Winter 2021 Funding Request for Applications

Alpha-synuclein Seed Amplification Assay Program

This RFA supports research that will facilitate integration of alpha-synuclein seed amplification assays into clinical studies for the purposes of predicting prognosis, tracking disease progression and monitoring therapeutic response in Parkinson’s disease.

BACKGROUND

Parkinson’s disease (PD) is the fastest growing neurological disorder. While therapeutic development marches forward, biomarkers of diagnosis, prognosis and progression remain critical unmet needs for patient care and clinical trials. Given the role of alpha-synuclein (a-syn) in the pathophysiology of the disease, it holds importance as a therapeutic target (with more than a dozen a-syn-focused drug programs in trials) and as a biomarker candidate for PD.

Recent cerebral spinal fluid (CSF) a-syn seed amplification assays (SAAs) have demonstrated high sensitivity and specificity to identify PD study participants. But these findings are from a small sample and with limitations associated with substrate standardization, scalability and quantification. Additionally, a thorough evaluation of performance in more accessible biospecimens is warranted.

A-syn SAAs have the potential to facilitate therapeutic development through enrichment of study subject selection for synucleinopathy and for risk of synucleinopathy prior to the onset of motor or cognitive symptoms. Further development of these assays may extend their utility for (a) prognosis of PD development, (b) monitoring disease progression, and (c) monitoring therapeutic response.

The Michael J. Fox Foundation (MJFF) announces this Request for Applications (RFA) to support a-syn SAA development, optimization to address existing challenges, validation and qualification of existing assays in relevant biosamples/tissues. Funding is also available to explore scalability of commercial *in vitro* diagnostic assays.

To facilitate faster and enduring integration of a-syn SAA into clinical trials, applicants are encouraged to form teams and submit proposals that address one or more of the following key goals reflecting SAA challenges and unmet needs:

* **Goal 1**: Development of a scaled-up, reliable and rapid a-syn SAA as a research use only *in vitro* diagnostic (IVD) with validation package toward an eventual point-of-care IVD integrable into clinical trials with potential for commercial use.

To achieve this (in CSF or other tissues/fluids), MJFF aims to identify partner organizations with technical capabilities, resources and strategic alignment to provide a scaled-up a-syn SAA for clinical studies. Successful applicants should plan to work closely with investigator(s) who originated the assay(s) to test and validate assay performance.

* **Goal 2**: Modification of a-syn SAAs from the current binary (positive/negative) readouts to an analytically validated quantitative assay format that measures a-syn seed concentrations.
* **Goal 3**: Identification of the most sensitive, specific, reproducible, stage-appropriate biomatrix through comparative assessment of an a-Syn SAA on a variety of biomatrices (e.g., CSF, skin, nasal mucosa, submandibular gland, etc.).

Please note, applicants may submit proposals toward a single goal or combination of the goals; addressing all three goals in a single application is not required.

MJFF can help support use of existing MJFF biosample resources, where available, but applicants are encouraged to identify appropriate biosamples through collaborative efforts. New collection for novel matrices may also be considered as needed (e.g., nasal mucosa).

Please note that proposals to measure post-translationally modified (e.g., pS129) or “total” a-syn by immunoassay or other non-SAA techniques are not eligible for funding through this program. Aggregation assays for other (non-synuclein) proteins are also outside the scope. MJFF will launch an RFA for our core funding programs, including around outcome measures, later this summer, where those projects may be considered.

DEADLINES & REVIEW SCHEDULE

* Proposals Due: September 13, 2021
* Anticipated Award Announcement: November 2021
* Anticipated Funding: December 2021

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

FUNDING AVAILABLE

**Duration:** Up to 3 years

**Award Amount:** MJFF plans to allocate at least $3M to efforts across the three identified areas. MJFF encourages applications for projects of all sizes. Requested budget amount will not correlate with prioritization for funding. Requested support should be commensurate with work proposed and must include clear explanation of costs.

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 [Administrative Guidelines](https://www.michaeljfox.org/page.html?administrative-guidelines) [FAQ](https://www.michaeljfox.org/foundation/faq.html?navid=footer-faq).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by researchers or clinicians in or outside the United States in:

* biotechnology/pharmaceutical companies, or other publicly or privately held for-profit entities
* 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 projects may require many kinds of expertise, MJFF encourages industry, academic, clinical and/or non-profit collaborations when appropriate. Applicants proposing prospective recruitment of participants should do so in partnership with clinical centers and/or sites that are equipped to collaborate on such collections.

BIOSAMPLE REQUESTS

Investigators are encouraged to leverage existing biospecimen and tissue resources and/or develop collaborations to acquire necessary samples where possible. Studies requesting access to biosamples available through MJFF-sponsored biospecimen 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 request biospecimens from MJFF download, complete, and upload the Biosample Request form in the Project Proposal Template tab of the online application. The form template can be found near the top of the online application under Documents. To review MJFF’s available biosample collections, please consult the MJFF [biorepository website](https://www.michaeljfox.org/biospecimens) and [biorepository inventory catalogue](https://mjffbiobank.org/#!/biospecimens-and-data). *Note: Biosample requests from MJFF’s Parkinson’s Progression Markers Initiative (PPMI) cohort are not available for this RFA and should not be leveraged for this RFA*.

ADDITIONAL INFORMATION

Our [Administrative Guidelines](https://www.michaeljfox.org/page.html?administrative-guidelines) provide general guidance about applying for funding from MJFF. Please note that the RFA always supersedes information contained in the Administrative Guidelines.

Please note, MJFF now 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.

MJFF will share an informational video to clarify and explain the goals of this funding program. Visit the grant page at [michaeljfox.org/funding](https://www.michaeljfox.org/funding-opportunities) for the latest on that resource.

For questions about the application process or project suitability for this call for applications, please email [grants@michaeljfox.org](mailto:grants@michaeljfox.org).