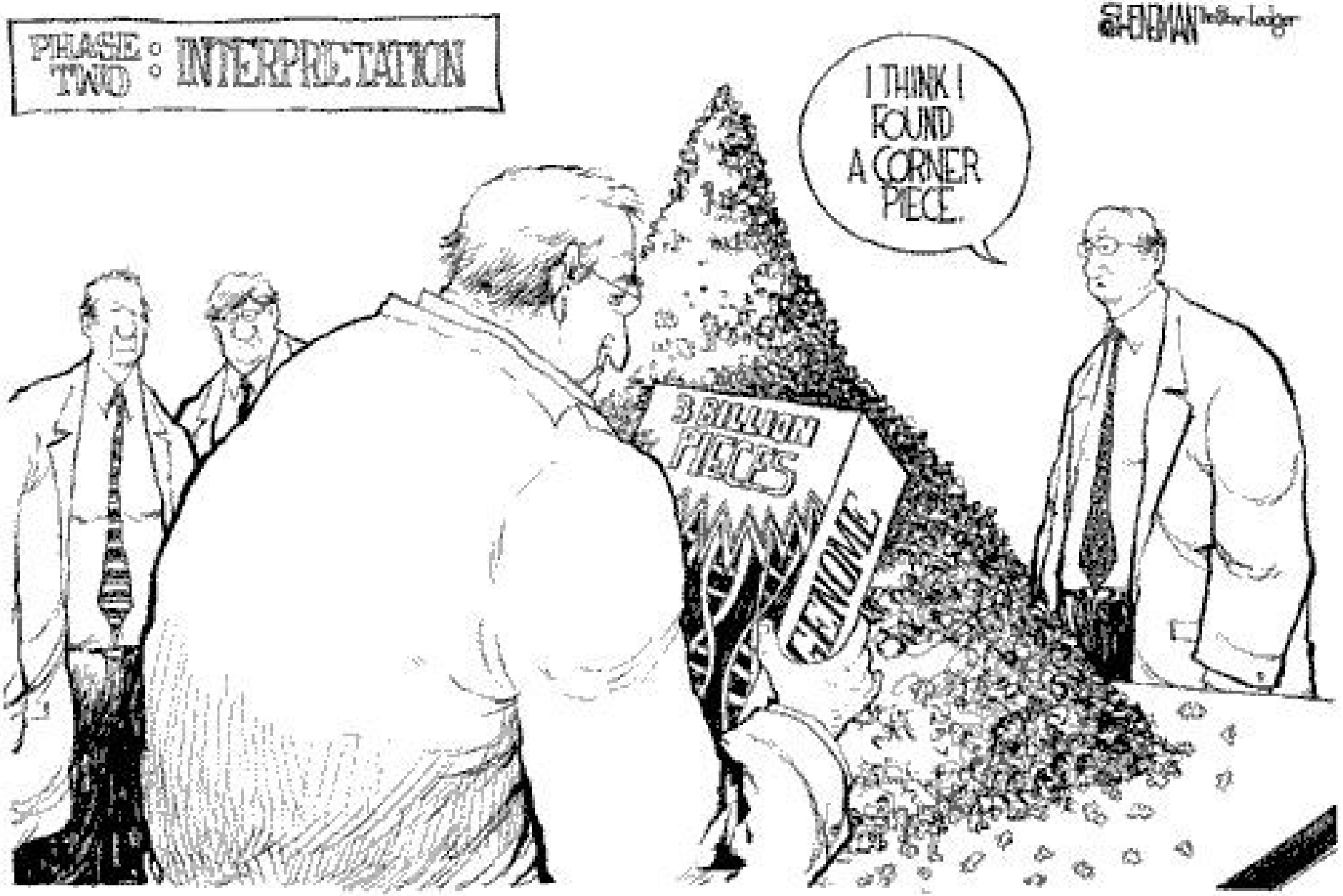
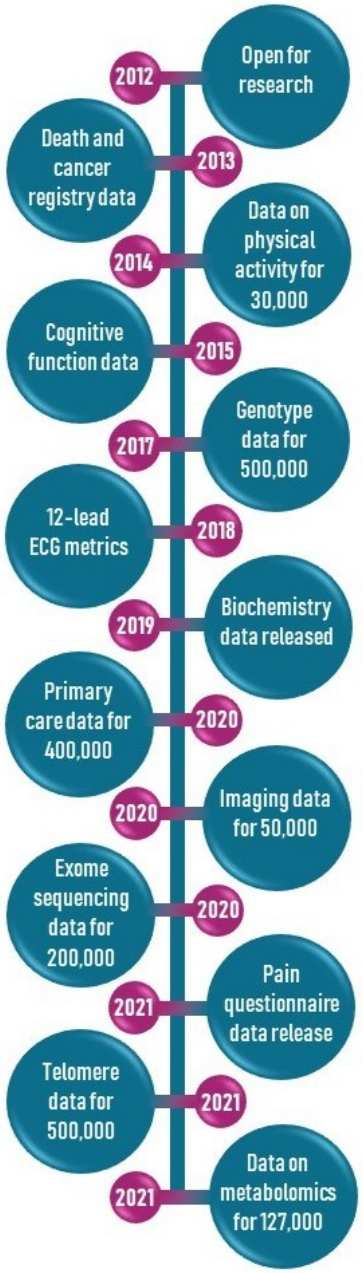
How genomics of admixed Brazilians improve precision health?

Prof. Michel Satya Naslavsky
Dept. Genetics and Evol. Biology
Human Genome Research Center (HUG-CELL)
Biosciences Institute
University of São Paulo
Visiting Researcher **Hospital Albert Einstein**



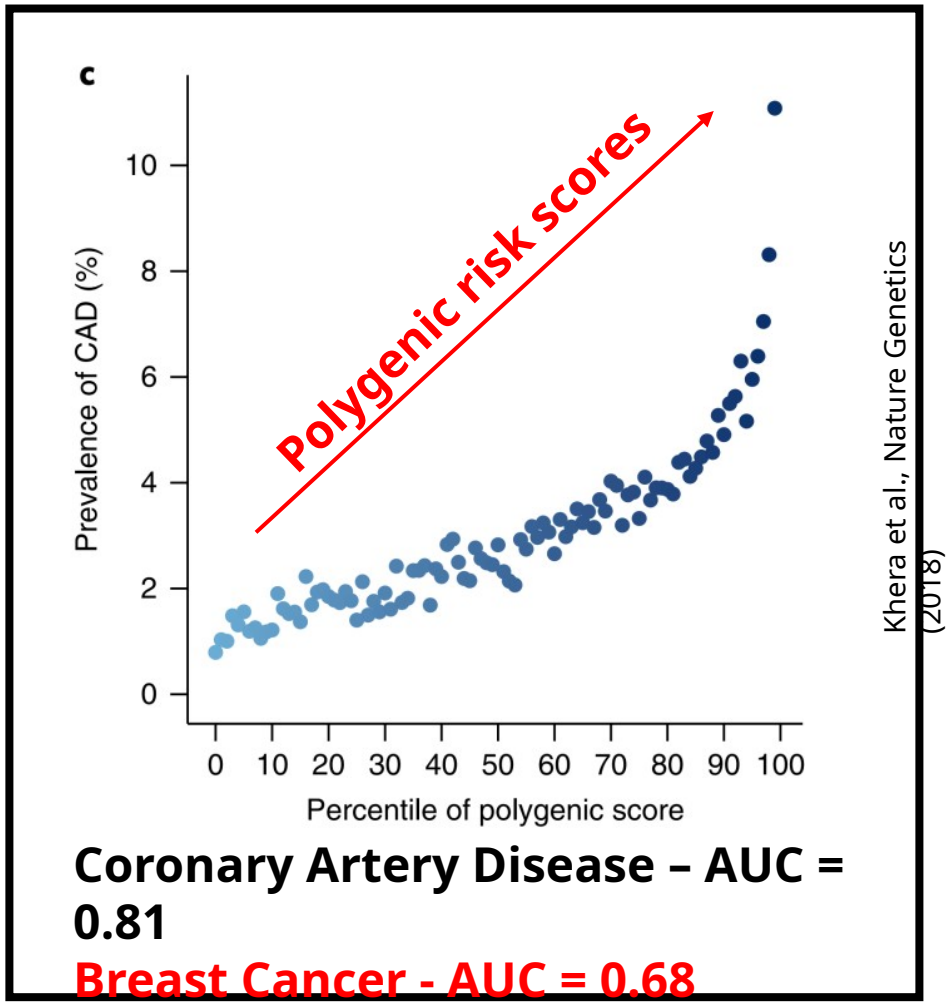
Operários, 1933 (Tarsila do Amaral)


