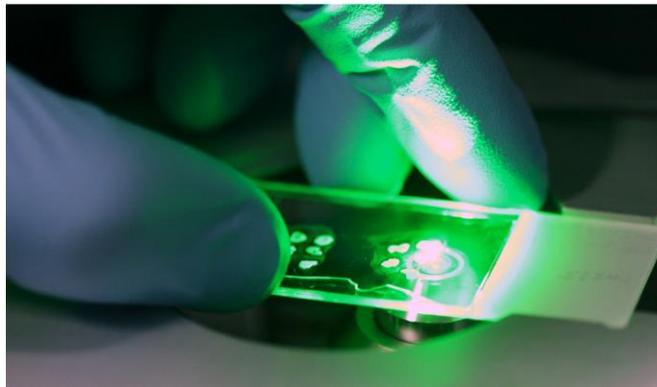




National Institute of
Neurological Disorders
and Stroke

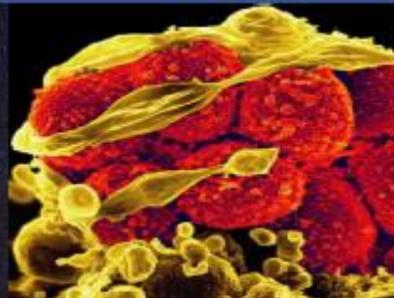
Resources and Funding Opportunities for Parkinson's Disease Biomarker Discovery

June 8, 2015



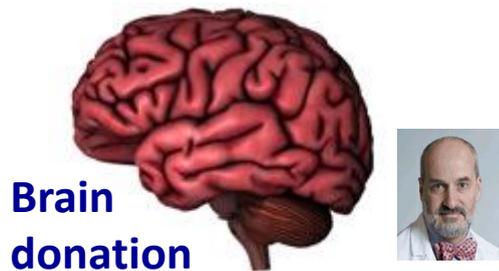
Webinar Agenda

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

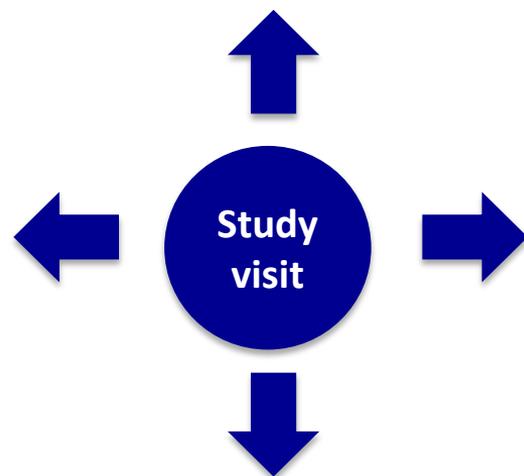


The Harvard Biomarker Study: *Participants are tracked clinically and with biospecimens collections over five years*

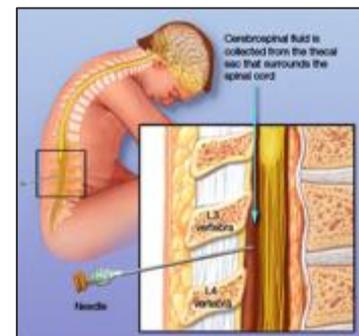
Co-directed by Clemens Scherzer, Brad Hyman, & Adrian Ivinson



