

SPRING 2022 REQUEST FOR APPLICATIONS CELLULAR PHENOTYPING IN HUMAN iPSCs FROM THE PPMI COHORT

This RFA aims to support additional phenotyping of human iPSCs from the PPMI cohort to facilitate future mechanistic studies and expedite drug screening and proof-of-concept efficacy testing for Parkinson's disease therapeutics.

BACKGROUND

Parkinson's disease (PD) is highly heterogeneous with individuals experiencing a wide array of motor and non-motor symptoms, many of which depend on disease severity and duration. This heterogeneity is not only reflected in the clinical presentation of the disease but also at the molecular and cellular level which is suggestive of the existence of disease subtypes. Through the [Parkinson's Progression Marker Initiative](#) (PPMI) study, the Michael J. Fox Foundation (MJFF) has recruited over 1400 control, prodromal and PD subjects and continues to deeply phenotype these individuals through clinical, genetic, imaging and biological assessment to identify biomarkers.

From a subset of individuals enrolled in the PPMI study, the Foundation has also generated and distributed [iPSCs](#) and shared data generated through the use of these iPSCs with the research community. More recently, the Foundation completed a series of deep molecular phenotyping studies in dopaminergic neurons derived from these iPSCs as part of the FOUNDIN-PD project. This study utilized PPMI iPSCs obtained from controls, sporadic patients as well as from manifesting and non-manifesting individuals carrying mutations in genes associated with PD, such as LRRK2, GBA and SNCA to create a foundational OMICs dataset for PD. The [outcomes](#) of this collaborative effort are already providing insights into markers of dopamine neurons, differentiation efficiency, cell-type enrichments and eQTL associations. Applicants may visit foundinpd.org or watch the [webinar](#) to learn more about the study findings and ongoing analyses.

The goal of this RFA is to expand on the observations made by the FOUNDIN-PD team and incorporate other molecular and functional phenotypic assays to further characterize the iPSCs/iPSC-derived cells from the PPMI cohort. We expect to fund a diverse array of assessments in established/characterized model systems such as a specific cell type (dopamine neurons, microglia, etc.), co-cultures, organoids to help establish a more expansive and robust dataset for future mechanistic studies or drug screening efforts. Note that the development of the model systems is not within scope of this RFA. MJFF envisions the funded teams to work collaboratively and as a network to validate and strengthen the dataset obtained on each iPSC line.

Program priorities:

- Assessments of known targets and pathophysiologic pathways of PD such as GCase, LRRK2, alpha-synuclein, endo-lysosomal system, mitochondria, immune cell function, etc
- Assays to characterize functional, electrophysiological, and/or neuroanatomical phenotypes
- Assays/endpoints that can be [compared to biofluid data](#) on the same individual to determine the value of iPSCs as models for the human disease
- Comparative assessments across different cell types- neurons, glia (CNS and PNS/ENS)
- Assessments in co-culture systems to study cell autonomous and non-cell-autonomous phenotypes
- Contribution of ageing to PD-relevant phenotypes

- Analyses on data generated through the FOUNDIN-PD study (Extensive protocols and all data generated through FOUNDIN-PD is available at <https://www.ppmi-info.org/> => Access-data-specimens / Download data / Genetic data / FOUNDIN-PD)

Requirements:

- Assays that are high-throughput or quantitative for PD relevant phenotypes
- Funded groups must work together to compare protocols and align on QC markers so data generated across lines and across teams can be compared to one another
- Teams are encouraged to deposit their differentiation protocols on protocols.io
- Teams must adhere to the PPMI [data](#) and [sample](#) use policies
- Teams must agree to deposit data back into LONI
- Teams are expected to work closely with MJFF and the FOUNDIN-PD group to support updates to the data portals and data browsers
- Teams will consult with the relevant members of the PPMI SC to promote best practices in use and interpretation of PPMI data
- Teams must be willing to participate in quarterly calls to provide updates on their study

Review criteria:

As part of the review process, MJFF will evaluate sample availability, rationale for use of a particular endpoint, robustness and quantitative nature of the assay, consistency in differentiation process, lab expertise in iPSC differentiations and endpoint assessments, and the utility of the assay in informing disease subtypes or fueling future mechanistic studies.

Gene-corrected controls for a few of the genetic lines will be available in 2H 2022 and we would encourage teams to utilize these lines as controls in their studies. Please see iPSC request form for more details.

DEADLINES & REVIEW SCHEDULE

- Pre-Proposals Due: September 28th, 2021 5 p.m. US EST
- Full Proposal Invitations: Week of November 15, 2021
- Full Proposals Due (by invite only): January 13th, 2022 5 p.m. US EST
- Anticipated Award Announcement: April 2022
- Anticipated Funding: April 2022

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

FUNDING AVAILABLE

Duration:

Up to 2 years

Award Amount:

Applicants may request budgets ranging from \$40,000 to \$200,000 for analysis of existing datasets from the PPMI iPSC sub-study and up to \$1,000,000 for phenotypic analysis. 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 [Application Guidelines](#) and [FAQ](#).

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 only and with the designation of an administrative primary investigator who directs the laboratory in which the fellow will conduct research. The administrative co-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.

As programs may require many kinds of expertise, MJFF encourages industry and academic collaborations when appropriate.

ADDITIONAL INFORMATION

Our [Application Guidelines](#) provide general guidance about applying for funding from MJFF, though the RFA always supersedes information contained in the Application Guidelines. Please note that MJFF updated our publication and indirect costs policies in early 2020. The new [open access publication policy](#) requires articles resulting from MJFF-funded work publish in a preprint repository then in an open access forum with free and immediate readership rights.

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.

DIVERSITY, EQUITY AND INCLUSION

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.

INFORMATIONAL WEBINAR

MJFF will host an informational webinar on August 24th, 2021, at 12 p.m. ET to clarify and explain the goals of our funding opportunities and answer applicant questions. The webinar will be available to view on-demand after the live airdate. Please register [here](#).

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