FARA, Ataxia UK and GoFAR invite proposals for projects to develop biomarkers by non-invasive approaches for evaluating the molecular and pathological features of affected neurons in Friedreich's ataxia patients.

Background:

Friedreich's ataxia (FRDA) is an autosomal recessive neurodegenerative condition caused by mutations in the frataxin gene (*FXN*). Most affected individuals (>95%) have a GAA repeat expansion mutation in the first intron of both copies of *FXN*, which results in extensive silencing of gene expression and reduced levels of frataxin. Frataxin is a highly conserved protein that is essential for iron-sulfur cluster biogenesis in the mitochondria. Individuals with FRDA produce about 5-15% of the normal level of frataxin, while unaffected carriers produce about 40-60%. The low level of frataxin in patients results in progressive neurodegeneration that affects multiple neuronal populations of the central and peripheral nervous systems, often accompanied by severe cardiomyopathy and diabetes mellitus. Drug discovery efforts have focused on various epigenetic and gene replacement approaches to restore frataxin to carrier or normal levels. Several candidate treatments are ready to move from pre-clinical development to early stage clinical trials in patients. Because we currently lack methods for measuring disease-relevant biochemical, molecular, and cellular changes in the nervous system, many of these early stage trials are relying on frataxin levels and other biomarker measures obtained from blood or buccal epithelial cells or other peripheral tissues not directly affected by the disease.

Request for Proposals (RFP):

The Friedreich's Ataxia Research Alliance (FARA), GoFAR and Ataxia UK are partnering to fund innovative research projects that seek to investigate directly in FRDA patients the molecular and pathological features of affected neuronal populations: specifically neurons of the dorsal root ganglia, corticospinal tracts, dentate nuclei, and the cerebellum. Cellular and pathological features may include but are not limited to measures of *FXN* expression/regulation, measures of functional consequences of frataxin deficiency (i.e., mitochondrial dysfunction and degeneration, iron accumulation, oxidative damage, etc.), measures of neuronal degeneration and loss, and measures of neuronal transmission deficits. The proposed measures should be non-invasive or minimally invasive and directly obtainable in living subjects. Of particular interest are approaches that enable the detection of early pathological signs in diagnosed individuals who have not yet developed extensive neuronal loss, and can therefore provide insights on the disease progression from a neuropathological perspective and ultimately to permit early intervention. Preference will be given to studies that are longitudinal and also include children. Animal studies to develop methods may be a component of the work proposed, but studies in human subjects must be included to be responsive to the RFP. It is expected that the proposed studies will provide invaluable information on the natural history of FRDA and indispensable clinical tools to evaluate therapeutic efficacy.

Collaborations between functional and structural neuroscientists and the FRDA clinical research community are encouraged in order to develop innovative approaches that achieve the objectives of this RFP.

Proposal Details:

Those eligible to submit proposals include investigators from biotechnology/pharmaceutical companies, other for-profit entities, public and private nonprofit universities, colleges, hospitals, laboratories, and government agencies, irrespective of the country of origin.

A Letter of Intent (LOI) is required for all proposals and must be submitted by November 1st 2013. The LOI must contain a brief description of the objectives, rationale, and key preliminary data for the project (1-3 pages is sufficient), an estimate of the budget, and the CV/biosketch for the principal investigator and any key collaborators. The LOI must be submitted as a PDF file via email to jen.farmer@curefa.org. The subject line should read as follows, LOI FARA/Ataxia UK/GoFAR RFP. The LOIs will be reviewed by the funding organizations Scientific Research Committees and, based on the outcome of this review, the submitting investigators will be either invited to submit a full proposal or informed that the LOI has been declined. This notification should be made within two weeks of the LOI deadline.

The deadline for receiving full proposals is January 15th, 2014. Awards will be announced March 20th, 2014, and will have a start date of April 1, 2014.

As a general guideline budgets should not exceed $150,000 for a 12-month period; however budgets >$150,000 will be considered if the applicant can present adequate justification of expenses required to support the proposal. While initial proposals will be accepted for one year, contingent upon significant progress and quality of results, funding may be extended for a second year to enable collection of additional longitudinal data. FARA, Ataxia UK, and GoFAR do not support indirect costs.