Serum
Plasma
Whole blood

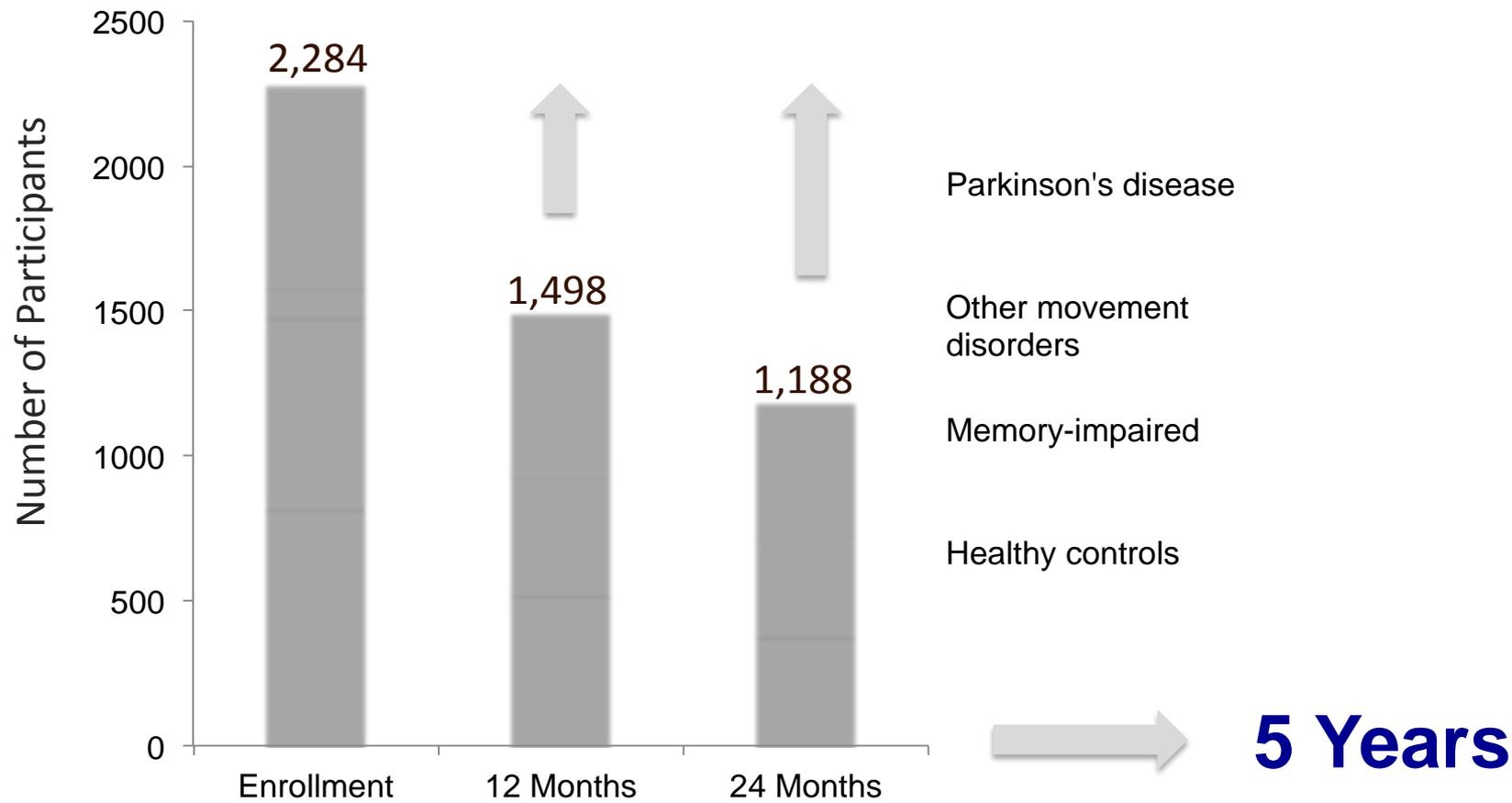


DNA
Buffy coat
RNA & miRNA

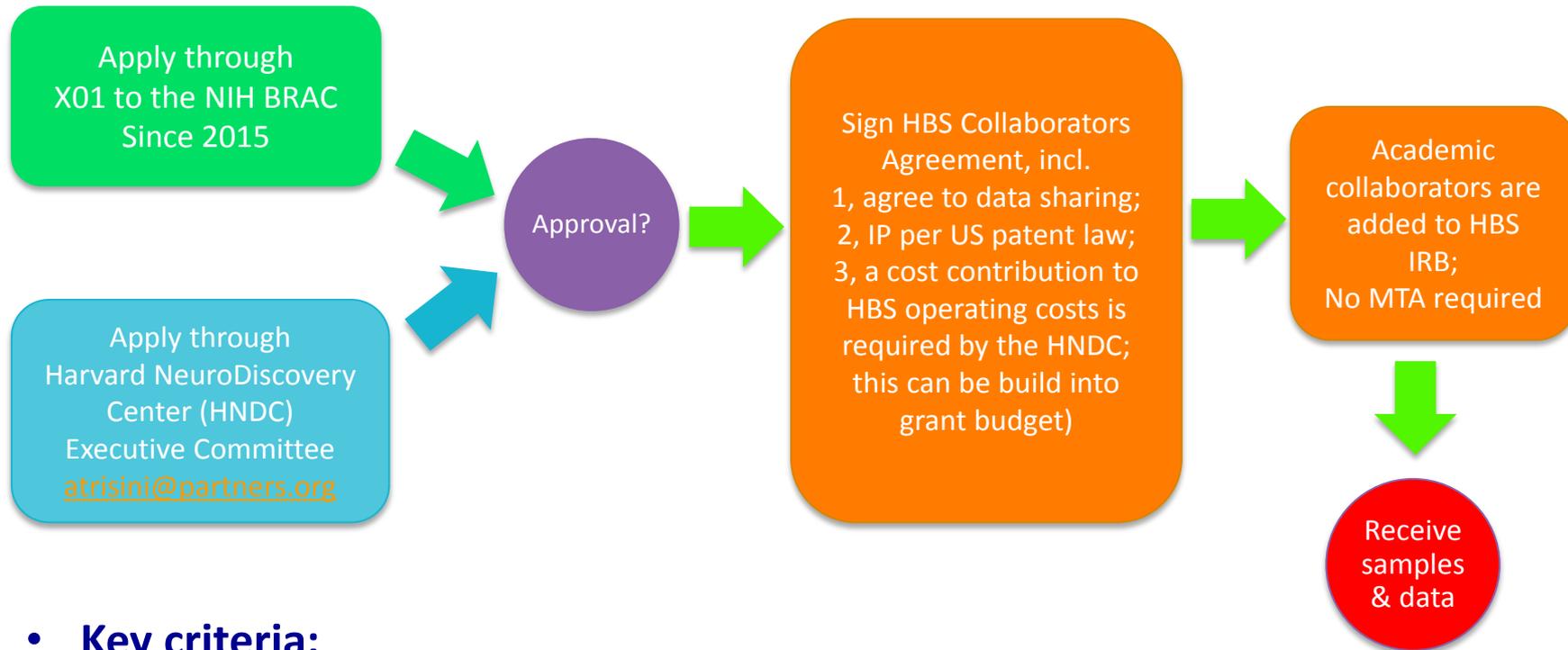


Personalized cell lines

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?

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 NBTR-PD draws on the Banner Sun Health Research Institute (BSHRI) Brain and Body Donation Program (BBDP) (www.brainandbodydonationprogram.org), a longitudinal clinicopathological study. See the 2015 free full text review article by Beach et al, Neuropathology 2015: <http://www.ncbi.nlm.nih.gov/pubmed/25619230>).
- 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

Cohort	DNA	RNA	CSF	Whole blood	Blood pellet	Plasma	Serum	Urine	Saliva
24-Hour Biofluid Sampling	-	-	12 PD 20 Control	12 PD 8 Control	-	12 PD 20 Control	12 PD 12 Control	-	-
BioFIND	122 PD 101 Control	118 PD 94 Control	109 PD 82 Control	-	115 PD 94 Control	117 PD 94 Control	-	27 PD 28 Control	23 PD 27 Control
