



MJFF – PRIORITIES AND FUNDING FOR CLINICAL STUDIES

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The Michael J. Fox Foundation

MJFF IS THE WORLD'S LARGEST NONPROFIT FUNDER OF PD RESEARCH

Our Mission

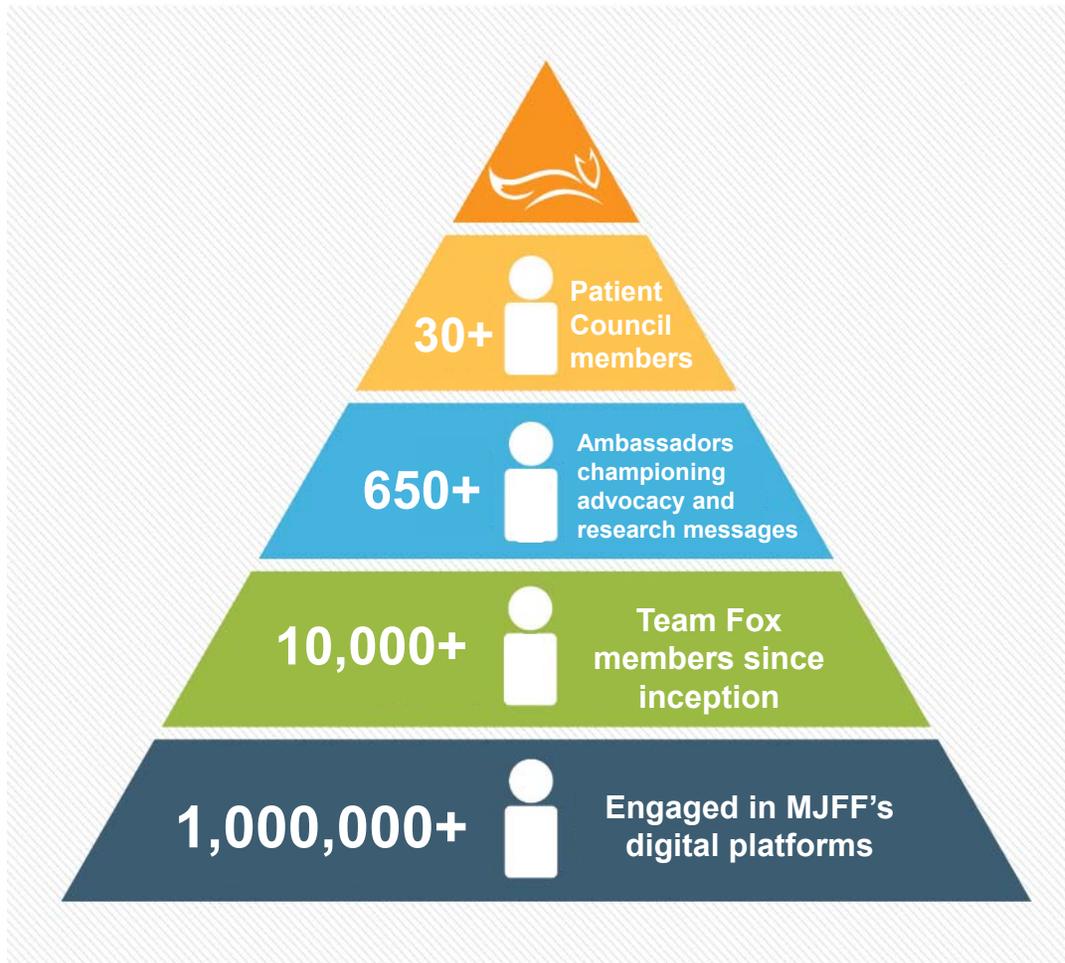
The Michael J. Fox Foundation is dedicated to finding a cure for Parkinson's disease through an aggressively funded research agenda and to ensuring the development of improved therapies for those living with Parkinson's today.

Vital Stats

- » Founded in **2000** by actor Michael J. Fox
- » Public charity
- » More than **85,000** donors in 2016 (individuals, corporations, nonprofits)
- » No chapters: team of **125** based in NYC
- » **4,200** grassroots fundraisers reaching **175,000** supporters worldwide in 2016
- » Over **30,000** emails were sent to members of Congress on critical Parkinson's issues in 2016
- » Nearly **\$800 million** in research programs funded to date
- » **\$84 million** in research programs funded in 2017
- » More than **2,600** projects funded to date
- » More than **600** active grants in current portfolio
- » **34%** of funded projects are led by researchers outside the United States
- » Fund academics, biotechs and pharma



