PD GENEration: Widescale Whole Genome Sequencing and Genetic Counseling for People Living with Parkinson's Disease

Kamalini Ghosh Galvelis[1], Megan Dini[1], Lark Caboy[1], Allison Dilliott[1], Nicola Bothwick[1], Rebeca De Leon[1], Ignacio Azcarate[1], Margaret Caulfield[1], Anny Coral-Zambrano[1], Melissa Nicewaner[1], Joshua Ruffner[1], Addison Yake[1], Cornelis Blauwendraat[2], James C. Beck[1], Roy N. Alcalay[3,4,5] and The Parkinson's Foundation PD GENEration Study.

1) Parkinson's Foundation, New York, NY; 2) Aligning Science Across Parkinson's, Bethesda, MD ; 3) Columbia University, New York, NY; 4) Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; 5) Parkinson Study Group, Boston, MA

Poster Number: 36

Background

PD GENEration (NCT04994015) is a multi-center observational clinical research study that offers genetic testing and counseling to people living with PD (PwP) in over 8 countries in the Americas and Israel. Testing includes a panel of 7 known PD associated genes, and with the transition from clinical exome sequencing to whole genome sequencing (WGS) in March of 2024, now also includes 2 optional secondary health findings (SHF) panels: 1) 21 genes linked to parkinsonisms or PD and 2) 10 non-PD actionable genes referred to as the CDC Teir 1 genes PwP consent to genetic counseling for the primary panel regardless of their results, and they have the option to consent to receive positive results for either or both secondary panels. Following study completion, participants may be eligible to participate in one of three sub-studies developed by PD GENEration. The full study pipeline is shown below. All de-identified data produced from this study is shared with researchers and scientists, most notably with the Global Parkinson's Genetics Program (GP2), a program of the Aligning Science Across Parkinson's (ASAP) initiative.

Methods

PD GENEration Participant Workflow

1) Baseline Visit
Consent for primary and secondary health findings, basic clinical data collection, and sample collection

2) Sample Analysis and Data Sharing
Fulgent Genetics CLIA-certified lab
WGS Samples are analyzed via NGS and deletion/duplication analysis
Biobank DNA
PDGENE Panel
gp2

3) Primary Results
Genetic Counseling Site-based or via telemedicine
Clinical Report *GBA1 SNCA PINK1 LRRK2 PRKN PARK7 VPS35*

4) SHF Confirmation
Participants reconfirm their consent to receive SHF results
Participant confirms SHF selections
OR
Participant declines SHF results

5) SHF Results
Negative Result Negative SHF letter sent to participant
OR
Positive Result Site-based or telemedicine Genetic Counseling

7) GP2 Analysis
Genome-Wide Genotyping with NeuroBooster Array
AND
Joint calling of Array and WGS data
AMP PDRD

6) Study Complete PD GENEration Proband

PDGENE Surveys
Participant reported outcomes from entire PDGENE cohort
Survey 1: Environment, RBD1
- Completed: Sep 2025
- 44% responded
- 36% completed

Survey 2: Feb 2026

PDGENE Family
Genetic testing and counseling of first-degree family members
First participant in:
Nov 2025

PDGENE Insights
Clinical phenotyping of proband and first-degree family members
First participant in:
Expected Apr 2026
Protocol and ICF in development

All de-identified data shared with GP2

PD GENEration Panels

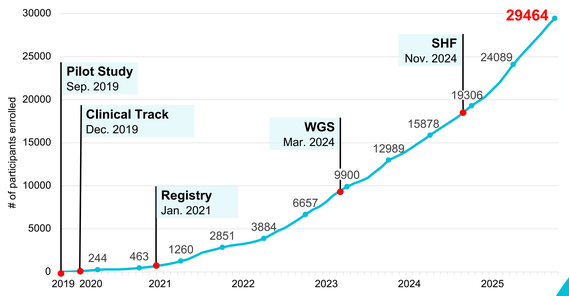
Primary Gene Panel	Optional Secondary Gene Panels
GBA1 *LRRK2* *PRKN* *SNCA* *PARK7* *PINK1* *VPS35*	**21 PD related** *RAB39B, VPS13C, PTRHD1, SYNJ1, POLG, DNAJC6, ATP13A2, DCTN1, ATP1A3, SLC6A3, TH, GCH1, FBXO7, PLA2G6, ATP7B, MAPT, GRN, TBK1, VCP, RAB32, CHCHD2* **10 Non-PD related (CDC Tier 1)** *BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS2, EPCAM, LDLR, APOB, PCSK9* Hereditary Breast and Ovarian Cancer Syndrome (HBOC) Lynch syndrome (LS) Familial hypercholesterolemia (FH)