DATATOP	~400 PD Baseline ~400 PD Endpoint	-	~500 PD Baseline ~350 PD Endpoint	-	-	-	~800 PD Baseline ~600 PD Endpoint	~350 PD Baseline ~350 PD Endpoint	-
LRRK2 Cross-Sectional	-	59 iPD 165 LRRK2+, PD 146 LRRK2+, no PD 154 Control	32 iPD 28 LRRK2+, PD 36 LRRK2+, no PD 31 Control	59 iPD 162 LRRK2+, PD 144 LRRK2+, no PD 155 Control	-	59 iPD 160 LRRK2+, PD 137 LRRK2+, no PD 155 Control	57 iPD 160 LRRK2+, PD 137 LRRK2+, no PD 154 Control	56 iPD 131 LRRK2+, PD 136 LRRK2+, no PD 155 Control	-
LRRK2 AJ Longitudinal	-	57 IPD 60 LRRK2+, PD 40 LRRK+, no PD 52 Control	-	57 IPD 61 LRRK2+, PD 40 LRRK2+, no PD 52 Control	-	57 IPD 58 LRRK2+, PD 36 LRRK2+, no PD 51 Controls	57 IPD 60 LRRK2+, PD 36 LRRK2+, no PD 51 Controls	53 IPD 56 LRRK2+, PD 37 LRRK2+, no PD 52 Control	-

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: COHORT OVERVIEW

- » 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.ioni.usc.edu



BIOFIND: AVAILABLE SAMPLES

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

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**.



