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LGMD News

Uniting the Limb-Girdle Muscular Dystrophy Community

Orchestrating a Cure for Dysferlinopathy

In the 17 Years Since its Founding, the Jain Foundation Has Funded Over 120 Projects and Invested Over $35 Million Dollars Towards Finding a Cure

FROM PATIENT TO PROFESSOR

Monkol Lek, PhD, with LGMD2G/R7, Changed His Career Path to Better Understand the Disease and Find a Way to Help Others

CLINICAL TRIAL RESOURCE GUIDE

What Trials Are Currently Available for Your Subtype?

The SPEAK Foundation

We Offer HOPE.

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

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

For additional information or to submit an application from August 1, 2022 through October 28, 2022, please visit **TheSpeakFoundation.com/grant-programs**.

The HOPE Project

A Program of The SPEAK Foundation

TheSpeakFoundation.com/grant-programs

Accepting applications from August 1, 2022 through October 28, 2022.
Available to US residents only.

LGMD News

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How To Donate

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

Thank you for your support!

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

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

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Working Together, Succeeding Together

As individuals living with LGMD, we should make every effort to find a solution cooperatively.

Most of the leaders in our community are either individuals or family members affected by LGMD. Some are parents of a child with the disease and work full-time jobs. Some are disabled adults who are working part-time jobs. Many fully volunteer their time. Every one of us is doing our very best to manage multiple responsibilities, such as family commitments, emergencies, our health, and more, alongside our tireless work to advance progress for the LGMD community. It is important that industry, patients, caregivers, and others are sensitive to the amount of time and effort that goes into advocacy work or leadership while also dealing with the challenges of a disability.

When I founded the Speak Foundation in 2008, also living with LGMD2I/R9, I was so eager to just provide encouragement to those of us living with a disease for which we were told there is no cure. Additionally, our foundation had to deal with the psychosocial impact of representing a disability that seemed to be of little interest to the pharmaceutical industry. Fortunately, these ideas about LGMD are changing.

As we anticipate treatments, we should take this time to learn from other disease communities. To be successful, we must work together. We should take the attitude that a rising tide raises all the ships. And to be effective, we must collectively communicate to industry and the Food and Drug Administration. As individuals living with LGMD, we should make every effort to find a solution cooperatively. If we are going to continue to succeed as a community, it will take all of us working together.

This Summer 2022 issue has wonderful articles on how others living with LGMD have dealt with the psychosocial stressors that come with having a disability. Additionally, we have included a Clinical Trial Resource Guide, an update on dysferlinopathy from the Jain Foundation, a new installment to our "Patients Who Have Gone Into Science" series, and more!

We invite you to share your thoughts on this issue by emailing us at ***ContactUs@TheSpeakFoundation.com***. ■

Kat Bryant Knudson

Kathryn Bryant Knudson
Editor In Chief

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Our Mission

The Speak Foundation was based on the principle of "Speak up for those who have no voice."

Speak up for those who cannot speak for themselves. — Proverbs 31:8

The LGMD Grant Award Program

Program overview

The LGMD Grant Award Program is a competitive program designed to inspire patient advocacy organizations or non-governmental organizations to address unmet needs in limb-girdle muscular dystrophy (LGMD) care. Multiple grants may be awarded through this program and a total of $100,000 (U.S. Dollars) may be distributed overall.

The path to a diagnosis of LGMD is often long and can involve multiple years of frustrating experiences. Many people living with LGMD are assigned a diagnosis of LGMD based on their symptoms, have not been offered genetic testing, or have a need for updated genetic testing.

Sarepta is introducing this LGMD Grant Award Program, an effort aimed to shorten the LGMD diagnostic journey and/or enhance participation in existing genetic testing programs. The goal of our efforts is to ultimately offer long-term impact for families, such as earlier access to specialized care, increased clinical trial participation, and improving access to potential future treatments for the LGMD community.

Individuals from the LGMD community may partner with an organization to apply.
Applications must be submitted between May 5, 2022 and September 5, 2022.

Proposal criteria are as follows: *

Proposals must be original, meaningful, and should include ways to shorten the LGMD diagnostic journey through one or more of the following:

- Promoting recognition of early signs and symptoms of LGMD
- Enhancing participation in genetic testing and genetic counseling programs
- Empowering families to take an active role in pursuing a confirmed diagnosis

The grant award program will accept submissions from patient advocacy organizations and non-governmental organizations from any country. Proposals may have a regional focus.

An organization's proposed work should not be specific to a certain subtype.

**Additional criteria apply. Please see our FAQ Document, found at https://Sarepta.com/LGMDGrantAwardProgram for more detail.*

Grant award(s)

Multiple grants may be distributed for a total of up to $100,000 USD to support the selected project or projects across the world.

Submission process

Thank you for your consideration of this grant award program! Please visit our website: **https://Sarepta.com/LGMDGrantAwardProgram** to review the full FAQ document and to submit your application.

If you have questions, please contact the Sarepta Patient Affairs team at advocacy@Sarepta.com.

SAREPTA THERAPEUTICS

A Letter to Young Adults with LGMD

I want to pass along a few affirmations that may help in those moments when you feel alone, upset, or hopeless. Had I known how important it was not to trust my inner critic earlier in life as a person living with a chronic illness, I might have suffered less.

It was the first few minutes after a fall in a public place that I hated myself the most. This internal dialogue followed: "Why didn't I pay more attention to where I was walking? How could I be so stupid? How did I think I could wear these shoes? Now what am I going to do?" I frantically masked my physical pain and assessed the situation for the least embarrassing way to get back onto my feet and on with my day.

However, I didn't *really* recover.

Inside, the collection of these experiences birthed a shame and sense of inadequacy that I did not want to talk about. While most other people in their twenties were considering a future with unlimited possibilities, I was stressed about the expected snow forecast and how I would make it from my handicap parking spot to the door entrance without slipping and falling.

To live with LGMD means to experience moments like mine as the condition progresses. Within the MD community, my story is not unique. Many of you can relate to how bad it feels to have your body and confidence come crashing down while walking down the sidewalk or falling in a busy bar or restaurant. It is how we define these experiences that plays a significant role in our collective mental health.

Living with LGMD is stressful, but only you experience and understand what happens on the inside as the condition shows itself time and time again to the outside world. For this reason, I want to pass along a few affirmations that may help in those moments when you feel alone, upset, or hopeless. Had I known how important it was not to trust my inner critic earlier in life as a person living with a chronic illness, I might have suffered less.

- **You are not weak, tired, or sore because you are doing anything wrong.**
- **Moments like these are difficult to bear. Be as kind to yourself as you would a friend.**
- **Giving help to someone in need can be rewarding.**
- **Everyone is on their own life path. Comparing yourself to others steals your joy.**
- **Not all bodies are great, and that is okay. You are so much more than your physical abilities.**
- **There are times you are going to feel deeply sad, scared, inadequate, and angry. Allow yourself the space to grieve.**

Living with a slowly degenerative, physical illness requires extra support on the outside *and* on the inside. Tend to your inner voice. Grow your mental health through intentional examination of your self-talk. Learning to reframe negative messages can have a powerful effect on your beliefs, behaviors, stress management, and overall well-being. ▪

Contributed by Kelsey Jager, PhD

Kelsey Jager, PhD is a licensed Professional Clinical Counselor and Supervisor in the state of Ohio and is living with LGMD2A/R1. She earned her PhD in Counseling and Human Development from Kent State University in 2019. Her dissertation, titled "The Experiences of Emerging Adults Living with Juvenile Onset Muscular Dystrophy: Implications for Counselors" provided an in-depth investigation into the emotional consequences of living with LGMD. She has taught undergraduate and graduate courses in counseling and education, and currently works in private practice providing counseling and psychotherapy to adolescents and adults. Working with individuals with chronic illness is her professional passion.

International Consortium of LGMD Organizations

United States

The Speak Foundation
Uniting the entire LGMD community
TheSpeakFoundation.com

Beyond Labels & Limitations
Funding research for LGMD 2A/R1 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 2S/R18
CamronsCure.com

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

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

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

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

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

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

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

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

Team Titin
A consortium of scientists and affected community members for LGMD2J/R10 Titin-related
TitinMyopathy.com

The Jain Foundation
Funding research for LGMD 2B/R2 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 2A/R1 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 1F/D2
ConquistandoEscalones.org

"GFB ONLUS"/ Family Group of Beta-Sarcoglycanopathy
Representing the LGMD 2C/R5 Gamma Sarcoglycan-related, LGMD 2D/R3 Alpha Sarcoglycan-related, LGMD 2E/R4 Bèta-Sarcoglycan-related, and LGMD 2F/R6 Delta-Sarcoglycanrelated 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 2A/R1 Calpain3-related community
AICA3.org

Japan

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

Netherlands

Stichting Spierkracht
Raising awareness and supporting the LGMD2D/R3 Alpha Sarcoglycan-related community
StichtingSpierkracht.com

Spain

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

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

Linda P. Lowes, PT, PhD

The Research Institute
at Nationwide Children's Hospital

Meet the Expert

Linda P. Lowes, PT, PhD is Associate Professor of Pediatrics at The Ohio State University and a principal investigator in The Center for Gene Therapy in the Abigail Wexner Research Institute at Nationwide Children's Hospital in Columbus, Ohio. As part of the Center for Gene Therapy, she has been a pivotal co-investigator on numerous, first-in-human gene therapy clinical trials in rare diseases, including the first-in-human trial that led to FDA approval of the first gene therapy for spinal muscular atrophy. She serves on the executive board for TreatNMD and was awarded the Excellence in Innovation award for her two inventions that use technology to quantify movement.

Q

Why are participants in natural history studies only divided into two groups — ambulatory and non-ambulatory? I would think limiting a study to just those two specific groups would result in excluding a large group of people who are semi-ambulatory, who can walk but use assistive devices for balance.

