Vol 5 / Issue 4

LGMD News

Uniting the Limb-Girdle Muscular Dystrophy Community

BUILDING A PATH TO A CURE
The Story of the Jain Foundation and Its Mission to Cure Dysferlinopathy

CENTERS FOR INDEPENDENT LIVING
What Makes Them Unique

INTRODUCING EVOLYRA THERAPEUTICS
A New Hope for LGMD

JOHN WALTON MUSCULAR DYSTROPHY RESEARCH CENTRE
New Projects to Advance Diagnosis and Care for Patients with LGMD

THE LGMD2L FOUNDATION
Driving Research, Building Community

SPECIAL EDITION

COLLEGE AND LGMD

PREPARING FOR COLLEGE WHEN YOUR CHILD HAS LGMD2A
A Parent's Perspective by Melina Garza

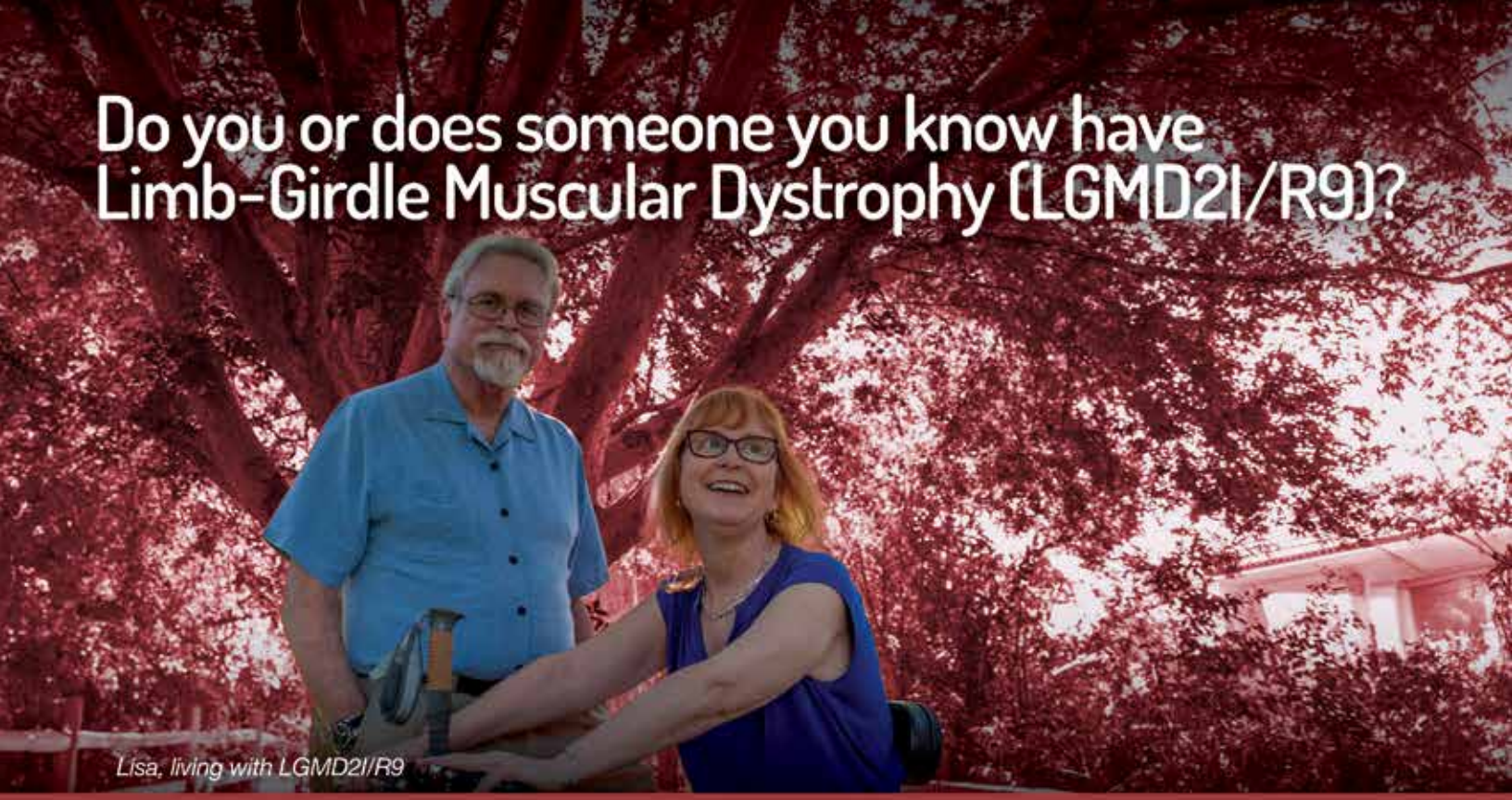
ATTENDING COLLEGE WITH CONFIDENCE
By Kathryn Bryant Knudson

BALANCING LIFE WITH LGMD
By Cerys Davage

CHOOSING COLLEGES
By Peter Frewing

NAVIGATING COLLEGE LIFE WITH LGMD
By Serena Desiderio

Do you or does someone you know have Limb-Girdle Muscular Dystrophy (LGMD2I/R9)?



Lisa, living with LGMD2I/R9

AskBio is actively recruiting clinical study[1] participants with a confirmed genetic diagnosis of LGMD2I/R9 for an investigational[2] gene therapy treatment.

Find out if you qualify today

- This study is designed to evaluate the safety and tolerability of investigational gene therapy AB-1003 to treat LGMD2I/R9.
- Participants will receive a one-time intravenous infusion (injected directly into your vein) of the investigational gene therapy called AB-1003. AB-1003 is designed to produce fukutin-related protein (FKRP) in the body, primarily in muscle, heart, and diaphragm (the muscle that helps you inhale and exhale).
- There are two cohorts in the study. Cohort 1 is complete. We are currently recruiting for cohort 2.
- Some visits will take place at the study site, while others may occur at home. Study visit support including transportation, lodging and meals may be available.

We invite you to learn more

Email us
askfirst@askbio.com
Visit us online
Askbio.com
Clinicaltrials.gov
clinicaltrials.gov/study/NCT05230459
Scan QR code

We celebrate LGMD patients and advocacy groups for their tireless efforts and dedication to the community!

AskBio
A Bayer Cell & Gene Therapy Platform Company

[1]Clinical Study: A clinical study is a research study for which people volunteer to help scientists find answers to certain health questions
[2]Investigational Treatment: An investigational treatment is a treatment being studied to see if your disease or medical condition improves while taking it. It has not yet been approved by regulatory authorities, such as the U.S. Food and Drug Administration (FDA).

LGMD News

Vol 5 / Issue 4

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!

Connect with Us

Email:
ContactUs@TheSpeakFoundation.com
Web:
TheSpeakFoundation.com
Facebook:
Facebook.com/TheSpeakFoundation
Instagram:
Instagram.com/TheSpeakFoundation
X:
Twitter.com/SpeakFoundation
Twitter.com/LGMDFoundation

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 personally. The Speak Foundation helps our voices to be heard.

Contents

Departments

College and LGMD Feature Articles

Feature Articles

Momentum, Advocacy, International Collaboration

We must keep sight of our ultimate goal, and support each other as we continue our journey.

Dear LGMD Community,

This issue of *LGMD News* focuses on independent living for young adults. For many living with limb-girdle muscular dystrophy, the journey toward independent living, especially in a college setting, looks different than the mainstream narrative. Independence isn't just about moving out or managing your own schedule. It's about advocating for access, adapting to new environments, and often, educating others about what inclusion really means.

We're also highlighting an excellent article about the founding and approach to research funding of the Jain Foundation, started 20 years ago by a family affected by dysferlinopathy (LGMD R2/2B). The Foundation has funded more than 150 scientific and clinical research projects ranging from the structure of the dysferlin protein to development of outcome measures for clinical trials, and has a patient registry with over 1,300 enrollees worldwide.

Our community has faced uncertainty and heartache in recent weeks; I share more about this in my letter on the following page. But what I want us all to clearly hear in the midst of this is that progress continues to move forward in many other areas. We want to share about a new company entering the LGMD space: **Evolyra Therapeutics**, based in Richmond, Virginia. Evolyra Therapeutics is developing full-gene replacement therapies for LGMD subtypes R3/2D and R5/2C. These subtypes—caused by mutations in relatively small genes—are particularly well-suited for complete gene replacement using AAV technology. Evolyra Therapeutics' approach uses next-generation AAV vectors designed for safer, more precise delivery to muscle, potentially reducing the liver-related complications that have impacted the gene therapy field.

When trying to do something that's never been done before—like find treatments for LGMDs—it's inevitable that there will be disappointments along the way. But we must keep sight of our ultimate goal, and support each other as we continue our journey. ▪

Kat Bryant Knudson

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

Connect with Us

ContactUs@TheSpeakFoundation.com

TheSpeakFoundation.com

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.

Navigating Heartbreak and Hope in Rare Disease

The LGMD community has been rocked by incredibly difficult news over the last couple of months—first, the heartbreaking loss of a fellow warrior in the LGMD R3/2D trial, and then Sarepta Therapeutics' abrupt decision to "pause" most of their LGMD gene therapy programs.

We are thankful that Sarepta is still maintaining their commitment to LGMD R4/2E (beta-sarcoglycanopathy). Still, the timing of these announcements, literally the day before our International LGMD Conference, was devastating.

Community member Faran Day, whose twelve-year-old son participated in several years of natural history testing, put it this way: "Our hopes and prayers for a clinical trial are cancelled." Each data point and each clinical endpoint represent people who have entrusted their bodies, time, and hope for progress in science.

The limb-girdle muscular dystrophy community now faces a sobering reality. While other conditions like Duchenne Muscular Dystrophy have multiple approved treatments, patients with any subtype of LGMD still have no approved therapeutic options. Yet, we remain hopeful. Several companies are actively working at various stages of the development pathway on treatments that hold significant promise for some LGMD subtypes. We are not at the end—we are at a turning point. More companies are entering this space, and our hope continues to grow.

We are not at the end—we are at a turning point.

To add to the complexity, Sarepta's continuation of treatment development for LGMD R4/2E creates a nuanced relationship between the company and our community. While many of us feel frustration and disappointment over the broader pause in their LGMD programs, we also rely on their ongoing commitment to this particular subtype.

This situation highlights a difficult truth: although we have invaluable research data on several LGMD subtypes gathered through many years of clinical studies, it's unlikely that researchers will have the opportunity to collect similar information from families again on such a scale.

This situation illustrates the vulnerability facing rare disease research, an issue that extends beyond just LGMDs. When companies step away from therapeutic areas, what becomes of the natural history studies, the biomarker data, and the years of carefully collected longitudinal information? When these data are lost, so too is much of our understanding about how to combat these diseases.

The LGMD community's response can provide a roadmap for other rare disease advocates who have experienced similar setbacks. Preserving research data is essential, as is sharing best practices within our community to minimize gene therapy safety risks. We must also work together to actively engage and support new drug developers entering our field.

We need to make sure that when hope becomes heartbreak, we must ultimately become a stronger and resilient movement that protects today's patients and tomorrow's treatments. ■

Written by Kathryn Bryant Knudson
Founder & CEO, The Speak Foundation

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 R18/2S
Facebook.com/LGMDCC

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

CureLGMD2i
Funding research for LGMD R9/2I
CureLGMD2i.org

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

LGMD Awareness Foundation
Raising awareness of and advocating for the LGMD community
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
Strengthening the titin community: LGMD R10/2J
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

South Korea

Korean Dysferlinopathy Patients Association
Providing patients with LGMD R2/2B information and research updates
Cafe.Naver.com/UniteDsyferlinopathy

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

For additional information about the International Consortium of LGMD Organizations: **ContactUs@TheSpeakFoundation.com**

Glenn Walter, PhD

Professor at the University of Florida

Q

I have LGMD R10/2J, titin-related. As my condition has progressed, I've noticed I can float upright in the pool without treading water—possibly due to increased fat infiltration in muscle. While I've had MRIs before, none were specifically to assess muscle loss or fat replacement. Could imaging focused on muscle composition provide benefits beyond diagnosis—for example, in guiding treatment, physical therapy, or even supporting documentation for insurance, adaptive equipment, or financial assistance?

A

You raise an excellent point. Imaging that specifically looks at muscle composition—such as MRI scans that measure the amount of fat versus muscle—can provide important information beyond just making an initial diagnosis. As LGMD progresses, muscle fibers are gradually replaced by fat and connective tissue—this replacement of muscle by fat is sometimes called the "fat fraction," a quantitative measure obtained from MRI scans that tells us how much of a specific muscle has been replaced by fat, compared to healthy muscle tissue. Ongoing studies are comparing how fat fraction changes in different subtypes. Fat fraction is the most broadly useful and emerging imaging marker for disease progression.

There are several ways in which MRI imaging, and fat fraction measurement in particular, can be helpful in guiding disease management:

- **Tracking Disease Progression:** By repeating these specialized MRIs over time, we can see how quickly or slowly fat is replacing muscle in different parts of the body. This helps doctors and researchers understand how your condition is changing—even before changes in strength or physical abilities might be obvious.
- **Predicting Future Function:** Studies, including those conducted at the University of Florida and through the GRASP network (with NIH support), have shown that changes seen in MRI—specifically increases in fat fraction—can help predict future physical function in people with muscular dystrophies such as Duchenne Muscular Dystrophy (DMD), Becker, and some types of LGMD. This means the MRI results could give advance warning of which muscles are most at risk and help anticipate future needs.
- **Guiding Physical Therapy and Treatment:** Knowing which muscles are being affected the most, and how quickly, can help tailor physical therapy programs or other treatments. Therapists and clinicians may be able to adjust exercises to focus on muscles that still have more healthy tissue or develop strategies to protect those that are showing early signs of fat replacement.

Meet the Expert

Glenn Walter, PhD is a Professor at the University of Florida with over 20 years of experience in skeletal muscle research. He specializes in developing advanced magnetic resonance imaging (MRI) and spectroscopy techniques to study muscle structure, function, and metabolism. Dr. Walter completed his Ph.D. in biophysics and metabolism at the University of Pennsylvania and a postdoctoral fellowship focused on dystrophic muscle physiology and gene therapy. He leads data coordination and analysis for multicenter NIH studies and has extensive expertise in MRI sequence design and processing for neuromuscular diseases. Many of these measures are now used in clinical trials for muscular dystrophy to access efficacy.

Have a Question for Our Experts?

Send Questions To:
ContactUs@TheSpeakFoundation.com

Question

Q

My 12-year-old daughter experiences episodes of severe pain in her neck, spine, and scapular region, which seem to coincide with new muscle weakness. Could regular MRI—perhaps every six months—be used to monitor muscle changes in those areas to help guide her pain management and physical therapy?

A

This is an important and understandable question. The relationship between episodes of pain, new muscle weakness, and changes seen on MRI is complex, and researchers are still learning about how these factors are connected—especially in children with muscle diseases.

While MRI is a valuable tool for detecting changes in muscle tissue, such as muscle loss or increased fat replacement, the link between these changes and episodes of pain is not always clear. There has been significant research on how MRI findings relate to back pain in the general population, but less is known about how MRI findings relate to pain and weakness in children with muscle disorders.

The relationship between episodes of pain, new muscle weakness, and changes seen on MRI is complex, and researchers are still learning about how these factors are connected—especially in children with muscle diseases.

Q

I've heard doctors say that cardiac MRI is better than other ways of looking for heart involvement in MD. Can you explain what advantages MRI has over ultrasound or other monitoring tests?

A

Echocardiography, or "echo," uses sound waves to create images of the heart. It is a fast, cost-effective test that is widely available. Echos can usually be done quickly at the patient's bedside and do not require sedation, making them especially convenient.

Cardiac MRI, on the other hand, uses magnetic fields and radio waves to create very detailed pictures of the heart. This test is especially helpful for getting clear images in patients where ultrasound images (from an echo) are not as good, such as in people with larger bodies. Cardiac MRI can also provide additional information about the heart muscle itself, such as detecting areas of scarring or damage, either naturally or with the help of special contrast agents which may need to be injected.

Q

Can you explain how MR spectroscopy is used to evaluate muscle metabolism in LGMD, and what abnormalities you commonly see?

