The Parkinson's Progression Markers Initiative: A Prospective Biomarkers Study

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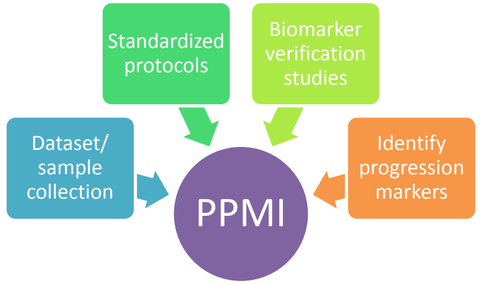
BACKGROUND AND RATIONALE

Current clinical outcomes for Parkinson's disease (PD) trials to assess potential disease modifying therapies require large sample size and long study duration. Reliable and well-validated biomarkers to monitor PD progression would dramatically accelerate research into both PD etiology and therapeutics. During the past two decades much progress has been made in identifying and assessing PD biomarkers, but as yet, no fully validated biomarker for PD is currently available. Given the recent advances in molecular genetics, neurobiology, imaging technology and radiochemistry that have provided new tools that may be useful for PD biomarkers, and the recognition that the lack of PD progression biomarkers has created a roadblock for further studies of disease modifying therapies, there is increasing consensus that a major initiative to develop PD progression biomarkers is both necessary and feasible. The PPMI study is designed to identify clinical, imaging, and biologic biomarkers of Parkinson's disease progression and to standardize the assessment of these tools for future disease modifying trials. The study was launched in June 2010.

OBJECTIVES OF PPMI



Deliverable: Identify a biomarker tool set that can be used to inform decisions at early stages of drug development and clinical testing

STUDY GOVERNANCE AND CORES

- **Steering Committee: ePI-K Marek, A Siderowf, C Scherzer, D Jennings, K Kieburtz, W Poewe, B Mollenhauer, C Tanner, B Ravina (core leaders, MJFF, ISAB)**
- **Clinical Coordination Core: University of Rochester's Clinical Trials Coordination Center, Bernard Ravina**
- **Imaging Core: Institute for Neurodegenerative Disorders, John Seibyl**
- **Statistics Core: University of Iowa, Chris Coffey**
- **Bioinformatics Core: Laboratory of Neuroimaging at UCLA, Arthur Toga**
- **BioRepository: Coriell/BioRep, Alison Ansbach, Pasquale De Blasio, Michele Piovella**
- **Bioanalytics Core: University of Pennsylvania, John Trojanowski, Les Shaw**
- **Genetics Core: NIA/NIH, Andy Singleton**

PPMI STUDY DESIGN

Study population	•400 *de novo* PD subjects (newly diagnosed and unmedicated) •200 age- and gender-matched healthy controls •Subjects will be followed for a minimum of 3 years and a maximum of 5 years
Assessments/ Clinical data collection	• Motor assessments • Neuropsychiatric/cognitive testing • Olfaction
Imaging	•DATscan image every 12 months •MRI •MRI/DTI every 12 months (sub-study)
Biologic collection/ Verification studies	• DNA collected at baseline • Blood collected at each visit; CSF collected on an annual basis • Samples aliquoted and stored in central biorepository • Lead biologic candidates potential to be tested: alpha-synuclein, DJ-1, urate

Key design features of PPMI

- **Subject recruitment eligibility includes DAT imaging status**
- **Comprehensive longitudinal biomarker and imaging assessments**
- **Longitudinal CSF acquisition in all study subjects**
- **Standardization of all data acquisition**
- **All data merged into PPMI database and rapidly available to scientific community via PPMI website**
- **Flexibility to incorporate novel biomarker candidates**
- **Public private partnership in pre-competitive space.**

CLINICAL SITES

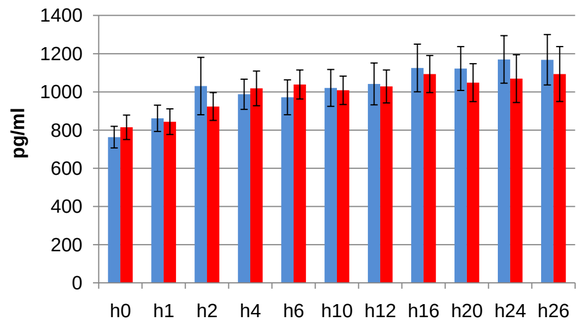
- **Arizona Parkinson's Disease Consortium (Phoenix, AZ)**
- **Baylor College of Medicine (Houston, TX)**
- **Boston University(Boston, MA)**
- **Emory University (Atlanta, GA)**
- **Innsbruck University (Innsbruck, Austria)**
- **Institute of Neurodegenerative Disorders (New Haven, CT)**
- **Johns Hopkins University (Baltimore, MD)**
- **Northwestern University (Chicago, IL)**
- **Oregon Health and Science University (Portland, OR)**
- **Paracelsus-Elena Clinic Kassel/University of Marburg (Marburg, Kassel, Germany)**
- **The Parkinson's Institute (Sunnyvale, CA)**
- **University of Alabama at Birmingham (Birmingham, AL)**
- **University of Napoli (Naples, Italy)**
- **University of Pennsylvania (Philadelphia, PA)**
- **University of Rochester (Rochester, NY)**
- **University of South Florida (Tampa, FL)**
- **University of Tübingen (Tübingen, Germany)**
- **University of Washington (Seattle, WA)**

PRE-PPMI SERIAL CSF COLLECTION STUDY

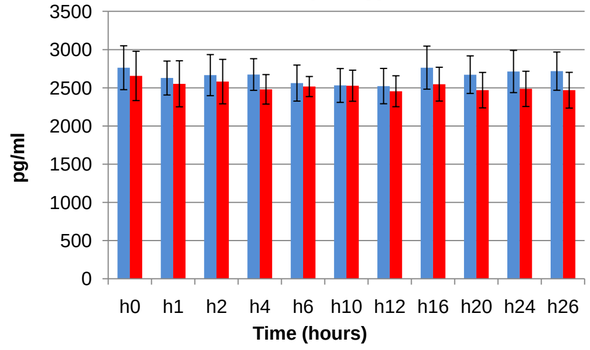
MJFF sponsored a preparatory study to collect serum, plasma, and cerebrospinal fluid from healthy volunteers to determine the diurnal fluctuation and inter- and intra-subject variability of lead markers over 24 hours

- CSF and blood collected over 24 hours in 13 healthy volunteers
- Follow up with same individuals two weeks later to determine test retest reliability of analyte assessments in healthy subjects
- Samples were analyzed to characterize the variability of lead biomarkers as shown below.

α-synuclein in CSF



DJ-1 in CSF



Future Plans/Timeline

- **Investigator Meeting – March 2010**
- **First subject recruited - June 2010**
- **All sites recruiting - Oct 2010**
- **Recruitment complete – Sept 2012**

Data will be available to the PD research community through a web portal

Biologic fluids will be available for biomarker verification studies by application

Coming Soon

www.ppmi-info.org