A

Definitions such as ambulatory or non-ambulatory are arbitrarily assigned based on which assessments are best for different levels of weakness. For example, one natural history study has individuals who can walk 10 meters in less than 12 seconds do standing balance activities that may not be safe for individuals with less walking ability. If it takes you longer than 12 minutes, you can still be in the study but would do the assessments that the individuals who are no longer walking are performing. This is mostly for safety, but also so that the data are consistent. Check with the study coordinator or investigator running the study. It is likely that someone who is "semi-ambulatory" can fit into one of the categories.

Q

Many of us with LGMD have heard the message that too much exertion or exercise can be detrimental and cause irreversible damage to muscle. We have also heard the seemingly contradictory message that we will "lose what we do not use." Fear of doing too much has kept me from trying physical therapy (PT). Please share your thoughts and guidance on how we can tell what is "too much."

A

The current guidance is that mild to moderate exercise is good for people with LGMD. You should avoid heavy lifting or maximal efforts, as it can break down your muscles. Listen to your body and do not push yourself to exhaustion. Exercising should not hurt. If you are still sore or in significant pain the next day, you are very likely overworking your muscles. Some general guidelines include choosing something you enjoy and starting slow. You can then increase your levels as your body adjusts. Also, make sure that the activity is safe. For example, if you have balance problems, hiking on a dirt trail may not be the best choice.

Q

I have tried PT in the past and was so exhausted afterwards that I could not drive home. How can I get a PT to do home therapy with me and have insurance pay for it?

A

Check with your health insurance company, as most have rules for when they will pay for home PT. You could also inquire if Telehealth is available through your insurance. If they will not approve home visits, you should talk to your PT and explain your concerns. The program is likely too strenuous for you. One solution might be to use the PT visit to teach you the activities, and then you can perform the repetitions at home.

Q

How can I tell if I should start using a wheelchair?

A

I know many patients do not want to use a wheelchair. I understand that this can be upsetting as it means the disease is progressing. I encourage people to get a wheelchair as soon as their walking ability is limiting their daily activities. If you are no longer going shopping or declining invitations because it will be too taxing, it is time to consider getting one. The most important thing is to be able to do the activities that you enjoy. Sometimes this means using a wheelchair. Keep in mind that you do not have to use it all of the time and it does not mean that you will stop walking faster.

Q

I am a physical therapist and father of a child with LGMD2B/R2. What is an optimal exercise program?

A

An optimal exercise program does not exist. Exercise should be tailored to the individual needs of the child. Even though you are a PT, it is not uncommon to have questions about treatment for rare diseases. I would encourage you to talk with a PT who works in a muscular dystrophy clinic. In general, I do not automatically recommend PT for a child with LGMD. Most children are active and self-monitor their own fatigue. I try to encourage community activities, as appropriate, such as swimming lessons or tai chi. If your child is having a specific problem, then a PT might be able to help.

Q

What are the best exercises I can do daily at home? Is there a website with home exercises that you recommend?

A

Exercise is best when it is tailored to your specific needs. If possible, please consult with a PT who is familiar with LGMD, as it is important to discuss any individual limitations with a professional before starting an exercise program. The Muscular Dystrophy UK site offers some general information on home exercise options. You can access it at **Musculardystrophyuk.org/get-support/everyday-living/exercise**. You can also find videos on Pilates for neuromuscular diseases at **YouTube.com/playlist?list=PLazCbfp_tqxyve043vSch45aPfMzFfHxX**.

The most important thing is to be able to do the activities that you enjoy. Sometimes this means using a wheelchair. Keep in mind that you do not have to use it all of the time and it does not mean that you will stop walking faster.

Connect with Us

TheSpeakFoundation.com

Question

Interview your PT at the first appointment and make sure that he or she is willing to learn about your disease and stay current. I believe that the therapist's personality and work ethic are more important than the specialty.

Have a Question for Our Experts?

Send Questions To:
ContactUs@TheSpeakFoundation.com

Q

When looking for a physical therapist, what kind of credentials, specialization, or expertise should I ideally be considering? I am not sure that I can find someone who knows a lot about neuromuscular disorders.

A

The best choice would be to see someone who is knowledgeable about LGMD. Many times, these physical therapists can be found in a muscular dystrophy center or clinic. Outside of this, a PT's knowledge of LGMD will vary. Interview your PT at the first appointment and make sure that he or she is willing to learn about your disease and stay current. I believe that the therapist's personality and work ethic are more important than the specialty. Do not feel bad "shopping around" until you find a good fit.

Q

I am a full-time wheelchair user who does not weight-bear any longer. My calves feel hard, tight, and quite sensitive if rubbed too deeply. What causes this tightness and what can I do at home to help loosen them up?

A

Over time, muscle is replaced by fibrotic tissue which feels hard and tight. Gentle stretching and massage can sometimes help. Your healthcare professional can give you specific techniques, but a general rule is that it should not hurt. Start slowly to your tolerance.

Q

I have LGMD2A/R1 and have had issues with intense pain in my hips when sleeping on my sides. Several friends with LGMD struggle with the same pain. What causes it and what are the best ways to manage it?

A

It is difficult to tell what is causing your hip pain. Some patients find relief by sleeping with a pillow between their knees so that the top leg stays in line with the body rather than dropping down. You can use a regular bed pillow or try a body pillow.

Q

I am a 75-year-old male living with LGMD2A/R1. I currently have constant pain in my shoulder and hip/girdle area. I take 220 mg of Aleve, twice a day. Is there anything else I can do to try to get rid of my pain and stiffness?

A

Unfortunately, as muscles weaken, they are not able to provide the proper support and are overused, which can lead to pain, especially if you are walking. If you are using a wheelchair, please make sure you have the best custom seating system for your needs. You can find this advice from physical or occupational therapists who specialize in wheelchair evaluations. Often a facility will have a "seating clinic" that will have options for you to consider. You may also want to try physical therapy to see if gentle stretching or exercise can help. Massage therapy or other modalities such as heating pads can also be beneficial. ■

Orchestrating a Cure for Dysferlinopathy

Dysferlinopathy refers to a muscular dystrophy caused by pathogenic mutations in the dysferlin gene (DYSF), no matter the clinical presentation. The most common clinical presentations associated with dysferlinopathy are limb-girdle muscular dystrophy type 2B (LGMD2B), also referred to as LGMDR2, and Miyoshi Myopathy type 1 (MM1). Detailed analysis of the different clinical presentations shows that they are the same disease. Therefore, the insights and potential therapies being developed for dysferlinopathy should be relevant to all individuals with pathogenic mutations in dysferlin, no matter what name they have been given for their clinical presentation.

A Nonprofit Driving Research Forward

The Jain Foundation (**Jain-Foundation.org**) was founded in 2005 by the Jain family after their son was diagnosed with Miyoshi Myopathy. Following his diagnosis, the family quickly realized that not only were there no treatments for his disease, but there was very little known about it, and almost no specific funding for research to understand the condition and determine treatments. Therefore, they started the Jain Foundation with the goal of identifying therapies for dysferlinopathy. In the 17 years since its founding, the Jain Foundation has funded over 120 projects and invested over $35 million dollars towards finding a cure.

> *In the 17 years since its founding, the Jain Foundation has funded over 120 projects and invested over $35 million dollars towards finding a cure.*

The Path Towards a Cure

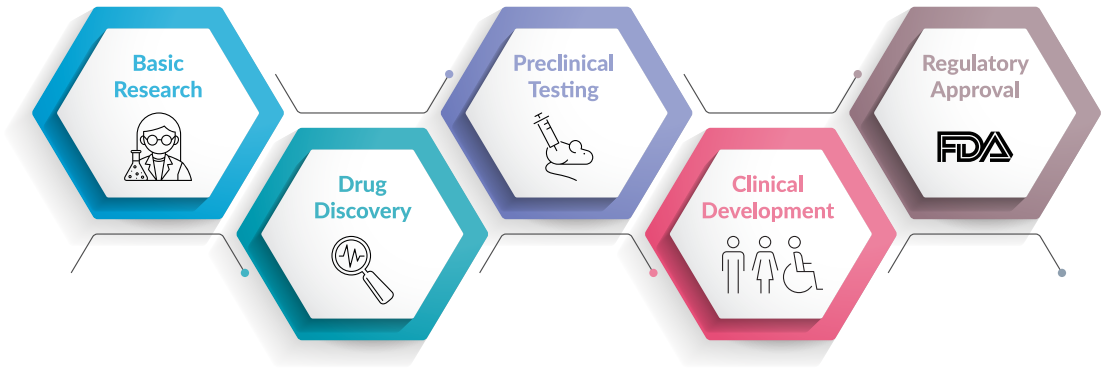
The process of developing treatments began by working backwards from the goal of treating patients and identifying and addressing the knowledge gaps at each step in the process that would prevent progress during the development of a treatment. Drug development involves many different steps, each with different players that have highly specific expertise, and they all must build upon each other. Thus, much of the foundation's work has focused on creating the necessary infrastructure and foundational knowledge required to identify treatments and determine if they are effective.

We are often asked if treatments being developed for other muscular dystrophies, such as Duchenne, can also be used in dysferlinopathy. This is called drug repurposing, which has some great advantages in that the safety and dosing of a drug may have already been solved. This can dramatically shorten timelines for testing and approving a potential treatment. We have embraced this approach and evaluated many treatments reported to work in Duchenne but have consistently found that they are either ineffective or detrimental in dysferlinopathy. These results highlight the importance of having a strong understanding of the disease mechanisms, as the choice of a repurposed drug relies on finding common disease intervention points between the disease the drug is approved for, and dysferlinopathy. If the connection is tenuous, then it is likely that the drug will not be effective. Our experiences with testing treatments being developed for Duchenne suggest that the underlying disease mechanisms are not similar and emphasize the importance of improving our understanding of dysferlin deficiency and why it leads to muscle problems. Hence many of the projects we fund seek to understand specific aspects of the disease mechanism that occur in dysferlinopathy in an effort to identify new treatments or repurpose known treatments that affect similar cellular functions in other diseases.

