Vol 1 / Issue 2

LGMD News

Uniting the Limb-Girdle Muscular Dystrophy Community

Recovering from an Injury with LGMD

Reviewing Risk Factors, Common Injuries, and Considerations for Rehabilitation Post-Injury

GRASP CONSORTIUM

Resolving Diagnostic Uncertainty for Patients is Our Priority

COALITION TO CURE CALPAIN 3

Overcoming Weakness with Strength

Team Titin

Variants in the massive gene titin (TTN) can cause a spectrum of muscle and heart disorders including LGMD 2J, also known as LGMD R10 Titin-related.

Team Titin is a consortium of scientists and affected community members aimed at making a worldwide difference in Titin-related muscle and heart disorders by: collaborating with other organizations, raising awareness, connecting with families, providing education, and supporting research. Our goal is to serve as a catalyst for stakeholders to develop a better understanding of Titin-related disorders, leading ultimately to a cure.

To learn more visit titinmyopathy.com

EMAIL:
CureMyopathy@gmail.com

FACEBOOK:
facebook.com/groups/teamtitin

REGISTRY:
Congenital Muscle Disease International Registry (cmdir.com)

Have you or someone you know been diagnosed with Limb-Girdle Muscular Dystrophy Type 2I?

ML Bio Solutions is developing an oral therapy for limb-girdle muscular dystrophy Type 2I (LGMD2I/LGMDR9).

A Lead-in Study (Natural History Study) is currently enrolling participants with LGMD2I. While there is no intervention in this study, participants will be eligible to participate in the late phase clinical trial of BBP-418 (Ribitol).

You may be eligible to participate in the Lead-in Study if you are 10-65 years old and have genetically confirmed LGMD2I.

Remote enrollment is available, all travel/study expenses are covered, and strict COVID safety precautions are observed.

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

ML Bio Solutions
a bridgebio company

Contact: Brittney.Holmberg@vcuhealth.org | 804-552-0014
info@mlbiosolutions.com | mlbiosolutions.com | clinicaltrials.gov

LGMD News

Vol 1 / Issue 2

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.

Contents

Departments

Feature Article

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Twitter.com/SpeakFoundation
Twitter.com/LGMDFoundation

Correction

The first human gene therapy trial for LGMD was done in 1999, led by Jerry Mendell, MD, chairman of the Department of Neurology at the Ohio State University Medical Center, and was a successful safety study like the trial that enrolled its first participant in 2008.

Show the World We Are Ready!

On September 17th–20th, with one united voice, let us make a difference by bringing a record number of individuals living with this disease to the forefront.

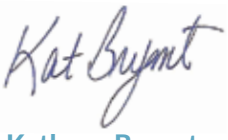
Many ask the question, "What can I do as an individual living with LGMD while I await a treatment?" Believe it or not, over the next few years, you will have a lot of opportunities! There are new paradigm shifts in the LGMD science community, and your voice will be needed in the drug development process.

Your first major opportunity is at the 2021 International LGMD Conference, being held virtually later this year, on September 17th – 20th. The Conference will engage patients, world-renowned experts, and top industry pharma and biotech companies from around the globe. Spread out over four days, you will be able to enjoy virtual, patient-focused sessions, hear patient stories, and participate in sponsored and vendor sessions that will update you on new plans and products developed to make living with LGMD easier.

You will also hear the latest information and top research on LGMD from world-renowned speakers from the GRASP-LGMD Consortium, as well as former FDA Commissioner, Dr. Scott Gottlieb. Dr. Gottlieb will be joining us to share how we can be a part of the regulatory process to get treatments out to patients quickly and safely. There are important advocacy opportunities in the next couple of years and you will learn all about how to get involved with them.

Starting April 15th, you will be able to register, free of cost, to attend this virtual conference at **InternationalLGMDconference.com**. This is a unique opportunity to engage with others in the limb-girdle community from many different nations, covering all subtypes. Your registration and attendance are important, as both will communicate to the world that individuals living with this disease are mobilized for clinical trials. The first 300 U.S. registrants receive a special swag bag and international patients receive a chance to win any number of gifts through our early registration contest. Early registration is encouraged.

On September 17th – 20th, with one united voice, let us make a difference by bringing a record number of individuals living with this disease to the forefront. ▪



Kathryn Bryant
Editor In Chief

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

JAIN FOUNDATION

ORCHESTRATING A CURE

LGMD2B/R2 DYSFERLINOPATHY MIYOSHI

The Jain Foundation is a nonprofit, scientifically led foundation whose mission is to cure muscular dystrophies caused by dysferlin protein deficiency, which includes limb-girdle muscular dystrophy type 2B/2R (LGMD2B/2R) and Miyoshi Muscular Dystrophy 1 (MMD1), collectively called Dysferlinopathies.

DYSFERLIN REGISTRY

by Jain Foundation

The Jain Foundation curates the Dysferlin Registry, an international registry for people with dysferlinopathy. The registry is critical to successful future trial recruitment. It also serves to educate and connect individuals who are navigating life with dysferlinopathy. The registry platform provides a quality, private media for open discussions. For more information about the registry, email ***Patients@Jain-Foundation.org***.

