

# **RYR-1-Related Diseases International Research Workshop:**

## **From Mechanisms to Treatments**

Hyatt Regency Pittsburgh International Airport  
**Pittsburgh, PA, USA • July 21 – July 22, 2022**







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# Agenda



**Thursday, July 21, 2022**

**7:00 am – 7:45 am      Breakfast**

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**7:45 am – 8:00 am      Welcome & Opening Remarks**

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**8:00 am – 9:00 am      Survey of Individuals Affected by RYR-1-Related Diseases**  
Drew Huseeth and Brentney Simon

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**9:00 am – 9:30 am      RYR-1 Community Testimonials (Chairs: Drew Huseeth & Brentney Simon)**

9:00 am – 9:10 am      Laurie Jones

9:10 am – 9:20 am      Sofia Leon

9:20 am – 9:30 am      Orlando Carneiro

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**9:30 am – 9:50 am      Coffee Social Break**

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**9:50 am – 12:00 pm      Phenotypic Variability (Chair: James Dowling, MD, PhD)**

9:50 am – 10:00 am      James Dowling, MD, PhD  
Session Introduction

10:00 am – 10:40 am      Heinz Jungbluth, MD, PhD • King's College London, London, UK  
*'RYR1-related disorders: an expanding phenotypical spectrum'*

10:40 am – 11:05 am      \*Anna Sarkozy, MD, PhD • Dubowitz Neuromuscular Centre, London, UK  
*'RYR1-related myopathies in childhood: review of available natural history data from the UK, USA and Canadian cohorts'*phenotypical spectrum'

11:05 am – 11:30 am      Nicol Voermans, MD, PhD, and Luuk van den Bersselaar, MD • Radboudumc, Nijmegen, Netherlands  
*'RYR1-related diseases in adulthood: neuromuscular symptoms in malignant hyperthermia and exertional rhabdomyolysis'*

11:30 am – 12:00 pm      Sheila Riazi, MSc, MD, FRCPC • University of Toronto, Toronto, CA  
*'The effect of exercise preceding MH: priming of muscle'*

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**12:00 pm – 1:00 pm      Lunch (Location: Allegheny ABC)**

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**1:00 pm – 1:30 pm      RYR-1 Community Testimonials (Chairs: Drew Huseeth & Brentney Simon)**

1:00 pm – 1:10 pm      Bob Hanich, MD

1:10 pm – 1:20 pm      \*Avi Swerdlow

1:20 pm – 1:30 pm      Drew Huseeth



# Regency Ballroom CDEF

\* = Remote participation

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## 1:30 pm – 2:40 pm **RYR1 Genetics and Variant Classification (Chair: Livija Medne, MS, LCGC)**

1:30 pm – 1:40 pm **Livija Medne, MS, LCGC**

Session Introduction

1:40 pm – 2:10 pm **Leslie Biesecker, MD** • NHGRI, Bethesda, MD, USA

*'Towards comprehensive interpretation of RYR1-related malignant hyperthermia variants'*

2:10 pm – 2:40 pm **Susan Treves, PhD** • University of Basel, Basel, Switzerland

*'Transcriptional analysis in muscles from patients with congenital myopathies'*

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## 2:40 pm – 3:00 pm **Coffee Social Break**

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## 3:00 pm – 4:40 pm **Drug Development and Validation (Chair: Filip Van Petegem, PhD)**

3:00 pm – 3:10 pm **Filip Van Petegem, PhD**

Session Introduction

3:10 pm – 3:40 pm **Oliver Clarke, PhD** • Columbia University, New York, NY, USA

*'Structural basis for modulation of the skeletal muscle ryanodine receptor by ligands and therapeutics'*

3:40 pm – 4:10 pm **Razvan Cornea, PhD** • Minneapolis, MN, USA

*'Targeting protein interactions in therapeutic discovery for RyR1-related disorders'*

4:10 pm – 4:40 pm **\*Takashi Murayama, PhD** • Juntendo University, Tokyo, Japan

*'Discovery of novel RyR1-selective inhibitor by high-throughput screening and structural development'*

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## 6:30 pm **Dinner (Location: Allegheny ABC)**

# Agenda



**Friday, July 22, 2022**

**7:00 am – 8:00 am      Breakfast**

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**8:00 am – 8:30 am      RYR-1 Community Testimonials (Chairs: Drew Huseh & Brentney Simon)**

8:00 am – 8:10 am      **Brentney Simon**

8:10 am – 8:20 am      **Mary Wright**

8:20 am – 8:30 am      **Courtney Perrin**

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**8:30 am – 9:40 am      Prevalence & Pathophysiology of RYR1-Related Diseases 1  
(Chair: Nicol Voermans, MD, PhD)**

8:30 am – 8:40 am      **Nicol Voermans, MD, PhD**  
Session Introduction

8:40 am – 9:10 am      **Heinz Jungbluth, MD, PhD** • King's College London, London, UK  
*'International prevalence study'*

9:10 am – 9:40 am      **Isabelle Marty, PhD** • Grenoble Institut des Neurosciences, Inserm, Grenoble, France  
*'Screening for pharmacological therapy to alleviate the consequences of RyR1 reduction'*

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**9:40 am – 10:00 am      Coffee Social Break**

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**10:00 am – 11:40 am      Prevalence & Pathophysiology of RYR1-Related Diseases 2  
(Chair: Robert Dirksen, PhD)**

10:00 am – 10:10 am      **Robert Dirksen, PhD**  
Session Introduction

10:10 am – 10:40 am      **James Dowling, MD, PhD** • Hospital for SickKids, Toronto, Canada  
*'Exploring RYR1 expression as disease modifier and therapeutic target'*

10:40 am – 11:10 am      **Susan Hamilton, PhD** • Baylor College of Medicine, Houston, TX, USA  
*'Role of Spieg Kinase in RyR1 function and congenital myopathy'*

11:10 – 11:40 am      **Johann Bohm, PhD** • IGBMC, Illkirch, France  
*'RYR1 mutations in centronuclear myopathy (CNM)'*

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**11:40 am – 12:10 pm      RYR-1 Community Testimonials (Chairs: Drew Huseh & Brentney Simon)**

11:40 am – 11:50 am      **Lauren Heft**

11:50 am – 12:00 pm      **Jacqueline Hoffman-Anderman**

12:00 pm – 12:10 pm      **Matthew Tompkins, PhD**

# Regency Ballroom CDEF

\* = Remote participation

**12:10 pm – 12:30 pm**    **Group Photo (wear your workshop t-shirt!)**

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**12:30 pm – 1:00 pm**    **Lunch (Location: Allegheny ABC)**

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**1:00 pm – 2:40 pm**    **Therapeutic Pipeline (Chair: Andrew Marks, MD)**

**1:00 pm – 1:10 pm**    **Andrew Marks, MD**  
Session Introduction

**1:10 pm – 1:40 pm**    **Jacques Tremblay, PhD** • University of Laval, Québec, Canada  
*'Correction of point mutations in the RYR1 gene using the CRISPR/Prime editing technology'*

**1:40 pm – 2:10 pm**    **\*Nanna Witting, MD, PhD** • Copenhagen University, Copenhagen, Denmark  
*'Exercise training and congenital myopathies'*

