CURRENT GENOME-ENABLED DISCOVERY ACTIVITIES RELATED TO BIORESOURCES

The Michael J. Fox Foundation for Parkinson's Research

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

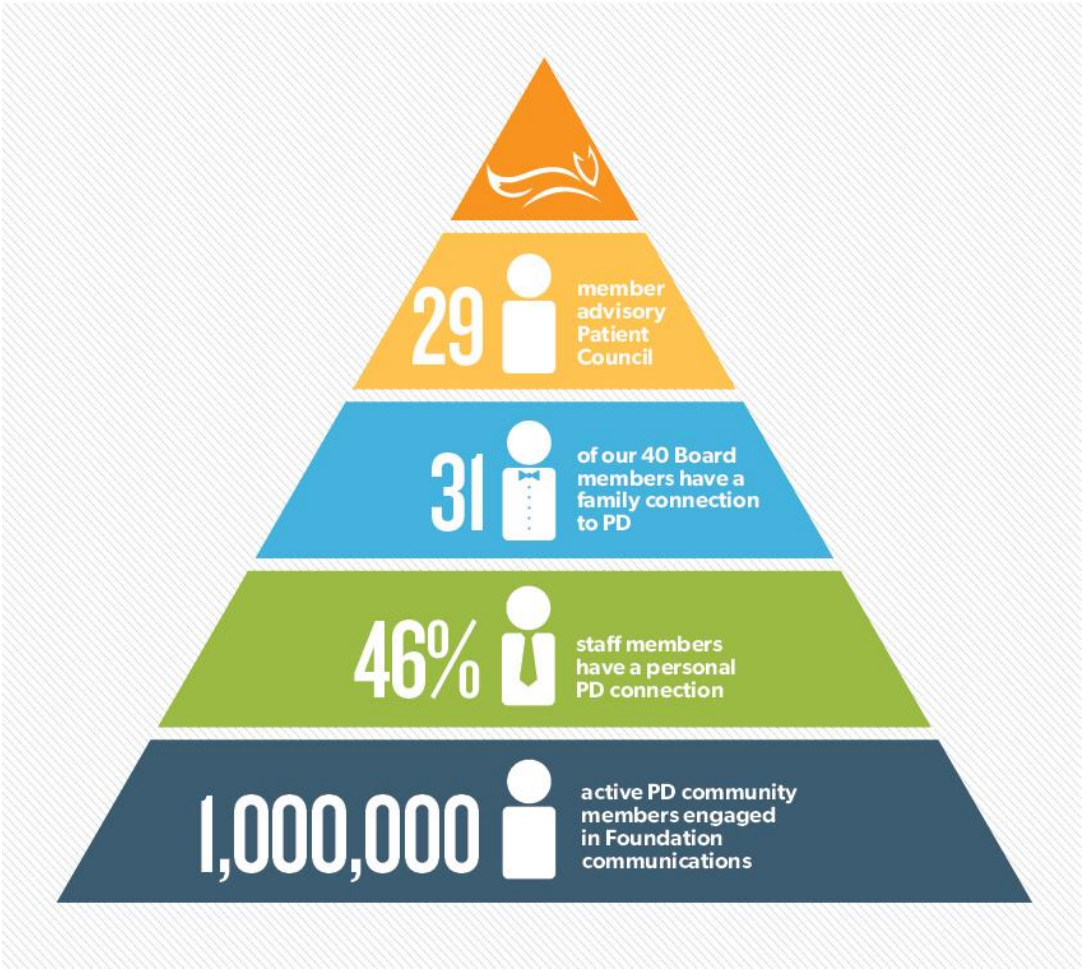
Our Mission

To accelerate the development of improved therapies, and ultimately a cure, for people living with Parkinson's disease today.

Vital Stats

- Founded in **2000** by actor Michael J. Fox
- Public charity
- Nearly **70,000** donors in 2015 (individuals, corporations, nonprofits)
- No chapters: team of **100** based in NYC
- **3,300** grassroots fundraisers reaching **150,000** supporters worldwide in 2015
- More than **$600 million** in research programs funded to date
- **$87.8 million** in research programs funded in 2015
- Nearly **2,100** projects funded to date
- **550** active grants in current portfolio
- **33%** 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.

