KCNT1 EPILEPSY
HOPE IS ON THE HORIZON

KCNT1 Epilepsy Foundation
2024 Seed Grant Full Application

The KCNT1 Epilepsy Foundation 2024 Seed Grant Program provides a one-year grant to support basic, translational, and clinical research topics related to KCNT1-related epilepsy with the ultimate goal of identifying and developing effective and safe treatments for KCNT1-related epilepsy. Our 2024 seed grant will fund up to $30,000. This grant is made possible by the KCNT1 Epilepsy Foundation and its generous supporters.

Eligibility
This RFA is open globally. International applicants are invited to apply. All individuals holding a faculty-level appointment at an academic institution or a senior scientific position at a non-profit institution or foundation are eligible to respond to this RFA. Prior award recipients must have current and updated project reporting to be eligible for selection.

Full Application Instructions and Review Procedure

Proposal Due Date: **April 29, 2024 no later than 8pm EST**
The application as a PDF file and budget as an PDF file should be emailed to ali@kcnt1epilepsy.org. Please send any questions to ali@kcnt1epilepsy.org.

CONTENT to be emailed to ali@kcnt1epilepsy.org:

☐ **Cover Page/Checklist/Institutional Signature Page [PDF].**

☐ **NIH-style Biosketch with Other Support of PI and key personnel** (5 pages max/PI, including Other Support). **[PDF]**
The PI must include accurate and complete information regarding all other sources of grant support (current and pending), including title, abstract, annual and total amount of grant, inclusive funding period, and percent effort.

☐ **Detailed Budget and Justification. [combined into one PDF]**
Complete Excel budget sheet (provided). Describe justifications in a Word document. Award will be for one year. Proposed funding period: October 1, 2024 – October 31, 2025. Up to $30,000.00 USD will be awarded.

Institutions may opt to take up to a maximum of 5% indirect costs (IDCs) and institutional overhead from award totals.

Allowable direct costs

- Salary for PI
- Salary/stipend and related benefits for graduate student/postdoctoral fellow/technical support
- Travel (up to $1500)
- Laboratory supplies and other research expenses
- IDCs of 5% are included in the total award amount

Unallowable costs

- Consultant costs
- Tuition
- Professional membership dues
- Equipment
- General office supplies institutional administrative charges (e.g., telephone, other electronic communication, IT network, etc.)
- Pre-award charges
- Any other expenses not directly related to the project

CONTENT:

☐ **Research Plan** (5 pages max) and **Bibliography** (1 page max). **[combined]**
Include the following sections: Specific Aims, Background and Significance, Preliminary Studies/Data, Research Design and Methods. Research plan should address the following questions: 1) Do you require access to reagents, cell lines, animal models, IRB/ethical board approvals, and/or equipment necessary to complete work? If so, please describe your plan to gain access within the timeframe of this grant period. 2) Have you identified qualified personnel to complete this project within the grant period? If not, please provide your plan to do so. Text citations should use a numbered format. Include all author names in the reference list.

☐ **Lay Abstract and Summary of Proposed Research** (375 words)

☐ **Potential Impact on KCNT1 Research and/or the care or treatment of those with KCNT1-related epilepsy.**

☐ **Lay Description of Potential Impact on KCNT1 Research and/or the care or treatment of those with KCNT1-related epilepsy** (2 paragraphs)

All previous grant awardees must include a statement of outcomes including publications, patents and additional funding granted as a result of data generated from those grants. Specific aims must be different from those in previous applications.

FORMAT for documents:
Font and Page Margins: Use Arial typeface, a black font color, and a font size of 11 points. A symbol font may be used to insert Greek letters or special characters. Use 0.5 inch margins (top, bottom, left, and right) for all pages, including continuation pages. Print must be clear and legible; all text should be single-spaced. The "Full Application" document may be used as a template.

Header: There should be a header at the top right on all pages of the PDF indicating the full name of the PI (e.g., **PI: Smith, John D.**).

File names: ALL files to be emailed should start with the LAST NAME of the PI followed by the brief name of the document. Examples: SMITH CV, SMITH Cover Page, SMITH Budget. **If files are not labeled properly, you will be asked to resubmit the PDFs before your application can be considered.**

Grant Program Award Terms

1. Indirect Costs are limited to up to 5% of direct costs.

2. Awardees are required to provide updates concerning other support, resulting publications, and research activities, as requested.

3. An interim programmatic report is due ~6 months after start date, potentially ~March 1, 2025. A final report is due one month after the close of the project. Each two-page report must contain a synopsis of scientific progress, a list of resulting collaborations, publications and grants, a description of the relationship of the project to the goals of the related-disease research, a financial report, and a statement regarding unspent funds.

4. Awardees will receive payment on a quarterly cost reimbursement basis. Awardees must submit invoices with a breakdown of incurred costs to the grant over the previous three-month period. A template and invoicing details will be provided in the award agreement.

5. The following citation must be included in all publications: This work was supported in part by a research grant from the KCNT1 Epilepsy Foundation.

6. Appropriate citation of all collaborations must be included in all publications.

7. All final data sets and observations must be shared openly with the full scientific community, and all reagents and/or research tools developed under support by this mechanism must be made accessible upon request. The KCNT1 Epilepsy Foundation makes no claim to rights on these items or intellectual property.

NOTE: Award terms are subject to change. If awarded, please refer to the grant award contract for actual project terms.