**2:10 pm – 2:40 pm**    **Tokunbor Lawal, PhD** • NINR, Bethesda, MD, USA  
*'MitoQ and polyunsaturated fatty acids: a novel therapeutic approach for RYR1-related myopathy'*

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**2:40 pm – 3:00 pm**    **Coffee Social Break**

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**3:00 pm – 4:40 pm**    **RYR1 Clinical Trials (Chair: Carsten Bönnemann, MD, habil)**

**3:00 pm – 3:10 pm**    **Carsten Bönnemann, MD, habil**  
Session Introduction

**3:10 pm – 3:40 pm**    **\*Eva Michael, MD** • University of Gothenburg, Gothenburg, Sweden  
*'Design of COMPIS\* trial and clinical experiences with salbutamol and pyridostigmine'*

**3:40 pm – 4:10 pm**    **Joshua Todd, PhD, CCRP** • NINDS, Bethesda, MD, USA  
*'NAC Phase II double-blind RCT and clinical trial readiness'*

**4:10 pm – 4:40 pm**    **Payam Mohassel, MD** • NINDS, Bethesda, MD, USA  
*'Rycal Phase I open-label dose-escalation trial and lessons learned'*

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**6:00 pm**    **Dinner & Kick-Off of the 2022 RYR-1 International Family Conference  
(Location: Regency Ballroom AB, Allegheny ABC, & Foyer)**

## Sponsor & Donors

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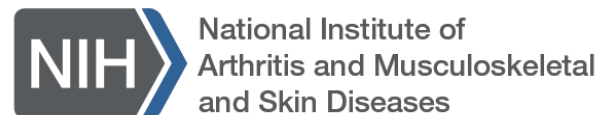
The RYR-1 Foundation would like to thank the Sponsor of the 2022  
RYR-1-Related Diseases International Research Workshop:  
From Mechanisms to Treatments.

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The RYR-1 Foundation would like to thank the following organizations for their grants in support of the 2022 RYR-1-Related Diseases International Research Workshop: From Mechanisms to Treatments.



Funding for this conference was made possible (in part) by **(1R13AR081619-01) from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)**. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

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The RYR-1 Foundation would like to thank the following individual donors for their generous contributions in support of scientific meetings hosted by The RYR-1 Foundation.

**Mr. and Mrs. Orlando and Sissi Carneiro**

**Dr. and Mrs. Stuart and Ellie Fine**

**Dr. and Mrs. Michael and Lindsay Goldberg**

**Mr. and Mrs. Bryan and Lauren Heft**

**Mrs. Jacqueline Hoffman-Anderman and Mr. Scott Anderman**

**Mr. Andrew Huseth**

**Mr. and Mrs. Michael and Connie Legum**

**Mr. and Mrs. Jo and Ken Merlau**

**Dr. and Mrs. Michael and Jennifer Orseck**

**Drs. Matthew and Zuhail Tompkins**

# Workshop Organizing Committee

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The RYR-1 Foundation expresses its deepest gratitude to the Co-Directors of the 2022 RYR-1-Related Diseases International Research Workshop: From Mechanisms to Treatments for their vision, expertise, and time. The workshop would have been impossible without this group.

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## Robert Dirksen, PhD

Dr. Robert Dirksen is the Lewis Pratt Ross Professor and Chair of Pharmacology and Physiology at the University of Rochester Medical Center. Dr. Dirksen obtained his BS in Biology and Chemistry from the University of Notre Dame, and MS and PhD in Pharmacology from the University of Rochester. Dr. Dirksen is an outstanding scientist who has focused much of his scientific efforts on understanding the underlying defects of skeletal muscle in patients with Myotonic Dystrophy, Malignant Hyperthermia, Central Core Disease, and other RYR-1-related diseases. His particular focus has been on understanding the control of calcium movements in muscle and the complex relationship between altered calcium movements and abnormal muscle function. His work has shown that dysfunction in calcium flow through RYR-1 calcium channels is the underlying cause of muscle weakness in patients with RYR-1 muscle disease.

His work has been funded by the National Institutes of Health, the Muscular Dystrophy Association, and The RYR-1 Foundation among others. He has published over 150 original research articles and reviews in leading scientific journals and has given numerous invited lectures. Dr. Dirksen served tenures as President of the Society of General Physiologists and Chair of the MHAUS Professional Advisory Committee. He currently serves on the editorial boards of several journals, including the Journal of General Physiology, Skeletal Muscle, and Frontiers in Skeletal Muscle Physiology. He was Chair of the 2015 Gordon Research Conference on Muscle: Excitation-Contraction Coupling and has served on several NIH Study Sections related to muscle biology and disease.

***Dr. Dirksen is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## Andrew Huseth, AICP

Drew Huseth is a Land Entitlement Manager for Woodside Homes of Arizona, a single-family residential development and homebuilding company. Prior to Woodside Homes, he spent 12 years working as a Land Entitlement Planner for a privately held consulting firm. Drew has a bachelor's degree in Housing and Urban Development from Arizona State University. He is a member of the American Institute of Certified Planners (AICP), the Arizona Chapter of the American Planning Association (APA), and also the Arizona Chapter of the Urban Land Institute (ULI). Drew has a recessive form of RYR-1 caused by mutations in the *RYR1* gene.

***Drew is on the Board of Directors of The RYR-1 Foundation.***

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## Anna Sarkozy, MD, PhD\*

Dr. Anna Sarkozy studied medicine at La Sapienza University in Rome, Italy, where she also completed her higher medical training and PhD in clinical genetics. She moved to the UK in 2008 working first at the Newcastle Muscle Centre and moved to the Dubowitz Neuromuscular Centre at the Great Ormond Street Hospital in 2014, where she works as a Consultant in Neuromuscular Diseases. She also is an Honorary Senior Lecturer at University College, London. Anna's clinical research interests lie in the identification of genes responsible for rare neuromuscular disease, in particular congenital myopathies and muscular dystrophies, and in deep phenotypization of this rare condition, to better understand their natural history and clarify genotype/phenotype correlations and improve trial readiness as well.

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## Brentney Simon

Brentney Simon is a former Information and Referral Specialist and Youth Leadership Coordinator at AccessAbility, a Center for Independent Living. She has advocated for disability rights by speaking at the SC State House on Advocacy Day in 2018. She and her family have hosted fundraisers for The RYR-1 Foundation and loved attending the international family conferences. Brentney said “Working within the RYR-1 community allows me to do what I’ve always wanted to do, regardless of my physical condition.” Despite the progression of her recessive Multi-minicore Disease, Brentney says that she enjoys spending her life supporting those with disabilities and motivating everyone to always focus on their abilities.

***Brentney is on the Board of Advisors of The RYR-1 Foundation.***

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## Filip Van Petegem, PhD

Dr. Filip Van Petegem is Professor at the University of British Columbia (UBC), Department of Biochemistry and Molecular Biology (Vancouver, Canada). Born in Belgium, he obtained his PhD in Biochemistry at Ghent University in 2002 and performed postdoctoral studies at the University of California San Francisco (UCSF).

Dr. Van Petegem leads a research lab at UBC, where he studies the structure and function of ion channels, with a focus on cardiac and skeletal muscle. This includes the Ryanodine Receptor (RyR) and voltage-gated calcium channels (CaV), two types of ion channels that have intimate communications inside muscle cells. Mutations in the genes that encode these channels cause malignant hyperthermia, central core disease, cardiac arrhythmia, and much more. A major approach consists of determining very detailed 3D structures of these channels, allowing his lab to peer into the direct effects of the disease mutations on the structure.

