Parkinson's Progression Markers Initiative

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Winter 2025 Request for Applications
PPMI Biofluid Biomarkers Program

BACKGROUND

The Parkinson's Progression Markers Initiative (PPMI) is a landmark study to identify biological markers of Parkinson's onset and progression. Initiated in 2010, PPMI has enrolled thousands of subjects spanning diagnosed Parkinson's disease (PD), healthy controls, at risk individuals, and specific mutation carriers. Participants are longitudinally evaluated through comprehensive clinical assessments and imaging studies, and biosamples are collected using standardized sample collection, handling, and processing procedures administered through centralized biorepositories. These include DNA, RNA, whole blood, serum, plasma, peripheral blood mononuclear cells (PBMCs), urine, cerebral spinal fluid (CSF), and skin biopsies. Central to its mission and core values, PPMI provides the research community with a comprehensive, standardized, open access data set and biosample library..

A new era of biologically defined PD is upon us, as exemplified by the development of biology-based paradigms (Neuronal Synuclein Disease and SynNeurGe) and an integrated biologic and clinical research staging platform (NSD-ISS). The staging system is anchored to two well characterized, validated measures of disease pathology: alpha-synuclein (aSyn) aggregation (as measured today by the aSyn seed amplification assay (SAA) in CSF) and dopamine dysfunction (using DaT SPECT imaging). The goal is that these two core biomarkers are measured in every PPMI participant. Looking ahead to a future state of individualized patient care, crucial needs remain toward refining this biological definition through integration of additional biomarkers of disease pathogenesis from the earliest stages of neurodegeneration, those that track disease progression, and ones that provide insights into the presence of additional neurodegeneration pathology. MJFF is eager to accelerate this work to capitalize on current momentum around the biological definition of the disease.

PPMI is uniquely poised to catalyze these efforts and the PPMI Steering Committee has articulated the following 2025 strategic goals that can be addressed with available longitudinal biosamples and dedicated funding resources. These are to:

- Identify and validate biomarkers of aSyn pathology (beyond aSyn SAA in spinal fluid).
- Further understanding of biologic endotypes underpinning initiation/progression prior to and after onset of Parkinson's disease symptoms using targeted and unbiased omics platforms.

- Comprehensively characterize known biomarkers of neurodegeneration (including amyloid, tau, TDP-43, NfL).
- Advance biomarker characterization across the spectrum and time-course of disease with a focus on both those that are aSyn SAA positive and those with genetic variants that are aSyn negative but with DAT imaging deficit to predict and/or correlate with progression in biomarker, motor, cognitive, and other clinical domain outcomes.

PPMI recently executed an ambitious, multipronged approach to address these goals through assessment of CSF and/or plasma by NULISAseq CNS and Inflammation panels, Olink Explore HT, and priority targeted neurodegeneration analytes (Abeta40, Abeta42, total tau, ptau-181, p-tau217 and MTBR-tau243, NfL, and GFAP). Concurrently, development/validation of blood-based and skin-based aSyn SAA studies are also underway. These new data will be available in real-time in PPMI's **open access data repository** alongside existing clinical and imaging data. View a complete list of already available and upcoming PPMI biospecimen data, **here.**

PROGRAM GOAL

The purpose of this Request for Applications (RFA) is to engage the research community in broadening the assessment of biomarkers in existing PPMI biosamples. This RFA will support (through the provision of PPMI biosamples and commensurate funding) studies that address the strategic goals of PPMI listed above and facilitate refinement in the biological definition of PD and related disorders prior to and following onset of symptoms.

The PPMI Biofluid Biomarkers RFA will support projects aiming to test biomarkers that have the potential to refine the current definition and staging paradigm of PD via:

- Detection of biological mechanisms from the earliest stages and understanding their relationship to the emergence of aSyn SAA status, dopamine deficiency and other biomarkers and symptom onset.
- Prediction of progression of biomarker and clinical (motor, cognition, and other) outcomes of PD.
- Correlation of progression of biomarker and clinical (motor, cognition and other) outcomes of PD.
- Identification of biologically defined subsets of PD participants.
- Detection of pathogenic/pathophysiologic mechanisms in PD cases without evidence of asyn aggregates (ex. aSyn SAA negative LRRK2 PD) or non-neuronal forms of parkinsonism such as multiple system atrophy.

To be considered for funding, the biomarker assay must satisfy one or more of the criteria above, be analytically validated and deployable in existing PPMI biosamples (see inventory here).

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

- Imaging or digital endpoints
- Use of biosamples from non-PPMI cohorts
- New biosample collection
- Cell line requests
- Proposals focused solely on analysis of existing PPMI data
- Development of novel biomarker assays from scratch
- Unbiased discovery proteomics efforts

PROGRAM PRIORITIES

The PPMI Biofluid Biomarkers Program will support the following work in PPMI biosamples:

- Quantitative, known biomarkers of neurodegeneration (ex. amyloid, tau, TDP-43, NfL) in existing biofluids.
- Biomarker discovery using targeted, multiplexed panels (excluding proteomics, which is well covered already in PPMI).
- Pathway focused biomarkers (ex. mitochondrial dysfunction, immune dysfunction/inflammation, endolysosomal dysfunction) to support biological subtyping.
- aSyn pathology biomarkers with priority to those that are quantitative.

When considering proposals submitted to this program**, MJFF will prioritize those that**:

- Situate the proposed molecular bioassay analysis within the breadth of existing PPMI clinical, imaging, genetic and other molecular data.
- Establish a clear link to at least one of the strategic goals listed above.
- Evaluate the proposed biomarker for a specific context of use.

Projects funded through this program will be established as **collaborations** between the awardee and PPMI. To this end, Study Leadership intends to work closely with funded investigators by providing active thought leadership throughout the project, guidance on sample selection and statistical support. All biosample/funding recipients must abide by PPMI's open data principles by depositing data into its publicly accessible database prior to becoming unblinded to subject IDs and PD status and adhering to MJFF's publication policy.

FUNDING AVAILABLE

Duration: 6 to 24 months
Award Amount: Up to $750,000. 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.

DEADLINES & REVIEW SCHEDULE

- Pre-proposals Due: May 27, 2025, 5 p.m. US ET
- Full Proposal Invitations: Week of July 18, 2025
- Full Proposals Due (by invite only): September 16, 2025, 5 p.m. US ET
- Anticipated Award Announcement: Week of December 16th, 2025
- Anticipated Funding: January 2026

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 ineligible to apply as Principal Investigators

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.

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. Grantees will be asked to provide proof of compliance with this policy, and future funding will be contingent upon adherence.

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.

CONTACT INFORMATION

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