MDS African Parkinson's Disease and Movement Disorders Conference (APMC)

Nairobi, Kenya | March 10-11, 2026

International Parkinson and Movement Disorder Society African Section

Global Parkinson's Genetics Program

Supported in part by the Global Parkinson's Genetics Program, a program of the Aligning Science Across Parkinson's initiative and implemented by the Michael J. Fox Foundation.

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PARKINSON'S DISEASE IN AFRICA

Unravelling the genetics of sporadic Parkinson's disease in Africa

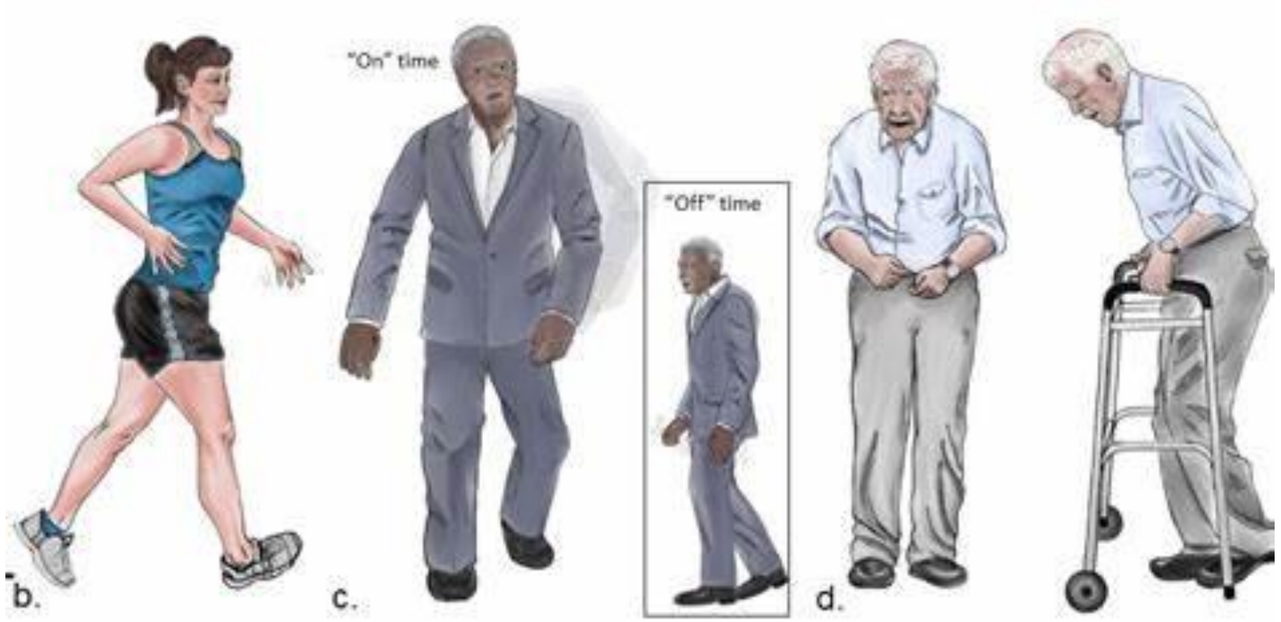
N. Okubadejo *MD, FMCP, FANA*
nokubadejo@unilag.edu.ng

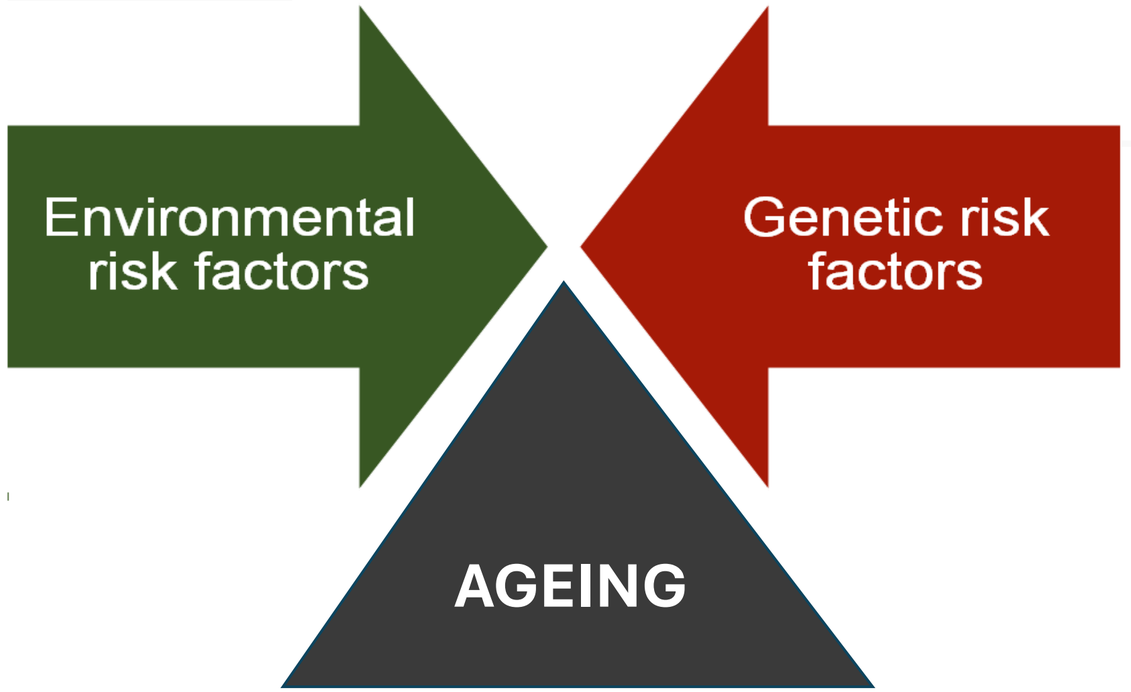
11/03/2026 – 28 days – 30 minutes talk

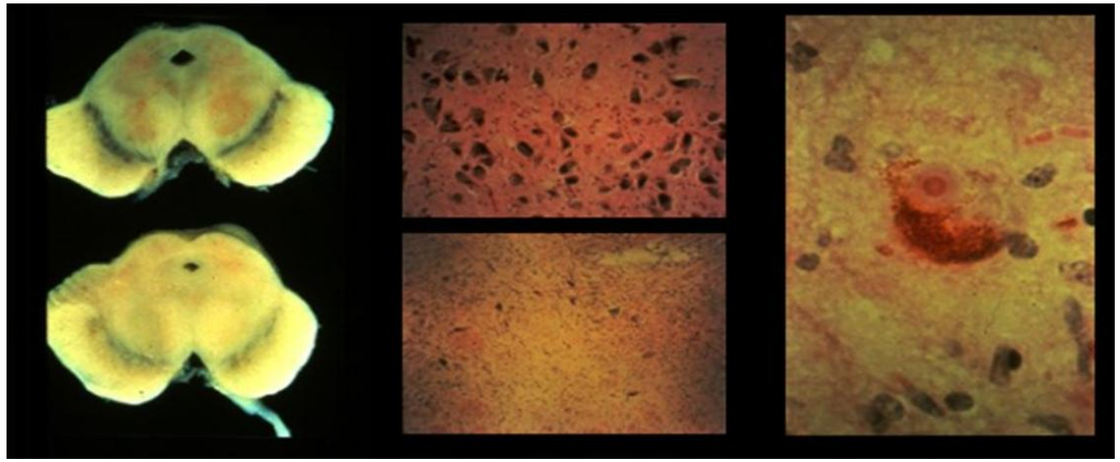
Outline

- Background – PD burden and main risk factors
- Timeline of genetic discoveries in PD
- Global insights into PD - monogenic and sporadic
- Historical insights of PD genetics in Africa
- Current knowledge of genetics of sporadic PD in Africa

