THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

Spring 2023 Request for Applications
Data-Driven Subtyping and Stratification Program

BACKGROUND

Parkinson's disease (PD) affects nearly 1 million people in the US and over 6 million worldwide, and those numbers are expected to rise over the coming decades. PD is highly heterogeneous: individuals experience a wide array of motor and non-motor symptoms, many of which depend on disease severity and duration. Though our understanding of PD and its causes is growing, many questions remain. There are no drugs available for Parkinson's known to alter the progression of the disease, and current symptomatic treatments provide limited relief but come with complications and side effects.

The Michael J. Fox Foundation (MJFF) funds research to better define, measure, and treat Parkinson's disease as well as critical tools and other resources to advance that research. The purpose of this Request for Applications (RFA) is to **expand our understanding of PD subtypes to support precision medicine approaches in PD research**. To this end, MJFF believes that promoting data-driven identification, characterization, and validation of these subtypes will address a critical gap in the field.

Parkinson's disease in living patients remains characterized largely by its core clinically assessed motor and nonmotor symptoms, despite clear heterogeneity of disease features. These include age at onset (AAO), rate or mode of progression, and presence or absence of specific symptoms. This observed heterogeneity supports a model where different pathways may be affected, and independent or overlapping biological features may represent different subtypes of disease. While some heterogeneity can be attributed to known or yet-to-be-identified genetic or environmental risk factors, it remains unclear what biological mechanisms may affect the presentation, progression, and treatment response of PD. Further, how specific subtypes correlate with symptoms, features, or potential biomarkers remains incompletely understood. Addressing the underlying neurodegeneration and damage of dopaminergic neurons may well be advanced by selective targeting of pathogenic mechanisms leading to this condition, bringing emerging precision medicine approaches to support improved symptomatic and mechanistic treatments.

To expand our understanding of this heterogeneity and support identification of molecular features and targets, we are seeking research proposals focused on identifying, characterizing, and/or validating subtypes of PD through expanded analysis of existing data sets.

PROGRAM GOAL

The Data-Driven Subtyping and Stratification Program seeks to build on previous efforts in Parkinson's disease subtyping through identification of robust, empirically derived subtypes. Funding will support projects poised to identify, characterize, and compare disease subtypes through use of existing clinical and molecular data sets.

PROGRAM PRIORITIES

The Data-Driven Subtyping and Stratification Program supports programs centered on:

- Analysis of existing clinical and molecular data sets to derive, characterize, or validate subtypes of PD
- Identification of clinical features which best cluster with, or within specified risk groups in PD
- Identification of clinical, behavioral, and molecular indicators, or combinations thereof, that are most significant in identifying subtypes of PD
- Analysis of clinical and molecular features linking, or distinguishing different genetic subtypes of PD (i.e., LRRK2, GBA), or identification of features consistent across carriers regardless of disease status
- Identification of shared and/or discriminatory features between PD, related parkinsonisms, and other synucleinopathies (i.e., multiple system atrophy)
- Identification of novel prodromal indicators or antediagnostic features enriched in PD patient populations
- Primary drivers of AAO for given background/risk group

When considering proposals submitted to this program, MJFF encourages investigators to:

- Leverage multiple cohorts with harmonized clinical and/or biological data when feasible
- Demonstrate access to and familiarity with proposed data sets and cohort features, such as enrollment criteria, medication status, and demographic representation. Explain how the analyses will control for these potential variables within and across cohorts
- Demonstrate expertise in analysis of data modalities included in proposal
- Demonstrate prior success for proposed analyses in PD or other relevant disease states
- Focus on objective, data-driven strategies to identify subtypes
- Utilize large and/or deeply characterized multi-modal data sets
- Ensure sample sizes are sufficiently justified

For this round, MJFF **will not consider** proposals focused on the following:

- Exploratory proposals lacking specific data analysis aims
- Prospective cohort development or molecular/imaging data generation
- Replication or review of published work without novel analysis aims
- Curation, harmonization, or visualization efforts without novel analysis aims
- Proposals including therapeutic development or identification of therapeutic compounds
- Requests for biosamples

FUNDING AVAILABLE

Duration: 12-18 months after initiation of award
Award Amount: $50,000 to $375,000. Requested support should be commensurate with work proposed.

These budgets include direct and indirect costs. For academic and for-profit institutions, no more than 15% or 10%, respectively, may go to indirect costs. Additional details about MJFF's indirect cost policy can be found in the Application Guidelines and FAQ.

DEADLINES & REVIEW SCHEDULE

- Pre-proposals Due: Tuesday, September 27, 2022, 5 p.m. US ET
- Full Proposal Invitations: Week of November 14, 2022
- Full Proposals Due (by invite only): Thursday, January 12, 2023, 5 p.m. US ET
- Anticipated Award Announcement: Week of April 17, 2023
- Anticipated Funding: April 2023

Applicants are encouraged to apply early to allow adequate time to correct errors found during the submission process.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by researchers or clinicians in:

- U.S. and non-U.S. biotechnology/pharmaceutical companies, or other publicly or privately held for-profit entities; and
- U.S. and non-U.S. public and private non-profit entities, such as universities, colleges, hospitals, laboratories, units of state and local governments and eligible agencies of the federal government.
- Post-doctoral fellows are eligible to apply as co-investigators with the designation of an administrative primary investigator who directs the laboratory in which the fellow will conduct research. The administrative PI will be responsible for assisting in providing all institutional documents required for the project and will be required to sign any award contract. Training or mentoring-only proposals will not be considered.

DIVERSITY, EQUITY, AND INCLUSION (DEI)

In pursuit of our mission to accelerate the development of better treatments and a cure for Parkinson's disease, MJFF aims to support a rigorous research agenda reflecting a wide and diverse range of perspectives on Parkinson's disease and carried out in diverse populations. Diversity may refer to characteristics including, but not limited to, race, religion, ethnicity, sex, gender identity, sexual orientation, socioeconomic circumstance, nationality, geographic background, ability and disability, political ideology and age. Parkinson's is a complex problem; the more angles from which we attack, the greater the chances of finding innovative scientific solutions to benefit everyone living with the disease. As such:

- The Foundation encourages applications from diverse investigators representing groups historically underrepresented in the research enterprise.
- Because research shows that diverse teams outperform homogeneous ones, we urge applicants to share information about the composition of the team that will carry out the funded work.
- Specific DEI considerations and/or objectives for this program include:
    - Proposals which utilize data from diverse, well-characterized cohorts in their analysis

ADDITIONAL INFORMATION

The Application Guidelines provide general guidance on applying for funding from MJFF, though the RFA always supersedes information contained in the Application Guidelines.

MJFF holds an open access publication policy requiring articles resulting from MJFF-funded work to be published in a preprint repository, then in an open access forum with free and immediate readership rights.

MJFF requires that the Principal Investigator be the primary applicant (i.e., the person who initiates and takes primary responsibility for the application). All application-related correspondence will be sent to the Principal Investigator.

INFORMATIONAL WEBINAR

MJFF has made available an informational video to clarify and explain the goals of our funding opportunities and application process. The video is available to view on-demand on the MJFF funding opportunities webpage.

For questions about the application process or project suitability for this call for applications, please email grants@michaeljfox.org.