Dr. Van Petegem has received New Investigator Awards from the CIHR (2008) and the Michael Smith Foundation for Health Research (2008) as well as a UBC Faculty of Medicine Award for excellence in basic science (2013). He received a new investigator award from the Canadian Society for Molecular Biosciences (CSMB) in 2016, and a Killam Research Fellowship in 2017. He serves on the Macromolecular Beam team committee at the Canadian Light Source and frequently consults with industry.

***Dr. Van Petegem is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## Nicol Voermans, MD, PhD

Dr. Nicol Voermans’s research at the Radboud University Medical Centre (The Netherlands) focuses around genotype-phenotype coupling and trial-readiness of rare inherited myopathies. As a clinical neurologist trained in neuromyology and experienced in translational research, she is well prepared to bridge the gap between the neuromuscular bench and bedside. Her passion for supporting patients with rare genetic disorders and her enthusiasm for interdisciplinary work is what drove her to this research field.

Dr. Voermans has focused on congenital myopathies, with a special interest in the clinical presentations and pathophysiology of RYR1-related myopathies. In 2014, Dr. Voermans gained experience in functional analysis of the RYR-1 channel in the lab of Dr. Susan Treves in Switzerland. Dr. Voermans has focussed on the wide spectrum of RYR1-related myopathies throughout life, including intermittent phenotypes such as exertional rhabdomyolysis. She is a medical advisor of the congenital myopathies group of the Dutch patient organization for neuromuscular disorders.

Recently, Dr. Voermans has extended her scope to include other congenital myopathies (centronuclear myopathies, nemaline myopathies, and SEPN1-related myopathies) and facioscapulohumeral muscular dystrophy (FSHD). Her research in these myopathies has increased the knowledge of geno- and phenotypes, natural history and outcome measures, all of which are crucial for future trials.

***Dr. Voermans is a member of The RYR-1 Foundation Scientific Advisory Board.***

# The RYR-1 Foundation Representatives —

## Nicole Becher

Nicole Becher joined The RYR-1 Foundation in January 2017 as the Program Director. As a full-time employee, Nicole coordinates daily operations and works closely with the Board of Directors, Board of Advisors, and Scientific Advisory Board of The RYR-1 Foundation. She is a graduate of the University of Pittsburgh with a BS in Psychology. She can be reached at [nicole@ryr1.org](mailto:nicole@ryr1.org).

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## Carsten G. Bönnemann, MD, habil

Dr. Carsten Bönnemann is a pediatric neurologist specializing in neuromuscular disorders and neurogenetics. He is a Senior Investigator in the Neurogenetics Branch and Chief of the Neuromuscular and Neurogenetic Disorders of Childhood Section at the National Institute of Neurological Disorders and Stroke at the National Institutes of Health in Bethesda.

Dr. Bönnemann is also an Adjunct Professor of Neurology at the University of Pennsylvania and the Children's Hospital of Philadelphia (CHOP), and he is a member of the Executive Board of the World Muscle Society as well as Co-Editor-in-Chief of the Journal of Neuromuscular Disease. Dr. Bönnemann is an internationally recognized expert in the diagnosis of neuromuscular diseases. His research is dedicated towards understanding the molecular genetics and cell biology of muscular dystrophies and early onset myopathies in order to develop molecular-based treatments. Dr. Bönnemann was a Pew Scholar in the Biomedical Sciences and received the Derek-Denny Brown Neurological Scholar Award of the American Neurological Association.

***Dr. Bönnemann is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## James Dowling, MD, PhD

Dr. James Dowling is a clinician-scientist who is focused on gene discovery and therapy for childhood muscle diseases. He is a Professor of Paediatrics and Molecular Genetics at the University of Toronto and a staff clinician at the Hospital for Sick Children in Toronto. He is also the inaugural Mogford Campbell Chair in Pediatric Clinical Neuroscience at Toronto's Hospital for Sick Children. In addition, he is a member of the Executive Board of the World Muscle Society and Chair of the Executive Committee of TREAT-NMD.

Dr. Dowling is considered one of the world's leading experts in RYR-1 muscle disease. His research spans the continuum from new gene discovery to disease pathogenesis to therapy development. He is engaged in both targeted and non-biased drug discovery for RYR-1 related myopathies. His laboratory employs both the zebrafish and mouse model systems, along with complementary in vitro analyses. Dr. Dowling is the recipient of numerous NIH and private foundation research grants, and has recently published detailed results of his RYR-1 related research.

***Dr. Dowling is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## Michael Goldberg, MD, MPH

Dr. Michael F. Goldberg is President of the Board of Directors and Co-Chair of Research of The RYR-1 Foundation. Mike is a board-certified neuroradiologist and is the Director of Neuroradiology at the Allegheny Health Network. As someone who is affected by an RYR-1-related disease, Mike understands first-hand the importance of building a community of similarly-affected individuals and families. As a physician, he has used his medical and scientific background to lead The RYR-1 Foundation's efforts to fund critically important RYR-1 research. In a short period of time, The RYR-1 Foundation's research program has had a major international impact and has led to important scientific and medical breakthroughs.

***Dr. Michael F. Goldberg is on the Board of Directors of The RYR-1 Foundation.***

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## Morton Goldberg, MD, FACS

Dr. Morton F. Goldberg is Vice President of the Board of Directors and Co-Chair of Research of The RYR-1 Foundation. He is also an ophthalmologist specializing in retinal disease and genetics. He is the Joseph Green Professor of Ophthalmology at the Johns Hopkins School of Medicine and the Director Emeritus of the Wilmer Eye Institute. He is a member of the Institute of Medicine of the National Academies of Science of the United States.

***Dr. Morton F. Goldberg is on the Board of Directors of The RYR-1 Foundation***

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## Johanna Lanner, PhD

Dr. Johanna Lanner is a preclinical expert in muscle pathophysiology, and her interdisciplinary and translational research program is focused on understanding mechanisms and identifying novel therapeutic interventions to combat muscle dysfunction and weakness. She is an Associate Professor at The Department of Physiology & Pharmacology, Karolinska Institutet, Stockholm, Sweden. Her background includes a master's degree in chemistry from Stockholm University, Sweden, and a PhD in medical sciences from Karolinska Institutet. She did her postdoc training in Professor Susan Hamilton's laboratory at Baylor College of Medicine in Houston, Texas, focusing on muscle dysfunction in RYR-1-related diseases.

Johanna has conducted research on different signaling pathways in muscles for over a decade and has made significant advances in this field by characterizing novel mechanisms of muscle weakness and linking oxidative stress and altered muscle metabolism to the impaired contractile function of muscle. She has published over 50 original articles and reviews in leading scientific journals and is frequently invited to present her research at acknowledged scientific conferences and congresses. Dr. Lanner is the recipient of national and European grants, and her research team recently identified a mitochondrial protein that potentially can be targeted to improve muscle function in genetic diseases and non-communicable disorders.

