Call for Proposals, October 2022

GREGoR Consortium's Small Research Grants to Advance Understanding of Unsolved Mendelian Diseases

The GREGoR Consortium solicits applications for small-to-medium scale projects **that will complement our ongoing efforts** to develop novel approaches to identify candidate variants/genes underlying rare genetic diseases and phenotypes, particularly those that remain unsolved following whole exome sequencing.

Letters of intent due: Dec. 2, 2022
Proposals due: Jan. 13, 2023
Awards announced: Mar. 1, 2023
Earliest start date: Apr. 1, 2023

The Genomics Research to Elucidate the Genetics of Rare diseases (GREGoR) Consortium is a network of researchers at five Research Centers and a Data Coordinating Center focused on developing strategies to more readily identify causal variants associated with rare genetic diseases that have not been solved using whole exome sequencing. Researchers in the GREGoR Consortium employ a variety of high-throughput sequencing approaches, analytical strategies, and functional assays to achieve this goal. Details about the Consortium can be found on the Consortium's website.

The GREGoR Opportunity Funds program is intended to provide funding for small-to-medium projects with well-defined scope that complement the ongoing work of the GREGoR Consortium. Priority will be given to proposed projects that use experimental or analytical approaches that complement ongoing efforts by the GREGoR Consortium. GREGoR samples span a wide spectrum of rare diseases, and we encourage proposals focused on a broad range of phenotypes, disease areas, and organ systems.

Topics

Priority research areas appropriate for this call include, but are not limited to:

New genomic technologies / molecular assays that can be applied to unsolved cases

- Projects to pilot the use of emerging or novel genomic technologies on existing GREGoR samples or other appropriately consented unsolved cases after exhaustive sequencing and analysis (i.e. samples that are unsolved after clinical exome alone are not appropriate for these pilot studies).

User-friendly interfaces for annotation and interpretation of candidate variants in non-coding regions that adapt/reuse existing datasets and domain-expert tools to create a web portal and accompanying interpretation guidance (cutoff scores/ranks/etc.) for use by a broad audience of clinicians and researchers. High priorities include:

- Given genomic coordinates of a (typically noncoding) SNV or indel:
    - Does the variant add or remove a transcription factor binding site, is the predicted change in the transcription factor binding likely to have a large effect on gene regulation consistent with a monogenic cause of disease?
    - For which gene(s) is the variant predicted to decrease or increase expression, by how much, and in which tissues?
- Create a comprehensive set of annotations of predicted regulatory elements for a variety of tissues of interest that could be used to identify candidate regions for novel/unsolved Mendelian phenotypes (e.g. developmental heart defect, cerebellar malformation, limb malformation, skin, immune system, reproductive organs, etc.)

Novel analytical approaches that would be useful for analyzing GREGoR molecular data (these data include, but are not limited to: short-read sequencing, long-read Nanopore and PacBio sequencing, RNA-Seq, methylation array and sequencing, metabolomics, optical genome mapping)

- Head-to-head comparisons of available tools for prediction of variant pathogenicity.
- Development or piloting of new computational tools for variant filtration/analysis (e.g. RNA-Seq data, methylation from Nanopore or PacBio sequencing data).

Proposals regarding other novel approaches and techniques that complement the goals of the Consortium are welcome.

Proposals to carry out routine diagnostic sequencing and analysis of individuals whose samples are not part of a GREGoR center's study cohort will not be considered for this call. Researchers or clinicians who would like to collaborate with GREGoR Research Centers on these types of projects should email the Consortium's Data Coordinating Center at gregorconsortium@uw.edu.

Letter of Intent

(Due date Dec. 2, 2022) Interested applicants must submit a Letter of Intent (LOI) containing a short description (up to half a page) of their proposed research and the names and affiliations of anticipated key personnel. The letter should specify whether or not the proposed research involves human subjects research and/or involves animals. Please use this LOI template and submit your LOI by email to: gregorconsortium@uw.edu and mention "Letter of Intent" in the subject line.

Application Format and Submission

Applicants whose proposal (as described in the Letter of Intent) is considered responsive to the Solicitation will be sent a link by Dec. 16, 2022, inviting them to submit a full application. More information about how to submit the application will be provided. Those invited to apply will be provided detailed information about how to do so.

Budget and Project Period
Applicants may request up to $175,000 in direct costs for one year or (on average) $125,000 per year for up to two years (or $250,000 direct cost combined over two years). The budget and project period should reflect the needs of the proposed project. The Consortium intends to spend a total of $900,000 for the awards for this funding cycle.

Application Due Dates
Jan. 13, 2023; Jan. 2024 and Jan. 2025 (specific dates for 2024 and 2025 will be announced later)

Eligibility
Any investigator who is not part of a funded GREGoR center (i.e., does not have 'core member' status in GREGoR) is eligible for this funding call. An awardee may, however, be at the same institution as a GREGoR center.

Researchers from academic institutions within and outside the US are welcome to apply. Multiple applications from the same institution and principal investigator are allowed provided the proposals are sufficiently distinct scientifically. However, depending on the number of meritorious applications, diversity in institutions and investigators will be taken into consideration.

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Principal Investigator(s) (PI(s)) is invited to work with their organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are encouraged to apply for these funding opportunities.

Questions
If you have questions regarding eligibility or appropriateness of your research idea, we strongly encourage you to email gregorconsortium@uw.edu.

A brief summary/comparison of GREGoR Grant Opportunities.