



**Individual Investigator Research Grant Awards
Request for Letter of Intent (LOI) for Research Grant
Application**

Deadline: May 18, 2024

The RYR-1 Foundation expects to fund a limited number of Individual Investigator Research Grants, **to be awarded in early-2025**. *Preference will be given to LOI grant applications that address the “Research Priority Areas.” Additional and detailed information can be found below on pages two through four (2 - 4).*

You are invited to submit a Letter of Intent (LOI) for our next round of research grant applications to The RYR-1 Foundation by **May 18, 2024**. Please make sure your LOI is no more than two (2) pages in length. *You will be notified of your status by June 1, 2024. For any questions please contact Patricia Raffaele at patricia@ryr1.org. The final deadline for applications is October 19, 2024.*

The following is required to be addressed in your LOI:

1. Title of the RYR-1-Related Diseases (RYR-1-RD) Project
2. Applicant/PI
3. Institution and Contacts
4. Key Personnel
5. Lay Abstract including: Research Priority Area(s) & Specific Aims

DESCRIPTION:

Individual Investigator Research Grant Awards are designed to concentrate research in areas that will have the greatest potential to move towards treatments and cures for RYR-1-RD.

As appropriate, applicants are encouraged to use one or more of RYR-1-RD murine models currently available from commercial, corporate, academic, and other sources, including recently developed animal models. **Recently developed murine models of RYR-1-RD demonstrating moderate-severe myopathy phenotypes, including mice with mutations on exons 34 and 96. Please see “Entry #1” and “Entry #2” on the spreadsheet entitled “Mouse Models of RYR-1-Related Diseases” at www.ryr1.org/mice.** For information on obtaining these mice, please contact Patricia Raffaele at patricia@ryr1.org.

The RYR-1 Foundation has identified Research Priority Areas (RPAs) that align with its mission; and the purpose of this targeted open call for applications is to address specific gaps in current research related to RYR-1-RD. While applications addressing the areas of particular interest (below) will be given priority consideration, **The RYR-1 Foundation will also consider proposals for research that do not fit easily within these goals.**

RESEARCH PRIORITY AREAS (RPAs):

Priority will be given to research that has direct application to clinical therapies for RYR-1-RD. Specific areas of research interest may include the following:

A. Novel therapeutic approaches to RYR-1-RD. All approaches will be considered, but potential interventions include:

- i. Novel mechanisms to *efficiently* deliver therapeutic technologies (e.g. gene editing, gene therapy, etc) to skeletal muscle throughout the entire body. Given the size of the *RYR1* gene, an emphasis should be placed on novel vectors with increased cargo capacities (e.g. non-AAV viral vectors, lipid nanoparticles, protein nanoparticles, antibodies, etc).
- ii. Gene editing (e.g., CRISPR/Cas9, Base editing, Prime editing, etc.).
- iii. Novel gene therapy strategies (e.g. split intein protein transplicing, etc.).
- iv. Epigenetic modifying therapies.
- v. mRNA-based protein replacement therapies
- vi. t-RNA-based therapies.
- vii. Development of therapeutic interventions that modify RyR1 receptor activity, reduce muscle degradation, and/or increase regenerative capacity of skeletal muscle.

B. Cell and molecular mechanisms of RYR-1-RD and other muscle disease: Basic research designed to define the underlying pathogenic mechanisms of RYR-1-RD and possible common, “downstream” pathways that are also present in other muscle diseases (e.g. calcium leak via the RyR1 receptor, ER stress, mitochondrial dysfunction, post-translational modifications of myosin and other proteins associated with muscle structure and function).

C. Regenerative Medicine (RM): Development of strategies that provide functional rescue or replacement of degenerating and/or dead muscle cells that can lead to improvement of muscle function.

LOI INSTRUCTIONS

KEY PERSONNEL

Each individual Investigator Research Grant Application must be directed by a **single Principal Investigator** who is responsible for the conduct and management of the project. Co-Investigators are allowed, and must be identified.

LAY ABSTRACT: RESEARCH PRIORITY AREA(S) & SPECIFIC AIMS

Provide an abstract of the proposed research project, written **in lay terms** for a non-scientific audience.

RPA: Identify specific RYR-1-RD research priority area(s) (see above for details).

SPECIFIC AIMS: 1) Describe the overall goal(s) for the proposed project. Numerically list the specific aims. 2) For clinical research projects, identify the specific disease(s) and patient population(s) to be studied. Include genomic diagnosis whenever possible.

ELIGIBILITY:

Applicants must hold a Ph.D., M.D., D.V.M., D.O., or equivalent degree and have a faculty position/equivalent at a domestic/foreign nonprofit organization, or public/private institution (such as a university, college, medical school, hospital, research institute, or laboratory).

AWARD:

The total award will be up to **\$120,000 USD over a period of two years** (up to **\$60,000 USD per year**). Exceptions may be made on a case-by-case basis. Research projects that are expected to exceed two years in duration will also be considered for funding.

Note: The RYR-1 Foundation and its Directors do not provide funds for indirect, administrative, or overhead costs. The RYR-1 Foundation does not provide funds for fringe benefits and annual “cost of living” increases. In addition, The RYR-1 Foundation does not pay for costs related to construction or renovation.

Purchase of capital equipment is generally not supported by The RYR-1 Foundation. Capital equipment is defined as a permanent or semi-permanent apparatus, device, or system costing more than \$5,000 per device or system. Applicants must obtain prior approval from the Chair/Co-Chair(s) of Research to submit an application to purchase capital equipment.

If any of the investigators have either an active or pending grant on RYR-1-RD matters, the list will need to be provided in the full application.