***Dr. Lanner is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## Andrew Marks, MD

Dr. Andrew Marks is Professor and Chair of the Department of Physiology and Cellular Biophysics, Professor of Biomedical Engineering, and Clyde and Helen Wu Professor of Medicine at Columbia University. He is board-certified in Internal Medicine and in Cardiovascular Diseases. He is a member of the National Academy of Sciences, the National Academy of Medicine, a fellow of the American Academy of Arts and Sciences. He received the Basic Research Prize from the American Heart Association, Stanley J. Korsmeyer Award, American Society for Clinical Investigation, Robert J. and Claire Pasarow Foundation Award in CV Research, Glorney-Raisbeck Award, NY Academy of Medicine, Doctor of Science, Honoris causa, Amherst College, Docteur Honoris causa, de l'Université de Montpellier and was Editor-in-Chief of the Journal of Clinical Investigation,

Dr. Marks discovered that "leaky" intracellular calcium release channels (ryanodine receptors) contribute to heart failure and impaired exercise capacity. His research has provided groundbreaking insight into RYR-1-related diseases for over 25 years, including the cloning of RYR1 gene in 1989 and the discovery in 2014 of the high-resolution structure of the RyR-1 channel.

Based on fixing the "leak" in the ryanodine receptor/calcium release channels, his research has resulted in a new class of drugs, known as Rycals®, now in Phase Ib clinical trials at the NIH for the treatment of RyR1 myopathy. He is the chair of the SAB for ARMGO Pharma, Inc., a company he founded in 2006 to develop novel therapeutics for diseases related to the ryanodine receptor, and is an inventor of over 20 U.S. patents for these new treatments.

He developed the rapamycin drug eluting coronary artery stents, and has served on SABs of Novartis and Centocor and the NHLBI Council. He designed and teaches a course at Columbia entitled "How to Make a Drug", serves on advisory boards of the Harrington

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Discovery Institute and Gladstone Foundation (UCSF). He has published over 200 peer reviewed articles. He founded SPURS, a summer research program for minority students that has trained over 200 undergraduates over the past 17 years to improve diversity of the biomedical research pipeline.

Since the start of the COVID-19 pandemic he has co-organized the Columbia COVID-19 virtual symposium which has hosted lectures by investigators from Columbia University and around the world.

***Dr. Marks is Chair of The RYR-1 Foundation Scientific Advisory Board.***

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## **Livija Medne, MS, LCGC**

Ms. Livija Medne is a senior genetic counselor in the Divisions of Human Genetics and Neurology and a co-director of the Roberts Individualized Medical Genetics Center (RIMGC) at The Children's Hospital of Philadelphia. For the last 15 years, she has specialized in neuromuscular and neurogenetic disorders and served as a CHOP co-investigator for several clinical research trials and patient registries. As a genetic counselor, her goal is to facilitate accurate and genetically confirmed diagnosis for all children with suspected neuromuscular disorders and other diagnoses. More recently, she has developed expertise in large-scale genomic testing and played a critical role in developing the RIMGC program at CHOP to allow for the incorporation of genomic testing into clinical practice. With an increasing number of testing options and modalities, it is critically important that each and every individual gets access to the right test at the right time. Ms. Medne has developed significant expertise in interpreting genetic testing results for neuromuscular disorders, including RYR1-related myopathies. While many genetic neuromuscular diagnoses still lack targeted therapies, they can be notably better managed and treated when the exact molecular diagnosis is known.

***Ms. Medne is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## **Payam Mohassel, MD**

Dr. Payam Mohassel is an adult neurologist and neuromuscular specialist at the National Institutes of Health (NIH). After his clinical training at Johns Hopkins University, Dr. Mohassel joined the NIH in 2014 to continue research training in muscle disease with Dr. Carsten Bönnemann, who is also a member of the RYR-1 Foundation's Scientific Advisory Board. His research focus in neuromuscular neurogenetic disorders spans gene discovery efforts, pre-clinical studies in cellular and animal models, and early-stage clinical trials. As a clinical neurologist trained in myopathies and muscular dystrophies and experienced in translational research, Dr. Mohassel is passionate about bringing new therapies to individuals with muscle disease such as RYR-1-related diseases. Dr. Mohassel is currently the principal investigator of a phase I clinical trial for RYR-1-related diseases (please see [www.ryr1.org/rycals](http://www.ryr1.org/rycals) for additional details) and was awarded the Young Myologist of the Year award by the World Muscle Society in 2020.

***Dr. Payam Mohassel is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## **Jessica R. Nance, MD**

Dr. Jessica Nance is a pediatric neurologist with specialized training in pediatric neuromuscular disorders. She is an Assistant Professor of Neurology and the Director of the Johns Hopkins Pediatric Neuromuscular Clinical Trials Group. Dr. Nance cares for children and families affected by genetic nerve and muscle diseases in her clinics at The Johns Hopkins Hospital and the Kennedy Krieger Institute in Baltimore, Maryland. She is an investigator in several multi-center, industry-sponsored clinical trials evaluating neuromuscular therapies. Dr. Nance's research focuses on the development and validation of measurements of motor function in patients with neuromuscular disorders.

***Dr. Nance is on the Board of Advisors of The RYR-1 Foundation.***

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## Sheila Riaz, MSc, MD, FRCPC

Dr. Sheila Riaz is a Professor at the Department of Anesthesia, clinician-scientist at Toronto General research institute, and a staff anesthesiologist at University Health Network. Dr. Riaz also directs the only Canadian diagnostic center for malignant hyperthermia (MH), where she assesses at-risk individuals and provides genetic testing and caffeine-halothane contracture test (CHCT). Her research interests include the pathophysiology of MH, links with exertional heat illnesses, and phenotypic variability in MH susceptible patients.

Dr. Riaz has received several teaching and research awards and has secured funding from Canadian and American grant agencies. She is also the chair of the MH International Professional Advisory Council, the board of directors of the MH Association of the United States (MHAUS), and an associate editor at the Canadian Journal of Anesthesia.

***Dr. Riaz is a member of The RYR-1 Foundation Scientific Advisory Board.***

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## Susan Treves, PhD

The main focus of Dr. Susan Treves's laboratory at the University of Basel (Switzerland) is to study intracellular calcium homeostasis in mammalian cells under normal and pathological conditions, with particular emphasis on skeletal muscle excitation-contraction coupling. One of the models she uses to study calcium dysregulation in skeletal muscle is unique to her laboratory since they use biopsy-derived human skeletal muscle cells differentiated into myotubes in vitro. As a result of her PhD work in the laboratory of Professor Tullio Pozzan, one of the pioneers in the development of fluorescent Ca<sup>2+</sup> indicators, she has a broad understanding on the use, pitfalls, and advantages of the available methods to study calcium homeostasis with fluorescent calcium indicators. This expertise coupled with access to patient material has allowed her laboratory to directly assess the effect of mutations in the human ryanodine receptor calcium channel in muscles obtained from patients affected by neuromuscular disorders. Her laboratory applies a broad range of techniques, including cell and tissue culture, molecular biology, cell biology, biochemistry, microscopy and imaging, and fluorescence measurements of intracellular [Ca<sup>2+</sup>].

