



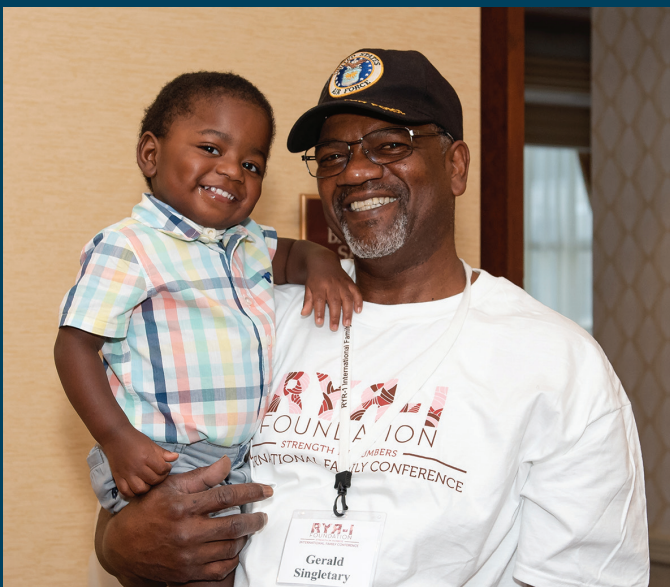
**SUPPORTING RESEARCH TO FIND A CURE  
FOR RYR-1-RELATED DISEASES**

**Global Headquarters**

P.O. Box 13312, Pittsburgh, PA 15243 | (412) 529-1482

[www.ryr1.org](http://www.ryr1.org)







## Dear Friends,

Although rare, RYR-1-related diseases (RYR-1-RD) are the most common form of “congenital myopathy” -- muscle disease caused by a genetic mutation. The most common manifestations include: mild-to-moderate muscle weakness (e.g., difficulty climbing stairs), severe weakness (e.g., requiring wheelchair assistance and breathing support), muscle cramping and pain, rhabdomyolysis (severe muscle breakdown that can lead to multi-organ failure), and a potentially fatal reaction to anesthesia, called malignant hyperthermia. Yet, despite the prevalence of this disease and the severity of these symptoms, The RYR-1 Foundation is the only organization that exists solely to support RYR-1-RD. Therefore we fund, promote, and highlight research in this area. Further, The RYR-1 Foundation serves the needs of and advocates for individuals and families affected by RYR-1-RD.

In a very short period of time, The RYR-1 Foundation has become a leader in the field of RYR-1-RD.

Due to the support of our many generous benefactors, the organization’s work has led to important breakthroughs in scientific knowledge. In addition, we have formed a worldwide community of affected individuals who can find comfort and support with the knowledge that they are not alone and that our organization now exists to help them.

The need for treatments or a cure is urgent. With your support, The RYR-1 Foundation can continue to fund world-renowned scientists, expand the RYR-1 community, and make our slogan, “Strength in Numbers,” a reality.

Sincerely yours,



**Michael F. Goldberg, MD, MPH**  
President, Co-Chair of Research, & Co-Founder  
The RYR-1 Foundation



To learn more about the story of The RYR-1 Foundation and the work we are doing, please visit our website at:

**[www.ryr1.org](http://www.ryr1.org)**.



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# Supporting Research

One major program of The RYR-1 Foundation is to support both basic science and clinical research of RYR-1-related diseases. Funding research gives us the best chance to find a treatment or a cure. This has already led to important advances in knowledge and potential therapies. To learn more about the research The RYR-1 Foundation has funded, please visit: [www.ryr1.org/grants](http://www.ryr1.org/grants).

The RYR-1 Foundation grant recipients include:

**“FUNCTIONAL AND PHARMACOLOGICAL CHARACTERIZATION OF THE T4709M MUTANT RYANODINE RECEPTOR AT SINGLE-CHANNEL LEVEL”**

János Almássy, PhD, University of Debrecen (Hungary)

**“DRUG DISCOVERY FOR RYR-1 MYOPATHIES USING ZEBRAFISH MODELS”**

Alan Beggs, PhD, Harvard University (United States)

**“HIGH-THROUGHPUT SCREENS TO DISCOVER NOVEL MODULATORS OF DYSFUNCTIONAL RYR-1 CHANNELS FOR THERAPEUTIC DEVELOPMENT”**

Razvan L. Cornea, PhD, University of Minnesota (United States)

**“CAS9-MEDIATED POINT MUTAGENESIS OF RYR-1”**

James Dowling, MD, PhD, University of Toronto (Canada)

**“DRUG DISCOVERY AND VALIDATION FOR RYR-1-RELATED MYOPATHIES”**

James Dowling, MD, PhD, University of Toronto (Canada)  
and Robert Dirksen, PhD, University of Rochester (United States)

**“DEVELOPING ANIMAL MODELS WITH AN RYR-1 MUTATION AND CLINICAL PHENOTYPE FOR THE PURPOSE OF EVALUATING CELL AND MOLECULAR MECHANISMS OF RYR-1 DISEASE”**

Angela Dulhunty, MD, PhD, Australian National University (Australia)

**“THE PREVALENCE OF RYR1-RELATED DISEASE – AN INTERNATIONAL, COLLABORATIVE MULTICENTRE STUDY”**

Heinz Jungbluth, MD, PhD, King’s College (England)

**“RYR-1 MYOPATHY DATABASE”**

Alexander Kushnir, MD, PhD, Columbia University (United States)

**“TARGETED REMOVAL OF PATHOGENIC RYR-1 ALLELES”**

William R. Lagor, PhD, Baylor College of Medicine (United States)