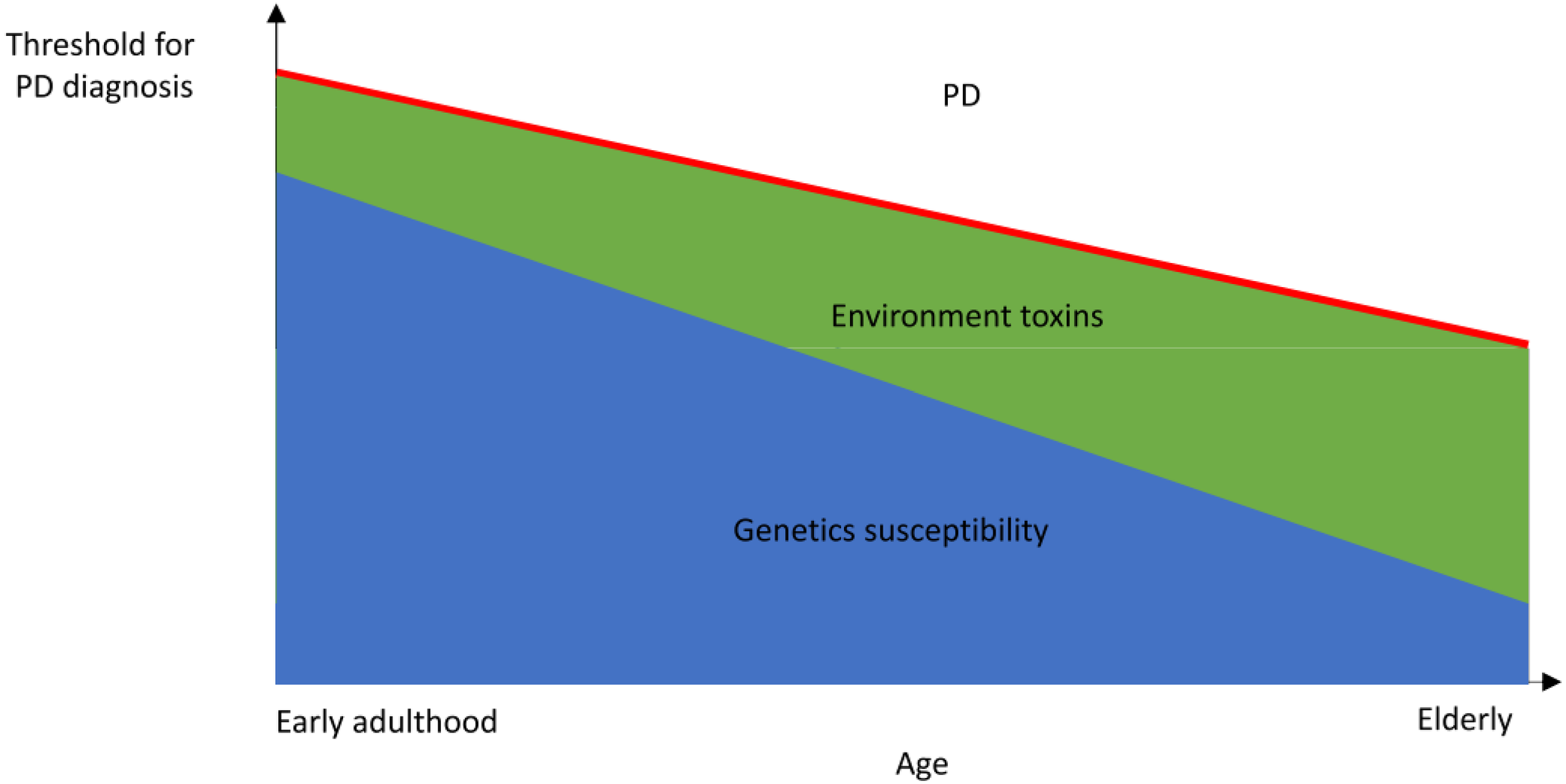
2nd most prevalent and fastest growing neurodegenerative disease







Interplay among aging, genetic susceptibility and environmental toxins in the pathogenesis of PD



Pang SY, Ho PW, Liu HF, et al. The interplay of aging, genetics and environmental factors in the pathogenesis of Parkinson's disease. *Transl Neurodegener*. 2019;8:23.

Position Paper: For/Against

J Parkinsons Dis. 2024;14(3):467-482. doi:10.3233/JPD-230376

Parkinson's Disease is Predominantly a Genetic Disease

Shen-Yang Lim[a,b] and Christine Klein[c,*]

Many patients with PD have a positive family history

10 – 15%

Pathogenic variants in some PD genes are highly penetrant for the disease

Environmental factors act on a background of genetic vulnerability

Besides causation/development of disease, genetic factors can also have a significant influence on the disease trajectory

Estimated population with PD in Africa

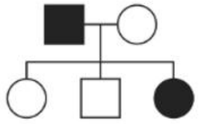
- PD affects ~ 1% of population ≥ 60 years
- PD affects ~ 0.04% of population <60 years

Category	Population size	PD Prevalence	Estimated number of PwPD
Population ≥ 60 years (4.9%)	66,000,000	1%	660,000
Population < 60 years (95.1%)	1,275,000,000	0.04%	510,000
Estimated number of people with PD in Africa			1,170,000

Monogenic (~20%)

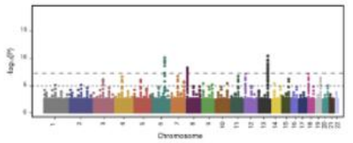
Apparently sporadic (~80%) (polygenic contributions)

Rare variants with high effect sizes (disease-causing)



Variants with moderate effect sizes and reduced penetrance

Common variants with limited effect sizes (risk-associated)

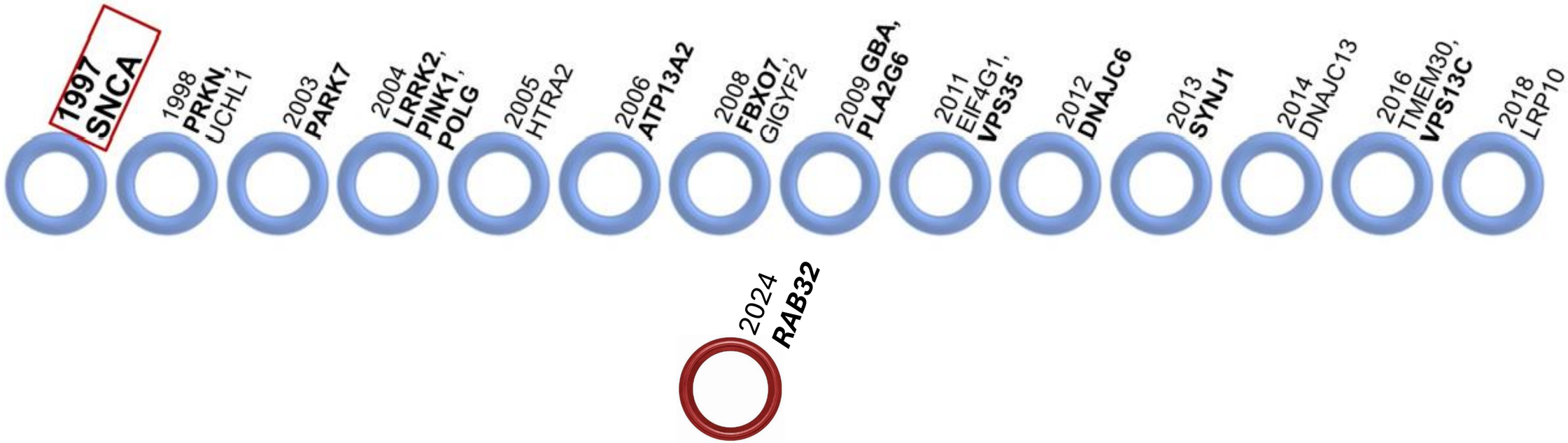


PINK1, PRKN, PARK7, SNCA

SNCA, LRRK2, VPS35, RAB32

GBA1, LRRK2, other GWAS hits

Mutations reported to cause PD



Bold: Mutations with ‘very high or high confidence as actual PD genes’

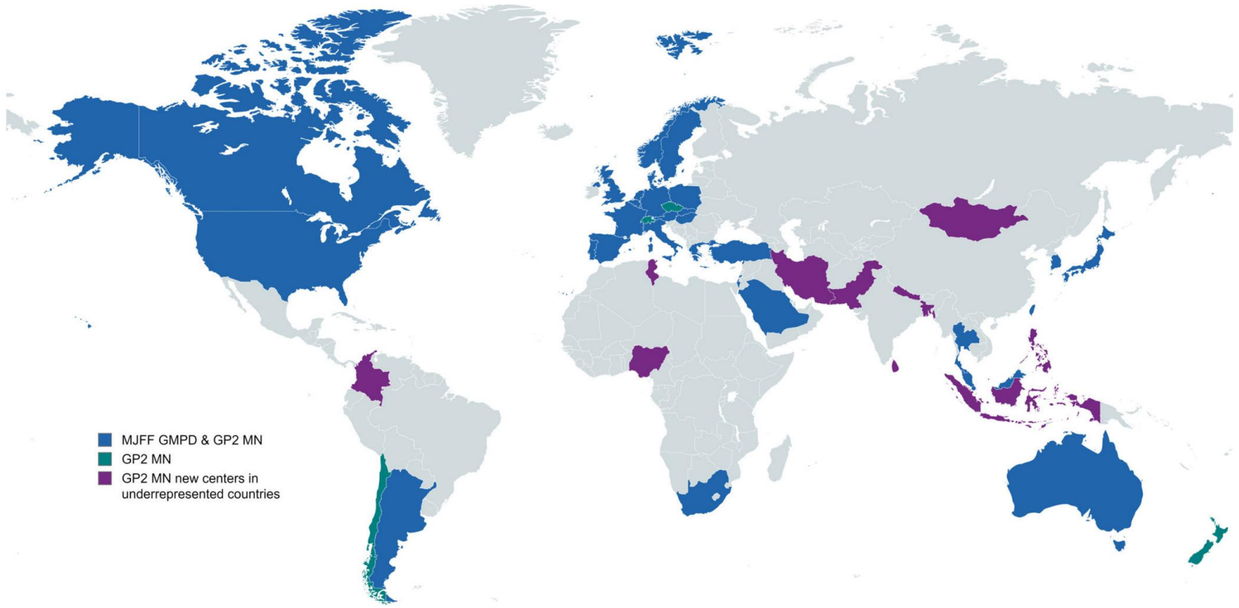
Top figure modified from: Blauwendraat C, Nalls MA, Singleton AB. The genetic architecture of Parkinson's disease. *Lancet Neurol*. 2020;19(2):170-178.
Gustavsson EK, Follett J, Trinh J, et al. RAB32 Ser71Arg in autosomal dominant Parkinson's disease: linkage, association, and functional analyses. *Lancet Neurol*. 2024;23(6):603-614.