***Dr. Treves is a member of The RYR-1 Foundation Scientific Advisory Board.***

# The RYR-1 Foundation Grant Recipients —

## Razvan Cornea, PhD

Dr. Razvan Cornea is a molecular biophysicist with extensive experience in basic and translational research of Ca-cycling proteins in muscles. He has received his BS degree from the University of Bucharest – Romania (1988), his PhD. from the University of Minnesota – Minneapolis (1996), followed by postdoctoral studies advised by Dr. Larry Jones at Indiana University – Indianapolis, and Dr. Charles Louis at the University of Minnesota. He is currently an Associate Professor with the University of Minnesota Department of Biochemistry, Molecular Biology, and Biophysics. He is also a Co-Founder and Vice-President for Research at Photonic Pharma LLC, a start-up biotech company focused on technologies for the early-stages of drug discovery. Dr. Cornea leads research that is focused on the development and application of fluorescence-based methods for understanding the structure, function, and dynamics of protein complexes involved in the regulation of intracellular calcium homeostasis, particularly in striated muscle.

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## Jocelyn Laporte, PhD\*

Dr. Jocelyn Laporte leads the research team “Physiopathology of Neuromuscular Diseases” at the IGBMC in Strasbourg, France ([www.igbmc.fr/laporte](http://www.igbmc.fr/laporte)). This international team comprises geneticists, biologists, bioinformaticians, and physicians who contribute with their expert knowledge to a comprehensive research program focused on congenital myopathies. They tackle three main bottlenecks in this field: improving the genetic diagnosis for patients lacking a diagnosis, deciphering the disease mechanism to suggest therapeutic approaches, and validating these therapies through proof-of-concept experiments in laboratory models. Jocelyn and his team have been the vanguards in the field of myotubular myopathy and centronuclear myopathy since 1993. They described the first mutations in the genes MTM1, BIN1, and DNM2, promoted new procedures for DNA analysis, and described several cellular, mouse, and dog models. The team was also involved in the development of several therapies, some of which translated to clinical trials. They also focus on potential therapies common to different congenital myopathies.

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## Joshua Todd, PhD, CCRP

Dr. Joshua Todd completed postdoctoral training as a Visiting Fellow and Research Fellow with the Neuromuscular Symptoms Unit of NINR on preclinical models and clinical trials for RYR1-related myopathies. Dr. Todd was an Investigator on the NAC phase 2 trial and Lead Associate Investigator on the Rycal phase 1 trial. He holds a Staff Scientist (Clinical) position jointly with the NINDS Clinical Trials Unit and Neuromuscular and Neurogenetic Disorders of Childhood Section (Bönnemann Team). His current focus is on translational and clinical development of gene and transcript-directed therapies for rare neurologic disorders.

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## Jacques Tremblay, PhD

Dr. Jacques P. Tremblay received a BSc in Honors Biochemistry from McGill University in 1970, and a PhD in Neuroscience from UCSD in 1974. From 1975 to 1976, he was a postdoctoral fellow at Laval University. Subsequently, he spent his entire career at Laval University where he is currently a full Professor of the Department of Molecular Medicine. He is currently a regular researcher at the Neuroscience Axis of the Research Center of CHUQ. His group has been working on cell and gene therapy treatment for Duchenne Muscular Dystrophy (DMD) since 1987. In 2006, Dr. Tremblay received the Henry Friesen Award from the Royal College of Physicians and Surgeons of Canada for his work on myoblast transplantation as a potential treatment for DMD. Dr. Tremblay's group has also been conducting research on Friedreich's Ataxia since 2010. This disease is due to an elongation of the GAA trinucleotide repeat in intron 1 of the frataxin gene, which reduces expression of this protein. His group demonstrated that it is possible to remove the trinucleotide repetition by cutting with the CRISPR / Cas9 system before and after this repeat. Tremblay's group also uses CRISPR / Cas9 technology to develop a treatment for Alzheimer's disease. This disease is due to the abnormal metabolism of the APP protein (Amyloid Precursor Protein) which leads to the formation of beta-amyloid peptides that form plaques. The formation of these peptides can be greatly reduced by the A673T mutation of the APP gene observed in a small portion of Iceland's population. Dr. Tremblay's group has demonstrated that this mutation could be produced with the CRISPR derived Prime editing technology.

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## Francesco Zorzato, MD, PhD

The research activity of Dr. Francesco Zorzato focuses on questions pertaining to the molecular physiopathology of excitation-contraction coupling of skeletal muscle in normal and diseased condition. Dr. Zorzato cloned cDNA which encoded the ryanodine receptor of skeletal muscle and found pathogenic mutation in pigs susceptible to malignant hyperthermia. This study was a crucial step in identifying the first pathogenic mutation in the human ryanodine receptors in malignant hyperthermia patients and in patients affected by other neuromuscular disorders. Since then, Dr Zorzato continued to research this protein. Initially isolating the affected gene and creating an animal model to develop a potential therapeutic approach to treat congenital myopathies linked to recessive ryanodine receptor mutations.

# Expert Guests

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## Leslie G. Biesecker, MD

Dr. Leslie Biesecker is a Distinguished Investigator, and Director of the Center for Precision Health Research at the National Human Genome Research Institute of the National Institutes of Health, which he joined in 1993. He uses genetic and genomic technologies to study the etiology of genetic disorders and has published over 300 primary research articles, reviews, and chapters and developed the ClinSeq® program, which began clinical genomics research in 2006, before the widespread availability of next generation sequencing. He is double board certified in Pediatrics and Medical Genetics. He was elected to the National Academy of Medicine of the National Academy of Science in 2018 and was the President of the American Society of Human Genetics for 2019.

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## Johann Bohm, PhD

Dr. Johann Bohm is a research director/professor at the French National Institute of Health and Medical Research (Inserm), and is working on rare muscle disorders at the IGBMC in Strasbourg, France. From the beginning, he was particularly interested in rare diseases, and he joined the Institute of Human Genetics in Freiburg (Germany) for a PhD in malformation disorders. He was then seeking for a professional experience abroad and the possibility to study a human disorder in its entirety - from gene identification to the development of therapies. The IGBMC in Strasbourg (France) provided the required scientific environment, and his postdoctoral project in the team of Jocelyn Laporte addressed congenital myopathies. At the beginning of the project, the genetic bases of congenital myopathies were barely known, and they applied innovative sequencing technologies to identify several causative genes and provided a molecular diagnosis for numerous affected families. Through functional experiments in cell models, they investigated the pathomechanisms underlying congenital myopathies. They also generated and characterized mouse models recapitulating the main signs of human disorders, and they established therapeutic approaches preventing and reverting disease development. His work enabled me to publish high-impact articles in scientific journals, present his results at international conferences, and obtain tenure track positions as a research associate (in 2014) and research director (in 2020).

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## Oliver Clarke, PhD

Dr. Oliver Clarke completed his PhD in Melbourne, Australia, where he trained as a crystallographer under Jacqui Gulbis and Brian Smith, investigating conformational changes in a bacterial potassium channel. After completing his PhD, he started my postdoc work in Wayne Hendrickson's lab in 2012, where he learned cryoEM, and applied it to help understand the architecture and gating of the mammalian ryanodine receptor, an intracellular calcium release channel that plays a key role in mediating excitation-contraction coupling. He has continued that work in my own lab, which opened in late 2017, as well as investigating other membrane protein complexes of interest, most recently the erythrocyte ankyrin-1 complex.