THE 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 PARTNERS

PPMI is sponsored and partially funded by The Michael J. Fox Foundation for Parkinson's Research. Other funding partners include a consortium of industry players, non-profit organizations and private individuals.

PPMI STUDY DETAILS: SYNOPSIS

STUDY POPULATION

- 400 de novo PD subjects (newly diagnosed and unmedicated)
- 200 age-and gender-matched healthy controls
- ~70-80 SWEDD subjects
- 60-100 individuals with non-genetic risk factors (hyposmic, RBD)
- 500 LRRK2 or GBA (PD manifest and non-manifesting family members)
- 100 Synuclein (PD manifest and non-manifesting family members)
- Subjects followed for 3 to 8 years

ASSESSMENTS/ CLINICAL DATA COLLECTION

- Motor assessments
- Neuropsychiatric/neurobehavioral testing
- Autonomic, olfaction, sleep
- DaTSCAN imaging, DTI/rs MRI

BIOLOGIC COLLECTION

- DNA collected at screening
- 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

INITIAL VERIFICATION STUDIES

- Lead biologic candidates to be tested:
  - Alpha-synuclein (CSF)
  - DJ-1 (CSF and blood)
  - Urate (blood)
  - Abeta 1-42 (CSF)
  - Total tau, Phospho-tau (p-181) (CSF)

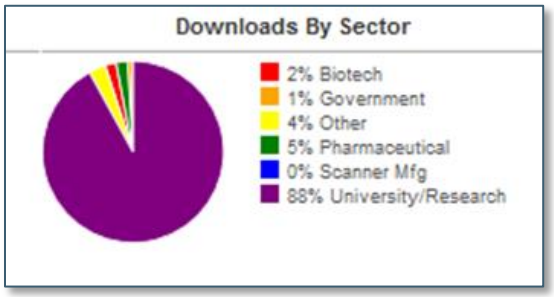
PPMI IS A GLOBAL RESOURCE FOR PARKINSON'S RESEARCH

