THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

Summer 2023 Request for Applications
Lysosomal Biomarkers Program

BACKGROUND

Parkinson's disease (PD) affects nearly 1 million people in the US and over 8 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 that 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, while also supporting critical tools and other resources to advance that research. In recent years, we have seen an explosion of drug development around lysosomal targets, despite the fact that the ways to measure this pathway remain limited. Given the role of lysosomal & protein clearance dysfunction in PD more broadly, a robust toolbox of lysosomal biomarkers will enable identification of patient populations as part of a precision medicine approach, while also supporting known and emerging lysosomal targeted therapeutics. The purpose of this Request for Applications (RFA) is to advance lysosomal pathway biomarkers, which are currently a critical gap across all intended uses.

PROGRAM GOAL

The Lysosomal Biomarkers Program seeks to develop, optimize, and validate biomarkers related to lysosomal function, protein clearance/autophagy and lipid homeostasis. Funding will support projects to:

- Develop, optimize or validate *molecular bioassays* (ex. mass-spectrometry or immunoassay approaches) for autophagy or lysosomal analytes
- Investigate *imaging* approaches in the brain or other areas (ex. lipidated microtubule-associated protein 1A/1B-light chain 3 (LC3), autophagosome number, lipofuscin, lysosomal content, glucocerebrosidase (GCase) tracer, etc.)

- Measure *functional endpoints*, *dynamic measures*, *in vivo activity* or *lysosomal flux* (ex. heavy labelling approaches)
- Analyze existing datasets (including non-PD human data) to identify molecular measures of lysosomal function in normal and disease states towards identification of *patient enrichment markers* for lysosomal targeted therapies

This program welcomes biomarkers to specifically support lysosomal targeted therapies (ex. TMEM175, TRPML1, GBA, etc.) and also those geared towards quantification of lysosomal dysfunction or lysosomal dysfunction states more broadly.

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

- Non-lysosomal associated biomarkers
- New unbiased discovery data generation efforts which may identify lysosomal 'hits'
- Basic biology projects to better understand lysosomal pathway/dysfunction without a clear link to translatable biomarkers

PROGRAM PRIORITIES

The Lysosomal Biomarkers Program will consider applications spanning all stages of the biomarker pipeline, including development, optimization and validation. MJFF encourages applicants to *get creative* and *think outside the box* when considering how to address challenges surrounding measurements of this pathway (ex. evaluation of lysosomal versus secreted GCase, methods to measure protein turnover, lack of readily available tools/antibodies, etc.).

This RFA will fund proposals related to:

- Markers of autophagy (including measures of upstream signaling cascade & more tractable targets like p62, cathepsins, LAMPs, etc.)
- Other lysosomal pathway markers/interactors (including lipid markers & GCase interactors)
- Please note: Due to the lack of available antibodies to measure many relevant analytes, antibody generation *may be considered* with relevant justification for why new development is necessary for the proposed assay work. If proposing novel antibody generation to support assay development, please consider long term access for relevant assay work (ex. use of monoclonals, path to commercialization & scalability, any IP considerations, etc.). Working with MJFF to deposit the resulting antibody in an MJFF-designated repository for community access is a requirement of the program.

When considering submissions to this program, MJFF will prioritize those that:

- Have potential to directly inform ongoing or upcoming clinical trials
- Directly inform precision medicine approaches for patient selection & stratification
- Include clear indication of how the proposed biomarker will be used to inform PD diagnosis, prognosis, monitoring, prediction, susceptibility and/or pharmacodynamic response

Note: Clear translational value and path to use of the assay in the clinic should be described if fibroblasts or iPSCs are used.

FUNDING AVAILABLE

Duration: 12 to 24 months
Award Amount: Up to $350,000. Requested support should be commensurate with the 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: January 17, 5 p.m. US ET
- Full Proposal Invitations: Week of March 10, 2023
- Full Proposals Due (by invite only): May 11, 5 p.m. US ET
- Anticipated Award Announcement: Week of August 14, 2023
- Anticipated Funding: August 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.

BIOSAMPLE REQUESTS

Applicants may propose studies designed to evaluate biomarkers in human biospecimens. Investigators are encouraged to leverage existing tissue and biosample resources if possible. New biosample collection should be limited to studies where clinical biosamples are unavailable for the intended purpose (ex. different sample collection protocol required, specific cohort required or novel biomatrix proposed).

Studies requesting access to biosamples available through MJFF-sponsored biospecimen and cell line collections are eligible to apply to this initiative. In these cases, access to samples will be reviewed in parallel to funding requests by the committees overseeing the biospecimen collection(s) requested. To review MJFF's available biosample collections, please consult the MJFF website and biorepository inventory catalogue. Groups requesting access to samples only (without funding) should contact resources@michaeljfox.org.

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 consideration that cohort(s) investigated are representative of all people with Parkinson's (ex. for recruitment of new subjects and reporting of demographics of existing samples)

Note: Proposals to validate known/existing biomarkers in underrepresented groups will be considered.

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.

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