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## Susan Hamilton, PhD

Dr. Susan Hamilton is the Chair of the Department of Molecular Physiology and Biophysics at the Baylor College of Medicine, and also serves as Professor in that department. For over 30 years, she has studied excitation-contraction coupling in skeletal muscle and the molecular mechanisms of human diseases related to E-C coupling. In doing so, she has become one of the world's leading experts in the mechanisms underlying the disease processes of malignant hyperthermia (MH) and central core disease (CCD), both of which are related to mutations in the RYR-1 gene. This has led to research for possible therapeutic interventions. Her lab created the first mouse model (a knock-in mutation into RYR-1) of malignant hyperthermia and has also created a mouse model of CCD.

Dr. Hamilton has been the senior author on numerous peer-reviewed publications, and her research has been funded continuously by NIH grants.

Dr. Hamilton is the former Senior Vice President and Dean of Research at the Baylor College of Medicine. She is also the recipient of numerous honors, including membership on the Board of Trustees of the Gordon Research Conference. She was also the recipient of the 2010 Mayerson-DiLuzio Award from Tulane University.

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## Heinz Jungbluth, MD, PhD

Dr. Heinz Jungbluth is a Professor of Paediatric Neurology at King's College London and Consultant Paediatric Neurologist at the Evelina Children's Hospital, Guy's & St Thomas' NHS Foundation Trust, with more than 25 years of clinical experience in Paediatric Neurology and the neuromuscular field.

His main research interest is in early-onset neuromuscular and neurodevelopmental disorders. He has been leading the genetic and phenotypic characterization of congenital myopathies, in particular those affecting excitation-contraction coupling due to mutations in the skeletal muscle ryanodine receptor (RYR1) gene, and related episodic disorders such as malignant hyperthermia (MH) and (exertional) rhabdomyolysis (ERM). He and his group have also introduced the novel concept of congenital disorders of autophagy, a class of inborn neurometabolic and neuromuscular conditions linking aberrant neurodevelopment with common adult-onset neurodegenerative and neuromuscular disorders such as dementia, PD, and ALS.

He has published more than 200 peer-reviewed papers and chapters in key textbooks. He is a member of national and international expert consortia concerned with improving the care and developing therapies for early-onset neuromuscular and neurological disease.

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## Tokunbor Lawal, PhD

Dr. Tokunbor Lawal is a Nurse Scientist with the National Institutes of Nursing Research at the NIH. His work focuses on the functional characterization of *RYR1* genetic variants of uncertain significance using cell- and animal-based models.

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## Angela Lek, PhD\*

Dr. Angela Lek is VP of research at the Muscular Dystrophy Association. She has extensive experience in elucidating the molecular mechanisms of neuromuscular diseases. Dr. Lek completed her PhD at the University of Sydney studying Limb Girdle Muscular Dystrophy, and her postdoctoral training at Boston Children's Hospital and Harvard Medical School studying Facioscapulohumeral Dystrophy. Her work at MDA involves developing a framework to accelerate the translation of gene therapies for ultra rare diseases. In addition to her day job, Angela is also a full-time carer for her husband who has been diagnosed with a neuromuscular disease and she is also passionate about patient advocacy and scientific communication to the patient community.

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## Isabelle Marty, PhD

Dr. Isabelle Marty is a basic scientist, working at INSERM, the French National Institute for Medical Research. She is part of the AFM-Telethon (French Muscular Dystrophy Association) scientific board. She manages a research team "Muscle and Pathologies", at the Grenoble Institute of Neurosciences. This team gathers basic scientists, geneticists, and clinicians, working on muscle pathologies related to defects in muscle calcium release, and more specifically on *RYR1*-related myopathies. The geneticists of the team are among the international references for the identification and analysis of *RYR1* mutations. Two approaches are developed at the research level: research on pathological human muscle, to identify the consequences of *RYR1* mutations, and the development of animal models to uncover efficient therapies.

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### **Eva Michael, MD\***

Dr. Eva Michael is an MD and PhD candidate at Queen Silvia's children's hospital in Gothenburg Sweden. She is a board-certified paediatrician since 2014 and a consultant in paediatric neurology since 2019. She has a special interest in neuromuscular disorders and has been working with the diagnostics and follow-up of paediatric neuromuscular disorders since 2015. She also has an interest in clinical trials and has been a sub-investigator in several international clinical trials for several disorders. Since 2021, she has taken over as principal investigator in all ongoing neuromuscular studies performed at our paediatric clinical research centre.

She is also a PhD candidate with ongoing projects in congenital myopathies. Her interest in clinical trials has led her and her supervisors to designing a smaller clinical trial for this patient group which is currently ongoing.

Her goal is to help her patients come to a correct diagnosis, receive follow-ups according to the international standards of care, and be able to contribute to new knowledge in treating neuromuscular disorders.

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### **Takashi Murayama, PhD\***

Dr. Takashi Murayama has been working on the characterization of RyR/Ca<sup>2+</sup> release channel at the Department of Pharmacology, Juntendo University, Tokyo. His current research focuses mainly to the elucidation of molecular mechanisms of RyR-linked diseases in skeletal muscle and heart. This line of research has recently identified novel drugs for RyR-linked diseases.

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### **Nanna Witting, MD, PhD\***

Dr. Nanna Witting received her medical degree from the University of Aarhus in 1994, delivered her PhD thesis on neuropathic pain 2001, received a Specialist in neurology degree in 2005, and received a diploma in neurology with distinction at the Queen Square Hospital of Neurology, London 2006. Since then, Dr. Witting has worked at Rigshospitalet, Copenhagen as a part-time clinician and part-time researcher focused on myopathies. Dr. Witting has worked on more than 70 peer-reviewed papers.



# Attendees

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## Paul Allen, MD, PhD

Prof. Paul Allen is an Anesthesia Clinician/Scientist who has been working for 40+ years on structure function relationships of RyR1 and the mechanisms associated with Malignant Hyperthermia (MH), a pharmacogenetic disease caused by exposure to anesthetics most commonly caused by mutations of RyR1. He has been NIH funded for 30+ years on these projects and led two 10 year Program Projects on EC coupling and MH. He is currently in Knoxville Tennessee, where he is Director of Anesthesia Research at the Graduate School of Medicine at the University of Tennessee.

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## Yu (Seby) Chen, PhD

Dr. Yu (Seby) Chen is a postdoctoral research fellow in the Van Petegem lab at the University of British Columbia. He is interested in understanding the molecular mechanism underlying human diseases for the development of therapeutics. This involves using biophysical techniques such as X-ray crystallography or cryo-electron microscopy to determine three-dimensional structures of proteins involved in human diseases. His current research focuses on structural and functional studies of RyR1 by pharmacological modulators.

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## Kookjoo Kim

Kookjoo received his BS degree in Pharmacology and Toxicology from the University of Wisconsin-Madison. He is interested in structural characterization of RyR1 ligand gating using cryoEM. When he is not in the lab, he enjoys trying out new foods from different cultures, taking pictures, and going on hikes outside of New York City.

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## Huan Li, PhD

Dr. Huan Li is an associate research scientist in the anesthesiology department of Columbia University Irving Medical Center (CUIMC). She obtained her PhD degree at the University of Chinese Academy of Science. During her PhD, she was studying the antiarrhythmic mechanism of compounds that interact with ion channels. She started her post doc in 2018 and began to work on the structure of membrane protein using cryo-EM. Currently, she is working on the structure and function of Ryanodine Receptors.