PATIENTS' NEEDS DRIVE OUR EFFORTS

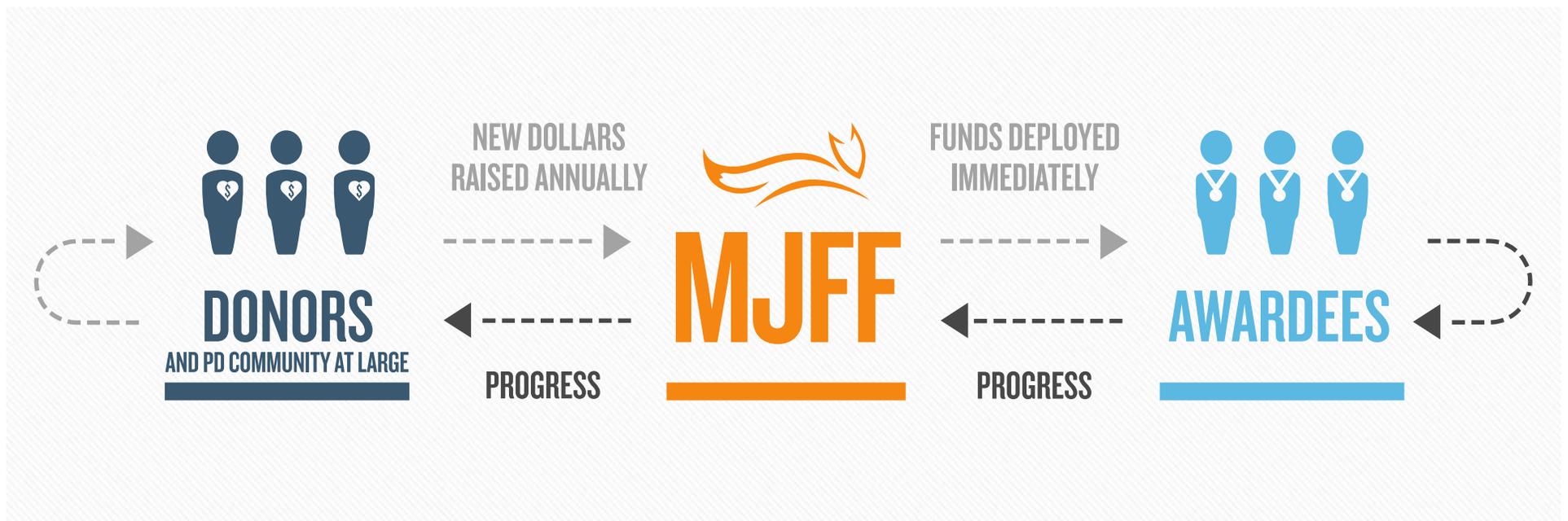


MJFF was founded by a person with Parkinson's disease.

Assessing all potential projects through a patient-focused lens, everything we do is driven by the many unmet medical needs of Parkinson's patients today.



