to fall down a lot and often asked me to hold him in my arms. As he was growing up, I noticed that other children were able to do certain things that Gerard had difficulties with. For example, he ran in a very strange way and could not jump. As he got older, I noticed that his calf muscles had developed a lot and that it was not due to his physical capacity or activity.

When Gerard was four years old, we went to a birthday party where he ended up extremely exhausted. As a consequence, he was unable to move his arms and he tiptoed, as he could barely walk. His urine was also very dark and we could see him suffering. We ended up taking him to a hospital emergency room where he was admitted to an intensive care unit. After he stabilized, the hospital referred us to a pediatric neurologist who diagnosed Gerard with LGMD R3/2D. When our whole family was tested, we discovered that our daughter, Claudia, also has the disease. Claudia is functional (walks, climbs stairs) as long as she does not do very strenuous physical activity. Even so, she complains of pain and falls frequently. Both of our children continue to be regularly followed by their neurologist.

I deeply hope that clinical trials for our children's disease will be here soon. We have not had the opportunity to participate in any trials but are willing to, if given the chance and our children qualify. I have to admit that I am concerned about potential adverse effects but being able to participate in trials opens a door of hope.

It is difficult to watch your children's frustration when they can't do activities. I am slowly learning not to set limits on their behalf. If they see themselves as capable of doing an activity, I give them the opportunity to do it, but reduce the amount of time they participate to avoid fatigue or look for alternatives if necessary. Gerard is able to walk, but he does not have the strength to ride a regular bike. That is frustrating for him, of course. So, two years ago, I adapted his bicycle with an electric motor, and now he can ride his bike. He also likes playing soccer, but in this case, he is the goalie so that he doesn't get as tired. Sometimes we look for more creative activities or play board games such as chess or card games.

Since my children were diagnosed with LGMD, communication with them has been very sincere and real, making them aware of the fact that they should not strain their muscles and should find a balance when doing an activity so as not to negatively impact their health. My children are knowledgeable about the disease they suffer from. We also share information about it with our close friends and relatives so that they understand and can help our children when they have difficulties.

To parents who may find themselves in the same situation, I would say that it is important to meet other families affected with the disease and join, if there is one, an association so as not to feel alone and to share concerns. Do not let the disease put limits to what your children want to do. Seek psychological support to deal with the situation in the best way. And last but not least, it's very important to inform your family circle, friends, and school contacts so that they understand and know how to best respond as the disease progresses. ▪

The Fuster family

***Do not let the disease put limits to what your children want to do. Seek psychological support to deal with the situation in the best way.***

*–Oriol Fuster*

# Parenting with LGMD

By Jessica Evans

By Rebecca Gregg

By John Graybill

*Living with a disability* can make parenting more challenging, but having a family is not "off limits" simply due to a diagnosis of LGMD. While having a family may not necessarily be where you land, these parents' stories provide a glimpse into a world of possibilities.

# Jessica Evans' Story

**• LGMD R1/2A**

**I have always wanted to be a mother.** I was diagnosed with LGMD at 12, but that never seemed to have any bearing on my belief that I would be a mom one day. And of all that I have done in my 40 years, I am most proud to be mom to Hudson (9) and Holden (5).

At the time of my first pregnancy, I was using a wheelchair most of the time but could stand, transfer, and take steps with a platform walker or full support. I was in aquatic and land PT as well. My OB-GYN was never discouraging about my desire to be a mom. She did not necessarily consider me "high risk" but encouraged a consult with a perinatologist (high-risk OB-GYN). He focused on what he thought the risks *could* be and shared considerations and recommendations given my progression but never told us whether we *should* or *should not* try to conceive, as he respected that it was our decision alone. We agreed that knowing our child may have MD would not change our minds about biological parenting, as I know firsthand that it is possible to live a joyful and productive life with this disease.

By my second pregnancy, both the passing of time and a broken femur had advanced my progression to full-time wheelchair use and seated transfers. While I was fairly low risk, my OB-GYN had me consult with a perinatologist who wanted to follow me every 4-6 weeks as well.

For both pregnancies, I was on a prophylactic dose of blood thinner due to my level of mobility and the increased risk of thrombosis and embolism. I made sure to consult not only with my neurologists before and during pregnancies but also with a cardiologist and a pulmonologist to be safe. While my OB-GYNs were comfortable allowing me a "trial of labor" to see if vaginal delivery was possible, my neurologists were more comfortable with planned c-sections.

I dreamed of going into labor on my own and being able to deliver vaginally. However, with my first, I was induced 5 days past my due date and, failing to progress past 5 cm, ended up with a c-section after 27 hours of labor. He weighed a whopping 9 lbs 9 oz! With my second, I went into labor 6 days after my due date and was overjoyed for a successful VBAC (vaginal birth after cesarean). As fate would have it, the delivering OB-GYN that day had been highly trained and skilled in forcep-assisted delivery. Imagine my surprise at learning that not only was my regular doctor off duty but also being told minutes before delivery that "you will not be pushing at all." That was not the plan! But it ended up being the perfect plan for me. My story is unique; forcep deliveries and doctors highly skilled in them are rare, so I want to caution others that this is not something to expect.

After my first was born, I was motivated to be a resource for other women with MD. Before becoming a mom, I had so many questions and felt frustrated that my searches yielded very little information. My own desire for a place where women with MD could ask questions and share pregnancy, delivery, and parenting stories led me to start a Facebook group.

**"Moms with MD"** is a closed group for moms, stepmoms, adoptive moms, and expecting moms living with MD — as well as women with MD who would like to have children one day and would benefit from asking questions.
**Facebook.com/groups/momswithmd**

The first two years of motherhood were especially challenging and confronted me with my limitations, but good support ("helping hands"), a faith-filled and hopeful attitude, and creative problem-solving make all the difference in parenting with MD. Now, as a single mom, I'm learning that I'm far more capable than I ever believed. Our strength and ability lie in far more than just our bodies and parenting is far more than just a physical job. It also helps to remember that children are adaptable; what they grow up with is their "normal," and they grow up and become independent (too) fast!

# Rebecca Gregg's Story

• **LGMD R2/2B**

**The phrase "ignorance is bliss"** gets used a lot in daily vernacular, to the point of becoming cliché. For me though, it has meant getting to have two children that I'd always dreamed about having — all because I didn't receive my LGMD diagnosis until I was in my forties. I never had to make difficult decisions like, "should I put my body through two pregnancies while also battling LGMD?" I just did it, blissfully unaware of how it would later affect my body. As a result, I am blessed beyond measure to have two daughters, ages 16 and 11.