PHASE TWO: INTERPRETATION
SIDNEY HARRIS
I THINK I FOUND A CORNER PIECE.
3 BILLION PIECES
GENOME



biobank uk

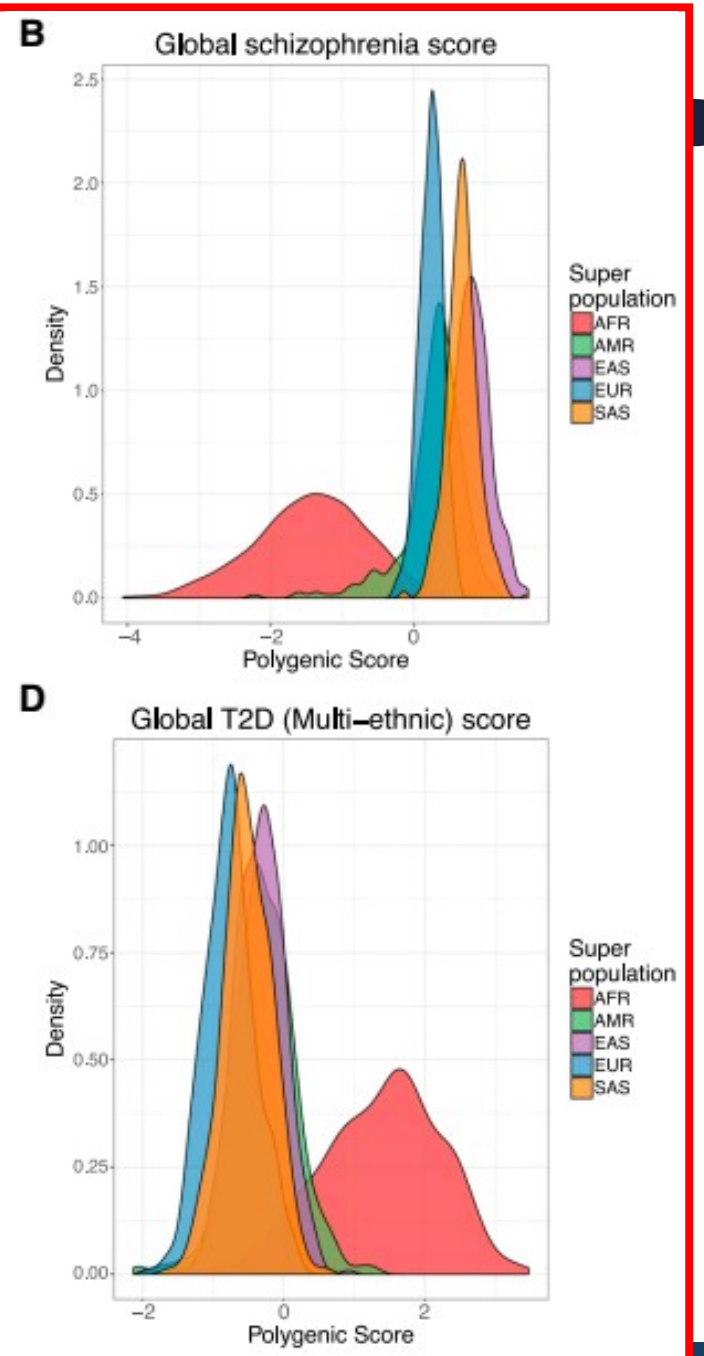
Enabling scientific discoveries that improve human health



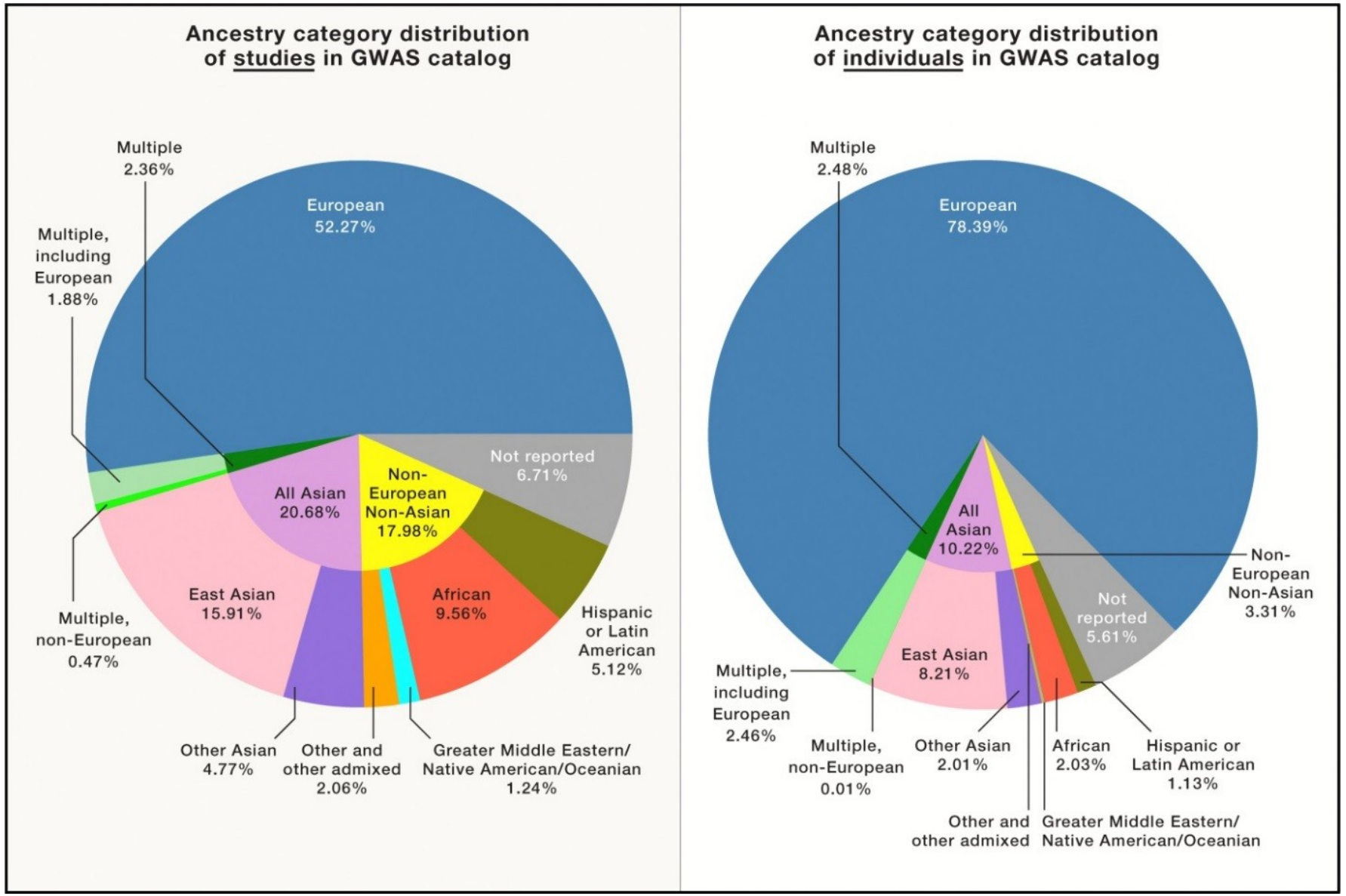
Khera et al., Nature Genetics (2018)

