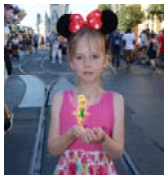
CURE CMD

SCIENTIFIC AND FAMILY CONFERENCE

JULY 7-9, 2017
Arlington, Virginia

CONNECT AND INSPIRE





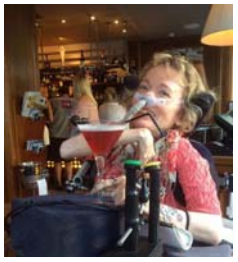





A cure is among us

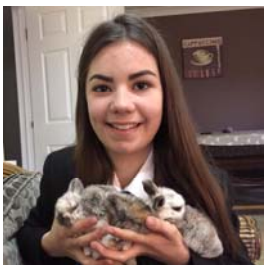











Conference Map

Welcome to CMD SciFam!

Welcome to the largest-ever gathering of CMD-affected individuals, families, caregivers, and CMD experts, clinicians, scientists, and researchers. Cure CMD's staff has been working toward this event for the past 18 months, so it is an understatement to say we are so excited and delighted that you are with us.

Every aspect of this conference has been designed with you in mind. This weekend, some of the most brilliant, dedicated minds in the world—including researchers, clinicians, and industry and government partners—have come together to focus on you so that they may gain a greater understanding of congenital muscular dystrophy. You will be able to discuss with them and each other how best to optimize care and improve quality of life when living with CMD. We will also answer your most pressing questions and encourage you to become advocates for yourselves and the CMD community. Finally, we aim to motivate and engage, and support momentum toward clinical trials. The next three days are going to be exhilarating, moving, educational—so make sure to rest when you can!

We hope that you find your highest priorities reflected in this weekend's agenda, from main stage presentations to breakout sessions to supporting activities like Sunrise Yoga and the BioBank/Tissue Repository booth. We encourage you to meet videographer Evan Burgher (***Thatch Creative***) and photographer Levi Gershkowitz (***Living in the Light***), and participate in **CMD Voices**, sharing your story in a safe, welcoming space.

But before we begin, we urge you to consider your goals for the weekend. What do you wish to achieve? Who do you want to meet? How you do wish to transform and transform others?

The connections you make this weekend are just as important as the information you learn. Look around you — the 300 people here this weekend are your tribe. And it is up to us, as a community, to come together and build momentum toward our goals.

Starting now, together:

Let's *Connect and Inspire*. Let's move forward.

With Warmest Regards,

The Cure CMD Staff and Board of Directors

Cure CMD thanks PCORI and our industry partners who have graciously stepped in to help fill the budget gap for this once-in-a-lifetime event. We are incredibly grateful for all of our partners – including you – who have made CMD SciFam possible.

About the 2016-2017 CMD Conference Series

In May 2016, Cure CMD received a Eugene Washington Engagement Award ((3353-C-CMD) from the Patient-Centered Outcomes Research Institute (PCORI), which made possible a five-conference series, designed to:

- Educate and connect affected individuals and families with each other and with CMD experts
- Increase knowledge and collaboration among the experts researching the five CMD subtypes
- Raise public awareness and build advocacy around CMD
- Build momentum toward clinical trials

The conference series:

- October, 2016: International Conference on LMNA Related Disorders, Paris
- February, 2017: International Conference on Collagen VI Disorders, Washington D.C.
- March, 2017: International Conference on LAMA2 Disorders, Washington D.C.
- May, 2017: International Conference on SEPN1 Disorders, Washington D.C.
- July, 2017: CMD Scientific and Family Conference, Washington D.C.

The first four meetings brought together more than 200 researchers, clinicians, affected individuals and their families to review the current state of research, share and interrogate data, and develop an international collaborative plan based on identified priorities.

In addition to the four subtype meetings, Cure CMD was welcomed to participate in the 5th International Workshop for Glycosilation Defects which covered topics related to the alpha-Dystroglycanopathies. We continue to engage with researchers and clinicians to find ways to improve care and identify targets for treatments in Dystroglycanopathy.

About Cure CMD

Cure CMD was founded in 2008 to advance research for treatments and a cure for the congenital muscular dystrophies (CMD) and, through engagement and support of the community, to improve the lives of those living with CMD. To date, the organization has funded more than $2 million in research, launched the Congenital Muscle Disease International Registry (CMDIR), and has connected more than 2,000 affected individuals to a supportive, helpful community. Visit curecmd.org for more information.

About PCORI

The Patient-Centered Outcomes Research Institute (PCORI) is an independent, nonprofit organization authorized by Congress in 2010. Its mission is to fund research that will provide patients, their caregivers, and clinicians with the evidence-based information needed to make better-informed healthcare decisions. PCORI is committed to continually seeking input from a broad range of stakeholders to guide its work.

This conference series was funded in part through a
Patient-Centered Outcomes Research Institute (PCORI)
Eugene Washington Engagement Award (3353-C-CMD).

cureCMD

a cure is among us

Cure CMD's mission is to advance research for treatments and a cure for the Congenital Muscular Dystrophies (CMDs). **Cure CMD** will also improve the lives of those living with a CMD through engagement and support of our community.

Cure CMD collaborates with dedicated parent, research and government advocates worldwide to achieve this mission.

Generous support from the community since 2008 has helped

- Launch two clinical trials
- Complete a five year natural history study with the NIH to identify clinical trial endpoints
- Grow the Congenital Muscle Disease International Registry (CMDIR) to 2,200 registrants worldwide
- Fund over $1.5 million in research grants

Congenital Muscular Dystrophy (CMD)

Congenital: *born with*

Muscular: *affecting muscle*

Dystrophy: *gradual wasting*

The Congenital Muscular Dystrophies are conditions which become apparent in infancy or early childhood. The most noticeable symptom is muscle weakness. Some children never walk, while others lose the ability to walk as they grow into adulthood. Some children with a CMD may also have various neurological or physical impairments. All CMDs are caused by genetic mutations. As of today, no treatment or cure is available for this group of diseases.

Types of CMD:

- Collagen VI (Ullrich/Bethlem)
- Dystroglycanopathy (α-DG)
- LAMA2 (Merosin Deficient)
- LMNA (L-CMD)
- SEPN1 (Rigid Spine)
- CMD Not Otherwise Specified

Show your support on social media!

www.curecmd.org ♦ info@curecmd.org

Conference WiFi

WiFi will be available at the conference on the Plaza level throughout the weekend:

NETWORK: Crystal Conference

PASSWORD: cmdscifam

Download the CMD SciFam App!

Access full event information including the agenda, speaker bios, special content, hotel info and more!

1. **Download the app.** Access via the App Store for iOS or the Play Store for Android.

   Search for: *Cure CMD SciFam*

   *For **Blackberry** or **Windows** devices, access the web version of the app found here:*

   crowd.cc/cmdscifam

2. **Install the app.** Once you've found the app, tap **Download/Install**. After installing, a new app icon will appear on your device.

Be sure to create a login to access all the features:

- **Connect with other attendees**
- **Track your schedule**
- **Post to the social wall**
- **Play the CMD SciFam game for a chance to win prizes!**

Closed Captioning Service

We will be providing closed captioning for all main stage sessions on Saturday and Sunday.

To access the feed, please visit the following URL on your smart device:

tinyurl.com/cmdscifamcc

Registration Desk

The Registration desk, located in the main hall, across from the Adams/Madison Ballroom will be staffed throughout the weekend to provide answers and assistance. Stop by and say "Hi!"

This is also where you can sign up for a CMD Voices time slot to record your story with Evan from *Thatch Creative*

Cure CMD Merch & Opportunity Drawing

Support Cure CMD by purchasing Cure CMD Swag!

T-shirts and Sports Bottles are available for sale at the Registration Desk

All proceeds benefit Cure CMD Programming

Participate in our Opportunity Drawing to raise funds for CMD research!

$1.00 per ticket or 5 tickets for $3.00

Available at the Registration Desk

Up to ten prizes will be given away throughout the weekend:

$25 Amazon Gift Card	***$25 iTunes Gift Card***
$25 Fandango Gift Card	***$25 Target Gift Card***
$25 Home Depot Gift Card	***T-Shirt or Sports Bottle***

Share & Engage on Social Media

Share your photos and thoughts using these hashtags and participate on our social wall:

#CMDVoices #CMDSciFam #CureCMD

Friday, July 7

Location	Adams	Madison	Wash I	Wash II	Wash III	Monroe I	Monroe II	Boardroom	Crystal	Location
7:30 AM	Researcher/Clinician Check-In/Breakfast									7:30 AM
8:00 AM										8:00 AM
8:30 AM										8:30 AM
9:00 AM										9:00 AM
9:30 AM										9:30 AM
10:00 AM	Researcher/Clinician General Session									10:00 AM
10:30 AM										10:30 AM
11:00 AM										11:00 AM
11:30 AM										11:30 AM
12:00 PM										12:00 PM
12:30 PM									Researcher & Clinician Lunch Posters/ Networking	12:30 PM
1:00 PM										1:00 PM
1:30 PM										1:30 PM
2:00 PM				CMD Science: Researcher Session	CMD Care: Clinician Session					2:00 PM
2:30 PM										2:30 PM
3:00 PM	Family Conference Check-In									3:00 PM
3:30 PM										3:30 PM
4:00 PM										4:00 PM
4:30 PM										4:30 PM
5:00 PM	Meet & Greet Dinner Buffet Comedy									5:00 PM
5:30 PM										5:30 PM
6:00 PM										6:00 PM
6:30 PM										6:30 PM
7:00 PM			CMD Voices: Telling Your Story Through Photography & Videography							7:00 PM
7:30 PM							Cure CMD Board Meeting			7:30 PM
8:00 PM										8:00 PM
8:30 PM										8:30 PM

Saturday, July 8

Location	Adams	Madison	Wash I	Wash II	Wash III	Monroe I	Monroe II	Boardroom	Crystal	Location
6:30 AM									Sunrise Yoga	6:30 AM
7:00 AM										7:00 AM
7:30 AM	Breakfast									7:30 AM
8:00 AM	CMD Voices: Affected & Caregiver Perspectives									8:00 AM
8:30 AM										8:30 AM
9:00 AM									TITIN: Research	9:00 AM
9:30 AM										9:30 AM
10:00 AM	Group Photo									10:00 AM
10:30 AM				Kids Camp			LMNA: Research	aDG: Research	SEPN1: Research	10:30 AM
11:00 AM	LAMA2: Research	COL6: Research								11:00 AM
11:30 AM										11:30 AM
12:00 PM	Lunch Genetics									12:00 PM
12:30 PM			CMD Voices: Share & Record Your Story	Kids Camp						12:30 PM
1:00 PM										1:00 PM
1:30 PM	Pulmonary Care									1:30 PM
2:00 PM										2:00 PM
2:30 PM	Orthopedics, Physical Therapy & Exercise									2:30 PM
3:00 PM										3:00 PM
3:30 PM	Feeding & Nutrition									3:30 PM
4:00 PM	Tissue/BioBanking									4:00 PM
4:30 PM							Vehicle Conversions & Modifications		TITIN: Neurology	4:30 PM
5:00 PM	Making for Special Needs									5:00 PM
5:30 PM										5:30 PM
6:00 PM	Dinner									6:00 PM
6:30 PM										6:30 PM
7:00 PM			Discussion: Parents of Newly Diagnosed	Kids Camp	Discussion: Veteran Parents	Discussion: Affected Young Adults 13-20	Discussion: Affected Adults 19-40	Discussion: Cognitive Impairment	Discussion: Affected Adults 35+	7:00 PM
7:30 PM										7:30 PM
8:00 PM										8:00 PM
8:30 PM										8:30 PM

Sunday, July 9

Location	Adams / Madison	Wash I	Wash II	Wash III	Monroe I	Monroe II	Boardroom	Crystal	Location
6:30 AM								Sunrise Yoga	6:30 AM
7:00 AM									7:00 AM
7:30 AM									7:30 AM
8:00 AM	Breakfast								8:00 AM
8:30 AM	Special Needs Financial Planning & Navigating Medicare, Medicaid & SSI	CMD Voices: Share & Record Your Story	Kids Camp						8:30 AM
9:00 AM								AFBS Meeting (Nemaline Myopathy)	9:00 AM
9:30 AM									9:30 AM
10:00 AM									10:00 AM
10:30 AM	COL6 & LAMA2: Care					LMNA: Care	aDG: Care	SEPN1: Care	10:30 AM
11:00 AM									11:00 AM
11:30 AM									11:30 AM
12:00 PM	Lunch/Transitioning to Adulthood							Lunch CMD in Adulthood	12:00 PM
12:30 PM			Kids Camp						12:30 PM
1:00 PM	CMD Programs: Registry								1:00 PM
1:30 PM	CMD Programs: Research								1:30 PM
2:00 PM	CMD Programs: Outreach								2:00 PM
2:30 PM	CMD Programs: Development								2:30 PM
3:00 PM	Closing Remarks								3:00 PM
3:30 PM						Cure CMD Board Meeting			3:30 PM
4:00 PM									4:00 PM
4:30 PM									4:30 PM
5:00 PM									5:00 PM

Special Thanks to Our Sponsors

Presenters: Researchers & Clinicians

Anne Bang, PhD

Director, Cell Biology
Sanford Burnham Prebys Medical Discovery Institute

Dr. Bang is an experienced cell biologist and stem cell expert who leads efforts to develop patient cell specific and human induced pluripotent stem cell based disease models for drug screening and target identification. Her research is primarily focused on neurological and neuromuscular disease, with the aim of designing human cell based models and assays that reflect higher order cellular functions and recapitulate disease phenotypes, yet have the throughput and reproducibility required for drug discovery.

Alison Blain, PhD

Research Associate
The John Walton Muscular Dystrophy Research Centre

Dr. Blain has worked in translational research for almost ten years, first in Duchenne MD. She was recently recruited to manage a Muscular Dystrophy UK project, supported by the Collagen VI alliance, to improve Trial Readiness for Collagen VI myopathies. The specific aims are to develop a new European-based registry which will feed directly into the existing CMDIR, to identify a new cohort of patients through existing large scale sequencing projects (such as MYO-SEQ and SEQ-NMD), to standardize outcome measures through international projects aimed at developing neuromuscular imaging, and to coordinate the collection of clinical data and bio-materials from the patient community.

Alan Beggs, PhD

Professor of Pediatrics
Director, The Manton Center
Beggs Laboratory, Boston Children's Hospital

As director of the Beggs Laboratory, Dr. Alan Beggs' goal is to study the basic biology of skeletal muscles and to use this information to understand the genes and proteins involved in the cause of neuromuscular disorders. By understanding the cause of neuromuscular disorders, Dr. Beggs hopes to develop better diagnostic tests, treatments and therapies for congenital myopathies.

Anne Bertrand, PhD

Investigator
Institut de Myologie

As a biologist in Dr Gisèle Bonne's lab, the work of Dr. Bertrand focuses on myopathies due to mutations in the LMNA gene, including Emery-Dreifuss muscular dystrophy and the LMNA-related congenital muscle dystrophy. Her primary goal is to understand the role played by lamin A/C at the nuclear membrane, and how mutations in these proteins induce the development of various neuromuscular disorders. She is also testing different strategies to correct LMNA mutations with the final objective of developing new therapies.

Carsten Bönnemann, MD

Senior Investigator
Neuromuscular and Neurogenetic Disorders of Childhood Section
National Institutes of Health

Dr. Carsten Bönnemann is a Board-Certified Pediatric Neurologist. Research in the Bönnemann laboratory revolves around molecular mechanisms underlying early onset muscle disease (congenital muscular dystrophies, congenital myopathies, and reducing body myopathy). The laboratory's goal is to identify the genetic and cellular mechanisms in these conditions in order to develop strategies for molecular-based treatments.

Presenters: Researchers & Clinicians

Dean Burkin, PhD

Professor of Pharmacology
Director, CMPP Graduate Program
University of Nevada, Reno

The primary goal of Dr. Burkin's research program is to understand the role integrin receptors and the extracellular matrix play in neuromuscular development and disease. His research focuses on Duchenne Muscular Dystrophy (DMD) and Merosin-Deficient Congenital Muscular Dystrophy type 1A.

Russell Butterfield, MD, PhD

Assistant Professor, Departments of Neurology and Pediatrics
University of Utah

Dr. Butterfield received his PhD in mammalian genetics, and medical degree from the University of Illinois. He is currently an Assistant Professor in the Departments of Neurology and Pediatrics, after completing a fellowship in neuromuscular disorders. Dr. Butterfield's clinical interests include all types of neurogenetic and neuromuscular disorders with an emphasis on muscular dystrophies of childhood onset. His research interests are in understanding genetic aspects of these disorders. His current efforts are in characterization of genotype/phenotype relationships and molecular pathogenesis in collagen VI myopathies such as Bethlem myopathy and Ullrich congenital muscular dystrophy.