A

Magnetic resonance spectroscopy (MRS) is a special imaging technique that lets us look at the chemical makeup and metabolism of muscle, rather than just its structure. In LGMDs, the most clinically relevant way to use this technology is with a method called 31-phosphorus MR spectroscopy. This approach focuses on naturally occurring phosphorus compounds in your muscles.

What does 31-phosphorus MR spectroscopy measure?

- This technique measures the levels of key energy-related chemicals in your muscles, especially phosphocreatine (PCr) and adenosine triphosphate (ATP). These are the molecules your muscles use to store and quickly access energy.

- It can also detect changes in the intracellular pH (how acidic or alkaline the muscle environment is), as well as information about free magnesium and how well ions are balanced inside the muscle cells.

Why is this useful in evaluating LGMD?

- At rest, 31-phosphorus MR spectroscopy can reveal early problems in muscle metabolism before they show up as symptoms. For example, it can detect if the muscle is more acidic than normal (a sign of impaired energy use) or if levels of high-energy phosphates are lower than expected.

- It can also point to ion channel dysregulation.

Common abnormalities possibly seen in LGMD:

- Reduced phosphocreatine (PCr) or ATP: These findings indicate that the muscle has less "energy reserve" available for quick, intense activity.

- Elevated intracellular acidity (lower pH): This can happen when muscles cannot efficiently clear byproducts of energy use, sometimes leading to early fatigue.

- Changes in free magnesium or abnormal ion handling may reflect deeper issues in how muscle cells are functioning at a biochemical level.

Overall, MR spectroscopy provides unique information about how muscles are functioning energetically. While it is mostly used in research settings and some specialized clinics, it helps researchers and clinicians understand the metabolic challenges faced by people with LGMDs and may eventually guide the development of new therapies or ways to monitor the effects of treatments aimed at mitigating metabolic problems.

Q

Is there a best practice recommendation for frequency of MRIs to track progression or to highlight new muscle group involvement?

A

There is no single "best practice" for how often to get MRI scans to track muscle changes, because that depends on many factors, including the specific type of muscle disease and how quickly it tends to progress.

Generally, MRI scans can help show when muscle tissue is starting to be replaced by fat, which is a sign that the disease is progressing. The speed of this change varies with the type of muscular dystrophy. For example, in some childhood forms of the disease — such as DMD or certain types of sarcoglycanopathies — muscles can change more rapidly, sometimes losing more than 10% of their normal tissue each year. In contrast, adults with other types of muscular dystrophy may see changes at a much slower rate, such as 1–2% per year.

Because of these differences, the decision about how often to do MRI scans is based on the individual patient's type of disease, age, and how quickly their muscles seem to be changing. There isn't a "one size fits all" answer, and the frequency of MRI scans should be tailored to each person's needs. In general, scans are performed annually if there is concern about muscle deterioration.

Generally, MRI scans can help show when muscle tissue is starting to be replaced by fat, which is a sign that the disease is progressing. The speed of this change varies with the type of muscular dystrophy.

Question

There are several exciting advances coming in MRI technology that could really help people with LGMD. New tools like artificial intelligence (AI) and machine learning are making MRI scans much faster, which means you won't have to spend as much time in the scanner.

Connect with Us

TheSpeakFoundation.com

Q

Based on your work, are there distinctive imaging or metabolic profiles that help differentiate between LGMD subtypes?

A

Different subtypes of LGMD often affect specific muscle groups in distinct patterns. This means that, by looking at which muscles are most involved—and how much muscle has been replaced by fat on MRI scans—clinicians can often distinguish between different forms of muscular dystrophy.

Imaging Profiles:

- Using advanced MRI techniques, especially those that quickly measure fat fraction in many muscles throughout the body, doctors can see "patterns" of muscle involvement that are characteristic for different LGMD subtypes.

- For example, sarcoglycanopathies (LGMD types R5/2C, R3/2D, R4/2E, R6/2F) tend to show a different pattern of muscle loss compared to Pompe disease (GAA deficiency, also known as Glycogen Storage Disease Type II) or dysferlinopathy (LGMD R2/2B and Miyoshi myopathy). Some subtypes affect muscles closer to the hips and shoulders first, while others may involve the calves or other areas earlier.

- These imaging patterns are highly specific and can be visualized efficiently with modern MRI techniques that survey multiple body regions in a short period of time.

Q

What advances in MR technology or analysis do you believe will have the biggest impact on LGMD research or care in the next 5–10 years?

A

There are several exciting advances coming in MRI technology that could really help people with LGMD. New tools like artificial intelligence (AI) and machine learning are making MRI scans much faster, which means you won't have to spend as much time in the scanner. This is especially important for people with contractures (tight or stiff joints), because being in the scanner for a long time can be uncomfortable or even painful. Faster scans can help reduce that discomfort.

In addition, researchers are working on making MRI machines that use lower magnetic fields or simpler technology. These "low-field" or less expensive MRI machines are more affordable and easier to install, which means more clinics and hospitals—even in smaller towns or countries with fewer resources—can offer MRI scans. This could make it much easier for more people around the world to get the scans they need for both research and medical care.

Finally, because MRIs produce so much detailed information, AI is also helping us spot the earliest changes in muscle—even before symptoms appear. All of these advances could lead to better care and more accessible research for people living with LGMD. ▪

Introducing Evolyra Therapeutics:

A New Hope for Limb-Girdle Muscular Dystrophy

Evolyra Therapeutics is a cutting-edge biotechnology company on a mission to bring life-changing treatments to people living with LGMD. Based in Richmond, Virginia, the company is developing next-generation gene replacement therapies designed specifically for rare neuromuscular conditions that currently have no cures.

Founded by a team of physician-scientists and biotech leaders, Evolyra Therapeutics is working to change the future for individuals with LGMD type R3/2D and type R5/2C, two severe subtypes of the disease that cause progressive muscle weakness, loss of mobility, and serious impacts on quality of life. Their approach is rooted in a deep understanding of muscle biology, patient need, and the limitations of past therapies.

What makes Evolyra unique is its second-generation AAV vector platform—engineered to deliver a full-length, functional gene directly to muscle tissue, while avoiding toxicity in other organs like the liver. This improved design reflects lessons learned from earlier gene therapy trials and offers the potential for safer, more effective treatments.

Evolyra Therapeutics is also distinguished by its close partnership with the GRASP-LGMD Patient Consortium, a global network of clinicians, scientists, and patient advocates focused on accelerating research in LGMD. This collaboration gives Evolyra access to clinical trial-ready infrastructure, natural history data, and patient voices that help guide every stage of therapy development.

Still in preclinical stages, the company is preparing for future clinical trials in the next year while advancing its manufacturing and regulatory plans. Their ultimate goal is to deliver curative gene therapies—not just symptom management—for families who have long waited for meaningful options.

In a field where progress has often been slow and uncertain, Evolyra Therapeutics offers a fresh wave of hope for the LGMD community. With innovative science, a committed team, and a patient-centered approach, they are working to turn the tide in one of the most challenging areas of neuromuscular medicine. ■

Written by Kathryn Bryant Knudson
Founder & CEO, The Speak Foundation

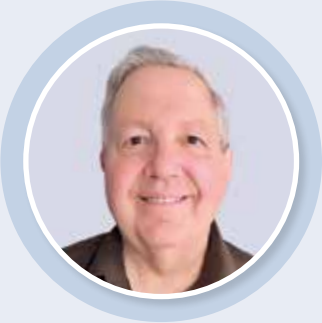
Nicholas Johnson, MD, MSci, FAAN
Professor and Vice Chair of Research
Virginia Commonwealth University

In a field where progress has often been slow and uncertain, Evolyra Therapeutics offers a fresh wave of hope for the LGMD community.

Written By Hal Tily, PhD

The LGMD2L Foundation:

Driving Research, Building Community



Longtime disability advocate **Ralph Yaniz** started the LGMD2L Foundation in 2018.

Like many forms of limb-girdle muscular dystrophy, LGMD R12/2L is not well understood. Scientists are still debating the exact role of the affected protein, anoctamin-5, in muscle function. To make things more confusing, symptoms can vary dramatically from person to person. Many of us experience pain and weakness that can prevent us from walking, dressing ourselves, or even lifting something as light as a cup of coffee. For some, symptoms begin in early adulthood, often in their 30s; for others, they may not appear until much later in life. But for every person with very obvious challenges, there is another whose symptoms are mild and only diagnosed by chance—in the course of a routine medical screening or through the diagnosis of a more severely affected sibling.

> **"This wide variation in severity raises an important question: is LGMD R12/2L underdiagnosed? Could there be countless people out there with milder symptoms who simply attribute their difficulties to aging or a lifestyle that could be healthier?"**

This wide variation in severity raises an important question: is LGMD R12/2L underdiagnosed? Could there be countless people out there with milder symptoms who simply attribute their difficulties to aging or a lifestyle that could be healthier? A 2019 study examining the frequency of mutations in large European genomic databases estimated that more than 1 in 40,000 people are expected to have the disease. This figure dwarfs earlier estimates of around 1 in 250,000.

Billy Zureikat is one of those whose symptoms were unmistakable. A lifelong athlete, he began to notice his performance was slipping, occasionally even falling during basketball games. The realization that something more serious was going on came at age 30, when he stepped out of his car and collapsed to the ground in agony, dislocating a toe. Like many, he took his diagnosis hard—learning that his condition would continue to worsen, with no treatment or cure on the horizon, hit him "like a ton of bricks."

When life handed Billy lemons, he decided to make lemonade. Realizing that his passion for sport would now have to play out as a spectator, he embraced a new love: cooking. Styling himself as "Tripping Billy" in reference to his frequent falls, he launched his innovative pizza pop-up restaurant that has turned him into a celebrity chef in his home city of Chicago. He uses that spotlight to raise awareness about the disease and to fundraise for the Muscular Dystrophy Association (MDA). Billy is now lending his voice to the LGMD2L Foundation to help support the search for a cure.

The Foundation was started in 2018 by Ralph Yaniz, a longtime disability advocate

and one of four affected siblings. In addition to providing a community for those living with 2L, the LGMD2L Foundation took a major step forward in late 2024 by expanding its mission: directly funding and advancing the research that will lead to treatments.

With guidance from its scientific panel—composed of leading doctors and researchers—the foundation has developed a clear roadmap of the work that needs to be done. While gene replacement therapy remains the most promising long-term solution, the current priority is research that will be broadly useful across a range of possible treatments.

The foundation then plans to make its results and resources available to researchers in both academia and industry. The goal is simple: to accelerate progress toward a cure by making it easier for all scientists to work on 2L.

The first phase of this work is already underway. With funding from the Foundation, Assistant Professor Ellie Carrell and Professor Nick Johnson (Virginia Commonwealth University, GRASP-LGMD Consortium) have begun developing a new animal model for studying 2L, using laboratory mice. An accurate model of the disease (meaning an animal with the same genetic defect) is essential for foundational research, testing of new medications, and securing regulatory approval of drugs from agencies like the U.S. Food and Drug Administration (FDA). These mice will lay the groundwork for the next phases of the foundation's roadmap—testing existing compounds that might improve symptoms, and separately, developing a novel gene therapy construct aimed at restoring lost muscle function.

Above: Billy Zureikat lends his voice to the LGMD2L Foundation to help support the search for a cure.

> **"The goal is simple: to accelerate progress toward a cure by making it easier for all scientists to work on 2L."**

Right: Morgan Harman enjoys actively contributing to the mission of advancing progress towards a cure.

> **It was a heartwarming feeling, finding out how many people were out there in my circle who supported me.**

The LGMD2L Foundation is a community organization, relying on the effort of patients and their friends and families to fund our work. Morgan Harman is one person who stepped up to answer that call. Diagnosed at 27 after chronic pain and shoulder injuries, she chose to face her fear of the future with action. Morgan launched her own fundraiser for the Foundation, raising nearly $4,000 USD, mostly from friends and family. That money helped fund the development of the Foundation's new animal model for 2L research. "It was a heartwarming feeling," she said, "finding out how many people were out there in my circle who supported me. It really solidified that." Morgan believes anyone in the community can achieve the same success—and enjoy the same deep sense of support and empowerment that comes from actively contributing to the mission of advancing progress towards a cure.

The Foundation now has a growing presence on Facebook, Instagram, Linkedin, and its website: **LGMD2L-Foundation.org**. There, visitors can join the community, learn more about the Foundation's work, and hear stories from Morgan, Billy, and others about life with LGMD R12/2L and how the community is working together to overcome it.

The LGMD2L Foundation wants you to know: Rare disease is a heavy burden to carry alone—but there are more of us than you might realize, and we are fighting together. ▪

Connect with Us

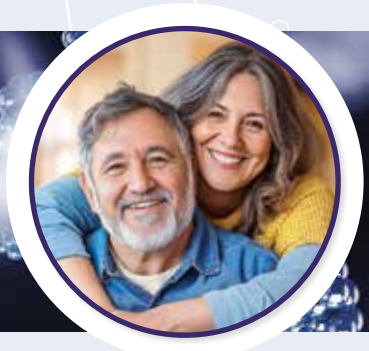
LGMD2LFoundation@gmail.com

LGMD2L-Foundation.org

Facebook.com/LGMD2LFoundation

Instagram.com/lgmd2l.foundation

Linkedin.com/company/lgmd2l



Donate and Help Find a Treatment!

The first phase of the LGMD2L Foundation's plan to develop a treatment will cost an estimated $25,000. This will pay for the animal model needed for further research and for testing medications. Please consider donating to cover the costs. Thanks to a sponsorship from an affected family, your donation will be matched! Donate today: Tinyurl.com/CureLGMD2L.

Volker Straub, MD, PhD

Director, John Walton Muscular Dystrophy Research Centre
Newcastle University
Newcastle upon Tyne, England, UK

Volker Straub is the Director of the John Walton Muscular Dystrophy Research Centre and Deputy Dean of the Translational and Clinical Research Institute at Newcastle University, Newcastle upon Tyne, UK. In his role as deputy dean for the largest of the three research institutes at Newcastle University's faculty of medical sciences, he supports the translation of fundamental disease mechanisms from the laboratory to patients through clinical observational studies and interventional trials. Volker is a member of the faculty's Global Strategy Committee, the Centre for In Vivo Imaging, and the Regional Network for Innovation in Advanced Therapies. He supports the National Institute for Health and Care Research (NIHR) Newcastle Biomedical Research Centre as the Co-Lead for the neuromuscular and rare disease theme and is a NIHR Senior Investigator.

His own clinical and academic interests focus on translational research in genetic neuromuscular disease. His research Centre delivers care and diagnosis whilst being at the forefront of clinical and basic research directed to therapy delivery for patients with genetic neuromuscular conditions and supported by internationally directed networking, tools and resources. His current research involves the application of muscle imaging, the use of zebrafish and mouse models, next generation sequencing and other –omics technologies for the characterization of genetic neuromuscular disorders. He is an investigator for several natural history studies and interventional trials. He is currently the president of the World Muscle Society and an author on more than 500 peer-reviewed publications.

Volker has been involved in the coordination and work plans of many EU-funded research projects and networks. He was the grant holder, founder and co-coordinator of TREAT-NMD, a network of excellence for genetic neuromuscular diseases funded by the EU with €10 Million (FP6). The network has now become a global alliance for translational research and provides services for industry, clinicians and scientists to bring novel therapeutic approaches into the clinic. In 2019, he established TREAT-NMD Services Ltd., the business arm of the alliance, and is one of the directors of the enterprise. He also coordinated the COST Action "Applications of MR imaging and spectroscopy techniques in neuromuscular disease: collaboration on outcome measures and pattern recognition for diagnostics and therapy development" (MYO-MRI, BM1304). ▪

Below: The Centre for Life, Newcastle upon Tyne, home of the John Walton Muscular Dystrophy Research Centre.

Connect with Us

JWMDRC.org
TREAT-NMD.org

New Projects to Advance Diagnosis and Care for Patients with LGMD

(Left to Right): Dr. Jordi Diaz Manera, Alejandro Gonzalez Chamorro, Dr. Ana Topf and Dr. Volker Straub from the John Walton Muscular Dystrophy Research Centre in Newcastle upon Tyne, UK, participated in the 5th Congress of the Latin American Neuromuscular Society in Mexico City, where they provided research updates on LGMDs.

These projects will play an important role in deepening our understanding of LGMDs and moving us closer to improved care and therapies.