**“THERAPEUTIC PROOF-OF-CONCEPTS FOR RYR1-RELATED MYOPATHY”**

Jocelyn Laporte, PhD, Institute of Genetics and Molecular and Cellular Biology (France)

**“ASSESSMENT OF THE ABILITY OF SMALL MOLECULE RYR-1 MODULATORS TO CORRECT THE CA<sup>2+</sup> FLUXES IN SKELETAL MUSCLE FIBERS WITH RYR-1 MYOPATHY”**

Bradley S. Launikonis, PhD, The University of Queensland (Australia)

**“RYCAL TREATMENT IN RYR-1-RELATED MYOPATHY MUSCLE BIOPSIES”**

Andrew Marks, MD, Columbia University (United States)  
and Katherine Meilleur, PhD, CRNP, NIH, formerly (United States)

**“MITOQUINOL MESYLATE AND N-3 POLYUNSATURATED FATTY ACIDS: A NOVEL THERAPEUTIC APPROACH FOR RYR-1 RELATED MYOPATHY”**

Joshua J. Todd, PhD, CCRP, NIH (United States)

**“PRIME EDITING CORRECTION OF THE T4709M MUTATION RESPONSIBLE FOR SOME CASES OF RYANODINE RECEPTOR TYPE 1 (RYR1) RELATED MYOPATHIES (RYR1 RM)”**

Jacques Tremblay, PhD, Laval University (Canada)

**“TREATMENT OF AN ANIMAL MODEL CARRYING RECESSIVE RYR1 MUTATIONS WITH HDAC/DNA METHYLTRANSFERASE INHIBITORS”**

Susan Treves, PhD, and Francesco Zorzato, PhD, University of Basel (Switzerland)

**“STRUCTURAL INVESTIGATION OF DISEASE-ASSOCIATED MUTATIONS IN THE RYANODINE RECEPTOR PORE AND EF HAND REGION”**

Filip Van Petegem, PhD, University of British Columbia (Canada)

**“A HOT DEBATE: THE ROLE OF RYR1 IN EXERTIONAL HEAT-ILLNESSES”**

Nicol Voermans, MD, PhD, Radboud University (The Netherlands)



# Rycal Treatment in RYR-1-Related Myopathy Muscle Biopsies

In 2016, The RYR-1 Foundation awarded a grant of \$80,000 to Dr. Andrew Marks, Chairman of the Department of Physiology and Cellular Biophysics at Columbia University, and Dr. Katherine Meilleur, former Assistant Clinical Investigator at the National Institute of Nursing Research, for their research project entitled “Rycal Treatment in RYR-1-Related Myopathy Muscle Biopsies.”

Dr. Marks discovered Rycals, a class of drugs that reverses the calcium “leak” in muscle cells with RYR-1 mutations. The grant from The RYR-1 Foundation allowed researchers to assess the effect of Rycals on samples of muscle biopsies taken from individuals affected by RYR-1-RD. The results of their study showed that Rycals not only reversed the calcium leak in those human muscle biopsies, but also repaired muscle damage and improved muscle function.

The data from this project served as the basis for and justification of a human clinical trial at the National Institutes of Health (NIH). This trial demonstrated that this drug was well-tolerated by the trial participants, with no report of serious adverse events. There is also early and preliminary evidence that some subjects demonstrated increased strength while on the drug. In hopes of confirming this, early enrollees in the trial, who received a low dose of the drug, returned to the NIH to receive a higher dose. The trial has now concluded, and results were presented at the annual meeting of the World Muscle Society in October 2022. Following the conclusion of the clinical trial, a Dutch venture capital firm, Forbion, invested \$35 million in ARMGO.

In addition to funding Rycal research, The RYR-1 Foundation played an important role in advocating for the initiation of this trial. In 2019, the Rycal trial was at risk of being permanently terminated. Working closely with ARMGO Pharma, Inc. (Rycal manufacturer) and contacts at the NIH, The RYR-1 Foundation immediately initiated a phone call and letter writing campaign, ultimately soliciting the invaluable assistance of members of the United States Senate and House of Representatives. It is clear that were it not for the successful advocacy efforts of The RYR-1 Foundation, this trial would not have been initiated. For more information on the vital role The RYR-1 Foundation played in this clinical trial, please go to: [www.ryr1.org/our-impact/rycals](http://www.ryr1.org/our-impact/rycals).

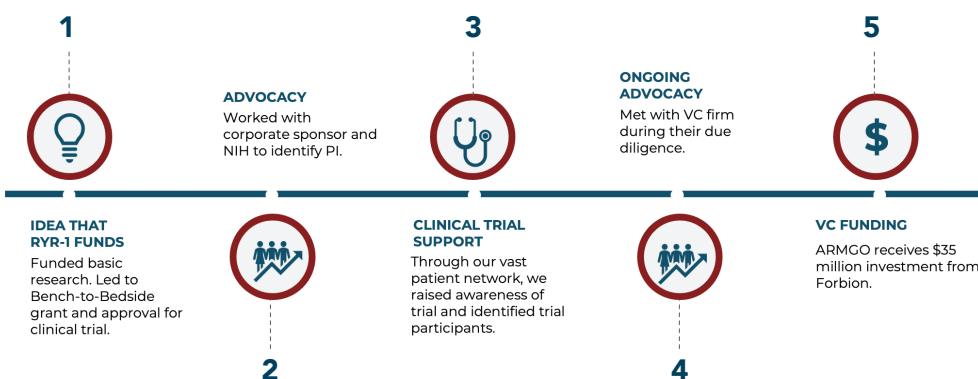


## ARMGO Pharma raises \$35 million to progress clinical studies of lead molecule ARM210 in cardiac and skeletal muscle diseases

December 20, 2021 07:00 ET | Source: ARMGO

ARMGO Press Release, dated December 20, 2021, announcing \$35 million investment from Forbion to progress clinical studies of lead molecule ARM210 in cardiac and skeletal muscle diseases.