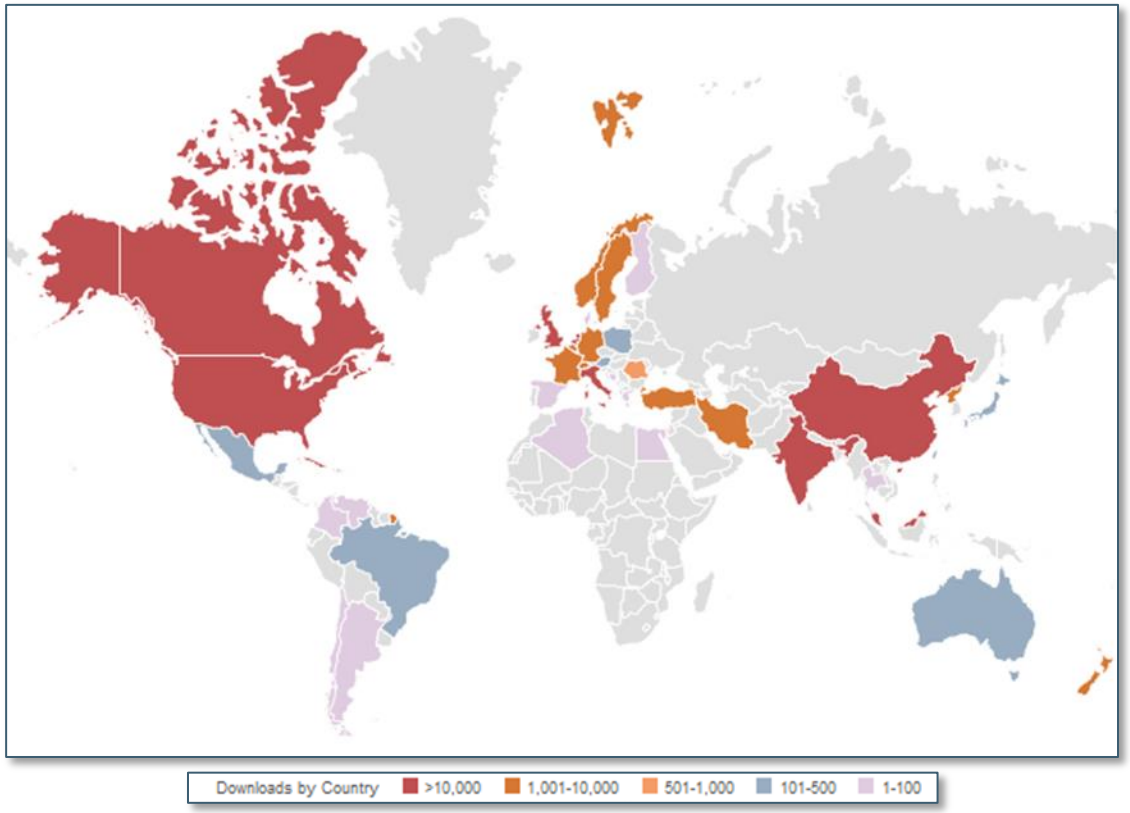
TOTAL # OF DATA DOWNLOADS

538,009

TOTAL # OF SPECIMEN REQUESTS

70





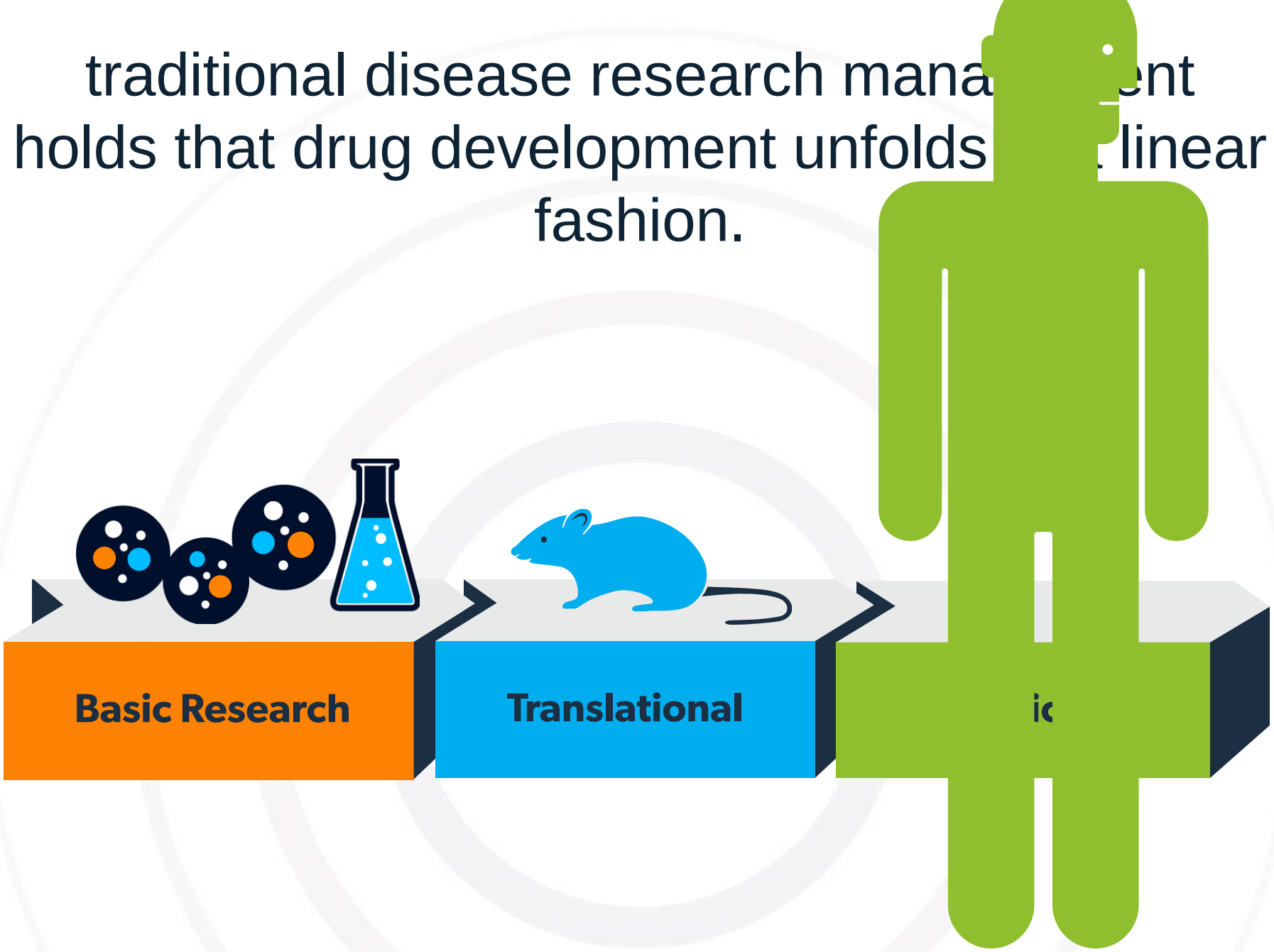
Researcher-facing website: www.ppmi-info.org