BRIEF REPORT

Team Science Approaches to Unravel Monogenic Parkinson's Disease on a Global Scale

- **MJFF Global Monogenic PD project**
- **GP2 Monogenic Network**
  - 100 centers
  - 46 countries

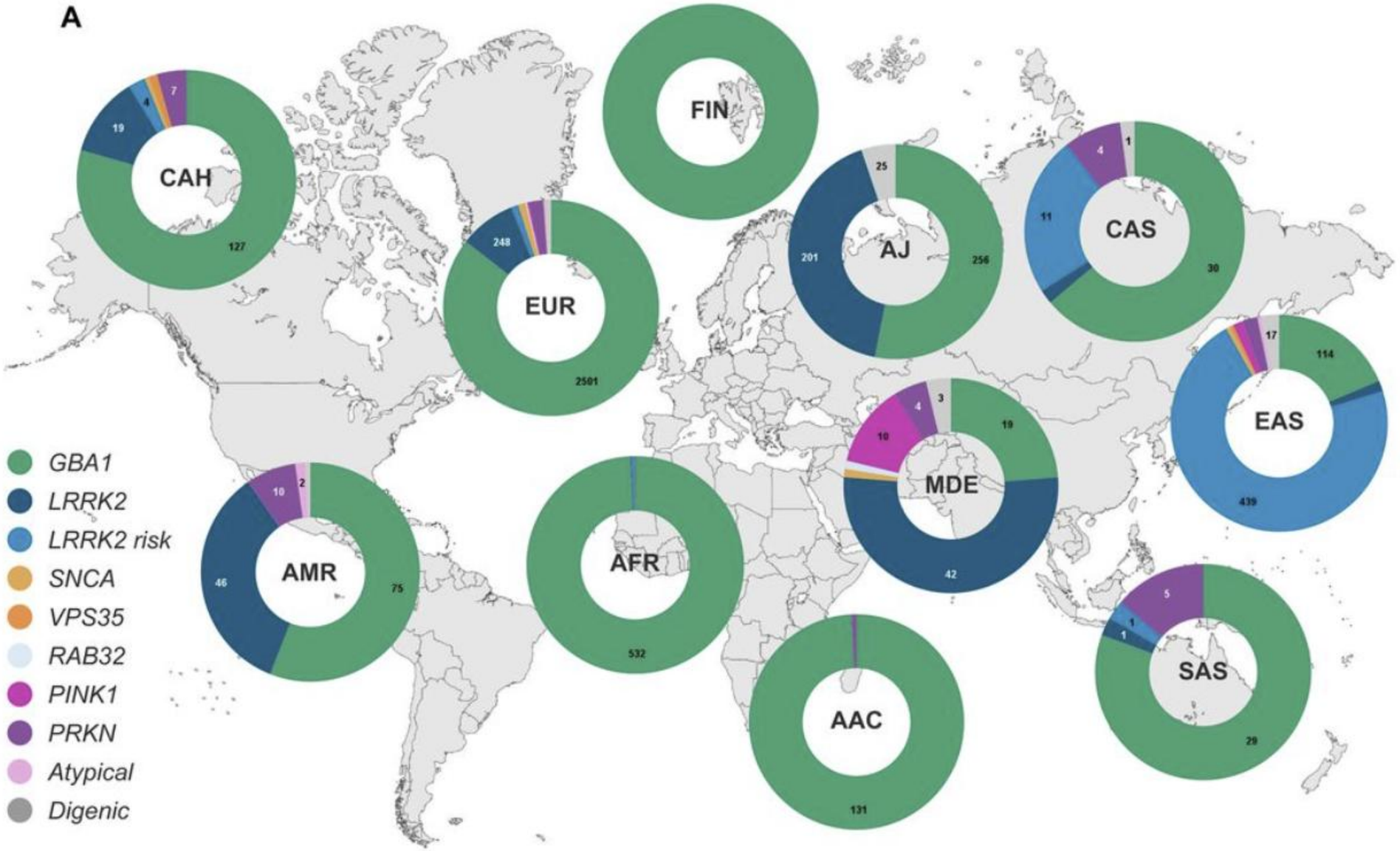
GP2's MN Cohort (n = 4824)	MJFF GMPD Cohort (n = 3185)	Individuals from MJFF GMPD and GP2's MN with Reported Genetic Findings (n = 539)



Top 5 reported

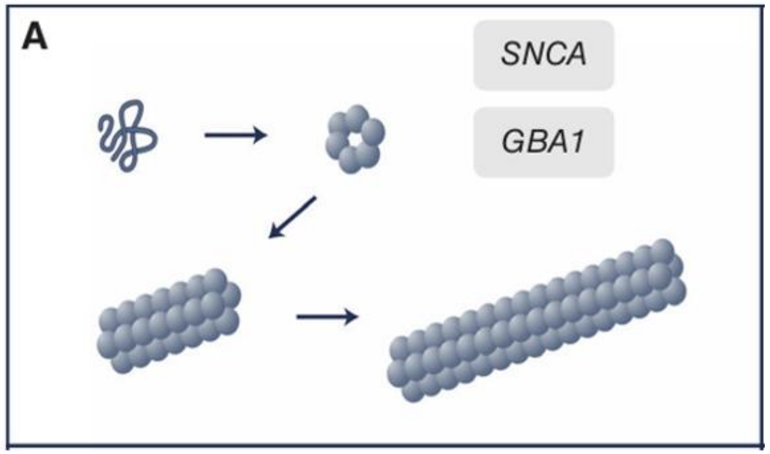
1. GBA1 (52%)
2. LRRK2
3. PRKN
4. PINK1
5. SNCA

Junker J, Lange LM, Vollstedt EJ, et al. *Mov Disord*. Published online July 30, 2024. doi:10.1002/mds.29925

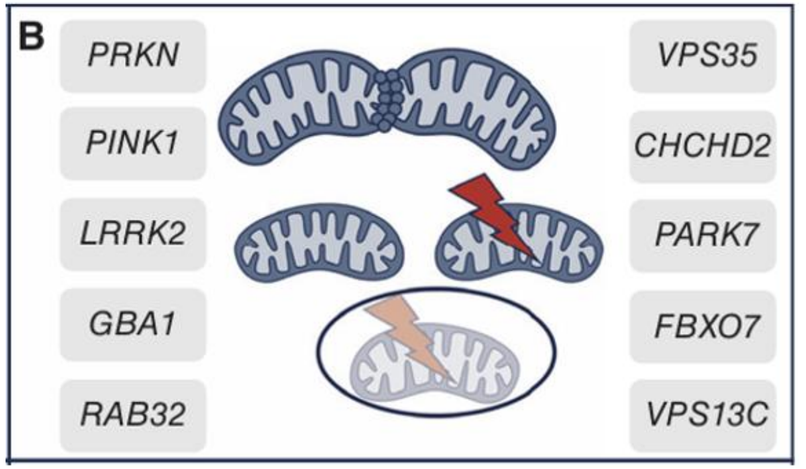


Lange LM, Fang Z-H, Makarious M, et al. The Global Landscape of Genetic Variation in Parkinson's disease: Multi-Ancestry Insights into Established Disease Genes and their Translational Relevance https://www.medrxiv.org/content/10.1101/2025.07.08.25330815v2.full.pdf

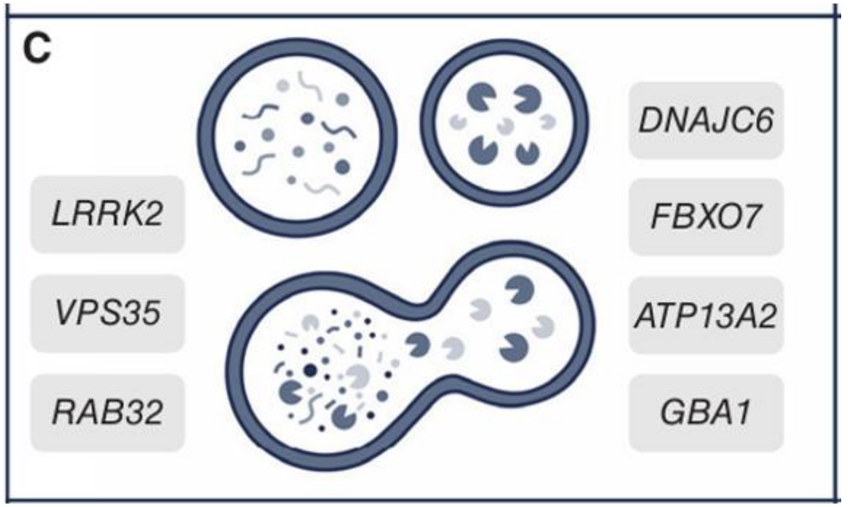
Oligomerization and fibrillation of α-syn



