The Parkinson’s Progressive Marker Initiative (PPMI) is an observational clinical study partnership that aims to identify biomarkers of disease progression by evaluating patients with Parkinson’s disease and controls using advanced imaging and biospecimen analysis with clinical and behavioral assessments. The initiative is sponsored and coordinated by the Michael J. Fox Foundation for Parkinson’s Research (MJFF), a non-profit patient foundation dedicated to improving the lives of patients with Parkinson’s disease.

**Mission**

The overall goals of Michael J. Fox Foundation for Parkinson’s Research is to fund research that:

- Slow, stop or reverse the progression of Parkinson’s disease
- Target unaddressed or under-addressed symptoms of Parkinson’s disease
- Address or avoid the debilitating side effects of current Parkinson’s disease drugs
As an effort of MJFF, the mission of the Parkinson’s Progressive Marker Initiative (PPMI) is to identify one or more biomarkers of Parkinson’s disease progression. This effort aims to improve the understanding of Parkinson’s Disease (PD) etiology and help create tools that accelerate clinical testing of new therapeutics. The specific goals of PPMI are to:

- Establish standardized protocols for acquisition, transfer and analysis of clinical, imaging and biospecimen data that can be used by the PD research community.

- Investigate existing and identify novel clinical, imaging and biospecimen PD progression markers that will demonstrate interval change in PD patients, in comparison to healthy controls or in sub-sets of PD patients.

- Optimize bioassays and conduct preliminary verification studies on biomarkers.

PPMI has identified the following analysis to be carried out with the data generated from the initiative and has determined that this will help identify biomarkers in PD and progress research towards finding treatments for PD.

- Comparing baseline characteristics among healthy controls and Parkinson’s Disease (PD) subjects.

- Determining whether short-term changes in progression endpoints are predictive of change in long-term endpoints. The goal of this analysis is to attempt to provide a subset of short-term progression endpoints and suggest biomarkers for future studies of interventions in PD patient populations.

SWEDD (Scan Without Evidence of Dopaminergic Deficit) cohort was added to the PPMI study to determine if there is a change in their diagnosis over a 24 month evaluation period. In addition, in 2013 additional cohorts will be added to PPMI – prodromal, genetics, hypsomia and dopamine deficit cohorts.

Parkinson’s Progressive Marker Initiative (PPMI) hallmarks:
2007, the Michael J. Fox Foundation for Parkinson’s Research’s (MJFF) Industry Scientific Advisory Board began formal discussions that led to the PPMI study. This led to a MJFF-sponsored workshops to discuss site selection and study parameters.

2009, PPMI study cores and steering committee were selected and the protocol taskforce was appointed.

2010, PPMI begins recruiting patients, completes enrollment in 2013.

2013, PPMI extension to include prodromal arm of 100 patients to study risk factors of Parkinson’s disease and a genetic arm comprised of 1200 subjects.

Structure & Governance

The Parkinson’s Progressive Marker Initiative (PPMI) study is led by a central principal investigator and coordinated by Michael J. Fox Foundation for Parkinson’s Research (MJFF) through its Senior Vice President (SVP) for Research Partnerships. The SVP of Research Partnerships also serves as the main point of contact for industry partners.

The PPMI Steering Committee, of which MJFF is a member, reports to the Principal Investigator and is responsible for the scientific rationale, study design, site selection, logistics, data management and analysis planning for the study. Committee membership includes the principal investigator and the heads of all of the study cores. The study cores (bioanalytics, bioinformatics, biorepository, clinical, DTI, genetics, imaging, olfactory, RBD, genetics clinical coordination and statistics) provide oversight of various functions within the study, and data analysis. MJFF’s Clinical Trials Strategy Team supports PPMI through efforts geared toward meeting subject recruitment and retention goals.

Study committees focus and provide oversight in the following areas:

- Clinical Study Oversight Committee, responsible for safety monitoring and protection of study subjects.
- Data Use and Publications Committee, responsible for oversight of use of study data,
permissions to access study data, review of publications and citations.