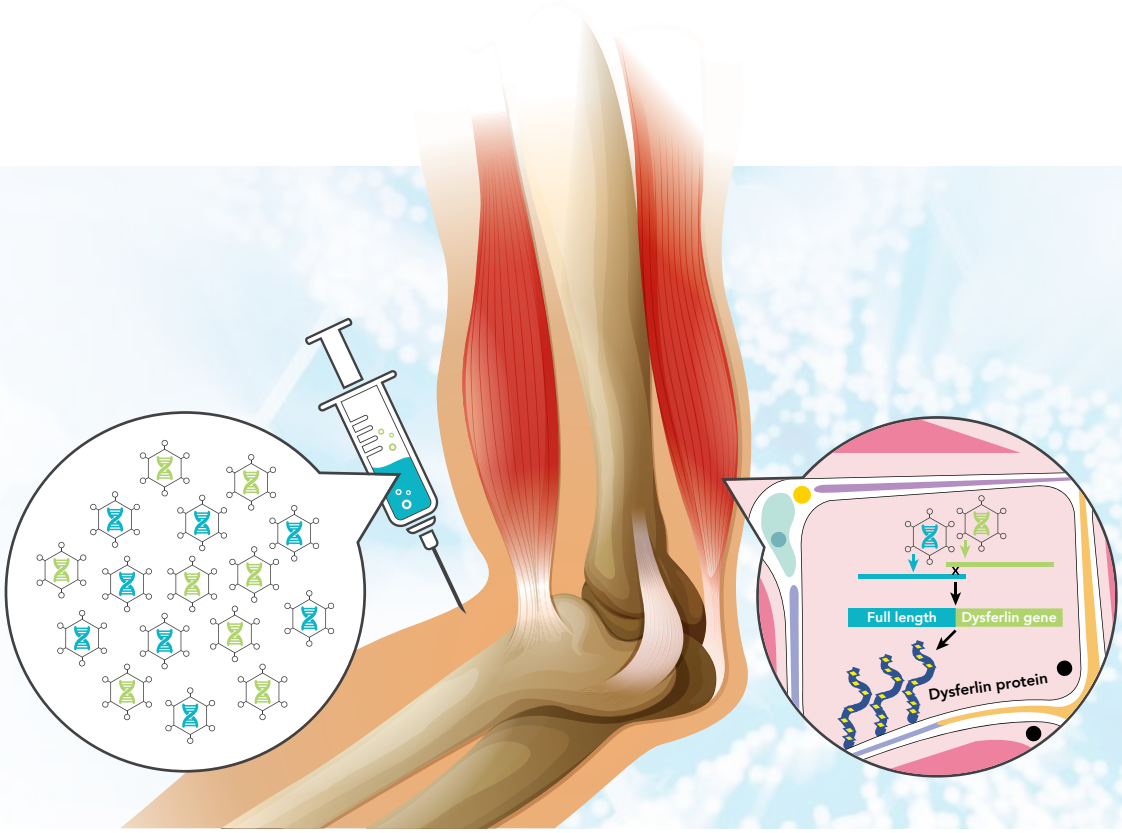
Drug development involves many different steps, each with different players that have highly specific expertise, and they all must build upon each other.

Genetic Therapies

Dysferlinopathy is a stereotypical genetic disease that is caused by mutations in the gene that makes the dysferlin protein. Therefore, therapies that restore dysferlin protein production by correcting the genetic mutations (gene editing), bypassing the mutations to produce functional or semi-functional dysferlin protein (exon skipping), or providing a working copy of the dysferlin gene (gene replacement) are all potential methods of addressing this disease. The Jain Foundation has explored all three strategies, however the large variety of dysferlin mutations found in dysferlinopathy, combined with the low efficiency of these strategies currently prevents exon skipping and gene editing from being viable treatments.



Below: Steps that build on each other during the drug development process.



Left: Schematic representation of AAV dual vector gene replacement strategy—overlapping halves of the dysferlin gene are put into 2 different AAV vectors. These vectors are injected into the blood stream. Both vectors must then get into the same muscle cell. Once there, they release their DNA cargo, which then needs to find each other and recombine to form the full-length dysferlin gene. From the full-length gene, the dysferlin protein is made.

Currently, the most promising avenue for a genetic therapy for dysferlinopathy appears to be gene replacement. The concept of restoring dysferlin in muscles by delivering a working copy of the gene is conceptually simple and bypasses many of the mechanistic questions about how the loss of dysferlin causes problems in the muscle. Yet the practical application of gene therapy is much more challenging than traditional therapy development and is an area that is truly on the cutting edge of science. The most advanced and successful gene therapies today use the very small AAV virus to deliver the required genetic cargo to the target tissue. The dysferlin gene is too large to fit in a single AAV virus, which left us with a problem to solve before we could take advantage of the latest gene therapy technologies. The Jain Foundation worked for many years with multiple research labs to develop an effective dual vector AAV system that can deliver both halves of the dysferlin gene to the nucleus of muscle cells. There, two pieces of DNA find each other and create a single, full-length copy of the dysferlin gene that the muscle cell can use to make the dysferlin protein. This dual AAV dysferlin gene therapy has successfully met the safety and efficacy criteria required by the FDA to move into human testing. It is licensed by Sarepta Therapeutics, who is continuing to develop it into a treatment. Sarepta recently announced that the first intravenous dosing of a small number of dysferlinopathy patients in a proof-of-concept trial is anticipated to begin late in 2022.

While we have high hopes for the Sarepta program, the Jain Foundation is also continuing to explore new technologies that may make dual vector gene therapy more efficient and effective. One example that we are following closely uses special protein sequences called inteins, which can join two pieces of protein into a single, full-length protein. It is not clear yet if an intein system working at the protein level will be more efficient than a system that works at the DNA level, but we feel it is important to continue exploring new technologies to bring the best therapies to patients.

The Jain Foundation worked for many years with multiple research labs to develop an effective dual vector AAV system that can deliver both halves of the dysferlin gene to the nucleus of muscle cells.

Right: Dr. Pam Van Ry, Jain Foundation funded researcher and Assistant Professor, Brigham Young University.

Below: Undergraduate student Dallin Jacobs and graduate student Jonard Valdoz research Galectin 1 protein therapy in the laboratory of Dr. Pam Van Ry, Brigham Young University.

Recent publications from the Van Ry lab, that were supported by the Jain Foundation, show that injecting dysferlin-deficient mice with Galectin-1 protein can produce some encouraging, short-term benefits.

Disease-Modifying Therapies

Traditional drug development for genetic diseases relies on a thorough understanding of the disease mechanism to find places to intervene and slow the disease process. In most cases, these strategies only solve a fraction of the problems that are happening at a cellular level, and thus have a limited capacity to improve the health of a patient. Even so, the relentlessly progressive nature of dysferlinopathy and the lack of any effective treatments means disease-modifying therapies still have the potential to dramatically improve a patient's quality of life. Some of the potential intervention points we are exploring in dysferlinopathy include calcium regulation, immune modulation, membrane repair, muscle regeneration, and cellular metabolism. In addition, many disease processes in the body have intervention points that are similar, raising the possibility of repurposing existing drugs to treat dysferlinopathy patients, if only we can understand the disease well enough to identify the right intervention points.

A disease-modifying therapy that we are excited about is treatment with a protein called Galectin-1. Galectin-1 is normally made by muscle and works both inside and outside of muscle cells to improve membrane repair, promote muscle growth and regeneration, and suppress some of the detrimental effects of inflammation, all of which may help slow the disease process that happens when dysferlin is absent. Recent publications from the Van Ry lab, that were supported by the Jain Foundation, show that injecting dysferlin-deficient mice with Galectin-1 protein can produce some encouraging, short-term benefits. The next step is to treat mice with Galectin-1 protein for longer periods of time to better assess and demonstrate the benefits of this treatment. If these experiments continue to go well, we hope to find an industry partner to take on the program and do the formal toxicity and dosing studies that are necessary to gain permission from the FDA to conduct tests in humans. We expect this work to take several years, at which point, we hope to be able to begin clinical trials in patients.

The Role of the Dysferlinopathy Community in Therapy Development

The dysferlinopathy patient community has a large role to play in therapy development. Sharing your experiences and perspectives helps researchers better understand dysferlinopathy, and the knowledge gained can improve the way your disease is managed and could positively impact the treatment development process by improving the way dysferlinopathy is evaluated. Thus, contributions by the patient community can help ensure that future interventional trials are designed to succeed.

One of the greatest bottlenecks that slows down clinical trials is the difficulty of finding individuals to participate in the trial. This is especially true for a rare disease like dysferlinopathy, which affects so few individuals. To overcome this challenge, the Jain Foundation curates the Dysferlin Registry, a patient registry dedicated to individuals who are genetically confirmed to have dysferlinopathy. In addition to being a recruiting resource, the Dysferlin Registry is also a tool that helps with diagnostic research and clarifications, provides a consistent source of disease-specific information, and is a place to interact with Jain Foundation staff and others with the same disease. The Jain Foundation encourages all individuals with dysferlinopathy to join the Dysferlin Registry and become part of the process of identifying treatments for this disease. It is only by all of us (researchers, clinicians, patients, caregivers, pharma, regulatory agencies, and advocacy) working together that we will reach our goal of finding a cure for dysferlinopathy. ■

Written by Laura Rufibach, PhD **and** Doug Albrecht, PhD
Co-Presidents of The Jain Foundation

Connect with Us

Jain-Foundation.org
DysferlinRegistry.Jain-Foundation.org

Patients@Jain-Foundation.org

An Exciting Time for LGMDs

With the advent of implementing next-generation sequencing, we can now arrive at a diagnosis much quicker than before, because all genes known to cause limb-girdle weakness can be analyzed at once.

It is an exciting time for LGMD, as we now come to the end of a long, but also exhilarating journey to correctly diagnose hereditary muscle diseases. With the advent of implementing next-generation sequencing, we can now arrive at a diagnosis much quicker than before, because all genes known to cause limb-girdle weakness can be analyzed at once. This accelerated method to diagnosis leaves very few patients undiagnosed.