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

30 years GENETHON

GENE THERAPY PATHFINDER

GENETHON, A 30-YEAR GENE THERAPY PATHFINDER, CREATES ATAMYO THERAPEUTICS TO HARBOR ITS LGMD PROGRAMS

A pioneer in the development of gene therapies, Genethon has been working to find treatments for LGMDs for over 20 years. Genethon's researchers identified both the genes and the mechanisms responsible for many of these diseases and are using their skills and expertise in gene therapy and LGMDs to develop innovative treatments.

To date, Genethon is working on 7 LGMDs.

Five of Genethon's LGMD programs have reached in vivo proof of concept, 3 of which are planned to be submitted for clinical trial within 24 months. Genethon is spinning off these programs into a new company, Atamyo Therapeutics, that will be focused on their development and marketing.

The first LGMD-R9/2i patient is expected to be injected by the end of 2021.

Genethon, 30 years Gene Therapy Pathfinder - Genethon.fr/en

Next Steps

Your Starting Point as a Newly Diagnosed Individual with LGMD

These subtype-specific organizations are dedicated to finding treatments and connecting with patients through registries. You can contact any of these organizations for unique support to match your personal diagnosis.

The first thing you need to know is you are not alone. This magazine was created by the Speak Foundation to help you get connected into our already existing community of individuals living with limb-girdle muscular dystrophy. There are over 30 different genetically distinct subtypes of limb-girdle muscular dystrophy and it can be hard to find resources and clinical trials that are available for your subtype. This magazine is the first source for you.

In this issue, on the page to the right, you will find the International Consortium of LGMD organizations. These subtype-specific organizations are dedicated to finding treatments and connecting with patients through registries. You can contact any of these organizations for unique support to match your personal diagnosis.

You will also find informative articles from some of the best researchers in the world. GRASP-LGMD is a consortium of doctors who are conducting clinical trials and are united to find a cure for LGMD. Your subtype may be one of the forms in a current trial.

Last, many of the biotech and pharmaceutical companies developing therapies for LGMD are included in this magazine. There are numerous companies working on a cure for various forms of LGMD. So there is hope.

The Speak Foundation — we are a voice for LGMD. ▪

LGMD Patient Network

Register at **TheSpeakFoundation.com** to receive updates on the limb-girdle muscular dystrophy patient community. By registering, you will receive our magazine and many important resources to help you. We offer multiple programs to enhance your quality of life, such as the International LGMD Conference and the Personal Care Attendant Stipend Program. The Speak Foundation is a patient-led team of individuals who are living successfully with LGMD — we know firsthand the importance of ***community***.

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

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

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

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

Two New Programs

Offered by The Speak Foundation

BEGINNING MAY 2021

The C.A.R.E. Program

Connecting and Reaching Everyone

Are you a newly diagnosed patient with limb-girdle muscular dystrophy? We understand LGMD and we are here to help. The C.A.R.E. program gifts newly diagnosed patients with a box of helpful tools that includes smart technology and items donated from the International Consortium of LGMD Organizations. This program is available to patients newly diagnosed with limb-girdle muscular dystrophy as of May 1st, 2021. Visit our website at **TheSpeakFoundation.com** for more information. Open to U.S. residents only.

BEGINNING MAY 2021

The HOPE Project

Do you need financial assistance for mobility or durable medical equipment (DME)?

Through the HOPE Project by The Speak Foundation, individuals living with limb-girdle muscular dystrophy can receive up to a $500 stipend per qualified applicant to help cover the costs of mobility and DME equipment. Applications will be available beginning May 1st at **TheSpeakFoundation.com** and will be accepted through September 30th. Grant funds to approved applicants will be released beginning May 20th. Open to U.S. residents only.

Connecting and Reaching Everyone
C.A.R.E.
A Program of The SPEAK Foundation

The HOPE Project
A Program of The SPEAK Foundation

Do You Have Questions? | Please Connect with a Team Member at The Speak Foundation | *ContactUs@TheSpeakFoundation.com*

Peter B. Kang, MD

Director, Paul & Sheila Wellstone Muscular Dystrophy Center
Vice Chair of Research, Neurology Department, University of Minnesota Medical School

Meet the Expert

Peter B. Kang MD, is a pediatric neuromuscular neurologist and physician-scientist who has been studying the LGMDs for over a decade in his laboratory. He has cared for patients with LGMD in his clinic for nearly 2 decades.

Q

Many have started to get the COVID vaccine by now. Have there been any adverse effects for LGMD patients who have received the vaccine? At this point, do you feel it is safe to get the vaccine?

A

Not much is known about adverse effects of the FDA-approved COVID vaccines specifically in the LGMD population. However, in a recent webinar hosted by the National Organization of Rare Diseases (NORD), officials from the U.S. Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) indicated that there is no evidence to date that patients with rare diseases are at higher risk of adverse effects from the vaccines compared to the general population. LGMD is classified as a rare disease. It is important for LGMD patients to be vaccinated when they have access to the approved vaccines except for those who are in specific high-risk situations, unless new information becomes available in the future that indicates otherwise.