I miss them being babies, but I'm also grateful that my LGMD symptoms were minimal with my first baby and only starting to advance with my second baby. As my daughters have grown older, giving them the childhood they deserve, while also dealing with my own day-to-day challenges of LGMD has been a hurdle to overcome. Early in my diagnosis, long before I made it to the "acceptance" phase in the stages of grief, I felt inferior to other moms, and I only focused on the things I was no longer able to do. I felt my kids were somehow getting a "raw deal."

***"I've never heard anyone say that having LGMD is easy, nor have I ever heard that said about parenting either, but prayers, lots of grace, and perseverance will hopefully help us all to be successful."***

Through time, prayers, and therapy, I was able to get into a better headspace. Being a good parent is about being there for them and with them. Life is so much more than focusing on the things I cannot do. I have learned to focus on how I can be a role model for my daughters; how I handle battling LGMD will teach them how they can face their own battles. I am very open with them about my struggles and successes. They see how hard I work at just doing my best to get through each day in the best way possible. Of course, some days are easier than others. They have seen me cry and get frustrated, and they've also seen me dust myself off and keep moving forward. I feel a responsibility to show them that life isn't often fair, but you take what you're given, and you make the most of it.

Also, it helps me to remember that I'm not like every mom, yet I am every mom, all at the same time. We all have our own struggles we deal with — mine just happen to be magnified for all to see. There has never been a perfect mom, but most of us try our best to be just that. If we have a bad day and make mistakes, we always have the next day to do better.

My kids know I am their biggest fan and biggest supporter, along with my husband. They know they are our whole world, and there is nothing we wouldn't do to help them. They also see how hard my husband and I work to ensure we never miss a dance recital or a school play. It often takes creativity to make it all happen, especially in places that are not accessibility-friendly, but we always find a way. I feel we are showing them what a good marriage looks like by seeing the "in sickness and in health" part of our vows in real time.

Living with LGMD is challenging and so is parenting. I've never heard anyone say that having LGMD is easy, nor have I ever heard that said about parenting either, but prayers, lots of grace, and perseverance will hopefully help us all to be successful.

# John Graybill's Story

• **LGMD R1/2A**

**When my wife, Darcie,** and I talked about having a child, we both shared two concerns. The first concern was whether our child would have LGMD. The last thing I wanted was to have a child who would have to go through the same mental, emotional, spiritual, and physical hardships I had experienced. And the second concern was whether I would be physically strong enough to help with caring for and raising our child.

> ***I am so glad that Darcie and I did not allow fear to prevent us from having a child. The roles we play as parents are not exactly the way they are for most people, but we make it work our way.***

Darcie and I talked about the first concern with my doctor. We concluded that the only way for our child to have LGMD was if Darcie were a carrier. My type, LGMD R1/2A, is recessive. We were taking a chance that Darcie was not a carrier, as we didn't do any genetic testing beforehand. This may have been a little cavalier on our part, but we felt that because the disease is rare, the odds were in our favor. As to the second concern, we wouldn't know the answer until the baby arrived, which for me was a little scary, being that there was no turning back.

Shortly after Chloe was born and we brought her home, my fear materialized. Thinking and believing I was ready to care for her and then seeing just how physically weak I was and all of the things I couldn't do was difficult to confront. Changing diapers, giving her a bath, picking her up, dressing her, and sometimes feeding her were physically exhausting, if not impossible for me to do on my own. I didn't have the strength to bring my arms together and instead could use only one arm to do the task since I needed the other one to hold the arm doing the work.

I quickly found myself in an undesirable place — doubt. Mentally, thoughts and feelings of not being a good dad tormented me when I couldn't take care of Chloe. Instead of listening to this constant chatter of how inept I was at being a father, I needed to find a way to contribute to my family. I discovered that I could help by cooking meals. Now, it wasn't the tough job of doing all that needs to be done to care for a child, but it was what I could do. However, whenever my physical limitations showed up, I had to mentally remind myself that I can only do what I can do, and that beating myself up over not being able to do more doesn't help the situation.

I'm not going to lie and say being a dad was or is easy when you have LGMD. There are many physical activities that I wish I could do with Chloe that I simply cannot. And these are the trying times for me as a father. I see the ideal father as one who is out there doing things with their child, running around and showing them how to play sports. But I've come to realize that being a dad is much more than physical strength — it's reading a story to them each night, brushing your teeth with them, listening to them share their day with you, and being there for them when they have a question (or 100 questions!).

I am so glad that Darcie and I did not allow fear to prevent us from having a child. The roles we play as parents are not exactly the way they are for most people, but we make it work our way. ■

**To learn more about parenting products** parents with LGMD have found most helpful, be sure to check out the **Adaptive Parenting** article on Page 22.

By Hillary Kendall • Cyndy Baxter

# Adoption & Surrogacy:

## More Than One Way to Grow a Family

**Growing a family through pregnancy and having biological children is not always possible or the best option. Thankfully, there are other beautiful ways one can grow a family. Here, two women with LGMD share their unique journeys to motherhood.**

### Hillary Kendall's Story

**LGMD R1/2A**

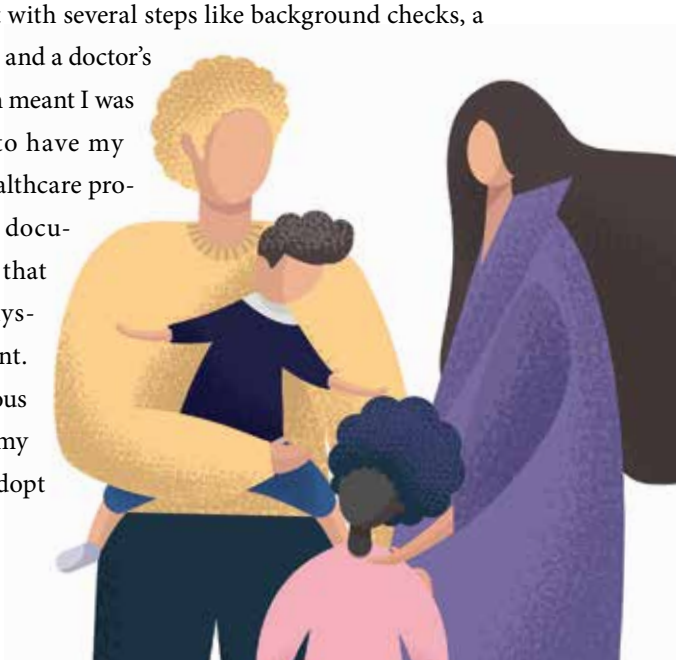
**I always knew I wanted to be a mom.** Throughout my youth, I was surrounded by amazing women, including my own mother, grandmothers, aunts, neighbors, friends, church leaders, and teachers who found joy amidst the chaos of raising kids. Their mothering influence stayed with me throughout my life. Even after my diagnosis, at 12 years old, my desire and hope to be a mom never waned. There were times I worried and feared that it may not happen because of my LGMD. Questions about my ability and strength would flood my mind, but I held onto the hope of someday being called "Mom."

