Resources and Funding Opportunities for Parkinson’s Disease Biomarker Discovery

June 8, 2015
Webinar Agenda

1. Resources Available
   a) The Harvard Biomarker Study
   b) National Brain and Tissue Resource for Parkinson’s Disease and Related Disorders
   c) MJFF Biomarker Resources: 24 hour biofluid sampling, BioFIND, DATATOP, LRRK2 Cross-sectional, LRRK2 AJ Longitudinal
   d) NINDS Parkinson’s Disease Biomarkers Program (PDBP)

2. Accessing Resources – Use of the X01 Mechanism

3. Funding Opportunities
The Harvard Biomarker Study: Participants are tracked clinically and with biospecimens collections over five years

Co-directed by Clemens Scherzer, Brad Hyman, & Adrian Ivinson

Brain donation

Study visit

Serum
Plasma
Whole blood
DNA
Buffy coat
RNA & miRNA

CSF

Personalized cell lines
The Harvard Biomarker Study: 2,300+ individuals with PD, individuals with memory decline, as well as healthy controls are participating as of 2015.
The Harvard Biomarker Study (HBS): how to apply for biosamples and clinical data?

- Key criteria:
  - Rigorous: is the technical quality of the assay sound?
  - Collaborate: Data sharing with HBS and all future collaborators?

Apply through Harvard NeuroDiscovery Center (HNDC) Executive Committee atrisini@partners.org

Apply through X01 to the NIH BRAC Since 2015

Approval?

Sign HBS Collaborators Agreement, incl.
1. agree to data sharing;
2. IP per US patent law;
3. a cost contribution to HBS operating costs is required by the HNDC; this can be build into grant budget)

Academic collaborators are added to HBS IRB; No MTA required

Receive samples & data
National Brain and Tissue Resource for Parkinson’s Disease and Related Disorders
National Brain and Tissue Resource for Parkinson’s Disease and Related Disorders


- The Arizona Parkinson's Disease Consortium (APDC), which includes BSHRI as well as the Arizona Mayo Clinic and Barrow Neurological Institute, oversees the Lewy body diseases component of the BBDP and includes the neurologists, neuropsychologists and neuropathologists who perform the annual standardized clinical assessments, autopsy, neuropathological examination and academic studies.
Resources Available

- Postmortem fixed and frozen brain and body tissue from over 290 (body 112) control subjects, 180 with PD (body 77) and 130 (body 46) with dementia with Lewy bodies. Postmortem blood serum, CSF and clinical data (e.g. MMSE, UPDRS) available on most subjects.
- Tissue quality is excellent for most molecular and biochemical purposes, with median postmortem interval of 3.0 hours and median brain RNA Integrity number > 8.5.
- Neuropathology (thomas.beach@bannerhealth.com; geidy.serrano@bannerhealth.com) and neurology (Dr. Charles Adler: cadler@mayo.edu) consultation is available for assistance with study design, subject/tissue selection and X01 proposal preparation.
MJFF Sponsored and Supported Biospecimen Resources
## SUMMARY OF AVAILABLE BIOSPECIMENS