Q

My bloodwork is abnormal in several areas and my doctor says it is related to my LGMD. Can you share what labs are typically "off" in individuals with LGMD?

A

Levels of serum creatine kinase (CK), also known as creatine phosphokinase (CPK), are usually elevated, sometimes significantly, in patients with LGMD. There are actually five serum biomarkers that are found in skeletal muscle tissue and may be elevated in patients with LGMD: CK/CPK, aldolase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH). CK/CPK and aldolase are well known as biomarkers of muscle dysfunction, but ALT, AST, and LDH are often included in a set of tests known as liver function tests or LFTs, and it is not as widely recognized that these three biomarkers are also found in skeletal muscle. Patients with LGMD may have elevations of some or all of these five serum biomarkers at baseline. Thus, these tests should always be interpreted in the overall clinical context and when possible, consider trends over time.

Q

What forms of LGMD can affect breathing muscles? I was told that some forms can cause respiratory problems. What do I need to look for in terms of symptoms?

A

Respiratory problems in LGMD are regarded as being relatively uncommon overall, though some subtypes are associated with more frequent respiratory complications than others, and patients who have lost ambulation are at higher risk overall for these complications. LGMD subtypes that are known to have relatively high rates of respiratory complications by early to mid-adulthood include LGMD2I/R9 (FKRP-related)

and the sarcoglycanopathies. These complications are less frequently seen in that age range for LGMD2A/R1 (CAPN3-related) and LGMD2B/R2 (DYSF-related). As data on patients with LGMD in later adulthood are sparse, not much is known about respiratory complications in that age group. Symptoms of respiratory problems include shortness of breath and changes in endurance/stamina. An episode of pneumonia, even if easily treated, may be a sign of changes in respiratory function. Sleep disorders are important manifestations of respiratory dysfunction. Signs of sleep disorders in this setting may include excessive snoring, restless sleep, morning headaches, and daytime sleepiness. Any patients who have concerns about respiratory complications should consult with their physician(s) about the advisability of a pulmonary evaluation, which may include an evaluation by a pulmonary or sleep specialist physician, pulmonary function tests (PFTs), and/or a sleep study.

Q

Is it possible to have a video consultation with a GRASP-LGMD clinic doctor if I live in another state? I live in the U.S., but don't live in an area close to a major city.

A

Rules and regulations regarding telemedicine practice have recently been relaxed in numerous states due to COVID-19, but there is a significant amount of variability from state to state. Some states will permit physicians from other states to conduct official telemedicine visits on patients within their borders without any official documentation with their state medical boards. Others require official registration by such physicians, albeit generally abbreviated. It is not clear how these rules and regulations will look in the long term, after the worst of the pandemic is over. Patients who are interested in consulting a GRASP-LGMD physician in another state via telemedicine should contact that physician's office, explain what state they reside in, and inquire about whether there are any options for telemedicine consultations.

Q

Are there any nutritional supplements or a special diet that you would recommend for a person with LGMD?

A

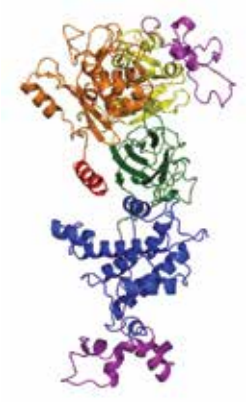
The most helpful general supplement for patients with LGMD and other muscular dystrophies is vitamin D, especially if they have low serum levels of 25-hydroxy vitamin D. Though vitamin D is available over-the-counter, patients should consult their physicians regarding dosing recommendations as the recommended dose may vary depending on factors such as serum levels and any history of fractures. A balanced diet is recommended for LGMD patients with all major food groups represented, and caloric intake should be sufficient to permit growth during childhood and adolescence, and stable and appropriate body mass indices during adulthood. ■

> *It is important for LGMD patients to be vaccinated when they have access to the approved vaccines except for those who are in specific high-risk situations, unless new information becomes available in the future that indicates otherwise.*

Have a Question for Our Experts?

Send Questions To:
ContactUs@TheSpeakFoundation.com

C3 Scientific Advisory Board Chair Dr. Melissa Spencer and student Leo Martinez review images captured by a microscope in her University of California Los Angeles laboratory.



Above: Illustration depicting the structure of calpain 3. Calpain 3 deficiency causes LGMD2A/R1 and LGMD1I/D4.

Coalition to Cure Calpain 3: Overcoming Weakness with Strength

A Therapeutics-Focused Patient Organization

Coalition to Cure Calpain 3 (C3) is a non-profit organization founded in 2010 by Kristine Kurnit and Michele Wrubel, two women living with LGMD2A/R1. Before C3, there was no organization dedicated specifically to understanding and curing this disease. Our founders recognized the need to make rapid progress on therapies specifically designed for LGMD2A/R1 patients, and C3 is focused on driving high-quality research with the goal to accelerate the development of therapeutics.

LGMD2A/R1 is the most common subtype of LGMD in many populations, affecting 1-7 of every 100,000 people. The onset of muscle weakness usually occurs between the ages of 8-15, but may range from 2-40 years old. Early symptoms often include walking on tiptoes, difficulty in running, protruding shoulder blades, and a waddling gait. Some patients also experience Achilles tendon shortening and joint contractures. Progressive weakness often leads to patients becoming wheelchair dependent. Respiratory problems can occur late in disease progression, however there are no heart abnormalities associated with this subtype.