Coronary Artery Disease – AUC = 0.81

Breast Cancer - AUC = 0.68



Martin et al, AJHG,



Sirugo et al., Cell 2019

Centro de Pesquisa sobre o Genoma Humano e Células-Tronco

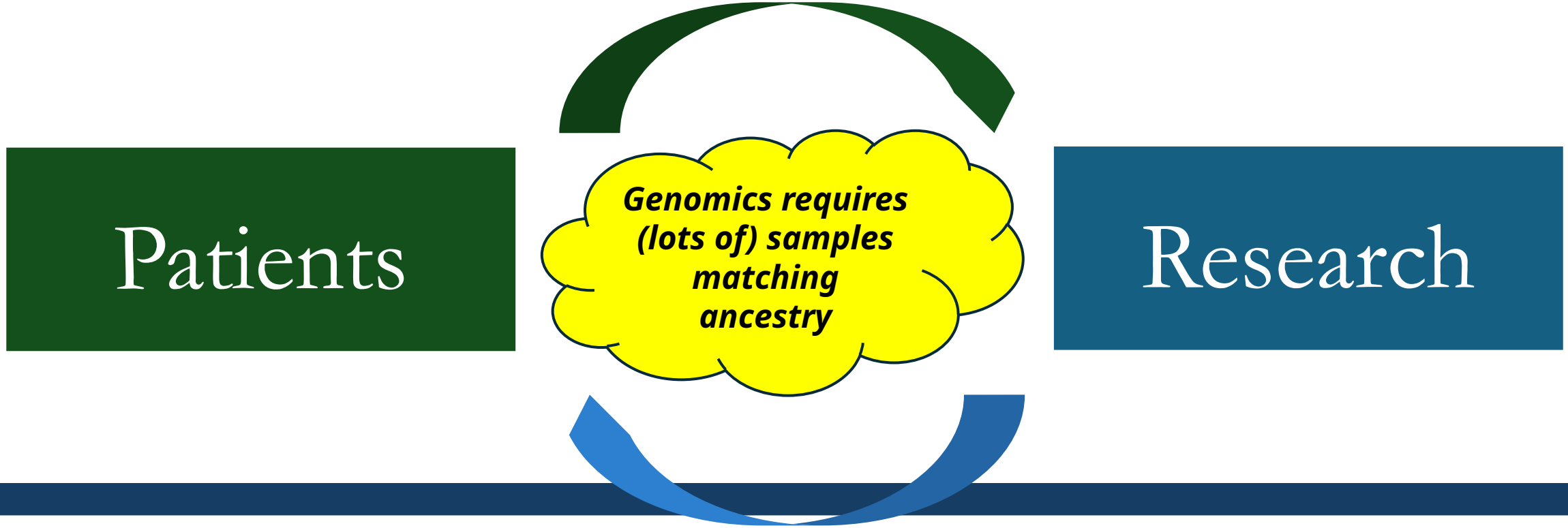
genoma

Human **G**enome and Stem **Cell** Research Center

HUG-CELL USP (former CEPID FAPESP)

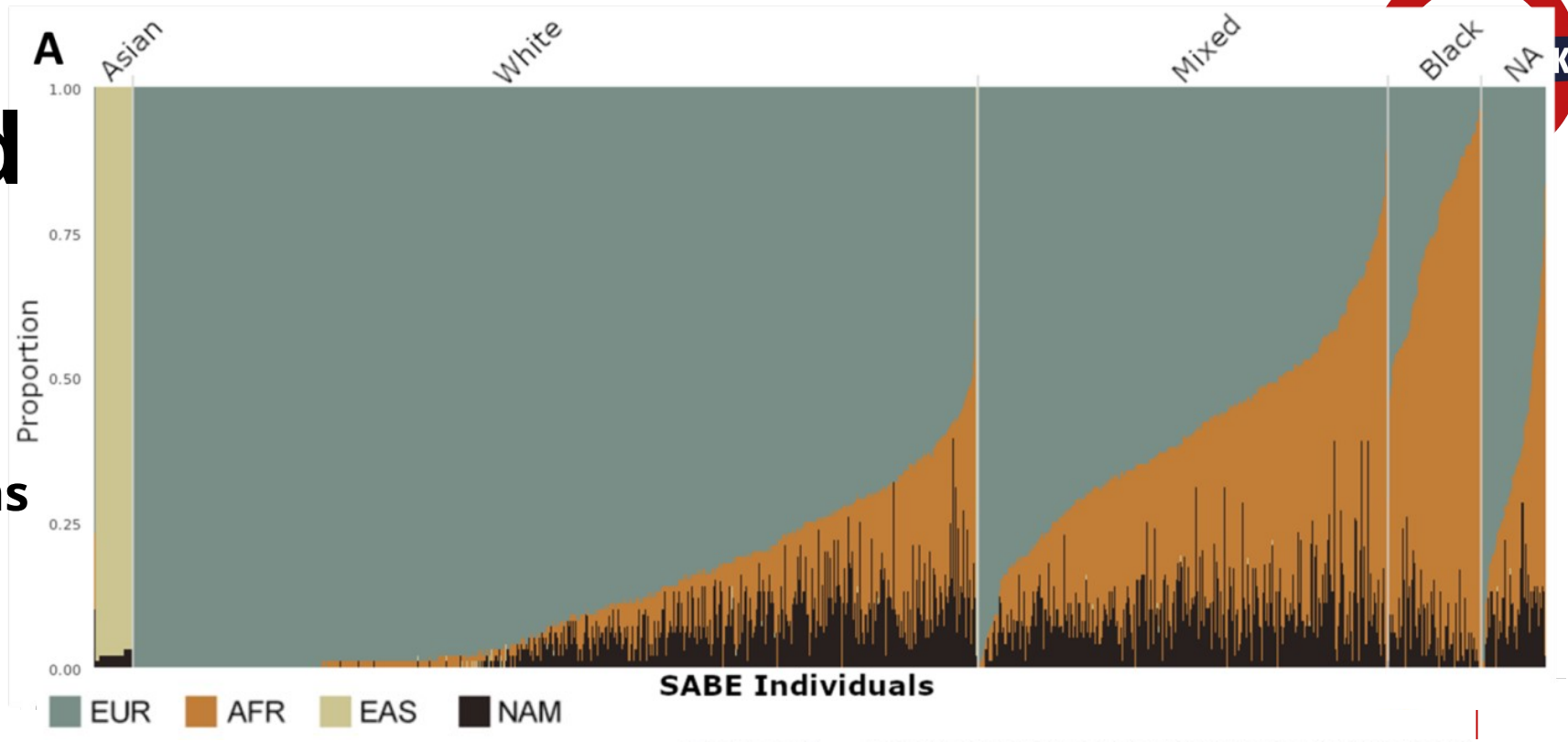
LONDON FAPESP WEEK June, 2-4th 2026

Since 1960s, enrolling families affected by genetic disorders (mainly neuromuscular and neurodegenerative)



We are indeed highly admixed

Naslavsky et al (Nat. Comms -2022)



Elderly admixed individuals improve molecular diagnosis

Non-Europeans are still harder to interpret

Naslavsky, et al. American Journal of Medical Genetics (2021)