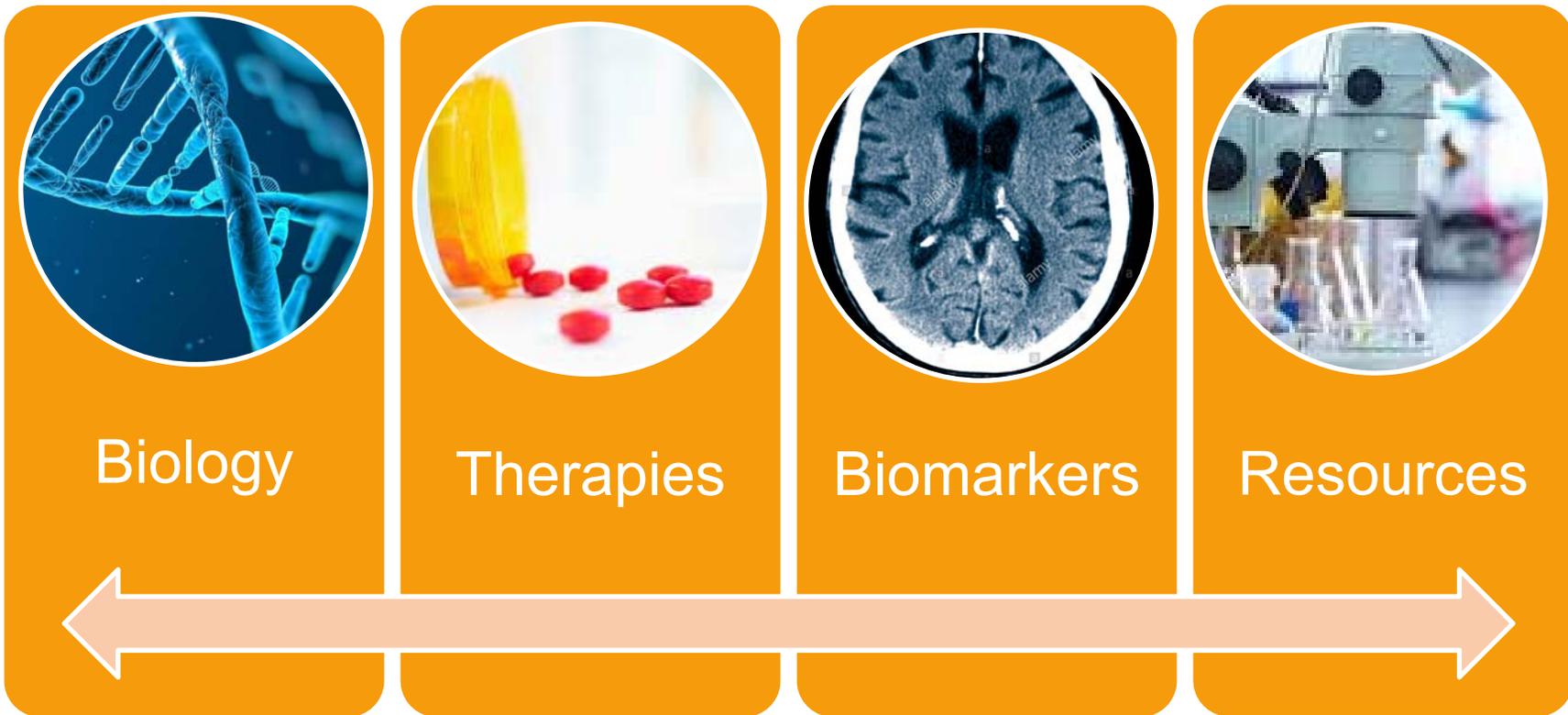
OUR BUSINESS MODEL: EFFICIENCY, URGENCY AND ACCOUNTABILITY



MJFF has **no endowment** and deploys **89¢ of every dollar spent** to research.



MJFF SUPPORTS CLINICAL RESEARCH ACROSS FOUR MAIN CHALLENGES



BIOLOGY



Focus: Addressing Critical Understanding of PD Pathobiology and Dissecting Clinical Heterogeneity

Increase the diversity and breadth of genetic information on people with PD

- Targeted gene sequencing, whole exome/genome sequencing, genetic modifier studies

Understand the role environment and lifestyle may play in modifying risk of PD

- Epidemiological studies to identify risk and protective factors

Assess molecular changes which may influence downstream cellular biology

- Omics (transcriptomics, proteomics, metabolomics) approaches

Identify and validate novel targets for PD pathobiology and symptoms

- Target expression, functional changes, pathway analyses, target validation, replication

Investigate the biology of genetic targets (aSyn, LRRK2, GBA1) to advance our understanding of idiopathic PD

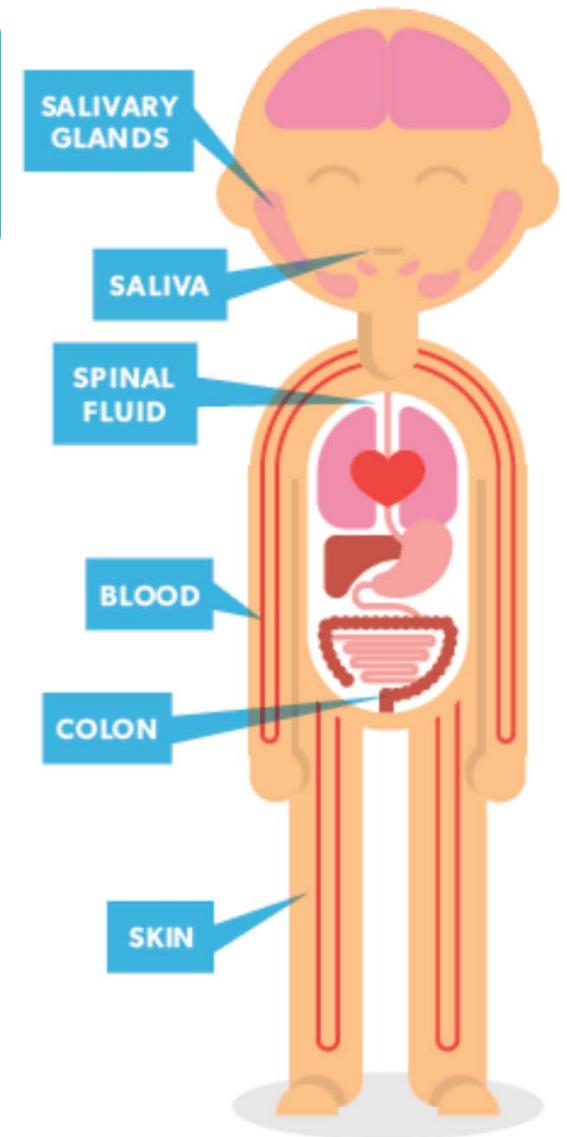
- Linking target and pathways in patient-derived tissues (e.g. iPSCs), genotype-phenotype studies



SYSTEMIC SYNUCLEIN SAMPLING STUDY (S4)

- **Goals**
 - Characterize aSyn burden both topographically and temporally within a given individual
 - Assess feasibility and safety of obtaining tissues and biofluids across a multi-center study