Sites per Country

Country	# of sites
United States	62 total sites *56 local sites* *6 national sites*
Chile	3 local sites
Canada	2 local sites
Israel	3 local sites
México	2 local sites
Colombia	1 local site
Dominican Republic	1 local site
El Salvador	1 local site
Perú	1 local site

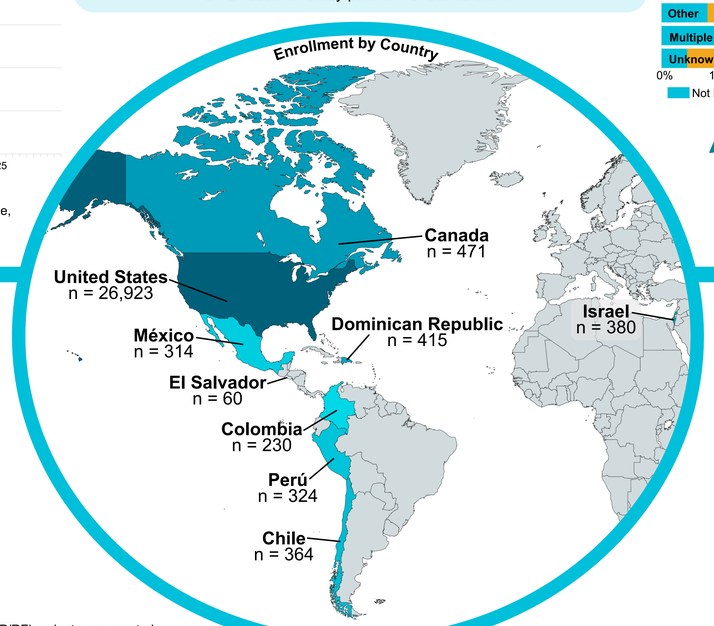
Results

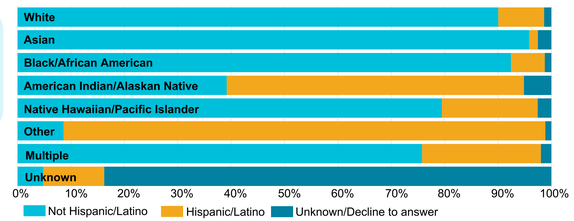
Enrollment

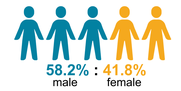


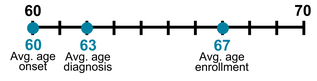
PD GENEration Cumulative Enrollment
Pilot Study – assessed feasibility. **Clinical Track** – continued the pilot at a larger scale, characterizing clinical phenotypes. **Registry** – made genetic testing and counseling available to 15,000 participants. **WGS** – transitioned to WGS and added SHF panel options. **SHF** – analysis and return of results for SHF panels began.

As of October 31, 2025, 29,464 participants have enrolled in PD GENEration, 9% internationally (left and below). Clinical exome sequencing was performed in 58% of participants while the remaining – and all ongoing testing – was performed by whole genome sequencing. Most participants (74%) have never participated in a PD research study prior to PD GENEration.



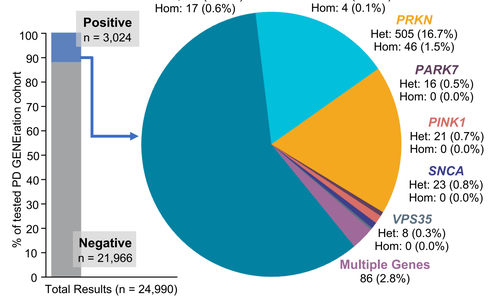






Participant Self-Reported Demographics
Participants self-report their race and ethnicity, biologic sex, and age at PD onset/PD diagnosis/current age as part of basic clinical data collection.