Kevin Campbell, PhD

Director, Paul D. Wellstone Muscular Dystrophy Cooperative Research Center
Howard Hughes Medical Institute, University of Iowa

Dr. Campbell is interested in elucidating the mechanisms that underlie muscular dystrophy. His laboratory currently focuses on understanding why O-glycosylation of the dystroglycan protein is essential for its function as an extracellular matrix receptor and how abnormalities in this modification cause muscular dystrophy. The goal of this research is to understand how dystroglycan functions, to identify and define the mechanisms that lead to muscular dystrophy, and to develop therapeutic strategies for these diseases.

James Collins, MD, PhD

Pediatric Neurologist
Mercy Children's Hospital

Dr. Collins graduated from the University of Cincinnati College of Medicine and completed his residency at Cincinnati Children's Hospital Medical Center. He specializes in the diagnosis and treatment of rare pediatric neuromuscular disorders. His goal is to help improve the quality of life for affected children as well as empower and educate their families, helping them find answers and meet their needs.

Stacy Cossette, MS

CMD Tissue Repository Coordinator
Medical College of Wisconsin
Congenital Muscle Disease International Registry (CMDIR)

Stacy is the manager for the CMD Tissue Repository located at the Medical College of Wisconsin. Stacy manages all aspects of the program including patient outreach and consenting, specimen acquisition and distribution, tissue handling and cell line generation, follow-up with hospitals and families, and other researcher services.

Soma Das, PhD

Director
University of Chicago Genetic Services

Dr. Das' laboratory at the University of Chicago was the first to develop genetic testing for congenital myopathy and has been providing this testing since 2000. Her laboratory currently performs comprehensive molecular testing for congenital myopathy and other neuromuscular disorders. She is committed to working with researchers to translate research findings into improved molecular diagnostics.

Presenters: Researchers & Clinicians

Jahannaz Dastgir, DO

Pediatric Neurologist
Medical Director, Pediatric Neuromuscular Medicine Program
Goryeb Children's Hospital

After finishing her medical and pediatrics training, child neurology fellowship, and neuromuscular sub-specialty training, Dr. Dastgir completed a three-year clinical research fellowship in neuromuscular and neurogenetic disorders of childhood at the National Institutes of Health. She gained experience in clinical trials and translational research. Dr. Dastgir's most recent research has been in muscle imaging (particularly ultrasound) for the diagnosis and prognosis of neuromuscular disorders.

Sandra Donkervoort, MS, CGC

Genetic Counselor
Neuromuscular and Neurogenetic Disorders of Childhood Section
National Institutes of Health

Sandra is a genetic counselor working at the National Institutes of Health, the Neuromuscular and Neurogenetic Disorders of Childhood Section. Sandra graduated from Sarah Lawrence College in 2007 and joined the Bönnemann team at the NIH in 2011. Her research is focused on identifying the underlying genetic cause in patients with unknown neuromuscular disease.

Ana Ferreiro, MD, PhD

INSERM Research Director, Pathophysiology of Striated Muscles Laboratory
Université Paris Diderot-CNRS
Neurologist, Institute of Myology, Pitié-Salpêtrière Hospital, Paris

During her neurology residency in Spain, Dr. Ferreiro developed a particular interest in muscle disorders. She joined the Institute of Myology in Paris to complete her PhD in Myology and Molecular Genetics, and through international collaboration, identified the first gene defects in multi-minicore disease. In 2003, Dr. Ferreiro launched her independent research laboratory at the Université Paris Diderot/CNRS. In parallel, she has served as a consultant neurologist at Pitié-Salpêtriere Hospital, where she provides diagnosis and follow-up to pediatric and adult neuromuscular patients, in particular those with atypical, difficult-to-diagnose forms. Dr. Ferriero's research is at the interface between clinical and basic research, with a strong translational component, "from bedside to bench and back". She and her team are developing multi- and interdisciplinary clinical, genetic and basic research on congenital and myofibrillar myopathies for which no treatment is available.

A. Reghan Foley, MD

Investigator
Neuromuscular and Neurogenetic Disorders of Childhood Section
National Institutes of Health

Dr. Foley is a child neurologist who trained in neuromuscular diseases with Dr. Carsten Bönnemann at the Children's Hospital of Philadelphia and with Professor Francesco Muntoni at the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital in London. She completed an MD-Research degree focused on the collagen VI-related dystrophies at University College London and then worked at the Children's University Hospital, Dublin to help expand neuromuscular diagnostic efforts there. Dr. Foley presently works with Dr. Bönnemann within the Neuromuscular and Neurogenetics Disorders of Childhood Section, NIH, where she is delighted to be able to be help affected individuals with neuromuscular conditions arrive at genetic diagnoses and journey towards clinical trials.

Casie Genetti, MS, CGC

Genetic Counselor, Program Manager
The Beggs Lab
Boston Children's Hospital

Casie is a genetic counselor and project manager specializing in rare disease research, genomic sequencing and gene discovery. She received her Master's degree in Genetic Counseling from Boston University and began working with the Beggs Congenital Myopathy Research Program at Boston Children's Hospital in 2015. Casie coordinates the recruitment and enrollment of families for the Beggs Lab research study, and is involved with the clinical studies that focus on identifying the genes and characterizing the symptoms associated with congenital myopathies.

Presenters: Researchers & Clinicians

Mahasweta Girgenrath, PhD

Director/Associate Research Fellow
Rare Disease Research Unit, Pfizer

In the last several years, Dr. Girgenrath has worked in the field of congenital muscular dystrophy, leading global CMD research with outreach to both scientific and patient communities. Her more than decade-long background in the CMD field allows Dr. Girgenrath a tangible understanding of the problems, timelines, and challenges of this disease and also opportunities that can be utilized to develop a therapy. For the last several years her lab has contributed significantly to target disease drivers in LAMA2-CMD, specifically focusing on understanding the repair axis targeted by insulin-like growth factor I (IGF-I) and other growth factors, as well as research into the role of matrix remodeling and fibrotic pathways in the progression of LAMA2-CMD.

Robert Graham, MD

Associate in Critical Care Medicine
Director, CAPE & Home Ventilation Program
Boston Children's Hospital

In addition to his clinical work in the intensive care setting, Dr. Graham is interested in improving the care for children and families living with chronic illness, disabilities, and technology dependence. Dr. Graham developed the Critical Care, Anesthesia, and Perioperative Extension (CAPE) and Home Ventilation Program, which provides home-visits, care coordination, and consultation for children with chronic respiratory insufficiency and other complex special healthcare needs.

Carla Grosmann, MD

Clinical Professor, UC San Diego
Neurologist, Rady Children's Hospital

Dr. Grosmann specializes in neuromuscular disorders and electrodiagnosis in children and adults at Rady Children's Hospital and at the University of California San Diego (UCSD), with a particular interest in undiagnosed muscular dystrophies and advocacy. She currently serves on the Cure CMD Board of Directors and is an advisor to the Congenital Muscle Disease International Registry (CMDIR).

Felice Heller, MD

Pediatric Cardiologist
Connecticut Children's Medical Center

Dr. Heller cares for children and adults of all ages with congenital and acquired heart disease. She has developed special expertise in caring for this unique population and works closely with the patients and their caregivers to achieve the best healthy outcomes.

Minal Jain, MPT, DSc, PCS

Investigator
Research Coordinator, Physical Therapy Section
National Institutes of Health

Dr. Jain is research coordinator and a senior staff physical therapist of the Physical Therapy Section in the Rehabilitation Medicine Department at the NIH Clinical Center. Her research interests are in the areas of pediatrics (metabolic disorders, oncology, and genetic disorders). She is the lead therapist for a study on congenital muscular dystrophy, juvenile dermatomyositis and NOMID.

Presenters: Researchers & Clinicians

Ajay Kaul, MD

Director, Neurogastroenterology and Motility Disorders Program
Cincinnati Children's Hospital Medical Center

Dr. Kaul is a pediatric gastroenterologist with thirty years of experience practicing medicine. His clinical interests are in motility disorders and GI problems in children with special needs.

Dwi U. Kemaladewi, PhD

Research Associate
The Hospital for Sick Children (SickKids), Toronto

Dr. Kemaladewi received her PhD in October 2012 from Leiden University, the Netherlands and is currently a Research Associate in Dr. Ronald Cohn's laboratory at the Hospital for Sick Children (SickKids), Toronto, Canada. Her research interest is to use genetic-based technologies to unravel novel molecular mechanisms of disease and translate it into therapeutic strategies. She is currently spearheading several projects pertaining to Congenital Muscular Dystrophy 1A, including the application of CRISPR/Cas9 technology to (1) correct mutations in LAMA2 gene and (2) modulate expression of compensatory genes and/or pro-fibrotic factors.

Chamindra Konersman, MD

Associate Professor of Neurosciences, UC San Diego
Clinical Director of Muscle Disease, Rady Children's Hospital

Dr. Konersman is a neurologist in San Diego, California. Her research and care is focused on the diagnosis and treatment of congenital myopathies, congenital muscular dystrophies, and congenital myasthenic syndromes.

Katherine Mathews, MD

Director, Neuromuscular Program
University of Iowa

Dr. Mathews is interested in all aspects of Clinical Pediatric Neurology. Particular interests include neuromuscular disorders, and her current academic efforts have been focused on improving the quality of care for patients with neuromuscular disease. Dr. Mathews is the co-PI on a project involving defining the phenotypes of patients with FKRP mutations.

Oscar H. Mayer, MD

Pulmonologist
Director of the Pulmonary Function Laboratory
Children's Hospital of Philadelphia

Dr. Mayer is an expert in the assessment and treatment of neuromuscular disorders with emphasis on the pulmonary manifestation in neuromuscular diseases. He is the co-principal investigator for the CMD Hyperinsuflation Trial that concluded last summer, and continues to support and advocate for proactive pulmonary care for the CMD Community.

Presenters: Researchers & Clinicians

Behzad Moghadaszadeh, PhD

Instructor
Harvard Medical School
Boston Children's Hospital

Dr. Moghadaszadeh's training focused on human genetics with a strong emphasis on muscle disease. He has been fortunate to work in different countries and his various projects have taken him into fields as diverse as gene discovery, cellular/animal models of human disease, assay development, protein and gene therapy.

Susana Quijano-Roy, MD, PhD

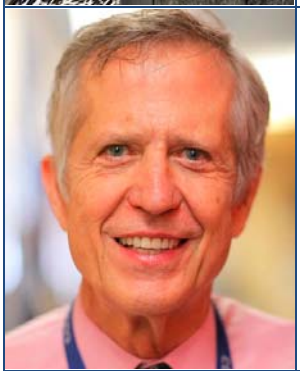
Full Professor
Neuromuscular Unit, GNMH Reference Center
Pediatric Neurology
Rehabilitation and Intensive Care Department
Raymond Poincaré University Hospital (APHP), Garches (FRANCE)
U 1179 INSERM, UVSQ (University of Versailles)

Dr. Quijano-Roy specializes in the diagnosis and comprehensive management of children with neuromuscular disease. Her special interests include muscle imaging, physiology of respiratory muscles, outcome measures of neuromuscular disease scaling, and pediatric EMG.

Deborah Requesens, PhD

Co-Principal Investigator, NIGMS Human Genetic Cell Repository
Principal Investigator, NIA Aging Cell Repository
Coriell Institute for Medical Research

Dr. Requesens is the co-principal investigator of the National Institute of General Medical Sciences (NIGMS) Human Genetic Cell Repository at Coriell, an extensive collection representing more than 1,000 unique human diseases. The NIGMS repository contains more than 11,000 cell lines and 5,500 DNA samples focusing on heritable diseases. She is also the principal investigator of the National Institute of Aging (NIA) Aging Cell Repository, a resource facilitating cellular and molecular research studies on the mechanisms of aging and the degenerative processes associated with it. Dr. Requesens collaborates with researchers and coordinates with investigators and advocacy groups to identify new submissions.



David Roye, MD

Professor of Pediatric Orthopedic Surgery
Columbia University

Dr. Roye specializes in treating pediatric spinal deformities, including scoliosis and performing hip surgeries on adolescents. Dr. Roye has dedicated his career to improving the lives of children both here and abroad. In 2009, Dr. Roye received the American Academy of Orthopaedic Surgeons' Humanitarian Award, which honors fellows of the academy who have "distinguished themselves by providing outstanding musculoskeletal care, both in the United States and abroad . . . (and) who help to improve the human condition by alleviating suffering and supporting and contributing to the basic human dignity of those in need." He has helped Pediatric Orthopedics at Columbia become nationally and internationally recognized for its research and clinical excellence.

Anna Sarkozy, MD, PhD

Consultant in Neuromuscular Disorders
Honorary Senior Lecturer
Dubowitz Neuromuscular Centre Institute of Child Health
Great Ormond Street Hospital London

Dr. Sarkozy trained as a clinical geneticist in Rome, Italy. She worked for seven years at the Neuromuscular Service in Newcastle upon Tyne as a specialty doctor in neuromuscular disorders, before joining the Dubowitz Neuromuscular Centre in London in February 2014 as a consultant. Anna has a clinical and research interest in muscular dystrophies and myopathies with genetic origin. She is particularly interested in clarifying the phenotypes of genetic neuromuscular diseases, identifying their genetic causes and elucidating possible genotype-phenotype correlations.

Presenters: Researchers & Clinicians

Hemant Sawnani, MD

Pulmonologist
Assistant Professor, UC Department of Pediatrics
Cincinnati Children's Hospital Medical Center

Dr. Sawnani is a pediatric pulmonologist specializing in pulmonary management of neuromuscular conditions. His areas of expertise include scoliosis and invasive & non-invasive mechanical ventilation. Dr. Sawnani is the co-principal investigator for the CMD Hyperinsuflation Trial that concluded last summer, and continues to support and advocate for proactive pulmonary care for the CMD Community.

David Spiegel, MD

Attending Physician, Orthopedic Surgery
Children's Hospital of Philadelphia

Dr. Spiegel specializes in neuromuscular diseases, trauma, and scoliosis. He has also dedicated considerable energy to volunteer work in low and middle-income countries, most frequently Nepal and Iraq. He has served as an Honorary Consultant in Orthopaedics and Rehabilitation at the Hospital & Rehabilitation Centre for Disabled Children in Banepa, Nepal, for nearly 20 years and is also an Honorary Professor at the University of Basrah, Basrah, Iraq. He has served on the Committee on Children's Orthopaedics in Underdeveloped Regions of the Pediatric Orthopaedic Society of North America (POSNA) for more than 10 years. He has also served as Chairman of the Bone and Joint Decade committee and the Global Courses Committee of POSNA. He has been on the Board of Orthopaedics Overseas, Global-HELP, the Ponseti International Association, and Miracle Feet. He currently serves on the International Committee of the American Academy of Orthopaedic Surgeons and is director of their international scholars program.

Christopher Tan, MS, CGC

Genetic Counselor
Clinical Genomics
Invitae

Chris is a board-certified genetic counselor with more than ten years of clinical and laboratory genetic counseling experience. He is currently a genetic counselor at Invitae and has a primary role in aspects related to its neuromuscular test offerings.

Jody Westbrook, PhD

Scientist
Invitae

Jody is a scientist with an extensive background in genetics and molecular biology. She has been at Invitae for over five years, and has worked on many aspects of developing its next generation sequencing platform for genetic diagnostics.

Sherryann Wert, MA

Project Associate
Coriell Institute for Medical Research

Sherryann is a Project Manager for the NIH-funded biorepositories of NIGMS and CHD GENES at the Coriell Institute for Medical Research. She has a diverse background in project and laboratory management, and research in pharmaceutical areas such as Oncology, Investigative Toxicology, and Inflammatory research. She currently maintains sample databases and associated clinical data for hereditary and rare diseases and collaborates with Coriell's internal teams and with external research foundations, genetic counselors, and scientific investigators.

Special Thanks to Our Sponsors

AUDENTES THERAPEUTICS

Audentes Therapeutics is a biotechnology company committed to the development and commercialization of innovative new gene therapy treatments for people with serious rare diseases.

We have four programs in our pipeline for the treatment of X-Linked Myotubular Myopathy (XLMTM), Pompe disease, CASQ2-related Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) and Crigler-Najjar Syndrome (CN). We are a focused, experienced and passionate team driven by the goal of improving the lives of patients.

audentestx.com

Presenters: Advocacy

David Brumbley

Filmmaker, Storyteller
Thatch Creative

After his first day on set Dave never turned back. Experiencing something new on every job, traveling the world and new challenges every day. Dave loves what he does, and is excited by every project he tackles.

