Global Parkinson's Genetics Program

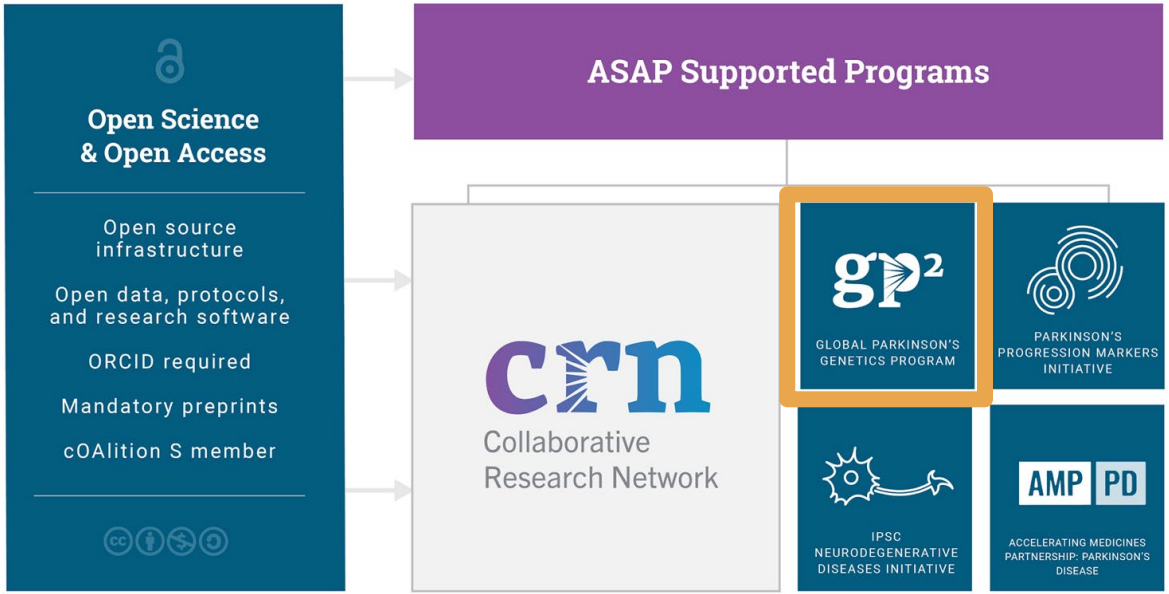
# The Global Parkinson's Genetics Program (GP2)

## NASEM Forum on Neuroscience & Nervous System Disorders

From Molecular Insights to Patient Stratification for Neurological and Psychiatric Disorders: A Workshop
October 5, 2021

Ekemini Riley, PhD
ASAP Managing Director

# GP2 is an ASAP Resource Project




WWW.PARKINSONSROADMAP.ORG

WWW.GP2.ORG

### ASAP Mission

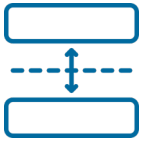
To accelerate the **pace of discovery** and inform the path to a cure for Parkinson's disease through **collaboration**, research-enabling **resources**, and **data sharing**.

### Implementation Partner

ASAP is leveraging the grantmaking infrastructure and clinical coordination expertise of The Michael J. Fox Foundation to implement its programs.

asap Aligning Science Across Parkinson's

# Filling Gaps within the Research Ecosystem



**95%** of large-scale genetic discovery work in PD is performed in populations of **Northern European Ancestry.**

*GP2 aims to fill this gap and provide a blueprint for how this can be done.*

To dramatically expand our understanding of the genetic basis of PD and to make that knowledge globally relevant.

*GP2 is on pace to genotype 150,000+ ancestrally diverse volunteers worldwide.*

1 Intentional engagement with various communities

2 Capacity building

*Key GP2 Structural Priorities:*
*Diversity in Research and Researchers*
*Collaboration & Cooperation*

# GP2 Mission & Path Forward

To dramatically expand our understanding of the genetic basis of PD and to make that knowledge globally relevant

## SCIENTIFIC OUTCOMES

### Complex Disease

dramatic expansion of known genetic risk

**whole genome genotyping of >150,000 individuals**

- Doubling in known risk loci
- Improved PRS for prediction and modeling
- Mutation carriers identified (every known assayable NDD mutation)
- Genetic basis of onset, progression
- Genetic modifiers of *LRRK2*, *GBA*
- Samples, tissues, cells available

### Monogenic Disease

enabling, accelerating, improving mutation discovery

**whole genome sequencing of >10,000 individuals**

- Rapid identification of new causal genes for PD
- Validation Resource for new genes/mutations
- Long read sequencing resource
- Exploration of SV and repeats in disease causation
- Samples, tissues, cells, with known genetic architecture

