Request For Proposals: Pharmacodynamic Biomarker Development

The Friedreich's Ataxia Research Alliance (FARA) is issuing a request for proposal (RFP) to support clinical drug development programs in Friedreich's ataxia (FRDA) by promoting the discovery of technologies to measure frataxin or surrogates of frataxin in inaccessible and disease relevant tissues.

Despite low levels of frataxin throughout the body in FRDA, only certain tissues appear to be impacted by its loss. These tissues include (but are not limited to) the proprioceptive system, deep cerebellar nuclei and the heart. Most of these clinically relevant tissues cannot be biopsied, making it difficult to assess whether therapeutic approaches that increase frataxin levels have done so in affected tissues. Blood, CSF, skin and buccal samples do not appear to be effective surrogates for frataxin levels in the CNS.

This RFP supports the discovery and validation of non-invasive and quantitative methodologies to measure the following in FRDA affected tissues (brain, spinal cord or heart):

A. Frataxin protein levels
B. Biochemical activities dependent on/downstream of frataxin function that can be surrogates of frataxin in inaccessible tissues. These surrogates must closely track frataxin level as it increases or decreases in disease-relevant tissues and must be responsive to therapeutic approaches, specifically frataxin gene and protein replacement therapies, and treatments aimed at increasing frataxin levels and restoring/substituting for frataxin function. For instance, in a gene therapy trial, the surrogate marker must reflect the degree to which frataxin levels have been restored in spinal cord, brain and/or heart.

Examples of areas of development include, but are not limited to:

- Validating established molecular imaging ligands that allow measuring frataxin and/or biochemical processes dependent on frataxin function in affected tissues
- Further validating promising biomarker assays at multiple clinical sites or expanding their use to clinical trials

FARA will consider proof of concept and high-risk proposals, without preliminary data, provided they show a strong rationale for the proposed use and development of such biomarkers. Applicants are encouraged to propose bold and creative approaches to these longstanding challenges, while applying scientific rigor and demonstrating plausibility and feasibility of the approach.

The development of peripheral (blood, CSF, skin, buccal samples) pharmacodynamic biomarkers will be considered only if they reflect the pathology of the affected tissues (brain, spinal cord or heart) and if a compelling biological rationale and connection to frataxin levels and/or frataxin function is established.

Please note: The development of pharmacodynamic biomarkers for pharmacological interventions that do not result in frataxin or frataxin function increase or restoration are not supported by this RFP and will not be considered.

All proposals will be evaluated for:

- Novelty and biological plausibility linking the biomarker to frataxin loss and disease pathophysiology in human studies
- Scientific and technical merit of the proposed approach
- Strength of preliminary data (where applicable)
- Level of innovation
- Feasibility in clinical studies, research design and methodology
- Investigators, organizational capabilities, and budget for the project

Informal inquiries regarding study relevance and interest to FARA are welcome and should be directed to grants@curefa.org.

For a list of available research resources that could be helpful in developing your proposal, please visit https://www.curefa.org/researchresources

Eligibility

Those eligible to submit proposals include investigators from public and private nonprofit universities, colleges, hospitals, laboratories, government agencies, biotechnology/pharmaceutical companies, other for-profit entities; irrespective of the country of origin. Investigators at all academic levels (or equivalent) may be named as the PI on the application. Collaborative efforts are encouraged.

Letter of Intent Submission Deadline

December 1, 2021

Application Submission:

Please submit your Letter of Intent (LOI) here (https://webportalapp.com/sp/login/fara_grants). See https://www.curefa.org/grant-apply for detailed instructions regarding the information that needs to be

included in the LOI and page limits. CVs/biosketches for the Principal Investigator and all other key personnel must be submitted.

All submitted LOIs will be review by FARA's Scientific Review Committee and selected applicants will be invited to submit a full application.

Budget

Grant amounts will be commensurate with the resources necessary to develop and validate such pharmacodynamic biomarkers to the degree that they can be used to support early-phase clinical trials. Allowed budget will depend on stage and scope of research. The anticipated direct costs should be detailed and adequately justified, and an estimate of the budget must be included with the LOI submission. Funding will be awarded for a maximum of 2 years. FARA does not fund indirect costs.

Please contact grants@curefa.org for questions or assistance with the application.