Evan Burgher

Filmmaker, Storyteller
Thatch Creative

Evan's introduction to photo & film came from his passion for travel. Seeing the world, and embedding himself in its cultures, has given Evan a unique approach to how he shoots and tell stories. Finding the best way to tell these unique and interesting stories is what motivates Evan to be a better photographer/filmmaker. Evan produced Cure CMD's Relaunch Videos in 2015 and we are delighted to be working with both Evan and Dave in our CMD Voices project.

Sarah Foye, OT

Governing Board President
Congenital Muscle Disease International Registry (CMDIR)
CMD Community Advocate

Sarah is an occupational therapist by training and has been working as a muscle disease advocate since 2006. She has a teenager with Titinopathy. Sarah has volunteered as the governing board president for our patient registry since 2012. Supporting families with muscle disease is her passion!

Levi Gershkowitz

Photographer, Writer, Storyteller
Rare Disease Patient Advocate
Living in the Light: From Patient to Person

Levi Gershkowitz is the founder and executive director of Living in the Light, an advocacy initiative utilizing the potency of photography, filmmaking and compelling personal narratives to educate about the realities of rare diseases and the unprecedented impact they have on families and daily life. This distinct concentration grew out of an understanding that the rare disease community is comprised of many people with many voices, while at the heart lies a unified experience of deep resilience and unique wisdom. Living in the Light presents a dignified and de-medicalized perspective of individuals living with major life challenges and conveys the unique wisdom and beauty they carry. We are delighted to welcome Levi to share stories in our CMD Voices project.

To learn more, visit **FromPatientToPerson.com** and **FB.com/LivingintheLightofRareDiseases**

Chase Phillips

Senior Financial Advisor
Menrick Friese Phillips Bock Group
Merrill Lynch

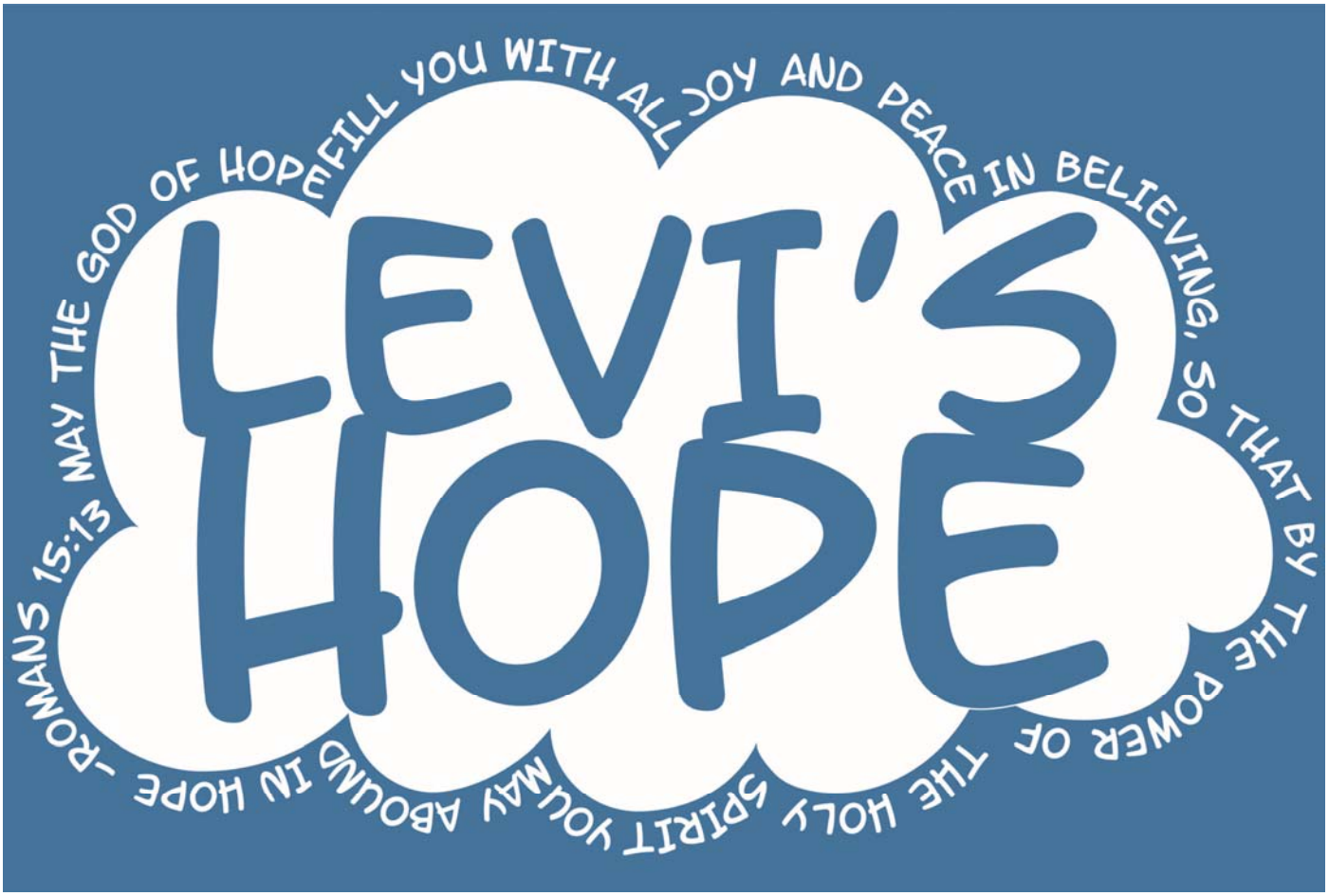
Mr. Phillips is an expert on financial planning for special needs individuals. He is well informed about the 529a, the Achieving a Better Living Experience Act (ABLE). The ABLE Act was designed to provide a new way for parents to save for special needs children. Mr. Phillips is not only experienced with the ABLE Act, but he also has knowledge of other planning tools to help families provide a financially secure future for their children.

Jodi Wolff, PhD

Director Patient Advocacy & Medical Science Liaison
Santhera Pharmaceuticals

As Director of Clinical Programs for the Muscular Dystrophy Association, Dr. Wolff coordinated and managed MDA clinic programs for 200 neuromuscular specialty clinics. Her current position with Santhera Pharmaceuticals allows her to collect and report research developments, trends, and new treatments in key therapeutic areas.

Special Thanks to Our Sponsors



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Presenters: Community

Kristin Andre

SEPN1 Community Member

Kristin is the mother of two sons affected with SEPN1-RM, ages 6 and 8. After the birth of her first child with SEPN1-RM, Kristin became a registered nurse to gain a better understanding of her sons' health condition, wanting desperately to find a diagnosis for them. Since diagnosis, Kristin has been an active participant in the Cure CMD community and is currently the moderator of the SEPN1/Rigid Spine Facebook Group. Kristin's goal is to help support those affected with SEPN1-RM and their families, as well as provide an arena to share the latest research in SEPN1-RM. She hopes to build numbers in the SEPN1 community and create a loud community voice to raise awareness and funding. "We are small, but we are mighty!"

Sara Bloomfield

LAMA2 Community Member

Sara has been an active volunteer for Cure CMD since 2012. She has a business degree from ASU and an MBA from Notre Dame. Her work experience includes roles within marketing, sales, product management, and business development. She has a young daughter that was diagnosed with LAMA2-CMD in 2012. Within Cure CMD, Sara has worked on projects including fundraising efforts and social media.

Simon Cantos

Collagen VI Community Member

Born in Sydney, Australia, Simon moved to the east coast of United States in 1990. Simon graduated from Villanova University in 2005 with a Bachelor of Science degree in Mechanical Engineering. He currently works full-time as an Inside Sales Engineer at Carrier Corporation where he assists in the design, construction, and sale of HVAC systems for large commercial applications. Simon actively participates at various disability conferences in the Philadelphia area, mentoring affected children and providing advice and support to their families to encourage their successful endeavors.

Kings Floyd

LAMA2 Community Member

Kings (Kingsley) Floyd is the Youth Transition Fellow for the National Council on Independent Living, and sponsored by the HSC Foundation. She graduated from High Point University in 2016 with a BA in English and concentrations in language, education and disability studies. She has worked with people with disabilities for over five years, advocating for youth with disabilities to have equal access to education and career opportunities. Kings has LAMA2-CMD, is originally from New England, currently lives in Washington, DC., and is excited to participate in SciFam!

Kyle Gagner

LMNA Community Member

Just a father who loves Jesus, his family, running, mountain biking, and history.

Jennifer Gluck

Collagen VI Community Member

Jennifer Gluck is mother to 11-year-old Owen, and 9-year-old John (Collagen VI). Jennifer began making solutions to fit the particular needs of John and her family early in John's diagnosis. Making is now a habit and she is making new things all the time. She is currently working on voice activated doors and shelves and doorbells in the house for John. Jennifer's initial solutions include a table seat for spica casting, pvc walkers, a swim platform, wheelchair baseball bat, and a changing table modification. Jennifer shares her solutions for others at www.jenmadeit.com. Jennifer works part time for the Navy, runs the house and the boys, she also designs games, writes songs and helps lead worship at her church.

Website: **jenmadeit.com**

Presenters: Community

Beth Gore, PhD

Patient Advocate, Professional Speaker
LAMA2 Community Member

Beth's role as a leading advocate for those affected by a rare disease is a personal one. She states "In the 14 years of being a parent to kids with special needs, I see the immense need for this population to have an advocate. I'm learning how to develop that role." Dr. Gore is the mother of six children, all adopted and all with special needs. Beth speaks for those who cannot speak for themselves.

Luke Hoban

Collagen VI Community Member

Luke is a recent graduate from the University of Pennsylvania. In addition to being a wicked wheelchair hockey player, Luke is fully engaged in the world around him and actively participates in the US political arena. He's been heavily active with Penn Democrats over the past year and interned at the DNC in Philadelphia. He has also worked at Sports Quotient, managing various writing and reporting staffs to cover many sports with a focus on the NHL. His creativity and communication skills have made him a positive role model for young adults trying to navigate independent lives on college campuses. He speaks openly about the challenges that someone with a rare disease might face in his/her daily life.

Gillian Keener

Collagen VI Community Member

Gillian is an eighteen years old recent high school graduate who has been driving a wheelchair since she was five. She loves music and going to concerts, makeup and fashion, and just being a teenager. Gillian also loves being an advocate for herself and others with physical disabilities. In January, Gillian attended the Women's March in Washington D.C. to fight for the rights of women and people with disabilities. She is interested in taking college courses in women's studies, and political science next year, and she hopes to continue helping people, disabled or not.

Susan Lee-Miller

Collagen VI Community Member

Susan Lee-Miller is the mother of Liam, a sophomore living and studying at Temple University in Philadelphia. She is currently a massage therapist and formerly worked as a dietitian in her professional life. Susan runs and bikes and enjoys life with her family and friends in southeast Pennsylvania.

Angela Maccarrone

SEPN1 Community Member

Angela lives in Seattle, WA, recently graduated from Gonzaga University with a B.A. in psychology and will be returning to Gonzaga this fall to pursue a master's degree in Clinical Mental Health Counseling. As a post-grad, Angela works as a Family Service Coordinator at the Seattle Children's Hospital Autism Center. She is the WA State Ambassador for the Muscular Dystrophy Association and is passionate about educating others about muscle disease. In her free time, Angela enjoys spending time outside in the beautiful PNW, playing with her yellow lab, and adding destinations to her travel bucket-list.

Liam Miller

Collagen VI Community Member

Liam is a sophomore at Temple University's College of Science and Technology. Liam, a proud owner of Collagen VI-CMD, lives independently on campus and is pursuing a degree in computer science. He is a passionate fan of hockey and acts as captain of his wheelchair hockey team based out of Philadelphia. Liam has also been an active member of the MDA community for the majority of his life, where he has participated as a public speaker and ambassador. Above all, Liam loves spending time with family and friends.

Presenters: Community

Joe Pinkelman

Dystroglycanopathy Community Member

Joe is originally from Denver, Colorado and has been a high school art teacher the past 24 years. His daughter, Maia, was born in 1998 and was diagnosed with CMD in 2006. They have always tried to live an active life with Maia, making the necessary modifications to make it happen.

Daniella Slon

SEPN1 Community Member

Born and raised in Johannesburg, South Africa, Daniella ditched a legal career in favor of seeing the world. She lived in Jerusalem, Israel, before ending up in Philadelphia, USA. For the past 15 years she has worked in the nonprofit field as a digital marketer and donor prospect researcher honing her innate curiosity and love of everything digital. Daniella was diagnosed with SEPN1-CMD at age 39 after perplexing doctors the world over for decades (and quite enjoying it)!

Nicola Smith

LAMA2 Community Member

Nicola Smith lives in North Louisiana with her husband, Jeff, and their three children, Kaden, Chase, and Camille. She is a co-owner of Muscle Club Apparel, a clothing company founded in response to their son's LAMA2-CMD diagnosis back in 2010. She has been a dedicated supporter and advocate for Cure CMD. Nicola has participated in several fundraisers for Cure CMD, one of which is their Stay Strong line of tees, where 100% of the sale of every shirt goes directly to Cure CMD.

Diane Smith-Hoban

Collagen VI Community Member

Diane lives in the Philadelphia suburban area with her young adult sons, Luke and Christian. Luke has Collagen VI CMD. She holds an MSW degree from Temple University and has worked as a child advocate social worker and educator in the Philadelphia child welfare system for over 20 years. Diane has volunteered with Cure CMD since its inception. She has organized conferences and fundraisers as well as worked on several publications, including the Family Guide for the Management of CMD.

George Vascik

Collagen VI Community Member

George was diagnosed in 2008 at the age of 54. His daughter was experiencing excruciating leg pain and she was fortunate enough to have a series of doctors eager to find the cause. After it was found through genetic testing that she carried the mutation, further tests revealed not only that George carried the mutation, but also his mother and sister. Although George's symptoms are mild, the existence of the mutation explains a variety of problems that both he and his sister experienced in youth and middle age that were ascribed to other ailments such as arthritis. George will discuss how his late-in-life diagnosis has informed the increasing difficulties that he faces as his symptoms progress.

Special Thanks to Our Sponsors

Cure CMD Staff & Board of Directors

Rachel Alvarez

Director of Operations
Secretary, Board of Directors
Cure CMD, Congenital Muscle Disease International Registry (CMDIR)
Collagen VI Community Member

Rachel graduated Magna Cum Laude from California Polytechnic University, and worked primarily in healthcare operations and accounting for several nonprofit organizations including The City Of Hope, prior to joining Cure CMD. She volunteered for Cure CMD for four years before becoming Cure CMD's first employee, and now serves as Director of Operations.

Sabine de Chastonay, PhD

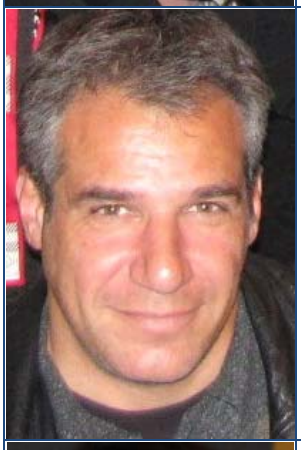
Director of Development
Cure CMD

Sabine received her bachelor's degree from the ETH in Zürich, Switzerland, and a Ph.D. in Molecular and Microbiology from the University of Bern, Switzerland. In 2012, she joined the Congenital Muscle Disease International Registry as a volunteer Research Associate. In 2015, Sabine joined Cure CMD as the Director of Development. Her role includes increasing fundraising revenue to ensure adequate support for Cure CMD's mission, resulting in a stronger CMD community.

Stephanie Dague

Board of Directors, Cure CMD
LMNA Community Member

Stephanie lives in upstate NY with her husband, Harris, and their three children, Charlie, Farrah and Max. She has been a dedicated supporter and advocate for Cure CMD since her eldest son, Charlie, was diagnosed with LMNA-CMD in 2010. Stephanie has a BA from SUNY, Albany and has worked in the non-profit field since 2003, serving ten years as Director of Development for a national 501(c)3 organization. Stephanie has put together several fundraisers for Cure CMD.



Gustavo Dziewczapolski, PhD

Scientific Director
Cure CMD
Congenital Muscle Disease International Registry (CMDIR)

Before becoming Cure CMD's Scientific Director, Dr. Dziewczapolski was a leading researcher for the Salk Institute for Biological Studies in La Jolla, California. In his role as Cure CMD's Scientific Director, he attends scientific conferences around the world related to discovery and translational research in neuromuscular diseases. In addition to being the liaison between Cure CMD and the researchers working in CMD, Dr. Dziewczapolski provides information to affected individuals and their families regarding the latest research and clinical trials in CMD. His goal is to widen the spectrum of treatments, to improve quality of life, and to ultimately find the cure for the Congenital Muscular Dystrophies.

