



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

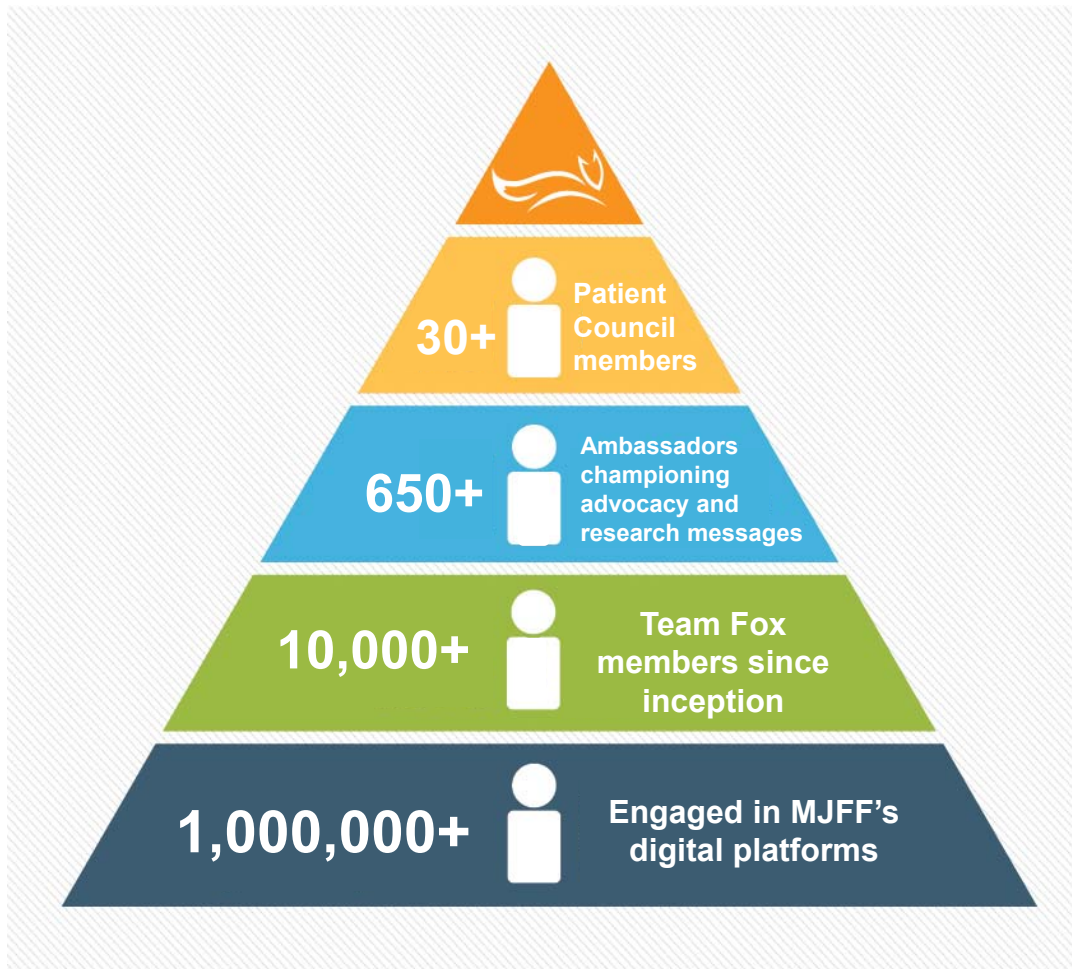
The Michael J. Fox Foundation is dedicated to finding a cure for Parkinson's disease through an aggressively funded research agenda and to ensuring the development of improved therapies for those living with Parkinson's today.