Logistics	<ul style="list-style-type: none"> ▪ 6 Centers (IND, UAB, UPenn, U Toronto, OSHU, Mayo) ▪ 4 visits: screening, biofluid & skin, colon biopsy, SMG biopsy
Study Population	<ul style="list-style-type: none"> ▪ 61 PD subjects <ul style="list-style-type: none"> - 20 <i>de novo</i> unmedicated - 20 moderate PD w/o motor fluctuations - 21 advanced PD with motor fluctuations ▪ 21 healthy controls
Assessments/ Clinical Data Collection	<ul style="list-style-type: none"> ▪ Motor assessments ▪ Neuropsychiatric/cognitive testing ▪ Clinical labs ▪ DaTSCAN imaging
Biofluid Sampling	<ul style="list-style-type: none"> ▪ Blood samples – whole blood, serum, plasma, RNA and DNA ▪ CSF ▪ Saliva
Tissue Sampling	<ul style="list-style-type: none"> ▪ Colonic submucosal biopsy by unprepped flexible sigmoidoscopy ▪ Skin punch biopsies on distal thigh and cervical paravertebral regions ▪ Submandibular gland biopsies under local anesthesia



BIOLOGY FUNDING OPPORTUNITIES

Target Advancement Program

- Supports novel target validation, protein expression in pathological samples, gene sequencing, replication of published findings, convergence of genetic targets to idiopathic PD.
- Funding up to \$150K for a 12-18 month grant
- Deadline: Sep 26, 2018

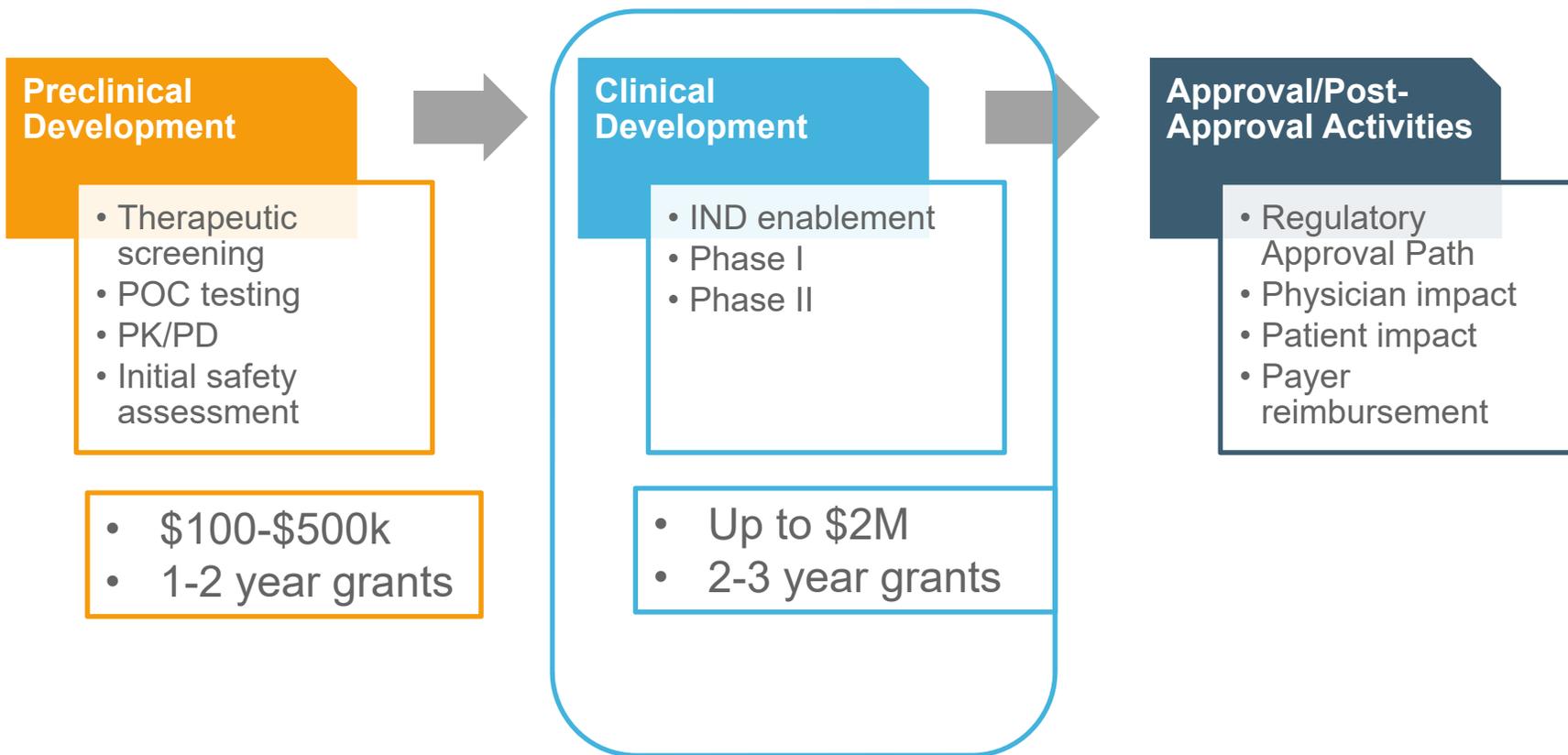
EPI Program: Using Epidemiological Datasets to Identify Risk and Protective Factors for Parkinson's disease