Carla Grosmann, MD

Clinical Professor, UC San Diego
Neurologist, Rady Children's Hospital
Board of Directors, Cure CMD

Dr. Grosmann specializes in neuromuscular disorders and electrodiagnosis in children and adults at Rady Children's Hospital and at the University of California San DIego (UCSD), with a particular interest in undiagnosed muscular dystrophies and advocacy. She currently serves on the Cure CMD Board of Directors and is an advisor to the Congenital Muscle Disease International Registry (CMDIR). Dr. Grosmann joined Cure CMD's Board of Directors in July, 2017.

Cure CMD Staff & Board of Directors

Eunice Kim

Vice Chair
Board of Directors, Cure CMD
Collagen VI Community Member

Eunice has served on the Cure CMD Board as Vice Chairman since April 2010. She is currently a Senior Manager at Google, and has held roles at Pepsico, Adobe Systems, and several Silicon Valley startups. Eunice also spent three years as the President of the Board for another non-profit corporation serving children with disabilities. She graduated with an MBA from the University of Chicago Booth School of Business, and received her BA from Columbia University in New York. She and her husband Andrew live in California with their two children. Her oldest child, Sophie, has Collagen VI-CMD.

Dione Kobayashi, PhD

Vice President, Preclinical Translation
Cydan Development, Inc.
Board of Directors, Scientific Advisory Board, Cure CMD

Dr. Kobayashi is the Vice President of Preclinical Translation at Cydan Development, a rare disease accelerator. Dr. Kobayashi is an accomplished executive scientist with deep knowledge and experience in drug development activities for rare diseases. Prior to joining Cydan, she worked as an executive scientist in several biotech and pharmaceutical companies as well as non-profit organizations. She was a director of neurology models at Alector, where she played key roles in leadership on discovery and lead characterization for Alzheimer's and other dementia programs. She was a director at the SMA Foundation, where she led in vivo drug screening and clinical biomarker validation and established numerous drug development collaborations with biotech and pharmaceutical companies, and served as the Alzheimer's and age-related macular degeneration research program leader at Rinat Labs, acquired by Pfizer. She also held research roles at Elan Pharmaceutical and Genentech, and has published various journal articles focused in neurodegenerative, neurodevelopmental, neuromuscular, and ocular rare genetic diseases.

Patrick May

Co-Founder, Chairman & CFO
Board of Directors, Cure CMD
LAMA2 Community Member

Pat is co-founder, Chairman, and Chief Financial Officer of Cure CMD. He is a Certified Public Accountant with twenty years of experience in private industry serving such roles as CFO, Treasurer and Controller for various for-profit corporations in the greater Kansas City area. He graduated Magna Cum Laude from the University of Notre Dame and is the father of a daughter diagnosed with LAMA2 congenital muscular dystrophy. Pat shares the vision for Cure CMD to promote awareness and ultimately accelerate therapies and a cure for the congenital muscular dystrophies.

Oscar H. Mayer, MD

Director of the Pulmonary Function Laboratory
Children's Hospital of Philadelphia
Board of Directors, Cure CMD

Dr. Mayer is an expert in the assessment and treatment of neuromuscular disorders with emphasis on the pulmonary manifestation in neuromuscular diseases. He is the co-principal investigator for the CMD Hyperinsuflation Trial, and continues to support and advocate for proactive pulmonary care for the CMD Community. Dr. Mayer joined Cure CMD's Board of Directors in July, 2017.

Jeff Rowbottom

Board of Directors, Cure CMD
Collagen VI Community Member

Jeff joined the Cure CMD Board to focus accelerating the promising and novel developments in science/ research into treatments for CMD patients. Jeff has a family member with Collagen VI-CMD. Jeff is a Partner at Pontifax, a venture capital investment firm focused on life sciences and biotech. Prior to joining Pontifax, Jeff was the Head of Capital Markets, Americas for KKR. He worked in senior capital markets roles at Goldman Sachs, Barclays Capital and Citigroup before joining KKR. Jeff holds a B.S. in Finance from SUNY at Albany and an MBA from Columbia University. In addition to Cure CMD, he is on the Board of the Melanoma Research Alliance, Project Renewal and The Elisabeth Morrow School.

Cure CMD Staff & Board of Directors

Terry Selucky

Grants & Public Relations, Cure CMD
Fine Point Consulting

Terry is a grant writer who has helped raise nearly $10 million for philanthropic organizations focusing on health, homelessness, domestic violence, and the arts. For Cure CMD, she wrote the application that won the PCORI Award, which allowed for the 2016-2017 five-conference series. Terry is honored to be a part of the teams that make a difference for people around the world. Terry is also a playwright whose work has been produced across the country. Her experience in advertising, nonprofits, and the theater have allowed her to become an effective leader and collaborator, building consensus across diverse interest groups to see a project from inception to success.

Robin Swallow

Volunteer Outreach Coordinator
Cure CMD, Congenital Muscle Disease International Registry (CMDIR)
SEPN1 Community Member

Robin is a retired librarian with a Master's degree in Library Sciences from UCLA. She is the grandmother of two boys who were diagnosed with SEPN1 in 2014. Robin is the Outreach Coordinator for the CMDIR and helps maintain the database. She assists in building the Cure CMD publication library and corresponds with scientific contributors.

Herb Stevenson, MD

Board of Directors, Cure CMD
LMNA Community Member

Dr. Stevenson is a Sports Medicine Physician and Associate Professor at the University of Massachusetts Medical school. He is the father of a son with LGMD2i. Dr. Stevenson has worked since 2011 with Cure CMD through the Stevenson Family Fund to support research in the congenital muscular dystrophies. Dr. Stevenson has an interest in muscular disorders and has helped work with scientists and clinicians to advance research with a particular focus on translating gene therapy for congenital muscular dystrophies into clinical trials. Dr. Stevenson is a graduate of the University of Vermont College of Medicine and resides in Massachusetts with his wife Meridith and 3 children Hannah, Amelia, and Carter.

Jodi Wolff, PhD

Director Patient Advocacy & Medical Science Liaison
Santhera Pharmaceuticals
Board of Directors, Cure CMD

At Santhera Pharmaceuticals, Dr. Wolff promotes and facilitates patient engagement in the drug development process. She earned her PhD in Rehabilitation from the University of Arizona, focusing her research on the transition to adulthood for youth with neuromuscular disease. Dr. Wolff has worked with young people who have muscular dystrophy for over 20 years and was formerly the Director of Clinical Programs at the Muscular Dystrophy Association. Dr. Wolff joined Cure CMD's Board of Directors in July, 2017.

Charlene York

Special Projects & Travel Coordination
Cure CMD, Congenital Muscle Disease International Registry (CMDIR)
Collagen VI Community Member

Charlene has been a volunteer with Cure CMD since 2009. She has a husband and daughter with Collagen VI Muscular Dystrophy. She has a Masters in Library of Science. Charlene has worked on several Cure CMD/ CMDIR projects, and currently coordinates all travel. She also curates for the Congenital Muscle Disease International Registry (CMDIR) and supports related study projects.

Janet Young

Operations & Development Coordinator
Cure CMD, Congenital Muscle Disease International Registry (CMDIR)

Janet Young is a proud mother of two grown daughters, native of Los Angeles and has a BFA from Cal State Long Beach in Interior and Architectural Design. Janet has volunteered for many organizations throughout her adult life and after returning from living abroad in Asia, she was happy to settle back in Southern California and begin a new chapter in her life with Cure CMD. Janet is passionate about Cure CMD and is grateful to be working towards a goal among staff and families she admires and respects. One of her duties is reaching out to families to keep their registry profile up-to-date.

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Valerion Therapeutics is a biotechnology company focused on developing targeted therapies for orphan genetic diseases

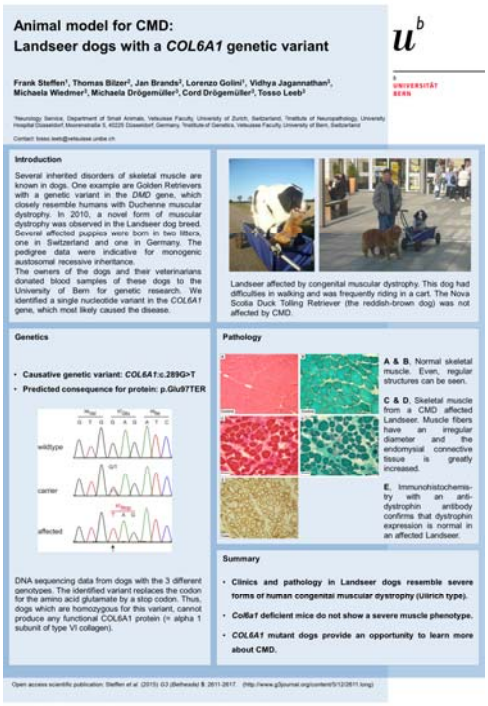
- Valerion Therapeutics is utilizing a proprietary antibody-mediated delivery platform to target therapies to specific tissues via a well-known and broadly studied transport pathway
- This platform is capable of enhanced intracellular delivery of a variety of active therapeutic payloads via a transport mechanism that is present in muscle and neurons
- Pipeline candidates include therapeutic agents aimed at addressing a host of orphan genetic disorders with limited or no current therapies

VAL-0620 Myotubular Myopathy (MTM1)

- VAL-0620 is a fusion protein of the platform delivery antibody 3E10 linked to MTM1, the enzyme missing in patients with myotubular myopathy
- The MTM program continues to make progress with VAL-0620 and once completed, will initiate confirmatory pharmacology studies. The Company plans to initiate IND enabling studies in Q1 2018.

Posters

Animal Models for CMD: Landseer dogs with a COL6A1 genetic variant



Frank Steffen[1], Thomas Bilzer[2], Jan Brands[2], Lorenzo Golini[1], Vidhya Jagannathan[3], Michaela Wiedmer[3], Michaela Drögemüller[3], Cord Drögemüller[3], Tosso Leeb[3]

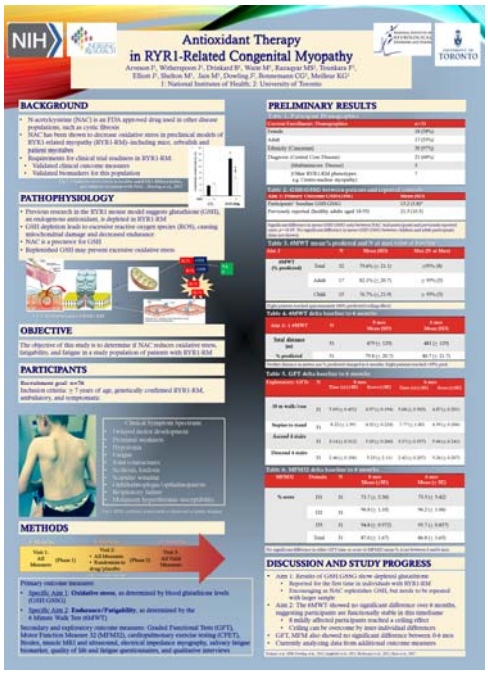
[1] Neurology Service, Department of Small Animals, Vetsuisse Faculty, University of Zurich, Switzerland
[2] Institute of Neuropathology, University Hospital Düsseldorf, Moorenstraße 5, 40225 Düsseldorf, Germany
[3]Institute of Genetics, Vetsuisse Faculty, University of Bern, Switzerland

A novel canine muscular dystrophy in Landseer dogs was observed. We had access to five affected dogs from two litters. The clinical signs started at a few weeks of age, and the severe progressive muscle weakness led to euthanasia between 5 and 15 months of age. The pedigrees of the affected dogs suggested a monogenic autosomal-recessive inheritance of the trait. Linkage and homozygosity mapping indicated two potential genome segments for the causative variant on chromosomes 10 and 31 harboring a total of 4.8 Mb of DNA or 0.2% of the canine genome. Using the Illumina sequencing technology, we obtained a whole-genome sequence from one affected Landseer. Variants were called with respect to the dog reference genome and compared with the genetic variants of 170 control dogs from other breeds. The affected Landseer dog was homozygous for a single, private nonsynonymous variant in the critical intervals, a nonsense variant in the COL6A1 gene (Chr31:39,303,964G>T; COL6A1:c.289G>T; p.E97*). Genotypes at this variant showed perfect concordance with the muscular dystrophy phenotype in all five cases and more than 1000 control dogs. Variants in the human COL6A1 gene cause Bethlem myopathy or Ullrich congenital muscular dystrophy. We therefore conclude that the identified canine COL6A1 variant is most likely causative for the observed muscular dystrophy in Landseer dogs. On the basis of the nature of the genetic variant in Landseer dogs and their severe clinical phenotype these dogs represent a model for human Ullrich congenital muscular dystrophy.

For more information, please contact:
Tosso Leeb, PhD
Email: tosso.leeb@vetsuisse.unibe.ch

Posters

Antioxidant Therapy in RYR1-Related Congenital Myopathy



Arveson I[1], Witherspoon J[1], Drinkard B[1], Waite M[1], Razaqyar MS[1], Tounkara F[1], Elliott J[1], Shelton M[1], Jain M[1], Dowling J[2], Bonnemann CG[3], Meilleur KG[1]

[1] National Institute of Nursing Research, NIH
[2] University of Toronto
[3] National Institute of Neurological Disorders and Stroke, NIH

In preclinical models of RYR1-related myopathies (RYR1-RM), N-acetylcysteine (NAC) has improved oxidative stress, muscle force and swim endurance. Given the limited side effect profile of NAC and lack of FDA approved treatment in RYR1-RM, the benefit of performing a clinical trial outweighs the risk. Lack of valid clinical outcome measures and biomarkers in this population pose a barrier to clinical trial readiness. A two-phase study including an outcome measure validation phase followed by a RCT is being conducted. Subjects are seen at 0, 6, and 12 months. All outcome measures are performed off-drug at the first two visits. At the end of visit 2, patients start drug or placebo and return at 12 months to perform all outcome measures on intervention. Primary outcome measures include plasma glutathione (GSH:GSSG) for oxidative stress and 6 Minute Walk Test (6MWT) for endurance. Data from the first thirty-one participants in the stud, including (18 (58%) adults, and 18 (58%) female). Analysis of the first participants' baseline values for GSH:GSSG show a decrease (13.2+5.8) compared to reported controls (21.3+10.3; $p<0.05$). Participants had a total mean distance on the 6MWT of 479m (+132m), with adults averaging 481m (+127m) and children averaging 476m (+142). 8 subjects (5 adults and 3 children) reached > 95% predicted distance. Results showing significant depletion of GSH:GSSG confirm findings in 3 preclinical models and allow for the potential of NAC to replenish GSH:GSSG. For milder participants, the 6MWT reaches a ceiling effect. The ceiling effect of the 6MWT may be overcome by analyzing inter-individual differences.

Presented By:

Katy Meilleur, PhD, PPCNP-BC

Following completion of a BS in biology and a BSN/MSN, Dr. Meilleur worked as an acute/chronic pediatric nurse practitioner in the newborn nursery of HUP while attending Johns Hopkins University for her PhD. Her interests in international health and genetics led to her dissertation at the National Institutes of Health, identifying a novel genetic locus for a hereditary spastic paraplegia in Mali, West Africa. After a postdoc at the National Human Genome Research Institute, she became a staff scientist at the National Institute of Neurological Disorders and Stroke and continued do gene discovery studies and scale development in the pediatric neuromuscular population. She is now a Tenure Track Investigator in the intramural program of the National Institute of Nursing Research. Her research program focuses on developing clinical outcome measures for congenital muscle diseases.

Posters

Building an Online Diagnostic & Geomapping Tool for Congenital Muscle Disease

image not available
at time of print

Chamindra Konersman[1], Tracey Willis[2], Brad Williams[3], Vivek Nirkhe[4]

[1]University of California, San Diego
[1]Birmingham Children's Hospital
[1]Jain Foundation
[1]Introp

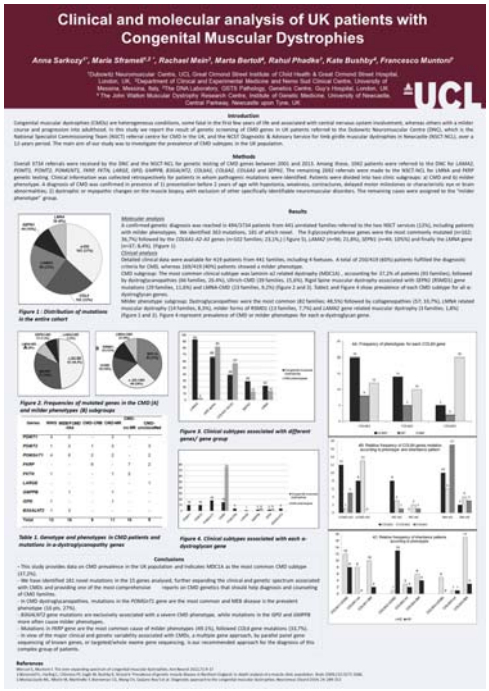
The congenital muscle diseases consist of congenital myopathies (CM), congenital muscular dystrophies (CMD), and congenital myasthenic syndromes (CMS); a rare group of disorders, with an estimated prevalence of 1 in 25,000 for CM and CMD and 1 in 500,000 for CMS. While these muscle diseases demonstrate considerable phenotypic and genotypic heterogeneity, classic presentations allow recognition and targeted diagnostic workups. Unfortunately, diagnostic expertise is limited, leading to under-recognition and often, lengthy, expensive workups that do not yield a definitive genetic diagnosis. We aim to construct an online diagnostic and geomapping tool to increase the efficiency and accuracy of genetic diagnosis for children and adults with presumed congenital muscle disease. We will launch it from the Congenital Muscle Disease International Registry (CMDIR) website www.cmdir.org. The tool assigns probabilities to key clinical symptoms to calculate the overall probability of a specific subtype based on the answers chosen by the user. During production, genetically confirmed cases will be run through the tool with positive and negative results to improve tool accuracy in an iterative fashion. Once launched, the tool will prompt each clinician or family member to register the affected individual prior to genetic testing. Demographic information will be anonymized prior to showing presumed subtype and location on a global map and updated upon receipt of genetic testing.