### Global Disease

making our understanding of genetics globally relevant

**ancestral diversity in all genetic analyses**

- Black Americans, Africa, South and Central America, East Asia, Central Asia
- Mapping heterogeneity
- Accelerated fine mapping to reveal effector gene and mechanism
- Identification of populations enriched for genetic factors
- Diverse patient samples, tissues, cells with known genetic architecture

## STRUCTURAL PRIORITIES

- **Democratization of Data**
- **Collaboration and Cooperation**
- **Safe, Responsible Data Sharing**
- **Diversity in Research and Researchers**
- **Transparency & Reproducibility**
- **Foundational, Actionable Resource Production**

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# Laying the Foundation with Diverse, Distributed Leadership

## Steering Committee
Andrew Singleton | Cornelis Blauwendraat | Tatiana Foroud | Alastair Noyce | Christine Klein | Enza Maria Valente | Peter Heutink | Huw Morris | Mike Nalls | Ignacio Mata | Nicholas Wood | Alexis Brice | Thomas Gasser | Nigel Williams | Brian Fiske | Bradford Casey | Alyssa Reimer | Ekemini Riley | Rejko Kruger | Ken Marek | Mie Rizig | Manu Sharma | Kin Mok

## Operations and Compliance
Tatiana Foroud | Alyssa Reimer | Claire Wegel | Justin Solle | Thomas Gasser | Schuyler Fox | Christine Klein | Enza Maria Valente | Njideka Okubadejo | Ignacio Mata | Mary Makarious | Hampton Leonard | Mie Rizig | Miriam Peleman | Niccolo Mencacci | Huw Morris

## Training and Networking
Alastair Noyce | Sara Bandres-Ciga | Sumit Dey | Claire Bale | Maggie Kuhl | Hampton Leonard | Patrick Lewis | Benjamin Stecher | Simon Stott | Sabina Adams | Alejandro Carrasco

## Monogenic Disease (MD) Hub
Christine Klein | Niccolo Mencacci | Katja Lohmann | Kishore Raj Kumar | Peter Heutink | Enza Maria Valente | Shen-Yang Lim

### MG Sample Prioritization
Christine Klein | Kishore Kumar

### MG Data Analyses
Peter Heutink | Zih-Hua Fang

### MG Portal Development
Enza Maria Valente | Shen-Yang Lim

## Complex Disease (CD) Hub
Andrew Singleton | Cornelis Blauwendraat | Caroline Pantazis | Dena Hernandez | Ruqaya Murtadha

### CD Cohort Integration
Huw Morris | Hirotaka Iwaki | Manuela Tan

### CD Data Analyses
Mike Nalls | Hampton Leonard | Sara Bandres-Ciga | Cornelis Blauwendraat | Jean-Christophe Corvol | Ignacio Mata | Hirotaka Iwaki | Jeff Kim | Mary Makarious | Yeajin Song | Dan Vitale | Nigel Williams

## Underrepresented Populations
Ignacio Mata | Artur F. Schumacher-Schuh | Shen-Yang Lim | Olaitan Okunoye | Sara Bandres-Ciga | Peter Heutink | Hirotaka Iwaki | Rejko Kruger | Kin Mok | Alastair Noyce | Njideka Okubadejo | Mie Rizig | Manu Sharma | Joshua Shulman | Bernadette Siddiqi

## Data and Code Dissemination
Bradford Casey | Mary Makarious | Jeff Kim

## Project Proposal, Approval, and Execution
John Hardy | Njideka Okubadejo | Mario Cornejo Olivas | Huifang Shang | Ruqaya Murtadha | Dena Hernandez | Sara Bandres Ciga | Yeajin Song | Thomas Gasser