<table>
<thead>
<tr>
<th>Cohort</th>
<th>DNA</th>
<th>RNA</th>
<th>CSF</th>
<th>Whole blood</th>
<th>Blood pellet</th>
<th>Plasma</th>
<th>Serum</th>
<th>Urine</th>
<th>Saliva</th>
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<tbody>
<tr>
<td>24-Hour Biofluid</td>
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<td>-</td>
<td>12 PD</td>
<td>12 PD</td>
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<td>12 PD</td>
<td>12 PD</td>
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<tr>
<td>Sampling</td>
<td>20 Control</td>
<td>8 Control</td>
<td>20 Control</td>
<td>12 Control</td>
<td>12 Control</td>
<td>12 Control</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>BioFIND</td>
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<td>118 PD</td>
<td>109 PD</td>
<td>115 PD</td>
<td>117 PD</td>
<td>-</td>
<td>-</td>
<td>27 PD</td>
<td>23 PD</td>
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<td>94 Control</td>
<td>82 Control</td>
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<td>94 Control</td>
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<td>28 Control</td>
<td>27 Control</td>
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<tr>
<td>DATATOP</td>
<td>~400 PD</td>
<td>~500 PD</td>
<td>~400 PD</td>
<td>~350 PD</td>
<td>~350 PD</td>
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<td>Baseline</td>
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<td>LRRK2 Cross-Sectional</td>
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<td>-</td>
<td>59 iPD</td>
<td>32 iPD</td>
<td>59 iPD</td>
<td>59 iPD</td>
<td>57 iPD</td>
<td>56 iPD</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>165 LRRK2+, PD</td>
<td>28 LRRK2+, PD</td>
<td>162 LRRK2+, PD</td>
<td>144 LRRK2+, PD</td>
<td>-</td>
<td>160 LRRK2+, PD</td>
<td>160 LRRK2+, PD</td>
<td>131 LRRK2+, PD</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>146 LRRK2+, no</td>
<td>36 LRRK2+, no</td>
<td>137 LRRK2+, no</td>
<td>155 Control</td>
<td>-</td>
<td>136 LRRK2+, no</td>
<td>136 LRRK2+, no</td>
<td>155 Control</td>
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<td>PD</td>
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<td>154 Control</td>
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<td>154 Control</td>
<td>155 Control</td>
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<td>-</td>
</tr>
<tr>
<td>LRRK2 AJ Longitudinal</td>
<td>-</td>
<td>-</td>
<td>57 iPD</td>
<td>57 iPD</td>
<td>57 iPD</td>
<td>57 iPD</td>
<td>57 iPD</td>
<td>53 iPD</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>60 LRRK2+, PD</td>
<td>61 LRRK2+, PD</td>
<td>58 LRRK2+, PD</td>
<td>60 LRRK2+, PD</td>
<td>-</td>
<td>58 LRRK2+, PD</td>
<td>56 LRRK2+, PD</td>
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<td>-</td>
</tr>
<tr>
<td></td>
<td>40 LRRK+, no PD</td>
<td>40 LRRK2+, no PD</td>
<td>36 LRRK2+, no</td>
<td>36 LRRK2+, no</td>
<td>-</td>
<td>36 LRRK2+, no</td>
<td>37 LRRK2+, no</td>
<td>37 LRRK2+, no</td>
<td>-</td>
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<tr>
<td></td>
<td>52 Control</td>
<td>52 Control</td>
<td>51 Controls</td>
<td>51 Controls</td>
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<td>51 Controls</td>
<td>52 Control</td>
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</tr>
</tbody>
</table>

For additional information on cohorts and available samples, please contact resources@michaeljfox.org or visit www.michaeljfox.org/dataspecimens
24-HOUR BIOFLUID SAMPLING STUDY: COHORT OVERVIEW

» MJFF sponsored an Assay Qualification study that collected CSF and blood over 24 hours at 11 different time points. The goal of this study was to understand the inter-subject variability and intra-subject variability of putative biomarkers in PD.

» **Study Subjects (Cohort 1):** 12 young healthy volunteers (2 sampling periods, 2 weeks apart)

» **Study Subjects (Cohort 2):** 12 PD, 8 elderly aged matched volunteers (1 sampling period)

» **Available Biospecimens:** CSF, serum, plasma, whole blood

Samples from this resource are appropriate for projects focused on **biomarker discovery**, **assay optimization**, and **circadian fluctuations** in biofluid matrices.
BioFIND is a cross-sectional clinical study, designed to discover and verify biomarkers of Parkinson's disease, sponsored by MJFF in collaboration with the National Institute of Neurological Disorders and Stroke (NINDS).

» **Study Subjects:** 119 clinically typical, moderate to advanced PD subjects and 96 healthy controls

» **Available Data:** For both PD and control subjects the clinical data includes demographics, neurological and medication history, MoCA, ADL, MDS-UPDRS, H&Y Stage, and Sleep/RBD, alcohol, and smoking questionnaires. All data are de-identified to protect patient privacy.