Presented By:

Chamindra Konersman, MD
Dr. Konersman is a neurologist in San Diego, California. Her research and care is focused on the diagnosis and treatment of congenital myopathies, congenital muscular dystrophies, and congenital myasthenic syndromes.

Posters

Clinical and molecular analysis of UK patients with Congenital Muscular Dystrophies



Anna Sarkozy[1]*, Maria Sframeli[1,2]*, Rachael Mein[3], Marta Bertoli[4], Rahul Phadke[1], Kate Bushby[4], Francesco Muntoni[1]

[1]Dubowitz Neuromuscular Centre[2]Department of Clinical and Experimental Medicine and Nemo Sud Clinical Centre, University of Messina, Messina, Italy
[3]The DNA Laboratory, GSTS Pathology, Genetics Centre, Guy's Hospital, London, UK
[4]The John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, University of Newcastle, Central Parkway, Newcastle upon Tyne, UK

Congenital muscular dystrophies (CMDs) are rare neuromuscular conditions with major clinical and genetic heterogeneity. CMDs range from severe forms with multisystem involvement to conditions with milder course. CMDs have now been associated with mutations in at least 20 genes, but the number of patients without a genetic diagnosis is still significant. In the UK, genetic diagnosis of CMDs is centrally offered in the neuromuscular centres in London and Newcastle upon Tyne. In this study, we have reviewed clinical and genetic data of 249 unrelated individuals who obtained a genetically confirmed diagnosis of CMD between 2001 and 2013. Laminin-α2 related CMD (MDC1A) was the most common subtype of CMD (37.4%), followed by dystroglycanopathies (26.5%), Ullrich-CMD (15.7%), SEPN1 (11.65%) and LMNA (8.8%) gene related CMDs. We also reviewed the frequency of milder allelic phenotypes, such as Bethlem myopathy and LGMD-dystroglycanopathies. We identified a total of 363 mutations, 160 of which novel. This study provides a comprehensive report on genetics and clinical features of CMD subtypes and should help diagnosis and counselling of families with this group of conditions, and also facilitate clinical trials and possible future treatments for specific genetic subtypes or mutations.

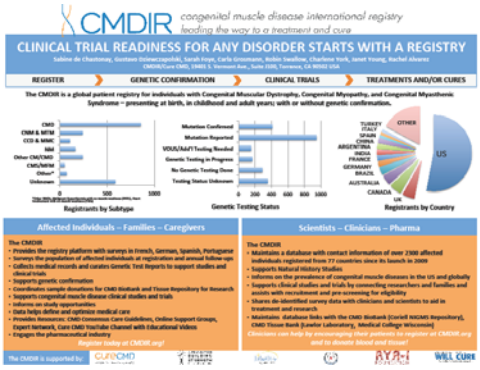
Presented By:

Anna Sarkozy, MD, PhD

Dr. Sarkozy trained as a clinical geneticist in Rome, Italy. She worked for seven years at the Neuromuscular Service in Newcastle upon Tyne as a specialty doctor in neuromuscular disorders, before joining the Dubowitz Neuromuscular Centre in London in February 2014 as a consultant. Anna has a clinical and research interest in muscular dystrophies and myopathies with genetic origin. She is particularly interested in clarifying the phenotypes of genetic neuromuscular diseases, identifying their genetic causes and elucidating possible genotype-phenotype correlations.

Posters

The Congenital Muscle Disease International Registry (CMDIR)



Sabine de Chastonay, Gustavo Dziewczapolski, Robin Swallow, Charlene York, Janet Young, Rachel Alvarez

Cure CMD

The CMDIR was launched to ready the global CMD community for clinical trials. With over 2,300 affected individuals from 77 countries with congenital through late onset muscle weakness registered to-date, the database contains self-reported contact and medical information as well as curated medical records, all stored in a HIPAA-compliant database. Registrants have access to resources such as care guidelines, online support groups, and alerts about clinical trial participation opportunities.

The CMDIR staff supports clinical studies by connecting families and researchers, by assisting with clinical trial pre-screening and recruitment, and by managing survey-based outreach studies aimed to gain a greater understanding of the natural history of these disorders.

Research is supported through links between CMDIR registrant profiles and donated biospecimens stored in the CMD BioBank at Coriell and the CMD Tissue Repository at the Medical College of Wisconsin.

Cure CMD hosts the CMDIR, with financial support and oversight from A Foundation Building Strength, The Joshua Frase Foundation, the RYR1 Foundation, Team Titin (Foye Family), and Where There's a Will There's a Cure.

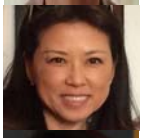
Presented By:

Rachel Alvarez
Rachel joined Cure CMD in 2009 first as a volunteer and then its first employee, initially to manage operations related to the CMDIR, bringing twenty years of experience in healthcare operations and non-profit organizations. She has coordinated the recruitment efforts for more than a dozen studies and trials in the CMD/CM/CMS communities and continues to provide valuable data mined from the registry for researchers and pharmaceutical companies.

Sabine de Chastonay, PhD
Sabine joined Cure CMD/CMDIR in 2012 as a volunteer research associate. She has coordinated three studies in myotubular myopathy, with authorship credits in two resulting publications. Sabine has supported Traveling Local Clinics in collaboration with the Bönnemann team in a number of cities including Calgary and São Paulo, and has represented Cure CMD and the CMDIR at several professional and family conferences.

Robin Swallow
Robin joined Cure CMD/CMDIR in 2014, and performs outreach to the CMD community, helping to maintain the registry through database updates and genetic report curation. She also assists with management of the CMD publication library.

Charlene York
Charlene has been a volunteer with Cure CMD/CMDIR since 2009, and has worked on several Cure CMD/CMDIR projects since joining the organization, including study travel coordination, medical records curation, and management of the CMD publication library.



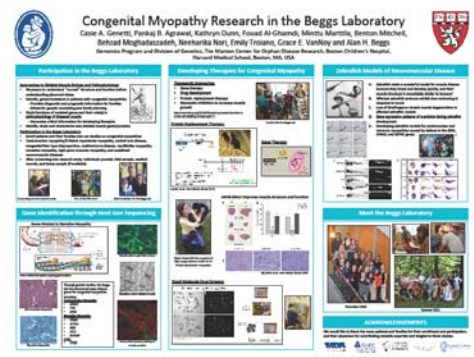
Janet Young
Janet joined Cure CMD/CMDIR in 2012 as a volunteer with duties including registry outreach to maintain registry profile data. Janet has traveled as far as Bejing and Buenos Aires to support Traveling Local Clinics in collaboration with the Bönnemann team to register affected individuals.

Carla Grosmann, MD
Dr. Grosmann specializes in neuromuscular disorders and electrodiagnosis in children and adults at Rady Children's Hospital and at the University of California San DIego (UCSD), with a particular interest in undiagnosed muscular dystrophies and advocacy. She currently serves as a physician advisor to the Congenital Muscle Disease International Registry (CMDIR).

Sarah Foye
Sarah is an occupational therapist and has been working as a muscle disease advocate since 2006. Sarah currently serves as the governing board president and vocal advocate for the CMDIR.

Posters

Congenital Myopathy Research in the Beggs Laboratory



Casie A. Genetti, Behzad Moghadaszadeh, Alan H. Beggs

Division of Genetics and Genomics
The Manton Center for Orphan Disease Research
Boston Children's Hospital
Harvard Medical School
Boston, MA, USA

The Beggs Laboratory for Congenital Myopathy Research at Boston Children's Hospital (bostonchildrens.org/research/beggs) hosts a long running clinical and molecular genetic research program aimed at discovering the genetic basis of congenital muscle diseases and developing therapies and treatments for these conditions utilizing cellular and animal models. The laboratory has a clinical research protocol in place to enroll participants with various forms of congenital myopathy, and their family members, into studies to examine their DNA, muscle biopsies if available, and medical records to discover and understand the genetic basis for their weakness. As new disease genes are discovered, their role in normal muscle function is explored, and cellular, zebrafish and mouse models carrying the human mutations are developed to better understand the causes of these conditions. The animal models are also used to screen for potentially therapeutic drugs and test new treatments. Over the years, the laboratory has identified dozens of new disease genes, and has focused in particular on congenital myopathies including nemaline myopathy, multiminicore myopathy, rigid spine muscular dystrophy, centronuclear and myotubular myopathy, congenital fiber type disproportion, and more. We welcome enrollment of families with any of these conditions, and particularly those with unknown or uncertain diagnoses related to primary skeletal muscle conditions.

Presented By:

Casie Genetti, MS, CGC

Casie is a genetic counselor and project manager specializing in rare disease research, genomic sequencing and gene discovery. She received her Master's degree in Genetic Counseling from Boston University and began working with the Beggs Congenital Myopathy Research Program at Boston Children's Hospital in 2015. Casie coordinates the recruitment and enrollment of families for the Beggs Lab research study, and is involved with the clinical studies that focus on identifying the genes and characterizing the symptoms associated with congenital myopathies.

Behzad Moghadaszadeh, PhD

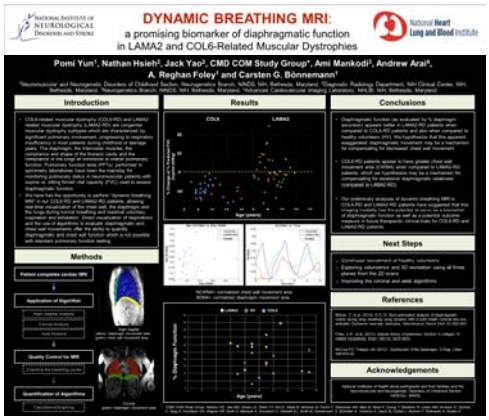
Dr. Moghadaszadeh's training focused on human genetics with a strong emphasis on muscle disease. He has been fortunate to work in different countries and his various projects have taken him into fields as diverse as gene discovery, cellular/animal models of human disease, assay development, protein and gene therapy.

Alan Beggs, PhD

As director of the Beggs Laboratory, Dr. Alan Beggs' goal is to study the basic biology of skeletal muscles and to use this information to understand the genes and proteins involved in the cause of neuromuscular disorders. By understanding the cause of neuromuscular disorders, Dr. Beggs hopes to develop better diagnostic tests, treatments and therapies for congenital myopathies.

Posters

Dynamic Breathing MRI: A promising biomarker of diaphragmatic function in LAMA2 and COL6-Related Muscular Dystrophies



Pomi Yun, Nathan Hsieh, Jack Yao, CMD COM Study Group*, Ami Mankodi, Andrew Arai, A. Reghan Foley, Carsten G. Bönnemann

***CMD COM Study Group:**
Meilleur KG, Jain MS, Hynan LS, Shieh CY, Kim E, Waite M, McGuire M, Fiorini C, Glanzman AM, Main M, Rose K, Duong T, Bendixen R, Linton MM, Arveson IC, Nichols C, Yang K, Fischbeck KH, Wagner KR, North K, Mankodi A, Grunseich C, Hartnett EJ, Smith M, Donkervoort S, Schindler A, Kokkinis A, Leach M, Collins J, Muntoni F, Rutkowski A, Norato G

Objective:
To explore the unique imaging modality of cine MRI of breathing called “dynamic breathing MRI” to directly visualize respirations and evaluate diaphragmatic and chest wall movements in children with COL6-related dystrophy (COL6-RD) and LAMA2-related dystrophy (LAMA2-RD).

Methods:
Automated algorithms were used to evaluate the thoracic cavity in particular with quantifications of the diaphragm movement area (DMA) and chest wall area movement (CWMA). These measurements were then compared across three cohorts of COL6-RD, LAMA2-RD, and healthy volunteers (HV).

Results:
Diaphragmatic function (as evaluated by % diaphragm excursion) appears increased in LAMA2-RD patients when compared to COL6-RD patients as well as healthy volunteers. COL6-RD patients appear to have greater CWMA when compared to LAMA2-RD patients as well as healthy volunteers. (Quantitative analyses of this data is in progress.)

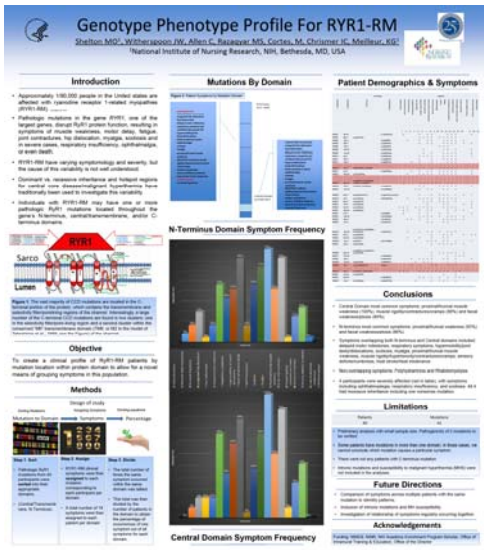
Conclusions:
We hypothesize that the apparent exaggerated diaphragmatic movement observed in LAMA2-RD patients may be a mechanism for compensating for decreased chest wall movement. Additionally, we hypothesize that the apparent exaggerated chest wall movement area observed in COL6-RD patients may be a mechanism for compensating for the excessive diaphragmatic weakness characteristic of this condition. These findings suggest that dynamic breathing MRI is an imaging modality which has the potential to serve as a biomarker of diaphragmatic function as well as a potential outcome measure in future therapeutic clinical trials for COL6-RD and LAMA2-RD.

Presented By:

Pomi Yun
Pomi is currently in her second year of a post-baccalaureate fellowship at the National Institutes of Health on Dr. Carsten Bönnemann's team in Pediatric Neuromuscular Disorders, and hopes to attend medical school after her fellowship.

Posters

Genotype Phenotype Profile for RYR1-RM



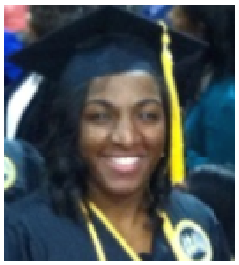
Shelton MO, Witherspoon JW , Allen C, Razaqyar MS, Cortes M, Chrismer IC, Meilleur KG

National Institute of Nursing Research, NIH

RyR1 is a calcium channel in skeletal muscle, crucial to muscle contraction. Mutations in the gene RYR1 disrupt RyR1 protein function, resulting in RYR1-related myopathies (RYR1-RM). Symptoms include muscle weakness, motor delay, fatigue, myalgia, scoliosis and, in severe cases, ophthalmoplegia and/ or respiratory insufficiency. RYR1-RM vary in presentation, but the cause of this is poorly understood. Mutations are located throughout N-terminal, transmembrane, and/or C-terminal protein domains. We evaluated genotype-phenotype profiles to identify whether mutation location by domain plays a role in symptom severity. Methods: RyR1 amino acid changes from 34 participants (ages 8-58 yrs., 71% female) were sorted into 3 protein domains above. 19 clinical symptoms were then assigned to each domain based on clinical presentation and mutation location. The total number of times a symptom occurred within a domain was tallied and divided by 19. Participants with multiple mutations in the same domain were counted once. Results: 100% of transmembrane domain mutations resulted in proximal/truncal muscle weakness. The most common symptoms for N- and C-terminus mutations were proximal/truncal weakness and facial weakness/ptosis. Differences were also noted, e.g. participants with C-terminus mutations did not experience neonatal hypotonia, suggesting a milder phenotype. Four participants with recessive inheritance were severely affected. Conclusion: Our patients exhibited both coinciding and differing symptoms across protein domains. Creating a clinical profile of RyR1-RM patients by protein domain may allow for a novel way to group symptoms in this population, which may assist clinicians with genetic counseling and prognosis. Additional work is needed to substantiate this finding.