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

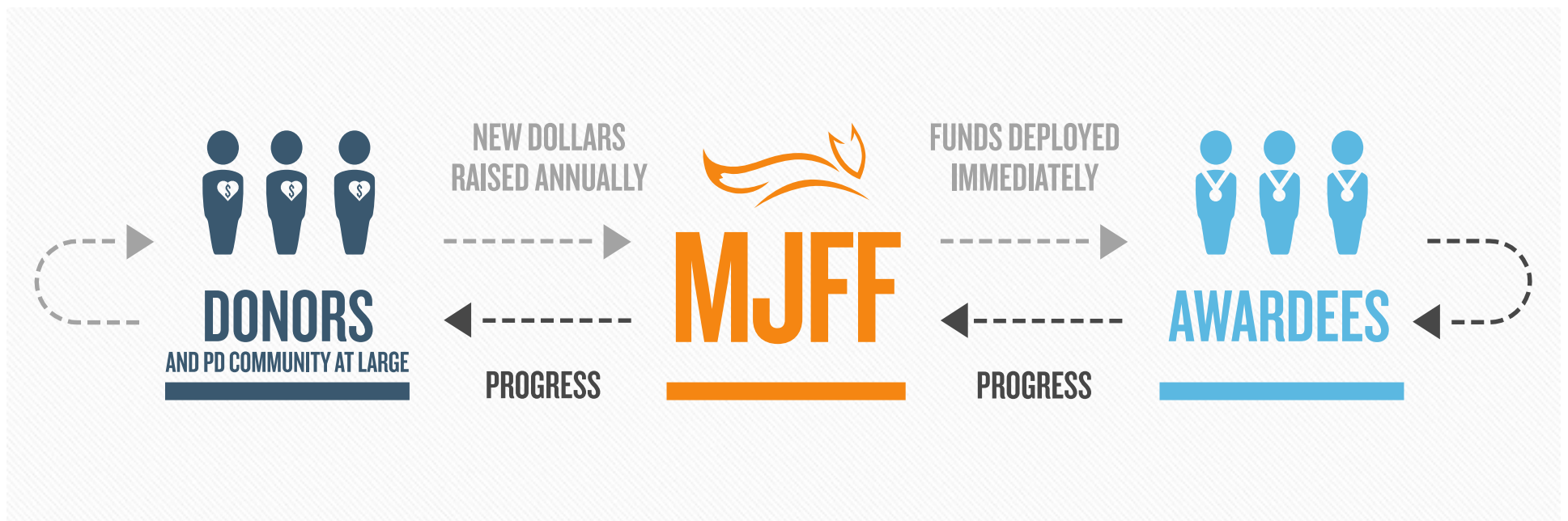


MJFF was founded by a person with Parkinson's disease.

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.