At the John Walton Muscular Dystrophy Research Centre, we are excited to launch new research initiatives aimed at improving the diagnosis and care of individuals living with limb-girdle muscular dystrophy (LGMD). As the host of the national diagnostic and advisory service for LGMD in the United Kingdom, and with a long-standing commitment to research in this heterogeneous group of genetic conditions, we are proud to continue leading efforts in this area.

We are delighted to share that three of our recent LGMD-related research proposals have received funding from the Jain Foundation and the Coalition to Cure Calpain 3 (C3).

The Jain Foundation has generously funded two projects: **COS-Prepared** and **Identifying Prognostic Biomarkers**.

COS-Prepared Project

In the COS-Prepared project, we are, for the first time, gathering data on young adults diagnosed with LGMD R2/2B *before* they exhibit clear disease symptoms. This study aims to document early signs of the condition by assessing muscle function, strength, and disease biomarkers. By better understanding early disease progression, we hope to improve diagnosis, clinical care, and future treatment approaches. We plan to recruit 20 participants in close collaboration with the Jain Foundation.

Identifying Prognostic Biomarkers Project

Prognosis of the rate of progression in dysferlinopathy between patients has been challenging. Previous studies have found that the initial presentation (proximal vs. distal weakness) and the type of *DYSF* mutation don't have strong predictive power as to how fast symptoms will progress. This new project, led by Prof. Jordi Díaz Manera, is using AI and machine learning to evaluate a large pool of data collected in earlier COS studies to identify biomarkers which can predict disease progression.

Our third funded project, supported by the Coalition to Cure Calpain 3, will investigate individuals who carry a single altered copy of the *CAPN3* gene—linked to autosomal dominant forms of the disease. We aim to reassess all known individuals with these "dominant" *CAPN3* variants, regardless of symptom status, to better understand the variability in disease expression.

We are incredibly grateful to all study participants and patient advocacy groups whose involvement and support make this research possible. These projects will play an important role in deepening our understanding of LGMDs and moving us closer to improved care and therapies. ■

Written by Volker Straub, MD, PhD
Director, John Walton Muscular Dystrophy Research Centre
Newcastle University
Newcastle upon Tyne, England, UK

Active GRASP-LGMD Natural History Study

UPDATED: SEPTEMBER 1, 2025

Recruiting:

Trial Readiness and Endpoint Assessment in LGMD R1/2A (GRASP-01-003)

Inclusion Criteria

- Age between 12 – 50 at enrollment
- Clinically affected (defined as weakness on bedside evaluation in a pattern consistent with LGMDR1)
- Genetic confirmation of LGMDR1 (presence of homozygous or compound heterozygous pathogenic mutations in CAPN3)
- Must be able to provide written informed consent and be willing and able to comply with all study requirements

Exclusion Criteria

- Have contraindications to MRI or MRS (e.g., non-MR compatible implanted medical devices or severe claustrophobia)
- Non-ambulatory, defined as unable to safely walk 10 meters without assistive devices (ankle foot orthotics allowed)
- Positive pregnancy test at any timepoint during trial
- Have dominantly inherited CAPN3 mutations (i.e. LGMD D4)
- Any other illness that would interfere with the ability to undergo safe testing or would interfere with interpretation of the results in the opinion of the site investigator

ENROLLMENT FOR THIS STUDY CLOSES: APRIL 30, 2026

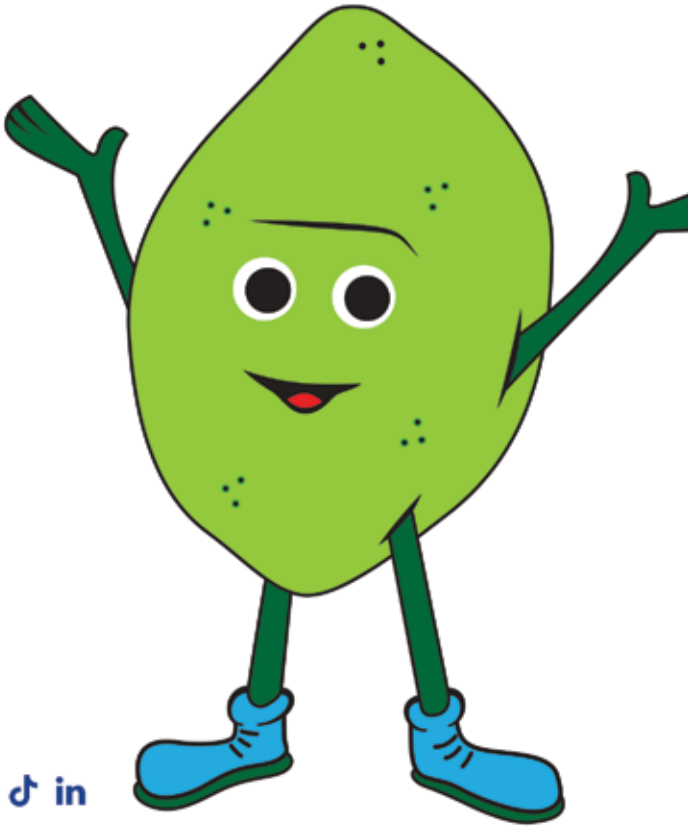
Ruby Langeslay
Network Coordinator, Grasp-LGMD Consortium
(804) 828-8481 | *Ruby.Langeslay@vcuhealth.org*

Jennifer Raymond
Network Coordinator, Grasp-LGMD Consortium
(804) 828-6318 | *Jennifer.Raymond@vcuhealth.org*

Together we are STRONGER!

Join the LGMD Awareness Foundation in our mission to elevate global awareness for limb-girdle muscular dystrophy.

Together we advocate for better access to diagnosis, care, and treatment for those affected.



Advocate **Educate** **Celebrate**

LGMD AWARENESS FOUNDATION

lgmd-info.org

Mark your calendar for the 11th Annual LGMD Awareness Day

LGMD
Awareness Day
September 30th

New Merch for 2025!

Shop Now:

Raise Awareness with the LGMD Awareness Day Toolkit

Even more free resources added this year!

Access Toolkit:

- Puzzles
- 30-Day Challenges
- Informational Flyers
- Social Media Posts
- Media Kits + more!

PLATINUM SPONSOR

GOLD SPONSORS

Thank you to our sponsors:

ML BioSolutions

AskBio

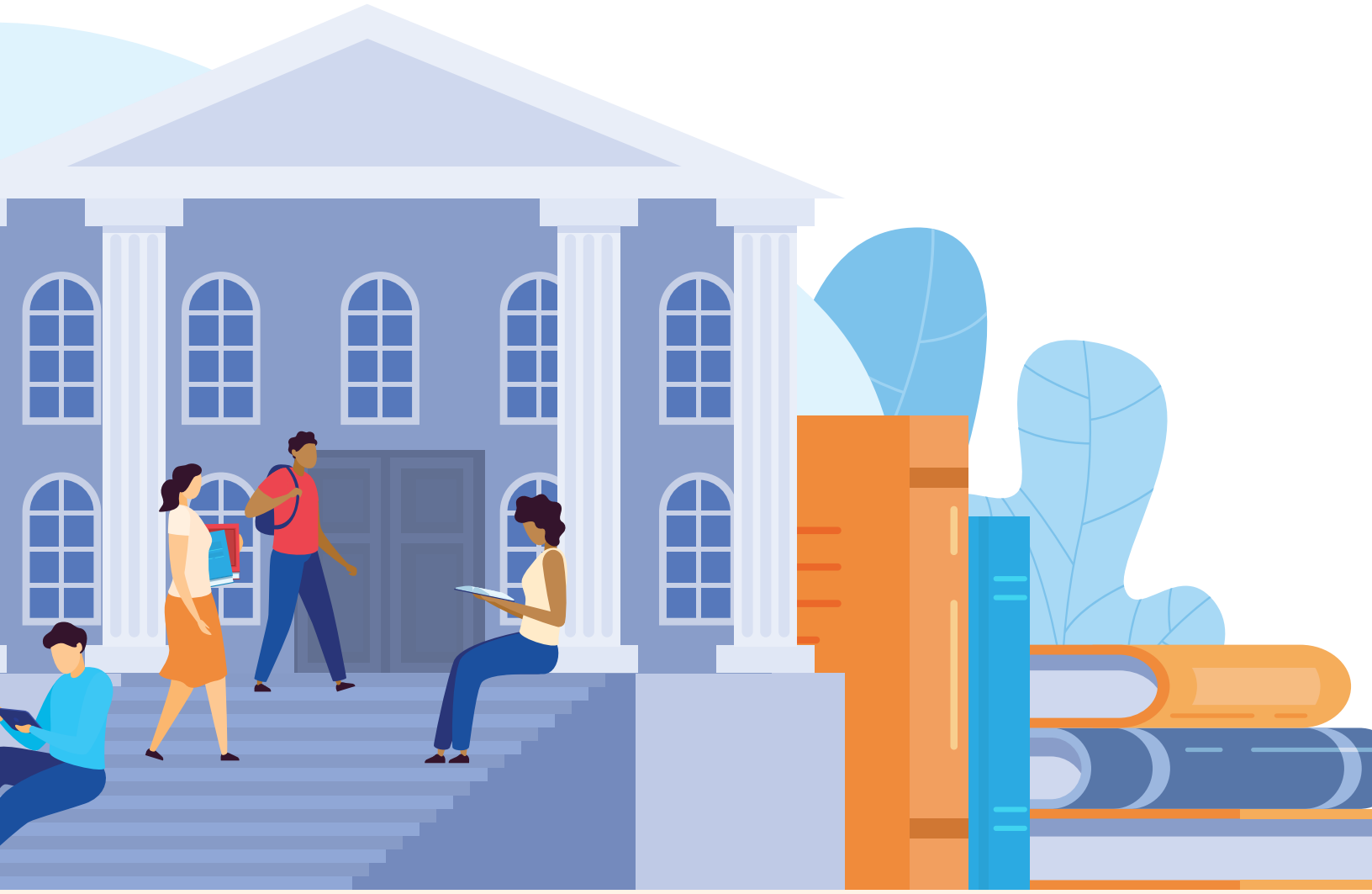
SAREPTA THERAPEUTICS

Support us:

Written By Kathryn Bryant Knudson

Attending College with Confidence

As a freshman living with LGMD R9/2I, I was overwhelmed by the sheer scale of everything when I first stepped onto my college campus. The sprawling buildings, packed schedules, and logistical challenges seemed insurmountable. As someone with accessibility needs, I wondered how I could navigate not just the physical campus, but the entire college experience. The realization that changed everything for me was that I didn't have to figure it out alone!



Finding Financial Support: The Unexpected Phone Call

Before I even got to college, there was the question of how to pay for it. Sometimes the most unexpected actions lead to life-changing opportunities. When I was in high school, my mom called the White House—yes, really! She asked if there were any programs that would help disabled students go to college. The next thing I knew, we were meeting with Virginia's Vocational Rehabilitation (VR) office.

A rehabilitation counselor came to my school to meet with me and assess whether I qualified for services. I was furious and embarrassed by the attention, but the outcome was positive: they told me and my parents that I was eligible because of my muscular dystrophy. Since this is a progressive disease, they suggested to consider a career I could do from a wheelchair. That went over like a lead balloon with me. But then they added that they would help pay for my college education. Who could say no?

Vocational Rehabilitation in Virginia covered my college tuition, room and board, and even my books. This was over 20 years ago, and I've since heard from hundreds of students whose college education was also supported by VR. In the U.S., this federally-funded program helps individuals with disabilities prepare for, obtain, and maintain employment. While funding and services can vary by state, support is available in many places. If you're navigating the financial challenges of college in the U.S. with disability-related needs, take time to research what VR services are available in your state. You might find valuable support to help you reach your goals.

The Power of Asking for Help

Once I got to college, I encountered many accessibility challenges, but the Disability Services offices consistently stepped up to support me. Instead of trying to figure out how to get to distant classrooms or wrestling with scheduling conflicts on my own, I learned to bring these issues to our campus Disability Services office. It wasn't giving up or taking the easy way out; it was working smarter, not harder.

At both George Mason University and the University of Virginia, I found more than just willingness to help; I found a genuine commitment to ensure that every student had a fair shot at success. Both schools provided support that went beyond what I initially expected, and it made all the difference for me.

Practical Accommodations that Made All the Difference

The accommodations I received in college weren't just checkboxes on a form—they were thoughtful, real-world solutions that addressed the challenges I faced every day. Some of the support that had the biggest impact included:

Priority Registration: I picked my classes before other students, which allowed me to optimize my schedule and choose the classroom locations and times that worked best for me. This wasn't just about convenience; it was about setting myself up for academic success. When you can plan your day to accommodate your accessibility needs, everything else falls more smoothly into place.

"Less time and energy spent on logistics meant more energy available for my studies, relationships, and involvement in campus life."

Flexible Exam Scheduling: I was able to reschedule finals if I had too many exams in one day. Anyone who's been through college knows how grueling exam week can be, but imagine facing that stress while also managing physical fatigue and accessibility challenges. This flexibility to spread out exams meant I could perform at my best when it mattered most.

Strategic Housing Placement: I had the ability to choose a dorm room closer to the dining hall. This might seem minor, but it made a *major* difference in my daily quality of life. Less time and energy spent on logistics meant more energy available for my studies, relationships, and involvement in campus life.

Campus Transportation: I was able to drive to my classes on campus and park near academic buildings. While many colleges restrict freshmen from having cars on campus, my disability required it—but I had to advocate for that need. Parking accommodations gave me the independence to fully participate in campus life and removed a significant barrier that many people overlook. If you require this type of accommodation, it's important to share your needs openly and explain why it's essential. Although this takes effort, it is worth doing as it also opens the pathway for others in the future.

Speaking Up: The Importance of Self-Advocacy

Something crucial I learned: you need to bring up these needs yourself. Disability Services staff are knowledgeable and well-intentioned, but they can't read your mind or anticipate every need. They might not even realize you need these accommodations.

When requesting accommodations, be specific and explain the why. Don't just ask for priority registration—describe how being able to choose your schedule helps you conserve energy and avoid physical strain. Don't simply ask for flexible exam scheduling—describe how having three exams in one day could prevent you from demonstrating your actual knowledge.

For example, I once told my disability services office: "I get tired easily due to my muscular dystrophy, so getting up at 7 AM and then having back-to-back classes all across campus puts me at risk for developing rhabdomyolysis. I cannot walk that far in one day." That level of detail helped them understand my request wasn't about convenience—it was about preventing a serious medical condition.

The "why" behind your requests helps staff understand not just what you need, but how these accommodations connect to your academic success and health. This context makes them partners in your education rather than just administrators processing requests.

Thinking About Career Planning: The Hidden Stress No One Talks About

When I got to college, a new kind of stress hit me—one that no one seemed to talk about: *what kind of career could I realistically pursue with a progressive disability?* It's hard enough for most 18-year-olds to choose a career path. But for those of us with disabilities, it's not just about what we *want* to do; it's about what we *can* do long-term. At a young age, many of us have to begin planning for the possibility of a future which incorporates wheelchair use. For others, limited mobility is a current reality, and mobility aids are already part of daily life. We're often forced to think years ahead, trying to predict what our bodies might be able to handle in five, ten, or twenty years.

"The 'why' behind your requests helps staff understand not just what you need, but how these accommodations connect to your academic success and health. This context makes them partners in your education rather than just administrators processing requests."

For me, that meant wrestling with the progression of my disability, the uncertainty of how fast it would advance, and the pressure of choosing a career that I could sustain even if I used a wheelchair part- or full-time. I can recall the enormous stress I felt trying to ask my neurologist if I could do a certain job for a decade or more before I might lose further mobility. But the hardest part? There was no definitive answer.

If you're a young person under 18 reading this—I see you. I've been there. The pressure is real, and your stress is valid.

"Be clear about your needs, and advocate for yourself!"

Here's the Advice I Wish Someone Had Given Me:

Start by asking yourself: *What are you passionate about?* Let that guide you. Then ask: *Can I see myself doing this work from a wheelchair if necessary?* Could I do it for many years?