LGMD2A/R1 is an autosomal recessive disease caused by mutations in the CAPN3 gene, which encodes the protein calpain 3. It was recently discovered that certain mutations in CAPN3 can also cause dominant inheritance of LGMD. The dominant subtype, LGMD1I/D4, usually has a later onset and is milder than LGMD2A/R1. The mechanism of disease is likely similar in both forms: loss of calpain 3 activity.

Supporting Research and Gene Therapy

In the search for a cure, C3 has committed over $1.7 million in grants to international leaders in the muscular dystrophy field. These grants have supported the development of essential research tools, the identification of outcome assessments which will be used in future clinical trials, and the testing of potential therapies in animal models to determine if they can be safe and effective for LGMD2A/R1.

Connect with Us

Inquiries or Questions?
Info@CureCalpain3.org

CureCalpain3.org
LGMD2A.org

Facebook.com/CureCalpain3

Twitter.com/CureCalpain3

Today, multiple companies are developing gene therapies for this disease. "We believe that gene therapy holds great promise, and in 2018, launched a Gene Therapy Initiative to advance the development of this technology," notes Scientific Director Dr. Jennifer Levy. "We are hopeful that this technology has life-changing potential for people living with this disease."

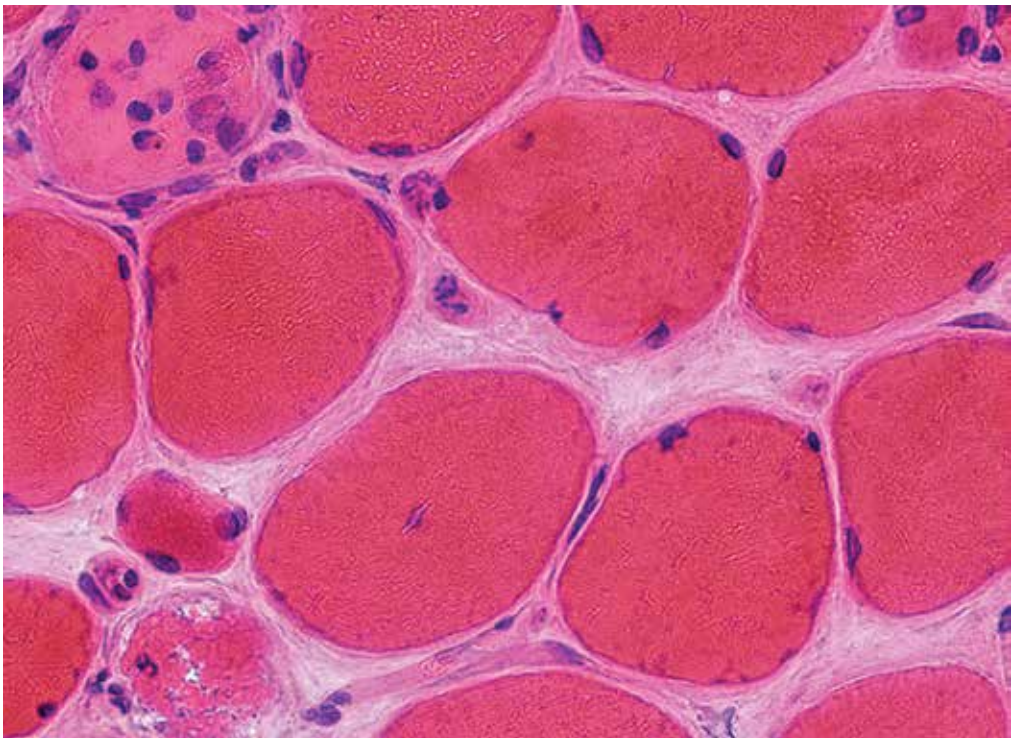
Managing a Global Patient Registry

A robust patient registry is essential to persuade researchers and pharmaceutical companies to take up C3's cause in search of a cure. The C3 Global Patient Registry is one of the most important tools to help the scientific world better understand the number of people living with LGMD2A/R1 and the symptoms they experience. The registry is used to contact patients when clinical trials are recruiting. Individuals diagnosed with LGMD2A/R1 or LGMD1I/D4 are encouraged to join this important initiative by signing up at **LGMD2A.org**.

"This is an extremely exciting time for the LGMD2A/R1 community," says C3 President Jordan Boslego. "Our understanding of the disease has increased significantly, and we have attracted the attention of large companies who are exploring multiple approaches to developing therapies for individuals living with this disease." ▪

Contributed by Jennifer Levy PhD
Scientific Director,
Coalition to Cure Calpain 3

> *The C3 Global Patient Registry is one of the most important tools to help the scientific world better understand the number of people living with LGMD2A/R1.*



Uncertainty in LGMD: GRASP-LGMD Consortium Will Improve Diagnostic Accuracy

Our consortium is committed to reducing diagnostic uncertainty and establishing clear genetic diagnoses for patients, clinicians, and families.

