Special Request For Applications:
Understanding Broader Genetic Impacts on Phenotype in Dravet Syndrome

The Dravet Syndrome Foundation (DSF) is issuing a special request for grant applications proposing research projects that will deepen our understanding of genetic impacts on the diverse phenotypic outcomes of individuals with Dravet syndrome.

Application Due Date: September 8, 2023
Award Budget: up to $1M distributed over 3 years (beginning in January 2024)

Purpose and Objectives: The clinical presentation of Dravet syndrome is well-defined, characterized by intractable seizures beginning in infancy as well as a range of comorbidities that include intellectual disability, behavior issues, movement and gait disorders, language and speech difficulties, sleep disruptions, and dysautonomia. However, the manifestation and severity of these clinical symptoms, as well as response to medical interventions, can differ among patients. Heterozygous loss-of-function variants in SCN1A are found in the majority (>80%) of patients diagnosed with Dravet syndrome. Causal mutations are varied (missense, nonsense, insertions and deletions) and have been identified in every exon of SCN1A. Research efforts have not been successful in uncovering clear phenotype-genotype correlations based on *SCN1A* variants alone. Environmental factors likely impact patient outcomes, but studies in animal models and families with inherited SCN1A mutations suggest the interplay of other genetic factors. A deeper understanding of these genetic interactions could contribute to our understanding of disease etiology, and potentially provide meaningful clinical insights.

Project Requirements:

- DSF will consider budget proposals of up to $1,000,000 (including direct and indirect costs) over a 3 year timeframe for projects that propose to address the topic of broader genetic impacts on diverse phenotypic outcomes in human subjects with Dravet syndrome.
- Projects are expected to generate substantial datasets from human samples using whole genome sequencing and/or other multi-omic approaches.
- Anticipated results should aim to uncover novel insights into disease that have the potential to impact clinical care and spur new lines of research.

- Projects should include plans for representation from diverse populations in the study cohort including patients from diverse geographical, racial and ethnic, and socioeconomic backgrounds.
- Proposals must include detailed plans for data sharing to ensure that resources developed within the project are accessible for future discovery.
- DSF encourages researchers to incorporate plans for biospecimen banking, that, similar to the data, could be used in future collaborative efforts.

Review of Applications: Grant applications will be scored principally on novelty of the hypotheses, innovative approaches with a direct relevance and application to Dravet syndrome, scientific quality, rigor of the overall approach and analytic methods, strength of expertise, and likelihood of success. Applications undergo a rigorous NIH-style scientific review process and final decisions are made by the DSF Board of Directors, ensuring projects funded by DSF meet high scientific standards and align with the most pressing needs of the patient community. Research Grant Awardees are required to give updates on their work throughout the grant cycle and present their findings at DSF's annual Research Roundtable meeting.

Application Eligibility: Applicants should hold an MD, PhD, DO, or equivalent degree and should be affiliated with a research or academic institution (excluding for-profit companies). Applicants may be US- or foreign-based, must be established in their field, and should be in good standing with their respective institution. Collaborative, multi-investigator and/or multi-center applications are highly encouraged.

Applications Due September 8, 2023

Questions?
Contact:
Veronica Hood, PhD- DSF Scientific Director
veronica@dravetfoundation.org

2023 Genetic RFA Application Instructions

Applications which do not include the following materials and meet the specified page limitations will be returned unprocessed, or will be deferred until a subsequent granting cycle.

- Please use a size 11 font or larger with margins of at least 0.5 inches.
- Use the section names and numerical order in the list below to label the documents within and collate your application.
- All required documents should be submitted as a single combined PDF via email to veronica@dravetfoundation.org with a subject line "DSF Genetic RFA Submission"
- Applications must be received by September 8, 2023 (by 11:59 US Pacific Time Zone).

Required Documents:

1. **Face Page – 1 page/per PI (found here)**
   Fillable PDF form that must be signed by applicant and an institutional grants program official. If submitting as a multi-PI grant, please include a Face Page for each collaborating PI.
2. **Scientific Abstract and Lay Abstract – 1 page**
   Please include a single page including a scientific abstract and a lay abstract.
   The scientific abstract should convey the hypothesis, goals, importance, and impact of the research.
   The lay abstract should convey the same information in language appropriate for someone without scientific training to understand clearly. The lay abstract is used in the Board of Director's decision making process following scientific review and care should be taken that the description is clear, accurate, and emphasizes the realistic impacts of the project.
3. **Budget– 1 page**
   Often displayed as a table, the budget page should include a simple numeric breakdown of how grant funds will be utilized, including indirect costs and a final total of the funds being requested.
   Indirect costs of no more than 10% of the total award are permitted, and must be accounted for within the $1M budget.
   If the total budget for your project exceeds the amount you are requesting from DSF, your budget page must include a breakdown of how all funds, including those from other sources, will be used.
4. **Budget Justification– 1 page**
   The budget justification page should provide an explanation and rationale of each line item of the budget including why specific personnel and/or supplies are critical to the proposed study.

5. **Hypothesis and Specific Aims – 1 page**
   Please use a single page to lay out the hypothesis and rationale for the proposal including the specific aims to be accomplished.
6. **Research Plan – 6 pages**
   This should include background, preliminary data, experimental approach, methods, expected outcomes and discussion of potential pitfalls.
7. **Data and Resource Sharing Plan –2 pages**
   Please include a detailed outline of plans for sharing data, tools, biological samples, or other resources that are created as part of the proposed project. Provide a brief summary of each type of data or resource that is anticipated to be generated, and describe to what extent and through what mechanisms (databases/repositories) they will be shared (including details such as the level of aggregation and data processing). *For additional guidance, the NIH has resources to aid in the development of data management & sharing plans as well as sharing genomic data.*
8. **Impact Statement – ½ page**
   A statement on how the research will impact the understanding, treatment or care of people with Dravet syndrome or related epilepsies
9. **Bibliography – no page limit**
   Please provide citations in NIH format (listing all authors)
10. **CV/Biosketch for PI and other key personnel– not to exceed 4 pages**
    Please use NIH format (an example can be found here).
    For multi-PI applications, please submit a CV/Biosketch for each PI.
11. **<Optional> Letter(s) of Support- 1 page/per letter**
    Please provide letters of support from any collaborators or advisory positions that are not otherwise included in the grant submission outlining how they are supporting the project with expertise or resources.

Review Process

Applicants will be informed of the status of their application by late November/ early December. Awarded submissions will be announced publicly at the annual DSF Research Roundtable that will be held on Thursday evening, November 30, 2023 just prior to the American Epilepsy Society Meeting in Orlando, Florida.

Grant applications will be scored principally on novelty of the hypotheses, innovative approaches with a direct relevance and application to Dravet syndrome, scientific quality, rigor of the overall approach and analytic methods, strength of expertise, and likelihood of success. Applications will undergo a rigorous NIH-style scientific review process by researchers with relevant expertise. Final funding decisions are made by the DSF Board of Directors, ensuring projects funded by DSF both meet high scientific standards and align with the most pressing needs of the patient community. Research Grant Awardees are required to submit annual updates on their work throughout the grant cycle, as well as a final report upon project completion. Awardees are also expected to present their findings at a future Research Roundtable meeting.