## The RYR-1 Foundation's Role in Drug Development



The RYR-1 Foundation played a key role at all stages in development of Rycals for RYR-1-related diseases. This collaborative approach with numerous stakeholders (academia, biotech industry, investors, and regulators) is a model that we hope to replicate with other promising therapies.



# Scientific Advisory Board

The Scientific Advisory Board (SAB) of The RYR-1 Foundation is a group of the world's leading authorities in RYR-1-related diseases. The SAB determines the research priorities of The RYR-1 Foundation. Meetings of the SAB occur on a biannual basis to evaluate grant applications, evaluate ongoing funded research, and discuss future research strategies.



Attendees of a meeting of The RYR-1 Foundation's Scientific Advisory Board. Participants included representatives from academia, the pharmaceutical industry, NIH, and patient advocacy organizations.

## ANDREW R. MARKS, MD (CHAIR) - Columbia University, United States

Dr. 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. Andrew Marks giving a lecture at an RYR-1 International Family Conference on Rycals, a drug that he discovered. The RYR-1 Foundation has helped support the development of the Rycal program (please see page 3 for more details).

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 the RYR-1 gene in 1989 and the discovery in 2014 of the high-resolution structure of the RYR-1 channel.

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Based on fixing the “leak” in the ryanodine receptor/calcium release channels, his research has resulted in a new class of drugs, known as Ry-

cals®, which was the subject of a human clinical trial at the NIH. 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 on 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” and serves on advisory boards of the Harrington 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.

### **CARSTEN G. BÖNNEMANN, MD, habil - National Institutes of Health (NIH), United States**

Dr. 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 the Childhood Section of the National Institute of Neurological Disorders and Stroke at the National Institutes of Health in Bethesda, MD.

Dr. Bönnemann is also Adjunct Professor of Neurology at the University of Pennsylvania and the Children’s Hospital of Philadelphia (CHOP). 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 to 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. Carsten Bönnemann gives an overview of RYR-1-related diseases at an RYR-1 International Family Conference.



Dr. Robert Dirksen discusses the role of calcium in RYR-1-related diseases at an RYR-1 International Family Conference.

### **ROBERT T. DIRKSEN, PhD - University of Rochester, United States**

Dr. 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 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-related diseases.



His work has been funded by the National Institutes of Health and the Muscular Dystrophy Association, among others. He has published over 80 original research articles in leading scientific journals. Dr. Dirksen is currently the Past-President of the Society of General Physiologists and 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 so important to The RYR-1 Foundation—his discoveries on how muscle cells with RYR-1 mutations function have helped many other scientists around the world!”

#### **RYR-1 INTERNATIONAL FAMILY CONFERENCE ATTENDEE**

#### **JAMES DOWLING, MD, PhD - University of Toronto/Hospital for Sick Children, Canada**

Dr. 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-related diseases. His research spans the continuum from new gene discovery to disease pathogenesis to therapy development. He is engaged in both targeted and unbiased drug discovery for RYR-1-related diseases. 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.

#### **JOHANNA LANNER, PhD - Karolinska Institutet, Sweden**

Dr. 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 disease.

Dr. Lanner 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.



Ms. Livija Medne, a genetic counselor, giving an introductory lecture on genetics at an RYR-1 International Family Conference.

### LIVIJIA MEDNE, MS, CGC - Children's Hospital of Philadelphia, United States

Ms. 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 (CHOP). 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 diagnoses 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 incorporation of genomic testing into clinical practice. With increasing numbers 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 RYR-1-related

diseases. While many genetic neuromuscular diagnoses still lack targeted therapies, they can be better managed and treated when the exact molecular diagnosis is known.

### PAYAM MOHASSEL, MD - Johns Hopkins University, United States

Dr. Mohassel is an Associate Professor of Neurology at Johns Hopkins University School of Medicine. After his clinical training at Johns Hopkins University, Dr. Mohassel joined Dr. Carsten Bönnemann's group at the NIH for eight years before he was recruited back to Johns Hopkins. His research focus in neuromuscular neurogenetic disorders spans gene discovery efforts, pre-clinical studies in cellular and animal models, and early-stage clinical trials. Dr. Mohassel was the principal investigator of a phase I clinical trial for RYR-1-related diseases (please see page 3 for additional details). He was awarded the Young Myologist of the Year award by the World Muscle Society in 2020 and The RYR-1 Foundation's 2022 Clinician of the Year Award.



Dr. Payam Mohassel (left) with Dr. Morton F. Goldberg (center) and Dr. Michael F. Goldberg (right). Dr. Mohassel received the Clinician of the Year Award at the 2022 RYR-1 International Family Conference.



Dr. Sheila Riaz, an anesthesiologist who specializes in malignant hyperthermia, giving a lecture at an RYR-1 International Family Conference.

### SHEILA RIAZI, MSC, MD, FRCPC - University of Toronto, Canada

Dr. 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.

### **SUSAN TREVES, PhD - University of Basel, Switzerland**

The main focus of Dr. Treves's laboratory at the University of Basel in 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, because she uses 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 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, imaging, and fluorescence measurements of intracellular [Ca<sup>2+</sup>].

### **FILIP VAN PETEGEM, PhD - University of British Columbia, Canada**

Dr. Van Petegem is a Professor in the Department of Biochemistry and Molecular Biology at the University of British Columbia (UBC) in 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 (Ca<sub>v</sub>), 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 ultra-structures of these channels, allowing his lab to peer into the direct effects of the disease mutations on these structures.