» **Available Biospecimens:** DNA and RNA from blood, plasma, whole blood pellet, CSF, saliva and urine

Access to the clinical data and detailed biospecimen catalog can be requested through the study database at biofind.loni.usc.edu
# BIOFIND: AVAILABLE SAMPLES

<table>
<thead>
<tr>
<th></th>
<th>DNA</th>
<th>RNA</th>
<th>CSF</th>
<th>Blood pellet</th>
<th>Plasma</th>
<th>Urine</th>
<th>Saliva</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>122 PD</td>
<td>118 PD</td>
<td>109 PD</td>
<td>115 PD</td>
<td>117 PD</td>
<td>27 PD</td>
<td>23 PD</td>
</tr>
<tr>
<td></td>
<td>101 Control</td>
<td>94 Control</td>
<td>82 Control</td>
<td>94 Control</td>
<td>94 Control</td>
<td>28 Control</td>
<td>27 Control</td>
</tr>
<tr>
<td><strong>Sample collected per subject</strong></td>
<td>100 – 300 µg</td>
<td>4 – 20 µg</td>
<td>10 ml</td>
<td>2 pellets</td>
<td>3 ml on meds</td>
<td>10 ml</td>
<td>1 – 3 ml</td>
</tr>
<tr>
<td></td>
<td>4 – 20 µg</td>
<td>10 ml</td>
<td>2 pellets</td>
<td>3 ml on meds</td>
<td>9 ml off meds</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Distributable aliquot size</strong></td>
<td>3 µg</td>
<td>1.1 µg</td>
<td>200 µl</td>
<td>Pellet</td>
<td>200 µl</td>
<td>1.5 ml</td>
<td>150 µl</td>
</tr>
</tbody>
</table>

Samples from this resource are appropriate for projects focused on **PD biomarker discovery and replication.**
DATATOP: COHORT OVERVIEW

» The DATATOP intervention trial, conducted by the Parkinson Study Group in the late 1980s, was a long-term study on the effect of Deprenyl and tocopherol (a form of vitamin E) on the progression of early PD. Data was collected at baseline and at a follow up visit, approximately 12-18 months later.

» **Study Subjects:** Approximately 800 PD patients were recruited in the trial. There are no matching controls that are a part of this cohort.

» **Available Data:** Clinical assessments in the DATATOP database include measures of neurological function, severity of PD, cognition, and mood.

» **Available Biospecimens:** DNA, serum, CSF, and urine

Samples from this resource are appropriate for research projects focused on understanding or developing biomarkers for disease progression.
The LRRK2 Cohort Consortium was launched in 2009 to study people with and without PD who carry mutations in the LRRK2 gene. The LRRK2 Cohort Consortium includes contributions from 17 international sites.

- Enrollment in the Cross-Sectional cohort closed in December 2014.
- Longitudinal collection of samples from the Ashkenazi Jewish (AJ) Consortium is ongoing and samples and data from this cohort will be available beginning August 1.

**Study Subjects:** Approximately 765 iPD, 777 LRRK2 mutation carriers with PD (primarily G2019S), 444 LRRK2 mutation carriers without PD, and 427 controls were enrolled in the cross-sectional component.

**Available Data:** Demographics, neurological history, medication history, MoCA, ADL, MDS-UPDRS, H&Y Stage, and Sleep/RBD questionnaire. All data are de-identified to protect patient privacy.