If you feel overwhelmed by all this—I did too! Most young adults are just wondering about a job, while we are planning our whole lives out because of a disability. In fact, while I was at the University of Virginia, I was so desperate and stressed by the enormous pressure of trying to figure out my future that I turned to a higher power to find peace. Through prayer, I felt led to become a Christian Marriage and Family Counselor. That career gave me meaning and purpose. I worked in that field for many years until I became the founder of the Speak Foundation, which I'm proud to say helps so many people with neuromuscular conditions now. (But that's a story for another time.)

You may not be religious, and that's fine. For me, that is how I coped; for you, it might be finding a career where you feel you're helping others, or you might realize you have a passion for something like computer design, technology, law, or science. Many people pursue complex, demanding careers while using wheelchairs. I've met physicians with muscular dystrophy who completed medical school while using mobility scooters. There are engineers, teachers, artists, and executives who use wheelchairs every day.

Don't feel like you have to limit yourself, but *do* think realistically about longevity. Consider how many years you want to work, what kind of physical demands you think you can accommodate over time, and what kind of flexibility a field might offer. Choosing a career when you have a disability isn't just about finding a job. It's about building a life that works for you. You don't have to figure it all out right away, and you don't have to do it alone. There is a community full of people with LGMDs who have gone before you. We're here to talk, share, and support you as you choose your own path forward.

Beyond Accommodations: Building Confidence

What struck me most wasn't just the practical support, but how these accommodations transformed my entire college experience. Instead of spending mental energy worrying about logistics, I could focus on what really mattered: learning, growing, and building relationships. The Disability Services offices didn't just solve problems—they removed barriers that could have limited my potential.

The Ripple Effect of Good Support

When colleges invest in comprehensive disability services, they're not just helping individual students—they're fostering more inclusive communities for everyone. The accommodations that helped me succeed also benefited my classmates, professors, and the broader campus community. When students aren't weighed down with basic accessibility struggles, they can contribute more fully to campus life, research, and the academic environment as a whole.

A Message for Future Students

If you're heading to college with accessibility needs, know that you don't have to navigate it alone. Reach out to Disability Services early, be clear about your needs, and *advocate for yourself!* Come prepared with specific accommodation requests and be ready to explain how they'll support your success. The resources are there, and with the right support, what once felt like an overwhelming challenge can become an empowering opportunity. ▪

Written By Serena Desiderio

NAVIGATING COLLEGE LIFE WITH

Living with a progressive neuromuscular disease like limb-girdle muscular dystrophy brings a unique set of strengths and challenges, especially during the transition to young adulthood. Entering college marked a major turning point in my life and in my disability. I was no longer just managing a diagnosis; I learned to advocate for myself and live independently, while also trying to build a fulfilling college experience. Through this article, I hope to offer insight and encouragement to others with LGMDs who are beginning their college journeys. From navigating accessibility on campus to finding your voice, here are some lessons I've learned along the way.

Where to Begin: Understanding Your Needs

The summer before you set foot on campus, take time to assess both your personal and professional needs. What kind of support will you need to succeed, whether it be academic, physical, and/or emotional? Do you need accessible housing, classroom accommodations, mobility assistance around campus, or support attending events like sports games? Knowing what you need—and what helps you thrive—is the first step to setting yourself up for success as a college student with a disability.

It's also important to remember that your needs may change over the time you are attending college. My disability progressed significantly throughout my four years. As a freshman, I was able to walk around the campus and use stairs. Over time, I became more reliant on the Disability Cart Service (this is much like a golf cart) provided by my university. By sophomore year, I needed AFO braces for my legs. By junior year, I transitioned to using a scooter to help me navigate the campus, and by my senior year, I was using a wheelchair to better support my mobility and independence.

Your needs may change too and that is okay. What matters is that you understand those changes and know that there are resources available to help you every step of the way.

Getting In Touch: Registering with Disability Services

One of the most important steps in preparing for college in the U.S. with LGMD is registering with your school's Disability Resource Center (DRC). I recommend starting this process as early as possible—ideally, the summer before your freshman year. When I registered, I had to provide documentation of my disability from a medical provider, although the intake process can vary depending on the institution.

During the process, be open and honest about your daily needs and potential barriers that you may face. The more specific you are, the more effectively the DRC can support you. They can help implement a range of accommodations, from accessible dorm arrangements and classroom placement to transportation on campus and extended testing time.

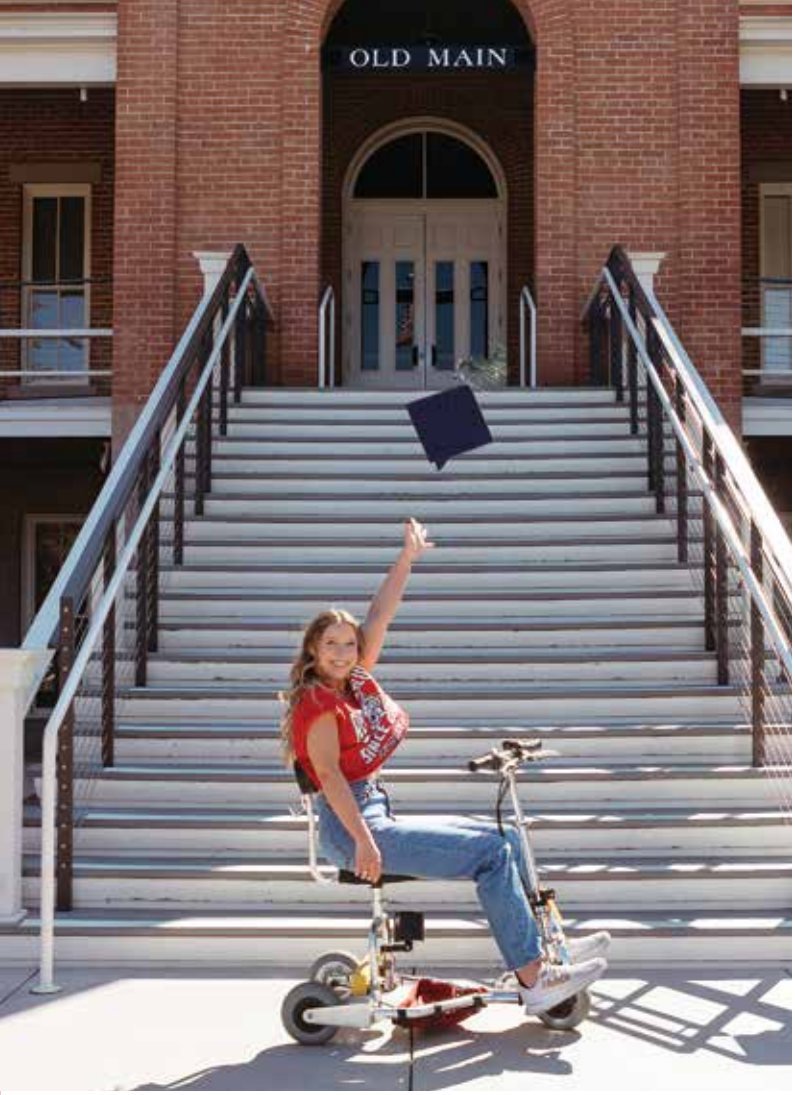
One of the best resources that I utilized from the DRC was their disability cart services and disability parking spots. I was fortunate to have a car on campus and a disability placard that I could use. This became such an essential part of my ability to navigate the campus. Whenever I needed assistance, the DRC acted quickly and ensured that they accommodated me to the best of their ability. Their support made a significant difference in my ability to succeed and feel included on campus.

Self-Advocacy and Its Impact

Self-advocacy does not come naturally to everyone, and I know this firsthand. I've struggled at times to speak up for myself, especially when it feels like I'm being a "burden" to others. But it's not just about asking for help; it's about knowing your worth and setting boundaries that protect your well-being. As my best friend likes to say, "protect your peace." Don't let anyone or anything disrupt your peace. You are your greatest advocate, and when you make your voice heard, others will follow your lead.

College introduced me to a whole new set of people and dynamics, from navigating social situations to interacting with professors. I quickly learned that speaking up for myself was not only necessary but empowering. One of the most impactful steps I took to ensure that I could enjoy the same experiences as my peers was calling ahead to restaurants, bars, and other venues to confirm they were accessible. More often than not, it was actually my friends who made those calls for me, making sure I could be included in all the adventures. Their support, combined with small but thoughtful actions, made a huge difference for me.

Over time, the more I advocated for myself, the more confident I became in explaining my condition and asserting my needs without apology. It's a learning process, but every small step builds a stronger, more self-assured voice.



Finding and Using Campus Resources

College is like Hermione Granger's bag from *Harry Potter*—it's filled with an endless range of resources, but you often have to dig around to find exactly what you need. These resources may include academic support programs, adaptive sports, mental health counseling, student clubs, and peer mentorship—all of which can make a world of difference in someone's college experience.

For me, discovering a pre-health honorary during my freshman year was one of the most valuable resources I found. This is a student organization that recognizes academic excellence and promotes professional development for students pursuing careers in health-related fields. The club connected me with job opportunities, introduced me to some life-long best friends, and gave me the space to grow into my disability without judgment. Finding a supportive community—even just one person who understands—can turn a hard day into a manageable one. Don't be afraid to ask questions or reach out.

Learning Through Experience: What I Wish I'd Known

There are many things I wish I had known at the start of my college journey. And while sometimes I wish I had been more prepared, I am incredibly grateful for those experiences that taught me more about the world and about myself.

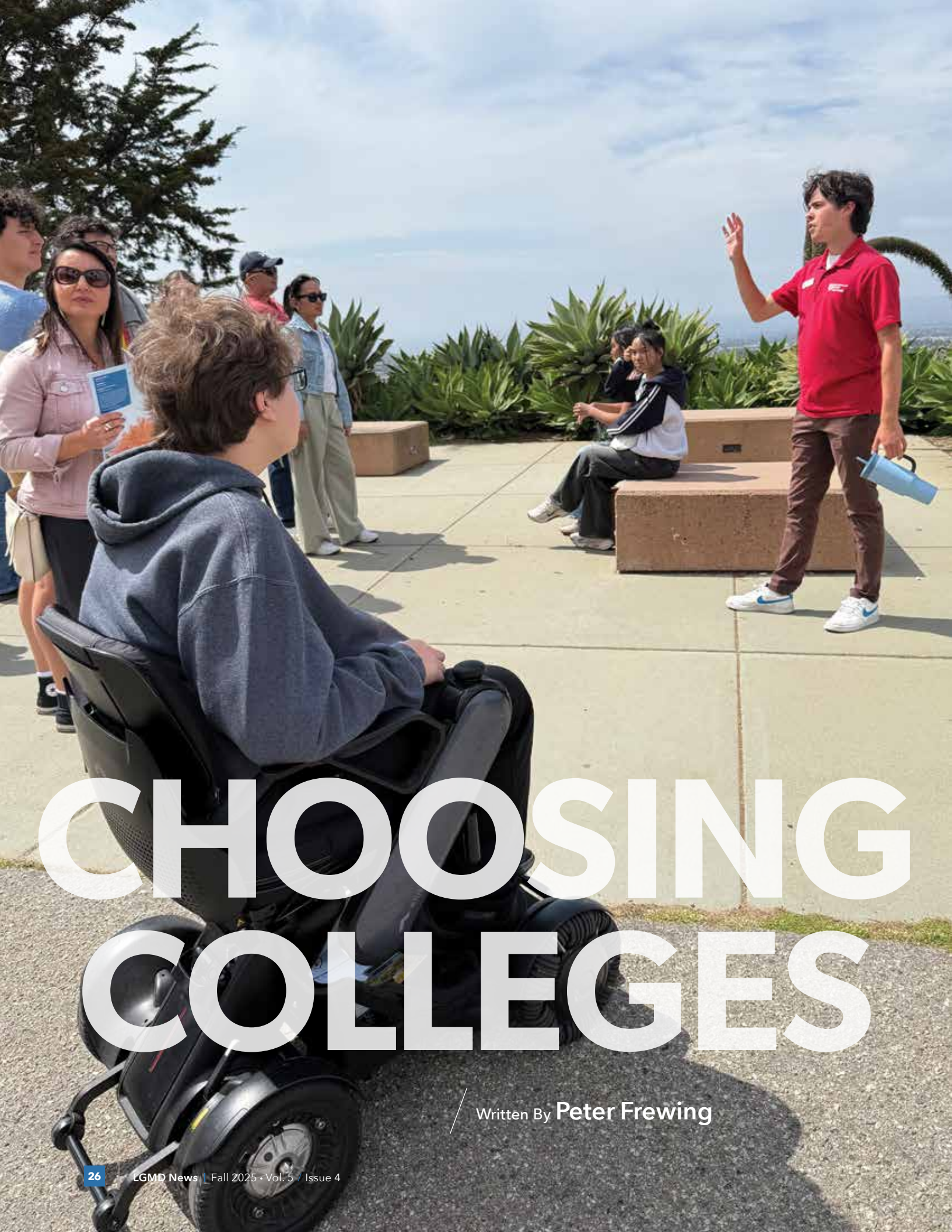
One unexpected challenge I faced was dealing with fire alarms and drills. During my first year, my dorm had around twenty fire alarms go off. Each time, everyone was required to evacuate using the stairs, but I lived on the fourth floor. I had not anticipated this situation and wished I had known to plan for it in advance so I could request the appropriate accommodation. This experience taught me that planning and anticipating your accommodation needs isn't just helpful, but a critical step in ensuring your safety on campus.

Apart from the chaos of frequent fire alarms, one of the biggest lessons and learning curves for me was the importance of asking for help and advocating for accessibility sooner, rather than trying to "tough it out" in spaces that weren't designed with people with disabilities in mind. What I hope others learn from my journey is that people are often more willing to offer help and support than you'd expect—if you let them in and give them a chance. Letting your guard down, trusting people, and asking for help can be so incredibly hard. But once you take that step, I promise it's worth it.

Closing Thoughts

Living with LGMD in college requires adaptability, flexibility, resilience, courage, and a deep sense of self awareness. It also offers a powerful opportunity to grow, connect, advocate, and inspire. Be the author of your own story; don't wait for someone else to come along and write it. Be loud, be silly, be confident, be unapologetically yourself—and others will follow.

By understanding your needs and the power of your own voice, while also using the resources available to you, you can create a college experience that is not only accessible, but entirely your own. ■



CHOOSING COLLEGES

Written By **Peter Frewing**

Like many high school juniors starting to think about college, I'm considering the majors offered, the size of the school, and the overall campus vibe. But, because I live with a severe form of limb-girdle muscular dystrophy (LGMD R5/2C), I also have to think about what it will be like to navigate college life in a wheelchair. Accessibility is my top priority, but another major consideration is having a strong support system to help me live as independently as possible.

College isn't just about classes; it's where I'll be eating, sleeping, studying, and spending most of my time. That's why I'm thinking carefully about housing, transportation, dining, and health services. I want a campus where I can get around independently, manage daily tasks, and be part of the community. The right college can't just be accessible on paper — it needs to be a place where I can succeed academically, stay healthy, and feel included.

So, when I tour a college campus, I'm not only looking at the academic opportunities, the quality of the classrooms and libraries, or the sports facilities. I'm also paying close attention to the things that that will affect my daily life as a person living with LGMD, such as:

- **Accessible Infrastructure**
  I am evaluating whether the campus goes beyond mere legal compliance with the Americans with Disabilities Act (ADA). I ask myself whether moving around campus will be intuitive and relatively easy, or if I'll constantly feel segregated from my peers as we all move between classes. In other words, is the campus not just technically accessible, but actually practical in daily life?

"The right college can't just be accessible on paper— it needs to be a place where I can succeed academically, stay healthy, and feel included."

"I value a disability services team that does not simply respond to requests, but that is helpful in anticipating needs."

- **Proactive Disability Services**

I'm interested in schools that not only have experience in supporting physically-disabled students but also use a forward-thinking approach. I value a disability services team that does not simply respond to requests, but that is helpful in anticipating needs. My older brother also lives with LGMD R5/2C (though he is somewhat less impacted than me), and is about to start college. His school seems to be taking a very proactive role in asking thoughtful questions about his needs and working with him to adapt a dorm room in advance.

- **Weather**

  Some of the top schools I'm looking at are on the East Coast. They have excellent math programs—my academic focus—and offer incredible opportunities, but the weather is something I can't ignore. Snow, ice, and freezing temperatures could make it harder to get around in a wheelchair. I'll have to weigh the strength of the school's math program against how the climate may affect my daily mobility and independence.