In the aftermath of this diagnostic revolution, we are on the verge of starting a new era of therapeutic opportunities for people with LGMD. However, so much is still unknown about the different trajectories of individual LGMD types, and the natural history course even differs a lot within individual subtypes of LGMD. Therefore, the GRASP-LGMD Consortium has invested a lot of energy and time to study this in several subtypes. One of these studies is the natural history study in FKRP (LGMD2I/R9). This study is ongoing but will be followed later this year by a Phase 3 treatment study of ML Bio Solutions' BBP-418, which is the substrate of FKRP. The idea behind this is to drive BBP-418 through the partially functional FKRP enzyme in people with LGMD2I/R9, so that the surface protein, alpha-dystroglycan, is properly glycosylated, simply by offering more substrate to the partially functioning enzyme. This is a very simple idea, but if it works, it has great potential.

Another initiative for LGMD2I/R9 is the upcoming gene therapy by Atamyo Therapeutics, which will be launched later this year as a Phase 1/2. The gene in question, FKRP, is an enzyme, and the advantage of replacing a freely floating enzyme, in comparison with a protein destined to be a building block in the cell, is that it does not have to be as precisely positioned in the cell and will have a therapeutic effect even at low levels of enzyme expression.

Stay tuned, as this is an exciting time for the LGMD community! ■

Written by John Vissing, MD, DMSci
University of Copenhagen, Denmark

UPDATED: JUNE 1, 2022

Active GRASP-LGMD Natural History Studies

Recruiting:

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

Inclusion Criteria

Ages 8 and older:

- Clinically affected (defined as weakness during evaluation consistent with Becker Muscular Dystrophy)
- Genetic confirmation of an in-frame dystrophin mutation
- Willing and able to give informed consent and follow all protocol instructions

Ages 8–16:

- All of the above and must be ambulatory

Exclusion Criteria

Ages 8–16:

- Out-of-frame dystrophin mutation
- Inability to walk 10 meters without assistive devices
- >16 hours of ventilatory support
- Other illness that would interfere with participation or results

Ages 17 and older:

- Loss of ambulation prior to age 16
- >16 hours of ventilatory support

Recruiting:

Defining Clinical Endpoints in Limb-Girdle Muscular Dystrophy (LGMD) (GRASP)

Inclusion Criteria

- Age between 4–65 at enrollment
- Clinically affected (defined as weakness on bedside evaluation in either a limb-girdle pattern, or in a distal extremity)
- A genetically or functionally confirmed mutation in ANO5, CAPN3, DYSF, DNAJB6, or SGCA-G
- Ambulatory

Exclusion Criteria

- Non-ambulatory at the time of enrollment
- 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

Subtypes

- CAPN3 (LGMD 2A/R1)
- DYSF (LGMD 2B/R2)
- ANO5 (LGMD 2L/R12)
- DNAJB6 (LGMD 1D/D1)
- Sarcoglycan (LGMD 2D/R3, LGMD 2E/R4, LGMD 2C/R5, LGMD 2F/R6)

Not Recruiting:

Biomarker Development in LGMD 2I/R9 (MLB-01-001)

Inclusion Criteria

- Age between 10–65 at enrollment
- Clinically affected (defined as weakness on bedside evaluation in either a limb-girdle pattern, or in a distal extremity)
- A genetically confirmed mutation in FKRP (LGMD 2I/R9)
- Up to 60 participants will complete the 10-meter walk test in greater than 4 seconds
- Up to 40 participants will complete the 10-meter walk test in over 12 seconds
- Up to 20 participants may be non-ambulatory

Exclusion Criteria

- 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
- History of a bleeding disorder, platelet count <50,000, current use of an anticoagulant
- Positive pregnancy test at start or at any time during the trial

Subtype

- FKRP (LGMD 2I/R9)

Contact: Jessica St. Romain | Project Manager, Grasp-LGMD Consortium | (804) 828-7887 | *Jessica.Stromain@vcuhealth.org*

GRASP-LGMD Consortium Members

Vijay Ganesh, MD, PhD | Brigham and Women's Hospital
Conrad "Chris" Weihl, MD, PhD | Washington University in St. Louis
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Urvi Desai, MD | Atrium Health
Volker Straub, MD, PhD | Newcastle University
Monkol Lek, PhD | Yale University, Non-Clinical Site

GRASP-LGMD Researcher Spotlight

Dr. John Vissing | University of Copenhagen, Denmark

Dr. John Vissing is Professor of Neurology at the University of Copenhagen, Denmark, and Director of the Copenhagen Neuromuscular Center at the National Hospital, Rigshospitalet, along with 42 dedicated neuromuscular employees. He obtained his MD in 1986 and was then a research fellow at UT Southwestern Medical Center in Dallas, Texas, where he worked primarily on metabolic myopathies. His research focuses on treatment, pathophysiology, and natural history of hereditary muscle diseases and myasthenia gravis. His research in limb-girdle muscular dystrophies includes designing appropriate exercise recommendations, discovery of new limb-girdle muscular dystrophy forms, natural history studies, MRI of muscle and treatment, and upcoming gene therapy and ribitol trials in LGMD2I/R9. His unit runs a clinical trial unit with 23 ongoing trials in a variety of neuromuscular conditions including LGMD.

Exploring Adaptive Vehicles

Learn more about the Chariot® Scooter Lift at Bruno.com.

Learn more about the Q'Straint One™ all-in-one wheelchair securement station at QStraint.com.

Featured Resources

Bruno.com
MobilityWorks.com
QStraint.com
UnitedAccess.com

Living with LGMD creates challenges in the mobility world. Walking becomes more difficult as leg strength declines, necessitating the use of devices to assist in ambulation. While options such as manual wheelchairs, scooters, and power wheelchairs offer the benefit of increased independence, transporting these mobility devices can present complications for standard vehicles. In such cases, specialized adaptive vehicles offer the optimal solution.

Accessible Vehicle Basics

What are your needs? There are many different types of accessible vehicles, so understanding your personal needs is key to selecting the right vehicle for you.

- **Ramp vans:** For full-time wheelchair users, options that allow you to drive into the vehicle via a ramp, without transferring, are best. Vans or SUVs with ramps on the side or rear (for nondrivers) of the vehicle are available. Typically, these have a tie down (i.e. Q'Straint) or floor lock (i.e. EZ lock) system for securing the wheelchair to the vehicle.
- **Lift for vans or trucks:** These vehicles use a lifting platform that remains level while lowering to the ground. Once lowered, wheelchair users can then drive onto the platform before the lift raises them back up to safely enter the vehicle. Typically, the lift is controlled by an attached remote. This is found on full-size vans, trucks, and SUVs.
- **Attached rear carriers:** For people who are slow or short distance walkers, a rear carrier is an option to carry a mobility device. Carriers attach to a hitch on the back of the vehicle (weight limits apply). The Bruno Chariot scooter lift, for example, acts like an independent trailer to allow smaller vehicles to tow a scooter or wheelchair.
- **In-vehicle stowage devices:** A wide range of scooter and wheelchair hoists can be installed to allow non-occupied mobility devices to be stored in the trunk.

To Drive or Not to Drive

Using a mobility device can make driving more difficult. However, specialty devices like hand controls can help make driving a safer experience. These devices should only be used by those who have had sufficient training by a certified driver rehabilitation specialist.

- **Manual hand controls:** Push-Pull and Push-Rock hand controls allow drivers to apply the gas and brake with only movements of the hand and arm. Users must have sufficient upper body strength to properly control these devices.
- **Hi-tech electronic hand controls:** Integrated into your vehicle's driving system, these sophisticated hand controls command the operations of the vehicle, including acceleration, braking, steering, and other functions. Individuals with more profound weakness can find success with driving using these devices.

Getting Into Your Vehicle

Transfer devices can help those who do not want to sit in their mobility devices inside the vehicle.

- **6-way transfer seat base:** This is installed on the factory seat and allows the user to transfer from the middle of the van to the front.
- **Valet turning seats:** These are designed to allow independence when entering and exiting the vehicle.

Purchasing an adaptive vehicle is a highly specialized and expensive process. Contact your local mobility dealer for more information. If you do not have a local dealer, national companies such as Mobility Works and United Access may offer solutions. ■

Written by Vovanti T. Jones, MD
Physical Medicine & Rehabilitation,
University of Missouri at Rusk Rehabilitation Hospital

Above: Learn more about ramp vehicles at MobilityWorks.com.





Clinical Trial Resource Guide

The 2022 LGMD Global Advocacy Summit featured seven different biotechnology companies who presented on upcoming clinical trials. The SPEAK Foundation has put together a summation of the program in this LGMD Clinical Trial Resource Guide. We have partnered with companies to provide this information to you, and we will continue to provide this resource to you in various ways in the future.

It is important to understand that companies take a lot of time to develop clinical trial protocols. Some companies do not have their clinical trial information ready to be published in this resource guide. This means they are still developing the protocol, or they are still in preclinical development. When a new therapy is in preclinical development, it indicates there is not a human trial ready. They are testing in vivo or in vitro for safety and toxicity. Before human clinical trials, a drug must first be determined to be safe.

You may also see trials advertised that do not have open enrollment yet. Even so, it is still a good idea to share your information with the trial site early. Patients should be assertive and can regularly reach out to the contact person at that site.

Another important point to note is that natural history studies are not clinical trials. There is a difference. Natural history studies assist researchers in collecting data to understand the natural disease progression without intervention. That being said, these observational studies are often conducted for clinical trial readiness. This means that sites are identifying patients within a particular subtype. While being in a natural history study does not guarantee acceptance into a clinical trial, it does position a patient to be within a cohort that is easily accessible. The site will have your data and will have followed you for a period of time. You will find that many natural history studies can lead into clinical trials.