My adoption journey did not begin the day my husband and I called our first adoption counselor or when we signed our first home study paperwork. Looking back on different experiences and moments I had through my adolescence and young adulthood, I firmly believe God was preparing me for an adoption path. One of those experiences was an internship in college that allowed me to work with two groups of young women — young expectant mothers considering an adoption plan and birth mothers who had already placed a child with a family.

As a newly-married couple, my husband and I moved to a new city and started attending a new MDA clinic. I specifically remember my new doctor encouraging us to consider alternatives to natural childbirth. This was unexpected. I processed this recommendation for some time and weighed the pros and cons of following the doctor's advice. As time passed, adoption experiences, stories, and connections seemed to pop up all the time. As my husband and I explored different options and prayed for guidance on how to start a family, we chose adoption.

First, I want readers to know that adoption is amazing and wonderful and has blessed my life in miraculous ways. Second, adoption is not necessarily an easy choice. The journey between our decision to adopt and the day we met our daughter and her birth parents was full of twists and turns, financial strain, stress, and a lot of faith and prayers. We also experienced multiple miracles which ultimately led us to our daughter's birth family.

Part of the adoption process is completing a home study. Depending on your state of residence, this involves a to-do list with several steps like background checks, a home visit, and a doctor's visit, which meant I was required to have my general healthcare provider sign documentation that I could physically parent. I was nervous to discuss my desire to adopt



with my doctor. I feared that he would discourage me from parenting. Luckily, he had no hesitation to sign the paperwork and shared in our excitement and joy.

We were open and honest in our profile and paperwork about my LGMD, but I still worried about meeting my daughter's birth parents and feared they would worry about my physical ability to parent. They too had no hesitation to move forward.

My husband and I decided to adopt again a few years after my daughter was born. Some of those fears resurfaced as we began the home study process; however I was once again supported by both my doctor and our son's biological mother.

I encourage anyone considering adoption to research, plan, and move forward! The journey may be bumpy, but it is worth every twist and turn.

## Cyndy Baxter's Surrogacy Story

### LGMD R9/2I

**I wasn't sure** that I was capable of being a good mom. That doubt nagged at me for many reasons and many years. The physical limitations that resulted from LGMD R9/2I were overwhelming at times. As I looked around, I didn't see a lot of other disabled parents that weren't able to pick up their baby, protect their baby from a hot stove, or change their baby's diaper. Luckily for me, my friends and my husband spent many hours convincing me that I could do this. For that boost of confidence, I am forever grateful. As a result of their persuasiveness, I entered into the rewarding journey of motherhood.

At the time that I decided to start a family in my thirties, I was still searching for a diagnosis. My doctors hypothesized that my undiagnosed neuromuscular disease might be genetic. I was concerned that I might pass my disease on to my children and that natural childbirth would significantly worsen my disease. My husband and I ultimately decided that natural childbirth was not the best option for us and began to explore the possibility of adoption.

Unfortunately, after several years of meetings with adoption agencies, home visits, and no interest from any birth mothers, we gave up on adoption. We suspected that we were being overlooked, in favor of other potential adoptive families, due to my disability. At this point, we were deflated and disappointed. That is when one of my friends mentioned the option of surrogacy and I responded, "No way! That's too expensive, too time consuming, and too fraught with legal pitfalls." Ironically, I now look back at that conversation and laugh. My friend likes to remind me of that and take the credit for being the catalyst that "created" my family!

So, we were off on another detour. This time, we were headed to India. Well, not literally. We engaged with an international surrogacy agency headquartered in India. Over the next two years, we chose egg donors located in India, shipped sperm from Philadelphia to India, and waited. Unfortunately, we faced yet another significant setback and disappointment, and terminated our agreement with that agency.

The following year, we reached our final destination in successfully creating our family: domestic surrogacy. If anyone had predicted at the beginning of this journey that we would spend tens of thousands of dollars and endure seven years of emotional rollercoasters and disappointments, I probably would have told them that they were mistaken.

As we selected our surrogacy and donor agencies in California, I was optimistic but simultaneously convinced that we were still not going to have a family. By that time, I was jaded, doubtful, and burnt out. But finally, we got the phone call that we had waited to receive for seven years — our surrogate was pregnant with twins! Surrogacy may not be the choice for everyone with MD, but it was for us! In the end, it was worth all the expense and struggle. And I often tell my kids about our journey, so that they know how much they were wanted and loved even before they arrived in our family! ■

# Products to Aid in Adaptive Parenting

**Featured Resources**

4moms.com
Boppy.com
GertieCribs.com
MyBrestFriend.com
NuRooBaby.com
PediaLift.com
PrimoBaby.com
Stokke.com
TetraSociety.org

**Every parent,** whether they have LGMD or not, wants to keep their children safe and healthy. But the obvious question is how do you care for a child when you also have unique needs? Below are some off-the-shelf baby gear, specialty items, and DIY hacks that have helped parents with LGMD navigate the delights (and disasters!) of the early years.

Depending on your progression and mobility needs, some of these solutions may or may not work for you. Consult your physical and occupational therapist to see whether you can safely and effectively use these items. ▪

Written by Jessica Evans and Yumi Shim

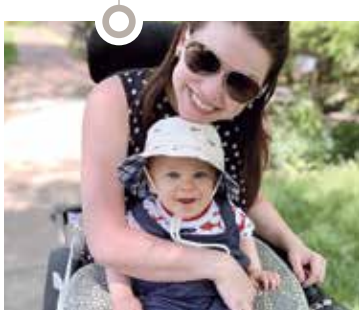
*The items below are intended to be examples. The Speak Foundation is not endorsing any specific product or responsible for the outcome of individual product use. It is recommended to check for recalls on products and use them as directed by manufacturers, with input from medical professionals where necessary.*

### Boppy Nursing Support and Boppy Anywhere® Nursing Support

Boppy is the original, U-shaped nursing pillow introduced 25 years ago. These pillows are useful not only for nursing but also for helping to prop up and support the baby on your lap as you hold him/her. Boppy offers their original nursing support pillow as well as a newer version, which can be tied or clipped around your back.

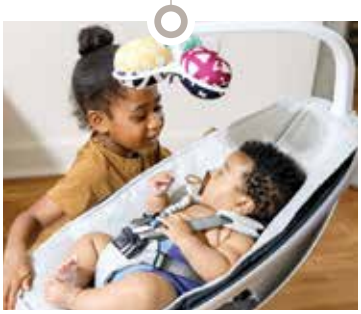
### My Brest Friend Nursing Pillow

This pillow is very helpful for nursing moms, as it clips around the body and stays securely in place. **Tip:** ***You can place a regular bed pillow underneath for additional support while nursing.*** Men and non-nursing mothers should not be deterred by the name! This product can also just be a handy tool to hold your baby close, easily and safely.