WE'VE DEVELOPED THIS IMPORTANT RESOURCE – SO NOW WHAT?

» This is an exciting and optimistic time for Parkinson's drug development
  – Have several disease-modifying trials in early-stage clinical testing
  – Genetic discoveries (SNCA, LRRK2, GBA) are tractable targets

» BUT… Genetics only take us so far when it comes to drug development
  – Parkinson's is a complex disease that goes far beyond what is occurring in a patient's brain
  – Heterogeneity of disease suggests distinct subtypes of patients

traditional disease research mana ent holds that drug development unfolds linear fashion.



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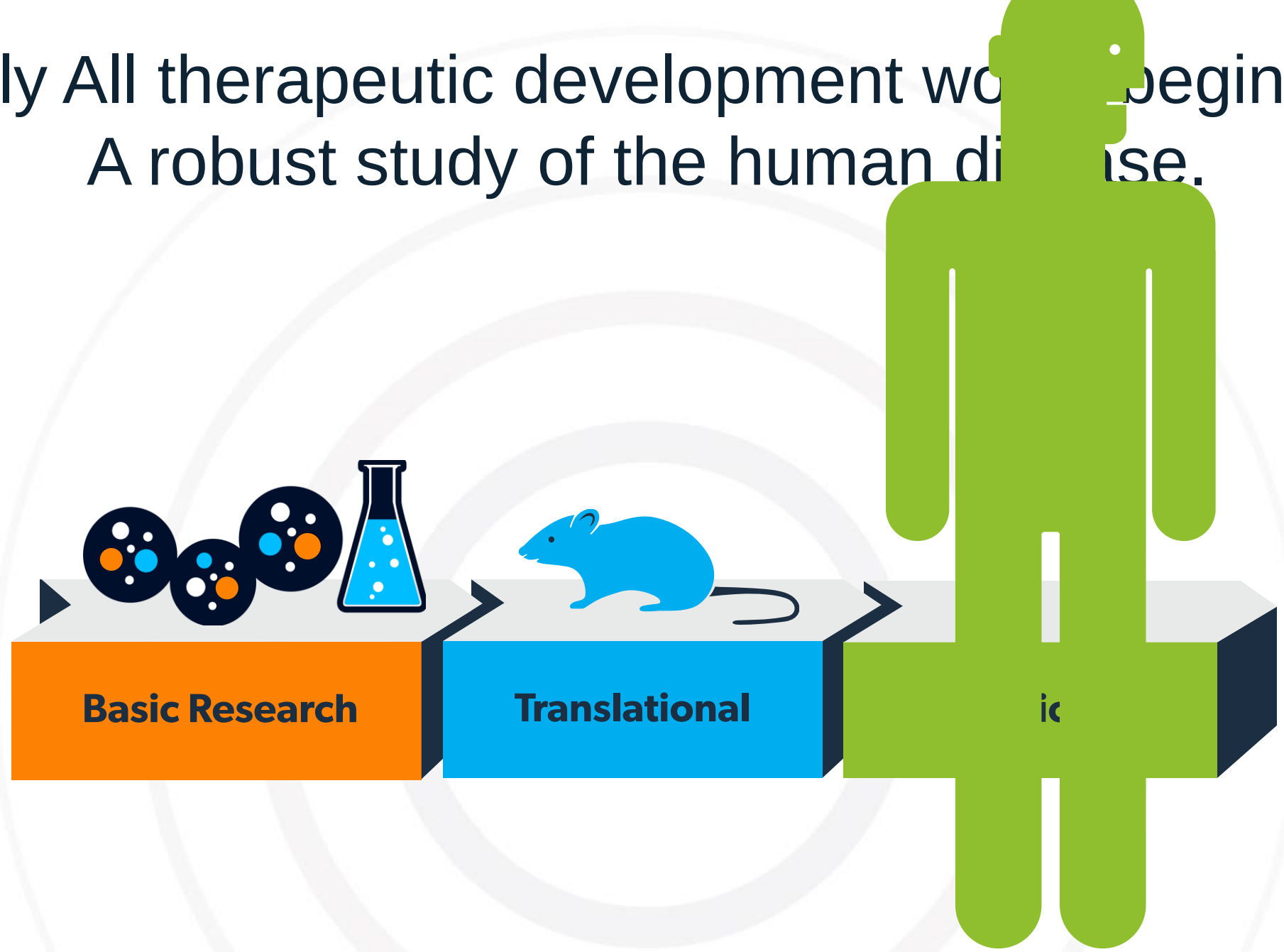