LRRK2 COHORT CONSORTIUM

- » 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

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

Qualified proposals should have a **strong rationale** for examining a particular marker(s) in a **LRRK2 population**. Visit www.michaeljfox.org/dataspecimens for details on accessing clinical data.



AJ LONGITUDINAL: ON-GOING COLLECTIONS

	Visit 2				Visit 3				Visit 4			
	iPD	LRRK2+ PD	LRRK2+ no PD	Control	iPD	LRRK2+ PD	LRRK2+ no PD	Control	iPD	LRRK2+ PD	LRRK2+ no PD	Control
Whole Blood	57	61	40	52	32	40	17	23	5	9	1	1
Plasma	57	58	36	51	32	40	13	22	5	9	1	1
Serum	57	60	36	51	32	40	12	22	5	9	1	1
RNA	57	60	40	52	29	40	11	18	5	8	1	1
Urine	53	56	37	52	31	35	15	21	4	8	1	1

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

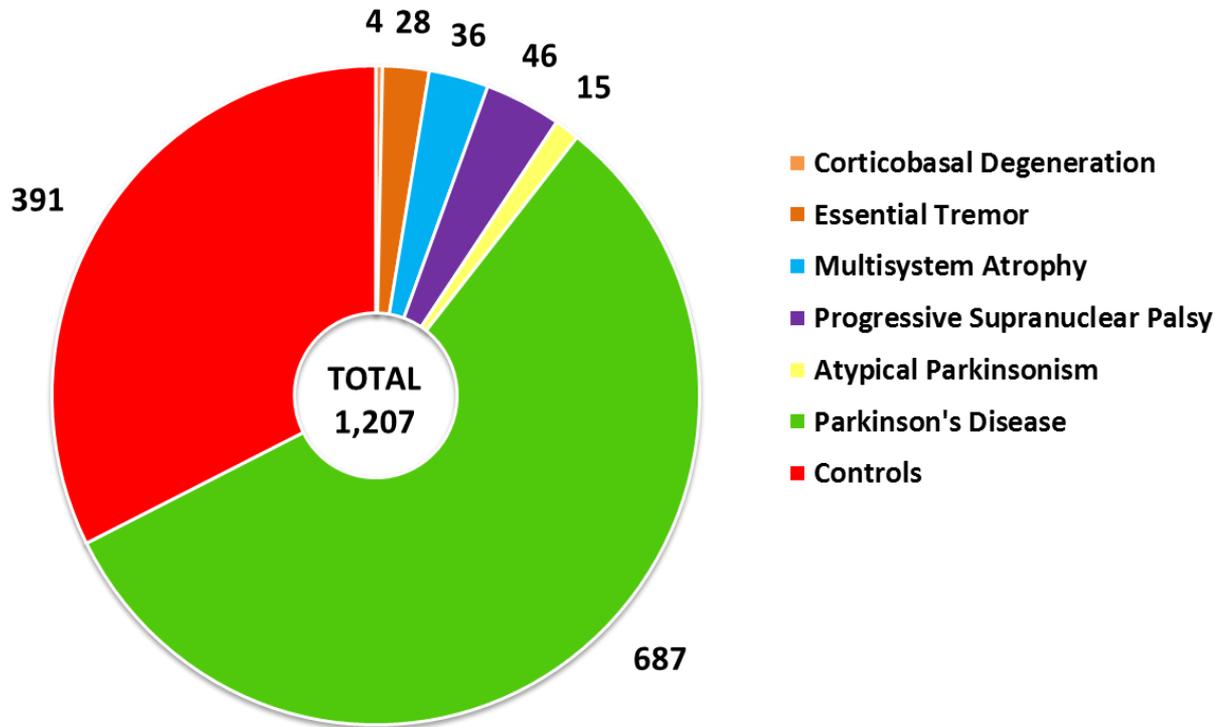
- » Templates for submitting budget requests are available from MJFF. Typical MJFF awards support up to a total of \$250,000 USD and a maximum project duration of 2 years, although funding guidelines may be flexible with appropriate justification.