- **Availability of Trained Personal Care Assistants**

  It's a challenge to face the reality of needing help from a caregiver outside of one's immediate family. I hadn't fully considered how this might affect my college decision. But now, I realize that access to reliable, trained personal care assistants—whether through the school, local agencies, or private hires—is going to be a significant factor. It's one of the practical challenges that my family and I must navigate as we plan for my transition to college life.

- **Proximity to a Hospital or Clinic Familiar with Neuromuscular Diseases**

  Until recently, being close to a medical facility with expertise in muscular dystrophy didn't seem especially important to me because there weren't any treatments that had any chance of changing the course of my disease. But as we get closer to having gene therapy trials start for LGMD R5/2C (and other subtypes), that may change. As a result, I'm now more likely to consider a college's proximity to potential clinical sites—or to hospitals where future treatments may be administered—as part of my decision-making process.

- **A Social Culture that Fits Me**

  I've learned from my high school experience that independence isn't just about ramps and elevators—it's also about friendships and feeling like part of a community. Somewhat ironically, I chose to go to a high school on a steep hill, but the school values and student body made me feel exceedingly comfortable despite the physical challenges. That experience taught me that finding a campus culture where I feel welcomed and understood is just as important as the physical layout of the environment. Both matter.

This spring, I visited a friend at Loyola Marymount University in Los Angeles who lives with LGMD R3/2D. Seeing how he manages college life gave me a useful glimpse into the issues I'll need to think about. He met me at the coffee shop on campus and then showed me around.

The university has wide, flat paths with minimal stairs, making it easy to navigate. His dorm room had been modified with an adapted bathroom and enough space for his PCA to stay with him. That visit made me realize that with the right planning and infrastructure, a well-supported, independent student experience is absolutely possible.

For others with muscular dystrophy who are thinking about college, I suggest dreaming big, but also planning smart. Ask yourself, your family, and the colleges hard questions early. If possible, visit campuses and talk to current students with disabilities. Know your legal rights under the ADA but also know your personal needs—because those aren't always the same thing. Independence isn't about doing everything alone; it's about building the life you want with the right support in place. ■

Written By Melina Garza

Preparing for College When Your Child Has LGMD2A:

A Parent's Perspective

I'm the mother of a teenager living with LGMD R1/2A. This fall, my daughter Brooklyn is beginning her freshman year of college—a milestone filled with pride, hope, and a mountain of logistics. We've both found the process of preparing for college exciting and daunting.


Sic Em
Bears
Brooklyn Carter
Dawson Hall

Early in Brooklyn's senior year, I attended a free Muscular Dystrophy Association (MDA) Virtual Learning session titled *Personal Care Attendants at College*. That's where I learned about a grant from the Christopher Reeve Foundation that allowed us to receive three free hours of coaching from Annie Tulkin, the founder of Accessible College. That session became one of our most valuable steps in preparing for the transition.

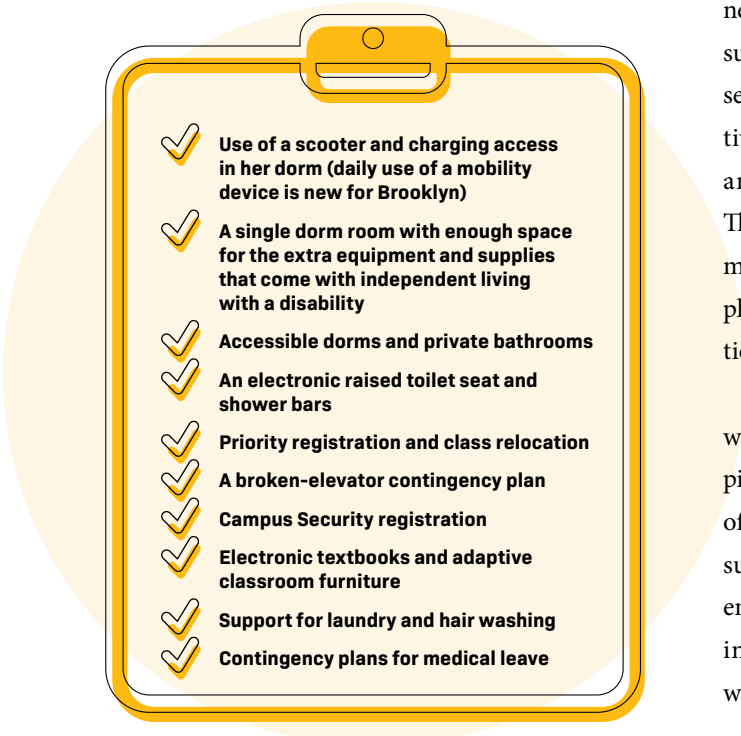
Annie helped us to look beyond academics and into what daily living and accessibility would mean for Brooklyn. One piece of advice that stuck with me: *You are not just interviewing the college—you're also interviewing their Office of Disability Services*. That guidance shifted how we approached college visits. It wasn't just about the campus vibe or academic programs — it was also about transportation, dorm accessibility, and how adaptive or rigid disability accommodations were on each campus.

For example, at one large public university, students with mobility challenges are expected to rely on the ADA-compliant bus system to get around campus. While technically this fulfills the need for accessible transport, it felt impersonal and inflexible for someone with fluctuating strength and energy. In contrast, a smaller private college we visited offered golf cart rides (like those used

This journey has taught me that preparing your child with LGMD for college is so much more than dorm shopping and orientation packets. It's about advocating ahead of time so your child doesn't spend their first semester in survival mode. It's about finding support systems that empower both you and your student.

for injured athletes) and allowed Brooklyn to purchase a faculty parking permit so she can park close to each building in ADA spaces—something that could make or break her ability to attend class on harder days.

Annie also helped us anticipate the "new accommodations" Brooklyn would need, which weren't on any standard school checklist. These included:



It was empowering—not just for me, but for Brooklyn. Annie encouraged her to start thinking through the big questions and hard decisions that come with adulthood and self-advocacy.

Through Accessible College, I was referred to Deborah McFadden with Abilities Count, who helped us navigate Supplemental Security Income (SSI) and Vocational Rehabilitation (VR). This referral opened doors I didn't even know existed. With their help, Brooklyn now has access to both physical and financial support to attend a private college that's a much better fit for her specific needs. Vocational Rehabilitation provides Brooklyn with support to prepare for and secure employment, offering services such as educational assistance, counseling, assistive technology and accommodations, job search guidance, transition planning, transportation, and more. Their goal is to empower individuals with disabilities to make informed choices and overcome barriers to employment by providing support throughout their educational journey and beyond.

This journey has taught me that preparing your child with LGMD for college is so much more than dorm shopping and orientation packets. It's about advocating ahead of time so your child doesn't spend their first semester in survival mode. It's about finding support systems that empower both you and your student. And perhaps most importantly, it's about acknowledging the emotional weight of it all.

Let yourself feel the nerves. It's normal to be anxious when your child moves out. But when your child lives with a progressive disease and depends on you daily, those nerves multiply. Give yourself grace. You *will* figure it out—and so will they. ■


RØDE

Written By Cerys Davage

BALANCING LIFE with LGMD

I'm 24 and live in Cardiff, Wales, in the UK. I found out I had LGMD R9/2I at seven after blood tests revealed high CK levels and a genetic test confirmed the condition, which my family later learned I share with my two younger sisters. I'd always struggled to keep up with my peers physically, but it wasn't until I was about 12 that I really began to notice symptoms.

In the early years of school, I didn't have to think about my condition every day. But gradually, it started to affect my daily tasks, and I had to find ways to adapt. For example, I progressed from being able to get to and from my lessons independently, to needing the help of a friend to climb stairs while holding onto the rail. Living with LGMD has meant that I constantly have to listen to my body and adapt to its changing needs.

University brought new challenges. Beforehand, I had applied for disability grants that enabled me to get a laptop, an ergonomic chair, and other appliances to make my life at university easier. The process can be a very slow and tedious one, requiring in-person visits so that the assessment centre can figure out exactly what you need. Having a very organised mother really helped me get that support! The university I attended was on a HUGE steep hill, which I couldn't walk all the way up, so asking for lifts either from friends or the university security was key!

At the start of university, I struggled to open up about my condition, as I just wanted to fit in like everyone else, and not stand out with something that set me apart. But as my condition became more obvious and I grew more comfortable with my new friends, I realised that they were there to help me. They gave me support on nights out and always put my needs at the forefront of their plans.

Over time, I've come to realize how important it is to advocate for myself—after all, if you don't speak up for yourself, who will? My relationship with this condition remains complicated, especially as I lose mobility and face an uncertain future. Still, I'm learning to take things one day at a time and focus on the present, because worrying about the future can feel overwhelming at times.

When I first started using a wheelchair, I was very self-conscious and embarrassed. I wanted people who stared at me to know that I could still stand and walk. There's a common stereotype that if someone uses a wheelchair, they can't walk at all—but the truth is, mobility aids like wheelchairs help me when I'm tired or when my legs and feet hurt too much. I also face prejudice the other way around; when I'm not using my wheelchair, my disability is hidden, and I'm criticized for using disabled toilets and parking spaces because I don't "look" disabled. I try to turn these moments into opportunities to educate people that not all disabilities are visible.

> ***THROUGH THE PODCAST I HOPE TO PROVE THAT HAVING A DISABILITY DOES NOT DEFINE YOU AND TO ENCOURAGE MY LISTENERS TO EDUCATE OTHERS AS A STEP TOWARDS A BRIGHTER FUTURE FOR PEOPLE WITH DISABILITIES.***
>
> —Cerys Davage

Growing up, I didn't know anyone else my age with a disability, and I felt alone in my experiences. So, two years ago, I decided to be the voice I wish I had growing up, and I started *Unbalanced with Cerys Davage*, a podcast that shows what life is really like with a disability as a young adult. The podcast is a mix of solo episodes diving into topics that young adults go through (some of which can be uncomfortable to address, making this podcast a safe space), and interviews with guests discussing their lives and how they've managed to deal with and overcome certain "life barriers." Through the podcast I hope to prove that having a disability does not define you and to encourage my listeners to educate others as a step towards a brighter future for people with disabilities. A big source of support for me has been the messages I receive from strangers on Instagram, telling me they've listened to my podcast and share similar symptoms. It is a great comfort to know that I'm not alone in this struggle. Community has become an essential part of how I manage life with LGMD.

I miss many of the things I used to be able to do when I was younger—things I never imagined I wouldn't be able to do anymore. So to my younger self, and other young people living with LGMDs, I'd say: make the most of your remaining physical abilities and never take them for granted. And above all, don't be afraid to ask for help—you are your own biggest advocate, and support is available when you seek it out. ■

Cerys's podcast ***Unbalanced with Cerys Davage*** is available on:

Spotify · Apple Podcasts · YouTube

Written By John Faver

Centers for Independent Living

What Makes Them Unique

Centers for Independent Living (CILs) operate on a fundamental principle that sets them apart from other disability organizations: they are run by and for people with disabilities. Federal law requires that 51% or more of their staff and board of directors be comprised of people with disabilities. This ensures that the organization can be most effective and relatable to the community it serves by utilizing the strengths of "disability experts" who understand firsthand the challenges that people with disabilities face.

The first CIL was founded in Berkeley, California, in 1972, and in 1978, federal funding was obtained to establish a nationwide network of CILs. Today, there are about 430 CILs throughout the U.S. CILs provide five core services to the community:

- Individualized and system-based advocacy
- Information and referral services
- Independent living skills training
- Peer support groups
- Youth (age 14-24) and institutional transition services

These services can assist with personal discrimination issues, the complex web of governmental benefits, transitions from a parent's living situation to an independent one, and personal relationships through courses such as Empowering to Connect.

The Independence Alliance in Cincinnati

To give a more detailed perspective on the work and services provided by Centers for Independent Living, we focus on one specific CIL: The Independence Alliance (TIA) which is based in southwestern Ohio (greater Cincinnati area) and is one of 12 CILs in Ohio. It serves the disability community in seven southwestern Ohio counties. The organization, which was known as The Center for Independent Living Options (CILO) until 2024, was brought to life in 1977 by two advocates with disabilities one night at the kitchen table. In keeping with the general philosophy of the CIL movement, its mission is "Empowering people with disabilities to lead independent and inclusive lives in the community."

TIA's funding comes primarily from the U.S. Dept. of Health and Human Services, but it also receives state funding (part B) through Opportunities for Ohioans with Disabilities (Vocational Rehabilitation for Ohio) allowing close coordination of vocational efforts to facilitate its consumers achieving their independent living goals on their own terms. Also, it receives program-based funding through the U.S. Department of Housing and Urban Development in support of housing-related efforts.

Suzanne Hopkins, who has served as Director of Programs at TIA since 2000, gives an overview of the organization's programs (see Figure 1, page 39). Suzanne joined the Alliance in 1992 as Personal Care Assistance (PCA) Services Coordinator, teaching incoming freshman at Wright State University (WCU) how to manage their PCA needs during their transition to university life. She has aspired to accomplish and implement needed changes as they were addressed in early ADA legislation and recognizes that "there is still much to be done."

John Faver with **Suzanne Hopkins**, Director of Programs at The Independence Alliance

1 Expanding Access for Youth with Disabilities

Our Youth Transition Services (YTS) Specialist continues to make waves in Greater Cincinnati schools. Recent initiatives include mock interviews, vision board workshops, and self-advocacy training in collaboration with Cincinnati Public Schools (CPS), Opportunities for Ohioans with Disabilities (OOD), and the Department of Developmental Services (DDS). Through events like the Workforce Academy Interview Day and an upcoming presentation at Clovernook Center for the Blind and Visually Impaired, we are building skills, confidence, and community among young people with disabilities – including those with rare neuromuscular disorders like LGMDs.

2 Ohio Permanent Supportive Housing (OH-PSH) Program

Our Ohio Permanent Supportive Housing (OH-PSH) Program is currently serving 33 households, supporting 85 individuals. Behind those numbers are stories of resilience. One long-term participant, once unhoused and navigating substance use, has now achieved sobriety, gained employment, and found stability with our support. Others are pursuing education in dental hygiene, nursing, and HVAC certification – goals first articulated in their Independent Living Plans, and made possible through trust, community, and the right supports.

3 Voter Accessibility: Local Change, Statewide Impact

Voting is a fundamental right – and for many people with disabilities, one that has been historically obstructed. Our longstanding collaboration with the Hamilton County Board of Elections has resulted in system-level improvements: the return of curbside voting signage, creation of an instructional training video, and implementation of accessible curbside voting at Early Voting sites. We hope to expand this work statewide, ensuring that people with disabilities – including those with mobility impairments or progressive conditions like LGMD – can vote safely and independently.

4 Celebrating Disability Pride and the ADA

In collaboration with community partners, we are planning a powerful celebration of the 35th Anniversary of the Americans with Disabilities Act (ADA), blending joy and justice with accessible indoor and outdoor spaces. Our focus extends beyond community-building to educating allies – those who may not live with a disability but hold the power to drive meaningful change in businesses and institutions. We are also laying the groundwork for Disability Pride 2025, set for September at the Main Public Library in downtown Cincinnati – a symbolically inclusive location for an event centered on identity, culture, and activism.

5 Disability Advocacy at the Forefront

At the Coalition on Homelessness and Housing in Ohio (COHHIO) Conference, Independence Alliance led discussions on the intersection of disability and housing, offering both policy recommendations and practical support for individuals navigating inaccessible housing systems. We are proud that our expertise led COHHIO to seek our consultation to improve accessibility for future events. Our Disability Rights and Advocacy (DR&A) team also hosts Disability Qmmunity, a peer support group created by and for people with disabilities. This vibrant community has expanded to meet twice monthly, offering a safe and affirming space for individuals with diverse identities and lived experiences.

6 Living Well in the Community

Finally, our Living Well in the Community (LWIC) workshop continues to be a cornerstone of our peer support programming. This year, 13 new participants joined our curriculum focused on goal setting across five domains of wellness: physical, intellectual, emotional, spiritual, and social. One participant even published a reflection in the Hamilton County DDS magazine – proof of the transformation possible when disabled people are given the space and support to grow.