Despite knowing the specific genes that cause LGMD subtypes, diagnostic uncertainty remains for many patients. We know that over 50% of patients with LGMD receive unclear results from their genetic testing. These are referred to as variants of unknown significance (VUS or VOUS) since it is unknown whether the genetic variant (formerly termed mutation) is causing the disease or is associated with random variation in human DNA.

Our consortium is committed to reducing diagnostic uncertainty and establishing clear genetic diagnoses for patients, clinicians, and families. We have established an international genetic working group that scrutinizes, validates, and certifies genetic variants in LGMD genes. Validated variants are deposited into ClinVar as expert panel reviewed and FDA-recognized.

Our future goal is to establish a workflow to resolve the genetic variant and diagnostic confusion for patients and families within the LGMD community. We hope to be able to offer a web portal that will enable patients to upload their genetic testing results for evaluation by our expert team. One clear challenge with genetic testing is that many physicians have not been trained how to interpret it. We are here to help. ■

Contributed by Dr. Conrad "Chris" Weihl
Professor of Neurology
Washington University School of Medicine, St. Louis, MO

Above: Hematoxylin and Eosin staining of muscle from a patient with LGMD2B/R2. Pale pink fibers represent necrotic fibers engulfed by dark blue phagocytic cells.

UPDATED: MARCH 1, 2021

GRASP-LGMD Clinical Trials

STUDY 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)

STUDY 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 the10-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: **Brittney Holmberg** | Project Manager, Grasp-LGMD Consortium | (804) 997-9384 | *Brittney.Holmberg@vcuhealth.org*

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University of California Irvine


Urvi Desai, MD
Atrium Health


Volker Straub, MD, PhD
Newcastle University


Monkol Lek, PhD
Yale University, Non-Clinical Site

GRASP-LGMD Researcher Spotlight

Dr. Conrad "Chris" Weihl
Washington University School of Medicine, St. Louis, MO

Dr. Conrad "Chris" Weihl is a Professor of Neurology at Washington University School of Medicine in St. Louis, Missouri, USA. He received his MD and PhD from the University of Chicago Pritzker School of Medicine followed by a neurology residency and neuromuscular fellowship at Washington University. During his post-doctoral fellowship, he began to study the molecular pathogenesis of hereditary myopathies and now has an active clinical and basic science research program focused on genetics and limb-girdle muscular dystrophies. His research has delineated the molecular mechanism of several myopathies and identified the genetic cause of LGMD1E/D1. He has received a number of honors including the Derek Denny-Brown Young Neurological Scholar Award from the American Neurological Association. He is currently a member of the WMS meeting planning committee and is the ANA scientific program advisory committee chair. Dr. Weihl has a strong commitment to the training of future neuromuscular clinicians and myologists.

Toilet Solutions

Thankfully, there are several products on the market which can make the bathroom much more user friendly by increasing safety and independence.

Going to the bathroom is a simple activity most people take for granted. For many individuals with LGMD, using a toilet may become challenging as they struggle to independently stand up from a seated position. Thankfully, there are several products on the market which can make the bathroom much more user friendly by increasing safety and independence.

Grab Bars

Grab bars are an important safety feature for bathrooms. They are available in a variety of styles and lengths to accommodate your space and physical needs. When properly installed, grab bars provide assistance with balance and support.

Toilet Seat Height

The height of a toilet can also make a huge difference. Usually, an individual with muscle weakness finds it easier to stand up from a taller toilet. A simple, plastic, raised toilet seat is a device that sits on top of the toilet bowl and provides about 5" of additional height. Although not as solid or permanent as the other devices, many find it to be a low-cost, portable solution. A raised toilet seat can easily be transported in a large tote bag or pillowcase, if necessary. Raised toilet seats are sold online as well as at your local pharmacy.

Another option is the **Toilevator**,® a special base to mount under an existing toilet base that adds 3.5" in height. This is a more stable and discreet option for raising the toilet. Learn more at **Hartmobility.com/Products/Toilevator** (MSRP: $140 – $209).

Power Toilet Lift

For a more mechanical solution, consider a power toilet lift. **Power Toilet Aid** by **Stand Aid of Iowa** is powered by a 12-volt rechargeable battery and raises your toilet seat up to 13" above your existing toilet height. It is operated with a lift switch control. The Power Toilet Aid is available in a standard model which attaches to your toilet or a mobile model which can also be used as a commode. Learn more at **stand-aid.com/power-toilet-aid.html** (MSRP: Standard $1,500, Mobile $1,650).

LiftSeat® stands securely over your toilet with no attachments necessary. With adjustable rotational arc or straight vertical lift motion paths, LiftSeat® accommodates a wide range of mobility limitations. It is equipped for both bathroom or bedside use, with features such as adjustable width armrests, adjustable seating height, AC or DC power or both, wheels for mobility, bidet accommodation and other customizable options. Learn more at **LiftSeat.com** (MSRP: starts at $1,349). ■

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

Toilevator® base mounts (Left) and LiftSeat® Powered Toilet Lifts™ (Above) are both ideal solutions for people living with limb-girdle muscular dystrophy.