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## Stefan Nicolau, MD

Dr. Stefan Nicolau completed his medical education and neurology residency at McGill University, followed by a fellowship in Neuromuscular Medicine at Mayo Clinic. He joined Nationwide Children's Hospital in 2020 as a Gene Therapy fellow. His research interests include the characterization of rare and ultra-rare inherited myopathies, as well as the establishment of genotype-phenotype correlations in Duchenne muscular dystrophy and the development of gene editing approaches to correct mutations in Duchenne muscular dystrophy.

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## Thomas O'Connor

Thomas O'Connor is from Buffalo, NY. He received his undergraduate degree in biotechnology from the University at Buffalo. He is currently pursuing a PhD in Genetics at the University of Rochester in the lab of Dr. Robert Dirksen. His research is focused on implementing endurance exercise as a means to mitigate and/or delay onset of disease. His work has involved studying juvenile irradiation, aging, tubular aggregate myopathy, RYR-1-related diseases, and dementia. He will be graduating and looking for employment in the spring of 2023.

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## Helga Silva, MD, PhD\*

Dr. Helga Cristina Almeida da Silva has graduated in Medicine (Medical School, Federal University of Bahia – Brazil, 1989), specialization in Neurology (Medical School, University of São Paulo - Brazil, 1994), PhD in Pathological Anatomy and Clinical Pathology (Medical School, University of São Paulo - Brazil, 1999) and post-PhD at Biophysics (Medical School, Federal University of São Paulo – Brazil, 2002).

She is a professor from Medical School, Federal University of São Paulo – Brazil and a member of the board of directors of the European Malignant Hyperthermia Group. She works as a physician, graduation/post-graduation professor, and coordinator of CEDHIMA (Brazilian Center of Study Diagnosis and Investigation of Malignant Hyperthermia).

She has experience in Medicine, focusing on Neurology, acting on the following subjects: malignant hyperthermia, central core disease, neuromuscular disorders, skeletal muscle pathology, and motor neuron disease (amyotrophic lateral sclerosis and post-polio syndrome).

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## Monika Sztretye, PhD

Dr. Monika Sztretye received her MSc diploma from the University of Oradea (Romania) in 2005. Between the years 2005-2007, she was awarded an international fellowship and joined the European Research Training Network on skeletal muscle financed by the European Union 5th Framework at the University of Debrecen (Hungary) under the mentorship of Prof. Dr. László Csernoch. In 2010, she was awarded the PhD degree in Biomedical Sciences with highest honors from the University of Debrecen. Between the years of 2007-2011, she was a postdoctoral fellow at Rush University Chicago (USA) in the laboratory of Dr. Eduardo Rios. In 2011, she returned to Debrecen and she is currently a full time research associate supervising two PhD students. In 2014, she was awarded a SCIEX fellowship and spent eight months at the University of Basel in Dr. Susan Treves' laboratory.

She has substantial experience with skeletal muscle excitation-contraction coupling and knowledge in RyR1 physiology, regulation, and pharmacology. Dr. Sztretye has done in vivo electroporation, confocal calcium imaging synchronized with whole-cell patch clamp, and measurements of intracellular calcium transients, calcium sparks, and mitochondrial dynamics in skeletal muscle fibers.

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## Luuk Van den Bersselaar, MD

Dr. Luuk van den Bersselaar is a Medical Doctor and PhD student at the Malignant Hyperthermia Investigation Unit at the Canisius Wilhelmina Hospital, Nijmegen, the Netherlands and the Department of Neurology at the Radboud University Medical Centre, Nijmegen, the Netherlands. His research mainly focuses on the neuromuscular phenotype of patients with RYR1-related malignant hyperthermia susceptibility and/or exertional rhabdomyolysis.

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## Yong-Xiao Wang, MD, PhD

Dr. Yong-Xiao Wang has been a Full Professor in the Department of Molecular and Cellular Physiology at Albany Medical College since 2006. Dr. Wang obtained his MD at Wannan Medical University and PhD at Fourth Military Medical University. He received his post-doctoral training at the Technology University of Munich and at the University of Pennsylvania.

His research interests are mainly focusing on basic, translational and drug discovery research in respiratory and cardiovascular biology and diseases, specifically on ryanodine receptor calcium release and other relevant ion channels, cell calcium, redox and other signaling. He has had numerous publications in highly peer-reviewed journals including Nat Commun, 2020; Proc Natl Acad Sci USA, 2009; Nature, 2002; and Circ Res, 1995.

His research team has explored the potential important functional contributions and molecular mechanisms of RyR1 in smooth muscle biology and diseases. Thus, the current RYR-1-Related Diseases International Research Workshop will significantly impact and improve our ongoing and future research projects, by which the findings may not only substantially increase our current knowledge on the functional importance of RyR1 in smooth muscle biology and diseases, but also help to develop new and more effective drugs and biologics specific for RyR1-linked smooth muscle diseases.

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### **Emily Wires, PhD**

Dr. Emily Wires's research focuses on altered cellular proteostasis as a consequence of ER/SR calcium dysregulation. She received her PhD in November 2016 from University of Maryland, Baltimore. Emily completed her NIH postdoctoral fellowship in 2021, during which she received an NIH Bench to Bedside Award seeking to identify potential biomarkers of RYR1-related diseases (manuscript in press). Additionally, in collaboration with the National Center for Advancing Translational Sciences (NCATS), she helped investigate the ability of FDA-approved drugs to stabilize ER/SR proteome. Emily also created the mouse models of RYR-1-related diseases spreadsheet. In her spare time, she enjoys running, cycling, and keeping up with her two young children.

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### **Melissa Wright, MD, PhD**

Dr. Melissa Wright is a physician-scientist with a specialty in pediatric neuromuscular disease. Dr. Wright began her training through MSTP program at the University of Colorado, where she completed a PhD thesis on the influence of early electrical activity in the development and plasticity of dorsal root ganglia neurons and motor neurons. Through her PhD work and her experiences in medical school she began to focus on pediatric neuromuscular disease and completed a residency in Pediatric Neurology at the University of Colorado followed by a clinical fellowship in Neuromuscular Medicine at Washington University. She is now an Assistant Professor of Pediatrics in the Section of Child Neurology at the University of Colorado with her clinical practice at Children's Hospital Colorado. Her basic science research focuses on developing models for rare congenital myopathies, particularly triadopathies such as RYR1-related myopathy, and her clinical work focuses on pediatric neuromuscular disorders with an emphasis on rare congenital myopathies and muscular dystrophies. She currently cared for about 15 patients with RYR1-related myopathy. She is working to build a center with both clinical and scientific excellence in congenital myopathies and muscular dystrophies.

# RYR-1 Community Representatives

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## Orlando Carneiro

Orlando Alves Carneiro Jr, 59, is Brazilian, married, graduated in business administration, and partner director of Vera Cruz Holding, a family company, which has investments in mining, agriculture, cattle raising, and real estate sectors. He lives on a daily agenda basis focused on work, family, and maintaining his physical condition. Orlando lived a great part of his life without knowing what was progressively affecting his physical condition, but at age 44 he was diagnosed with recessive Centronuclear Congenital Myopathy, caused by a mutation in the *RYR1* gene.

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## Robert Hanich, MD

Dr. Robert Hanich retired as a cardiologist with Asheville Cardiology Associates, a 39 physician group serving Western North Carolina. He holds an AB (Harvard College) and MD (University of Pennsylvania), completing his Internal Medicine residency and Cardiovascular Disease fellowship from Penn and Johns Hopkins, respectively. He retired medically in 2019 secondary to an RYR-1-related disorder after thirty years as an electrophysiologist and interventional cardiologist.