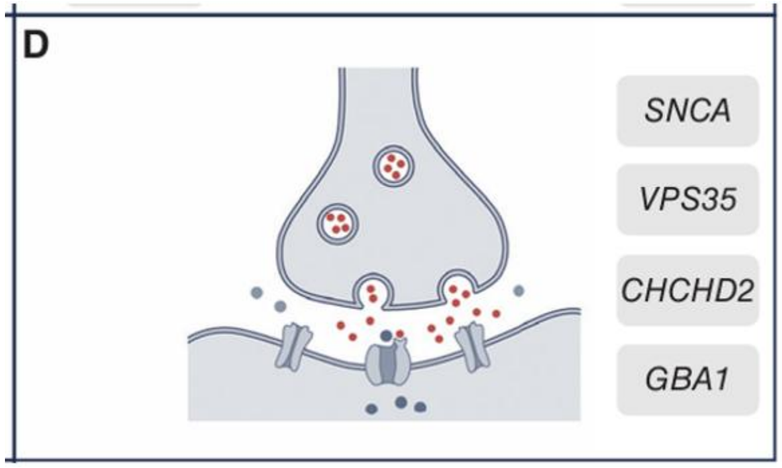
Mitochondrial dysfunction and clearance



Endosomal/lysosomal dysfunction



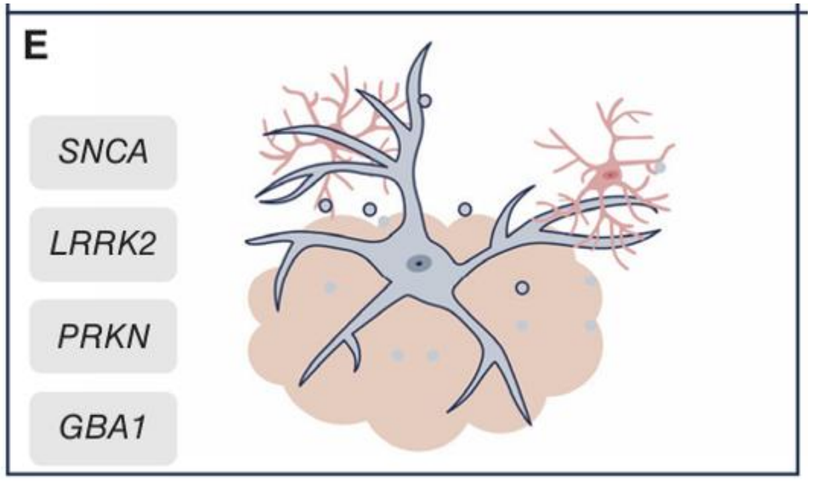
Impaired neurotransmission



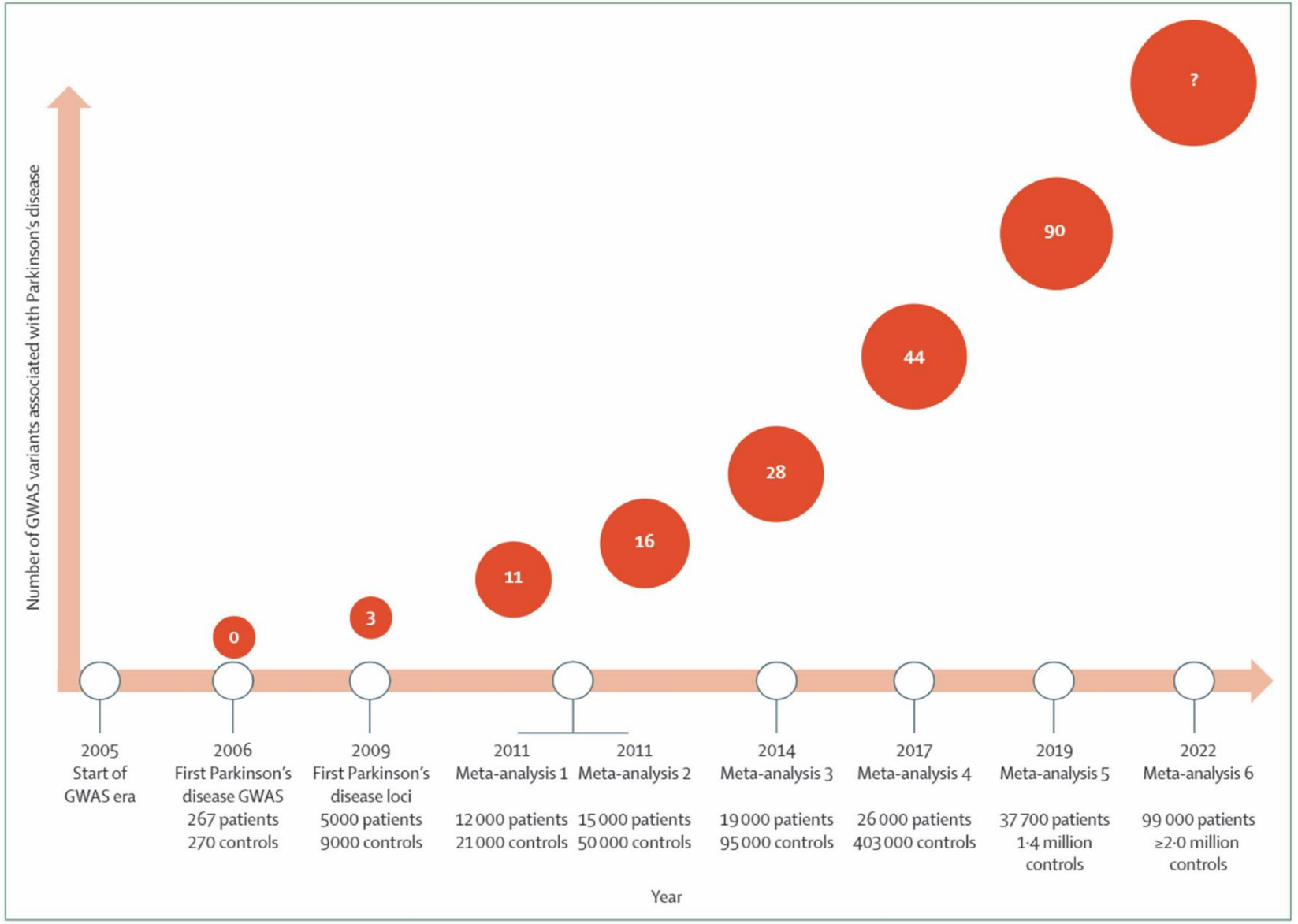
Modified from:

Westenberger A, Brüggemann N, Klein C. Genetics of Parkinson's Disease: From Causes to Treatment. *Cold Spring Harb Perspect Med*. 2025;15(7):a041774. doi:10.1101/cshperspect.a041774

Neuroinflammation



Timeline of genetic discoveries from PD GWASs



Blauwendraat C, Nalls MA, Singleton AB. The genetic architecture of Parkinson's disease. *Lancet Neurol*. 2020;19(2):170-178.

Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies

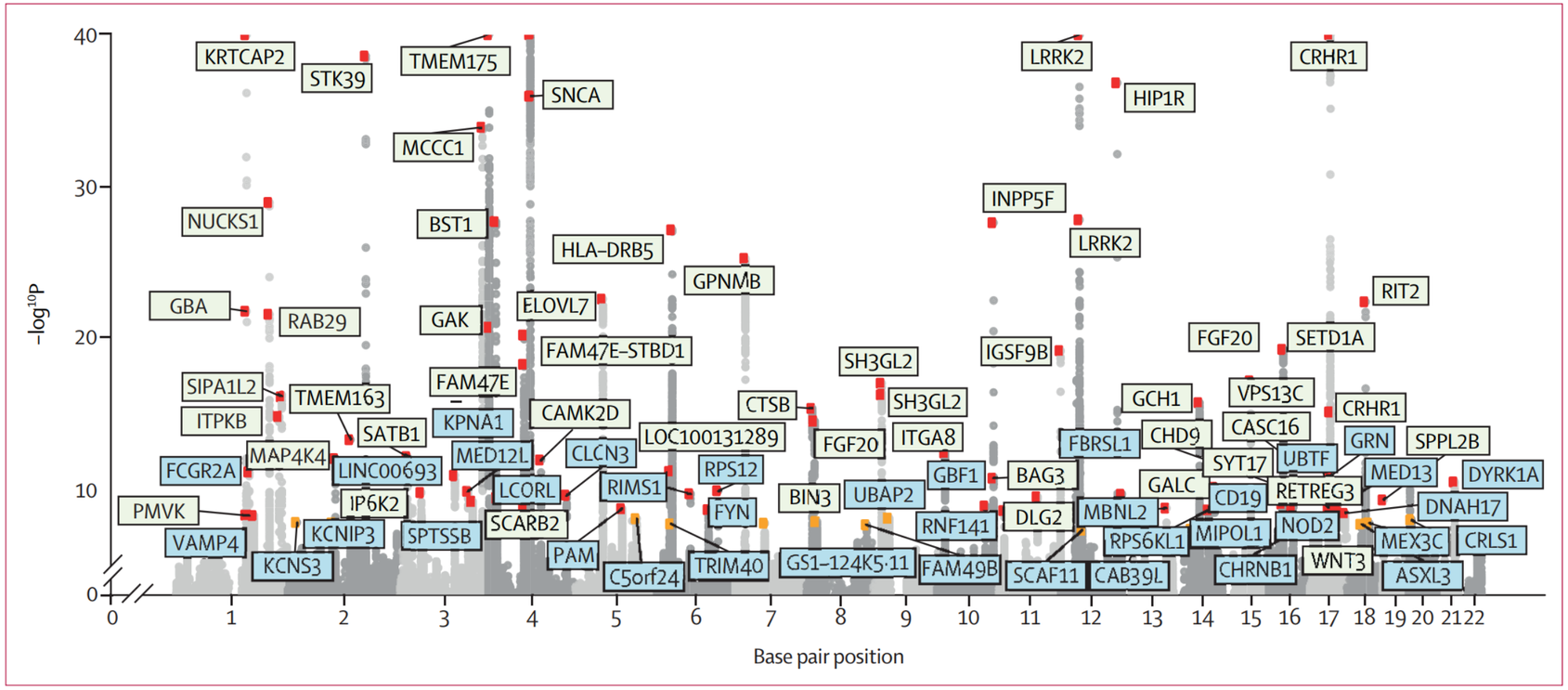


Figure 2: **Manhattan plot for significant variants**

- **Increased count of independent common risk variants to 90**
- **Added 38 novel risk variants**
- **Refined heritability estimates (common variants account for ~22% PD risk**

Gene – known loci

Gene – novel loci

p=5× 10– 8 to 10– 9

p <5× 10– 9

European ancestry datasets

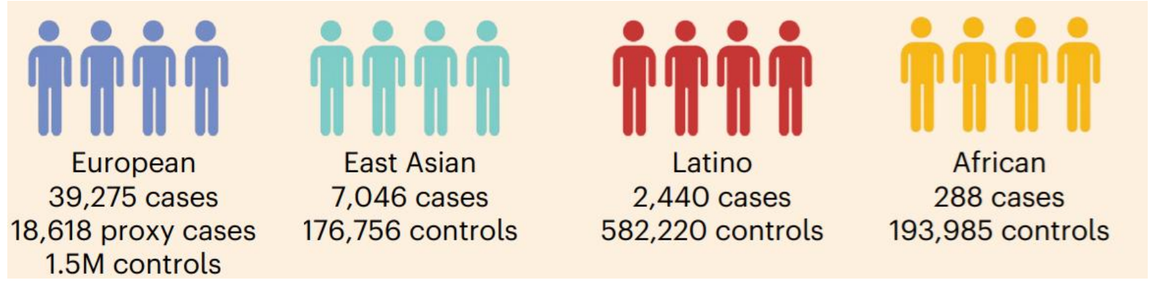
Nalls MA, Blauwendraat C, Vallerga CL, et al. *Lancet Neurol*. 2019;18(12):1091-1102.
Consortia: 23andMe Research Team; System Genomics of Parkinson's Disease Consortium; IPDGC

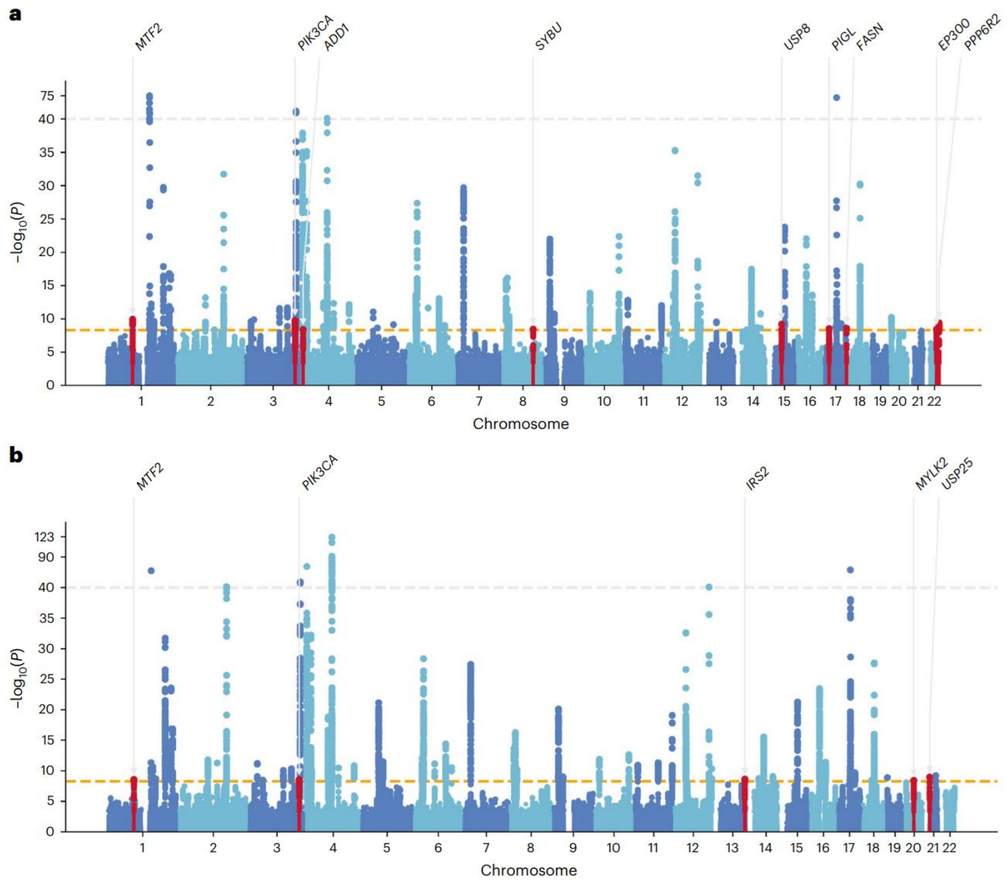
nature genetics

Article

https://doi.org/10.1038/s41588-023-01584-8

Multi-ancestry genome-wide association meta-analysis of Parkinson's disease





49049 Parkinson's disease
18785 proxy cases
2,458,063 controls

- **78 independent genome-wide significant loci**
- **Including 12 potentially novel loci**
- Fine-mapped 6 putative causal variants at 6 known PD loci
- **Identified 25 putative PD risk genes in the novel loci**

Kim JJ, Vitale D, Otani DV, et al. Multi-ancestry genome-wide association meta-analysis of Parkinson's disease. *Nat Genet*. 2024;56(1):27-36.
Consortia: 23andMe Research Team; GP2

What do we know about the genetic architecture of PD in the African population?

OPEN ACCESS Freely available online

PLoS one

Analysis of Nigerians with Apparently Sporadic Parkinson Disease for Mutations in *LRRK2*, *PRKN* and *ATXN3*

Njideka Okubadejo[1], Angela Britton[2], Cynthia Crews[2], Rufus Akinyemi[3], John Hardy[4], Andrew Singleton[2], Jose Bras[2,5]*

1 Neurology Unit, Department of Medicine, College of Medicine, University of Lagos, Lagos, Nigeria, 2 Laboratory of Neurogenetics, National Institute of Aging, National Institutes of Health, Bethesda, Maryland, United States of America, 3 Neurology Unit, Department of Medicine, Federal Medical Centre, Abeokuta, Ogun State, Nigeria, 4 Reta Lila Weston Institute and Departments of Molecular Neuroscience and Neurodegenerative Disease, Institute of Neurology, London, United Kingdom, 5 Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal

PLOS ONE

RESEARCH ARTICLE

Leucine rich repeat kinase 2 (LRRK2) GLY2019SER mutation is absent in a second cohort of Nigerian Africans with Parkinson disease

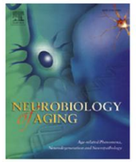
Njideka U. Okubadejo[1☯]*, Mie Rizig[2☯], Oluwadamilola O. Ojo[1], Hallgeir Jonvik[2], Olajumoke Oshinaike[3], Emmeline Brown[2], Henry Houlden[2]