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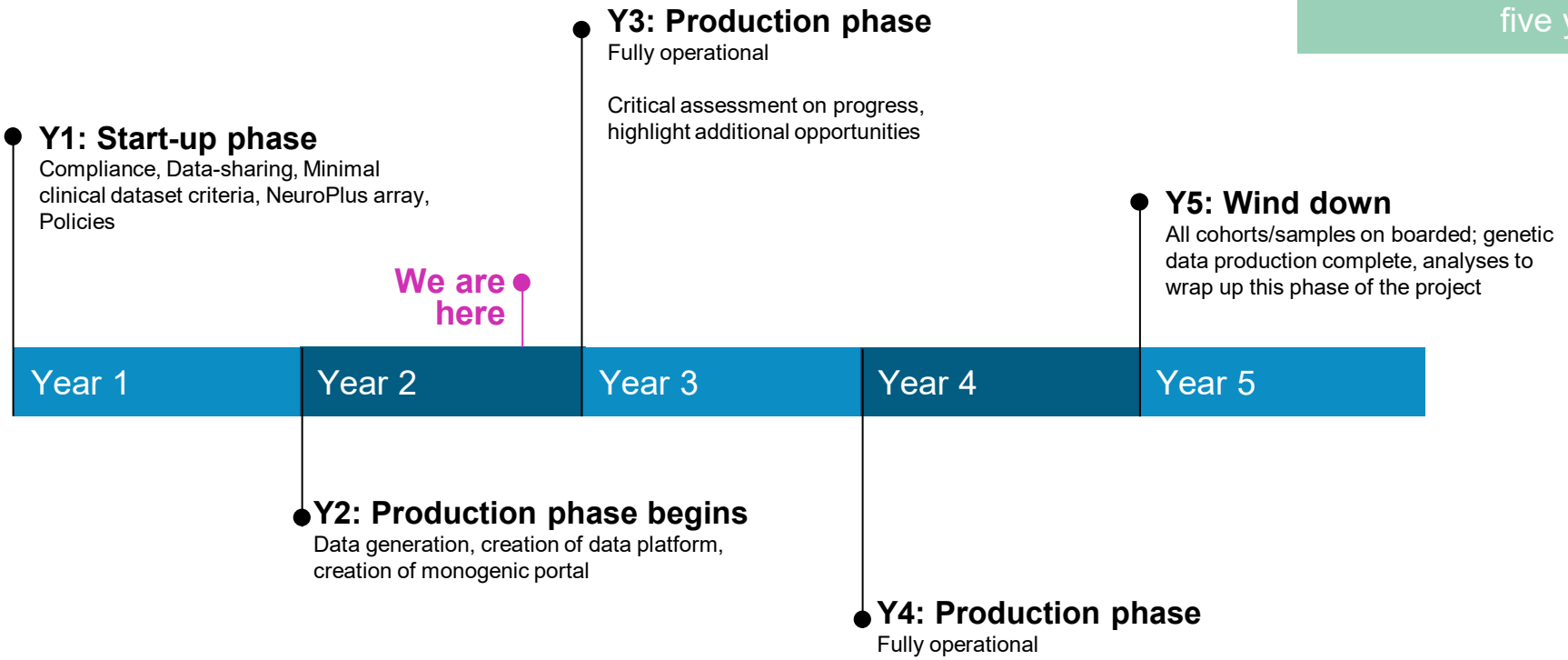
# Time & Scale

$35M committed over five years



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# Intentional Engagement

# Intentional engagement through strategic partnerships…

**Y1: Start-up phase**
Compliance, Data-sharing, Minimal clinical dataset criteria, NeuroPlus array, Policies

We are here


**Y2: Production phase begins**
Data generation, creation of data platform, creation of monogenic portal

International Parkinson and Movement Disorder Society

Shared training materials, outreach to cohorts and underserved populations, joint meetings, free membership to GP2, access to scales, translation of scales

AMP PD

Data access through a controlled environment, user access to include browsing of results and in situ analysis of data to democratize analysis

illumina

Creation of a global diversity array with neurodegenerative disease content

Parkinson's Foundation

Collaboration on the PD GENEration study, that aims to provide genetic results and counseling to 10,000 PD patients

PARKINSON'S PROGRESSION MARKERS INITIATIVE
Play a Part in Parkinson's Research

Generation of genotype, whole genome sequencing, and long read sequencing data on the most well-characterized PD cohort in the world

iPDGC
iPDGC Africa
iPDGC East-Asia
LARGE-PD
GEoPD

Collaborative partnerships with existing international consortia in the PD genetics field



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# …leading to the launch of programs & commitments to contribute cohorts and samples globally


## Understanding Genetic Implications of the Black and African American Connections to Parkinson's Disease Study (BLAAC PD)

By Sara Bandres-Ciga, Justin C. Solle, Alyssa Reimer, and Bernadette Siddiqi | **GP2 Values**, **GP2 Values** | July 23, 2021

## Increasing Underrepresented Hispanic Participation in Parkinson's and Genomic Research Through the LARGE-PD Study

By Ignacio Fernandez Mata, Philippe Salles, Shilpa Rao, Miguel Inca Martinez, Nicolas Gutierrez, and Thiago Peixoto | **Uncategorized** | September 27, 2021