### 4moms MamaRoo® Multi-Motion Baby Swing™

The MamaRoo® baby swing can be paired with the 4moms app to adjust motion, speed, sound, and even set a timer right from your phone or tablet.



### Toddler Harness Backpack with Hand Tether for Parent

Once your little ones are on-the-go, a toddler harness backpack with a hand tether for you can help keep them closer during your adventures.

## DIY Hacks

***Everyday life with LGMD requires creative problem solving. Here are some out-of-the-box ideas for solutions that LGMD parents have devised to adapt.***

**Yumi Shim** *acquired a hand-me-down crib with a front panel that they sawed in half and hinged to open to the front, like french doors, securing it with an eye hook.*

**Jessica Evans** *worked with a Tetra Society volunteer who engineered a structure that attached to her wheelchair so that she could safely and securely keep her son close to her.*

## Wall-Mounted Changing Tables

Wheelchair users might find it helpful to purchase the same type of wall-mounted diaper changing stations that fold down in public restrooms. They can be securely mounted to the wall so that you can roll your wheelchair underneath to help change your baby's diaper. **Tip:** ***You can purchase a soft changing-pad separately to lay on the fold-down table.***

## Products on Wheels

Highchairs or bassinets and cribs on wheels, like the Stokke® Sleepi™ Bed, can be used to move your baby around the house, closer to arm's reach or eye level. Some moms use a stroller inside their home to transport the baby around or to gently push them back and forth to sleep, which may be done sitting or standing, depending on ability.

## Sippy Cup Straps/Tethers

These products secure around sippy cups and easily attach to strollers, highchairs, car seats, shopping carts, and more. They can help minimize fall risk by reducing the need to bend over for fallen toys or cups.

## Swivel Base Baby Car Seat

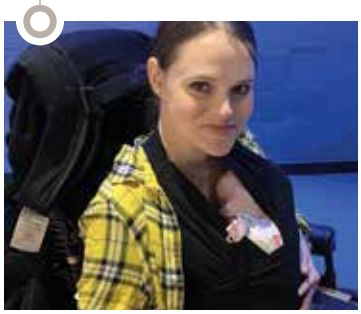
Several car seat brands offer a swivel base feature so that you can adjust your baby's positioning toward you for greater ease, especially when your little one is rear-facing.

## Cantilever Chair

If standing and soothing your baby is not an option, a cantilever chair can be used to "bounce" them.

## Baby Wraps and Carriers

There are countless types of wraps and carriers for babies these days! We recommend trying different types to find what works best for you — from stretchy wraps, ring slings, pouch slings, and mei-tais to structured carriers. There are even baby-wearing shirts available, such as the NüRoo® Pocket or VIJA Design shirt, which work up until your baby is about 15-20 pounds.

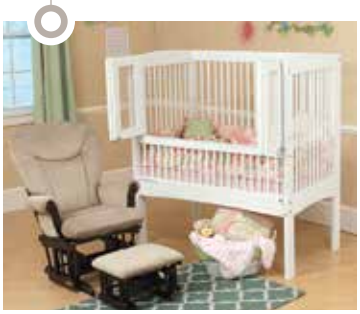


## Bedside Sleepers/ Cosleepers

Bedside Sleepers that attach or sit up against your bed and keep your baby nearby may be an easier option for those that have difficulty getting out of bed. There are sleeper options where the side of the product drops down to be even with the bed.

## Cribs Made for Parents with Disabilities

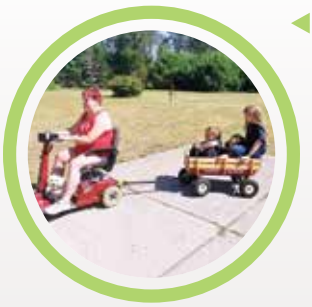
The PediaLift Crib™ and Gertie Crib are two options for wheelchair accessible cribs that are designed to provide a safe way for parents with disabilities to transfer their baby. With the push of a button, the PediaLift Crib™ raises to allow a wheelchair to pull underneath it in order to safely get your child out of the bed. The Gertie crib can be set to various heights to make it easier for parents who use a wheelchair.



## PRIMO Lapbaby

This product is a seating aid that supports your baby, hands-free, on your lap.

**Eva Achoch** *had her wheelchair adapted to have her daughter close since she was unable to push a stroller.*



**Michele Erdman** *and her nieces are adventurous and creative. Here Michele pulls a wagon with her wheelchair.*

**"Whether it is standard baby gear or an ingenious use of a tool that gets you through the day, people with LGMD are already familiar with the dedication and creative thinking necessary to problem solve everyday barriers."**

By **Douglas Sproule, MD, MSc**
*Chief Medical Officer, ML Bio Solutions*

# What is Substrate Supplementation Therapy and How Could it Work as a Treatment for LGMD2i?

ML Bio Solutions is developing BBP-418, a new investigational therapeutic approach that intends to target LGMD2i at the source of the disease. This investigational oral therapy is intended to work by a process called substrate supplementation therapy. In order to understand substrate supplementation therapy, it is helpful to understand what a substrate is and how it works in a healthy muscle.

In healthy muscles, the fukutin-related protein (FKRP) enzyme is responsible for an important step in a process called glycosylation. During glycosylation sugar chains attach to the backbone of a protein called α-dystroglycan (aDG). Glycosylation is critical for the normal function of (aDG). Once glycosylated, aDG stabilizes muscle cells by acting as a "shock absorber" for muscle fibers during contractions.

In individuals with LGMD2i, the FKRP enzyme works a little bit, but it doesn't work well enough. As a result, aDG is not properly glycosylated in individuals with LGMD2i. Without enough glycosylation, aDG is not able to anchor to the muscle cell, limiting its role as a "shock absorber" and making the muscle fragile and prone to damage — even with normal everyday use.