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)

Number of PDBP Participants based on Neurological Diagnosis
as of May 7, 2015

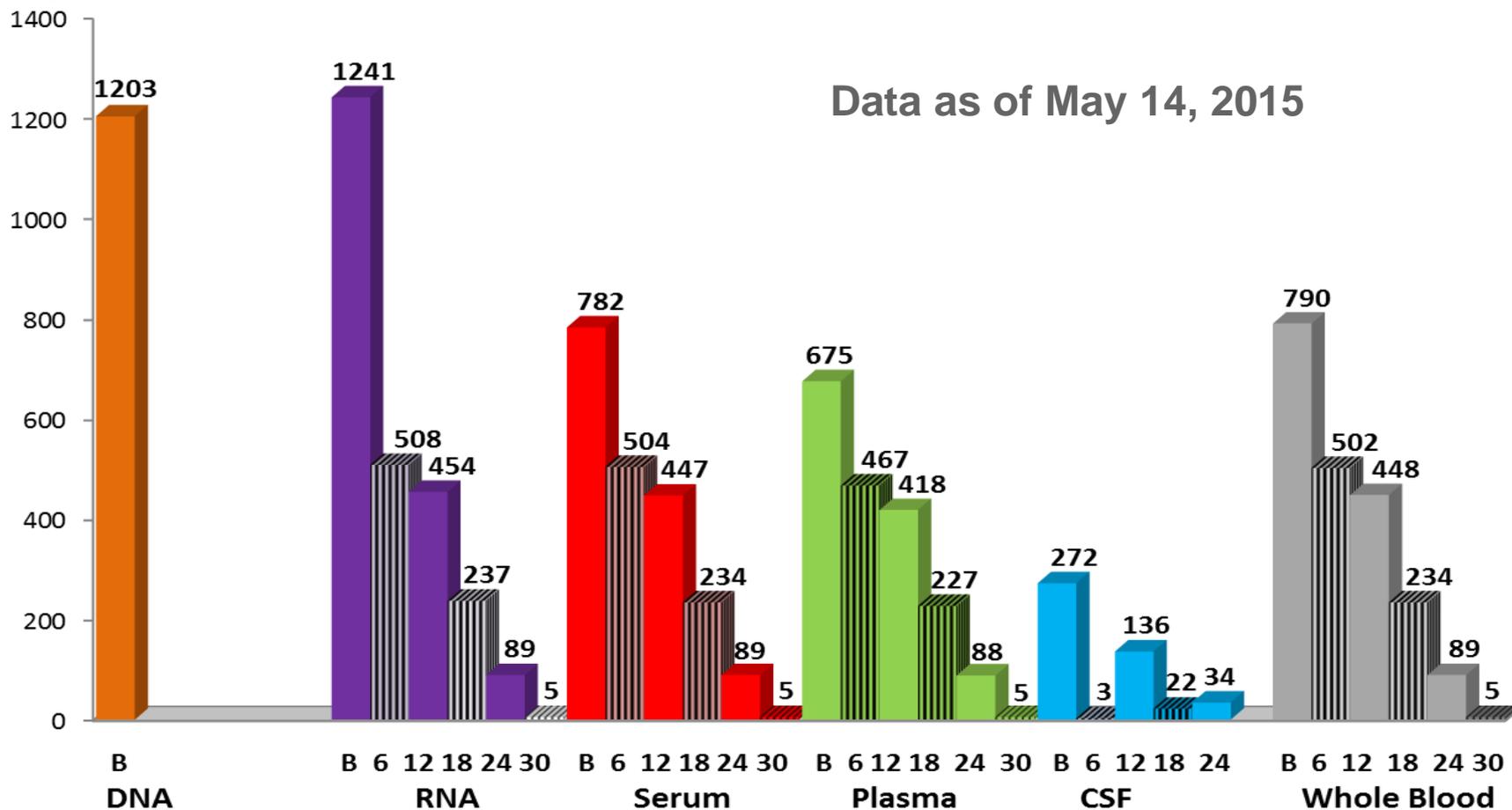


Features of PDBP

- 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 the NINDS Parkinson's Disease Biomarkers Program (PDBP)