If you identify multiple natural history studies, it is fine to participate in more than one. Patients often think that these studies are linked, but often they are not, and data is not easily shared back and forth. At the SPEAK Foundation, we encourage patients to be intentional about learning about studies and clinical trials, and to ask questions. Please know that we are here to help as an organization as well.

We suggest doing a search on a regular basis on **ClinicalTrials.gov** to see what trials are available for your subtype. Things may be available that were not at the time of this publication.

If you would like to help us continue to grow and help patients, please consider donating at TheSpeakFoundation.com/donate to help us continue this important work.

Clinical Trial Resource Guide

AskBio

A summary of the trial(s) that you are offering, including what type(s) of trial(s):

AskBio is conducting a clinical study (**LION-CS101**) of an investigational gene therapy for individuals with a confirmed genetic diagnosis of LGMD2I/R9.

LION-CS101 is a one-time intravenous infusion of gene therapy designed to produce fukutin-related protein (FKRP) in the body, primarily in muscle.

The initial part of the study, to assess the safety of LION-CS101, will be conducted only in adults (ages 18–65 years). The study is designed to investigate at least 2 different doses of LION-CS101 as compared to placebo.

Is this a natural history study or a clinical trial for a potential new therapy?

This clinical trial is for a potential new gene therapy.

Enrollment dates and other information:

AskBio expects to start enrolling patients in the 2nd half of 2022. Please review **ClinicalTrials.gov** (Identifier: **NCT05230459**) for specific details.

Trial(s) dates:

AskBio expects to start enrolling patients in the 2nd half of 2022. Please review **ClinicalTrials.gov** (Identifier: **NCT05230459**) for specific details.

Location(s) of the trial(s):

Please review **ClinicalTrials.gov** (Identifier: **NCT05230459**) for specific details.

What LGMD subtype(s) are included in the trial(s)?

AskBio is currently focused on LGMD2I/R9.

Interested?

For additional information or to sign up for our newsletter, please send an email to ***askfirst@askbio.com***.

Clinical Trial Resource Guide

Atamyo Therapeutics

A summary of the trial(s) that you are offering, including what type(s) of trial(s):

This is a Phase 1-2 (2 stages) multicenter study to evaluate the safety and efficacy of intravenous GNT0006, adeno-associated viral vector carrying the FKRP gene, in patients with FKRP-related limb-girdle muscular dystrophy (LGMD2I/R9). This Phase 1-2 study includes a dose escalation safety and proof-of-concept Phase (Stage 1, open label), followed by a double-blind, randomized, placebo-controlled, confirmatory Phase (Stage 2).

Is this a natural history study or a clinical trial for a potential new therapy?

This is an interventional clinical trial.

Enrollment dates and other information:

Enrollment begins in June 2022.

Trial(s) dates:

The trial is expected to run about 7 years, but first results are expected by end of 2025.

Location(s) of the trial(s):

There are currently 3 clinical sites—one in Denmark (at Rigshospitalet, University of Copenhagen), another in France (at Institute of Myology Pitié-Salpêtrière Hospital in Paris), and the third in the United Kingdom (at Royal Victoria Infirmary in Newcastle Upon Tyne).

What LGMD subtype(s) are included in the trial(s)?

This trial is for patients diagnosed with LGMD2I/R9.

Interested?

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Clinical Trial Resource Guide

Sarepta Therapeutics

A summary of the trial(s) that you are offering, including what type(s) of trial(s):

NCT04475926: A Global Multicenter Longitudinal Study of the Natural History of Patients with LGMD2E/R4, LGMD2D/R3, and LGMD2C/R5, ≥ 4 Years of Age, Who Are Managed in Routine Clinical Practice. This study will follow patients who are screened and confirmed with a genetic diagnosis of limb-girdle muscular dystrophy type 2E (LGMD2E/R4), limb-girdle muscular dystrophy type 2D (LGMD2D/R3), or limb-girdle muscular dystrophy type 2C (LGMD2C/R5).

These enrolled patients will be followed to evaluate mobility and pulmonary function for up to 3 years after enrollment. Additional patient data will be collected from the time the individual began experiencing LGMD symptoms to the present.

Is this a natural history study or a clinical trial for a potential new therapy?

This is a natural history study.

Enrollment dates and other information:

The study start date was April 22, 2021, and the estimated end date is December 24, 2025.

Location(s) of the trial(s):

Updated study date locations may be found on either **ClinicalTrials.gov** (by searching the study number **NCT04475926**) or by visiting **ClinicalTrials.Sarepta.com/JourneyLGMD**.

What LGMD subtype(s) are included in the study?

Limb-girdle muscular dystrophy type 2E (LGMD 2E/R4), limb-girdle muscular dystrophy type 2D (LGMD2D/R3), or limb-girdle muscular dystrophy type 2C (LGMD2C/R5).

Interested?

1-800-690-2003 or ***SareptAlly@sarepta.com***.

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its **ClinicalTrials.gov** identifier (NCT number): **NCT04475926**.

MED-US-NP-0097.

Clinical Trial Resource Guide

Vita Therapeutics

A summary of the trial(s) that you are offering, including what type(s) of trial(s):

This is a Phase 1/2 trial of intramuscular administration of induced pluripotent stem cell-derived satellite cells (VTA-100) for the treatment of LGMD 2A/R1. The primary goal is to determine the safety and tolerability of intramuscular administration of VTA-100. We will also study dosing, genetic expression of the replaced Calpain-3 gene and functional improvement in the treated muscles. Fifteen patients will be enrolled and studied for two years.

We will enroll patients with a clinical and genetic diagnosis of LGMD2A/R1 with a confirmed bi-allelic pathogenic variant in the CAPN3 gene. We will seek patients with upper extremity disease involvement. Ambulatory status is not an exclusion. We will exclude patients with other significant comorbidities, for instance lung or cardiac involvement.

The study will take place in 2 phases. In the first phase, patients will be randomized and treated in muscles of one arm, with the other arm serving as a control. Patients will be divided into 3 groups to receive low, medium, or high dosing of VTA-100. In Phase 2, after determination of safety, patients will be treated in the other arm with the optimal dosing determined during Phase 1. Additionally, if the patients are determined to be eligible, they will also be treated in the lower extremities, bilaterally.

Baseline and follow-up studies will be conducted including physical examination, blood chemistries, biopsy of the biceps muscles, whole body MRI, and functional strength testing.

Is this a natural history study or a clinical trial for a potential new therapy?

This is a therapeutic trial of a novel cellular therapy.

Enrollment dates and other information:

Enrollment will likely begin in early 2023, pending FDA IND approval.

Trial(s) dates:

The trial is expected to last 2-3 years total, with extended follow-up possible.

Location(s) of the trial(s):

We are currently targeting 3 clinical sites, two on the east coast and one in a midwestern state.

What LGMD subtype(s) are included in the trial(s)?

LGMD2A/R1 with a confirmed bi-allelic pathogenic variant in the CAPN3 gene.

Interested?

Contact:
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Patients Who Have Gone Into Science Series
PART 3 Monkol Lek, PhD
LGMD2G/R7

Written By Rebecca Gregg
and Brad Williams, PhD
Director of Research, Jain Foundation

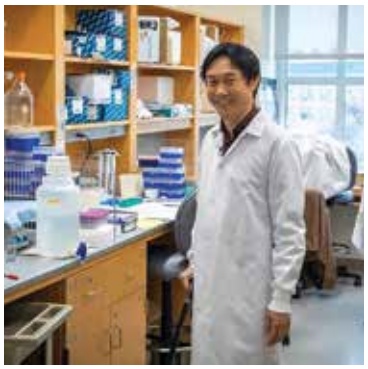
From Patient to Professor

Being diagnosed with a rare disease can be life-changing in so many ways. For some, this means changing your career path so you can better understand your own disease and find a way to help others.

In this installment of our ongoing "Patients Who Have Gone into Science" series, we introduce Monkol Lek, PhD, Assistant Professor in the Department of Genetics at Yale School of Medicine, who is living with LGMD2G/R7.

Monkol Lek was born in Cambodia, but as a baby, he and his family moved to Australia as refugees. He is the youngest of seven children. When he was ten years old, his sister was diagnosed with a muscle disease. At the time, his family did not know about genetic diseases. When Monkol was 19, he started noticing that he had trouble walking up and down stairs, had muscle pain, and lost his balance easily. As Monkol waited for a diagnosis, he was consistently told, "Leave it to the experts." Little did he know how much this statement would change the course of his future.

It took Monkol longer than he imagined to finally get his diagnosis of limb-girdle muscular dystrophy. He was married at this point, and he and his wife, Angela, considered the LGMD2G/R7 answer as cause for celebration. They even had a cake made. It was around this time that he decided to become an expert himself. The slow pace of learning his diagnosis and all the unknowns in the world of rare diseases was enough to motivate him to pursue a career in this field. In 2004, he left his "dream job" at IBM, where he had worked for several years, to return to the University of New South Wales where he would study a double major in science (Physiology) and engineering (Bioinformatics). Later, Monkol went on to pursue a PhD in Medicine from the University of Sydney. He says, "If it weren't for having LGMD, I would not have switched to a career in science from software development. The switch occurred while I was quite established in my career, so living with LGMD also provided the motivation and drive to go back to university to study."



As a result of this career change, Monkol worked on a project at the Broad Institute of MIT and Harvard, which has been responsible for creating a database of human protein-coding genetic variation from over 60,000 individuals. With this information, they created a resource that is used by all clinical genetic labs around the world to help interpret and discover pathogenic variants in rare-disease patients. The scientific community uses this resource to determine the likelihood of novel disease-gene associations.

Monkol now leads his own research group at Yale School of Medicine. He says the hard work has been worthwhile and fulfilling for him. "The most rewarding moment in my

"If it weren't for having LGMD, I would not have switched to a career in science from software development. The switch occurred while I was quite established in my career, so living with LGMD also provided the motivation and drive to go back to university to study."