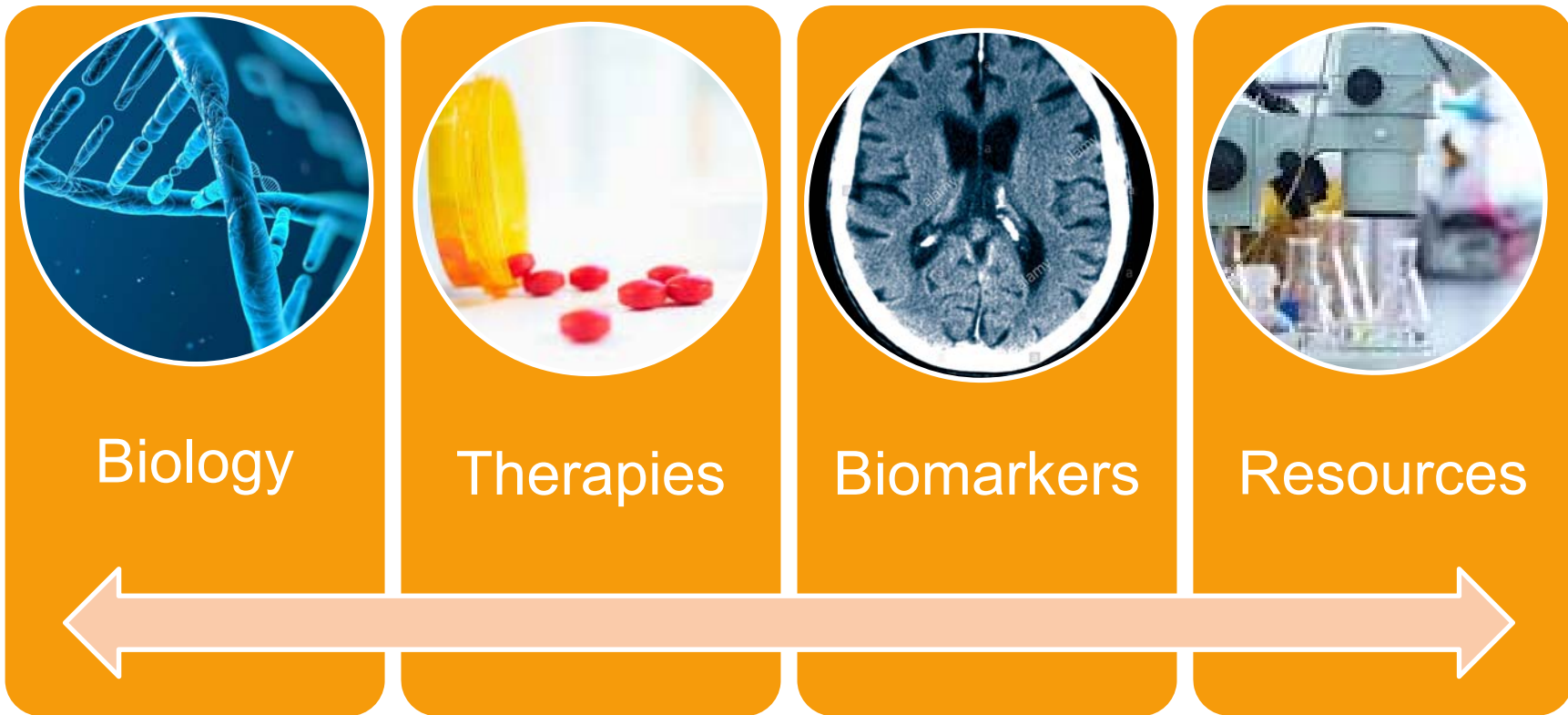
OUR BUSINESS MODEL: EFFICIENCY, URGENCY AND ACCOUNTABILITY



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

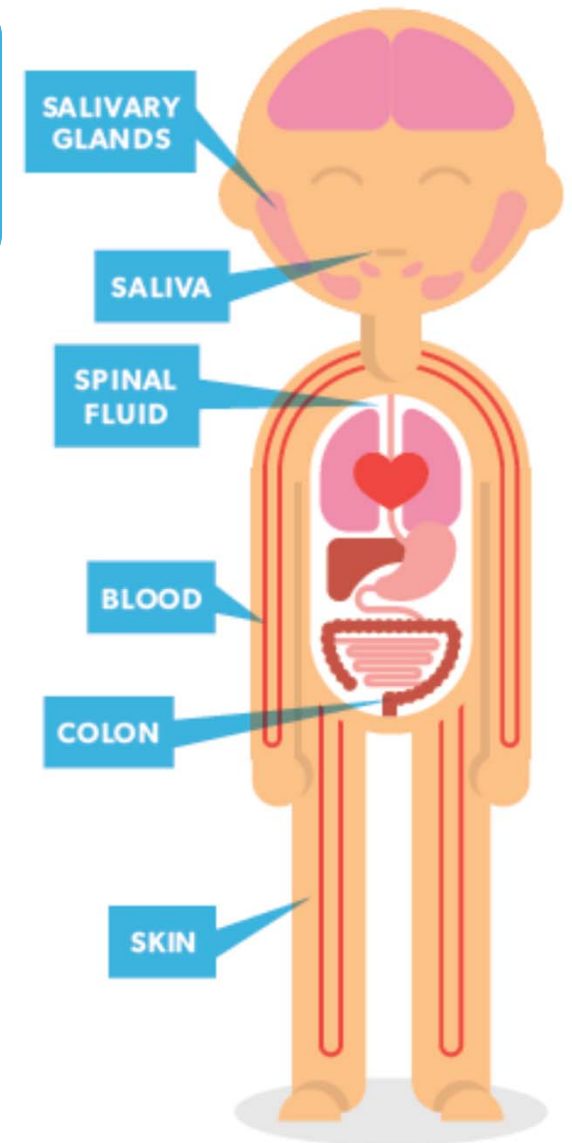


SYSTEMIC SYNUCLEIN SAMPLING STUDY (S4)