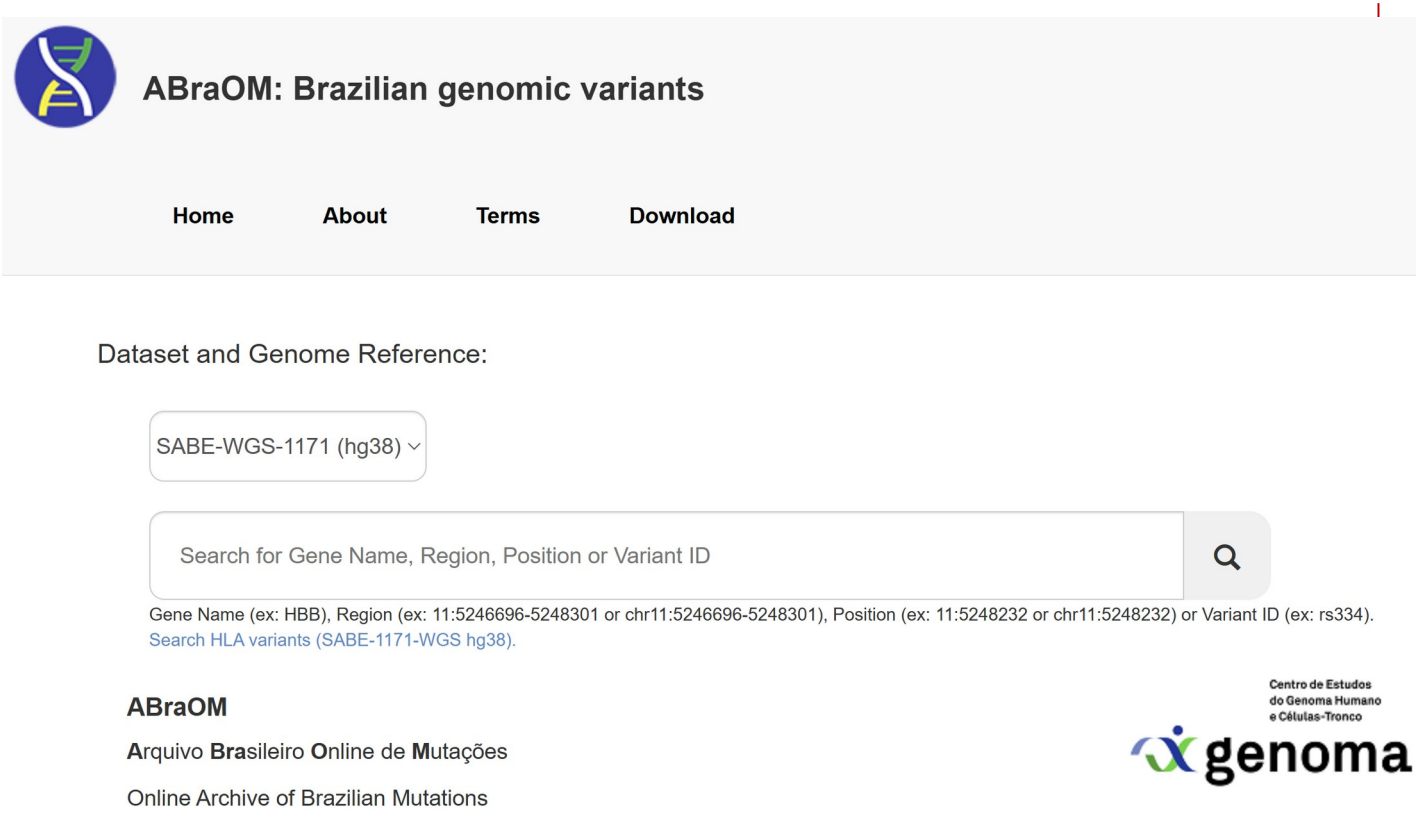
TABLE 2 Genotype counts per individual local ancestry and variant's non-benign assertions on ClinVar

(a)	ClinVar assertions		
Local ancestry	0	1	Total genotypes
Non-European	2,187	128	2,315
European	3,025	502	3,527
Total genotypes	5,212	630	5,842
Odds ratio = 0.353			
CI (95%) 0.288–0.431, *p*-value <.0001			

ABraOM (Arquivo Brasileiro Online de Mutações)

http://abraom.ib.usp.br/

- Search 609 WES (hg19) or 1171 WGS (hg38)
- Search HLA variants
- Search MEI variants
- Directly request download aggregated files
- Individual-level data under request thru EGA (~170Tb)



Impact of admixture in moderate effect variants (*APOE* x Alzheimer-related pathology)

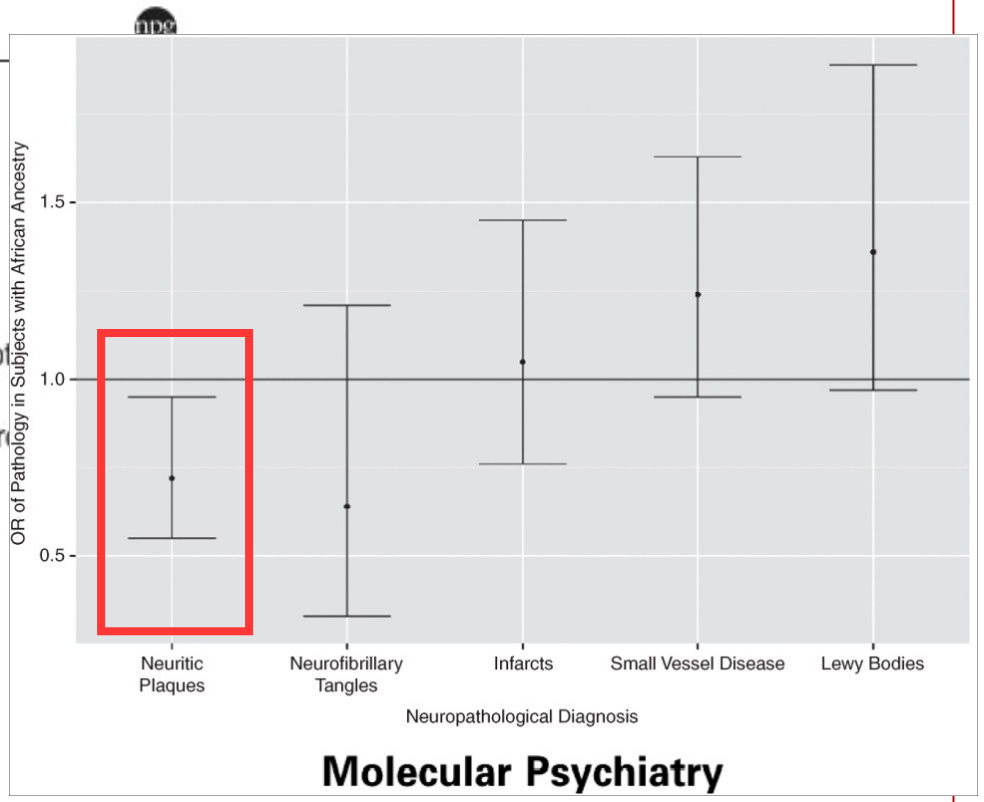
Open

Molecular Psychiatry (2013) 18, 79–85
© 2013 Macmillan Publishers Limited All rights reserved 1359-4184/13
www.nature.com/mp

