

Fall 2023 Request for Applications Alpha-Synuclein Post-Translational Modifications Quantification Program

Overview

- **Target:** Projects need to quantitatively map post-translational modifications of alpha-synuclein in people across all stages of PD as well as people without PD
- **Funding Available:** Up to \$1,000,000 over 18-24 months. Requested support should be commensurate with the work proposed
- **Deadline:** Pre-proposals Due on April 18, 2023 at 5 p.m. US ET
- Teams with selected pre-proposals will be required to attend a two-day Synuclein Solutions Bio-Hackathon in-person at MJFF's office in New York City on September 6 and 7
- Invited groups will present, discuss, and further develop their project plans with others in attendance for critical evaluation and feedback



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 a highly heterogeneous syndrome: individuals experience a wide array of motor and non-motor symptoms and rates of progression, many of which depend on disease severity and duration. Though our understanding of the pathogenic mechanisms of PD 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 as well as critical tools and other resources to advance that research. Alpha-synuclein is one of the primary components of protein aggregates known as Lewy bodies that are the pathological hallmark of Parkinson's disease. Although several alpha-synuclein post-translational modifications have been reported, their impact on the physiological and pathological role of alpha-synuclein remains unclear. Lack of reliable protocols, orthogonal assays and associated reagents/tools have driven this knowledge gap. The purpose of this Request for Applications (RFA) is to fund collaborative, interdisciplinary projects that will **quantitatively** map post-translational modifications of alpha-synuclein in people without PD and people at all stages of the disease. Successful projects will provide deeper insights into the normal and pathogenic function of alpha-synuclein, leading to new targets for therapeutic intervention as well as new biomarker candidates.



PROGRAM GOAL

The Alpha-Synuclein Post-Translational Modification Quantification Program seeks to establish robust methods and tools that can quantify the amount and regional distribution of post-translational modifications in alpha-synuclein in Parkinson's disease-relevant brain regions in healthy human subjects and those at different stages of PD. The data generated from these projects should enable more accurate staging of alpha-synuclein pathology, provide insights into therapeutic approaches targeting pathogenic alpha-synuclein and generate information on alpha-synuclein species as biomarker candidates for assessing PD stage and progression.

Applicants with selected pre-proposals will be required to attend a two-day, in-person meeting at MJFF's office in New York City on September 6 and 7, called the Synuclein Solutions Bio-Hackathon. At the hackathon, invited groups will present, discuss, and further develop their project plans with others in attendance for critical evaluation and feedback. The intention is for all invited groups to collaborate in order to revise and improve their project plans through harmonization of protocols and data-sharing. This meeting will be held under a confidentiality agreement.

MJFF envisions that this meeting will support the generation of robust project plans to address this fundamental knowledge gap in alpha-synuclein biology, and that subsequently funded teams will work collaboratively and as a network to validate and strengthen the dataset(s) generated through this program. Teams are also expected to work closely with MJFF and MJFF advisors to deposit data, protocols and field-enabling tools in easily accessible repositories, as well as publish results in open access formats.

Funding will support projects that aim to:

- Optimize and refine reproducible protocols for the isolation of alpha-synuclein (soluble/insoluble) species from brain tissues and inclusions that preserve its biochemical diversity
- Develop, characterize, and validate assays to accurately detect and quantify alpha-synuclein post-translational modifications (PTMs) reliably
- Use reproducible methods to develop quantitative maps of alpha-synuclein post-translational modifications in disease-relevant brain regions
- Utilize new technologies and/or cutting-edge methods to address previously intractable roadblocks

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

- Assessments of alpha-synuclein post-translational modifications in biofluids or non-CNS tissue
- The study of alpha-synuclein post-translational modifications in pre-clinical or cellular models of Parkinson's disease
- Purely qualitative assessments of alpha-synuclein post-translational modifications present in human brain tissue
- Development of antibodies or nanobodies toward alpha-synuclein post-translational modifications



PROGRAM PRIORITIES

When considering proposals submitted to this program, MJFF will prioritize projects and teams that:

- Have previously demonstrated success with the techniques and technologies proposed for use
- Have assembled cross-disciplinary teams with relevant expertise
- Have access to post-mortem brain tissue containing relevant brain regions from subjects with Parkinson's and age-matched controls
- Propose the use of techniques and technologies that can be easily deployed in other laboratories
- Propose the quantification of alpha-synuclein post-translational modifications across multiple stages of the disease
- Show willingness to collaborate with other teams and stakeholders for this program



FUNDING AVAILABLE

Duration: 18 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% 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: April 18, 2023 at 5 pm US ET
- MJFF Synuclein Solutions Bio-Hackathon Meeting Invitation: Week of May 29, 2023
- Synuclein Solutions Bio-Hackathon: September 6 - 7, 2023
- Full Proposals Due: October 6, 2023 at 5 pm US ET
- Anticipated Award Announcement: Week of November 6, 2023
- Anticipated Funding: November 2023

Note that invitation to the Bio-Hackathon does not guarantee funding.



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 the coordinating PI but are eligible to be co-PIs in the team.



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.

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.