Featured Resources

Hartmobility.com/Products/Toilevator

stand-aid.com/power-toilet-aid.html

LiftSeat.com

By **Vovanti T. Jones**, MD
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Recovering from an Injury with LGMD

Despite our best efforts, injuries happen. As healthcare professionals, we are often asked about managing recovery post-injury and how LGMD can impact that recovery. In this article, we review risk factors and common injuries, as well as considerations for rehabilitation post-injury.

Risk Factors

In people with LGMD, symptoms are progressive. With each change in body function, there is increased risk of injury. As muscles weaken, the body compensates in many ways, putting strain on body structures. Overuse injuries are common in stronger muscle groups that attempt to compensate for other, weaker muscles.

Contractures can occur when a joint is not consistently moved through its entire range, often due to muscle weakness or reduced mobility. This results in the muscle and surrounding skin and tissues tightening down to restrict the flexibility and mobility of a joint. Contractures can change the way a body moves, which may increase the risk of injury. Similarly, people with reduced mobility or wheelchair users should regularly monitor their skin as there can be issues around reduced circulation and wound repair, especially in the lower limbs.

Osteoporosis is another disorder that may increase the risk of injury. Osteoporosis is caused by the imbalance of normal bone formation and bone resorption. This results in low bone density, making bones more fragile and at an increased risk for fracture. This is especially important in females who have a higher risk of osteoporosis as they age in the general population.

Common Injuries

The most frequent injuries in persons with LGMD tend to result from unexpected events, such as falls or other accidents. Individuals with LGMD have a high risk of fractures. There are various degrees of fractures, but all should be brought to the attention of your medical provider for follow-up. Symptoms of a fracture may include a change in shape of your limb, swelling, bruising, intense pain in a specific region, or change in mobility of a limb. Where appropriate, early fixation with orthopedic surgery may allow for quicker mobilization after injury. Make sure your orthopedic surgeon liaises with your neuromuscular team to ensure management is appropriate for your specific circumstances.

Far Left: Bruising may result following a muscle, tendon, or ligament strain or sprain.

Left: Dr. Vovanti Jones examining a patient's X-rays at the University of Missouri at Rusk Rehabilitation Hospital

Muscle, tendon, and ligament strains or sprains frequently occur due to overuse of muscles or trauma from a fall or other accident. Symptoms of strains or sprains may include pain, swelling, bruising, and pain. Other overuse injuries, such as shoulder impingement (compression of the tendons of the rotator cuff the shoulder muscles against the acromion causing pain and restriction of movements) or hip bursitis (inflammation of a fluid filled sack between the tendon and bone of the hip that typically reduces friction when moving), occur from inflammation. As certain muscle groups work harder to complete a movement or activity, those muscles or supporting structures can become inflamed and painful. Shoulder pain, when attempting to lift an arm overhead or after completing overhead activities, can be a sign of shoulder impingement. Similarly, pain on the side of the hip or thigh can be a sign of bursitis in the hip due to compensation or reduced mobility.

Injuries can occur quickly or progress slowly over time. Be sure to seek medical attention if you have any new symptoms, especially if occurring after a fall or other event. It is important to talk with your multidisciplinary neuromuscular team about any pain or change in symptoms to determine the appropriate treatment plan. Often, pain or discomfort may be caused by a treatable injury rather than being a symptom of LGMD.

Rehabilitation

After an injury, early rehabilitation (rehab) is important to the recovery process. The goal of rehab is to help people adapt to their disability as well as to restore function and regain as much independence as possible. Rehab is a collaborative process that includes not only you, but often your therapist (physical and/or occupational) and your physician. LGMD creates a unique group of symptoms and patterns of muscle weakness. It is important to have healthcare professionals who understand this disorder as well as other medical conditions, including cardiac and respiratory dysfunction, which might impact the rehab process. Rehab focuses on exercise as well as other modalities like massage and heat/cold treatments.

Early rehabilitation is important to the recovery process after an injury.

Often pain or discomfort may be caused by a treatable injury rather than being a symptom of LGMD.

Exercise

When it comes to exercise after an injury, it is important to find a skilled provider or team to guide and supervise your recovery. As most LGMDs are rare, you will likely be the expert on your individual body, while your team will be the expert in exercise. Work together to find the right balance of exercise and activity, without overworking or re-injuring your body.

Mild and/or moderate exercise can be safe after injury, but exercise comes in many shapes and sizes, therefore, here are a few general guidelines.

- **Isometric Strengthening:** These strengthening exercises are simple contractions of your muscles without your limbs moving. Some studies have shown that mild isometric contractions of muscle groups around the area of injury may provide a means of safe strengthening.
- **What to Avoid:** High intensity resistance training or eccentric contractions (squeezing your muscles while lengthening or extending at the joint) are thought to create too much muscle damage and may result in more weakness.
- **Exercise:** In general, supervised mild aerobic exercise or activities are likely helpful after injury. It is recommended that you pick a low-resistance activity that you enjoy and that is available in your area, like walking, water aerobics, or biking.
- **What to Avoid:** Overuse or too much exercise could be harmful. Signs of overuse may include increased fatigue, muscle pain or cramping, or changes in your abilities after exercise. If any of these occur, work with your team or provider to alter your program.