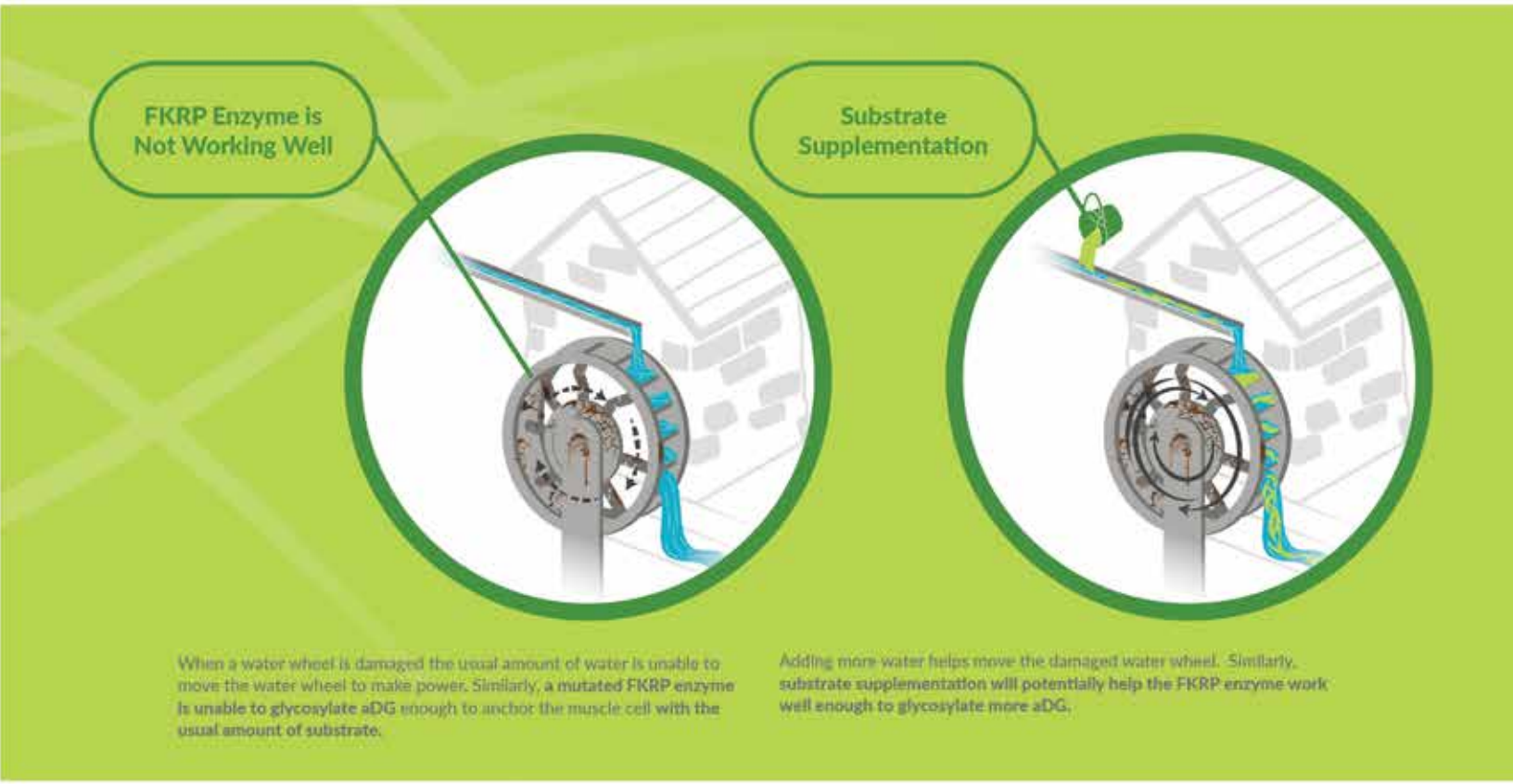
## What is the problem with an FKRP enzyme that is not working well?

Water wheels are not seen much anymore but in the past, some types of machinery were powered by water wheels. Also called hydropower, the force of water flowing over a large wheel would rotate the wheel and generate power to help humans carry out important tasks. Historically, water wheels have been used to mill flour, make paper, prepare fiber for cloth making, and much more.

In a water wheel which is built well and working properly, the water wheel utilizes an upstream source of flowing water to generate power. Similarly, in a muscle in which the FKRP enzyme is working well, the FKRP enzyme uses upstream molecules, called substrates, to glycosylate aDG. These substrates help activate the FKRP enzyme to cause the glycosylation process.

A water wheel uses water to turn the wheel. Similarly **the FKRP enzyme uses upstream substrate molecules to glycosylate aDG.**


ML Bio Solutions




When a water wheel is damaged the usual amount of water is unable to move the water wheel to make power. Similarly, **a mutated FKRP enzyme is unable to glycosylate aDG** enough to anchor the muscle cell **with the usual amount of substrate.**

Adding more water helps move the damaged water wheel. Similarly, **substrate supplementation will potentially help the FKRP enzyme work well enough to glycosylate more aDG.**

Now imagine a situation in which the water wheel doesn't work properly. Perhaps the spokes in the water wheel are bent. The same amount of water is flowing over the water wheel, but because the wheel is not working properly, it is no longer able to move the wheel well enough to power the machinery. Something similar happens in individuals with LGMD2i. When the FKRP enzyme doesn't work well, the substrate is not able to glycosylate aDG well enough to anchor the muscle cell and this makes the muscle fragile and prone to damage.

When aDG's role as a "shock absorber" is compromised muscle damage occurs with daily tasks such as walking, going up stairs, or standing up from a chair. With recurring muscle damage, muscle is replaced by scar tissue. Over time there is so much scar tissue and so little muscle that the muscle can no longer do its job.

## How might substrate supplementation therapy work in individuals with LGMD2i?

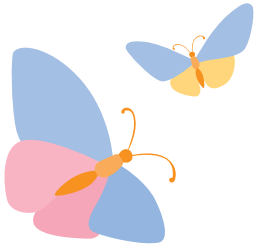
How might substrate supplementation therapy help the damaged water wheel to work well enough to get the machinery to work again? Potentially forcing more water over the damaged wheel might help to get the wheel moving to generate the necessary power for downstream machinery to work again.

This is similar to how a supplementation therapy for the treatment of individuals with LGMD2i may be designed to work. In this therapeutic strategy, the FKRP enzyme is supplemented by the addition of extra substrate molecules upstream of the enzyme. Just as adding extra water to push the damaged waterwheel helps get it moving well enough to do its job, adding key substrate molecules may help FKRP work better.

Substrate supplementation therapy is one of several potential strategies under investigation for the treatment of LGMD2i and each approach has advantages and disadvantages. It is important to note that all therapies currently in development for the treatment of LGMD2i are investigational, meaning that they have not been approved by any health authority.

## How might ML Bio Solution's investigational therapy work?

ML Bio Solutions is developing an oral, investigational therapy called BBP-418 for the treatment of LGMD2i. BBP-418 is expected to work by adding more of the substrate molecules upstream of the mutated FKRP enzyme to potentially help it work a bit better. This additional substrate may support the glycosylation of more aDG allowing it to better stabilize muscle cells and act as a "shock absorber" for muscle fibers. By increasing the shock absorbing mechanism in muscle cells, muscles may be less prone to damage, and may be able to function better in everyday activities.