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

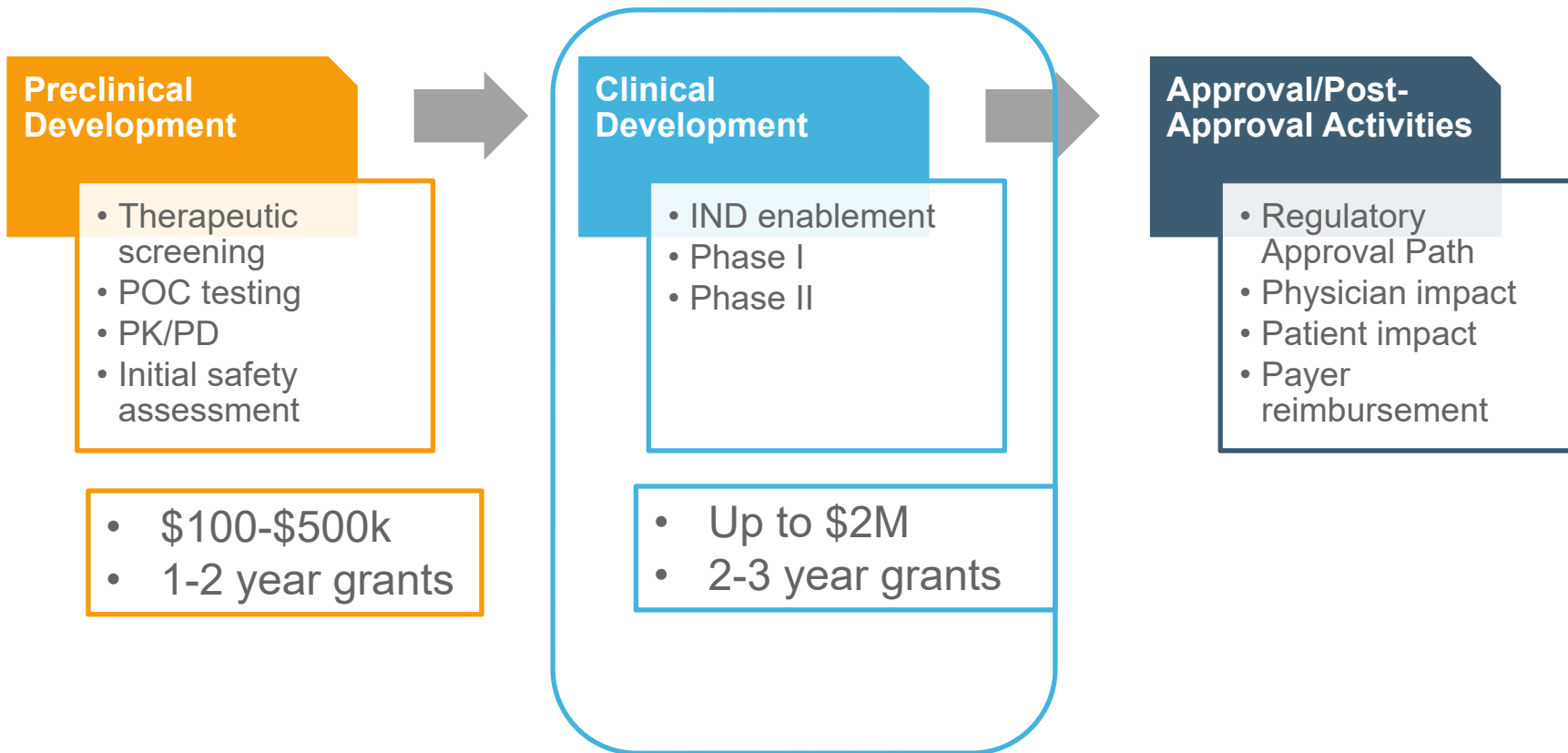
EPI Program: Using Epidemiological Datasets to Identify Risk and Protective Factors for Parkinson's disease