**Available Biospecimens:** Serum, plasma, RNA from blood, whole blood, CSF and urine
# LRRK2 CROSS-SECTIONAL: AVAILABLE SAMPLES

<table>
<thead>
<tr>
<th></th>
<th>IPD</th>
<th>LRRK2+ with PD</th>
<th>LRRK2+ without PD</th>
<th>Controls</th>
<th>Sample collected per subject</th>
<th>Distributable aliquot size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Blood</td>
<td>59</td>
<td>162</td>
<td>144</td>
<td>155</td>
<td>6ml</td>
<td>TBD</td>
</tr>
<tr>
<td>Plasma</td>
<td>59</td>
<td>160</td>
<td>136</td>
<td>155</td>
<td>4.5-6ml</td>
<td>200ul</td>
</tr>
<tr>
<td>Serum</td>
<td>57</td>
<td>160</td>
<td>137</td>
<td>154</td>
<td>4.5-6ml</td>
<td>200ul</td>
</tr>
<tr>
<td>RNA</td>
<td>59</td>
<td>165</td>
<td>146</td>
<td>154</td>
<td>2-10ug</td>
<td>1.1ug</td>
</tr>
<tr>
<td>Urine</td>
<td>56</td>
<td>131</td>
<td>136</td>
<td>155</td>
<td>10-15ml</td>
<td>1.5ml</td>
</tr>
<tr>
<td>CSF</td>
<td>32</td>
<td>28</td>
<td>36</td>
<td>31</td>
<td>10ml</td>
<td>200 µl (100 and 500 µl aliquots available)</td>
</tr>
</tbody>
</table>

Qualified proposals should have a strong rationale for examining a particular marker(s) in a LRRK2 population. Visit [www.michaeljfox.org/dataspecimens](http://www.michaeljfox.org/dataspecimens) for details on accessing clinical data.
**AJ LONGITUDINAL: ON-GOING COLLECTIONS**

<table>
<thead>
<tr>
<th></th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Visit 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>iPD</td>
<td>LRRK2+ PD</td>
<td>LRRK2+ no PD</td>
</tr>
<tr>
<td>Whole Blood</td>
<td>57</td>
<td>61</td>
<td>40</td>
</tr>
<tr>
<td>Plasma</td>
<td>57</td>
<td>58</td>
<td>36</td>
</tr>
<tr>
<td>Serum</td>
<td>57</td>
<td>60</td>
<td>36</td>
</tr>
<tr>
<td>RNA</td>
<td>57</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>Urine</td>
<td>53</td>
<td>56</td>
<td>37</td>
</tr>
</tbody>
</table>

Samples and longitudinal data will become open access on **August 1, 2015**. Please email resources@michaeljfox.org to be notified when samples become available for request.
AVAILABLE FUNDING FOR USE OF BIOSPECIMEN

Funding to support PD biomarker research is available through MJFF

» Eligibility
  – Both non-profit and for profit organizations are eligible for funding
  – International institutions are also eligible for funding

» Direct vs. indirect costs
  – 25% indirect costs for academic/non-profit institutions
  – 10% indirect costs for for-profit organizations

» Templates for submitting budget requests are available from MJFF. Typical MJFF awards support up to a total of $250,000 USD and a maximum project duration of 2 years, although funding guidelines may be flexible with appropriate justification.

Please submit budget requests to resources@michaeljfox.org for consideration in tandem with proposals submitted through the X01 mechanism.
The National Institute of Neurological Disorders and Stroke (NINDS) Parkinson’s disease Biomarkers Program (PDBP)

Features of PDBP
- Standardized data collection across 7 clinical sites
- Standardized biosample collection (CSF, plasma, serum, RNA, DNA, whole blood)
- Longitudinal study with participants representing the full disease spectrum
- 1289 participants as of May 7, 2015
- Data management resource provides real time access to clinical, genetic, imaging data and biosample information
- De-identified Clinical data includes: MDS-UPDRS, MoCA, RBD, HAM-A, HDRS, Epworth SS, Modified Schwab and England ADL, demographics, medication history, H&Y stage, UPSIT, family history, PDQ-39
- Biosamples available for discovery and replication
Number of unique biosamples in PDBP: B= Baseline; 6= 6 months; 12=12 months; 18=18 months; 24=24 months; 30=30 months
Aliquot volumes: CSF, Serum and Plasma 1 aliquot = 200 μl, Whole blood 1 aliquot = 5 ml, DNA 1 aliquot = 3 μg, RNA 1 aliquot = 1 μg