By Alayne Meyer, MS, CGC
*Specializing in Neuromuscular Genetics, Nationwide Children's Hospital*

# Genetics of LGMD and Family Planning with Muscular Dystrophy

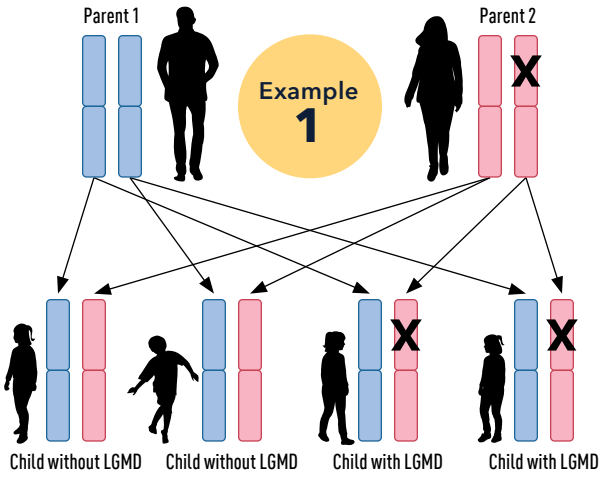
Understanding the genetics and inheritance of limb-girdle muscular dystrophy (LGMD) can be an important part of making informed family-planning decisions.

With more than 30 subtypes of LGMD, understanding the genetics of the diagnosis can be complicated! Most genes associated with LGMD either cause an autosomal dominant **or** an autosomal recessive form of the condition, so we will focus on those two scenarios in more detail. It is important to know the method of inheritance of a patient's particular form of the disease, as well as which gene is causing the disease, to allow for accurate family planning.

For a patient with an autosomal dominant form of LGMD (also known as LGMDD/LGMD1), each of their biological children have a 50% chance to have the same form of LGMD as their parent.

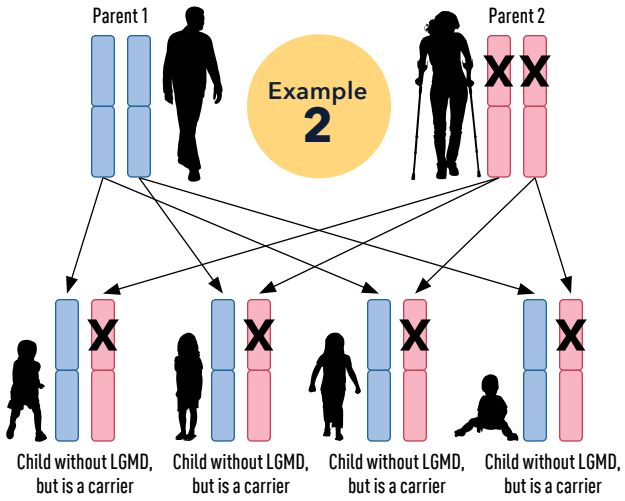
# Possible Genetic Outcomes

**Each parent has two copies of the genes associated with LGMD and passes on one of the two copies (by chance) to a future child. This diagram shows the possible genetic outcomes that could occur in a child.**



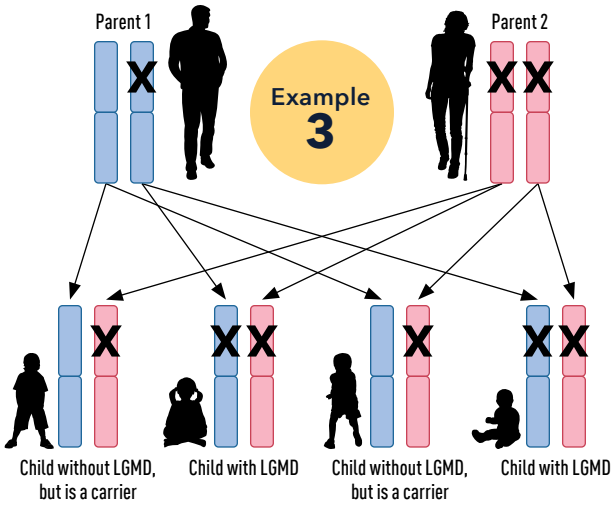

## Autosomal Dominant Inheritance

In this example, parent 2 has an autosomal dominant form of LGMD (with the "X" representing a genetic change/variant). The partner (parent 1) does not have LGMD. In this scenario, there would be a 50% chance to have a child with LGMD and a 50% chance to have a child who does not have LGMD.



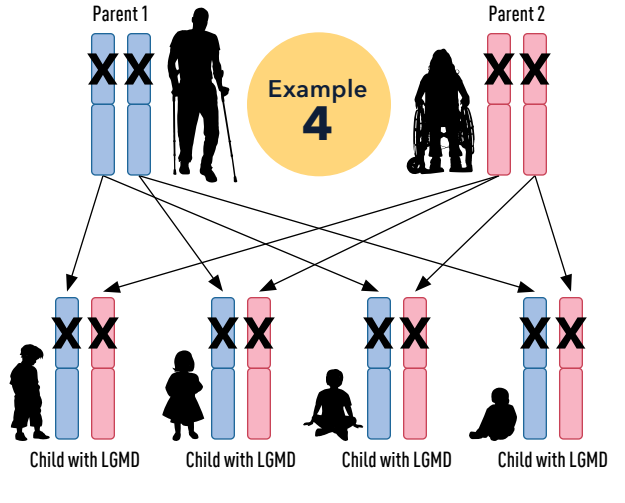

## Autosomal Recessive Inheritance
(Partner is Not a Carrier)

In this example, parent 2 has an autosomal recessive form of LGMD (with the "X" representing a genetic change/variant). The partner (parent 1) does not have LGMD and is not a carrier for LGMD. In this scenario, there would be a 100% chance to have a child who is a carrier for LGMD.




## Autosomal Recessive Inheritance
(Partner is a Carrier)

In this example, parent 2 has an autosomal recessive form of LGMD (with the "X" representing a genetic change/variant). The partner (parent 1) does not have LGMD but is a carrier for the same type LGMD that the partner has. In this scenario, there would be a 50% chance to have a child with LGMD and a 50% chance to have a child who is a carrier for LGMD.




## Autosomal Recessive Inheritance
(Partners with Same Type LGMD)

In this example, both parents have the same form (involving the same gene) of autosomal recessive LGMD (with the "X" representing a genetic change/variant). In this scenario, there would be a 100% chance to have a child with LGMD.

For a patient with an autosomal recessive form of LGMD (also known as LGMDR/LGMD2), the chance to have a child with the same type of LGMD would depend on their partner's status for this gene.