ELSEVIER

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging



Negative screening for 12 rare *LRRK2* pathogenic variants in a cohort of Nigerians with Parkinson's disease

Mie Rizig[a,b], Oluwadamilola O. Ojo[c,d], Alkyoni Athanasiou-Fragkouli[a,b], Osigwe P. Agabi[d], Olajumoke O. Oshinaike[e,f], Henry Houlden[a,b], Njideka U. Okubadejo[c,d,*]

J Neurol (2012) 259:569–570
DOI 10.1007/s00415-011-6210-y

LETTER TO THE EDITORS

Screening *LRRK2* gene mutations in patients with Parkinson's disease in Ghana

Roberto Cilia · Francesca Sironi · Albert Akpalu · Momodou Cham · Fred Stephen Sarfo · Tiziana Brambilla · Alba Bonetti · Marianna Amboni · Stefano Goldwurm · Gianni Pezzoli

Total PD screened: 329 (Ghana: 54; Nigeria: 275

Total controls screened: 361 (Ghana: 46; Nigeria: 315) 275 PD

No pathogenic *LRRK2* mutation (at the time)

Contents lists available at SciVerse ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Analysis of *LRRK2*, *SNCA*, *Parkin*, *PINK1*, and *DJ-1* in Zambian patients with Parkinson's disease

Ekaterina Yonova-Doing [a], Masharip Atadzhanov [b,**], Marialuisa Quadri [a], Paul Kelly [b], Nyambura Shawa [b], Sheila T.S. Musonda [b], Erik J. Simons [a], Guido J. Breedveld [a], Ben A. Oostra [a], Vincenzo Bonifati [a,*]

18 (2012) 567–571

- 38 PD; 181 controls
- No *LRRK2* G2019S mutation

J Neural Transm (2010) 117:847–853 DOI 10.1007/s00702-010-0423-6

MOVEMENT DISORDERS - ORIGINAL ARTICLE

LRRK2 G2019S mutation: frequency and haplotype data in South African Parkinson's disease patients

Soraya Bardien · Angelica Marsberg · Rowena Keyser · Debbie Lombard · Suzanne Lesage · Alexis Brice · Jonathan Carr

- 205 SA PD; 79 controls
- *LRRK2* G2019S mutation frequency 1.95% (4/205); 2.8% in familial (2/72), 1.5% sporadic (2/155); **0/16 black**

neurogenetics https://doi.org/10.1007/s10048-019-00588-z

SHORT COMMUNICATION

Frequency of the *LRRK2* G2019S mutation in South African patients with Parkinson's disease

Nicola du Toit [1] · Riaan van Coller [2] · David G. Anderson [3] · Jonathan Carr [4] · Soraya Bardien [1]

- 647 PD (Different ancestries; 91 African ancestry)
- *LRRK2* G2019S mutation frequency 1.2% (8/647). **0/91 African ancestry**
- EOPD: 1.9% (3/154); LOPD 1% (5/493)

PINK1, *PRKN* and others

- Tunisia: 231 familial PD (*PINK1* mutation frequency 18%; *PRKN* mutation frequency 3.9%) *Hentati et al 2010*
- Nigeria: 57 sporadic PD (No *PRKN,* No *ATXN3* mutations). *Okubadejo et al 2008*
- South Africa: 229 PD (*PRKN* mutations in 3.1%) *Haylett et al 2012*
- South Africa: 154 PD (*PINK1* mutations (<1%; homozyg 1; heterozyg 2) *Keyser et al* 2010
- Zambia: 39 PD (2 *PRKN* mutations. No *SNCA*, *PINK1, DJ1* mutations) *Yonova-Doing 2012*
- Case reports/families: Familial *PRKN/PINK1* PD (Morocco – *Bouhouche et al 2017, Smaili et al 2020*); *PINK1* (Sudan – *Bakhit et al 2023*); *PRKN* (Tanzania – *Dekker et al 2020*)
- Tunisia: *RAB32* Ser71Arg variant (109 probands,18 North African) *Gustavsson et al 2024*

1st African ancestry PD GWAS: 2023

Identification of genetic risk loci and causal insights associated with Parkinson's disease in African and African admixed populations: a genome-wide association study

Lancet Neurol. 2023;22(11):1015-1025

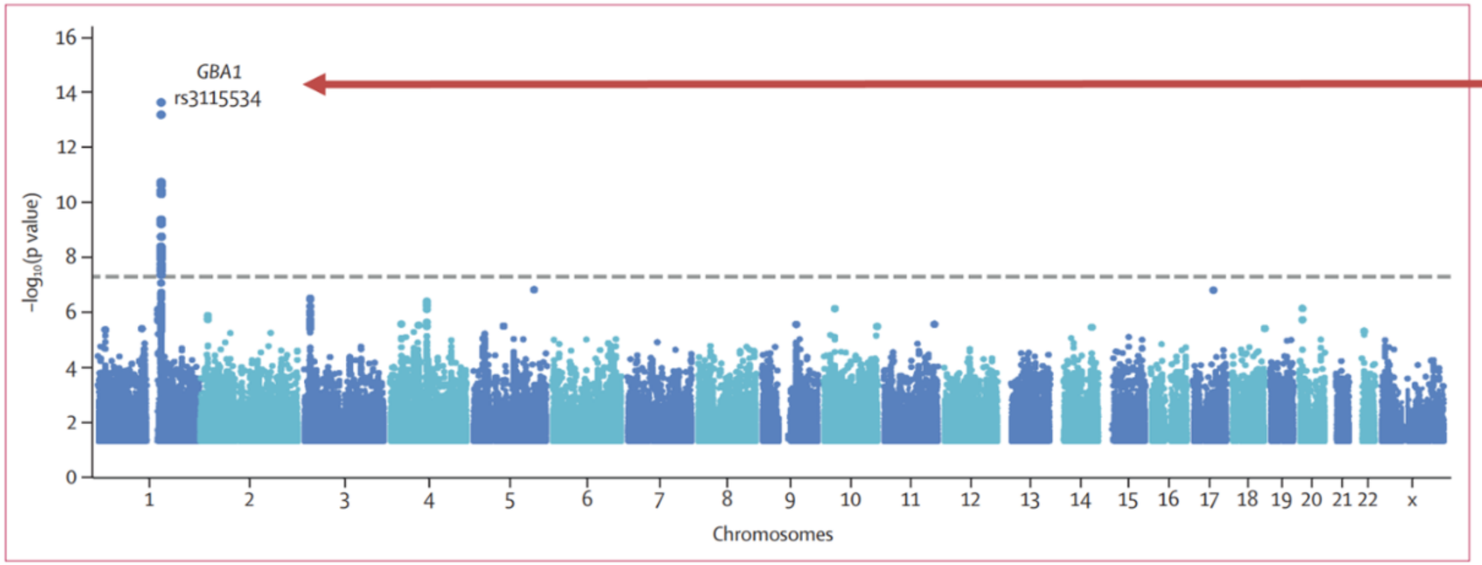


Figure 2: African and African admixed GWAS meta-analysis assessing Parkinson's disease risk

Novel African-specific GWAS signal in the GBA1 locus

197918 individuals
(1488 cases and 196430 controls)

- Virtually absent in other ancestries
- Common (present in about 50% of Nigerian PD cohort (~10% homozygous and 40% heterozygous
- Associated risk: 1.4x in heterozygous and ~3.5x risk in homozygous carriers
- Associated with an earlier age at onset in PD
- Most important genetic risk factor for PD in this African and African Admixed populations

gp2 Global Parkinson's Genetics Program

nature structural & molecular biology

https://doi.org/10.1038/s41594-024-01423-2

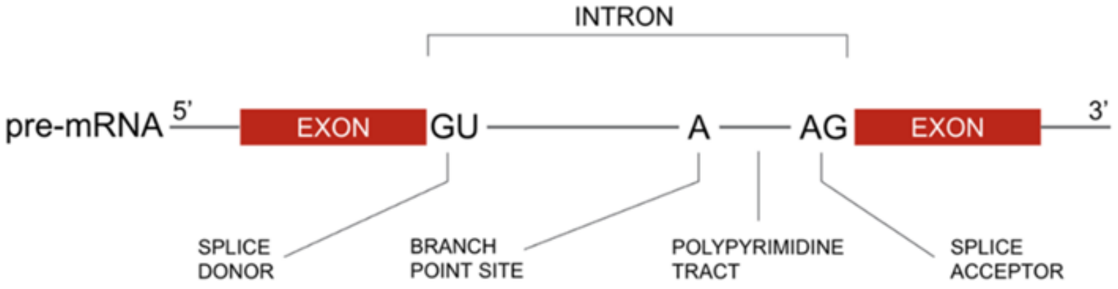
African ancestry neurodegeneration risk variant disrupts an intronic branchpoint in *GBA1*