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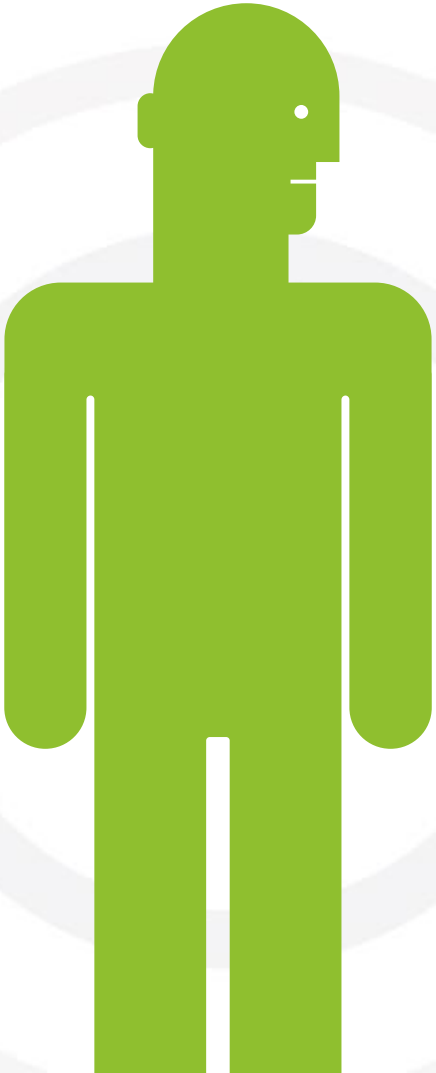
Epidemiology

Diagnosis and
Clinical Symptoms



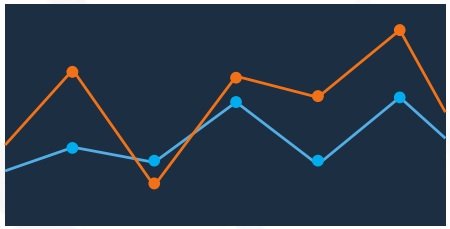
Progression

Patient-reported Data

Response to
Available Treatments

better clinical understanding enables informed biological characterization of disease.