- 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

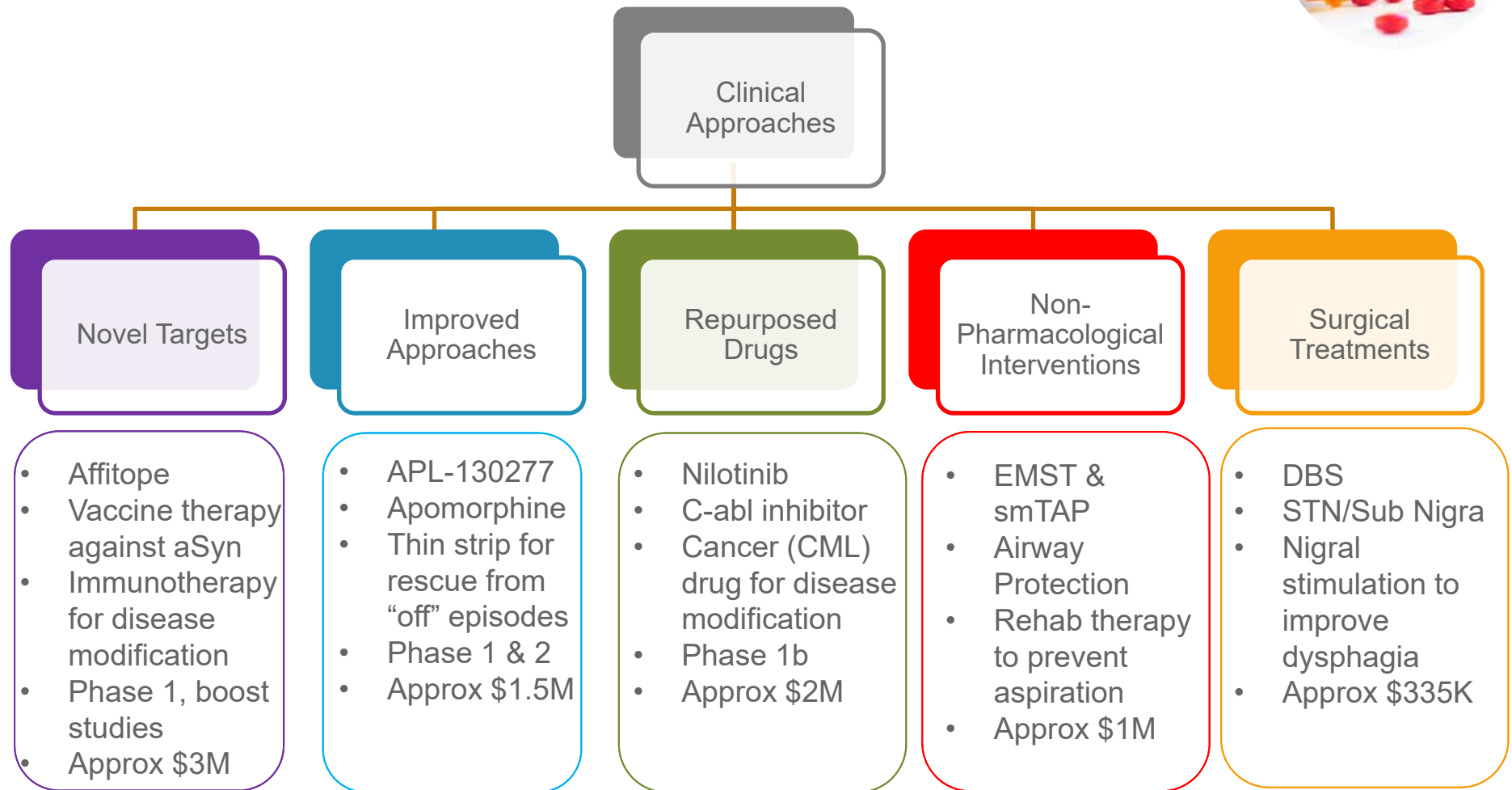


THERAPEUTICS

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

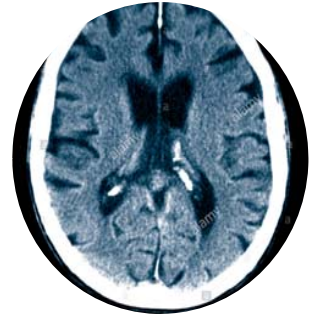
- Supports preclinical and clinical drug development (drug and non-pharmacological therapeutics, including gene therapy, biological, surgical and non-invasive approaches).
