THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

Spring 2025 Request for Applications
Seed Amplification Assay Innovation Program

BACKGROUND

Parkinson's disease (PD) affects nearly 1 million people in the US and over 6 million worldwide, with these numbers expected to rise in the coming decades. PD is highly heterogeneous, meaning individuals experience a wide array of motor and non-motor symptoms, which depend on disease severity and duration. While our understanding of PD and its causes is improving, many questions remain. Currently, no drugs exist that can alter the progression of PD, and available treatments focus only on alleviating symptoms, providing limited relief while often coming 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. MJFF's funding to develop, analytically qualify and validate alpha-synuclein seed amplification assays (aSyn-SAA) in cerebrospinal fluid (CSF) contributed to the recent Letter of Support by the FDA toward the use of CSF aSyn-SAA for patient enrichment in therapeutic trials. Specifically, CSF aSyn-SAA has >90% sensitivity and specificity for identifying recently diagnosed sporadic PD cases. Importantly, CSF aSyn-SAA can detect neuronal alpha-synucleinopathy prior to clinical diagnosis, thereby providing an important anchor for the biology-founded Neuronal Synuclein Disease Integrated Staging System (NSD-ISS). However, two critical gaps need to be addressed to integrate aSyn-SAA into clinical practice and therapeutic development:

1. Current aSyn-SAAs provide binary (positive/negative) results, rather than quantitative assessment. This precludes their use for monitoring disease progression and evaluating treatment effects.
2. The invasiveness of spinal taps limits its utility in routine clinical practice, can delay or deter subject recruitment in clinical trials, has poor accessibility/acceptance in some geographies and is not amenable to frequent repeated sampling.

The purpose of this Request for Applications (RFA) is to overcome these obstacles by funding projects that directly address these challenges through the development of *quantitative* aSyn-SAA in CSF as well as in *more accessible* biofluids or tissues. Applicants may seek to address one or both challenges in a single application towards the goal of enabling feasible, efficient and quantitative measures of aSyn in SAA for clinical trials.

PROGRAM GOAL

The SAA Innovation Program seeks to advance the development of high performance, quantitative seed amplification assays for aSyn, addressing the critical need for less invasive, highly sensitive and quantitative biomarkers in clinical trials. MJFF's priorities for this RFA are aligned with the current state of the field as described below:

- Existing aSyn-SAA in CSF exhibits extremely high sensitivity and specificity for neuronal synuclein disease and can identify individuals who are at high risk for developing PD and Dementia with Lewy Bodies (DLB) years before symptom onset. Nonetheless, CSF-SAA cannot be used as a biomarker of disease progression or pharmacodynamic/therapeutic response without technical advances that enable robust quantitation. Proposals addressing this critical need that can advance the quantitation of SAA in any biological matrix (including CSF) will be given top priority.
- aSyn-SAA in other biofluids and tissues have the potential to augment CSF assays but require further analytical development and validation. While studies have demonstrated feasibility in matrices such as skin, blood, tears, saliva and olfactory mucosa, the field still grapples with issues of sensitivity, specificity and reproducibility. Pre-analytical variables, such as optimal methods for sample collection, storage and processing are poorly understood and vary between studies. These gaps in standardization hinder scalability and clinical applicability of SAA in peripheral matrices, making it critical to address these challenges to fully realize the potential of these less-invasive matrices. SAAs in peripheral matrices are also not yet quantitative.

MJFF **will prioritize** proposals that:

- Develop high-performance, quantitative seed amplification assays for alpha-synuclein.
- Tackle challenges in sensitivity, specificity and reproducibility of SAA in peripheral biofluids and tissues.

MJFF **will NOT consider** proposals focused on:

- CSF SAA that is strictly binary
- Semi-quantitative SAA in CSF that is based on the analysis of serial endpoint dilutions
- Immunoassays to measure post-translationally modified forms of aSyn (e.g. pS129-aSyn) or 'total' aSyn
- Other non-SAA techniques
- aSyn imaging proposals
- SAA for misfolded proteins other than aSyn – *Please note that although SAA for other proteins such as TDP-43 and tau are out of scope for this program, you may reach out to us at* grants@michaeljfox.org *to discuss future opportunities.*

FUNDING AVAILABLE

Duration: 6 to 24 months
Award Amount: Up to $1,000,000. 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%, 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

- Full Proposals Due: January 30, 2025, 5 p.m. US ET
- Anticipated Award Announcement: April 2025
- Anticipated Funding: June-September 2025

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 **NOT** eligible to apply as co-investigators.

BIOSAMPLE REQUESTS

Investigators are encouraged to leverage existing tissue and biosample resources if possible. While priority will be given to researchers with access to existing biobanks, studies requesting access to biosamples available through MJFF-sponsored biospecimen are eligible to, through this initiative. In these cases, please respond to the relevant biosample questions in the proposal template document. Please note that 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 biorepository and biorepository inventory catalogue.

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.

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