Right: Monkol Lek, PhD, sharing his 2019 TEDx talk in Sydney, Australia, titled, "Taking Control of Our Genetic Destiny."

career to date was being given this current opportunity to run my own research group and having the freedom to do research on things that interest me. It has made the late career change and long journey in training to get here all worth it."

To Learn More About Monkols' Work:

LekLab.org

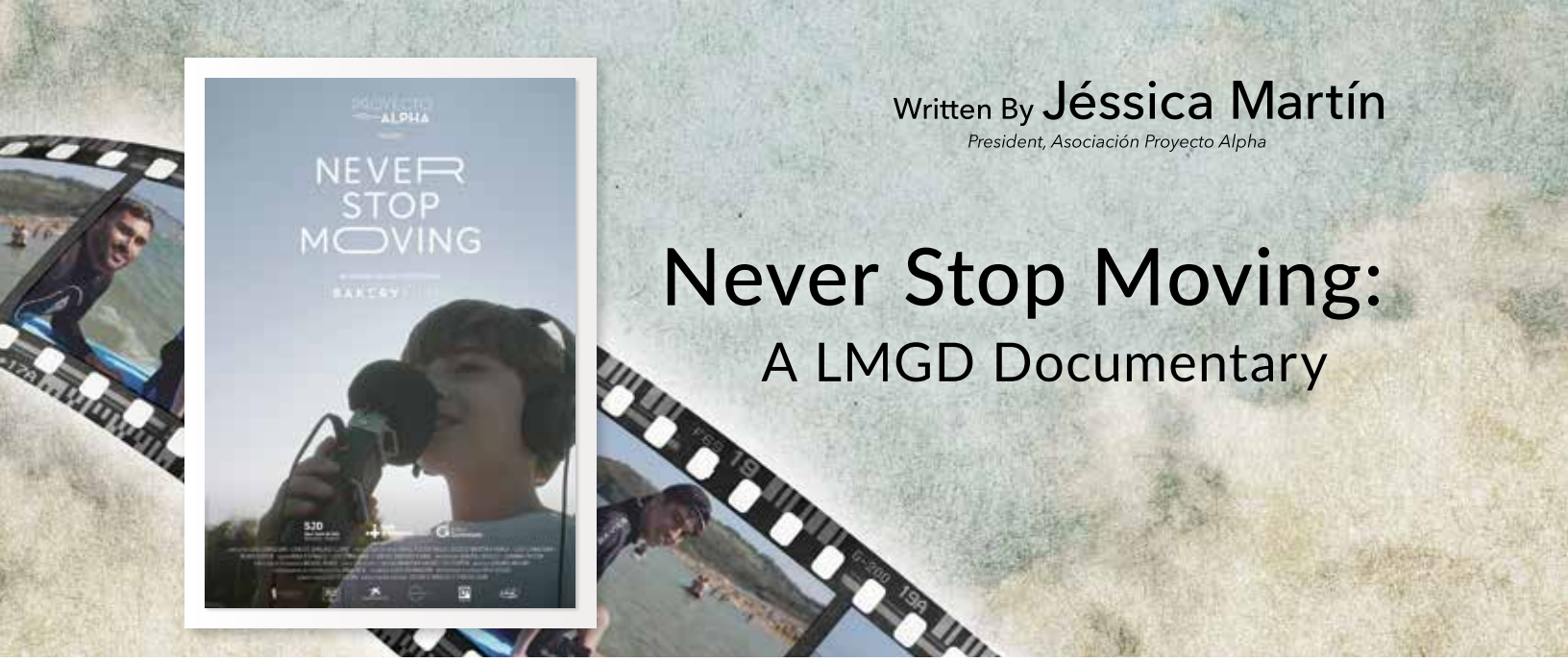
"I want to be known for working on discoveries that help rare disease patients. For me, the treatment for my muscle disease would mean I could repay all the people who have been so kind to me, helping with my disease."

One thing Monkol learned after getting involved in the scientific community is just how challenging it is to obtain research funds. He says, "Running a scientific research group is like running a small business. I needed to find research funds, not just to support projects that we are doing, but also to pay everyone's salaries. What surprised me the most before taking this job is that I also needed funds to pay my own salary, as the university does not pay it."

When asked about other people with LGMD wanting to pursue a career in the science field, Lek offers, "People who still have good mobility should train in experimental science while they can, as later on, you don't have to physically do the experiments; you will just be mentoring others to do it in the lab. Also, developing computational and analytical skills will ensure that you can contribute to research, no matter how far progressed your muscle weakness becomes."

As for his legacy, Lek says, "I want to be known for working on discoveries that help rare disease patients. For me, the treatment for my muscle disease would mean I could repay all the people who have been so kind to me, helping with my disease."

For more information about Monkol's continued work, visit **LekLab.org**. ▪



Written By Jéssica Martín
President, Asociación Proyecto Alpha

Never Stop Moving:
A LMGD Documentary

Proyecto Alpha (Spain) has released *Never Stop Moving*, a documentary to bring awareness and visibility of limb-girdle muscular dystrophy (LGMD) to the world. It highlights the importance and value of research as the main pathway to a treatment or cure for LGMD.

The film was produced by Bakery Group, a Spanish communication agency with extensive experience in documentary production. Some of their projects have even focused on other rare diseases.

Never Stop Moving showcases the daily efforts of three individuals affected with LGMD: Laura, Lucas, and Gerard. Despite their difficulties with mobility, the protagonists never give up. They share their personal experiences with three internationally known Spanish athletes: soccer player Lucas Vázquez, surfer Aritz Aranburu, and fitness influencer Patry Jordán. The documentary shows a parallel between the disease symptoms that people affected by LGMD endure daily and the demands that high-performance athletes experience. *Never Stop Moving* narrates from an optimistic perspective, capturing the subjects' fears, frustrations, and joys of overcoming difficulties.

As an interesting feature of the film, Laura, Lucas, and Gerard were involved in the recording of sounds associated with sports, which served as the basis for the film's theme song about LGMD, composed by producer Carlos Jean with vocals by Delafé y las Flores Azules, a Spanish indie pop and hip hop band based in Barcelona. The song, titled "Nunca Dejes de Moverte" (or "*Never Stop Moving*"), will soon be available on Proyecto Alpha's Spotify channel.

The film also features many professional voices. Pediatric neurologists Dr. Andrés Nacimento and Dr. Carlos Ortez, along with researcher Cecilia Jiménez from the Sant Joan de Déu Pediatric Hospital in Barcelona, explain the value of research in limb-girdle muscular dystrophy, and the importance of emotional and psychological support for LGMD families. Neurologist and researcher Francina Munell speaks about gene therapy and about her research at the Vall d'Hebrón Hospital in Barcelona, the first center in the world to apply Phase 3 gene therapy for Duchenne muscular dystrophy. Finally, the Institut Guttmann Neurorehabilitation Hospital in Badalona, a European benchmark center, emphasizes rehabilitation to maintain independence for LGMDs.

Proyecto Alpha hopes to show *Never Stop Moving* in different cities in Spain, as well as screenings abroad, as the documentary will soon be available with English subtitles. The final showing of the film will take place on September 30, 2022, on LGMD Awareness Day, as a grand finale. Proyecto Alpha hopes this important documentary will be used as an educational tool to raise awareness everywhere for LGMD. ■

Proyecto Alpha is a Spanish nonprofit organization that represents those affected by LGMD due to Sarcoglycan deficiencies.

ProyectoAlpha.org @asociacion.proyectoalpha @proyectoalpha_ **Trailer:** YouTube.com/watch?v=X-W_WAwlQsE&t=2s

Written By Rebecca Gregg

and Melissa Grove, M.S., LPC

Executive Director of Legacy Counseling Center

Cultivating Resiliency

"Resilience" is one of those words that has gained popularity in recent years. The healthcare and finance industries, for example, have added resilience training as part of their employees' education, to teach them how to effectively handle stress and coworker relationships. What exactly does this buzzword mean?

According to the National Association of Psychologists, "resilience" is defined as the process of adapting well in the face of adversity, trauma, tragedy, threats, or significant sources of stress, such as family and relationship problems, serious health problems, or workplace and financial stressors. This capacity is especially beneficial, as it not only helps in "bouncing back" from difficult experiences, but can also promote profound, personal growth. Fortunately, psychological research shows that resources and skills associated with resilience can be cultivated and practiced.

Melissa Grove, M.S., LPC, Executive Director of Legacy Counseling Center, lives with LGMD2I/R9.

How Can I Tell If I Should Seek Professional Help?

Most of us feel sad, lonely, or depressed at times. This is a normal reaction when faced with the losses and struggles of life. Living with LGMD certainly adds stressors with which the average person does not have to deal. According to the Centers for Disease Control and Prevention (CDC), adults with disabilities report experiencing frequent mental distress almost five times as often as adults without disabilities. Studies have also shown that adults with disabilities more often report depression and anxiety than adults without disabilities. So how can you tell if what you are experiencing is a normal reaction or a cause for concern?

When feelings of sadness become overwhelming, long-lasting in duration, and interfere with your daily functioning, these are good indicators that it may be time to seek professional support. The following are symptoms of depression that may warrant treatment:

- **Lack of interest and pleasure in activities once enjoyed**
- **Changes in appetite and/or significant weight loss or gain unrelated to dieting**
- **Insomnia or excessive sleeping**
- **Lack of energy or increased fatigue**
- **Feelings of worthlessness or excessive guilt**
- **Difficulty thinking, concentrating, or making decisions**
- **Recurrent thoughts of death or suicide**

There is help available if you are struggling emotionally. Know that you are not alone.

As a therapist with LGMD, she has had to cultivate resiliency over the years. She says, "People experience emotional pain, grief, and a sense of loss that comes after a tragedy, but their mental outlook allows them to work through such feelings and recover. Life is never perfect and being resilient allows one to gather the strength to not only survive, but to prosper. People with LGMD truly need resilience to cope with the ongoing challenges they face."