Figure 1: Overview of The Independence Alliance's Programs

TIA has served clients living with muscular dystrophy. There is no record of specific LGMD subtypes, although broader categories such as congenital MD, DMD, and SMA were named specifically in our interview. TIA wants the SW OH disabled community to know that "we are Cincinnati's best kept secret." People living with disabilities often gravitate toward organizations that focus on their specific disease or set of diseases and may overlook more broadly helpful organizations like CILs when seeking assistance with their goals. Although people may have different diagnoses, they share many of the same difficulties and struggles, and organizations like CILs are more equipped to help with these types of things than other smaller organizations may be. With all services being free of charge, they hold a unique position in the disability community.

TIA's advice regarding LGMD (or MD in general) with childhood onset is this: "Start early, around age 14, with youth transition services. Adapting to life with a disability often starts in high school, and training, community, and peer mentor coordination are so important. This helps to prevent feelings of isolation and being overwhelmed. If you are already an adult and need our services, we are here for you in every way, especially in terms of advocacy." ▪

Q&A

With Kelly Brazzo, Co-Founder and CEO, Dan Pope, Vice President and Kristen Olsen, Secretary/Treasurer of CureLGMD2i Foundation

As the CureLGMD2i Foundation marks its 15th anniversary, it stands as a testament to the power of unwavering dedication in the face of a challenging rare disease. Founded by the Brazzo family after their daughter Samantha's diagnosis with Limb-Girdle Muscular Dystrophy Type 2I/R9 (LGMD2I/R9)—a debilitating genetic condition causing progressive muscle weakness—the foundation's mission has always been clear: to empower families, advance scientific understanding, and bring global attention to a disease once largely invisible. Over the past fifteen years, CureLGMD2i has evolved from a focus on basic awareness and research to pioneering standards of care, funding diverse and strategic research, and amplifying the patient voice to drive policy and accelerate the approval of future treatments. Through this comprehensive approach, the foundation continues to offer informed support and a profound sense of hope to those navigating the arduous journey of LGMD2I/R9.

Q What are Cure's biggest 2-3 wins for the LGMD community in the last 15 years?

A

Collaboration is one of our core values at the CureLGMD2i Foundation and working in conjunction with other LGMD advocacy organizations, drug developers, regulators and policy makers has led to some amazing wins over the last fifteen years.

In September of 2022, the CureLGMD2i Foundation participated in the first-ever Externally-Led Patient Focused Drug Development meeting, which documented the perspectives of people living with LGMD and has directly impacted and informed numerous clinical trials across the LGMD spectrum. A few years later, in February of 2024, the CureLGMD2i Foundation participated in the LGMD Scientific Drug Development Workshop that brought together stakeholders, including leaders from the U.S. Food & Drug Administration. Recently, we worked with other LGMD advocacy groups, clinicians, and industry to obtain approval of a new ICD-10 diagnosis code specifically for LGMD2I/R9, FKRP-related. These codes are crucial because they help track who is seeking treatment for LGMD2I/R9, which leads to better research and public health initiatives that can ultimately improve the care available for everyone.

Q What has changed in the lives of people living with LGMD2I/R9 and their families, and how did CureLGMD2i help make that happen?

A

Previously, a diagnosis often left patients and families grappling with uncertainty regarding the disease and potential treatments. However, over the last fifteen years, CureLGMD2i has served as a critical source of knowledge and support. We aim to empower families, advance scientific understanding, develop standards of care, and elevate global awareness, fostering a more informed, supported, and hopeful outlook for the community, even as an approved treatment is still anticipated.

Q What surprised you most about advocating for the LGMD2I/R9 community over the past 15 years, and how did your organization adapt, or how did your focus change?

A

CureLGMD2i's foundational work in LGMD2I/R9 involved building awareness and supporting scientific research. However, we've adapted our strategy to confront the reality that many drugs fail to gain approval. Our approach now includes diverse research funding that investigates the disease from multiple angles. We've also expanded our reach through strategic collaborations and robust advocacy programs, empowering the patient voice to influence policy and regulation, in the hope of accelerating the approval of much-needed treatments.

Q Looking back, what's the most important lesson you've learned that will guide your next 15 years?

A

Over the past fifteen years, CureLGMD2i has come to understand the vital importance of patience and collaboration. It's a sobering truth for many of us that the disease often progresses faster than treatments can be developed, but we at CureLGMD2i find comfort in knowing our efforts will benefit future generations. This journey has shown us that we cannot do it alone. With the support of our dedicated board and volunteers, all personally affected by LGMD2I/R9, we have significantly expanded our reach. We actively involve patients and families not just as recipients of aid, but as essential teammates, working together to inform industry, shape priorities, and advocate for meaningful change.

bridgebio MLBioSolutions CURELGMD2i

Join us in celebrating

bridgebio ML BioSolutions
a bridgebio company

LGMD-info.org

When Time Matters

The Role of Accelerated Approval in Patient Care

By Darcy Frear, PhD
Associate Director, Regulatory Policy & Intel, BridgeBio

Follow the roadmap to see the path from clinical trial to FDA approval.

The Accelerated Approval Program was developed in 1992 after HIV/AIDS advocates pushed the Food & Drug Administration (FDA) to speed up access to new, promising treatments for serious and incurable diseases.

In the 1980s, those suffering from HIV/AIDS were in urgent need of new treatments. Members of AIDS Coalition to Unleash Power (ACT UP) held a large protest at FDA headquarters in 1988 to demand faster drug approval and greater access to AIDS treatments. Before AIDS and ACT UP, all experimental medical decisions were made by physicians. ACT UP's efforts not only contributed to the accelerated approval pathway but also led to recognition that for patients facing serious and life-threatening conditions, unavailability of treatments may present more risk than an experimental drug.[2]

How the Accelerated Approval Pathway Works

This pathway "accelerates" access to medicines for serious and life-threatening conditions by allowing approval based on a **surrogate endpoint that is reasonably likely to predict clinical benefit**, while meaningful clinical benefit is being confirmed.[3]

Accelerated approval allows use of a surrogate endpoint to predict clinical benefit of a drug, shortening time to initial FDA approval. Drug developers must then confirm clinical benefit, either in the same trial or in another trial, to convert to traditional approval.

Think of it this way: instead of waiting years to see if cancer patients live longer on a drug (clinical benefit), the FDA may grant accelerated approval based on clinical trial data showing the drug significantly shrinks tumors (surrogate endpoint reasonably likely to predict clinical benefit). While tumor shrinkage doesn't directly measure longer survival, it is **reasonably likely** that tumor shrinkage may improve the course of disease. Surrogate endpoint measurements may predict clinical success of a therapy faster than waiting for clinical benefit results, which in turn can shorten the time patients must wait for important therapies.

Accelerated Approval Meets FDA's Evidentiary Standard

FDA uses the same standard of evidence for an accelerated approval that the agency uses for a traditional approval: the FDA must conclude that the drug is safe and effective for a particular indication while acknowledging that there is some uncertainty in the ultimate clinical benefit.

Some have criticized that the accelerated approval pathway use of surrogate endpoints does not guarantee clinical efficacy.[5] In response to these criticisms, the FDA has worked to strengthen the program by putting in place guardrails which require drug developers to confirm clinical benefit of the drug based upon clinically meaningful endpoints (e.g., survival) in order to convert accelerated approval to traditional approval. Additionally, the FDA has adopted new procedures for withdrawing products that fail to demonstrate clinical benefit.[3]

If drug developers cannot confirm clinical benefit in a confirmatory trial, the developers can try to work with the FDA to find another path forward.

Importance of Accelerated Approval for Rare Disease Drug Development

The vast majority (95%) of rare diseases lack FDA-approved treatments.[4] The accelerated approval pathway allows patients to access treatments as early as safely possible while ongoing research is conducted to confirm clinical benefit. On average, the clinical development time of an innovative drug is about nine years; using a surrogate endpoint and accelerated approval reduces this time by about three years on average.[7] Those three years can make a huge difference to patients, especially in slowly progressing neurodegenerative diseases.

The accelerated approval pathway also helps overcome several rare disease drug development challenges:

- **Small Patient Populations:** Conducting large, long-term clinical trials to demonstrate direct clinical benefit can be exceptionally challenging in rare diseases. There are limited numbers of patients who can enroll in trials, and these patients are spread out geographically. Surrogate endpoints can provide meaningful evidence of efficacy in smaller, shorter trials.
- **Complex Disease Mechanisms:** Rare diseases often involve complicated, not well understood processes. Identifying reliable surrogate endpoints linked to the disease's progression, or the disease's root cause, can be more feasible than waiting for direct evidence of long-term clinical outcomes.

The accelerated approval pathway offers the potential for critically needed therapies to be made available for patients potentially years earlier than the traditional pathway for drug approvals. Equally critically, this pathway offers a potential path for developers to advance therapies for conditions where the rarity of the disease or other factors would preclude a traditional developmental approach.

References: **1.** M. Takach, "How AIDS Activists Fought for Patients' Rights," November 2022. [Online]. Available: https://www.history.com/articles/act-up-aids-patient-rights. [Accessed April 2025]. **2.** M. D. Greenber, AIDS, experimental drug approval, and the FDA new drug screening process : a legal research guide, Buffalo: W.S. Hein & Co, 1999. **3.** Beakes Read, Neisser, Frey and Guarducci, "Analysis of FDA's Accelerated Approval Program Performance December 1992–December 2021," *Therapeutic Innovation & Regulatory Science*, p. 698–703, 2022. **4.** EveryLife Foundation, "The Accelerated Approval Pathway and Rare Diseases," 1 March 2025. [Online]. Available: https://everylifefoundation.org/wp-content/uploads/2025/03/AAPathway_About.pdf. **5.** PinkSheet, "Gene Therapy: Years After Accelerated Approval, Will US FDA Still Be Asking 'Does It Work?'," February 2023. [Online]. Available: https://insights.citeline.com/PS147744/Gene-Therapy-Years-After-Accelerated-Approval-Will-US-FDA-Still-Be-Asking-Does-It-Work/. [Accessed April 2025]. **6.** FDA, "Accelerated Approval – Expedited Program for Serious Conditions," December 2024. [Online]. Available: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/accelerated-approval-expedited-program-serious-conditions. [Accessed April 2025]. **7.** Brown, Wobst, Kapoor, Kenna and Southall, "Clinical development times for innovative drugs," *Nat Rev Drug Discov*, vol. 21, no. 11, pp. 793-794, 2022.

For more information visit bridgebio.com/lgmd2i-r9/

Written By Sarah Shira Emmons, MPH
Vice President of Patient Affairs and Community Strategies, The Jain Foundation

and Brad Williams, PhD
Senior Editor, LGMD News

Building a Path to a Cure

The Story of the Jain Foundation and Its Mission to Cure Dysferlinopathy

In the year 2000, Ajit Jain's life took an unexpected turn. His son, Akshay, had just been diagnosed with a rare form of muscular dystrophy: Miyoshi Myopathy type 1/Limb-Girdle Muscular Dystrophy Type 2B (LGMD2B), now called LGMD R2 or dysferlinopathy.

At that time, this diagnosis provided more questions than answers. The gene responsible—dysferlin (DYSF)—had only been discovered two years earlier. There was no treatment, no roadmap, and almost no one actively working toward a cure. But Ajit Jain was not one to accept this status quo.

Akshay Jain

Rather than waiting for the traditional research system to catch up, Ajit decided to create a dedicated organization with a singular mission: to find treatments and, ultimately, a cure for dysferlinopathy. And so, in 2005, the Jain Foundation was born—a nonprofit that would take a novel, hands-on approach to rare disease research.

His first instinct, as with many parents navigating a rare disease diagnosis, was to identify experts in the field and to search relentlessly for information. Fortunately, Ajit didn't have to walk this path alone. His cousin, Plavi Mittal, PhD, a biologist by training, helped him to make sense of the landscape of dysferlinopathy research. Plavi scoured the internet, dug through medical literature, and began reaching out to researchers across the world. Through this, Ajit and Plavi discovered two things: first, that dysferlinopathy was severely under-researched, and second, that the global patient and research community was tiny—almost nonexistent. While promising studies on dysferlinopathy were underway in labs in Newcastle, Chicago, Boston, and Iowa City, progress was slow, fragmented, and hampered by the structural barriers all too common in rare disease research.

The critical question emerged for the two cousins:

What could they do to speed up the path to a treatment—not just for Akshay, but for everyone living with dysferlinopathy?

A New Kind of Foundation

Rather than waiting for the traditional research system to catch up, Ajit decided to create a dedicated organization with a singular mission: to find treatments and, ultimately, a cure for dysferlinopathy. And so, in 2005, the Jain Foundation was born—a nonprofit that would take a novel, hands-on approach to rare disease research.

From the beginning, the Jain Foundation was structured to address key bottlenecks that slow the progress of rare disease science.

Building a Global Patient Community

For rare diseases, finding and connecting patients is one of the biggest hurdles. Without a critical mass of diagnosed individuals, it is difficult to run clinical trials or even understand the disease. When a pharmaceutical company asked how many patients they knew with the condition, there were only four: in addition to Akshay, two of these were Brad Williams and Josh Thayer—both of whom had participated in a study which had identified the DYSF gene. Brad now is Director of Research for the Jain Foundation, while Josh serves as its General Counsel. Ajit had met Brad through a website Brad had established

after finally getting his diagnosis (after 19 years), and Brad introduced Ajit to Josh.

It quickly became clear that there were enormous barriers to getting a diagnosis since the DYSF gene was very large and sequencing was not readily available. Relationships were forged with the researchers Dr. Nicolas Levy and Dr. Martin Krahn (in Marseille, France) to perform DYSF sequencing. Soon after, the foundation began a patient registry (now known as the Dysferlin Registry) and began supporting sequencing of DNA samples to confirm diagnoses.

Subsequent advances in genetic testing have greatly facilitated diagnosis of dysferlinopathy throughout the world. There are now more than 1,300 genetically confirmed individuals representing over 65 countries in the Dysferlin Registry. The Dysferlin Registry is a vital resource—not only for understanding the patient population but also for helping connect patients to potential clinical studies and emerging therapies, and with one another.

Defining Natural History and Outcome Measures

Understanding the natural history of a rare disease and knowing which tests can demonstrate a treatment's effectiveness are critical to designing clinical trials. In 2012, the Foundation began the Clinical Outcome Study in Dysferlinopathy (COS), which to date has involved > 300 individuals with dysferlinopathy at 21 clinical centers worldwide. COS has produced numerous publications on dysferlinopathy and has also established MRI (Magnetic Resonance Imaging) and the NSAD (North Star Assessment for the Limb Girdle Muscular Dystrophies) as sensitive outcome measures for clinical trials not only in dysferlinopathy but in other LGMD subtypes as well.

Providing Essential Research Tools

One of the greatest challenges in rare disease research is the scarcity of reliable resources. Without access to key resources such as animal models, cell lines, and antibodies, scientists who are beginning their journey studying dysferlinopathy face enormous barriers to entry. The Jain Foundation tackled this problem head-on by developing and distributing essential research tools.

By providing mouse models (transgenic mice created to have the defective dysferlin gene), cell lines, and specialized antibodies to the scientific community, the foundation made it easier for new labs to engage in dysferlin research. This open-access approach has helped to grow the field and attract fresh talent.

Clinicians participating in the Clinical Outcome Study in Dysferlinopathy meeting with Jain Foundation personnel in connection with the most recent Dysferlin Conference in Houston in 2024.

Building In-House Scientific Expertise

Many rare disease foundations rely on external scientific advisory boards, which can sometimes be subject to competing academic interests. Ajit wanted to remove these barriers, so he assembled an internal Scientific Advisory Board (SAB)—a team of scientists who work full-time for the Foundation and are solely focused on dysferlinopathy. This structure has eliminated conflicts of interest and allowed the Jain Foundation to develop a deep, internal knowledge base with a global view of the disease area.

Instead of simply reviewing grant applications, the Foundation's scientific team works closely with researchers to shape proposals, refine methodologies, and set clear milestones.

Throughout each project, the Jain Foundation remains in close contact, offering support, tracking progress, and proactively identifying opportunities and obstacles. This hands-on approach ensures that the funded work stays on course and that setbacks can be addressed quickly and collaboratively.

Fostering Scientific Collaboration

Bringing researchers together is essential. The Jain Foundation began to host dysferlin-specific scientific conferences at different locations around the globe, where experts share findings, spark new collaborations, and align on research priorities. These focused meetings have helped cultivate a community of scientists committed to accelerating progress and who are rewarded for collaborating.