Presented By:

Monique Shelton



Monique earned a graduate assistantship at Murray State University as a teaching and research assistant following graduation with honors in with a joint bachelor's degree in Biology and Spanish from Fisk University. She then attended a summer practice research session at Vanderbilt University in the clinical pharmacology department. In 2014, Monique was awarded the National Institutes of Health (NIH) Intramural Research Training Award (IRTA), as a post baccalaureate fellow where she worked alongside researchers at the National Institute of Allergy and Infectious Disease (NIAID) in the Vaccine Research Center (VRC), researching the immunogenicity of a vaccine for Respiratory Syncytial Virus (RSV) on mice. Monique is now completing her fellowship at the National Institute of Nursing Research (NINR), researching the genotype-phenotype of patients with RYR1-RM.

Posters

The influence of personal assistance services on employment for young adults with neuromuscular disease

Jodi Wolff[1], Linda Shaw[2]

[1]Santhera Pharmaceuticals, University of Arizona
[2]University of Arizona, Tucson, Arizona, USA

Thanks to advances in therapies and clinical care, youth with neuromuscular disease now are living into adulthood. If properly supported in their environment, young adults with neuromuscular diseases requiring significant caregiving can successfully engage in competitive employment.

This study uses a qualitative, phenomenological approach to examine the lived experiences of young adults with neuromuscular disease and their perceptions of the ways in which their use of personal assistance services (PAS) impacted employment. Nine employed participants with neuromuscular disease who use paid PAS were interviewed regarding their experiences with PAS and employment.

Three themes emerged following an analysis of the qualitative data: (1) impact of PAS on employment – with five sub-themes of the importance of working to QOL; a high level of stress associated with coordinating PAS; the critical importance of access to PAS to employment; the reliance on informal and non-paid caregivers such as friends and family; and minimizing the need for PAS in the workplace; (2) restrictions on career mobility – with two sub-themes of how PAS limits the ability to be spontaneous and limits the geographic mobility of the individual; and (3) public policy related to PAS – with three sub-themes of how income restrictions create work disincentives; the vital need for transportation to support employment and QOL; and the difficult and complex nature of PAS support programs.

Young adults in the U.S. with neuromuscular disease are able, willing, and motivated to engage in employment and to reap the benefits of participating in traditional adult social roles. However, the reliance on personal assistance services and the structure of support programs in the U.S. negatively impacts their ability to sustain employment. With changes in these programs and our expectations of youth, more youth with neuromuscular disease can achieve employment.

Presented By:

Jodi Wolff, PhD

Dr. Wolff is the Director of Patient Advocacy at Santhera Pharmaceuticals where she promotes and facilitates patient engagement in the drug development process. She earned her PhD in Rehabilitation from the University of Arizona, focusing her research on the transition to adulthood for youth with neuromuscular disease. Dr. Wolff has worked with young people who have muscular dystrophy for over 20 years and was formerly the Director of Clinical Programs at the Muscular Dystrophy Association.

Posters

The influence of personal assistance services on higher education for youth with neuromuscular disease

Jodi Wolff[1], Linda Shaw[2]

[1]Santhera Pharmaceuticals, University of Arizona
[2]University of Arizona, Tucson, Arizona, USA

Objective:
Striking disparities exist in higher education rates between young adults with disabilities and their non-disabled peers. This study is a qualitative analysis using a phenomenological approach to examine the lived experiences of young adults with neuromuscular disease and how their use of personal assistance services (PAS) impacted their pursuit of higher education.

Methods:
A series of three interviews were conducted with nine participants ages 24-35 with neuromuscular disease who have completed undergraduate and/or advanced degrees, are employed, and utilize at least 20 hours per week of paid PAS.

Results:
Participants overall had positive college experiences and report the easiest time coordinating PAS and staffing caregiving needs was during college, even while utilizing a significant amount of informal caregiving from family and friends. Families of participants expected college attendance and the need for PAS influenced the choice of college; however, the pursuit of advanced degrees was discouraged due to income restrictions to qualify for PAS. The lack of experience with PAS prior to college significantly impacted higher education experiences. Participants expressed preferences for both consumer-driven and agency-based models of providing PAS, reported negative interactions with vocational rehabilitation counselors, and speculated that societal stereotypes and low expectations of people with disabilities influence educational opportunities.

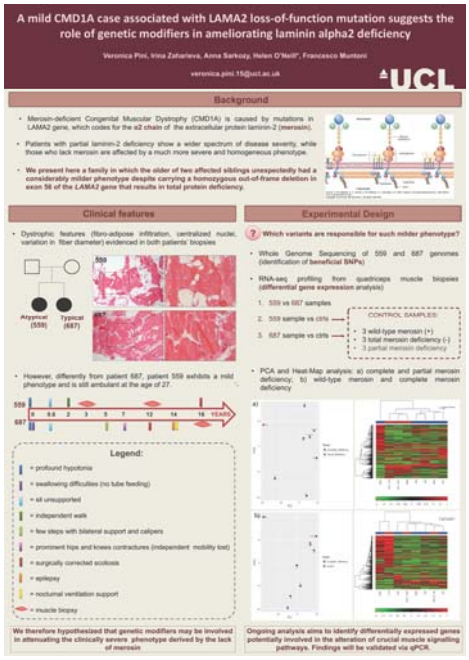
Conclusion:
Young adults with neuromuscular disease are willing, wanting, and capable to participate in higher education as a path to gainful employment and could not have completed their degrees without PAS. Efforts to prepare families and youth to manage, recruit, and fund PAS could help ease the transition to college.

Presented By:

Jodi Wolff, PhD
Dr. Wolff is the Director of Patient Advocacy at Santhera Pharmaceuticals where she promotes and facilitates patient engagement in the drug development process. She earned her PhD in Rehabilitation from the University of Arizona, focusing her research on the transition to adulthood for youth with neuromuscular disease. Dr. Wolff has worked with young people who have muscular dystrophy for over 20 years and was formerly the Director of Clinical Programs at the Muscular Dystrophy Association.

Posters

A mild CMD1A case associated with LAMA2 loss-of-function mutation suggests the role of genetic modifiers in ameliorating laminin alpha2 deficiency



Veronica Pini[1], Irina Zaharieva[1], Anna Sarkozy[1], Helen O'Neill[2], Francesco Muntoni[1]

[1] Greet Ormond Street Institute of Child Health – University College London
[2] Institute for Women's Health – University College London

Among the highly heterogeneous group of congenital muscular dystrophies (CMDs), CMD1A subgroup is associated with mutations in the LAMA2 gene, coding for the 2 subunit of the extracellular matrix component laminin-2 (merosin).
In CMD1A patients, laminin-2 can be either absent or partially produced: loss-of-function mutations abolish protein production, typically resulting in total laminin 2 deficiency, while missense mutations allow the production of a partially functional protein. The clinical CMD1A is associated with the residual ability to produce the defective protein: typically, patients with partial laminin-2 deficiency show a wider spectrum of disease severity, while those who lack merosin are affected by a much more severe and homogeneous phenotype.

We present a family in which one of two affected siblings unexpectedly had a considerably milder phenotype despite carrying a homozygous out-of-frame deletion in exon 56 of the LAMA2 gene that results in total protein deficiency. This sibling is still ambulant at the age of 27 and has features of a mild phenotype, with no respiratory insufficiency, similar to that reported in patients with partial protein deficiency. The other sibling followed the typical MDC1A course, never acquired independent ambulation and exhibits a clinically severe phenotype, with respiratory insufficiency from the age of 12.

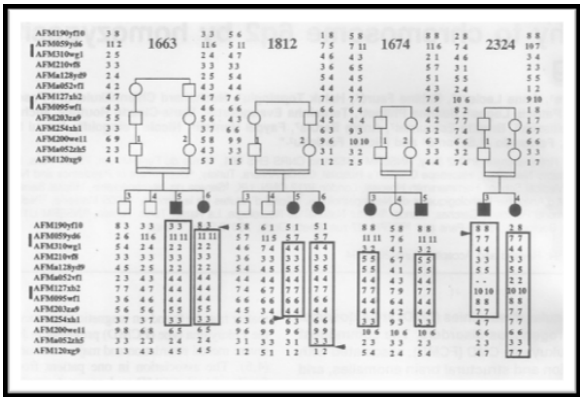
In both siblings, brain MRI revealed white matter abnormalities and muscle biopsy showed a clear dystrophic pattern with absent of laminin 2. We therefore hypothesize that genetic modifiers are acting in the older patient's muscles to counteract the deleterious effects associated with the absence of laminin 2.
To understand which variants are responsible for such milder phenotype, whole genome sequencing was performed on siblings' DNA. Moreover, transcriptome analysis (RNA-seq) was performed on patients' muscle samples, and compared to healthy controls and a cohort of CMD1A patients with both total and partial laminin 2 deficiency. Ongoing data analysis will be focusing both on the identification of beneficial SNPs variants and significant differentially expressed genes that may be involved in the alteration of crucial muscle signaling pathways.

Presented By:

Veronica Pini
Following her Master's degree in Molecular Biology and Genetics from the University of Pavia, Veronica joined the UCL Dubowitz Neuromuscular Centre at Great Ormond Street Institute of Child Health, where she is currently working under the supervision of Professor Francesco Muntoni. Veronica's current interests are the development of new gene therapy approaches for muscular dystrophies by using the CRISPR/Cas9

Posters

The original Turkish CMD family who served to identify the merosin gene; a follow-up of 25 years

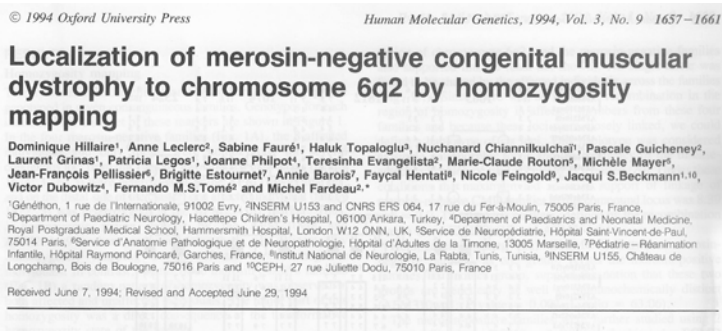


Haluk Topaloglu

Hacettepe Children's Hospital
Ankara, Turkey

I have seen and diagnosed the very first merosin deficiency patients proven by genetics in 1992-1993, and later published in 1994-1995. I witnessed the initial efforts to solve the molecular basis of this interesting form of CMD with leukodystrophic changes.

In the original linkage study there were two Turkish families, one family from France and one family from Portugal. There were two sisters, neither achieved ambulation and have multiple joint contractures. They are currently age 27 and 24.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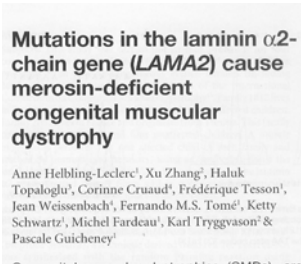
Human Molecular Genetics, 1994, Vol. 3, No. 9 1657–1661

Localization of merosin-negative congenital muscular dystrophy to chromosome 6q2 by homozygosity mapping

Dominique Hillaire[1], Anne Leclerc[2], Sabine Fauré[1], Haluk Topaloglu[3], Nuchanard Chiannilkulchai[1], Pascale Guicheney[2], Laurent Grinas[1], Patricia Legos[1], Joanne Philpot[4], Teresinha Evangelista[2], Marie-Claude Routon[5], Michèle Mayer[6], Jean-François Pellissier[6], Brigitte Estournet[7], Annie Barois[7], Fayçal Hentati[8], Nicole Feingold[9], Jacqui S.Beckmann[1,10], Victor Dubowitz[4], Fernando M.S.Tomé[2] and Michel Fardeau[2,*]

[1]Généthon, 1 rue de l'Internationale, 91002 Evry, [2]INSERM U153 and CNRS ERS 064, 17 rue du Fer-à-Moulin, 75005 Paris, France, [3]Department of Paediatric Neurology, Hacettepe Children's Hospital, 06100 Ankara, Turkey, [4]Department of Paediatrics and Neonatal Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 ONN, UK, [5]Service de Neuropédiatrie, Hôpital Saint-Vincent-de-Paul, 75014 Paris, [6]Service d'Anatomie Pathologique et de Neuropathologie, Hôpital d'Adultes de la Timone, 13005 Marseille, [7]Pédiatrie – Réanimation Infantile, Hôpital Raymond Poincaré, Garches, France, [8]Institut National de Neurologie, La Rabta, Tunis, Tunisia, [9]INSERM U155, Château de Longchamp, Bois de Boulogne, 75016 Paris and [10]CEPH, 27 rue Juliette Dodu, 75010 Paris, France

Received June 7, 1994; Revised and Accepted June 29, 1994



Mutations in the laminin α2-chain gene (*LAMA2*) cause merosin-deficient congenital muscular dystrophy

Anne Helbling-Leclerc[1], Xu Zhang[2], Haluk Topaloglu[3], Corinne Cruaud[4], Frédérique Tesson[1], Jean Weissenbach[4], Fernando M.S. Tomé[1], Ketty Schwartz[1], Michel Fardeau[1], Karl Tryggvason[2] & Pascale Guicheney[1]

Presented By:

Haluk Topaloglu, MD

Dr. Topaloglu is a professor of pediatrics and neurology at Hacettepe University School of Medicine in Ankara, Turkey since 1996. After completing his residency in pediatrics at Hacettepe University Children's Hospital in 1982, Dr. Topaloglu completed a fellowship in child neurology at the University of Calgary Department of Pediatrics in Alberta, Canada, in 1985; the Christine Saunders Memorial Fellowship in Neuromuscular Disorders at the Royal Postgraduate Medical School of Hammersmith Hospital, Department of Pediatrics and Neonatal Medicine, in London, England, in 1995; and a senior staff fellowship with the Developmental and Metabolic Neurology Branch of the National Institute of Neurological Disorders and Stroke, National Institutes of Health, in Bethesda, Maryland, in 2000. His research interests include pediatric neuromuscular disorders, neurogenetics, and developmental aspects in child neurology. He is the current secretary of the World Muscle Society (WMS). He received the Gaetano Conte Academy of the Mediterranean Society of Myology (MSM) award in clinical neuromuscular disorders in 2015. Dr. Topaloglu is the head of the muscular dystrophy consortium of the French Muscular Dystrophy Association (AFM).

Posters

Randomized Controlled Trial of Lung Hyperinflation In Children With Congenital Muscular Dystrophy

John E. Pascoe MD[1], Hemant Sawnani MD[1], Oscar H. Mayer MD[2], Anne M. Rutkowski MD[3], Monir Hossain PhD[4], Rhonda Szczesniak PhD[3] Keith McConnell MS[1], Joseph M. McDonough MS[2], Avani C. Modi MD[5], Raouf Amin MD[1]

[1]Division of Pulmonary Medicine, Cincinnati Children's Hospital Medical Center
[2]Division of Pulmonary Medicine, Children's Hospital of Philadelphia
[3]Cure CMD Foundation and Kaiser SCPMG
[4]Division of Epidemiology and Biostatistics, Cincinnati Children's Hospital Medical Center
[5]Division of Behavioral Medicine and Clinical Psychology, Center for Treatment Adherence and Self- Management, Cincinnati Children's Hospital Medical Center

Introduction:
Congenital muscular dystrophy (CMD) is a distinct genetic neuromuscular disorder presenting from birth with progressive loss of motor function, skeletal deformities debilitating contractures and early onset respiratory failure. We hypothesized that daily passive stretch of the chest wall through lung hyperinflation therapy could slow down the annual rate of decline in lung volume.

Methods:
A randomized controlled trial was conducted. One group received hyperinflation therapy prescribed as two-15 minute sessions per day for one year. A second group received standard of care served as controls. Participants had lung function measured at baseline and every 4 months for one year. The pressure that achieved maximum lung inflation was individualized for each subject and readjusted as needed at each visit. We estimated that the difference in the rate of decline of vital capacity between the 2 groups will yield an effect size of > 0.5 and thus needed a sample size of 17 subjects in each arm. Adherence to treatment was measured electronically and with a daily phone diary. The treatment by visit interaction was assessed by normal regression model.

Results:
Thirty-four participants were recruited, with a mean age of 11.5 ±3.9 years, 52% male and 76% Caucasians. Eighteen subjects were randomized to the hyperinsuflation protocol and 16 to the control group. After eliminating dropouts, there were 15 subjects in the hyperinflation group and 14 controls. With adherence and baseline forced vital capacity (FVC) controlled, a statistically significant difference was observed compared to controls for FVC ($p<0.001$), and inspiratory capacity ($p<0.001$). The effect size was < 0.5. The mean change in absolute FVC from baseline in the treatment group ranged 1.3 to 6.1% (p=NS). Mean adherence was 50% at visit 1, 36% at visit 2, and 38% at visit 3.