Project Disclosures and No Cost Extensions (NCE):

- NCEs will be granted at the discretion of the KCNT1 Epilepsy Foundation.
- Awardees will be limited to 1 NCE request for their award.
- Maximum NCE time awarded will be 6 months.
- NCEs will be granted after a formal request prior to the NCE deadline with adequate justification.
- If granted a NCE, you are still required to submit an interim scientific report 6 months into the duration of the original award period, regardless of your new project end date.
- You will be required to certify that you have identified qualified personnel to complete this project within the grant period **PRIOR** to the start date of the award. If you have not, you will be required to provide your plan to engage said personnel. Only under extenuating circumstances will personnel issues be considered for NCE requests.
- In your letter of interest, you will also be required to state whether or not you require access to reagents, cell lines, animal models, IRB/ethical board approvals, and/or equipment necessary to complete your work. If so, you will be required to describe your plan to gain access within the time-frame of this grant period.

Research Focus Areas for Seed Grants:

The goal of this grant is to support research that can lead to the development of effective treatments for KCNT1 disorders. The project should focus on one or more of the following areas:

- Define the non-conductance functions of KCNT1 to further disease understanding and find alternative treatment targets. Proposals should emphasize therapeutic potential.
- Understand cellular mechanisms, splice variants, and gene modifiers that potentially influence KCNT1 and could serve as a potential therapeutic target. Proposals should emphasize therapeutic potential.
- Repurposing screens of safe/FDA or EMA-approved drugs, previously shelved drugs with safety records, nutraceuticals, or other libraries of interest to identify a safe drug option that can be used quickly in KCNT1 patients
- Exploration of safe/ FDA or EMA-approved drugs previously identified in repurposing screens: This may include in vitro and/or in vivo work, to investigate efficacy for multiple patient mutations. The proposal should state why additional preclinical testing is necessary before patients are treated.
- Organization and execution of clinical trials for drugs already identified in repurposing screens: The proposal should include details of the clinical trial design, recruitment strategy, inclusion and exclusion criteria, primary and secondary outcomes, and statistical analysis plan.
- Validation of assessment tools in KCNT1 patients for use in clinical trial outcome measures, especially non-seizure outcomes. Proposals should include details of the assessment tools to be validated, the validation process, and the expected outcomes.
- Investigation of symptoms/pathophysiology outside of the brain, such as the role of KCNT1 in the lungs or cardiac symptoms. Proposals may include clinical studies or translational lab research.
- Novel therapeutic approaches for KCNT1-related disorders: The proposal should include details of the approach, preclinical data, and the proposed plan for clinical translation.
- Variant Classification. In addition to functional characterization of variants, there is a need for a more comprehensive method of classifying KCNT1 variants, including relevant criteria for incorporating data from sources including computational predictive models, cellular electrophysiology, and animal models, especially for VUS reclassification.
- Discovery and validation of biomarkers (molecular and functional). To date, no KCNT1-specific biomarkers have been identified.
- Investigation into the mechanisms underlying a caregiver-identified phenomenon wherein seizures are reduced during fever in children with KCNT1 epilepsy. Proposals may explore potential mechanisms to explain why seizures are reduced during fever and whether these mechanisms can be harnessed towards a potential therapeutic that can also suppress seizure.
- Other topics are welcomed and encouraged.

Applicants are encouraged to collaborate with existing KCNT1 researchers and to leverage existing disease models and data (e.g., animal models, Ciitizen natural history study data, registry data, biospecimens available from our biobank, KCNT1 cell lines, etc.) and should include a statement on resource sharing in their proposal.

Grant Review Process:

1) Grants will be reviewed for scientific content and relevance to the goals of the RFA.
2) Full applications proceed through a two-step review process. The first step includes scientific review and rating with an assessment of the strengths and weaknesses of each application based on the defined review criteria described below. During the second step, funding recommendations are determined based on an assessment of the reviewer scores and written comments. Final decision of funding will be made by the KCNT1 Epilepsy Foundation's Board of Directors.
3) Proposal Content and Review Criteria: The following criteria will be utilized in proposal review.
    - **Project Proposal -** Is the proposed project of high scientific quality? Is the budget fully justified and reasonable in relation to the proposed project?
    - **Background -** Is the fundamental objective of the study and hypothesis to be addressed clearly defined?
    - **Scientific Approach -** Will the proposed specific aims answer the study hypothesis? Will the scientific approach effectively test and answer each specific aim? Are the study goals supported by existing data?
    - **Clinical Impact -** Is the answer to the study hypothesis important to our ability to treat or reduce rare disorders/disease incidence and/or mortality? Will the proposed research lead to substantial advances and/or contribute to large leaps of understanding or knowledge that will contribute to reductions in disease incidence and/or mortality within the decade?
    - **Research Significance -** Does the study address an important question that is not likely to be addressed without this funding? Does the proposed study offer a unique opportunity to explore an important issue and/or employ a novel approach to this disease research? Will the study outcomes advance our knowledge of this disease and/or contribute to changes in the focus of future research questions or the way we conduct research on this issue?
    - **Investigator Qualifications –** Does the investigator hold a track record of outstanding accomplishment as evidenced by peer-reviewed publications and funding awards? Does the investigator have access to the resources and environment necessary to complete the study as outlined?

Anonymous reviewer feedback is shared upon the request of the applicant at the discretion of the KCNT1 Epilepsy Foundation where appropriate.

Confidentiality:
The KCNT1 Epilepsy Foundation Grant Program is a confidential process and all content of the Full Applications will be kept confidential. Our expert reviewers sign a CDA in advance of the review process. In order to encourage sharing of new techniques and findings to advance science, after funding decisions are made, the KCNT1 Epilepsy Foundation will share a non-confidential lay summary of the research proposals received (required), including those that were not funded, with each participating funding organization upon request.

Fund Disbursement:
Funds will be issued through a cost reimbursement mechanism executed by purchase order from the KCNT1 Epilepsy Foundation. Details of invoicing schedules and reporting requirements will be made available upon award. For additional information, please contact Sarah Drislane at Sarah@KCNT1epilepsy.org.