Dr. Van Petegem has received New Investigator Awards from the Canadian Institutes of Health Research (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.

## NICOL C. VOERMANS, MD, PhD - Radboud University, The Netherlands

Dr. Voermans's research at the Radboud University Medical Centre in The Netherlands focuses around genotype-phenotype comparisons 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 are 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 RYR-1-related diseases. 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 focused on the wide spectrum of RYR-1-related diseases throughout life, including intermittent phenotypes such as exertional rhabdomyolysis. She is a medical advisor to 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, SEPN1-related myopathies, and facioscapulohumeral muscular dystrophy (FSHD)). Her research in these myopathies has increased the knowledge of genotypes and phenotypes, natural history, and outcome measures, all of which are crucial for future trials.



The RYR-1 Foundation President Dr. Michael Goldberg is joined by members of The RYR-1 Foundation Scientific Advisory Board and Dr. Susan Hamilton in Naarden, Netherlands at the RYR-1 Workshop of the European Neuromuscular Centre. This workshop was co-sponsored by The RYR-1 Foundation.

From left to right: Dr. Robert Dirksen, Dr. James Dowling, Dr. Susan Hamilton, Dr. Michael Goldberg, and Dr. Andrew Marks.





Dr. Ronald Litman, former Vice President of the Malignant Hyperthermia Association of the United States, speaking at a patient "Q & A" session at the 2016 RYR-1 International Family Conference.



Dr. Sheila Riazzi (center), member of The RYR-1 Foundation Scientific Advisory Board, at an RYR-1 International Family Conference.



## Other Major Programs



### PATIENT REGISTRY

Developing a registry of patients with RYR-1-RD is critical for research, as it allows physicians to learn about the natural history of these disorders. Furthermore, as any potential therapy must be tested in a clinical trial prior to FDA approval, having a patient database is essential in encouraging pharmaceutical companies to develop therapies for this “orphan disease.”

### RYR-1 RESEARCH MEETINGS

International research meetings are essential for the dissemination of new scientific discoveries. They are also important for networking and the sharing of ideas among clinicians, basic science researchers, and the pharmaceutical industry. The RYR-1 Foundation has sponsored various meetings, including: Gordon Research Conference, World Muscle Society, International Congress on Neuromuscular Diseases, and European Muscle Conference. The RYR-1 Foundation has also co-hosted and sponsored a meeting at the European Neuromuscular Centre, specifically on RYR-1-RD.

In addition, The RYR-1 Foundation hosts biannual meetings of the Scientific Advisory Board (SAB). In July 2022, The RYR-1 Foundation hosted a two-day patient-led research workshop with over 45 in-person attendees from around the world (please see page 17 for more details). These are critically important forums for the world’s leading RYR-1 researchers and clinicians to share research, to collaborate, and, ultimately, to advance the field of RYR-1-RD.

### FACILITATING COLLABORATIONS BETWEEN BIOTECH AND THE RYR-1 COMMUNITY

Importantly, The RYR-1 Foundation is focusing its efforts not only in supporting research at academic centers, but also in the biotech industry. Several biotech companies have recently approached The RYR-1 Foundation about applying their technology to RYR-1-RD. Several of these companies have made presentations to The RYR-1 Foundation’s SAB to receive invaluable feedback from the world’s leading RYR-1 experts. Facilitating these kinds of interactions between the biotech industry, academia, and the RYR-1 community will be the key to expediting the development of effective therapies.