  Generally, weightlifting should be avoided, as attempts can be hazardous. Weightlifting typically can cause the breakdown of muscle fibers in order to rebuild into stronger ones. People with LGMD are at risk of being unable to successfully remodel these muscles leading to atrophy and further weakness.

  Contact your Physical Medicine and Rehabilitation (PM&R) physician, neuromuscular team, or your physical and occupational therapist prior to starting any exercise regimen.

Low-resistance activities, such as water aerobic exercises, are helpful following an injury.

A quick and safe return to activity is important to optimize your function and independence after injury. This could include a full return to previous abilities, maintenance of the new level of function, or anything in between. Remember to always work with your multidisciplinary neuromuscular team to determine the plan that works best for you, with specific exercises and activities that are safe for your individual body, and with regular monitoring over time. Some changes may be seen quickly and some may take longer. Stay positive and motivated, and don't be afraid to ask your team questions! ■

ICD Codes for LGMD: Coming Soon to Clinics?

We have complex therapies that are in clinical trials right now. We cannot be caught unprepared without specific LGMD codes when treatments become available.

Connect with Us

TheSpeakFoundation.com
MDA.org

Have you, like me, ever noticed that when seeing physicians, your diagnosis is never coded as limb-girdle muscular dystrophy? You might see a general code for muscular dystrophy being used, but never more specific than that. This is because there are no ICD codes to identify the LGMDs. That is and has been a huge problem for patients over the years.

So what exactly is an ICD code? It is an important classification tool used by clinicians in many areas, from billing to how your doctor manages your care. It is especially important when considering the possibility of future treatments, and can make a huge difference for you as a patient.

Advocates for a code for LGMD stress that the specificity of a diagnosis is critical to helping patients with targeted care management and treatments. For example, with an accurate code, a rural doctor faced with an ultra-rare form of LGMD can now identify risk factors that are commonly missed.

Specific codes facilitate the identification and monitoring of these diseases. How often have we all wondered how many people in the world are living with LGMD? With a code established, we will begin to see the numbers potentially increase dramatically over the next ten years. In other words, we would be able to identify patients more easily and establish reliable incidence, prevalence, and mortality.

While ICD-10-CM was not established for the purpose of payment, the code set can certainly impact it. Have you ever had a problem with insurance covering a procedure because the right code was not used? It happens. Before we get treatments on the market, we need to make sure that the LGMD community is ready. We have complex therapies that are in clinical trials right now. We cannot be caught unprepared without specific LGMD codes when treatments become available.

Recently, many advocacy organizations, including the Speak Foundation, along with experts in the field of limb-girdle muscular dystrophy, participated in a committee to nominate many forms of LGMD to be included in the ICD. The committee was led by Paul Melmeyer, Director of Regulatory Affairs, of the Muscular Dystrophy Association. We want to thank the MDA for leading this effort to give LGMD a voice. ▪

Nomination Committee Participants

The Sarepta Patient Affairs team is always excited to connect with individuals and families impacted by limb-girdle muscular dystrophy. **We would love to interact with more individuals who are living with LGMD2E in order to understand the experience and needs of the community.**

If you'd like to connect, email us at Advocacy@Sarepta.com

KEISHA
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Sarepta is advancing the research for multiple LGMD subtypes. We welcome connections with all individuals living with LGMD and encourage you to reach out to us directly and/or visit **limbgirdle.com** to sign up for Sarepta communications.
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My LGMD Story: John Graybill

John Graybill, II, is a busy man. In addition to being a devoted husband and father, he runs a nonprofit organization and manages a podcast and YouTube page — all for the benefit of helping others who have limb-girdle muscular dystrophy (LGMD) like himself. John is a valuable member of the LGMD community and has helped countless people all over the world.

Below: John Graybill with wife Darcie and daughter Chloe

Is your condition your greatest punisher, or your greatest teacher?

Speaking with John, it is quite evident that he is in a place of peace and acceptance about his condition. But he notes that this has been a journey, and not without difficulties.

When John was a teenager, he struggled for several years with physical activities before he knew what was wrong. His parents sought answers and took him to the University of Pennsylvania, where he underwent a number of tests. He was then diagnosed with LGMD2A/R1 in 1995, at the age of seventeen. Hearing this news at such a young age was devastating to John, and he struggled with fears about his future — that he would have to live with his parents for the rest of his life and that he would never get married.

In most populations, LGMD2A/R1 is the most common form of limb-girdle muscular dystrophy, accounting for about 30 percent of cases. People with LGMD2A/R1 often have initial symptoms of weakness and wasting in the hip, thigh, and shoulder muscles. This weakness is usually even on both sides of the body and leg weakness is usually present before shoulders and arms. The condition is caused by mutations in the CAPN3 gene.

About ten years after his diagnosis, John began to focus on improving his wellbeing as a whole, beyond just the physical. A trip to Brazil marked a significant moment of realization for him. John says, "While I was there, I thought, 'what if this disease is here in my life trying to teach me something?' I realized I needed to look at the disease differently. Before, I kept taking this disease personally, like it was taking things away from me. Once I changed my perspective to think of myself like a kid learning something in school, asking 'what do I need to learn from this?,' it changed everything for me."