Progress and Purpose

Over the past two decades, the Jain Foundation's model has proven to be both nimble and effective. Their investments have led to meaningful advances in understanding the biology of dysferlinopathy, identifying potential therapeutic approaches, and improving diagnosis. Their provision of free genetic testing, via the Lantern Project, for a wide variety of LGMDs has made a huge difference in many peoples' lives.

The foundation's work has helped lay the groundwork for promising clinical trials, including gene therapy and other potential treatments currently in development. What was once an isolated and underfunded research area is now an active, collaborative field—with more hope than ever on the horizon.

Empowering the Patient Voice

Throughout this journey, the Jain Foundation has always placed patients and families at the center. By providing education, resources, and opportunities to participate in research, the foundation has cultivated a strong, empowered patient community. For many people living with dysferlinopathy, the Jain Foundation has become a trusted partner and source of hope.

Their commitment goes beyond science. The foundation has an open line of communication with patients, facilitates lab tours and informational sessions to help people understand the latest research and connect with one another. These events create a sense of belonging in a community that was once scattered and silent.

A Message to the Rare Disease Community

The story of the Jain Foundation is one of determination, innovation, and the power of asking, "What more can we do?"

It is also a reminder that meaningful change in rare disease research is possible when families, scientists, and patients come together with purpose and urgency. By building a patient-driven, science-first organization, the Jain Foundation has reshaped the landscape of dysferlinopathy research and inspired others to follow.

For anyone navigating the uncertainties of a rare disease diagnosis, the Jain Foundation's journey offers this essential message:

> **You are not alone. Progress is possible. And sometimes, when the path forward doesn't exist—you can build it yourself.**

JAIN FOUNDATION

LGMD2B/R2 | DYSFERLINOPATHY | MIYOSHI

RESEARCH

Jain Foundation funds research into potential therapies for dysferlinopathy

REGISTRY

Jain Foundation maintains a registry specific to people living with dysferlinopathy

DYSFERLIN REGISTRY
by Jain Foundation

RESOURCES

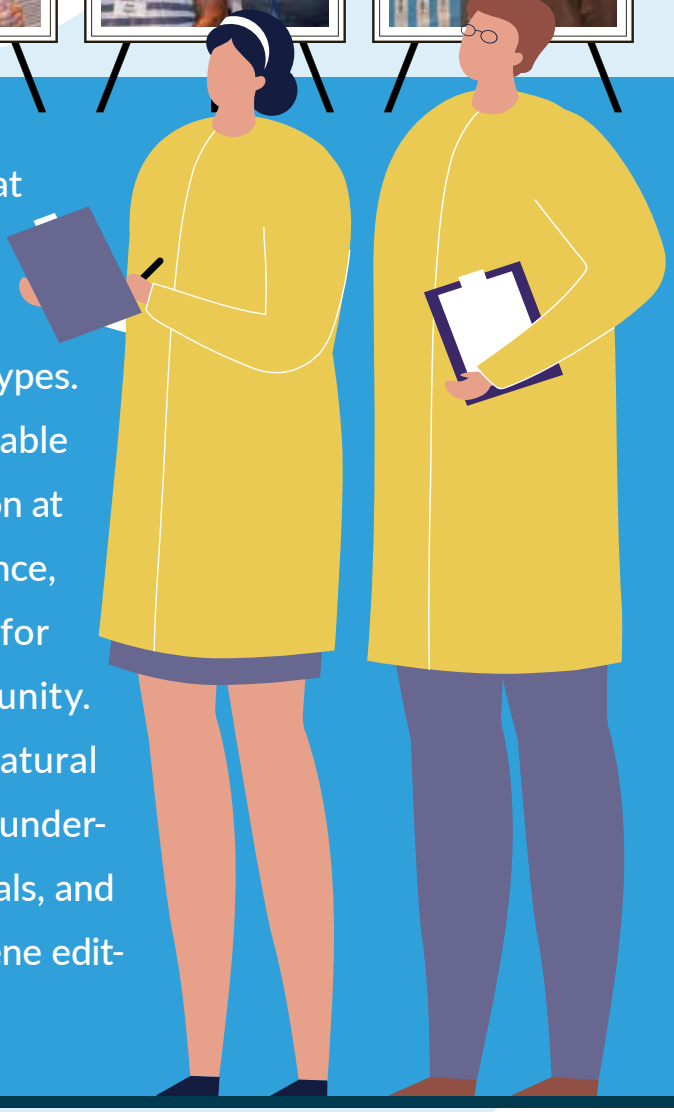
Jain Foundation supplies scientific resources and has funded over 10 years of natural history data collection contributing to developing outcome measures for clinical trials.

Written By Jean-Pierre Laurent, PhD
Director, LGMD2i Fund

Posters

at 2025 International LGMD Conference Show Progress in Research and Therapy Development

The first-ever scientific poster session at an International LGMD Conference featured 25 posters covering a wide range of topics and focused on many LGMD subtypes. Posters were presented (with authors available to discuss with attendees) at a special session at the end of the first full day of the Conference, which also included achievement awards for prominent members of the LGMD community. Topics featured in the posters included natural history studies, advances in diagnosis and understanding of disease mechanisms, clinical trials, and novel approaches to treatment including gene editing and cell therapies.



SCIENTIFIC POSTER SESSION SUMMARIES

Clinical Research

1 James, M. K., Alfano, L., Iammarino, M., Reasch, N., Steiner, C., Beale, A., Smith, M., Moat, D., Sodhi, J., Wong, K., Grover, E., Robinson, E., Mayhew, A. G., Eagle, M., Straub, V., Guglieri, M., Marini Bettolo, C., Muni Lofra, R., Diaz-Manera, J., & Lowes, L. (2025, July 19). *Motor function in limb girdle muscular dystrophy LGMD R1/2A (calpainopathy): Validation of clinical outcome assessments for clinical care and trial readiness* [Poster presentation]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

To assist in the design of clinical trials in LGMD R1/2A, this project showed the suitability of common physical therapy assessments including the North Star Assessment for LGMD (NSAD), 100-meter walk/run test and the Performance of Upper Limb (PUL) as outcome measures to capture disease presentation and progression in individuals with LGMD R1/2A.

• • • • •

2 James, M. K., Wong, K., Richardson, M., Grover, E., Richardson, E., Hilsden, H., Mayhew, A. G., Straub, V., & Alcock, L. (2025, July 19). *Progression of walking impairment in patients with dysferlinopathy over 12 months: Clinical outcome study for dysferlinopathy (LGMD R2/2B)* [Poster presentation]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Outcomes need to detect changes over time in dysferlinopathy to be useful as clinical trial assessments. This project looked at 21 temporal-spatial features of gait as a specific measure of mobility and showed the ability to detect changes in individuals' gait measurements over 12 months. These findings provide evidence supporting the use of gait analysis and gait outcomes in future clinical trials.

• • • • •

3 Sproule, D., Leiro, B., Mathews, K., & Vissing, J. (2025, July 19). *Development of pediatric and adult LGMD2I/R9 disease-specific physical function questionnaires using PROMIS item banks* [Poster presentation]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Assessment of the impact of functional deficits on daily life reported directly by the patients are called Patient-Reported Outcome or PROs, which can be important outcome measures in clinical trials. No PROs have been established and validated yet for LGMD 2I/R9. LGMD 2I/R9 specific physical function questionnaires for adults and children were created using the PROMIS Item Banks. Validation studies and correlation of PRO data with standardized performance measures are planned. If validated, this PRO can be a useful addition to clinical trials, such as FORTIFY.

• • • • •

SCIENTIFIC POSTER SESSION SUMMARIES

4 Hopkins, S., Merchant, P., Abby, S., & Witcoff, K. (2025, July 19). *Integrating patient insights into AB-1003 gene therapy clinical trial design in limb-girdle muscular dystrophy type 2I/R9 (LGMD 2I/R9)* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

People living with LGMD 2I/R9 experience a wide range of physical and emotional challenges, which are not always reflected in traditional clinical measures. To better address these needs, AskBio designed the LION-CS101 clinical trial for a new gene therapy (AB-1003) by actively involving patients, caregivers, and advocacy groups in the research process. Through interviews, advisory groups, and caregiver discussions, the company gathered insights into their daily life, including preferences for less invasive procedures, the importance of flexible trial logistics, and the need for clear communication about gene therapy. These insights led to meaningful changes in the trial design, such as offering home-based testing, travel support, and switching to a needle biopsy. The trial has completed its first group with no serious side effects and is now enrolling its second group of participants. AB-1003, an investigational gene therapy, has shown promise in a preclinical study and is currently being evaluated in a clinical study. AskBio remains committed to incorporating patient voices throughout the research process to ensure that future treatments are safe, scientifically sound and meaningful to patients living with LGMD 2I/R9.

• • • • •

5 Brazzo, K., Mathews, K., Fernández-Eulate, G., Wahbi, K., Muni Lofra, R., Johnson, N., Weihl, C., de Visser, M., Evangelista, T., Alfano, L., Lowes, L., Vissing, J., Ørstavik, K., James, M., Adcock, K., Geuens, S., Willis, T., Knudsen, L., Niks, E., Rosenberger, A. D., van der Holst, M., Dupitier, E., Leijenhorst, A., Laurent, J. P., Bryant, K., Bordes, M., Stojkovic, T., & Straub, V. (2025, July 19). *Provisional standard of care guidelines for the diagnosis and management of LGMD R9/2I* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Several potential disease-modifying therapies have now entered clinical trials for LGMD R9/2I, so there is a fundamental need for internationally agreed upon standards of care (SOC) guidelines. SOC guidelines are a framework to assist clinicians providing appropriate and safe management of patients. Moreover, their implementation facilitates interpretation of clinical research results by ensuring similar baseline care for patients across trial sites, particularly important in a rare disease requiring international sites. The participating experts agreed that LGMD R9/2I should be suspected in patients with autosomal recessive LGMD, high CK levels, and common clinical features such as proximal and calf hypertrophy. Detection of pathogenic mutations in both alleles of the FKRP gene via direct sequencing or next generation sequencing (NGS) is the only definitive way to diagnose LGMD R9/2I; muscle biopsy and muscle MRI can help guide the diagnosis. Cardiac and

respiratory involvement is common in LGMD R9/2I, so they should be monitored and managed proactively. Physiotherapy and input from occupational therapists can help maximize motor function and minimize the impact on daily living by using outcome measures to inform forward planning. A significant number of patients will experience pain, fatigue, and psychosocial concerns; clinicians should address these aspects when symptoms impact on daily living and provide support where indicated.

• • • • •

6 Rock, K., Bellam, P., Lott, D., Willcocks, R., Barnard, A., Forbes, S., Harris, A., Kamal, O., Hinkle, J., Senesac, C., Vandenborne, K., & Walter, G. (2025, July 19). *Using quantitative MRI to understand muscle changes in limb girdle muscular dystrophy (type R1/2A) and Becker muscular dystrophy (BMD)* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

The goal of this project is to demonstrate that MRI techniques can quantify muscle changes in diseases such as LGMD R1/2A and BMD. MRI techniques, developed in our lab, can quantify the amount of fat infiltration in muscle, called "fat fraction." The study's findings demonstrate that fat fraction, measured by MRI, is increased in people with LGMD R1/2A and BMD. We also demonstrate that these MRI methods can highlight important differences in muscles and muscle groups in LGMD R1/2A and BMD. These findings can help clinicians and researchers know which muscles to monitor to determine whether their treatment helped to stabilize or prevent progression.

• • • • •

Demographics and Quality of Life

1 Vola, B., Bianchi, M., Cerletti, M., Sermeryak, O., Sanchez Riera, C., Triki, C. C., & Torrente, Y. (2025, July 19). *Quality project for sarcoglycanopathies LGMD R3/2D, LGMD R4/2E, and LGMD R5/2C* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Studying quality of life in patients with muscular diseases is critical to understanding patients' needs and developing proper treatments. This is a 3-year project focused on the quality of life of more than 200 patients living with sarcoglycanopathies. From the patient's perspective, through questionnaires every 6 months, we have studied upper limb mobility, the ability to perform daily activities, sleep quality, mood, and energy levels, and how these factors change over a 3-year period. At the same time, we have conducted a comprehensive analysis of the participants, associating disease progression with specific genetic mutations.

• • • • •

2 LaMarca, N., Wyzanski, T., Carmichael, C., Bottomley, C., Levy, J., & Dabbous, M. (2025, July 19). *The patient experience of living with LGMD 2A/R1: Findings from a focus group* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

A patient focus group study was conducted to understand the patient experience of living with LGMD R1/2A, including symptoms, diagnosis, disease progression, disease impacts, and treatment expectations. This is critical to further the development of proper treatments. The findings highlight the need for a deeper understanding of the diagnostic challenges and unmet needs in this patient community. The FG findings may help healthcare providers and researchers to improve the diagnostic journey of patients as well as guide future research and clinical practices.

• • • • •

3 Gouverneur, C., Harden, M., Sproule, D., Rosen, A., Nelson, L., Bryant Knudson, K., & Brazzo, K. (2025, July 19). *Understanding the burden of living with LGMD R9/2I and the impact of a potential therapy* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

We conducted a survey to better understand the day-to-day experiences of people living with LGMD R9/2I and which symptoms have the most impact on their lives, as well as their expectations of the benefits from potential new treatments or disease-modifying therapies. Most of the patients surveyed expressed that they would want a treatment that enhances muscle strength as well as the recovery of their lost mobility and independence. If a treatment could not reverse muscle loss, there was a substantial interest in therapies that would slow or halt the progression of LGMD R9/2I. Survey results demonstrated that LGMD R9/2I profoundly affects the physical and mental well-being of those living with LGMD R9/2I and causes severe limitations on their independence and quality of daily life.

• • • • •

Diagnostic Tools

1 Bruels, C. C., Littel, H. R., Walls, C., Stafki, S. A., Estrella, E. A., Brady, L., Tarnopolsky, M., Dowling, J. J., Zingariello, C. D., Darras, B. T., Ghosh, P. S., Karachunski, P. I., Manousakis, G. E., Richardson, R. C., Kunkel, L. M., Pacak, C. A., Faulk, C., & Kang, P. B. (2025, July 19). *Improving genetic diagnosis in LGMD using nanopore long read sequencing* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

In this project, a new method of DNA sequencing was used to identify causative variants in individuals who did not get a genetic diagnosis after traditional clinical genetic testing. The nanopore long-read whole genome sequencing was used to sequence DNA from 68 individuals with muscular dystrophy. We identified and/or clarified pathogenic and likely pathogenic variants in 43% of the patient samples we sequenced. This increase in diagnostic capability will enable additional individuals with LGMDs to participate in clinical trials and to receive targeted care including better informed genetic counseling and family planning guidance.

• • • • •

SCIENTIFIC POSTER SESSION SUMMARIES

2 Weihl, C. C., Clause, A., & the ClinGen LGMD Variant Curation Expert Panel. (2025, July 19). *Improving LGMD diagnosis through systematic variant resolution* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

A significant fraction of individuals affected by LGMDs do not receive a definitive genetic diagnosis. One reason is that the pathogenicity of many mutations (whether they cause disease) is uncertain. They are called VUS for Variant of Uncertain Significance. The goal of this project is to help resolve these VUS and understand their clinical significance by creating a improved process for analyzing them. Through the ClinGen LGMD Variant Curation Expert Panel (VCEP), we have improved the non-specific rules used to assess variants and have the power to resolve VUS by aggregating unpublished evidence, strengthening the impact of a patient's clinical phenotype, and defining appropriate functional assays for LGMD. Critically, the clinical validity of the improved methodology and the resulting variant classifications are FDA recognized, and both the methods and results will be shared publicly. Our efforts over the past four years have resulted in the public release of improved variant interpretation guidelines and expert classification of over 250 variants, 125 of which are publicly available in ClinVar with 3-star expert panel review status. Of variants with either VUS or conflicting status, we have successfully resolved them to a definitive classification for 64% and 94% respectively.