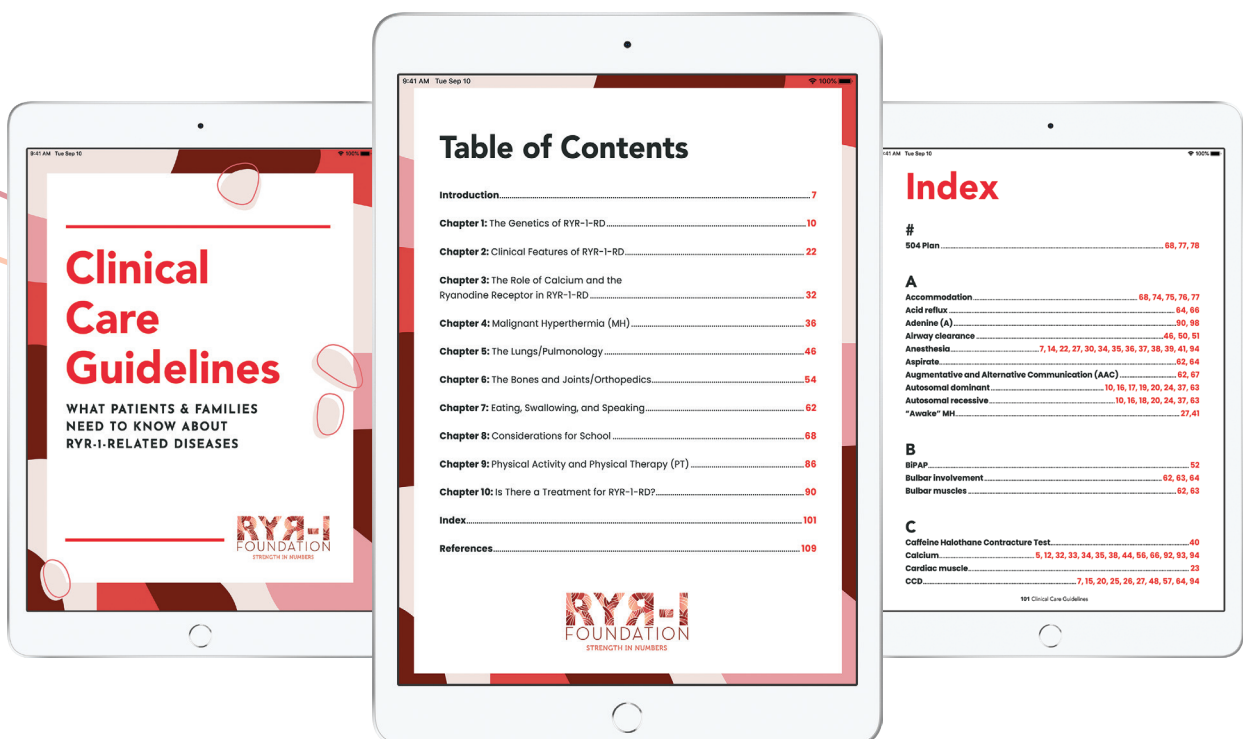


# Clinical Care Guidelines: What Patients and Families Need to Know About RYR-1-Related Diseases

In September 2020, The RYR-1 Foundation published the long-awaited *Clinical Care Guidelines (CCG)*, made possible by a \$50,000 grant from The Oscar and Elsa Mayer Family Foundation. These guidelines were written exclusively for individuals and families affected by RYR-1-RD. The CCG has over 100 pages of original content that will help the RYR-1 community better understand RYR-1-RD. This free online handbook utilizes numerous educational graphics and illustrations. Many topics are covered, including the role of calcium in RYR-1-RD, modes of genetic inheritance, and potential therapies. Each chapter contains a link to extensive online resources that The RYR-1 Foundation has provided. **A copy of the CCG is freely available and easily downloadable at [www.ryr1.org/clinical-care-guidelines](http://www.ryr1.org/clinical-care-guidelines).** On this webpage, there is also a brief video that introduces the CCG. To maximize the impact of the CCG on the international RYR-1 community, it has been translated into the following languages: Arabic, Chinese (Simplified), English, French, German, Russian, Spanish, and Vietnamese.

"I've found the site so informative - the most informative information I've found... I've read the *Clinical Care Guidelines* and have been digging into all the resources on your website. I plan on providing the guidelines and a number of other resources to our primary care providers so they can be more knowledgeable."

## INDIVIDUAL AFFECTED BY AN RYR-1-RD







# RYR-1 International Family Conferences

To date, The RYR-1 Foundation has held three RYR-1 International Family Conferences. Combined, these events have hosted over 550 attendees, representing 150 RYR-1-affected families from ten countries. These conferences are unique opportunities for affected individuals and families to meet, form friendships, and develop a true RYR-1 community.

For a rare condition like RYR-1-related diseases, providing a forum for affected individuals and families to meet others like them has significant psychological value. When an affected individual or their family members seek to find someone else who understands what they are experiencing, a family conference becomes an invaluable and necessary resource. It is a goal of The RYR-1 Foundation to enhance and enrich these relationships within the RYR-1 community by continuing to host RYR-1 International Family Conferences.

To view a documentary about the RYR-1 International Family Conferences, please go to: [www.ryr1.org/family-conferences](http://www.ryr1.org/family-conferences).

Below: Photos from prior family conferences.



“We are extremely grateful for this conference and the opportunity to meet other families who have a member with this disability and to be understood. We are especially thankful for the brilliant doctors and researchers -- experts in this myopathy -- who were willing to share their high level of expertise with all of us.

RYR-1 INTERNATIONAL FAMILY CONFERENCE ATTENDEE





Group photograph of attendees of the 2018 RYR-1 International Family Conference, July 13–15, 2018, in Pittsburgh, PA.

“To meet a whole staff of doctoral level scientists spending their lives researching the disease that impacts our families’ lives so drastically was so powerful!

**RYR-1 INTERNATIONAL FAMILY CONFERENCE ATTENDEE**







Group photograph of attendees of the 2022 RYR-1 International Family Conference, July 22-July 24, 2022, in Pittsburgh, PA.

“If not for attending the conference, there is no telling how long these concerns would have gone unchecked. I can’t thank y’all enough for all that we have learned from the conference!”

**RYR-1 INTERNATIONAL FAMILY CONFERENCE ATTENDEE**



Peter L. Saltonstall, President and CEO of the National Organization for Rare Disorders (center), receiving an award after delivering the keynote address at the 2018 RYR-1 International Family Conference. He is joined by Nicole Becher, Program Manager of The RYR-1 Foundation (left), and Dr. Michael F. Goldberg, President of The RYR-1 Foundation (right).



Myrna Goldberg (left) and Dr. Morton F. Goldberg, Directors and Co-Founders of The RYR-1 Foundation. Dr. Goldberg received the Guardian of Strength Award at the 2022 RYR-1 International Family Conference.



# Support and Advocacy for Affected Individuals and Families

Due to the rarity of RYR-1-RD, the diagnosis can be anxiety-provoking and isolating for individuals and their families. The RYR-1 Foundation serves as a resource, primarily through our website ([www.ryr1.org](http://www.ryr1.org)) and social media platforms, in which individuals can access a wealth of information.



## FIND THE THE RYR-1 FOUNDATION ONLINE

Website: [www.ryr1.org](http://www.ryr1.org)

Facebook: [www.facebook.com/ryr1foundation](https://www.facebook.com/ryr1foundation)

Instagram: [@theryr1foundation](https://www.instagram.com/theryr1foundation)

Twitter: [www.twitter.com/RYR1foundation](https://www.twitter.com/RYR1foundation)

Documentary: [www.ryr1.org/documentary](http://www.ryr1.org/documentary)

Educational videos about RYR-1-RD can be viewed directly on The RYR-1 Foundation's website:  
[www.ryr1.org/video-gallery](http://www.ryr1.org/video-gallery).