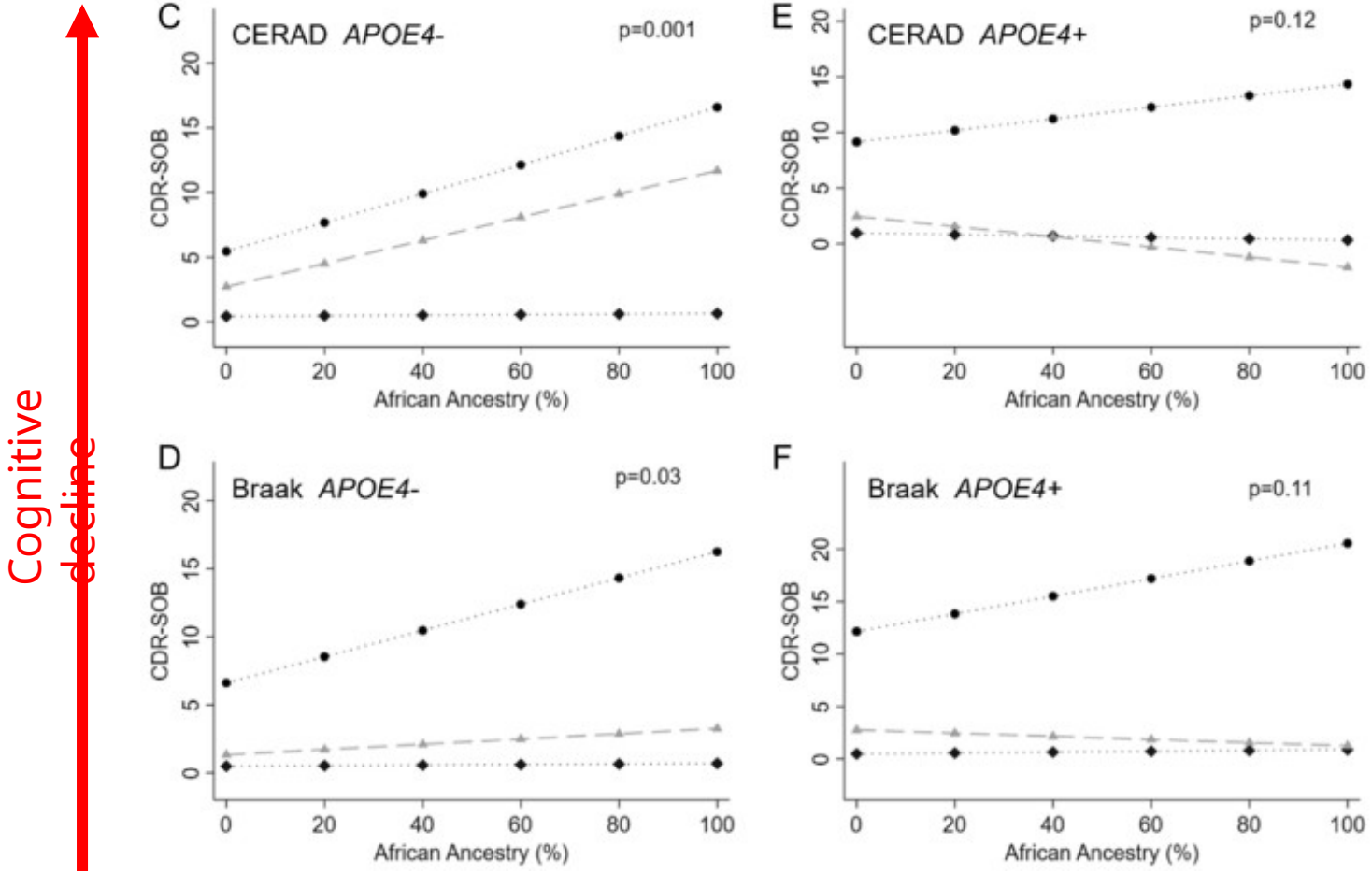
ORIGINAL ARTICLE

African ancestry protects against Alzheimer's disease-related neuropathology

D Schlesinger[1,2,11], LT Grinberg[3,4,5,11], JG Alba[3], MS Naslavsky[1], L Licinio[1], JM Farfel[3,6], CK Suemot
RE de Lucena Ferretti[3,6,7], REP Leite[3], MP de Andrade[3], ACF dos Santos[8], H Brentani[8],
CA Pasqualucci[3,9], R Nitrini[3,10], W Jacob-Filho[3,6], M Zatz[1] and the Brazilian Aging Brain Study Gr



Impact of admixture in moderate effect variants (*APOE* x Alzheimer-related pathology)



African ancestry predicts cognitive decline only in more **severe** burden of **neuropatholog y**. And the effect is clearer in **APOE4 noncarriers**

Impact of admixture in moderate effect variants (*APOE* x Alzheimer-related pathology)

Ongoing project (**Alzheimer's Association**, **Instituto Serrapilheira + FAPESP grant)**

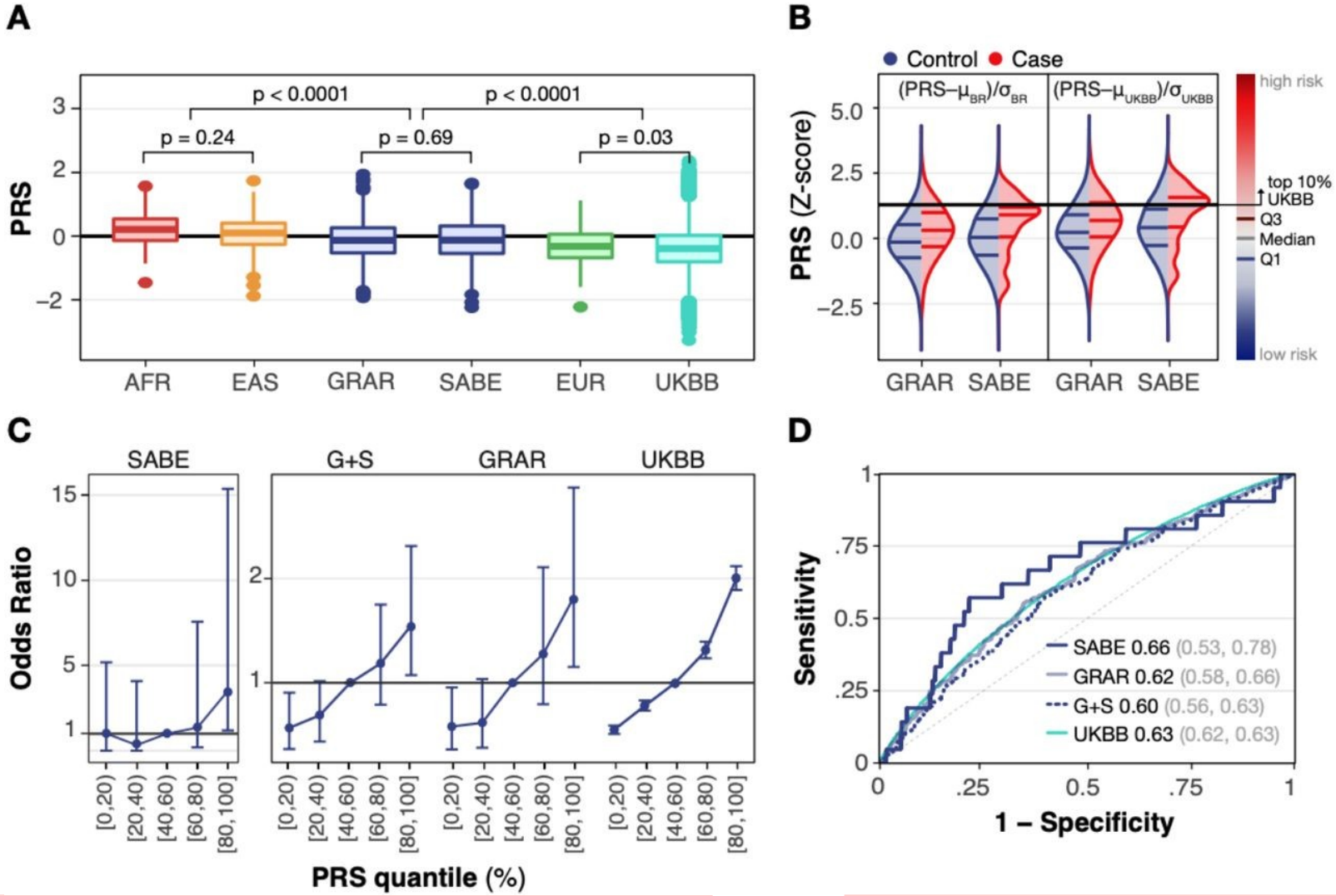
How do genomic ancestry and admixture modulate the effects of the APOE gene on white matter, myelination, and cognitive decline?