So, how do you train yourself in resiliency? According to Melissa, building resilience includes:

- **Seeking support** from family, friends, and/or a therapist. Being able to speak freely about your struggles helps greatly. Also, simply reaching out to the LGMD community via the many LGMD groups on Facebook offers an excellent opportunity for you to share your struggles, get advice, or even be a sounding board for others who are having a rough time. Communicating about the many challenges of LGMD does not make them go away, but it can help you gain understanding and learn new ways to manage these issues.

- **Reminding yourself** of who you are and what you have already overcome. You have made it through plenty of obstacles in the past, therefore, you can conquer this as well. Keep in mind the saying, "This too shall pass." Remember a time you thought you were ruined but survived it. Don't dwell on negative thoughts. Instead, tell yourself repeatedly, "I can do this!"

- **Focusing on** what you can control. Things will always change and fluctuate. Try to focus on the things you can control by creating goals with realistic expectations. Do not avoid problems that arise. Instead, be willing to meet challenges head on, learn from your mistakes, and move on. It is important to be present in your day-to-day life, nurturing your health and happiness.

You can also build a healthier and more resilient you through physical activity, good sleep hygiene, and proper nutrition. Get outside, go for a walk (if you are able), do chair exercises, etc. Exercise releases endorphins that can help your state of mind. Get plenty of sleep. You will be better equipped to cope and problem-solve if you are well rested. Finally, make it a priority to maintain good nutrition. It is important to keep your energy stable with quality food choices and frequent hydration.

It is often the case that we grow in resiliency as we reach outside of ourselves, too. Helping others who share similar circumstances can help you to refocus and strengthens you personally. Also, looking forward to treatments that are in development can give you a more hopeful outlook and incite action.

By incorporating all of these different practices, while also taking care of your mind, body, and wellness, your resilience can build and be a constant support and source of strength on your LGMD journey. ▪

To Find Treatment

If you are in crisis, seek immediate help. For potentially life-threatening situations, immediate emergency assistance is available 24 hours a day by calling **911**.

National Alliance on Mental Illness HelpLine

The NAMI HelpLine provides general mental health information and resource referrals. It can be reached Monday through Friday, 10 a.m.–10 p.m. EDT, at **(800) 950-6264** (NAMI) or at **Helpline@nami.org**.

Crisis Text Line

Visit **crisistextline.org** or text **HOME** to **741741** for 24/7, anonymous, free crisis counseling.

American Association of Christian Counselors

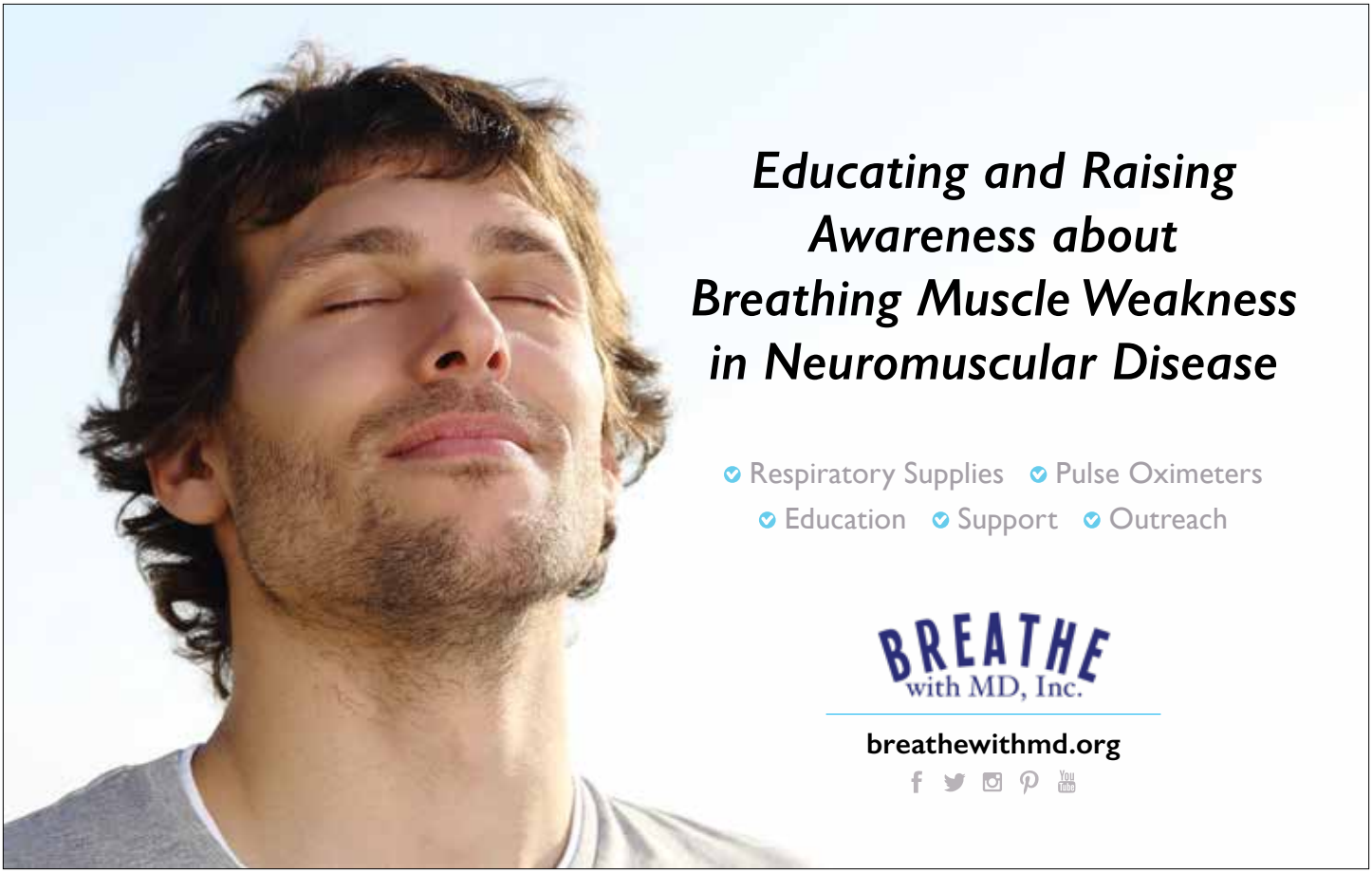
Search for a Christian counselor near you at **Connect.AACC.net**.

American Psychological Association

Search for a psychologist near you at **Locator.APA.org**.

National Suicide Prevention Lifeline

If you are thinking about suicide, are worried about a friend or loved one, or would like emotional support, the National Suicide Prevention Lifeline network is available 24/7 across the United States at **(800) 273-8255** (TALK) for English or **(888) 628-9454** for Spanish. Live, online chat is available at **SuicidePreventionLifeline.org/Chat**.



Educating and Raising Awareness about Breathing Muscle Weakness in Neuromuscular Disease

- Respiratory Supplies
- Pulse Oximeters
- Education
- Support
- Outreach

BREATHE with MD, Inc.

breathewithmd.org

LGMD Awareness Day: September 30

- **Advocate**
- **Educate**
- **Celebrate**

"I AM LGMD"

LGMD is what brought us all together, and Together We Are Stronger!

There is great strength in awareness, understanding, and unity. The LGMD community demonstrates global connectivity each year when we campaign together and gain recognition for limb-girdle muscular dystrophy.

Join our campaign today!

LGMD-Info.org

SCAN ME

2022 Girdie Sticker Campaign sponsored by SAREPTA THERAPEUTICS

LGMD Awareness Day is a *project* of LGMD AWARENESS FOUNDATION

Let's Advocate • Educate • Celebrate LGMD

There is great strength in awareness, understanding, and unity. The LGMD community demonstrates global connectivity each year when we campaign together and gain recognition for limb-girdle muscular dystrophy (LGMD). With more than 30 different genetic types of LGMD, the act of collaborating globally makes us stronger than we could ever be alone. Whether you are a longtime community member, or new to the scene, your participation in the 2022 LGMD Awareness Day activities is important. Awareness is power, and power brings cures, treatments, and policy changes. Awareness can spread much faster when more individuals, from all parts of the world, share their story and spirit through reposts, shoutouts and snaps of the LGMD Awareness sticker to your favorite platforms.

When is LGMD Awareness Day?

The 8th annual LGMD Awareness Day will be celebrated worldwide on September 30, 2022. This is an opportunity to Advocate • Educate • Celebrate LGMD!

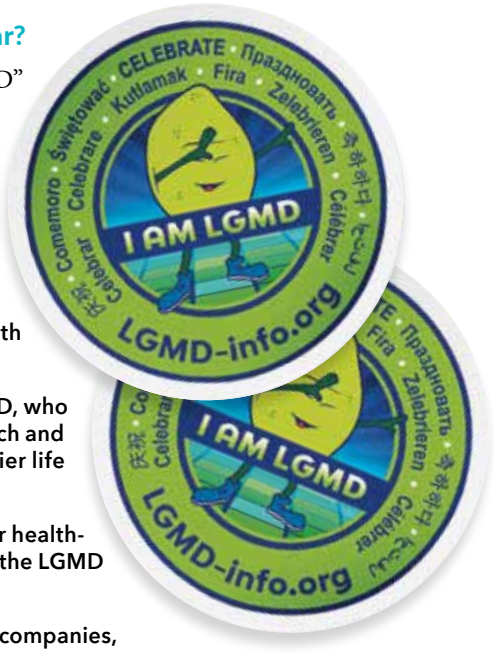
Where is LGMD Awareness Day being held?

There will not be a single event, but instead, individuals are encouraged to set up activities in their community to commemorate the day.

What is the theme this year?

The 2022 theme is "I AM LGMD" to celebrate:

- **Individuals who have been diagnosed with LGMD and do their best every day to make 'limeade out of limes.'**
- **Caregivers, who support and assist the individuals living with LGMD.**
- **Parents of children with LGMD, who never stop fighting for research and cures in hope of a better, easier life for their kids.**
- **Doctors, therapists, and other healthcare professionals, who treat the LGMD community.**
- **Researchers, pharmaceutical companies, and the scientific community dedicated to discovering a cure and treatment for LGMD.**
- **Families and friends, who proudly wear lime green for us and lend an ear when we are having a bad day.**



LGMD is what brought us all together, and together we are stronger! "I AM LGMD" is in all caps for a reason. We accept that this condition is part of us, and we CELEBRATE that we are stronger than LGMD.