- Supports analysis to identify lifestyle factors (e.g. diet, exercise) or use of pharmacological or other medical interventions that reduce risk of PD.
- Funding up to \$500K for one- to two-year grants
- Deadline: Sep 26, 2018

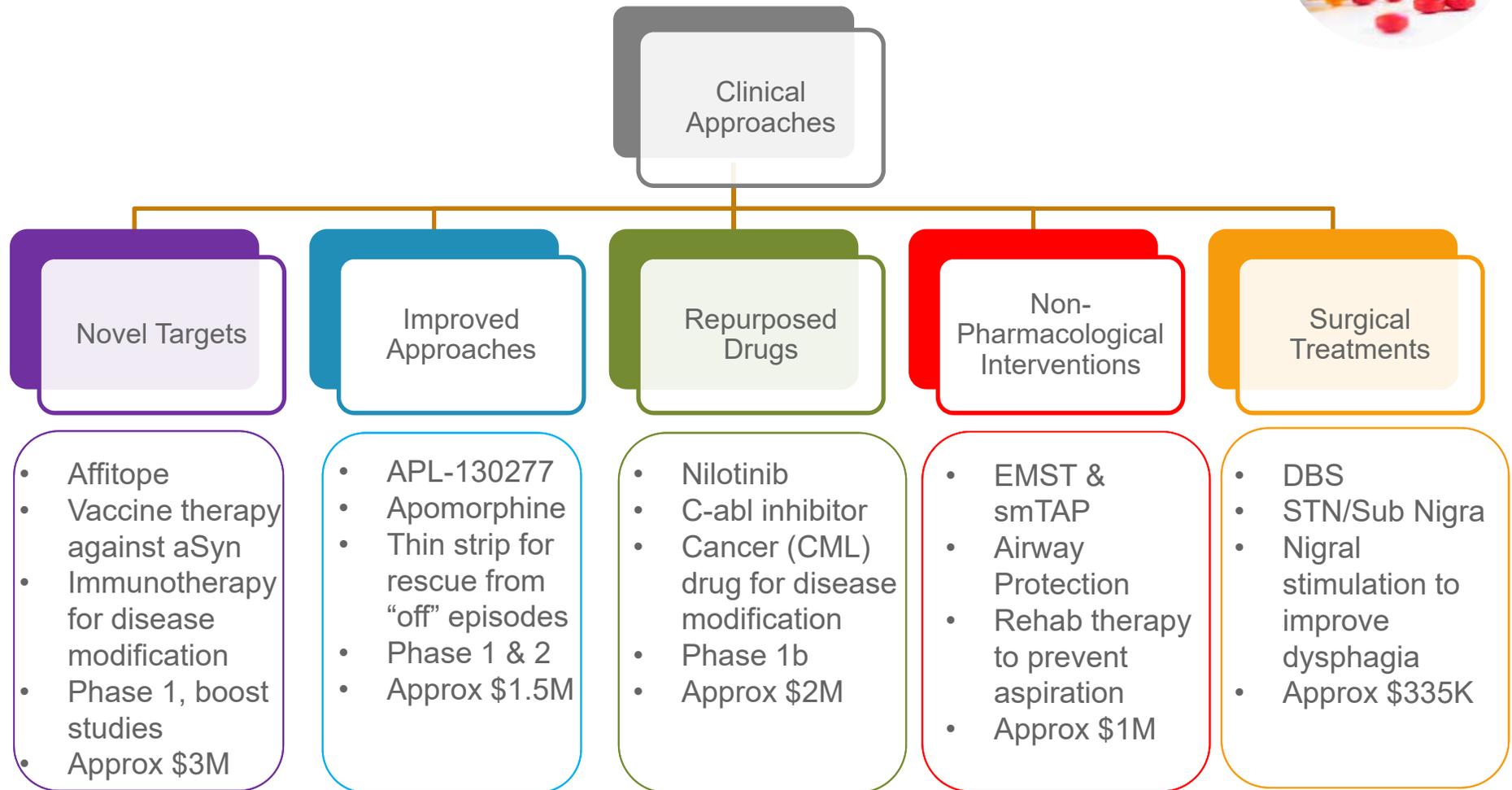


THERAPEUTICS

Focus: Fund and Support Preclinical or Clinical Drug Development for Disease-modification & Symptomatic Therapies



MJFF FUNDS CLINICAL TRIALS ACROSS DIVERSE APPROACHES



THERAPEUTICS FUNDING OPPORTUNITIES

Therapeutic Pipeline Program

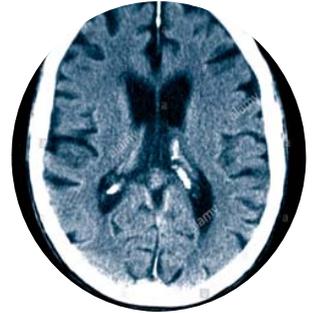
- Supports preclinical and clinical drug development (drug and non-pharmacological therapeutics, including gene therapy, biological, surgical and non-invasive approaches).
- Funding up to \$500K for preclinical and up to \$2M for clinical grant
- Deadline: Sep 26, 2018