Data as of May 14, 2015

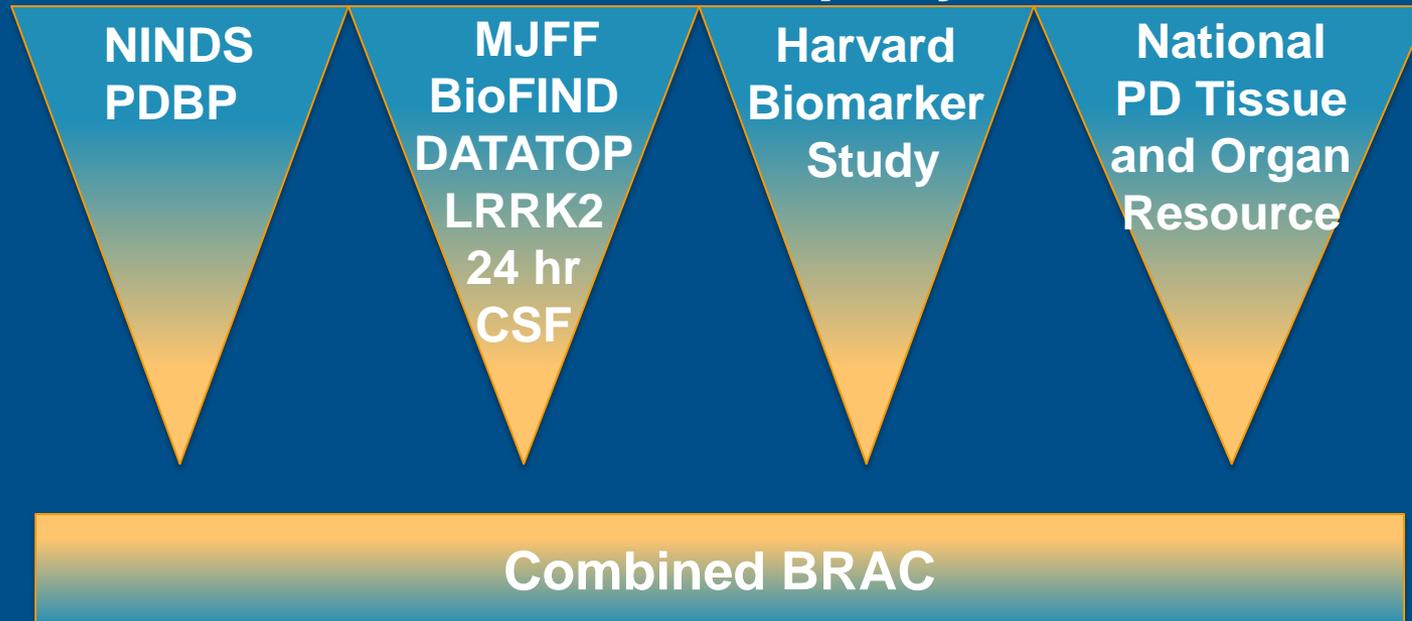


Number of unique biosamples in PDBP: B= Baseline; 6= 6 months; 12=12 months; 18=18 months; 24=24 months; 30=30 months

Aliquot volumes: CSF, Serum and Plasma 1 aliquot = 200 μ l, Whole blood 1 aliquot = 5 ml, DNA 1 aliquot = 3 μ g, RNA 1 aliquot = 1 μ g

Request to Access Parkinson's Disease Related-Biospecimens (X01) PAR 14-340

**XOI application – rolling application submission
review 6 X per year**



Biospecimen Access
**Specific Resource MTAs, fees, publication
agreements/acknowledgments apply**

Information to include in X01 Application

- 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/feasability 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

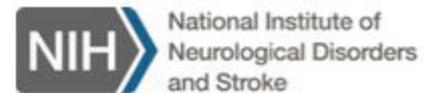
Submissions between September 16 - November 15, 2015

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>



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.

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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

<https://www.michaeljfox.org/page.html?access-parkinsons-clinical-data-and-biospecimens>

The National Brain and Tissue Resource for Parkinson's Disease and Related Disorders, at the Banner Sun Health Research Institute

<http://www.bannerhealth.com/Research/Research+Institutes/Banner+Sun+Health+Research+Institute/Research/Research+Programs/Brain+and+Body+Donation/Brain+and+Tissue+Bank.htm>

The NINDS Parkinson's Disease Biomarkers Program (PDBP)

<https://pdbp.ninds.nih.gov/index.jsp>

Biosample Access

X01 PAR 14-340 <http://grants.nih.gov/grants/guide/pa-files/PAR-14-340.html>

Funding for Parkinson's disease Biomarker Research

MJFF resources@michaeljfox.org

NINDS Parkinson's disease Biomarkers Program (PDBP) Discovery Projects (U01) PAR 14-259 <http://grants.nih.gov/grants/guide/pa-files/PAR-14-259.html>

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