Genetics



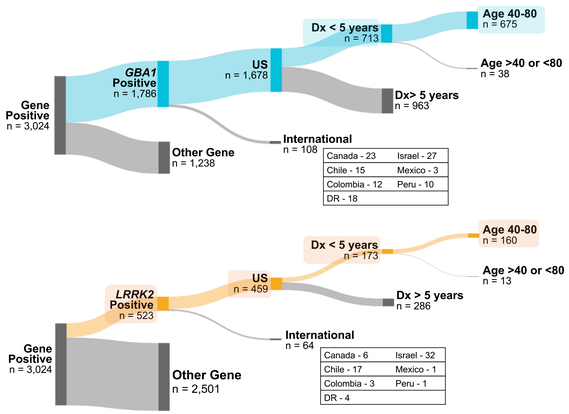
Primary Gene Panel Results Only pathogenic/likely pathogenic/risk factor (P/LP/RF) variants are reported to participants. Homozygous values also include confirmed compound heterozygous variants.

CDC Tier 1 SHF Results	
Variant Type	**Carriers (n)**
BRCA2* Het	21
BRCA1* Het	16
BRCA1* Mosaic	1
PMS2 Het	10
MSH6* Het	6
MLH1 Het	1
MSH2* *Het*	1
EPCAM* *Het*	1
LDLR* Het	32
APOB* *Het*	6
PCSK9* Het	2
Variant Negative	6,483

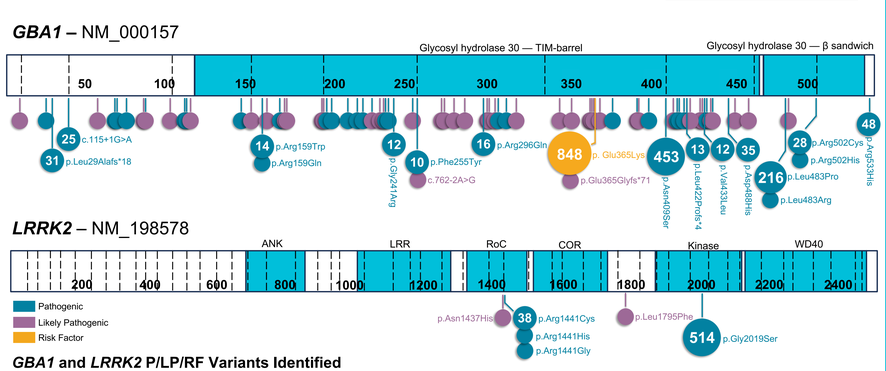
Genes with an asterisk (*) are known to display autosomal dominant inheritance

PD-related SHF Results	
Variant Type	**Carriers (n)**
POLG* Het	101
ATP7B Het	90
ATP7B Mosaic	1
VPS13C Het	30
PLA2G6 Het	16
GCH1* *Het*	10
TH Het	6
FBXO7 Het	5
GRN* Het	2
MAPT* Het	2
ATP1A3* Het	1
ATP13A2 Het	1
PTRHD1 Het	1
SYNJ1 Het	1
VCP* Het	1
Multiple genes	5
Variant Negative	6,352

PD GENEration Cohort Precision Trial Eligibility
Sankey diagrams demonstrating potential baseline stratification of the PD GENEration cohort based on simple inclusion criteria for genetic-based clinical trials and potential eligibility relevant to *GBA1* (top) and *LRRK2* (bottom). Abbreviations: DR, Dominican Republic; Dx < 5 years, year of diagnosis reported between 2021-2025.



PD Trial Navigator, an extension of PD GENEration, will accelerate precision medicine trials by identifying eligible participants from PD GENEration and ensuring they are sufficiently educated to understand and make enrollment decisions.



***GBA1* and *LRRK2* P/LP/RF Variants Identified**
Each circle represents a unique variant identified in at least one PD GENEration participant, with inset numbers indicating variant carriers, limited to n≥10. Some participants carried multiple variants. **Top:** 88 unique P/LP/RF single nucleotide variants (SNVs) have been identified in *GBA1*, as well as nine unique P/LP copy number variants (CNVs; not shown). **Bottom:** Six unique P/LP SNVs have been identified in *LRRK2*, with no CNVs reported to date.

Conclusion

PD GENEration offers a flexible research study framework that can integrate internationally, taking into consideration each country's infrastructure, cultural differences, and genetic counseling training needs. A decentralized study model and "train the trainer" methods allows PD GENEration to expand beyond the parameters of traditional genetic testing and genetic counseling. The study's recruitment rate demonstrates the enthusiasm of the community in disseminating genetic results to PwP. By analyzing an expanded panel and selectively collecting deeper phenotypic information, we aim to advance discoveries in PD genetics and accelerate enrollment into genetic specific clinical trials.

More about study findings and genetics

More about PD GENEration