### ROLE OF CALCIUM IN RYR-1 MYOPATHY:

Dr. Robert Dirksen



### MALIGNANT HYPERTHERMIA:

Dr. Ronald Litman



### INTRODUCTION TO RYR-1 MYOPATHY:

Dr. James Dowling



### WHAT ARE RYCALs:

Dr. Andrew Marks

# Patient-Led Research Workshop

The RYR-1 Foundation hosted the first-ever patient-led, *2022 RYR-1-Related Diseases International Research Workshop: From Mechanisms to Treatments*, on July 21 - July 22, 2022, in Pittsburgh, PA preceding the 2022 RYR-1 International Family Conference. With 45 *in-person* attendees and ten virtual attendees from 11 different countries, this workshop provided a much-needed forum for the leading international RYR-1 experts and a group of affected individuals to share knowledge, exchange ideas, form collaborations, and develop new strategies for finding therapies. The Workshop Organizing Committee included a diverse group of researchers/clinicians in RYR-1-RD, members of The RYR-1 Foundation's SAB, and RYR-1-RD community representatives. To learn more, please visit: [www.ryr1.org/2022-research-workshop](http://www.ryr1.org/2022-research-workshop).

This meeting was funded by grants from the Muscular Dystrophy Association (MDA) and the National Institutes of Health (NIH); sponsorships from Eagle Pharmaceuticals and Ingenious Targeting Laboratory; and donations from several generous benefactors.



The RYR-1 Foundation President & Co-Chair of Research Dr. Michael Goldberg (left) and The RYR-1 Foundation SAB Member and Workshop Co-Chair Dr. Filip Van Petegem (right).



The RYR-1 Foundation SAB Member and Workshop Co-Chair Dr. Robert Dirksen.



Attendees of the 2022 RYR-1-Related Diseases International Research Workshop: From Mechanisms to Treatments.





The RYR-1 Foundation SAB Member and Workshop Co-Chair  
Dr. Filip Van Petegem.



Dr. Johann Böhm - Institute of Genetics and Molecular  
and Cellular Biology (Strasbourg, France).



Attendees of the 2022 RYR-1-Related Diseases International  
Research Workshop: From Mechanisms to Treatments.



Dr. Tokunbor Lawal - NIH.



The RYR-1 Foundation President & Co-Chair of Research Dr. Michael Goldberg.



The RYR1-1 Foundation Advisor Jacqueline  
Hoffman-Anderman.



# Brentney's Story

When Brentney was born in 1993, her parents noticed something was wrong right from birth. Doctors told her family that they did not think she would ever be able to walk or talk. Nevertheless, each and every day, Brentney has continued to exceed everyone's expectations.

Like many other individuals with RYR-1-RD, Brentney was initially misdiagnosed. Due to her rapid health decline in 2015, she and her family became skeptical about her initial diagnosis, which led to genetic testing with Greenwood Genetics Center and the Mayo Clinic. It was not until January 2016, at the age of 22, that Brentney received her true diagnosis – Recessive Minicore Disease, a severe form of an RYR-1-RD. A rare situation indeed, she inherited a mutation from each of her parents who are both unaffected carriers.

Brentney and her family continue to remain optimistic, hopeful, and inspirational. In 2016, Brentney graduated with her associate's degree as she worked on stabilizing her health, even finishing classes from a hospital bed. In 2017 she began working for AccessAbility, a local non-profit center for independent living. Unfortunately, her health took another decline in 2019 and led to operations with lengthy recoveries, forcing her to resign. Today she continues to optimize her current health and do as much as she can while taking necessary precautions due to the current COVID-19 Pandemic.

Although there were some serious health roadblocks along the way, Brentney never felt defeated and her faith never wavered with loved ones always by her side. She accomplished many milestones in her life that no one can ever take away from her. Since her diagnosis, she has dedicated her life to making a difference for others. She has taken the opportunity to speak as an advocate for disability rights on the steps of the South Carolina State House, and raised money for The RYR-1 Foundation. She enjoys attending the RYR-1 International Family Conferences and reuniting with the RYR-1 community.

**"After discovering The RYR-1 Foundation, I was finally able to interact with and meet individuals who could identify with the same things I was going through, and that makes my personal battles easier to fight,"** Brentney explains.

Brentney is on the Board of Advisors of The RYR-1 Foundation and a Co-Director of the 2022 RYR-1-Related Diseases International Research Workshop.

To watch a video on "Brentney's Story," please go to: [www.ryr1.org/brentney](http://www.ryr1.org/brentney).



Dr. Michael F. Goldberg President (left) with Brentney Simon (middle) and Brentney's family.



Brentney Simon (center), Co-Director of the 2022 RYR-1-Related Diseases International Research Workshop, joined by the other Co-Directors and The RYR-1 Foundation staff, at the workshop.



# Cody's Story

As the 10th overall pick in the 2008 NHL Draft, Cody Hodgson had a bright career ahead of him in the NHL. Cody played for the Vancouver Canucks, Buffalo Sabres, and Nashville Predators over the course of a six-year career. Although Cody had experienced muscle cramps his entire life, he dismissed them as a regular part of being a competitive athlete. As his symptoms became more severe during his professional playing days, he recalled, "I knew I had to get medical help." He experienced many distressing signs and symptoms, including: trouble breathing, heart arrhythmias, severely low blood pressure resulting in "blacking out," and tea-colored urine. The severity of these symptoms culminated in a hospitalization in 2015, when doctors diagnosed him with rhabdomyolysis, a severe and potentially fatal condition related to abnormal muscle breakdown.