Pilar Álvarez Jerez, Peter A. Wild Crea, Daniel M. Ramos, Emil K. Gustavsson, Mandy Radefeldt, Mary B. Makarious, Oluwadamilola O. Ojo, Kimberley J. Billingsley, Laksh Malik, Kensuke Daida, Sarah Bromberek, Carol Hu, Zachary Schneider, Aditya L. Surapaneni, Julia Stadler, Mie Rizig, Huw R. Morris, Caroline B. Pantazis, Hampton L. Leonard, Laurel Screven, Yue A. Qi, Mike A. Nalls, Sara Bandres-Ciga, John Hardy, Henry Houlden, Celeste Eng, Esteban González Burchard, Linda Kachuri, Global Parkinson's Genetics Program (GP2), Andrew B. Singleton, Steffen Fischer, Peter Bauer, Xylena Reed, Mina Ryten, Christian Beetz, Michael Ward, Njideka U. Okubadejo, Cornelis Blauwendraat

doi: https://doi.org/10.1101/2024.02.20.24302827

Cornelis Blauwendraat

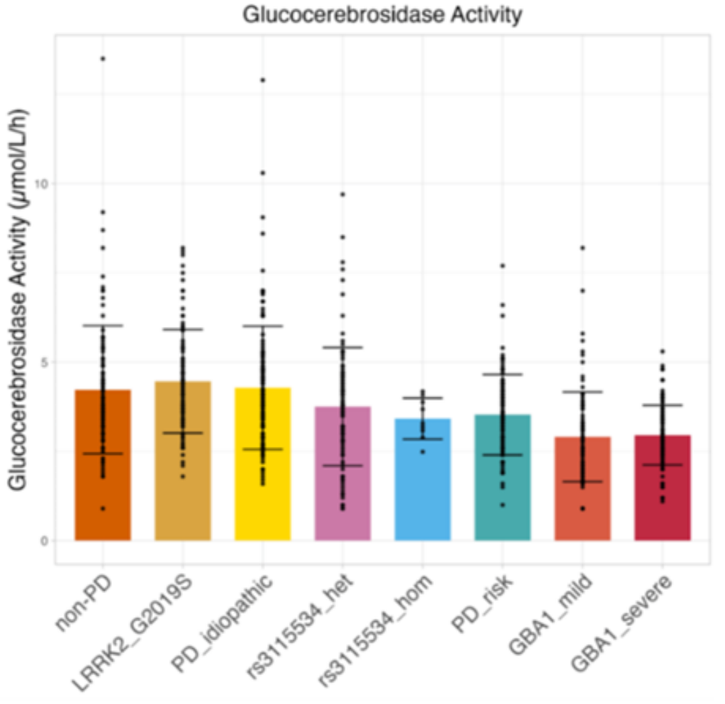
Co-lead, GP2



risk variant ⇒ disrupts branch point leading to mis-splicing

mis-splicing ⇒ apparent increase in *GBA1* RNA - but non-functional transcripts?

net-result ⇒ decreased GBA1 protein
⇒ decreased GCase activity

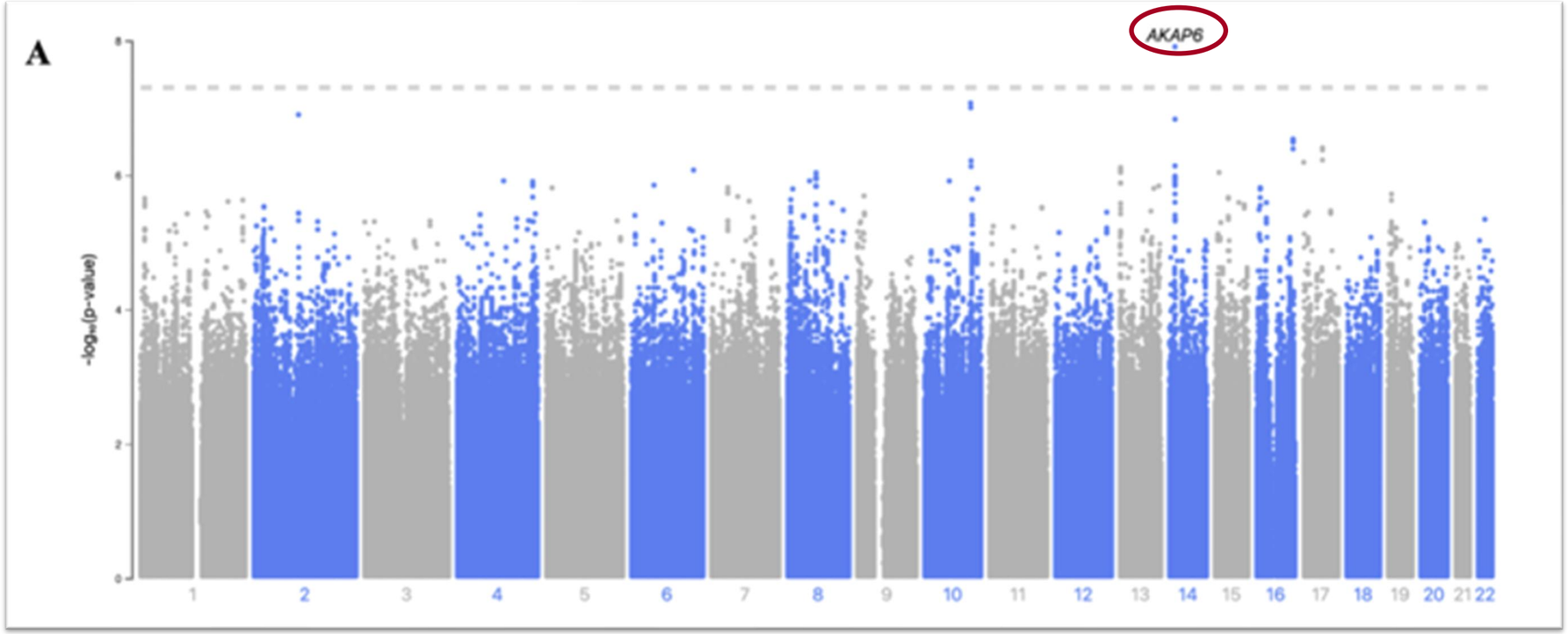


Why is this finding important?

Introduces a novel pathogenetic mechanism for a specific ancestry and population
Establishes a foundation for exploring the possibility of personalized interventions through clinical trials in this population
Underscores the scientific and ethical imperative of including underrepresented populations in genomics research
Adds to our understanding of the potential role of non-coding variants in PD risk
Highlights the notion that findings cannot be generally extrapolated to other populations
Provides impetus for refining polygenic risk scores for PD risk prediction in persons of black African ancestry

Genome-wide association analyses reveal susceptibility variants linked to Parkinson's disease in the South African population using inferred global and local ancestry

691 PD cases and 826 controls



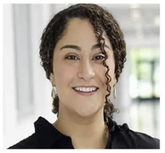
The conventional GWAS successfully identified one locus (rs17098735-T) with genome-wide significance on chromosome 14 (within the *AKAP6* gene)

Step K, Leal TP, Waldo E, et al. *medRxiv*. 2025;2025.08.01.25331910. Published 2025 Aug 2. doi:10.1101/2025.08.01.25331910

medRxiv

THE PREPRINT SERVER FOR HEALTH SCIENCES

gp2 Global Parkinson's Genetics Program



GP2 Complex Disease DAWG

https://www.medrxiv.org/content/10.64898/2026.03.01.26347367v1

Insights Into Parkinson's Disease Genetics in African Populations: Expanded GWAS Identifies Ancestry-Specific and Cross-Population Risk Loci

Posted March 03, 2026.