APOE Local ancestry + PRS → DTI (Diffusion Tensor Imaging) in SABE

→ Lipidomics (in BAS)

Next steps: Single Nuclei from Cortex in APOE groups (FAPESP Proposal)

PRS in Brazilians: breast cancer

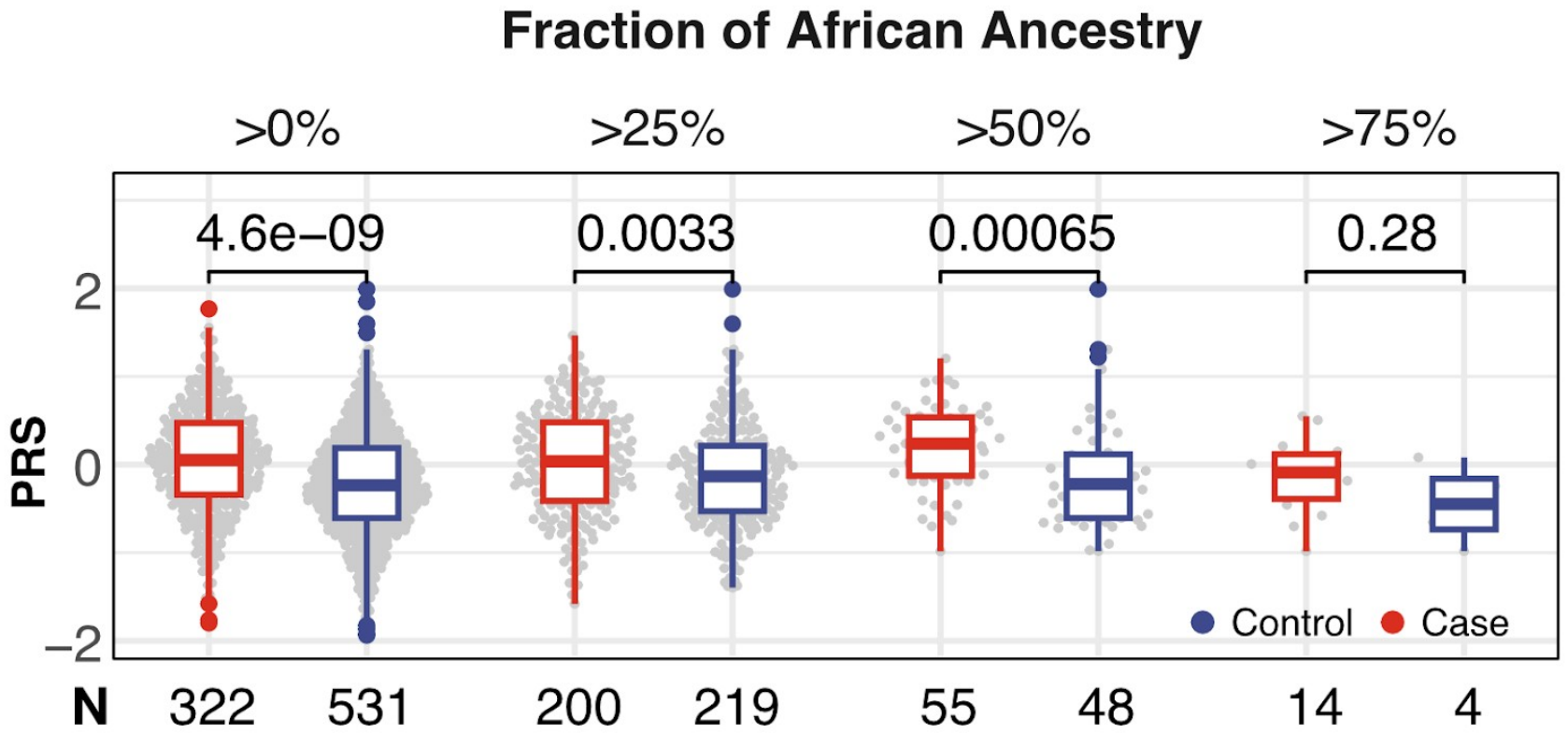


Breast cancer PRS-313 (based on Mavaddat, 2019)

Barreiro et al, 2024 → J Mol Diagnosis

Yes, but…

PRS in Brazilians: breast cancer



Sample size still limited

Yes, but…

Large initiatives in Genomics:
Support from Ministry of Health and FAPESP

Genomas Brasil is a program from the Ministry of Health – Department of Science and Technology that promotes and supports strategic projects in Genomics for accelaration of implementation in the Brazilian Universal Healthcare System (SUS)

Since 2024, it supports Genomas SUS with two anchor centers in São Paulo state (USP São Paulo and USP Ribeirão Preto) →

21k Genomes (Year 1) + 50k Genomas (Years 2-3)

In 2025, FAPESP announced support for 15k Genomes from São Paulo and expansion of anchor centers (equipment and data center)