During the 2015-2016 season with the Predators, Cody was referred to Dr. Sheila Riazi, an anesthesiologist and one of the world's leading experts on malignant hyperthermia, a muscle condition most commonly due to a mutation in the RYR-1 gene. Dr. Riazi, a member of The RYR-1 Foundation's Scientific Advisory Board, quickly realized that Cody's numerous injuries, severe symptoms, and episodes of rhabdomyolysis were all likely due to RYR-1-related malignant hyperthermia. She ordered genetic testing and a muscle biopsy, which confirmed the diagnosis.



Cody (right) at an RYR-1 International Family Conference with Lindsay Goldberg (left) and Cody's brother, Clayton (middle).

Receiving this diagnosis from Dr. Riazi was a source of tremendous relief for Cody. "You put up with a lot of injuries, and it takes a physical toll when you play hockey," Cody said, "but it really scares you when you are not sure what is going on with you."

Dr. Riazi informed Cody of The RYR-1 Foundation and put him in touch with its President, Dr. Michael Goldberg. After meeting with Dr. Goldberg in early 2018 and learning more about the work of The RYR-1 Foundation, Cody said, **"Hopefully, The RYR-1 Foundation and I can help to not only push for a cure, but also help the parents, patients, and families affected by it now so that they can better understand their condition, take the appropriate precautions, and have a treatment available to them."**

Cody is on the Board of Advisors of The RYR-1 Foundation and the recipient of the 2022 Advocate of Strength Award from The RYR-1 Foundation.

To watch a video on "Cody's Story" and an interview with Dr. Michael Goldberg, President of The RYR-1 Foundation, and Cody Hodgson, please go to: [www.ryr1.org/cody](http://www.ryr1.org/cody).





# How a Gift to The RYR-1 Foundation Can Help

## \$1,000

Expense for a doctor/researcher to attend a domestic scientific meeting.

## \$3,000

Expense for a doctor/researcher to attend an international scientific meeting.

## \$50,000

The annual cost of maintaining a colony of mice with RYR-1 muscle disease.

## \$200,000 – \$300,000

The annual cost of a basic science research project (lab equipment, staff salaries, supplies, etc.).

To make a donation to The RYR-1 Foundation, please scan the QR code below or go to:  
[www.ryr1.org/donate](http://www.ryr1.org/donate).



For questions about making a donation, please contact Nicole Becher, Program Manager, at [nicole@ryr1.org](mailto:nicole@ryr1.org) or (412) 529-1482.

The official registration and financial information of The RYR-1 Foundation may be obtained from the Pennsylvania Department of State by calling toll free, within Pennsylvania, 1 (800) 732-0999. Registration does not imply endorsement.



# Who We Are



Dr. Michael F. Goldberg (right) and Dr. Morton F. Goldberg (left).

## **MICHAEL F. GOLDBERG, MD, MPH, PRESIDENT, CO-CHAIR OF RESEARCH, CO-FOUNDER, DIRECTOR**

Dr. Michael F. Goldberg is a board-certified neuroradiologist, Associate Professor of Radiology at Drexel University College of Medicine, and is the Director of Neuroradiology at the Allegheny Health Network. As someone who is affected by an RYR-1-RD, 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. Mike can be reached at [mike@ryr1.org](mailto:mike@ryr1.org).

## **MORTON F. GOLDBERG, MD, FACS, VICE PRESIDENT, CO-CHAIR OF RESEARCH, CO-FOUNDER, DIRECTOR**

Along with Mike, Mort is the Co-Chair of Research. He is also an ophthalmologist specializing in inherited retinal diseases. He is the Joseph Green Professor of Ophthalmology at the Johns Hopkins School of Medicine and the Director Emeritus of the Wilmer Eye Institute at Johns Hopkins University. He is a member of the National Academy of Medicine of the National Academies of Science of the United States.

He was awarded the 2022 Academy Laureate Award by the American Academy of Ophthalmology and The RYR-1 Foundation's 2022 Guardian of Strength Award.

## **DREW HUSETH, AICP, SECRETARY, DIRECTOR**

Drew 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 RYR-1 gene.

## **RANDOLPH PEPPER, CPA, TREASURER, DIRECTOR**

Randy is recently retired as the Director of Finance & Accounting for Central Processing Services, LLC, a privately held company in suburban Detroit. He has a BA degree from the University of Michigan, and a MBA from Wayne State University. He has over 30 years experience in a variety of Controller/CFO positions for mid-size privately held companies.





Pictured left to right: Dr. Morton Goldberg, Mr. Michael Legum, Dr. Michael Orseck, Ms. Jennifer Ryan, Mrs. Lindsay Goldberg, Mr. Randolph Pepper, Mrs. Emily Pedersen, Dr. Michael Goldberg, Mrs. Myrna Goldberg, Mrs. Nicole Becher at the 2018 RYR-1 International Family Conference.

### **MICHAEL LEGUM, ASSISTANT TREASURER, DIRECTOR**

Mike is a senior portfolio manager for Park Circle Investments, a Baltimore-based private investment company. Prior to Park Circle, he worked in the film business, spending five years at New Line Cinema. He is a graduate of the University of Pennsylvania with a BA in English.



### **MYRNA GOLDBERG, MSW, CO-FOUNDER, DIRECTOR**

Myrna is a retired social worker, having previously worked in hospitals, protective services, and school social work settings. She serves on the Board of Advisors of the University of Maryland School of Social Work, is an active member of the Baltimore Women's Giving Circle, and is a docent at the Baltimore Museum of Art.