- Ancillary Studies Committee, responsible for assessing add-on studies that are proposed by investigators.

- Biospecimen Review Committee, responsible for reviewing and approving all biospecimens requests.

- Patient Advisory Committee, responsible for providing the patient perspective on elements of study design, recruitment and retention efforts, and communication.

Working groups focus on targeted scientific and design aspects of the study:

- Cognitive Behavioral Working Group

- Sleep Working Group

- Imaging Working Group

- Biologics Working Group

- Genetics Working Group

- Recruitment/Retention Working Group

- Website Working Group

- Statistics Working Group

In addition to communicating with the research director, industry partners can also provide feedback on study parameters through PPMI’s Industry Scientific Advisory Board (ISAB), where each industry partner is represented by one to two individuals from each company.
Financing

PPMI is sponsored and partially funded by The Michael J. Fox Foundation for Parkinson’s Research (MJFF). Other funding partners include a consortium of industry players, non-profit organizations and private individuals. Industry partners are contributing to PPMI through financial and in-kind donations and are playing a lead role in providing feedback on study parameters through the Industry Scientific Advisory Board (ISAB).

Intellectual Property

PPMI was designed as a pre-competitive study; as such, new IP is not expected to be generated through the study. PPMI was designed to accelerate the verification of PD biomarkers. Existing IP on markers utilizing PPMI collected data and biospecimens for verification remains with the holder of the IP; no new IP can be generated on findings using PPMI data and/or biospecimens.

Patent Engagement

As a longitudinal study, Parkinson’s Progressive Marker Initiative (PPMI) has instituted several strategies to incentivize patients to enroll and continue their participation in the study.

These include:

- Bi-Annual Newsletters informing subjects of study updates and results
- Recruitment Packets
- Annual dinners for study participants
- Travel assistance and Lunch coupons for study visit days
- “Thank you” gifts at study visits such as chocolates, PPMI logo cups or bags
In addition to direct participation by individual subjects, the PPMI also uses a Patient Advisory Committee to provide a patient perspective on their strategies, including input into study design, recruitment and retention efforts and communication.

Enrollment of PD and control subjects closed in May 2013 with PPMI reaching its enrollment target of 423 PD and 196 controls. Current focus is on analyzing the complete baseline dataset and initial comparisons between different data modalities. Initial baseline analyses were presented at the 2013 annual meeting of the Movement Disorders Society and a baseline data publication is planned for submission in autumn 2013.

Sohini Chowdhury
schowdhury@michaeljfox.org

The Michael J. Fox Foundation for Parkinson's Research
Grand Central Station
P.O. Box 4777
New York, NY 10163-4777

Data Sharing

The goal of the Parkinson’s Progressive Marker Initiative (PPMI) is to make a longitudinal dataset and stored biosamples available to scientists researching Parkinson’s disease. The PPMI database provides researchers with access to correlated clinical and imaging data, along with annotated biospecimens, all available within an open access system that encourages data sharing (http://www.ppmi-info.org/access-data-specimens/). Potential users of collected biospecimens submit a request to PPMI’s Biospecimen Review Committee, which convenes every other month to review requests to use available specimens being housed at the PPMI biorepository. As of 2015, over 435,000 data downloads of PPMI data from…and 67 requests for samples have occurred.

PPMI aims to release data as quickly as possible following its collection and Quality Control. In addition to analyses conducted by the study cores, other investigators are also encouraged to access the study data and specimens to conduct their own analyses. The website hosts an “Ongoing Analysis” section to keep the scientific community apprised of analyses being completed, in hopes of stimulating collaborations between researchers who are using PPMI data and specimens.
Sponsors & Partners

PPMI is sponsored by the Michael J. Fox Foundation for Parkinson’s Research and is funded by MJFF and a consortium of industry partners. Under the leadership of PPMI’s Principal Investigator, Dr Ken Marek, 32 clinical sites in the US, Europe, Israel, and Australia and 10 study cores partner to manage and run the study.

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Updated: 04/08/2016