BRASIL BEM CUIDADO
MAIS SAÚDE PARA QUEM MAIS PRECISA

SUS

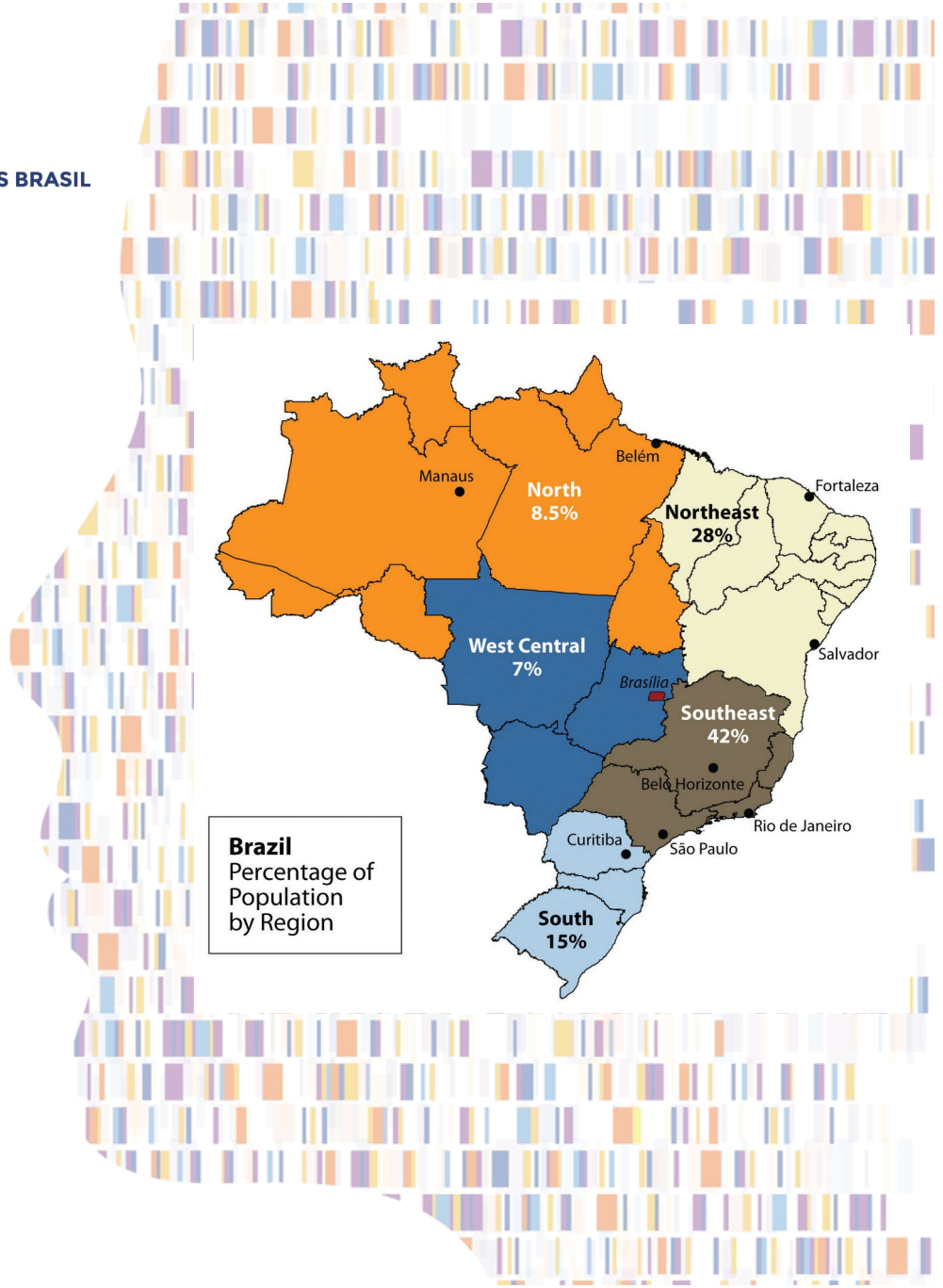
MINISTÉRIO DA SAÚDE

GOVERNO FEDERAL
BRASIL
UNIÃO E RECONSTRUÇÃO

GENOMAS BRASIL

Genomas SUS

Precision public health





Adriana Carvalho

UFRJ



Ândrea Ribeiro dos Santos

UFPA



David Livingstone

Unicentro/IPEC



Leandro Colli

USP-RP



Norma Lucena

Fiocruz-PE



Eduardo Tarazona

UFMG



Fábio Passetti

Fiocruz-PR



Juliana Mazzeu*

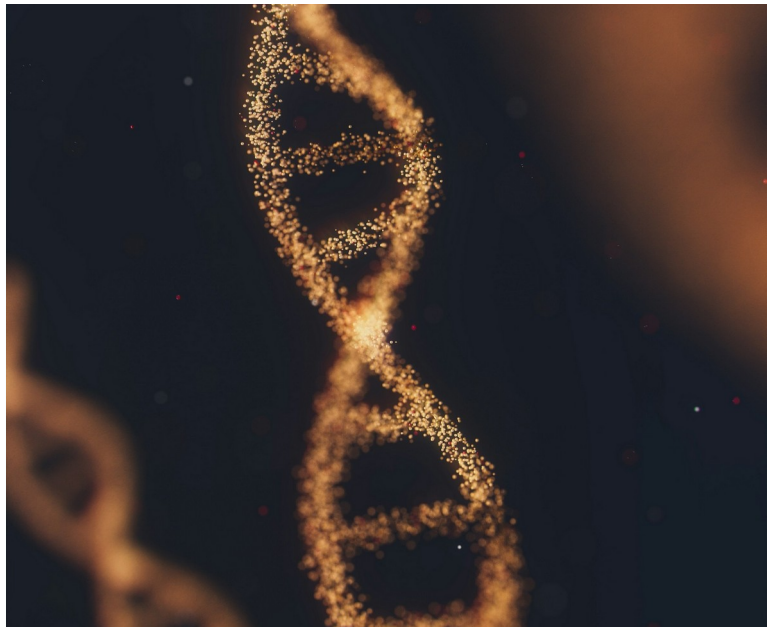
UnB



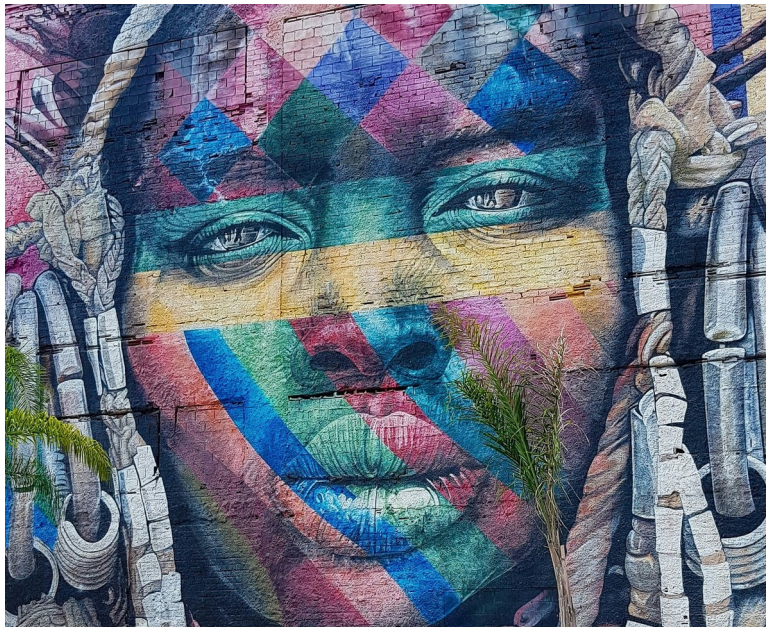
Michel Naslavsky

USP-SP

Specific goals



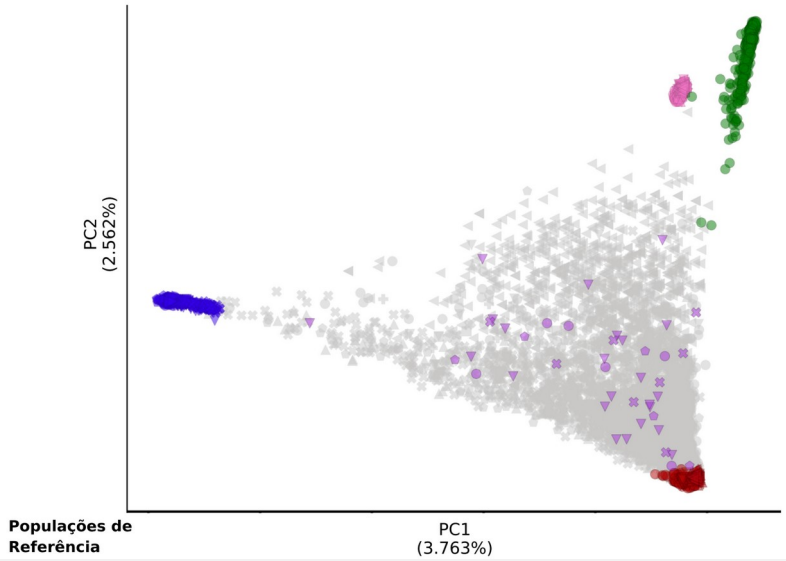
Whole-genome sequencing 21k Brazilians (Y1)