Conclusion:
Lung hyperinflation in children with CMD is associated with a small improvement in lung function after adjusting for baseline severity and adherence. The small effect size could be due to low adherence rates, and significant baseline restrictive lung disease and/or thoracic deformity that inherently limited mobility of the thorax. Future directions include adherence interventions and recruiting participants with lesser degrees of restriction.

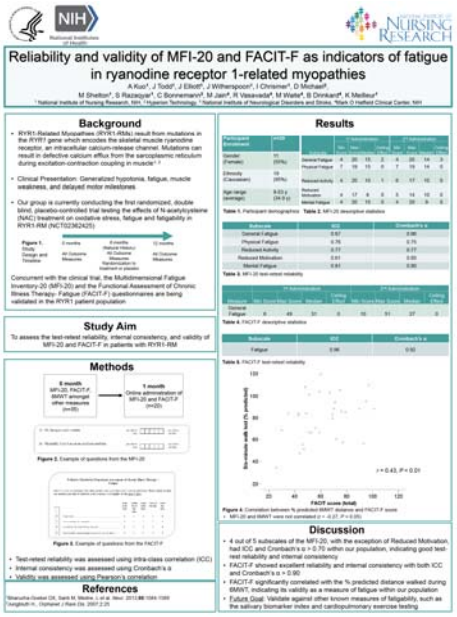
Presented By:

Hemant Sawnani, MD
Dr. Sawnani is a pediatric pulmonologist specializing in pulmonary management of neuromuscular conditions. His areas of expertise include scoliosis and invasive & non-invasive mechanical ventilation.

Oscar H. Mayer, MD
Dr. Mayer is an expert in the assessment and treatment of neuromuscular disorders with emphasis on the pulmonary manifestation in neuromuscular diseases.

Posters

Reliability and validity of MFI-20 and FACIT-F as indicators of fatigue in ryanodine receptor 1-related myopathies



A Kuo[1], J Todd[1], J Elliott[1], J Witherspoon[1], I Chrismer[1], D Michael[2], M Shelton[1], S Razaqyar[1], C Bönnemann[3], M Jain[4], R Vasavada[4], M Waite[4], B Drinkard[4], K Meilleur[1]

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[4] Mark O Hatfield Clinical Center, NIH

Background:
Daily, severe fatigue is a commonly reported symptom across all subtypes of ryanodine receptor 1-related myopathies (RYR1-RM), including central core disease, multi-minicore disease, centronuclear myopathy, and congenital fiber type disproportion. RYR1-RM comprise the most common group of congenital onset myopathies and affect approximately 1/90,000 individuals in the United States. Subjective fatigue questionnaires such as the Multidimensional Fatigue Inventory (MFI) and Functional Assessment of Chronic Illness-Fatigue (FACIT-F) may be useful indicators of fatigue in this population. However, these have not been assessed in RYR1-RM to date.

Study aim:
To test the reliability and validity of MFI and FACIT-F as indicators of fatigue in RYR1-RM.

Methods:
As part of an ongoing clinical trial of n-acetylcysteine in RYR1-RM, MFI and FACIT-F scores (n=32) were obtained from participants at baseline. Participants also completed a six-minute walk test (6MWT) and cardiopulmonary exercise testing (CPET), which are gold standard measures of endurance and fatigability, respectively.

Results:
MFI (except for Reduced Motivation domain) and FACIT-F demonstrated initial good test-retest reliability (ICC > 0.70; 0.96, respectively) and internal consistency (Cronbach's a > 0.70; 0.96, respectively) in RYR1-RM patients. FACIT-F scores (x = 62.5, [26-101]) significantly correlated with the percent predicted distance walked during 6MWT ($r = 0.43$, $p < 0.01$) and peak power asserted during CPET ($r = 0.57$, $p < 0.001$). However, this was not the case for MFI (all $P > 0.05$).

Conclusion:
These findings support the reliability and validity of FACIT-F as a subjective fatigue measure for RYR1-RM. Further studies with larger sample sizes are needed to assess the use of MFI as a valid measurement of fatigue in this population.

In both siblings, brain MRI revealed white matter abnormalities and muscle biopsy showed a clear dystrophic pattern with absent of laminin 2. We therefore hypothesize that genetic modifiers are acting in the older patient's muscles to counteract the deleterious effects associated with the absence of laminin 2.

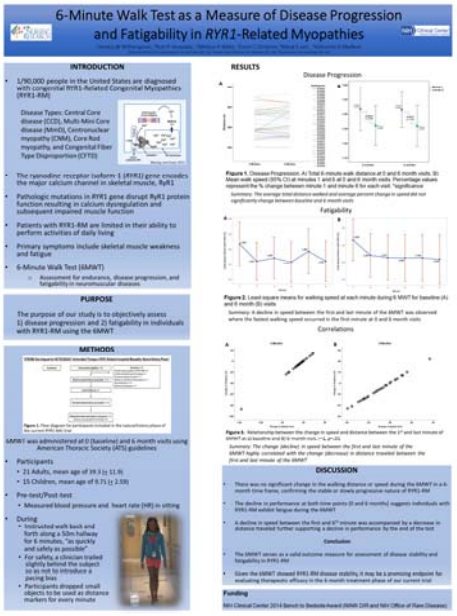
To understand which variants are responsible for such milder phenotype, whole genome sequencing was performed on siblings' DNA. Moreover, transcriptome analysis (RNA-seq) was performed on patients' muscle samples, and compared to healthy controls and a cohort of CMD1A patients with both total and partial laminin 2 deficiency. Ongoing data analysis will be focusing both on the identification of beneficial SNPs variants and significant differentially expressed genes that may be involved in the alteration of crucial muscle signaling pathways.

Presented By:

Ana Kuo
Anna Kuo is currently a Post-baccalaureate IRTA Research Fellow at the National Institute of Nursing Research at the NIH. She graduated from Vassar College with a B.A. in Neuroscience and is currently applying to physician assistant programs. Ana's research interests include musculoskeletal conditions, sports and exercise rehabilitation, child and adolescent health, and preventative health.

Posters

Six-Minute Walk Test as a Measure of Disease Progression and Fatigability in RYR1-Related Myopathies



Jessica W Witherspoon[1], Ruhi P Vasavada[2], Melissa R Waite[2], Irene C Chrismer[1], Minal S Jain[2], Katherine G Meilleur[1]

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[2]Rehabilitation Medicine, NIH, Bethesda, MD, USA
[3]Biomechanics, NIH, Bethesda, MD, USA

RYR1-related Congenital Myopathies (RYR1-RM) result from pathogenic mutations in the ryanodine receptor isoform-1 (RyR1) gene where consequent RyR1 protein calcium dysregulation leads to impaired excitation-contraction coupling, oxidative and nitrosative stress, and mitochondrial depletion. These physiological deficits perpetuate RyR1 dysfunction causing further muscle injury, muscle weakness, and muscle fatigue. Muscle weakness and fatigue are two primary complaints in patients with RYR1-RM, and are major symptoms that limit the ability of individuals to perform activities of daily living. The six minute walk test (6MWT) recently served as a fatigability measure in neuromuscular diseases (NMDs) with limited results in RYR1-RM. The purpose of our study is to determine if the 6MWT can objectively measure fatigability, as determined by a decline in speed, in individuals with RYR1-RM. The 6MWT was administered to 36 RYR1-RM affected participants (> 7yoa) using the standardized ATS guidelines protocol, without use of orthotics or assistive devices, at baseline and 6 months. The distance walked at each minute interval was documented. Paired t-test analyses revealed no significant difference between % change in speed at 0-months (-5.98 + 2.99) compared with the 6-month visit (-8.95% + 1.97). However, a significant decline in speed between the first and last minute of the 6MWT was observed at both time points where p=.025 and p<.01, respectively. Correlative analysis showed a strong correlation (r=1, p<.01) between decreased speed and distance. The significant decrease in walking speed between interval minutes 1 and 6 observed at baseline and 6-month visits, supported by the strong correlation between decreased speed and distance, implies the 6MWT is an appropriate outcome measure for fatigability in patients with RYR1-RM. Based on our results, the 6MWT may serve as a valid outcome measure for use in patients with RYR1-RM to assess disease stability and fatigability.

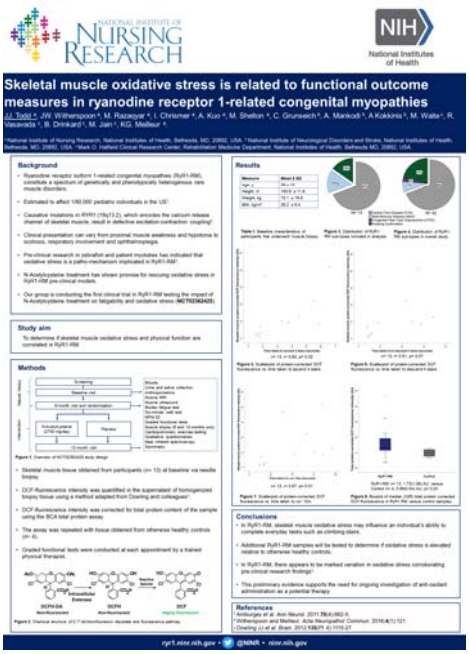
Presented By:

Jessica Witherspoon, PhD

Jessica Witherspoon is a Research Fellow at the National Institutes of Health in the National Institute of Nursing Research division. Her long-term goal is to study physical activity and functional ability in patients with RYR1-Related Congenital Myopathies (RYR1-RM). Dr. Witherspoon currently plays an intricate part in an ongoing clinical trial for antioxidant therapy in RYR1-RM. Her primary focus is rehabilitation outcome measures with an interest in RYR1-RM associated physiological mechanisms. She is also in the process of developing new treatment protocols for patients with RYR1-RM.

Posters

Skeletal muscle oxidative stress may be related to functional outcome measures in ryanodine receptor isoform 1-related congenital myopathies



JJ. Todd [a], JW. Witherspoon [a], M. Razaqyar [a], I. Chrismer [a], A. Kuo [a], M. Shelton [a], C. Grunseich [b], A. Mankodi [b], A Kokkinis [b], M. Waite [c], R. Vasavada [c], B. Drinkard [c], M. Jain [c], KG. Meilleur [a].

[a] National Institute of Nursing Research, NIH
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[c] Mark O. Hatfield Clinical Research Center, Rehabilitation Medicine Department, NIH

Ryanodine receptor isoform 1-related congenital myopathies (RyR1-RM), constitute a spectrum of genetically and phenotypically heterogenous rare muscle disorders. In RyR1-RM, causative mutations in RYR1 (19q13.2), which encode the major calcium release channel of skeletal muscle, result in dysregulated calcium release and excitation-contraction coupling. Subsequent clinical manifestations typically include proximal muscle weakness, hypotonia, delayed motor milestones and fatigue. Pre-clinical findings indicate that affected individuals may exhibit greater cellular oxidative stress than the general population. Yet the clinical impact of this disparity regarding physical function has not been investigated to date. Therefore, the primary aim of this study was to determine if skeletal muscle oxidative stress and physical function were correlated in RyR1-RM. Skeletal muscle tissue was obtained by needle biopsy from the tibialis anterior of participants (n= 13) attending an ongoing clinical trial (NCT02362425), with cellular oxidative stress determined in participant tissue and otherwise healthy donor tissue (n= 4) by measuring protein-corrected dichlorofluorescin (DCF) fluorescence intensity. During the study visit, participants also completed a series of graded functional tests, as measures of physical function, administered by a trained physical therapist. Median (IQR) DCF fluorescence intensity was 1.73 (1.06) AU and was not significantly different from control 0.99 (0.54) AU, P= 0.23. Time taken to ascend stairs and run 10 m were both positively correlated with DCF fluorescence intensity (r= 0.64, P= 0.02 and r= 0.67, P= 0.01, respectively) and trended toward significance for time taken to descend stairs (r= 0.51, P= 0.07). These findings indicate that, in RyR1-RM, skeletal muscle oxidative stress is associated with an individual's ability to complete everyday tasks such as climbing stairs; supporting the need for ongoing investigation of anti-oxidant administration as a potential therapy.

Presented By:

Joshua Todd, PhD
As a visiting fellow in Dr. Katy Meilleur's laboratory at the National Institute of Nursing Research (NIH/NINR), Dr. Todd is working on the first clinical trial in Ryanodine Receptor Isoform 1-Related Congenital Myopathies. His research background and interests include nutrition, musculoskeletal health, clinical trials and orphan drug development.

Posters

Spectrum of alpha-dystroglycanopathies: Clinical insights and diagnostic pathway

Goknur Haliloglu, Didem Ardicli, Haluk Topaloglu

Hacettepe University Children's Hospital
Department of Pediatric Neurology
Ankara, Turkey

Our aim is to present our experience on alpha-dystroglycanopathies, including 32 patients from 29 families with a confirmed clinical, radiological, pathological diagnosis combined with or without a molecular diagnosis.

The mean age of the patients (19 boys, 13 girls) was 7 years (3 months-19 years), of 23 being symptomatic before 6 months of life. Presenting symptoms were; developmental delay (n=15), hypotonia (n=4), difficulty in climbing stairs (n=4), respiratory and feeding problems (n=2), arthrogryposis, intrauterine diagnosis of CNS malformation, failure to thrive (n= 1), autistic-spectrum disorder (n= 1), seizure (n=1). The phenotypic categorization of patients in order of clinical severity is; Walker-Warburg Syndrome (n=2), muscle-eye-brain syndrome (n=3), CMD with mental retardation (n=9), CMD with cerebellar involvement (n=5), LGMD-MR (n=6), LGMD-No MR (n=4). Consanguinity was present in 22 families, and 38% (n=11) had affected sibling. MRI was available in 24 patients, and 18 (75%) had abnormal findings. Homozygous and compound heterozygous mutations in αDG genes were detected in 20 of 24 (83%) probands. Five patients' genetic work-up is pending. Mutations in POMT1 were the most prevalent (n=6) in our cohort, followed by FKRP (n=3), POMT2 (n=3), POMGNT1 (n=3), TMEM5 (n=1), FKTN (n=1), GMPPB (n=1), B3GALNT2 (n= 1) and SGK196 (n=1).

Positive diagnostic yield from molecular genetic studies, depends on detailed clinical evaluation, which further helps for genetic counseling and prenatal diagnosis.

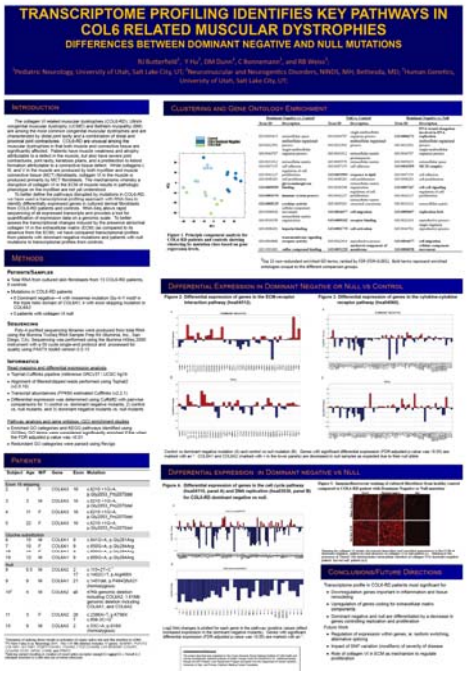
Presented By:

Goknur Haliloglu, MD

Dr. Haliloglu is currently working as a Professor of Pediatrics and Pediatric Neurology, at Hacettepe University Children's Hospital, Department of Pediatric Neurology, Ankara-Turkey. She is involved in the diagnosis, care and management of patients with neuromuscular diseases. Her main interest areas are clinical characterization and deep-phenotyping in early-onset neuromuscular diseases including mainly congenital muscular dystrophies and congenital myopathies.