John started eating healthier, taking supplements, exercising, exploring alternative therapies, and working on his mental health. As he puts it, he "went to work on his life." He hoped that if he did everything within his power to help himself, maybe he could stave off the decline of his condition.

In 2007, he and his family founded the nonprofit *Beyond Labels & Limitations*, which is dedicated to raising awareness, and funding research to find a cure for LGMD2A/R1. He also started a YouTube page, where he shares videos of stretching exercises, as well as helpful tips on getting in and out of a car, walking,

climbing stairs, etc. In addition, he manages a podcast with Jen Ives that is devoted to sharing stories about parenting, relationships, travel, and interviewing others who are making a difference in the LGMD community.

John says, "I realized there were no podcasts that focused on muscular dystrophy, so I decided to start one. In the podcast, we talk about living with LGMD, what it's like, the struggles we encounter, and solutions we've found helpful. We also talk about normal life, too, since most of us are trying to lead as normal of a life as possible."

The two fears John had when he was first diagnosed were put to rest in 2011, when he met Darcie during his trip to Brazil. After dating for a year, John moved from Pennsylvania to Colorado to live with her, and they got married in 2015. They now have a 5-year-old daughter named Chloe. "I am so grateful for Darcie and Chloe because they have taught me that I can have the family I've always wanted," John says. "They love me in spite of my physical limitations and it has helped me love *myself* more because of that."

John continues his quest to keep meeting and helping people any way he can through his online channels. On one of his recent podcasts, he asked his listeners, "Is your condition your greatest punisher, or your greatest teacher?"

What is LGMD for *you*? ■

Contributed by Rebecca Lucas Gregg

Connect with Beyond Labels & Limitations

BeyondLabelsLimitations.com

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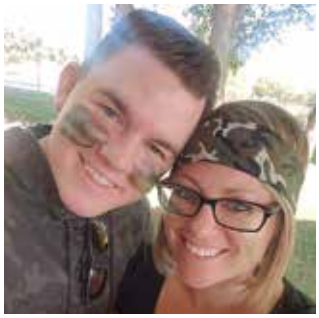
YouTube.com/c/JohnGraybillII

Fundraising for Hope



I realized very quickly that I had an opportunity to use this terrible situation to help others who were facing the same circumstances.

Three years ago, my life changed because of a disease I knew nothing about. On April 10, 2018, I was diagnosed with limb-girdle muscular dystrophy, type 2B/R2. I read the message from my specialist at The Mayo Clinic, overwhelmed with emotions. All I could do was cry. Standing in the arms of my parents, I was devastated, lost, and thinking, "Why me?"

Fortunately, I was not sad for long. I realized very quickly that I had an opportunity to use this terrible situation to help others who were facing the same circumstances. One of the first steps I took in my mission to help others was to reach out to charities and organizations that fight for people with this disease.

Fundraising is a huge part of my hope. I was fortunate to be a guest speaker at local MDA events in my area, and soon was writing proclamations to governors, creating my own muscle walk team, and eventually, planning my first fundraising event, a poker fundraiser. I received local donations from charities for raffle items, hung up flyers, and reached out to people via social media. I was able to raise over five hundred dollars and could not have been happier.

Due to COVID, we had a very challenging year. I knew I had to do something to help encourage others. I called my friends and family, and together, we decided that we were going to host a huge event to help other people with muscular dystrophy. We decided to plan a golf tournament, a monumental task considering that most local charities had shut down due to the pandemic. Our local MDA had shut down, which felt like a huge setback.

I learned quickly to accept the word "no" while also staying resilient and optimistic. With the many roadblocks I encountered, I knew I needed some help. I heard about The Speak Foundation and reached out to them. I was quickly offered support and a sponsorship for the tournament. They provided masks, goodie bags filled with items for my attendees, and encouragement. Together with The Speak Foundation, local organizations, family, and friends, we pulled off a hugely successful event. We raised over four thousand dollars in one day! All proceeds went to The Speak Foundation to help others with limb-girdle muscular dystrophy.

I have learned that even in the worst of times, you can have hope. My advice is to reach out to loved ones, minister to people like yourself who may be suffering, and strive for positivity. Even though you may have been dealt a tough hand, focus on the good things in life and remind yourself that you are not alone — others are experiencing the same struggles. Do what you can to help your fellow brothers and sisters. Your help brings hope. ■

Contributed by Aric Hershley

Mark your Calendar!

LGMD Awareness Day September 30th

Awareness is power, and power brings cures, treatments, and changes policies. LGMD Awareness Day is an annual effort to globally raise awareness of individuals living with Limb Girdle Muscular Dystrophy. The seventh annual Limb Girdle Muscular Dystrophy Awareness Day will be celebrated worldwide on September 30th, 2021. As an Ambassador for LGMD Awareness Day, we encourage you to adapt activities in accordance with your customs. Our goal is to reach the widest audience possible. Make an impact—get involved today!

"Together we are STRONGER!"

LGMD-Info.org

LGMD Awareness Day is a project of the LGMD Awareness Foundation, Inc.

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