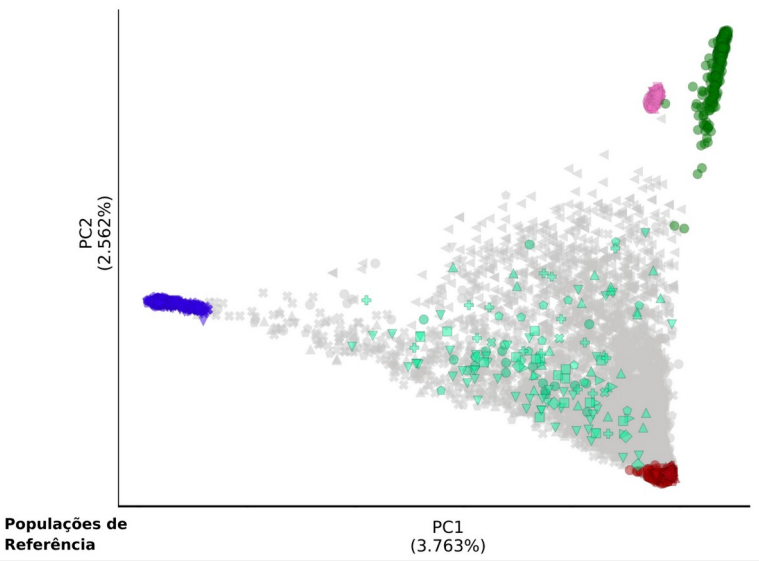
Characterize Brazilian population genomics and clinically relevant variants



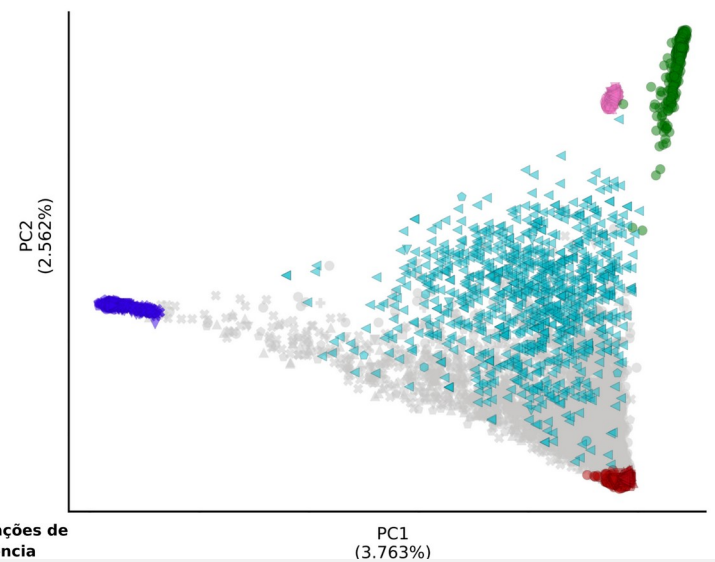
Establish reference laboratories for SUS integration



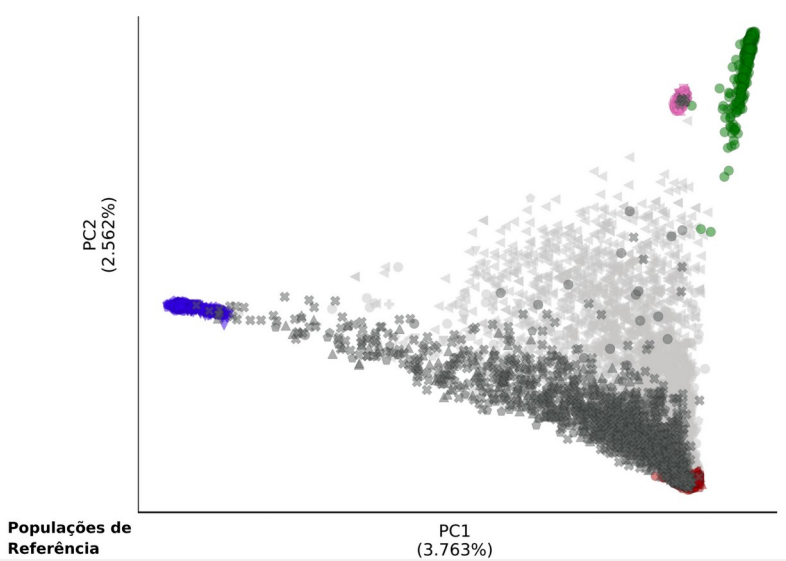
Centro-oeste



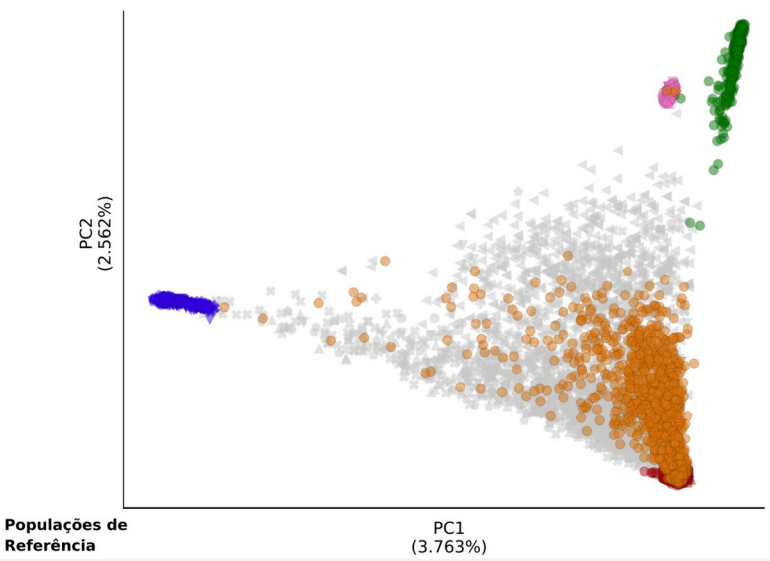
Nordeste



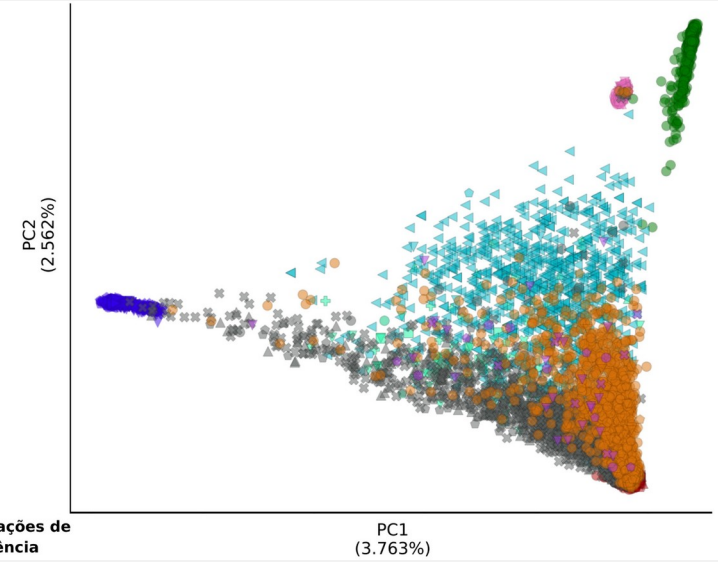
Norte



Sudeste



Sul



Nacional

Prospective efforts

Implementation of a pilot carrier screening program for couples in the world largest universal health care system: the Brazilian Our Genes Project



Acknowledgments

LAMP4: Lab for Genomic analyses in P4 Medicine

SABE: Mayana Zatz, Yeda Duarte, Maria Rita Passos Bueno, Guilherme Yamamoto, Marília Scliar, Jaqueline Wang

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AAMO – Einstein: Tatiana Almeida, Helena Brentani, Gabriela Tunes, Rodrigo Barreiro, Catarina Gomes, Gabriel Mesquita

Genomas SUS: Leandro Colli + 7 PIs + 90 collaborators

Nossos Genes: Regina Mingroni, Angelina Acosta, Flavia Errera, Juliana Mazzeu + 30 collaborators

Obrigado!

mnaslavsky@usp.br