• • • • •

3 Borland, H., Bolaño-Diaz, C., Verdú-Díaz, J., Gonzalez-Chamorro, A., Fitzsimmons, S., Veeranki, G., Straub, V., & Diaz-Manera, J. (2025, July 19). *MRI-based criteria to differentiate dysferlinopathies from other genetic muscle diseases* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

MRI scans can show patterns of muscle damage that are specific to particular genetic muscle diseases. To help in the diagnostics of patients with dysferlinopathy, MRI scans from hundreds of patients with dysferlinopathy were used to create a 5-step decision tree formula. The findings of this study show that MRI scans can help doctors decide whether a patient has dysferlinopathy instead of another genetic muscle disease.

• • • • •

4 Borland, H., Bolaño-Diaz, C., Verdu-Diaz, J., Gonzalez-Chamorro, A., Kocak, G., Fitzsimmons, S., MYO-Share Working Group, & Diaz-Manera, J. (2025, July 19). *Myoguide.org: A web-based portal supporting the analysis of MRIs for the diagnosis of neuromuscular patients* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Myoguide.org is a website containing several resources to help understand muscle MRIs from patients with NMDs. It has an artificial intelligence (AI) tool to help predict the type of NMD a patient might have based on their MRI scan, as well as training resources for doctors and other

healthcare professionals. This tool will facilitate diagnosis of individuals with NMDs when genetic test results are difficult to interpret. The website www.myoguide.org is already accessible to the public. Currently, MYO-Guide can predict the diagnosis of 20 different neuromuscular diseases based on the patient's MRI. It has a top 3 accuracy of 92%, meaning that in 92 out of 100 cases the correct diagnosis is one of the top three suggestions given by MYO-Guide.

Disease Knowledge

1 Gloriani, M., Cheli, B., D'Ercole, C., Ruggieri, V., Cosentino, M., Serrat Pineda, M., Blozanoska-Ochser, B., Grassi, F., Bouché, M., Madaro, L., & Sánchez Riera, C. (2025, July 19). *Sarcoglycans are enriched at the neuromuscular junction* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Nerves and muscles connect at the neuromuscular junction. Recently, the presence of sarcoglycans was shown to be critical for the nerve to establish proper contact with the muscle. Without sarcoglycans, the nerves do not connect to the muscles, and the muscle fibers get depolarized more easily, indicating that pathological decline in sarcoglycanopathies should no longer be understood in terms of sarcolemma damage only. This new report opens the door to exploring new strategies to approach these debilitating diseases.

2 Marshall, S. A., Iammarino, M. A., Smith, M. A., Steiner, C. L., Reash, N. F., Knight, A. B., James, M. K., Hunn, S. M., Mockler, S. R. H., Hilsden, H., Alfano, L. N., & Lowes, L. P. (2025, July 19). *Comparing phenotypes in limb girdle muscular dystrophy disease progression* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

A collaborative team of physical therapists completed a battery of tests on participants recruited during the International LGMD Conferences in 2019 and 2023, including the 100-meter timed test, the North Star Assessment for limb girdle-type Dystrophies, the Timed up and go, the Performance of Upper Limb, spirometry, and patient-reported outcomes. This study showed that standardized assessment of functional outcomes can be successfully captured at patient conferences with the advantage of reducing supplemental travel burden by meeting patients where they are. It shows also that validated outcomes such as the 100m, NSAD, and the PUL are informative across LGMD subtypes. Similarly, they appear to differentiate performance over time and across progression of disease in our cross-sectional cohort.

3 Borland, H., Moore, U., Gordish, H., Diaz-Manera, J., James, M., Mayhew, A., Guglieri, M., Fernandez-Torron, R., Rufibach, L., Feng, J., Blamire, A., Carlier, P., Spuler, S., Day, J., Jones, K., Bharucha-Goebel, D., Salort-Campana, E., Pestronk, A., Walter, M., Paradas, C., Stojkovic, T., Mori-Yoshimura, M., Bravver, E., Pegora, E., Lowes, L., Mendell, J., Bushby, K., & Straub, V. (2025, July 19). *Miyoshi myopathy and limb girdle muscular dystrophy R2/2B are the same disease* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Manual muscle testing (MMT), North Star assessment for limb girdle muscular dystrophy (NSAD), and MRI scores were compared and found to be similar between MMD1 and LGMD R2/2B. These results suggest that MMD1 and LGMD R2/2B should be treated as one disease (dysferlinopathy) in clinical trials. Separating them might create unnecessary distinctions and could limit treatment options for patients who could benefit from the same therapies. Since both conditions are caused by variants in the same gene (DYSF) and show similar patterns of muscle weakness and progression, the initial diagnosis does not reliably predict how a patient's condition will develop. Therefore, for research and treatment purposes, patients with dysferlinopathy should be grouped together, rather than being divided by LGMD R2/2B and MMD1.

• • • • •

Research Tools

1 Vola, B., Pompilio, G., Cerletti, M., Sanchez Riera, C., Gros-Louis, F., & Torrente, Y. (2025, July 19). *Human iPS-derived model to study sarcoglycanopathies* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

To improve research into disease mechanisms and expedite drug development, the GFB Foundation developed three induced pluripotent stem cell (iPSC) lines derived from the blood cells of patients affected by beta-sarcoglycanopathy with cardiomyopathy and respiratory involvement. Two of the three patients exhibit an aggressive phenotype with symptom onset before the age of 10. These cell lines were differentiated into cardiomyocytes, muscle cells, and neural cells and characterized, a necessary step towards their being used in research.

• • • • •

2 Levy, J., Boslego, J., Guglieri, M., Martin, A., Mathews, K., & Wrubel, M. (2025, July 19). *The LGMD2A/Calpainopathy registry: A patient-powered natural history study and trial recruitment tool* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

LGMD2A/Calpainopathy Registry is a global, patient-reported registry with two main goals: to collect data over time from individuals living with Calpainopathy (including LGMD R1/2A and LGMD D4/1I) and to support recruitment for clinical research studies. The Registry collects

information about motor function, activity, and quality of life. Participants are encouraged to upload a digital copy of their genetic report and enter their own data. In the first twelve months after opening, over 300 participants created a profile and entered data. Data collected through the Registry increases our understanding of the disease's burden and mechanism and helps to develop management guidelines to improve the care and quality of life for people living with Calpainopathy. Additionally, the study helps identify individuals with Calpainopathy who might be willing to take part in research studies or clinical trials. To date, it has been utilized to assist in participant recruitment for three clinical studies.

Therapy Development

1 Tasfaout, H., Reyes, T. R. L., & Chamberlain, J. S. (2025, July 19). *Development of gene therapy for FKRP disorders* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Mutations in FKRP lead to muscle disorders associated with defects in the dystrophin complex of proteins that are critical for normal muscle health and function. This study focused on treating advanced stages of FKRP disorders by using an aged animal model. In old mice we saw a significant reversal of pathology and an increase in strength. However, those studies required very high doses of AAV, which have been associated in some cases with serious adverse events in clinical trials. Therefore, our present studies have focused on comparing different variations of the different parts that constitute gene therapy: more efficient gene delivery and more efficient FKRP expression. Together, these approaches could lead to safer and more effective protocols for gene therapy of FKRP-related muscle disorders.

2 Goldstein de Salazar, R., Kramerova, I., Perez, J., Hauschka, S. D., Chamberlain, J. S., & Spencer, M. (2025, July 19). *Design of synthetic promoters for AAV-driven treatment of limb-girdle muscle dystrophy type R1/2A* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

These synthetic DNA elements enable the development of a new LGMD R1/2A gene therapy that restores calpain-3 protein to skeletal muscle while remaining inactive in the heart, as heart expression of calpain-3 has been shown to cause toxicity in mouse studies. A preclinical study in an animal model was successful and helped us identify a lead candidate for LGMD R1/2A gene therapy. Functional studies are ongoing to confirm that restoration of the calpain-3 protein eases LGMD R1/2A symptoms.

SCIENTIFIC POSTER SESSION SUMMARIES

3 Jordan, M., & Zingariello, C. D. (2025, July 19). *Use of lamotrigine to treat painful muscle contractions in LGMD 1C "Rippling muscle disease"* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

LGMD1C is caused by heterozygous pathogenic variants in the CAV3 gene, which encodes the protein caveolin-3. Caveolin-3 plays a crucial role in regulating calcium levels in the sarcoplasmic reticulum leading to muscle hyperexcitability. This is a case report of a patient who had episodes that she described as "muscles jumping." Lamotrigine was added to a Baclofen regimen. At 6-month follow-up, the frequency of episodes had significantly decreased to one or two over the course of months. Larger studies are needed to prove the benefit of lamotrigine for symptomatic treatment of LGMD1C, but this case suggests that lamotrigine is possibly a safe and effective option.

4 Gauthier, L., Huang, S., Ma, K., Ng, K., Koczwara, K., Johnson, N., & Lek, M. (2025, July 19). *Developing a modified CRISPR-Cas9 editing approach to correct a CAPN3 c.550del. A mutation associated with limb-girdle muscular dystrophy* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

This project could help meet two objectives: to ultimately develop a promising therapeutic approach for correcting the c.550delA mutation underlying LGMD R1/2A, a mutation very common in Eastern Europe, and to create a process to assess all missense variants within CAPN3 helping to interpret variants of uncertain significance (VUS), necessary for LGMD R1/2A patients to receive a definitive diagnosis.

SCIENTIFIC POSTER SESSION SUMMARIES

5 Lee, A., Blankenbiller, T., Rainey, A., Reklis, L., & Sproule, D. (2025, July 19). *FORTIFY: A phase 3 study to evaluate efficacy & safety of BBP-418 in individuals with limb girdle muscular dystrophy 2I (LGMD 2I), LGMD R9 FKRP-related* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

BBP-418 is an oral, experimental medication intended to saturate the partially functional FKRP protein. The goal is to force increased glycosylation of αDG to potentially stabilize or improve muscle integrity. FORTIFY is a Phase 3 randomized, placebo-controlled study that will assess the safety, tolerability, and efficacy of BBP-418 in LGMD R9/2I. In addition to evaluating the effect of BBP-418 on motor performance using the NSAD, the effect of BBP-418 treatment on glycosylated αDG levels, the hallmark of disease at the molecular level, will be investigated at 12 months with potential to use this biomarker as a surrogate endpoint in LGMD R9/2I.

• • • • •

6 Bouchard, C., Jiang, J., Rousseau, J., & Tremblay, J. P. (2025, July 19). *Correcting mutations responsible for LGMD R2/2B (dysferlinopathy) with prime editing* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

Prime editing is a type of gene correction, not replacement. This project aims at developing a precise correction of mutations in the dysferlin gene to treat LGMD R2/2B. Correction of several mutations was achieved. It is now important to make this prime editing technology even more efficient and very safe. The scientific advances of this project could help lead to treatments for all LGMDs.

• • • • •

7 Joynt, A. T., Guo, D., Daman, K., Yan, J., Emerson Jr., C. P., & Wolfe, S. A. (2025, July 19). *Developing prime editing therapeutics for LGMD R9/2I* [Poster session]. International Limb Girdle Muscular Dystrophy Conference, Orlando, FL, United States.

The goal of this project is to create a therapeutic for LGMD R9/2I by correcting the L276I mutation in FKRP using genome editing. Many patients with LGMD R9/2I carry the L276I mutation, so a therapeutic that can correct this mutation would address a large fraction of the patient population. Prime editing is a genome-editing approach that can precisely correct a mutated sequence within the genome. Prime editing functions much like a word processor: it can locally rewrite the "text" of the genome to correct errors. Using this method, we successfully corrected the L276I mutation in LGMD R9/2I patient-derived cells with high efficiency, at a rate of >50%. Currently, we are working on novel delivery of these genome-editing reagents and on bringing this novel experimental therapy to clinical trials.

• • • • •

From groundbreaking research to heartfelt connection, the 2025 International LGMD Conference brought together the brightest minds, the most dedicated clinicians, and inspiring patient leaders from around the globe. Together, we shared knowledge, raised our voices, and stood united in our mission to accelerate progress for those living with LGMD.

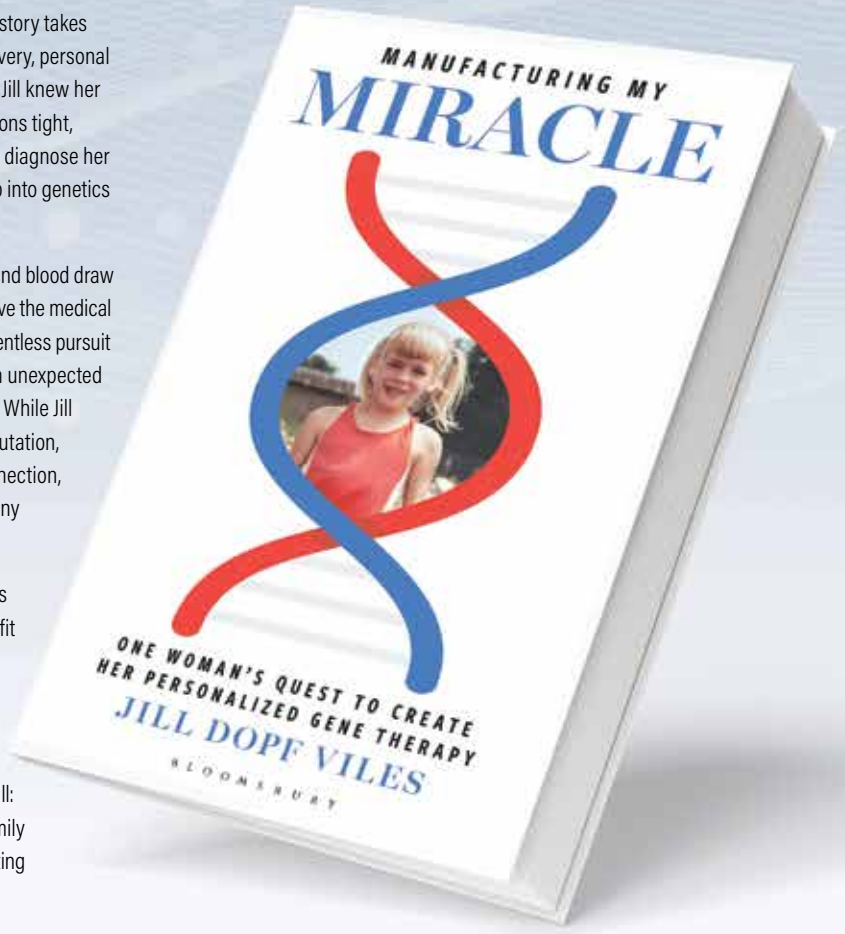
WHO LIVES? WHO DIES? WHO DECIDES?

ONE WOMAN'S QUEST TO SAVE HER FAMILY FROM A RARE HEREDITARY DISORDER AND WHAT IT MEANS FOR OUR COLLECTIVE GENETIC FUTURE

Jill Dopf Viles's genetic detective story takes readers on an extraordinary journey of scientific discovery, personal determination, and bioethical debate. From childhood, Jill knew her body was different—her muscles were weak, her tendons tight, and her body fat nearly absent. When doctors failed to diagnose her condition, she became her own researcher, diving deep into genetics in her search for answers.

Nearly thirty years ago, Jill Viles navigated an underground blood draw and genetic study with a team of Italian scientists to solve the medical mystery that plagued her family for generations. Her relentless pursuit of answers led to astonishing discoveries, including an unexpected genetic link to Olympic hurdler, Priscilla Lopes Schliep. While Jill battles a rare form of muscular dystrophy, Priscilla's mutation, in the same gene, enhances her athleticism. Their connection, highlighted on *This American Life,* is just one of the many remarkable stories in this book.

Viles explores urgent questions such as: Who deserves access to life-giving treatments? What role should profit play in healthcare? Who is ultimately responsible for payment-private health insurers, the government, or the patient? As Jill stores her self-designed viral vector in her rural Iowa kitchen, beside her ground beef and frozen waffles, she faces the most looming question of all: should she risk her own health to save her beloved family members who share the same genetic diagnosis by testing out the genetic therapy on herself?



ORDER YOUR COPY OF ***MANUFACTURING MY MIRACLE*** TODAY!

Available at amazon

The SPEAK Foundation
3551 Blairstone Road #105-62
Tallahassee FL 32301

Global Advocacy Meeting

We Are Interested In Hearing From You!

All LGMD organizations outside the USA are invited to attend this meeting.

October 17th 12:00 pm ET

The SPEAK Foundation

Sign Up Today to Attend!

TheSpeakFoundation.com/advocacy

SIGN UP TO ATTEND