- Funding up to \$500K for preclinical and up to \$2M for clinical grant
- Deadline: Sep 26, 2018

Non-Pharmacological Interventions For Gait and Balance Disturbances

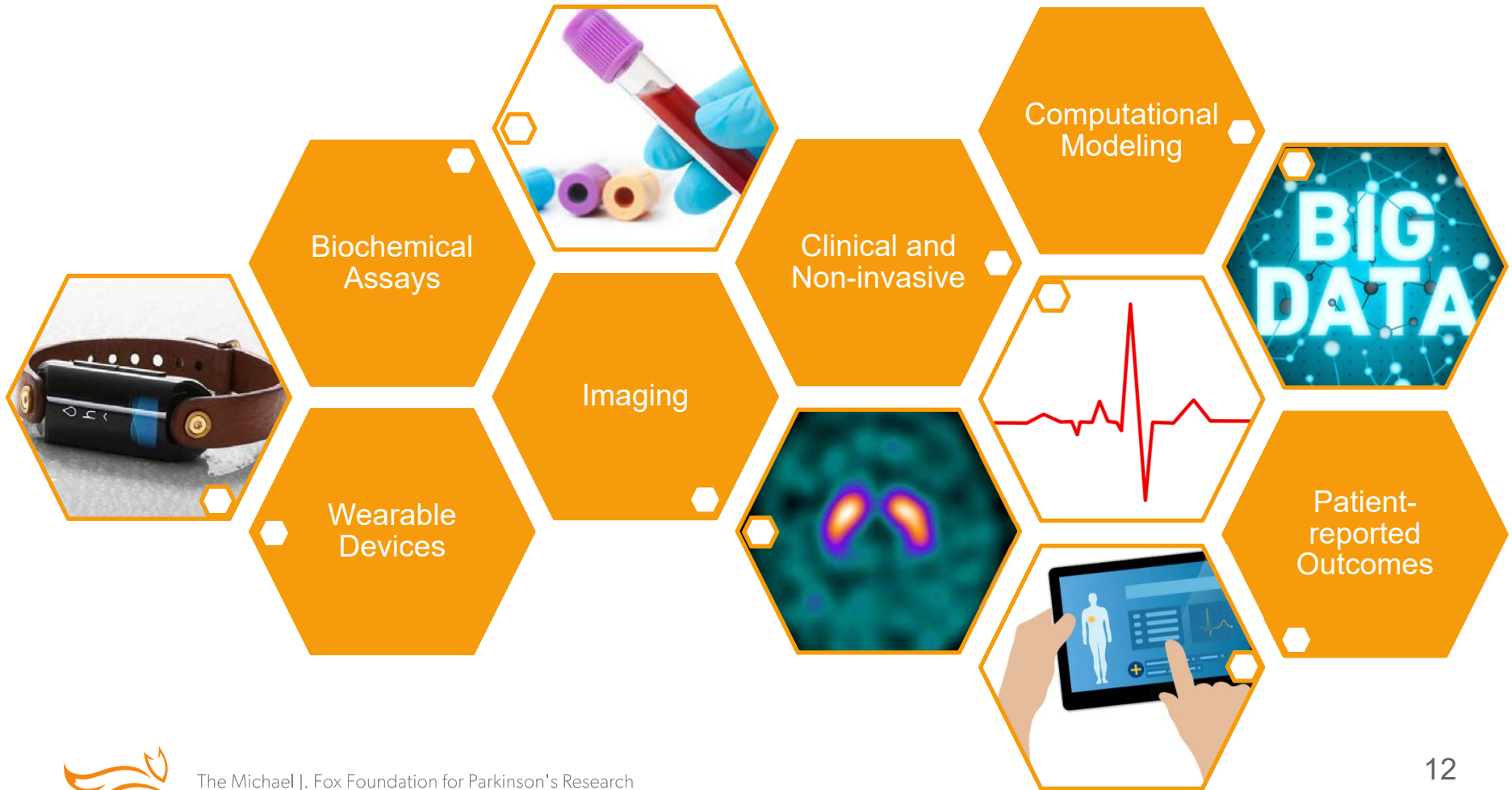
- Support proposals for studying therapeutic benefit of assistive devices, novel technologies and rehabilitative therapy programs.
- Funding up to \$500K for one- to two-year grants
- Deadline: Program closed, Funding in Oct/Nov 2018