Take a moment to shine a light on yourself and the importance of LGMD Awareness! Be proud to say, "I AM LGMD."

Where can I get more information?

To request your 2022 Girdie Sticker and learn more about our Awareness Day campaigns, visit the LGMD Awareness Foundation's website at **LGMD-Info.org** and follow **@LGMDawareness** on social media. ■

Written by Carol Abraham, *Retired OTR; Director of Community Outreach, Coalition to Cure Calpain 3; Founder, LGMD Awareness Foundation*

Connect with Us

LGMD-Info.org

Facebook.com/LGMDawareness

Instagram.com/LGMDawareness

Twitter.com/LGMDawareness

TikTok.com/@lgmdawareness

BE THE HOPE While We Wait for a Cure

At their recent Walk-a-Thon event, the First Coast Teen Homeschoolers group of Florida walked a collective 44 miles in just two hours for those living with LGMD.

What can you do to hold onto hope and to instill hope in others?

Connect with Us

BelieveThereIsHopeforaCure.com
TheSpeakFoundation.com

Waiting is a difficult game. Right now, we find ourselves waiting for many things — promising research, clinical trials, treatments, drug development, and, ultimately, a cure. In this interim time, the things we wait for can feel so beyond reach that it is easy to lose hope. But hope can be powerful. Hope can be inspiring. And hope is at hand.

What can you do to hold onto hope and to instill hope in others? How can you help drive forward those things we are so greatly anticipating? You can do this by supporting those LGMD organizations that are funding research, patient advocacy, and directly assisting families who are living with LGMD. The Speak Foundation and other organizations are working tirelessly with clinicians, researchers, pharmaceutical companies, and this year, even the Food and Drug Administration (FDA) to advance efforts for this disease. You can support these endeavors within your own social circles simply by planning fun events that double as fundraisers.

Recently, I planned a Walk-a-Thon event for my daughter's teen homeschooling group. It gave the kids an opportunity to hang out with their friends and to combine efforts for a good cause. In advance of the event, the teens collected pledges from family, friends, and neighbors, who promised to pay a certain amount per mile walked. I offered Amazon gift cards to the top earners as incentive, which encouraged them to work harder to gain pledges. Additionally, The Speak Foundation awarded service hours to each teen for their time, a requirement now for college admissions. The event was a huge success! The teens collectively walked 44 miles in two hours and raised a lot of money for LGMD. The experience was fun and rewarding for everyone.

A Walk-a-Thon is not the only way to raise funds for this movement. There are many fundraisers that can have the same effect — golf tournaments, poker fundraisers, bake sales, raffles, bowling tournaments, social media fundraisers, and more. So, where do you start? How can you set up your own fundraiser that speaks to your social circle, that promises success? The Speak Foundation is here to help. We are kicking off our **BElieve THEre Is HOPE for a Cure** campaign in an effort to empower the entire LGMD community by raising funds for new research, advocacy efforts, and to directly assist individuals living with LGMD. When you sign up to participate, a Speak Foundation team member will help you personalize your fundraising experience and goals. We will help you make it easy and fun.

JOIN US! Visit **BelieveThereIsHopeforaCure.com** to learn how to get started on being a hope and instilling hope in others living with these rare diseases. ■

Written by Rachel Sapp, *The Speak Foundation*

BELIEVE THERE IS HOPE

BELIEVE THERE IS HOPE FOR A CURE

Limb Girdle Muscular Dystrophy™

Be a Part of Our New LGMD Fundraising Campaign!

It's personal. If you are reading this, you or someone you know is living with a form of limb-girdle muscular dystrophy, and that affects all of us. We are family in the LGMD community. With over 30 different subtypes of LGMD, there is a need for ALL forms to see innovation. The 2022-23 **BElieve THEre Is HOPE for a Cure** campaign endeavors to empower the entire LGMD community by raising funds for new research, advocacy efforts, and to directly assist individuals living with LGMD.

Join Us! When you participate, a Speak Foundation team member will reach out to you to help you personalize your fundraising experience and goals. You will "Raise Your Way"— that is, find and use the unique fundraising method that works best for you. **Help us make history for the LGMD Community!**

www.BelieveThereIsHopeforaCure.com

The **BElieve THEre Is HOPE for a Cure** fundraising campaign is a project of The Speak Foundation.

Casey's Cure Foundation

In February of 2017, my heart sank as my daughter Casey, then 35, told me the news.

"Mom. I got my test results back. I didn't tell you I was getting tested because I didn't want you to worry. But I have Dad's gene. I have Hereditary Myopathy with Early Respiratory Failure. HMERF." (HMERF is one of the many Titin (TTN) gene-related muscular dystrophies.)

Memories of her father's journey with this disease, which ended in his passing in 2004, flashed through my head — years of him being bedridden and in pain, years of my tears, panic, and anger. I had always worried about the possibility of my children inheriting this damaged gene. We all believed it was a possibility, but doctors told us back in 1985 that girls could only be carriers of the gene and the only one who could possibly be fully affected would be our son, Casey's brother.

> *How was I going to keep my daughter from dying from this dreadful disease?*

I felt many emotions during this time. I did not know who to be angrier with — the doctors for giving us misleading information or God for allowing my child to be affected by this disease. I asked myself how I was going to deal with this. How was *Casey* going to deal with this? How was I going to keep my daughter from dying from this dreadful disease?

Once I calmed down and decided to become proactive, I started looking on the internet. Superficial searches on Google showed that little to no research was happening in the US. Some work was being done across Europe, but because HMERF shows up in little "pockets" of family groups, the number of affected patients worldwide is small. We discovered that HMERF falls into the "ultra-rare" category of rare diseases. This motivated me to move closer to Casey and get to work on raising awareness of HMERF.

Inspired by the work of Kathryn Bryant Knudson of The SPEAK Foundation, I started The Foundation for Casey's Cure, Inc., registering it as a 501(c)(3) nonprofit organization in August 2019. The goal of Casey's Cure Foundation is two-fold — to spread awareness of muscular dystrophy at the community level and raise money to fund research that shows promise in treating HMERF. Working together with other patient advocacy groups to raise money for research means that science can progress faster and hopefully save more lives, something we all strive for. My hope is that we will see an effective treatment for Casey's rare disease in my lifetime.

To learn more about Casey's Cure Foundation, please visit **Caseys-Cure.org**. ▪

Written by Christine Duane, *Founder/Executive Director, The Foundation for Casey's Cure, Inc.*

Above: Casey currently works as a pulmonary nurse with WellStar Pulmonary Medicine.

Connect with Us

Contact@Caseys-Cure.org

Caseys-Cure.org

Facebook.com/CaseysCureMD

Hereditary Myopathy with Early Respiratory Failure (HMERF)

HMERF is a condition that can be misdiagnosed for LGMD based on phenotype. There are many genetic conditions that share some phenotypical characteristics with LGMDs. It is important in raising awareness that we educate families and practitioners on overlapping symptoms and the critical need for genetic testing in the diagnosis of neuromuscular diseases.

JOURNEY

We welcome you to join our Journey...

Journey is a clinical outcomes assessment study, also referred to as a natural history study. Journey studies the natural progression of the disease and how it affects the muscles, lungs, and heart over a period of time (~3 years). The study does not involve the use of an investigational study drug. Individuals affected with Sarcoglycan Limb-girdle muscular dystrophy are invited to participate.

The Journey to uncover your potential treatment options

Currently there are no therapies for individuals with Limb-girdle muscular dystrophy. Participation will provide you access to highly experienced clinical trial physicians and clinicians with expertise in your condition and knowledge about future drug therapy research. Your participation in Journey will not hinder your ability to participate in future clinical studies, including those with investigational study drugs.

Who may be eligible

- Male or Female
- Age 4 years and older
- Genetic diagnosis of LGMD2E/R4, LGMD 2D/R3, or LGMD2C/R5

*Other inclusion/exclusion may apply and will be discussed with a study doctor at screening.

Journey Participation

Study participants will undergo medical and functional procedures during the screening visit, and at scheduled study visits throughout the lifetime of the study.

On-site visits: For screening and every 6-month visit:
- meet with the study doctor and research team
- complete motor assessments.

In between on-site visits: For every 3-month visit:
- study research team will contact you every 3 months by phone
- ask you questions on your health and wellbeing.

Journey Locations

The Journey study is currently enrolling at research centers in the United States and Europe, and is planned to be active in Canada, and parts of South America and Asia.

To learn more about the study and how you can join the Journey, go to journeyLGMD.com

You can also find more information about this study and participating locations, by visiting ClinicalTrials.gov and searching NCT04475926.

Sponsored by SAREPTA THERAPEUTICS

SAREPTA THERAPEUTICS

The SPEAK Foundation
PO BOX 600062
ST JOHNS FL 32260-0062

Your Voice Will Make a Difference!

The LGMD community will be leading an Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting on September 23, 2022.

What will happen at this EL-PFDD meeting? This important, monumental effort will give individuals diagnosed with limb-girdle muscular dystrophy types 2A, 2C, 2D, 2E, 2F, and 2I an opportunity to share with the FDA and other stakeholders about the experiences and challenges of living with LGMD.

What do we hope to gain? The EL-PFDD meeting is designed to engage patients and elicit their unique perspectives. With this information, our goal is to enable knowledgeable development and review of LGMD therapies that meet the needs and expectations of our patient community.

Coalition to Cure Calpain 3 — Overcoming Weakness With Strength
kurt+peter Foundation
LGMD2D Foundation
The SPEAK Foundation
CURELGMD2i
McColl-Lockwood Laboratory for Muscular Dystrophy Research

www.lgmdpfdd.com