Non-Pharmacological Interventions For Gait and Balance Disturbances

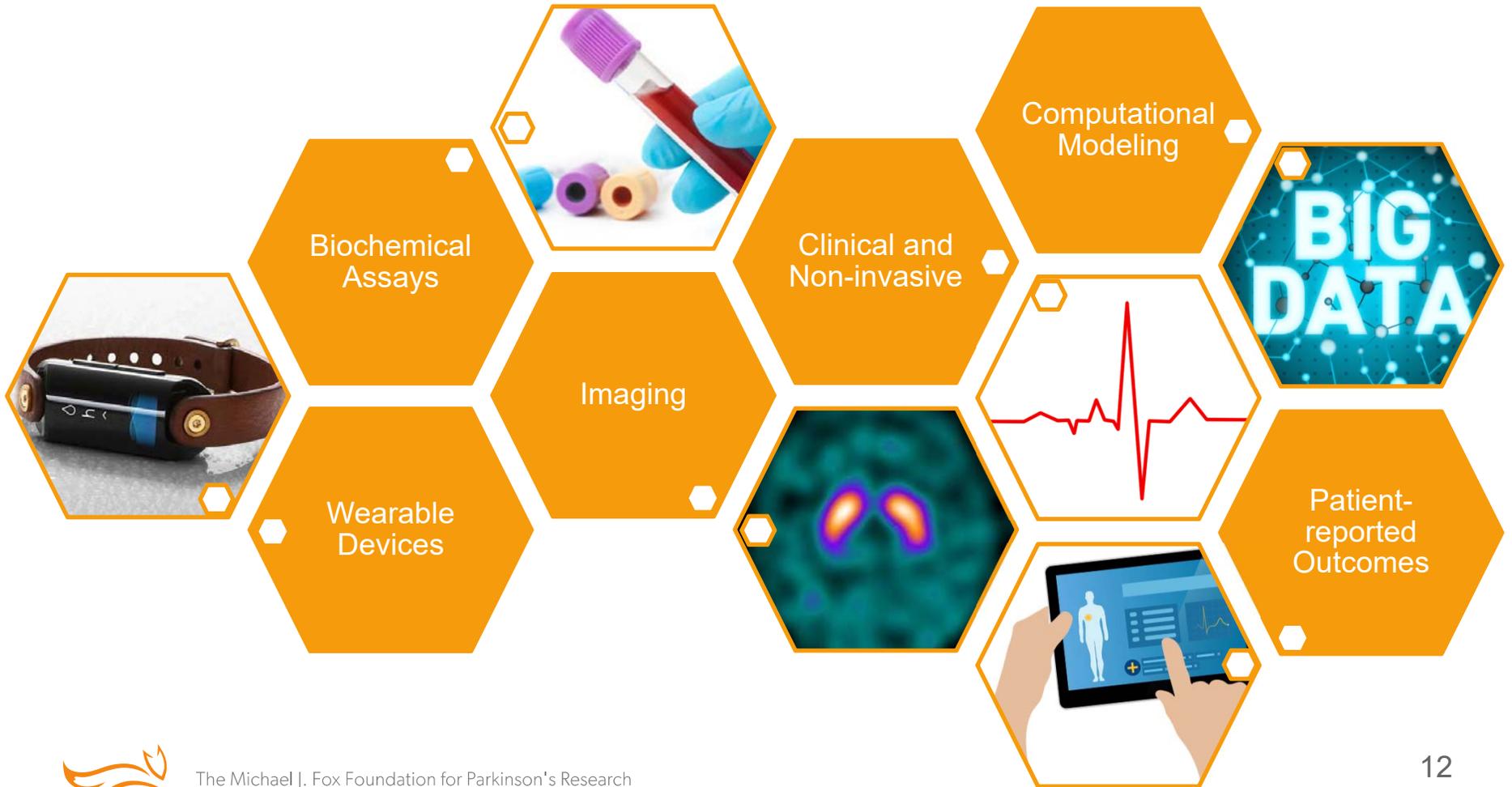
- Support proposals for studying therapeutic benefit of assistive devices, novel technologies and rehabilitative therapy programs.
- Funding up to \$500K for one- to two-year grants
- Deadline: Program closed, Funding in Oct/Nov 2018



BIOMARKERS



Focus: Fund and Support Development and Validation of Biomarkers and outcome measures



PARKINSON'S PROGRESSION MARKERS INITIATIVE (PPMI)

- » Disease modifying PD therapeutics remain a major unmet need
- » A major obstacle to current phase 2/3 neuroprotection studies is the lack of biomarkers for:
 - » Disease mechanism
 - » Drug mechanism
 - » Dosage determination
 - » Study eligibility
 - » Stratification into PD sub-types
 - » Correlation with clinical signals