Data as of May 14, 2015
Request to Access Parkinson’s Disease Related-Biospecimens (X01) PAR 14-340

XOI application – rolling application submission review 6 X per year

NINDS PDBP
MJFF BioFIND DATATOP LRRK2 24 hr CSF
Harvard Biomarker Study
National PD Tissue and Organ Resource

Combined BRAC

Biospecimen Access
Specific Resource MTAs, fees, publication agreements/acknowledgments apply
1. **Rationale**: Briefly describe the studies proposed and the rationale for these analyses (Overview).

2. **Biosamples/tissue/data requested in a table**

3. **Background**
   - The question being posed by the investigator must be appropriate to the source of the biospecimens, how they were collected, prepared, analyzed and stored; their age; and the phenotypic and other accompanying data.
   - Preliminary/feasibility data (if available)

4. **Sample Information** (if preliminary data includes samples from other cohorts)

5. **Project details**
   - Hypothesis
   - Methodology
   - Power and effect size
   - Data analysis
   - Plan for next Phase

6. **Project Support**
Review dates and approved requests under X01 Application

Submissions between October 13, 2014 - January 15, 2015
Review date: January 22, 2015
Submissions between January 16 - March 15, 2015
Review date: April 2, 2015
Submissions between March 16 - July 15, 2015
Review date: July 30, 2015
Submissions between July 16 - September 15, 2015
Review date: October 1, 2015
Submissions between September 16 - November 15, 2015
Review date: December 3, 2015

Biosample requests approved under the X01 15 request approved since October 2014

For full list of approved requests see: https://pdbp.ninds.nih.gov/jsp/brac.jsp
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Please submit budget requests to resources@michaeljfox.org for consideration in tandem with proposals submitted through the X01 mechanism.
NINDS Funding Opportunity for Biomarker Discovery: Parkinson’s Disease Biomarkers Program Discovery Projects (U01) - PAR 14-259

Purpose: To support discovery, assay optimization and replication studies for Parkinson’s Disease biomarker development
- Discovery and pilot projects may use biosamples from extant cohorts, as long as the patient consent allows for broad data sharing.
- Data from all studies funded under this announcement must be submitted to the PDBP data management resource (DMR)
- Funding announcement supports human studies only
- Use of PDBP pooled samples must be included in the analysis

Eligibility: Academic, Non-profit and For-profit organizations are eligible
Foreign institutions and components are eligible

Budgets: Up to 3 year grants – depending on stage of development
- Application budgets are not limited but need to reflect the actual needs of the proposed project. Application budgets are expected to be between $200,000 to $490,000 per year in direct costs.

Submission Dates: September 4, 2015, February 4, 2016, May 4, 2016 (resubmissions are allowed)
Resource Websites and Funding Web links

Resources
The Harvard Biomarker Study
http://cbmi.catalyst.harvard.edu/cores/cat/core.html?core_id=252&uri_id=0000012c-e17f-6dab-2162-17a280000000&category_id=6&navMode=cat
The Michael J. Fox Foundation (MJFF) Biospecimen Resources
The National Brain and Tissue Resource for Parkinson's Disease and Related Disorders, at the Banner Sun Health Research Institute
The NINDS Parkinson's Disease Biomarkers Program (PDBP)
https://pdbp.ninds.nih.gov/index.jsp

Biosample Access

Funding for Parkinson’s disease Biomarker Research
MJFF resources@michaeljfox.org
Contact emails for resources

Resource Contacts Information

The Harvard Biomarker Study
  • csherzer@rics.bwh.harvard.edu

The Michael J. Fox Foundation (MJFF) Biospecimen Resources
  • resources@michaeljfox.org

The National Brain and Tissue Resource for Parkinson's Disease and Related Disorders
  • Thomas.Beach@bannerhealth.com

NINDS Parkinson's Disease Biomarkers Program (PDBP)
  • NINDS-PD-BRAC@ninds.nih.gov