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## Lauren Heft

Lauren Heft is the parent of a child with RYR-1 myopathy. Her son Charlie is 11 years old and was diagnosed at age 5 with RYR-1 myopathy caused by a de novo mutation. She lives with her family in Dublin, Ohio and for the past nine years she has been a stay-at-home parent. She and her husband Bryan are proud supporters of The RYR-1 Foundation and its mission.

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## Jacqueline Hoffman-Anderman

Jackie is a registered nurse who currently works for Serenity Mental Health Care Centers as a Telehealth RN. She previously worked as an outpatient infusion nurse and an inpatient hospital nurse for 10 years specializing in Gynecological-Oncology at both the Hospital of the University of Pennsylvania and Banner University Medical Center- Phoenix. Jackie has participated in legislative advocacy, meeting with local, state, and federal representatives to promote community accessibility and rare disease research legislation in her home state of Arizona. She is the mother of Maddie, who is affected by recessive RYR-1 Related Myopathy.

***Jackie is on the Board of Advisors of The RYR-1 Foundation.***

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## Laurie Jones

Laurie Jones is from Ponoka, Alberta, Canada. She is the third generation in her family diagnosed with Central Core Disease and Malignant Hyperthermia. Her family's journey to a diagnosis of Central Core Disease started before she was born after her dad and his youngest sister had malignant hyperthermia reactions during surgery.

For the past 15 years, she has worked part-time as a Social Worker.

Her family has been grateful for the support of Muscular Dystrophy Canada over the years. They have been active Chapter members and fundraisers.

She enjoys reading, watching movies and researching her family tree in my spare time. She is a big hockey fan, with the Edmonton Oilers being her favorite team. She especially enjoys escaping the cold prairie winters for trips to much sunnier destinations.

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## Sofia Leon

Sofia Leon comes from a large family in Mexico City with more than 25 members affected with CCD. Moved to Austin, TX in 1983 and has two children, one of them, Tommie Leon, with CCD. In 1995, she began working with Dr. Susan Hamilton, head researcher at Baylor School of Medicine and brought to her multiple blood samples of family members which allowed researchers to find where was the mutation that caused CCD.

***Sofia is on the Board of Advisors of The RYR-1 Foundation.***

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## Courtney Perrin

Courtney Perrin is affected with RYR-1. Currently, she has no official known diagnosis related to her RYR-1 whole-exome sequence results. Courtney is in the process of earning her bachelor's degree in molecular biology and Spanish to one day become a genetic counselor. With the help of her family and her community, the Perrin Family has raised over \$30,000 in five-cent bottles and can redemptions to donate to The RYR-1 Foundation. It is important for Courtney to return the support The RYR-1 Foundation has always given to her. Courtney enjoys public speaking and has spoken on behalf of the Muscular Dystrophy Association to educate people about her rare muscle disease. Courtney is a second degree black belt in karate, which she was encouraged to take by a specialist to strengthen her core. In her free time, Courtney has a passion for music and enjoys playing electric and acoustic guitars. Courtney also loves to read and always has a book in her hand. Her favorite books are Crime and Punishment by Fyodor Dostoevsky and The Phantom of the Opera by Gaston Leroux. Courtney loves animals and has two dogs: a corgi (Ellie) and a dachshund (Stanley). Recently, Courtney just returned from going cross-country with her family and enjoys camping and seeing new sights.

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## Avi Swerdlow\*

Avi Swerdlow is a product manager at YouTube. Before moving into tech, Avi worked on the creative side of the film industry at Walt Disney Pictures and Sony Pictures Entertainment. He received his masters from the University of Southern California and his bachelor's degree from Brandeis University. Avi lives in Atlanta with his wife, Hadar, and daughter, Noa.

***Avi is on the Board of Advisors of The RYR-1 Foundation.***

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## Matthew Tompkins, PhD

Dr. Matthew L. Tompkins, PhD, is the Chief Operating Officer for TC Defense in Arlington, VA where he works as a Consultant for Naval Weapon Systems. Matthew has spent more than 20 years in the field of Science and Technology for Naval Systems. He is an Editorial Board Member for IEEE Transactions on Engineering Management and enjoys conducting research and doing peer reviews for research. Matthew is also an Adjunct Professor at The George Washington University School of Engineering and Applied Science. Matthew has several family members who are affected by RYR-1 and is passionate about finding solutions that provide support for those suffering from RYR-1.

***Matt is on the Board of Advisors of The RYR-1 Foundation.***

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## Mary Wright

Mary Wright is 80 years old and was born in 1942 in Lewiston, Idaho. She is the Mother of two, grandmother of five, and great grandmother of two. Thanks to a muscle biopsy, she knows for certain neither of her sons have Central Core Disease. She is the only CCD patient in her family going back to her great grandparents. She was the oldest attendee at the first RYR-1 International Family in 2016.

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She flew by herself from Boise, Idaho (leaning on a walker). And for the first time she met others with CCD. She wasn't alone!

A "war baby" (the Japanese had bombed Pearl Harbor four months before she was born), the delivery doctor left for War the day after she was born and never talked to her mother about the delivery. It was obvious there was a problem, but no one was available to answer questions. It was up to her parents to do their best, with her mother bearing the brunt of the burden of a child who wasn't walking or meeting other benchmarks of development. (Her mother always said she did talk early and in complete sentences!)

In 1970 at age 27 she was diagnosed at Ann Arbor University Hospital in Michigan and met Dr. Shy. (Dr. G. Milton Shy and Dr. Kenneth R. McGee had named the disease in 1956.) Dr. Joel Saper (later authored "Central Core Disease—A Congenital Myopathy" published in Nov 1976 in Diseases of the Nervous System) who was her doctor indicated it wasn't progressive or life shortening. Consensus was that CCD was dominantly inherited but here she was, the exception! No family history and her sons' muscle biopsies were negative. Her luck was that her Air Force husband happened to be stationed in Michigan and her doctors had referred me to Ann Arbor, where Dr. Shy was on staff.

To show how little she knew, in 1979 she just happened to pick up an MDA pamphlet and found Central Core Disease listed in the Jerry Lewis Family! She called the MDA Idaho office, got an MDA Clinic appointment, and most importantly began a life-long subscription to their magazine, Quest. Before gall bladder surgery in 2000, she was able to alert my anesthesiologist about the Malignant Hypothermia risk among CCD patients thanks to Quest information. And now, just like everyone else here, she wants to know more!

# Industry Support

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## Michael Greenberg, MD

Mike Greenberg, MD, an emergency physician by training, is the Vice President of Medical Affairs at Eagle Pharmaceuticals where he focuses heavily on hyperthermic/hypermetabolic diseases including malignant hyperthermia. In addition to his experience as an emergency physician and medical affairs professional, Dr. Greenberg has also worked with the Federal Agency for Healthcare Research and Quality (AHRQ) to raise awareness of comparative effectiveness research, and as acting as a consultant to teams focusing on Risk Evaluation and Mitigation Strategies (REMS) and Drug Safety Communications at the FDA Center for Drug Evaluation and Research (CDER). Mike earned his medical degree at the State University of New York Upstate Medical University and completed a residency in Emergency Medicine at the University of Massachusetts.



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