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



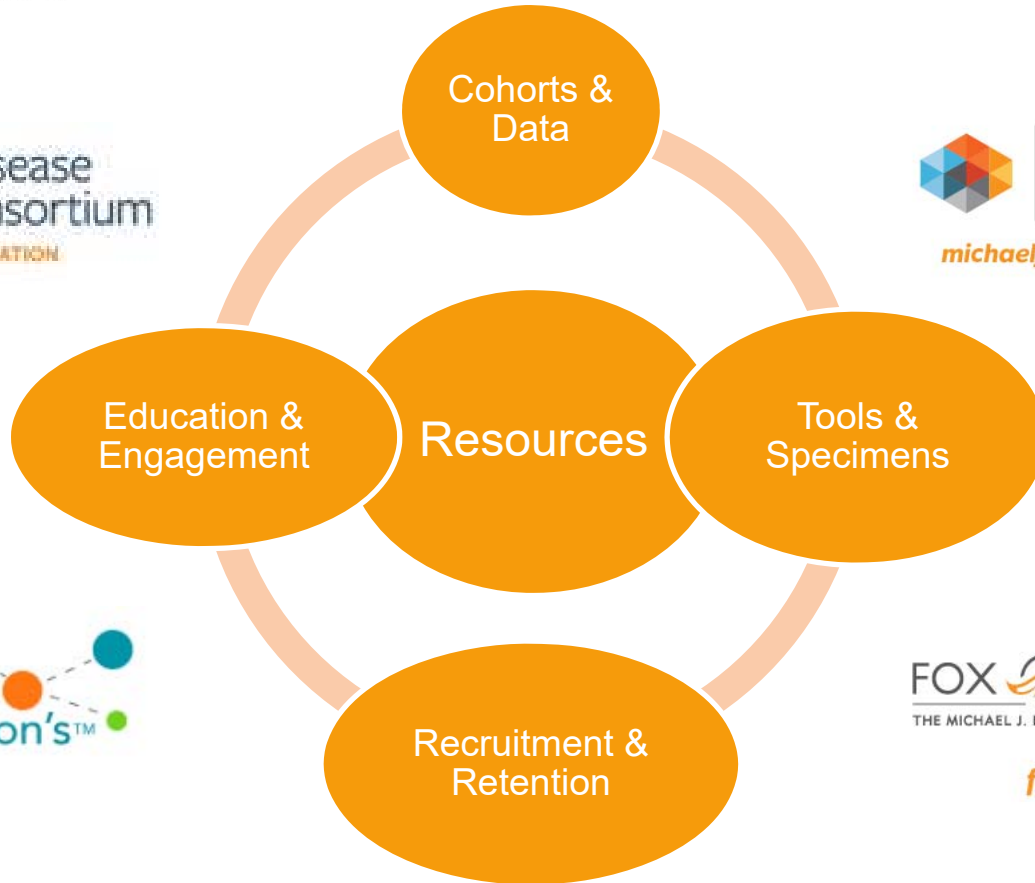
Parkinson's Disease
Education Consortium

THE MICHAEL J. FOX FOUNDATION



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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.