CARE

In partnership with
**CARE:** Community Access, Recruitment, and Engagement

iPDGC iPDGC Africa iPDGC East-Asia LARGE-PD GEoPD




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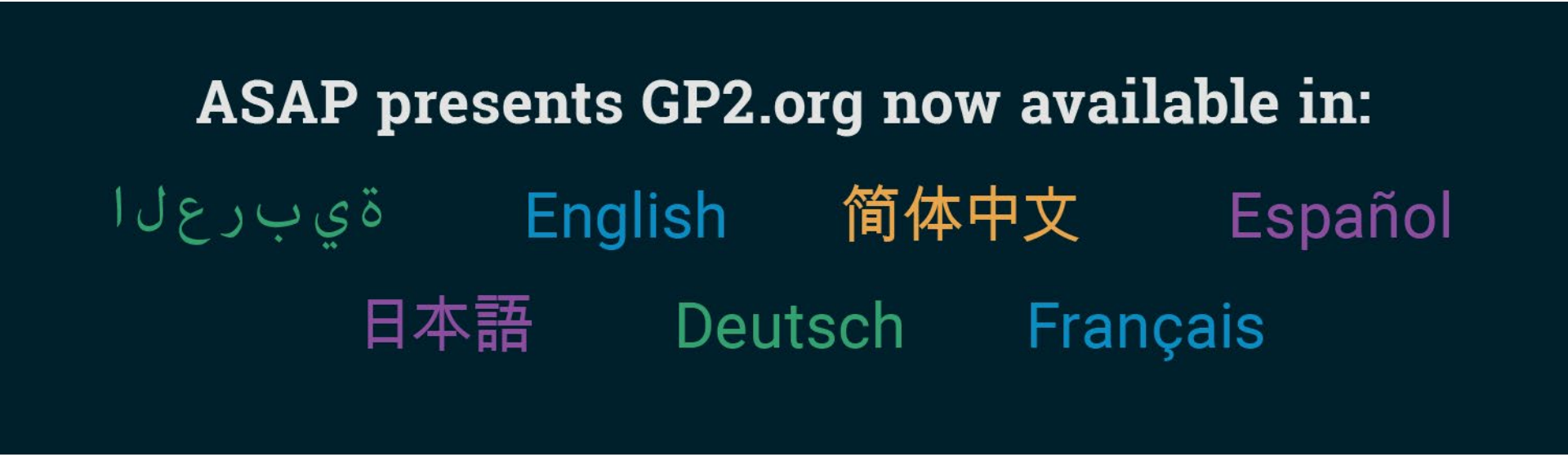
# Considering Access from the End User Perspective



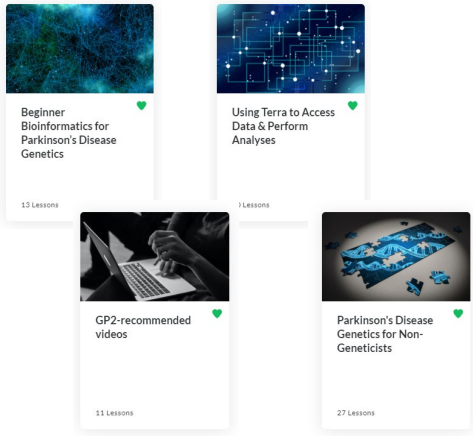

Expanding global reach with language accessibility

# Capacity Building

# Building global will and capacity

## ACCESS

Access for learners worldwide through online learning platform.




training.gp2.org

*Join 400+ learners | 4 courses*

## TRAINING

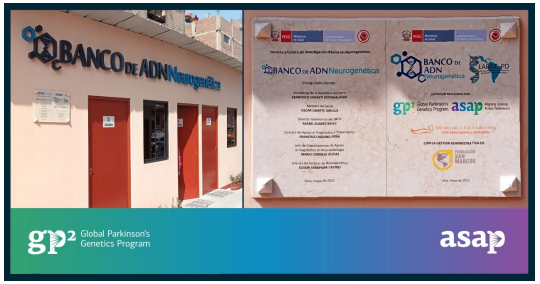
Fund genetics MSc & PhD programs for clinicians and researchers in low-to-middle income countries.


Trainees announced next week!

*Building diverse researcher & clinician pool*

## INFRASTRUCTURE

Contribute to infrastructure development to enable current & future research.




Helped to fund the construction of the first DNA Biobank in Peru!



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# An Actionable Blueprint

INTENTIONAL ENGAGEMENT

CAPACITY BUILDING

Journal of Parkinson's Disease 11 (2021) 905–908
DOI 10.3233/JPD-212593
IOS Press

Michael J. Fox Foundation – Position Paper

## A Call to Action: Promoting Diversity, Equity, and Inclusion in Parkinson's Research and Care

Bernadette Siddiqi* and Andrew Koemeter-Cox
*The Michael J. Fox Foundation for Parkinson's Research, New York, NY, USA*

**4** Major Areas of Action:

- Identifying barriers and solutions to research participation
- **Funding inclusive research with greater participant diversity**
- Building a clinician/researcher workforce committed to health equity
- **Supporting a more holistic understanding of PD**



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# Want More Information?

- **GP2 website:** www.gp2.org
- **GP2 blog series:** www.gp2.org/blog
  - 15 blog posts now available!
- **GP2 Programmatic Overview**
  - *Movement Disorders, 2021*. (PMID: 33513272)
- **Questions? Feel free to reach out to:**
  - Ekemini Riley, ASAP Managing Director: eriley@parkinsonsroadmap.org
  - Andy Singleton, GP2 Principal Investigator: singleta@mail.nih.gov

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