### **JUSTIN C. MCARTHUR, MBBS, MPH, FAAN, DIRECTOR**

Dr. Justin McArthur is the Neurologist-in-Chief at the Johns Hopkins Hospital and John W. Griffin Professor of Neurology at the Johns Hopkins University School of Medicine. He is also a Professor of Pathology, Medicine, and Epidemiology. He has become nationally and internationally recognized for his work in the epidemiology and treatment of HIV infection, multiple sclerosis, and other neurological infections and immune-mediated neurological disorders.

### **EMILY PEDERSEN, DIRECTOR**

Emily worked as a Recreation Therapist and Child Life Specialist at Weisman Children's Rehabilitation Hospital in Marlton, New Jersey for eight years. She has participated in and organized fundraising runs to support research for RYR-1-RD. Emily has a daughter who was diagnosed with Central Core Disease, a form of an RYR-1-RD.



Emily Pedersen (right) with Jackson (left), a boy affected by RYR-1.



### **JENNIFER RYAN, MBA, DIRECTOR**

Jeni is a trustee of the Schooner Foundation and has an MBA in Operational Management from Simmons College. She is the former COO of Integral Resources, a tele-marketing firm specializing in small donor acquisition for nonprofits. Both she and her daughter have Central Core Disease, a form of an RYR-1-RD.

### **DONALD J. ZACK, MD, PhD, DIRECTOR**

Dr. Donald Zack is the Guerrieri Family Professor of Genetic Engineering and Molecular Ophthalmology at the Wilmer Eye Institute, Johns Hopkins University School of Medicine. His research concerns the mechanisms of retinal degenerative disease and glaucoma, and efforts to develop new drug and stem cell-based therapeutic approaches.

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## **Staff**



### **LINDSAY GOLDBERG, RN, BUSINESS MANAGER, PATIENT LIAISON, CO-FOUNDER**

Lindsay is in charge of the organization's finances and compliance. She is also a liaison between affected individuals/their families and physicians, genetic testing companies, and scientists. She has a BSN from the University of Michigan and is a registered nurse who formerly specialized in pediatric cardiac intensive care (10 years). She can be reached at [lindsay@ryr1.org](mailto:lindsay@ryr1.org).



### **NICOLE BECHER, PROGRAM MANAGER**

Nicole joined The RYR-1 Foundation team in 2016. She focuses on programming of the organization, coordinates daily operations, and works closely with the Officers and 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).



### **LENA LEGHART, ADMINISTRATIVE ASSISTANT**

Lena joined The RYR-1 Foundation in 2022. She coordinates daily operations and works closely with the Board of Directors, Board of Advisors, and Scientific Advisory Board of The RYR-1 Foundation. She can be reached at [lena@ryr1.org](mailto:lena@ryr1.org) and (412) 529-1482.





The RYR-1 Foundation Co-Founders, husband and wife team, President and Co-Chair of Research Dr. Michael Goldberg and Business Manager and Patient Liaison Lindsay Goldberg.



The RYR-1 Foundation Assistant Treasurer Michael Legum (left) and Vice President and Co-Chair of Research Dr. Morton Goldberg (right).



The RYR-1 Foundation Business Manager and Patient Liaison Lindsay Goldberg (left) and Program Manager Nicole Becher (right).



# Advisors

## MARCIE EPSTEIN

Wife of Steve and Mother of Jackson, who are both affected by RYR-1

## MATTHEW GOLDBERG, JD

Reliability and Operations Compliance at a public utility company

## CODY HODGSON

Director of Alumni Hockey Relations, Nashville Predators

## JACQUELINE HOFFMAN-ANDERMAN, RN, BSN

Mother of Maddie, affected by RYR-1

## SOFIA LEON

Mother of Tommie, member of a large family with more than 20 members affected by Central Core Disease

## JESSICA R. NANCE, MD

Assistant Professor, Johns Hopkins Pediatric Neurology and Neuromuscular Disorders, Kennedy Krieger Center for Genetic Muscle Disorders

## JEREMY NATHANS, MD, PhD

Professor in the Departments of Molecular Biology and Genetics, Neuroscience, and Ophthalmology, Johns Hopkins Medical School

## AMY A. PERRIN, MS, FNP-C

Mother of Courtney, affected by RYR-1

## BRENTNEY SIMON

Individual affected by RYR-1 (recessive minicore)

## AVI SWERDLOW

Product Manager, Google

## Yael SWERDLOW

Special Education Consultant

## MATTHEW TOMPKINS, PhD

Chief Operating Officer, TC Defense



Emily Pedersen (Director), Amy Perrin (Advisor), Megan Norris, and Jacqueline Hoffman-Anderman (Advisor) at an RYR-1 International Family Conference.





## The mission of The RYR-1 Foundation is to:

- 1 Support research leading to an effective treatment or a cure for RYR-1-related diseases
- 2 Bring awareness and serve as a resource for medical professionals
- 3 Provide education, outreach, and advocacy for individuals and families affected by RYR-1-related diseases



“We are in awe of the strides  
The RYR-1 Foundation has  
made and your devotion to  
the RYR-1 population!

RYR-1 INTERNATIONAL FAMILY CONFERENCE ATTENDEE

“It is a great blessing to have The RYR-1 Foundation  
dedicated to research and to educating families  
and patients on all aspects of the disease.

RYR-1 INTERNATIONAL FAMILY CONFERENCE ATTENDEE







**Global Headquarters**

P.O. Box 13312, Pittsburgh, PA 15243 | (412) 529-1482

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[www.ryr1.org](http://www.ryr1.org)