REQUIREMENTS FOR BIOMARKER INFRASTRUCTURE

SPECIFIC DATA SET

- » Appropriate population (early stage PD and controls)
- » Clinical (motor/non-motor) and imaging data
- » Corresponding biologic samples (DNA, blood, CSF)

STANDARDIZATION

- » Uniform collection of data and samples
- » Uniform storage of data and samples
- » Strict quality control/quality assurance

ACCESS/SHARING

- » Data available to research community data mining, hypothesis generation & testing
- » Samples available for studies



PPMI STUDY DETAILS: SYNOPSIS

STUDY POPULATION

- » 423 de novo PD subjects (newly diagnosed and unmedicated)
- » 196 age-and gender-matched healthy controls
- » 64 SWEDD subjects
- » 67 individuals with non-genetic risk factors (hyposmic, RBD)
- » 550 LRRK2 or GBA (PD manifest and non-manifesting family members)
- » 50 Synuclein (PD manifest and non-manifesting family members)
- » Subjects followed for 3 to 5 years

ASSESSMENTS/ CLINICAL DATA COLLECTION

- » Motor assessments
- » Neuropsychiatric/neurobehavioral testing
- » Autonomic, olfaction, sleep
- » DaTSCAN imaging, AV133, Amyloid, DTI/rs MRI
- » Sensor data

BIOLOGIC COLLECTION

- » DNA, RNA
- » Serum, whole blood and plasma collected at each visit; urine annually
- » CSF collected at baseline, 6mo 12 mo and then annually
- » Samples aliquotted and stored in central biorepository
- » Post mortem tissue

SHARED DATA AND BIOSAMPLES

- » >1,700,000 data downloads
- » >100 samples requests via BRC
- » Ancillary study development



FOX INSIGHT STUDY



- » **Increasingly, Parkinson's patients seek to be active contributors to improved disease understanding, therapy development and care**
- » **Fox Insight facilitates patient and care partner information sharing about the lived experience of Parkinson's**
 - » Functional impact and real-world efficacy
 - » QoL and health outcomes
 - » Direct and indirect burden of disease
 - » Treatment awareness and access
 - » Patient-perspective value frameworks

RIGOROUS PATIENT-CENTERED DATA GENERATING ENGINE

SCALE AND ACCESS

- » Aims to recruit up to 125K patients and controls, including care partners, to contribute data
- » Open to anyone 18 or older worldwide with or without PD (Available in English only)

ASSESSMENTS

- » PD-relevant validated instruments of patient-reported outcomes (PROs)
- » Novel PROs and patient preference information
- » Multi-modal data collection including genetics

SHARING/FLEXIBILITY

- » Data available to research community for data mining, hypothesis generation & testing
- » Mechanism for deploying investigator-driven surveys will be available



FOX INSIGHT STUDY SYNOPSIS

STUDY POPULATION

Fox Insight Eligibility Criteria:

- » 18+ years of age
- » With or without PD
- » English-speaking
- » Internet access

Cohort Targets:

- » Enrollment: 125K
- » PD/Control ratio: 80/20
- » Demographics: Representative of PD epidemiology

ePRO ASSESSMENTS

- » Medical history
- » Medications
- » QoL and activities of daily living
- » Motor and non-motor symptoms
- » Physical activity
- » Neuropsychiatric measures
- » Environmental exposure
- » Novel PRO and patient preference instruments

MULTI-MODAL DATA COLLECTION

- » Genetic profiles from up to 17,000 US-based PD volunteers – **23andMe**
- » Sensor-derived activity level data
- » Interactive voice response
- » Expanding future possibilities ...

ANCILLARY SURVEY MECHANISM

- » Opportunity for researcher-driven questionnaires (*submission process available in 2019*)
- » **Proof of concept:** 1,500 responses from PD volunteers to a novel survey instrument collected in 8 days (over 4,500 responses total)

Data from this unique, longitudinal Parkinson's study will be made available to the research community in early 2019.



BIOMARKERS FUNDING OPPORTUNITIES

Outcome Measures Program

- Supports research to develop biomarker tools and clinical outcome measures to assist in diagnosis and therapeutic development.
- Funding up to \$750K for one- to three-year grants
- Deadline: Sep 26, 2018

Biomarkers Across Neurodegenerative Disorders (BAND)

- Partnership with Alzheimer's Association, Alzheimer's Research UK and Weston Brain Institute
- Support research across neurodegenerative disorders to increase understanding of pathogenic similarities and differences.
- Funding up to \$150K for one- to two-year grants
- Deadline: Sep 10, 2018



HOW YOUR GRANT FUNDING GETS APPROVED

RFA

- Formulate intent and application process
- Communicate the launch to research community

Preproposal

- MJFF staff evaluates initial ideas
- Most interesting/novel ideas are invited

Full Proposal

- MJFF staff and external advisors review proposals
- Experimental design, experience considered