Posters

Transcriptome profiling identifies key pathways in COL6 related muscular dystrophies: differences between dominate negative and null mutations



RJ Butterfield[1], Y Hu[2], DM Dunn[3], C Bönnemann[2], RB Weiss[3]

[1] Pediatric Neurology, University of Utah
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[3] Human Genetics, University of Utah

The collagen VI related muscular dystrophies (COL6-RD), Ullrich congenital muscular dystrophy (UCMD) and Bethlem myopathy (BM) are among the most common congenital muscular dystrophies and are characterized by distal joint laxity and a combination of distal and proximal joint contractures. 4COL6-RD are unusual among the muscular dystrophies in that both muscle and connective tissue are significantly affected. Patients have muscle weakness and atrophy attributable to a defect in the muscle, but also have severe joint contractures, joint laxity, keratosis pilaris, and a predilection to keloid formation attributable to a connective tissue defect. To better define the pathways disrupted by mutations in collagen VI, we have used a transcriptional profiling approach with RNA-Seq to identify differentially expressed genes in cultured dermal fibroblasts from COL6-RD patients (8 with dominant negative mutations and 5 with null mutations) and 4 controls. RNA-Seq allows rapid sequencing of all expressed transcripts and provides a tool for quantification of expression data on a genomic scale. To better assess the transcriptional changes induced by abnormal collagen VI in the extracellular matrix (ECM) (as compared to its absence from the ECM); we compared transcriptional profiles from patients with dominant negative mutations and patients with null mutations to transcriptional profiles from controls. Differentially expressed transcripts between patient and control fibroblasts include upregulation of ECM components and downregulation of factors controlling matrix remodeling and repair. Dominant negative and null samples are primarily differentiated by downregulation of genes involved with DNA replication and repair. Differentially expressed genes identified here will provide new targets for development of therapies and biomarkers to assess the efficacy of treatments.

Presented By:

Russell Butterfield, MD, PhD
Dr. Butterfield received his PhD in mammalian genetics, and medical degree from the University of Illinois. He completed his residency training in pediatric neurology at the University of Utah in June 2009. He is currently an Assistant Professor in the Departments of Neurology and Pediatrics, after completing a fellowship in neuromuscular disorders sponsored by the Muscular Dystrophy Association.

Dr. Butterfield is board certified in Neurology with special qualification in child neurology, with clinical interests include all types of neurogenetic and neuromuscular disorders with an emphasis on muscular dystrophies of childhood onset. His research interests are in understanding genetic aspects of these disorders. His current efforts are in characterization of genotype/phenotype relationships and molecular pathogenesis in collagen VI myopathies such as Bethlem myopathy and Ullrich congenital muscular dystrophy.

Special Thanks to Our Sponsors

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Glossary of Terms

General	
AAC	**A**ugmentative or **A**lternative **C**ommunication devices used by affected individuals whose speech and/or hearing is inhibited
alpha-Dystroglycanopathy/aDG	A CMD subtype that results from gene defects in a number of genes that affect glycosylation of a protein called alpha-dystroglycan, fundamental in skeletal muscle cells and neurons
ambulation/ambulatory	The ability to walk
apoptosis	A process causing cell death, specifically a "programmed cell death" in contrast with necrosis which is a "traumatic cell death"
atrophy	Small skinny muscles due to wasting
CMD	Congenital Muscular Dystrophy
CMD Subtype	A unique muscle disorder under the umbrella term "CMD"
Collagen VI/COL6, Ullrich CMD, Bethlem Myopathy	A CMD Subtype that results from gene defects affecting the production of collagen type 6 protein in the extracellular matrix of the muscle
congenital	Present from birth or within the first 2 years of life
dystrophy	The degeneration and replacement of muscle tissue by fatty cells or fibrosis
EDMD/Emery Dreifuss Muscular Dystrophy	A CMD Subtype caused by genetic defects in the Emerin, LMNA, or FHL1 gene that causes muscle weakness and cardiac dysfunction
encephalopathy	A broad term to describe any of a number of disorders or diseases of the brain
failure to thrive	Infants or young children who are not growing or gaining weight as expected
fibrosis	The formation of scar tissue
hydrocephalus	An accumulation of fluid within the cranium, especially in infancy, due to obstruction of the movement of cerebrospinal fluid, often causing enlargement of the head; water on the brain
hyperkeratosis pilaris	A condition causing dry, rough patches or raised bumps on the skin
hyperlaxity or hypermobility	A condition that causes joints to hyperextend or bend farther than normal
hypertrophy	Enlarged muscles (or any other organ or tissue)
hypotonia	A state of low muscle tone, "floppy"
keloids	A condition causing thickened, raised scars
LAMA2/Merosin Deficient/ MDC1A	A CMD Subtype that results from gene defects in the laminin-alpha2 gene affecting the production of merosin protein in the muscle cell
LMNA/Laminopathy	A CMD Subtype that results from gene defects in the lamin A/C gene affecting production of lamin A and lamin C proteins within the nucleus of cells
malignant hyperthermia	An allergic reaction to certain types of anesthesia or overexposure to heat
myopathy	A disease of muscle in which muscle fibers do not function properly
neuromusclular disorder	A broad term that encompasses many diseases that impair muscle function
palliative care	A specialized form of care for people with a serious illness to provide relief from symptoms
ptosis	A condition causing droopy eyelids
RYR1 Related Myopathy	A CMD Subtype that results from gene defects in the RYR1 (Ryanodine receptor 1) gene affecting a protein that manages a calcium release channel during muscle contraction
SEPN1 Related Myopathy	A CMD Subtype that results from gene defects in the SEPN1 gene affecting production of the protein selenoprotein N, involved in the process of oxidation-reduction and calcium homeostasis (balance)
Titin/Titinopathy	A CMD Subtype that results from gene defects in the Titin gene affecting the production of the protein connection, responsible for the passive elasticity of muscle

Glossary of Terms

Genetics	
allele	A variant form of a given gene (found at the same place on a chromosome pair). Sometimes, different alleles can result in different observable phenotypic traits, such as different pigmentation (see genetic variant).
autosomal dominant	A genetic inheritance pattern requiring only one abnormal gene to manifest disease, passed on by only one parent or occurring spontaneously (see de novo)
autosomal recessive	A genetic inheritance pattern requiring two abnormal copies of a gene to manifest disease, one mutation passed on from each parent
benign	Referring to a genetic change that does not cause disease
cell	The structural, functional, and biological unit of all organisms
DNA	Deoxyribonucleic acid is a molecule that carries the genetic instructions used in the growth, development, functioning, and reproduction of all cells (and many viruses)
de novo/spontaneous mutation	A genetic mutation found in an affected individual that is not present in either parent
genetic inheritance	The passing of traits to offspring from parents or ancestors
genetic variant	A variation in the DNA sequence of a given gene, such as a mutation or polymorphism (see allele)
heterozygous	A mutation in only one allele (maternal or paternal)
homozygous	Identical mutations in both the paternal and maternal alleles
mutation	An alteration or change to a gene's coding instructions
nucleotide	A building block of DNA or RNA
pathologic/pathogenic	Referring to a genetic change that causes disease
polymorphism	A discontinuous genetic variation resulting in the occurrence of several different forms or types of individuals
VUS/VOUS	A variant of unknown significance; a mutation found during genetic testing whose pathogenicity is unknown
X-linked	A genetic inheritance pattern pertaining to genes on the sex chromosome "x" (females are "XX", males are "XY")

Glossary of Terms

Pulmonary Care	
airway clearance	A technique for managing secretions in the airway and lungs
alveoli	Small sacs within the lungs where gas exchange takes place
arterial blood gas	A test that measures CO2 levels in the blood and is taken (typically) from the radial artery
aspiration	The entry of material, such as food, liquid or mucus, into the larynx, respiratory tract, or lungs
atelectasis	The collapse or closure of a portion of the lung resulting in reduced or absent gas exchange
AVAPS	Average Volume Assured Pressure Support, a type of BiPAP breathing support
BiPAP	Bi-level Positive Airway Pressure, a machine that provides breathing support
breath stacking	A technique to expand lung capacity and to help form a productive cough for someone with weakened respiratory muscles
capnography	The measure of CO2 levels in the airway
CO2 retention	The increased body storage of carbon dioxide resulting from impaired carbon dioxide elimination
cough assist machine	A device that helps to clear secretions from the lungs by gradually applying positive air pressure to the airway and then rapidly shifting to negative air pressure
CPAP	Continuous Positive Airway Pressure; a device that provides breathing support, typically for those with obstructive sleep apnea
forced vital capacity	A measure taken during Pulmonary Function Testing that indicates the maximal volume of gas that can be exhaled from full inhalation by exhaling forcefully and rapidly
Hypercapnea	See CO2 retention
hyperinsuflation	A passive stretch of the chest wall through use of a cough assist machine or bag valve mask used as an intervention to slow the rate of decline in breathing capacity
hypoxemia	an abnormally low concentration of oxygen in the blood
hypoventilation	breathing at an abnormally slow rate, resulting in an increased amount of carbon dioxide in the blood
IPPB/IPPV	Intermittent positive pressure breaths/ventilation; a type of breathing exercise to promote more effective aeration of the lungs
MPV	Mouthpiece ventilation, also known as sip ventilation or sip and puff; a straw-like device used to take supported breaths from a ventilator or BiPAP machine
mucociliary elevator	The biological mechanism for clearing secretions from the lungs
mucus	The free slime of the mucous membrane
NPV	Negative Pressure Ventilation/Iron Lung
percussive vest	A device that utilizes high frequency chest wall vibration that worn, promotes airway clearance and improvement of bronchial drainage
pneumothorax	Collapsed lung; an abnormal collection of air in the pleural space that causes an uncoupling of the lung from the chest wall
polysomnography	Sleep study; a test used to diagnose sleep disorders through the measurement of oxygen and CO2 levels, heart and breathing rate, eye and leg movements, and incidents of apnea (temporary cessation of breathing)
pulmonary function testing/PFT	See Spirometry
pulse ox/pulse oximeter	A device that measures oxygen saturation of the blood
sip ventilation/ sip and puff	See Mouthpiece Ventilation
spirometry	Pulmonary Function Testing (PFT); used to assess how well your lungs function by measuring how much air you inhale, how much you exhale and how quickly you exhale
supine	Lying down on one's back, facing upward
tracheostomy	An opening into the trachea through the neck with insertion of a tube to facilitate breathing or secretion management
ventilator	A device that provides breathing support or artificial respiration

Glossary of Terms

Cardiac Care	
ACE inhibitors	Medications that help relax blood vessels (ACE=Angiotensin-Converting-Enzyme)
AICD	Automatic implantable cardiac defibrillator
arrhythmia	A change in the rhythm of the heart's beating
beta-blockers	Medications that decrease the heart rate
cardiac monitor	A device for the continuous observation of cardiac function
cardiomyopathy	A disease of heart muscle that causes enlargement of the heart and rigidity of the walls of the heart
echocardiogram	An ultrasound image of the heart that demonstrates the size, motion, and composition of cardiac structures
ejection fraction	As measured during an echocardiogram, the blood present in the ventricle at the end of diastole and expelled during contraction of the heart
electrocardiogram (EKG/ECG)	An electrocardiogram (EKG or ECG) is a test that checks for problems with the electrical activity of your heart, showing the heart's electrical activity as line tracings on paper; the spikes and dips in the tracings are called waves
fractional shortening	As measured during an echocardiogram, like the ejection fraction, this is a measure of the heart's muscular contractility
holter monitor	A portable device that records the electrical activity (EKG) of the heart
LINQ Monitor	An implantable cardiac device to monitor (up to 3 years) heart rhythms and function

Feeding/Nutrition	
bolus feed	A dose of a nutritional or medication preparation given via feeding tube
dysmotility	A condition in which muscles of the digestive system become impaired
failure to thrive	Indicates insufficient weight gain or inappropriate weight loss, particularly referred to in growing children
fundoplication	A surgical procedure of tucking or folding the fundus of the stomach around the esophagus to prevent reflux
G-Tube, NG Tube, Feeding Tube	A device implanted into the stomach or inserted via nose or mouth to the stomach for providing food, supplements or medication
GERD	Gastro-Esophageal Reflux Disease; a digestive disorder that affects the lower esophageal sphincter (LES), the ring of muscle between the esophagus and stomach.
hypoglycemia	A condition resulting from low blood sugar
hypothyroidism	A condition resulting from underactive thyroid gland production

Glossary of Terms

Orthopedics	
AFO braces	An ankle-foot orthotic (see orthotic)
bisphosphonate	A class of drugs that prevent the loss of bone mass, used to treat osteopenia and osteoporosis
cervical	Pertaining to the bones in upper spine and neck
contracture	A chronic loss of joint motion due to structural changes in muscles, ligaments, and tendons
DEXA scan	A test to measure bone density or mineral loss as a result of mobility loss or aging
growth sparing	A technique whereby devices such as magic rods are implanted to straighten spine curvature without fixing the spine's height and allowing the patient to continue to grow
kyphosis	An abnormal, curvature of the upper or thoracic region of the spine resulting in a hunched posture
lordosis	An abnormal curvature of the lower or lumbar region of the spine resulting in a swaybacked posture
lumbar	Pertaining to the bones in the lower region of the spine
magic rods/growing rods	A surgical instrument used in growing children with scoliosis that allows the spine to continue growing while managing the curve until the child is old enough for spinal fusion
orthotic	An artificial support or brace for the limbs or spine
osteopenia	The reduction of bone density, less severe than osteoporosis
osteoporosis	The reduction of bone density, more severe than osteopenia
scoliosis	An abnormal curvature of the spine that makes the spine look like a “C” or “S” shape
spinal fusion	A surgical procedure in which vertebrae are permanently fixed to correct scoliosis
subluxation	The incomplete or partial dislocation of a joint or organ
T-score	A measure taken during a DEXA scan, referring to the density of bone as compared with what is normally expected in a healthy young adult (30 yo) of the same gender; T-score is the number of units — called standard deviations — that bone density is above or below the average
thoracic	Pertaining to the chest (thorax) or the bones in the middle region of the spine
torticollis	A type of neck contracture in which the neck is twisted or tilted
winged scapula	Having a prominent vertebral border usually owing to weakness of one of the muscles holding the scapula in place
Z-score	A measure taken during a DEXA scan, referring to the density of bone as compared with what is normally expected in a healthy adult of the same gender; Z-score is the number of units — called standard deviations — above or below the average

Physical Therapy	
active vs passive stretch	Active stretching stimulates and prepares muscles for use during exercise; static stretching is when an external force exerts upon the limb to move it into the new position
concentric exercise	The shortening of muscle as it acts against resistive force (like a weight). For example, during a biceps curl, the biceps contract concentrically during the lifting phase of the exercise
eccentric exercise	The lengthening of muscle while producing force, usually by returning from a shortened (concentric) position to a resting position. Using the same example above, the lowering the weight back down during a biceps curl
stander, gait trainer	Standing devices which enable individuals by facilitating their ability to stand upright at various intervals throughout the day
hoyer lift	A device with a motorized seat mechanism enabling the lifting of the body from a sitting to a standing position or to transport an immobile person to another place

Glossary of Terms

Research	
CALLISTO	Congenital Muscular Dystrophy Ascending Multiple Dose Cohort Study analyzing Pharmacokinetics at Three Dose Levels In Children and Adolescents With Assessment of Safety and Tolerability of Omigapil, the clinical trial testing the drug Omigapil in Collagen VI and LAMA2 CMD Subtypes
doxycycline	A drug currently being tested to slow apoptosis (muscle cell death)
EMA	**E**uropean **M**edicines **A**gency, a federal agency responsible for approving the trial and use of drugs and other interventions in the European Union
fast track, fast track status	A designation by the FDA of an investigational drug for expedited review to facilitate development of drugs which treat a serious or life-threatening condition and fill an unmet medical need
FDA	**F**ood and **D**rug **A**dministration, a federal agency responsible for approving the trial and use of drugs and other interventions in the United States
gene therapy	The administration of a gene or genetic material to replace, correct or inactivate a mutated (defective) gene or to supply a gene which produces a protein that can compensate for a missing or abnormal protein
losartan	A commonly prescribed FDA-approved medication (an angiotensin II receptor antagonist) for hypertension which demonstrated clinical improvement and amelioration of fibrosis in the LAMA2-CMD mouse model.
NAC/N-Acetyl Cysteine	An antioxidant drug currently being tested in clinical trials to slow progression of some types of CMD
omigapil	A drug currently being tested in clinical trials (see CALLISTO) to slow apoptosis (muscle cell death)
orphan disease	A condition that affects fewer than 200,000 people in the United States or less than 1:2,000 in Europe
orphan drug, orphan drug status	A pharmaceutical agent that has been developed specifically to treat a rare medical condition, the condition itself being referred to as an orphan disease, as designated by the FDA
PMDA	**P**harmaceuticals and **M**edical **D**evices **A**gency, a federal agency responsible for approving the trial and use of drugs and other interventions in Japan
TXA127, Angiotensin (1-7)	A pharmaceutical formulation of the naturally occurring peptide, Angiotensin (1-7), being tested for use as a treatment in several rare disorders

Tissue/Bio Banking	
biopsy	An examination of tissue removed from a living body to discover the presence, cause, or extent of a disease
fibroblast	A cell in connective tissue that produces collagen and other fibers
iPSC/iPS Cell line	**i**nduced-**P**luripotent-**S**tem-**C**ell is a cell that has been reprogrammed to behave like an embryonic stem cell from an adult cell
lymphoblast/lymphocyte	A white blood cell
stem cell	An undifferentiated cell capable of giving rise to indefinitely more cells of the same type, and from which certain other kinds of cells arise by differentiation

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