GWAS in African and African Admixed populations

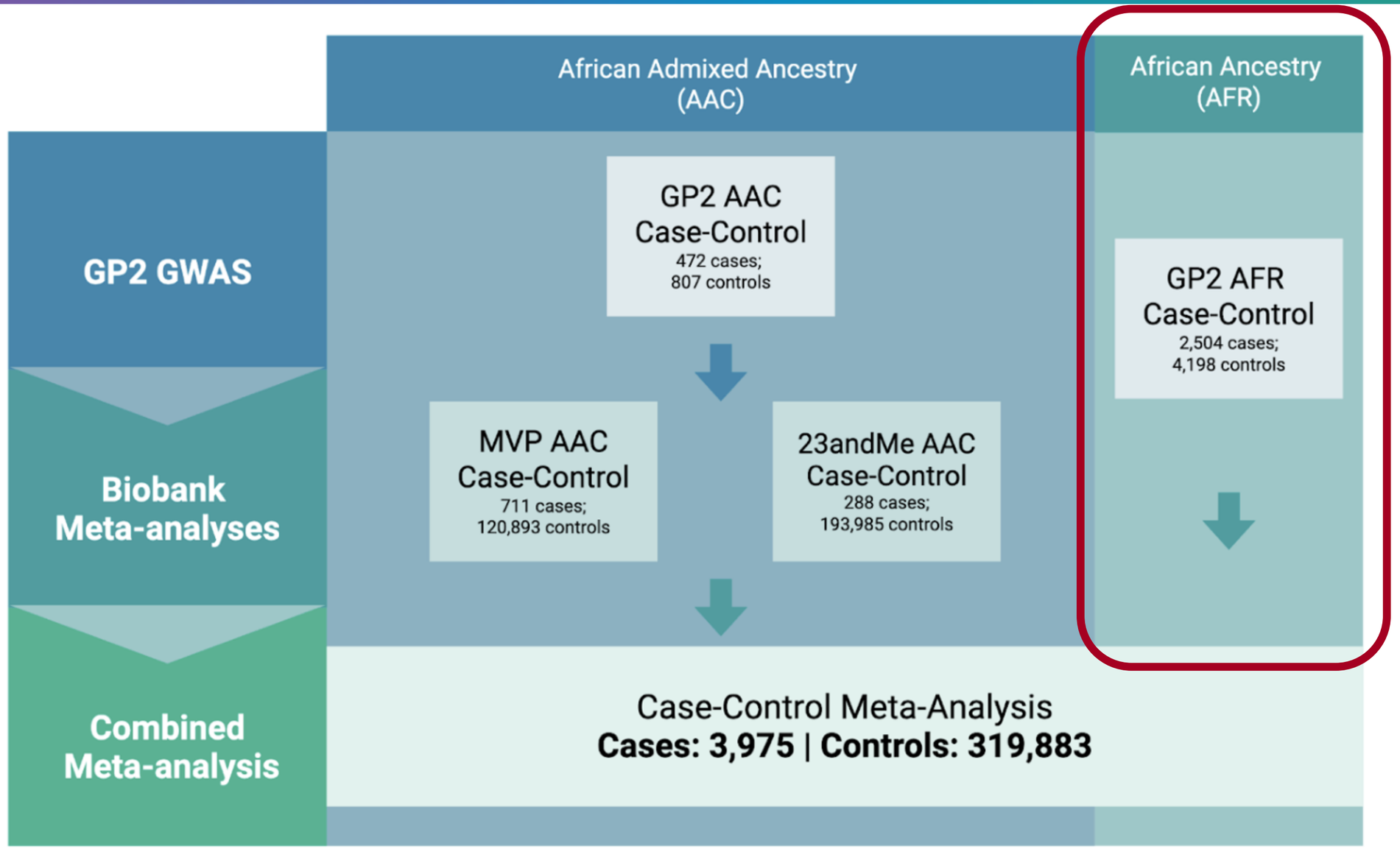
Genotype data (individual level) from GP2

Summary statistics from 23andMe and the Million Veterans Program (MVP).

Combined dataset: 3,975 cases and 319,883 controls

64% increase in total sample size compared with prior analyses

Separate GWAS for AFR and AAC cohorts + combined AFR/AAC meta-analysis.



Expanded GWAS and Metanalysis workflow (AAC and AFR)

Global Parkinson's Genetics Program

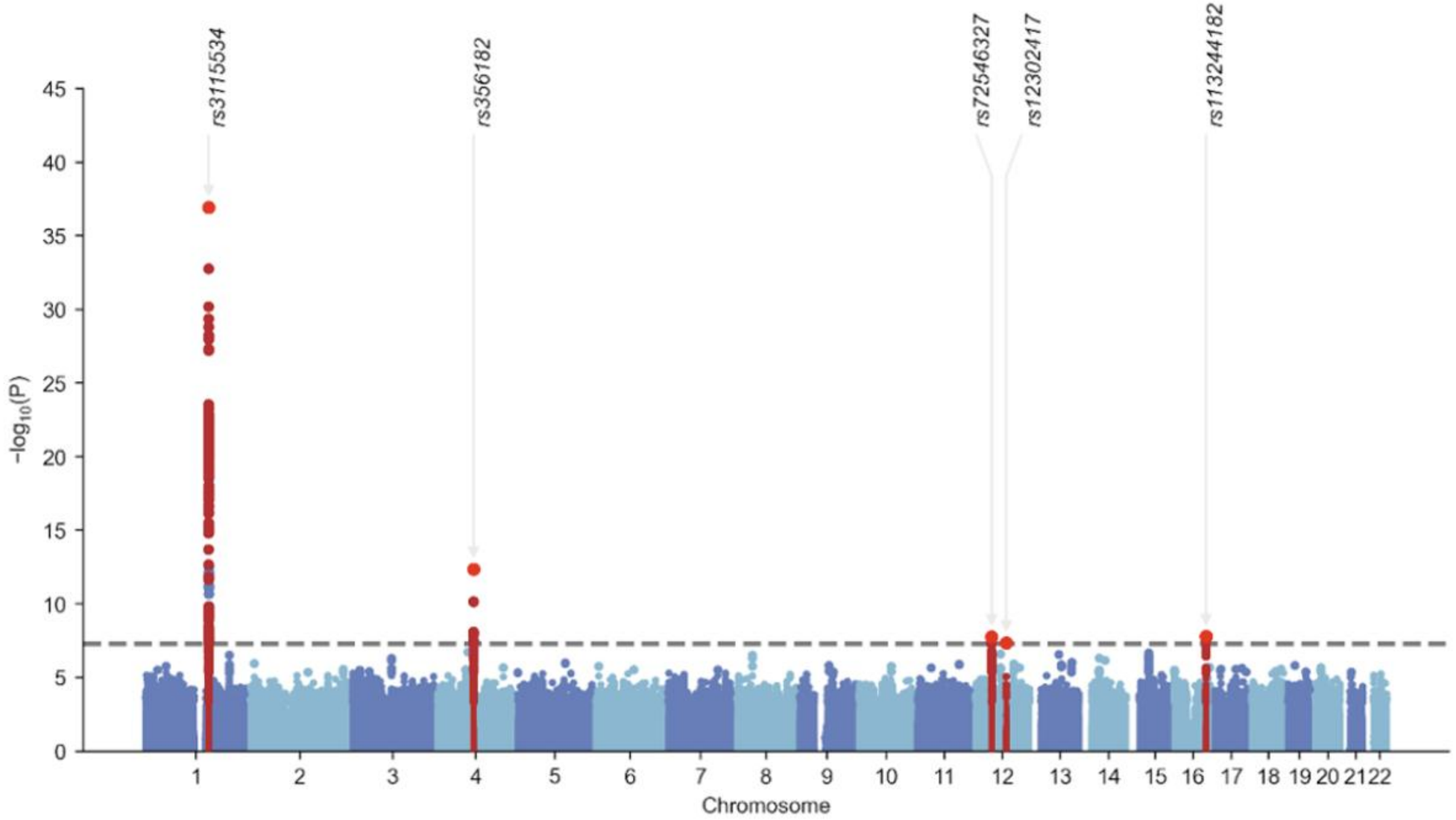
GWAS 2: Cohort characteristics (R11 GP2 AFR)

Cohort	Ancestry	Cases	Controls	% Female cases	% Female controls
GP2 AFR	African (AFR)	**2,504**	**4,198**	30.4	48.4

- Covariates used for cohort-level GWAS: *Sex, PC1-20*
- Array type: *NeuroBooster Array*

Global Parkinson's Genetics Program

AFR GWAS – genome-wide significant hits



Global Parkinson's Genetics Program

Genome-wide significant hits (AFR ancestry)

SNP ID	Effect allele	rsID	P	Close to known locus?
chr1:155235878:G:T	T	rs3115534	1.20E-37	Yes; GBA1
chr4:89704960:G:A	A	rs356182	4.33E-13	Yes; SNCA
chr12:40309145:C:T	T	rs72546327	1.72E-08	Yes; LRRK2
chr12:75689052:G:A	A	rs12302417	4.49E-08	No; novel (RPL10P13)
chr16:76969646:G:C	C	rs113244182	1.67E-08	No; novel

AFR ancestry expanded PD GWAS

Strongest association: *GBA1* functional branch site variant (rs3115534)

Intronic *SNCA* variant (established trans-ancestry PD risk variant)

LRRK2 missense variant (p.T1410M) (rare in non AFR ancestries)

Non-coding variant within *RPL10P13* pseudogene

Intergenic variant on chromosome 16 (rs113244182)

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Importance of findings

01 Convergence of evidence around genes involved in glucocerebrosidase (Gcase) trafficking and α-synuclein clearance

02 Supports current therapeutic strategies targeting lysosomal pathways

03 Provides critical targets for precision medicine in African ancestry populations

04 Identifies novel loci that warrant further study

05 Reinforces importance of inclusion of URPs in PD genomics research

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Global collaboration has significantly improved our understanding of the genetics of apparently sporadic (complexly inherited) PD in Africa

We anticipate that diversifying the African populations included in PD genetic studies will provide even greater insights

Collaborative research largely driven by the Global Parkinson's Genetics Program (GP2) are enabling this effort to widen the scope across Africa