Genetics



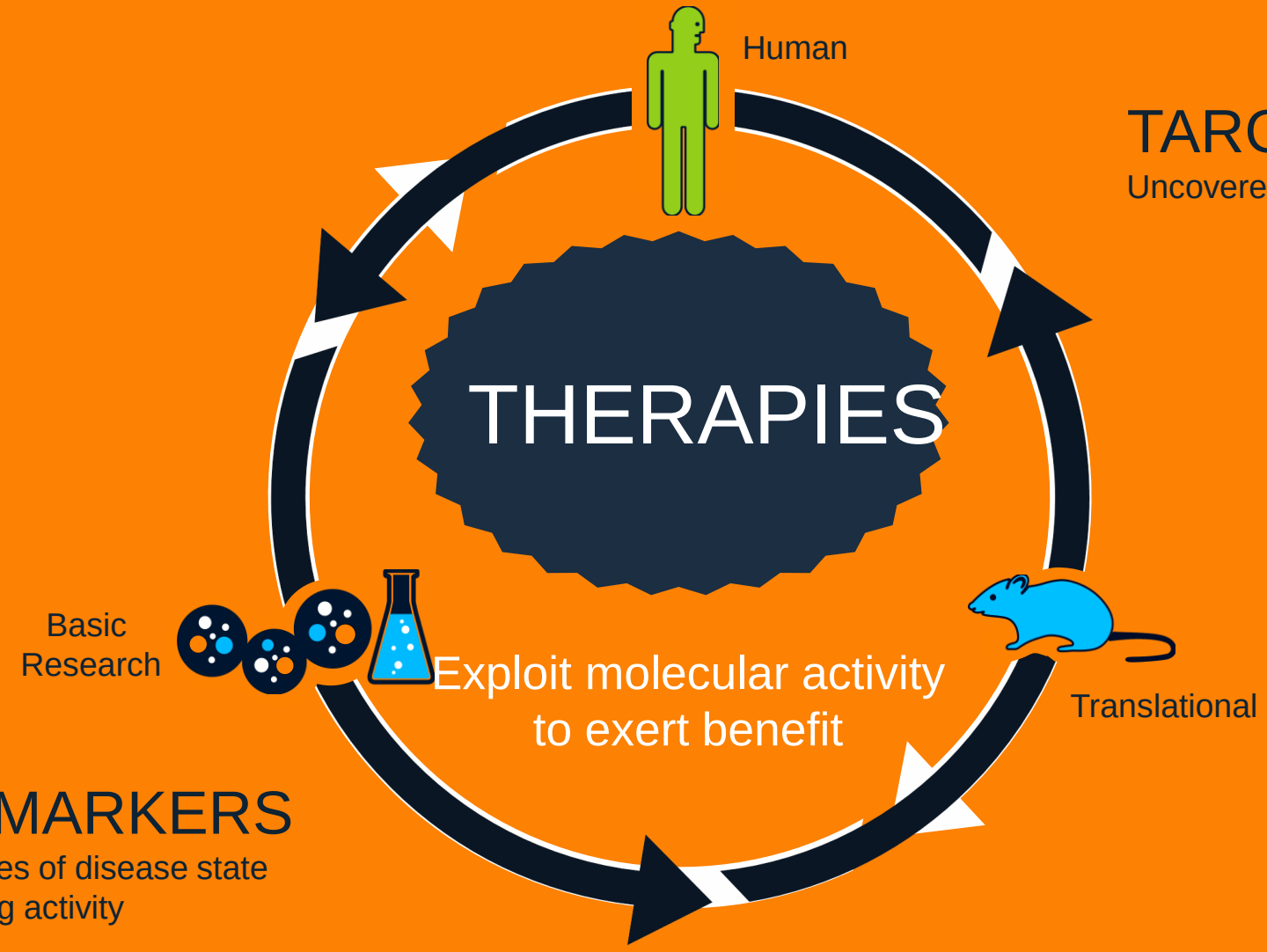
Biomarkers

Cellular Mechanisms and Pathways

Imaging

Disease Models

Defining the biology creates a virtuous cycle o drug target and biomarker identification.



ter-informed by biology we can develop and te
new therapies in the context of human disease

Treatment impact on biological measures

Cellular mechanisms and pathways

Understand and predict risk

Treatment impact on clinical characterization, diagnosis and progression

Patient selection for clinical trials

AS A PATIENT-DRIVEN RESEARCH FUNDING ORGANIZATION, WE WANT…

- To break down the siloes that exist between bench science, clinical research, drug development and biomarkers

- Ensure that all areas of drug development – from basic scientific discovery to therapeutic programs and biomarker research – are being informed by the patient

- Example:
  - Discovery of LRRK2 shines a spotlight on a new target around which to develop drugs. BUT the genetic target is just the 1st shot on goal
  - Work around the genetics will illuminate additional pathways for drug development