Funding Decision

- External advisors help us make the study better
- MJFF staff makes final decision to fund

Contracting

- Speedy contracting, confidentiality protected, MJFF does not seek IP rights
- Promote data sharing, tool distribution, return payment

Active Management

- Efficiency, accountability and milestone-based payments
- Interim, midpoint and final assessments of projects





PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research



THE FOX INVESTIGATION FOR NEW DISCOVERY OF BIOMARKERS

Play a Part in Parkinson's Research



Systemic Synuclein Sampling Study



FOX INSIGHT

YOUR EXPERIENCE FUELING RESEARCH



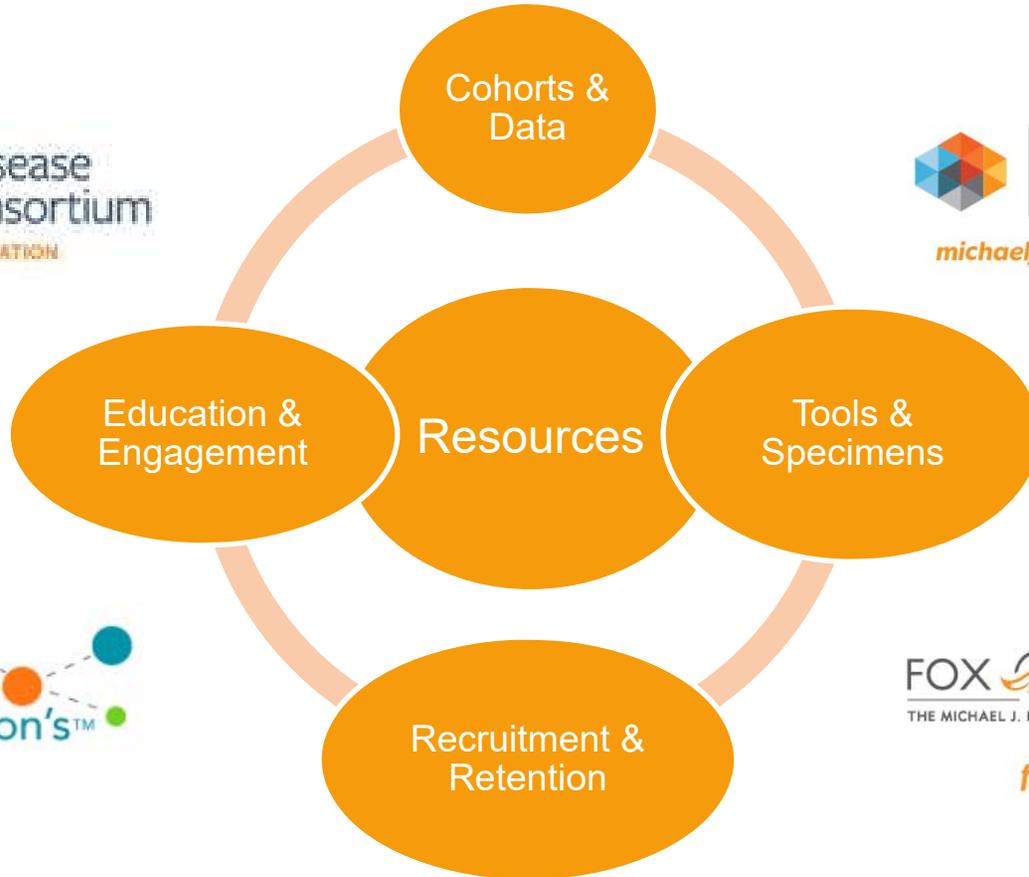
Parkinson's Disease Education Consortium

THE MICHAEL J. FOX FOUNDATION



PARKINSON'S DISEASE RESEARCH TOOLS CONSORTIUM
THE MICHAEL J. FOX FOUNDATION

michaeljfox.org/tools-consortium



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RESOURCES FOR TRIAL TEAMS



Identify Patient Advisor(s)

- Assess patient interest in proposed study
- Understand participant burden



Evaluate Study Design

- Identify study strengths to leverage
- Anticipate study challenges to address



Develop R&R Plans

- Outline multi-modal strategies to recruit & retain participants
- Create lay-friendly study materials



Provide Ongoing R&R Support

- Advise on recruitment & retention challenges that arise
- Motivate sites on monthly calls



Optimize Fox Trial Finder

- Share trial posting best practices
- Share messaging best practices

MJFF collaborates with trial sponsors on clinical trial recruitment and retention by **sharing best practices and facilitating meaningful patient engagement.**



TRAINING OPPORTUNITIES

Movement Disorders School for Neurology Residents

- Two-day course in Spring 2019
- Lectures and panel discussions
- Case studies

Edmond J. Safra Fellowship in Movement Disorders

- Fund two-year fellowships at leading universities
- Supported 20 fellows thus far
- International reach



ACKNOWLEDGEMENT

We would like to thank all the Parkinson's disease patients and our donors that continue to inspire us with their endless optimism.