(1) If a partner does not have a harmful change ("pathogenic variant") in the same gene, then the chance to have a child with the same type of LGMD is low (<1%), but all children would be unaffected carriers (they will inherit only one pathogenic variant from the parent with LGMD).

(2) If a partner were to be an unaffected carrier for the same type of LGMD, then each child would have a 50% chance to also have LGMD.
   - If a partner is a carrier for a *different* type of recessive LGMD (change in a *different* gene), this does not increase a child's risk to have either type of LGMD. Genetic testing will help clarify their carrier status (if they are a carrier for both types of LGMD or just the type of their affected parent).

(3) If a partner has the same type of LGMD, then 100% of children would also have that type of LGMD.

For both autosomal dominant and autosomal recessive forms, it is important to know that these chances are the same for each child you have and do not change based on the outcomes of prior pregnancies. For example, a couple at risk for having a child with an autosomal dominant LGMD has a 50% chance to have a child with LGMD for *each* pregnancy, even if they already have a child or children with the diagnosis.

Some genes involved in LGMD can cause either autosomal dominant or autosomal recessive forms of LGMD, which can further confuse matters. The specific change(s) or variant(s) in the gene usually determine the inheritance pattern (in other words, someone with autosomal recessive LGMD usually would only have a chance to have a child with autosomal recessive LGMD as well). However, there are examples in CAPN3-related LGMD where the same variant has been described in both recessive and dominant forms. If this is a concern or question for your family, meeting with a genetic counselor can help clarify these chances.

For individuals who have a chance of having a child with LGMD, there are a variety of reproductive technologies and testing options available. Prior to pregnancy, in-vitro fertilization with preimplantation genetic diagnosis (IVF with PGD) is available. This process allows embryos to be tested for genetic conditions prior to embryo selection and implantation. Therefore, this allows couples to choose an embryo that does not have a specific genetic condition. Diagnostic testing is also available during a pregnancy through two procedures: chorionic villus sampling (CVS) and amniocentesis. CVS is usually performed earlier in a pregnancy (often between 10-12 weeks gestation), while amniocentesis is performed later (often any time after 16 weeks gestation). Following a pregnancy, a child can be tested by cord blood, blood, saliva, or buccal sample. Whether a couple wants to pursue any of these options is a personal choice, but being aware of what is available can be helpful in family planning discussions. You should discuss the risks and benefits of these procedures with your physician to allow for counseling based on individualized medical history.

If you are interested in discussing the chance of having a child with LGMD, wish to seek genetic testing for a partner, or want to discuss prenatal and preconception testing options, I recommend meeting with a genetic counselor. Your OB-GYN, neurologist, or geneticist can help refer you to a genetic counselor. You can also find someone locally through the National Society of Genetic Counselors at: **FindAGeneticCounselor.nsgc.org**. ▪

# Brittany's Story:

## Finding a Diagnosis – and a Community

**Brittany Kerrigan's** diagnostic story started innocently enough, with her foot falling asleep following a long neighborhood walk during the COVID-19 lockdown. But over the next week and a half, her foot never woke up, and a tingly feeling spread to the middle of her right calf.

Brittany first sought medical attention at urgent care and the emergency room, resulting in a lengthy list of speculative diagnoses, from blood clot or brain tumor to breast cancer or multiple sclerosis. Later, Amyotrophic lateral sclerosis (ALS) was also mentioned, a far more devastating possibility than the earlier thought that she'd injured a nerve through impact or pressure.

It was all terrifying for Brittany, 36, to wrap her head around — and it didn't get any easier over the next few months. After several visits to doctors in various fields of medicine and numerous tests, the closest her neurologist could venture to a diagnosis was a likely distal familial myopathy, based on MRIs revealing atrophied calf muscles and Brittany's sister having similar symptoms. Another doctor Brittany consulted thought she might have Charcot-Marie-Tooth disease (CMT), a peripheral neuropathy which, like LGMD, has a number of genetic forms.

But confirmation of the diagnosis required genetic testing, so Brittany sought out a neurologist at the nearby University of Colorado Denver who is an expert in CMT. When Brittany got an appointment with the neurologist — quite an undertaking in itself — they didn't think she had CMT, but that it was in the right "neuromuscular ballpark." The next step was for Brittany to undergo genetic testing for a number of neuromuscular diseases and wait on the results.

On April 2, 2021, Brittany finally got *the* call. She was told the testing found recessive mutations in the ANO5 gene associated with both a type of limb-girdle muscular dystrophy, LGMD R12/2L, and a distal muscular dystrophy, Miyoshi Myopathy Type 3 (MMD3).

After the diagnosis, the neurologist who oversaw the testing referred Brittany to Dr. Matthew Wicklund, another neurologist at the University of Colorado. Wicklund has been very involved in LGMD research and is a member of the GRASP-LGMD (Genetic

*On April 2, 2021, Brittany finally got the call. She was told the testing found recessive mutations in the ANO5 gene associated with both a type of limb-girdle muscular dystrophy, LGMD R12/2L, and a distal muscular dystrophy, Miyoshi Myopathy Type 3 (MMD3).*

**Above, Left:** Brittany Kerrigan and Dr. Matthew Wicklund

*While LGMD typically involves weakness in the proximal muscles of the arms and legs, as well as in the shoulders and hips, some genetic subtypes, including R12/2L and R2/2B, can first show symptoms in distal muscles, as in Brittany's case.*

Resolution and Assessments Solving Phenotypes in LGMD) Consortium of neurologists.

The diagnosis of ANO5 muscular dystrophy accounted for the high creatine kinase (CK) levels (as well as elevated "liver enzymes") her doctors hadn't been able to explain and the slow realization she could no longer walk on her tippy toes, two common characteristics of the disease. "I just always thought I was bad at barre," Brittany joked.

Though Brittany didn't turn out to have CMT, Wicklund explained why it was initially considered as a potential diagnosis. "CMT affects nerves, and ANO5-related muscle disease affects muscles," he said. "However, both can lead to weakness at the ankle. This can cause the confusion in diagnosis."

While LGMD typically involves weakness in the proximal muscles of the arms and legs, as well as in the shoulders and hips, some genetic subtypes, including R12/2L (also referred to as anoctaminopathy) and R2/2B (dysferlinopathy), can first show symptoms in distal muscles, as in Brittany's case.

According to Wicklund, the question of why Brittany's anoctaminopathy presented distally — or really why any neuromuscular disease affects particular muscles — is a great one, but it's also one that doesn't yet have an answer. "Over the next 10-30 years, the questions of 'Why does my disease affect certain muscles and not others?' and 'Why did my disease symptoms start when they did?' are two of the biggest questions in muscle disease," he said.

The distal presentation of Brittany's diagnosis has made it difficult for her to find others in the LGMD community with whom she can fully relate. Although Brittany's distal presentation differs from its proximal counterpart, Wicklund ultimately believes that both forms should be treated the same because of their shared genetic cause.

Wicklund also notes that because symptoms often first appear between ages 20-50, "roughly half of all patients with ANO5-related muscle diseases are presymptomatic, and therefore undiagnosed."

Receiving diagnostic clarity as Brittany did isn't always guaranteed, but it's worth pursuing, according to Wicklund. The benefits of a definitive genetic diagnosis include:

- Having a diagnostic home
- Understanding how the disease is passed down through generations, important in family planning
- Having a better idea about prognosis and timelines
- Being able to participate in clinical trials
- Understanding what organ systems are or aren't involved
- Being aware of when a therapy is available

As it turns out, the GRASP-LGMD Consortium was conducting a natural history study of several forms of LGMD, including R12/2L, with Denver as one of the study sites. With only a short drive to the study, Brittany was easily able to participate.

Brittany has had to adjust the intensity of her physical activities and subsequent resting periods due to muscle weakness stemming from her ANO5-related muscle disease. How lack of ANO5 causes that muscle weakness "is not yet fully understood," according to Wicklund.

"ANO5 is thought to be involved in muscle membrane repair," he explained. "Defective repair leads to breakdown of muscle and the need for more repair. It is thought that at some point, the ability of the body to repair muscle runs out."

Once Brittany received her diagnosis, her next mission was to find a "home" patient advocacy group or foundation. Other than her older sister, who also has MMD3, Brittany has so far come across only two other people with LGMD R12/2L and no one else with MMD3.

Early on in the process, Brittany connected with Chris Anselmo, whom she found the first time she googled Miyoshi Myopathy. Anselmo — who lives with MMD1, or LGMD R2/2B (caused by dysferlin mutations), and was featured in the Winter 2022 issue of *LGMD News* — encouraged Brittany to attend The Speak Foundation's virtual 2021 International Limb-Girdle Muscular Dystrophy Conference.

Brittany wound up in a breakout discussion led by Kathryn Bryant Knudson of The Speak Foundation. Ever the extrovert, Brittany shared the high points of her diagnosis saga and subsequent struggles to find a "home" foundation inclusive of her distal presentation. Knudson's reply was exactly what Brittany had been waiting to hear.

"Kathryn and The Speak Foundation were the first people to tell me, 'This is where you belong,'" Brittany recalled. "It was very comforting and kind. I think I was almost caught off guard because it was easier than I expected."

Approaching two years since her diagnosis, Brittany is still learning how to navigate life with a progressive neuromuscular disease that so far appears "invisible." Most days are OK and "some days are very bad," but Brittany does her best to maintain a positive perspective — no matter how challenging her journey has been.

"I feel a little hesitant to talk about myself because I know how difficult it can be for other people," she said. "I mean, I have a very rare disease. It's a strange genetic fluke. It takes a lot of time and a lot of effort. But in a lot of ways, I'm extremely lucky. I live near Dr. Wicklund. My diagnosis process was only six months long. I have a flexible job. I have access to healthcare. I'm able to advocate for myself. I have strong family, friends and partner support. But it's also okay to acknowledge that in a very ableist world, there are — and will still be — a lot of difficulties.

"At the end of the day, I think I'm very fortunate in an unfortunate situation." ▪

**Written by** Rob Ketcham

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Daniel Ferguson

# The Daniel Ferguson LGMD Foundation

*The Daniel Ferguson LGMD Foundation (DFF) was established in late 2020 to improve support for those living with limb-girdle muscular dystrophy and their families.*

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**Daniel was a healthy, active child** who enjoyed climbing trees, riding his bike, and leading a normal, mischievous childhood. As Daniel entered adolescence, his general mobility declined. He was genetically confirmed to have LGMD R1/2A (calpain-3-related) at age 17.

As the years passed and Daniel's condition progressed, his limbs significantly weakened and normal day-to-day activities became increasingly difficult. With his steady deterioration, falls became more frequent. Now, at the age of 38, Daniel is unable to climb stairs, easily stand up from a chair, sit down upon a chair, or walk long distances.

Daniel's disability led to him losing his job as a maker of high-quality jewelry. However, Daniel has maintained a level of independence that allows him to live in his own home and to start up and operate his own home-based jewelry manufacturing business.

## Setting up the DFF

The Daniel Ferguson LGMD Foundation (DFF) was established in late 2020 to improve support for those living with limb-girdle muscular dystrophy and their families. Daniel not only provides evidence of the challenges of living with LGMD but also, through his determination, has shown that it is possible for those affected by this disease to lead fulfilling and productive lives. The Foundation is registered with the Australian Charities and Not-for-profits Commission and also has deductible gift recipient (DGR) status with the Australian Taxation Office, which means that donations to DFF are tax-deductible. The Foundation's Strategic Plan, available on our website, gives details on our programs and aims.

## DFF Scientific & Medical Advisory Board (SMAB)

Dr. Michelle Lorentzos serves as the Medical and Scientific Advisor on the Board of DFF. Her role, based upon her clinical and research experience, is to consider the current medical landscape and work with the broader team to facilitate opportunities and information that can support the lives of people affected by LGMD. Dr. Lorentzos is a pediatric neurologist and the Clinical Trials Medical Lead at The Children's Hospital at Westmead, Sydney. Most of her work focuses on finding new treatments for neuromuscular diseases. Dr. Lorentzos' collaboration with DFF is a natural extension of her passion and optimism with regard to this evolving field.

## DFF Mechanical Assistive Devices

DFF has also developed several prototype mechanical devices which assist those with severe mobility limitations. There is considerable interest in these devices from around the world, and we are working towards their manufacture. To enable this, DFF is collaborating with a leading Australian university and another not-for-profit organization which specializes in technical assistive devices. We look forward to providing more detailed information as the project develops. ■

**Written by** Rick Ferguson, *CEO*
**and** Dr. Michelle Lorentzos, *Medical and Scientific Advisor, The Daniel Ferguson LGMD Foundation*

# We Offer HOPE.

**Are you an individual living with** limb-girdle muscular dystrophy who needs assistance covering the costs of mobility and durable medical equipment (DME)? The SPEAK Foundation is here to help.

Through **The HOPE Project**, we are able to award a one-time stipend of up to $250 to qualified applicants living in the United States who have a diagnosis of limb-girdle muscular dystrophy and need assistance affording DME expenses for mobility.

For additional information or to submit an application from July 1, 2023 through July 31, 2023, please visit **TheSpeakFoundation.com/grant-programs**.

**The HOPE Project**

A Program of The SPEAK Foundation

**TheSpeakFoundation.com/grant-programs**

Accepting applications from July 1, 2023 through July 31, 2023.
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