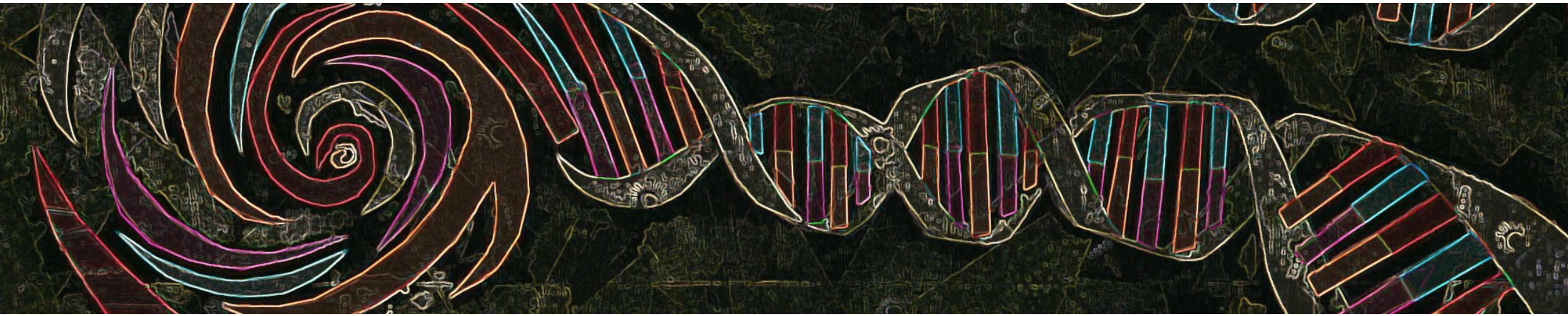


"Genetics of Alzheimer's Disease in Minoritized Populations "

Margaret A. Pericak-Vance, Ph.D.

Director, John P. Hussman Institute for Human Genomics

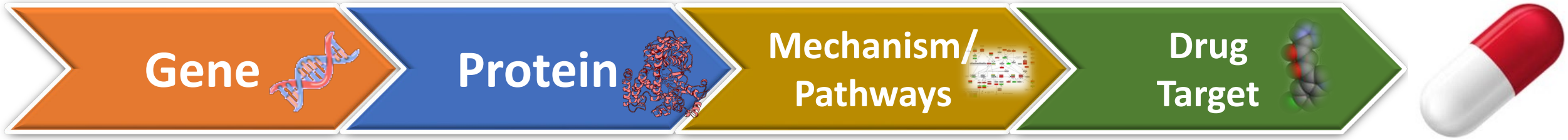
Dr. John T Macdonald Foundation Professor of Human Genetics

University of Miami Miller School of Medicine

10/17/2022

Human Genetics Disease Research Goals

- Study human disease mechanism directly in humans
- Prediction
- Mechanism
- Drug targets



Genetic Studies in Alzheimer Disease

❑ Why study genes?

To identify new targets for drug discovery

Genetic targets are 2X as successful in drug trials versus non-genetic targets.

❑ Why study Diverse Groups

More than 30 genetic risk factors for AD discovered- primarily in individuals of European ancestral descent

Different ancestral groups have different genetic risk factors

So that treatments are universally translational

- Black Americans and Hispanic Americans are more likely to develop AD and dementia compared to non-Hispanic white (European) Americans

- Greater familial risk for AD
- Limited health care access
- AD patients identified at later stages
- Poorer treatment outcomes

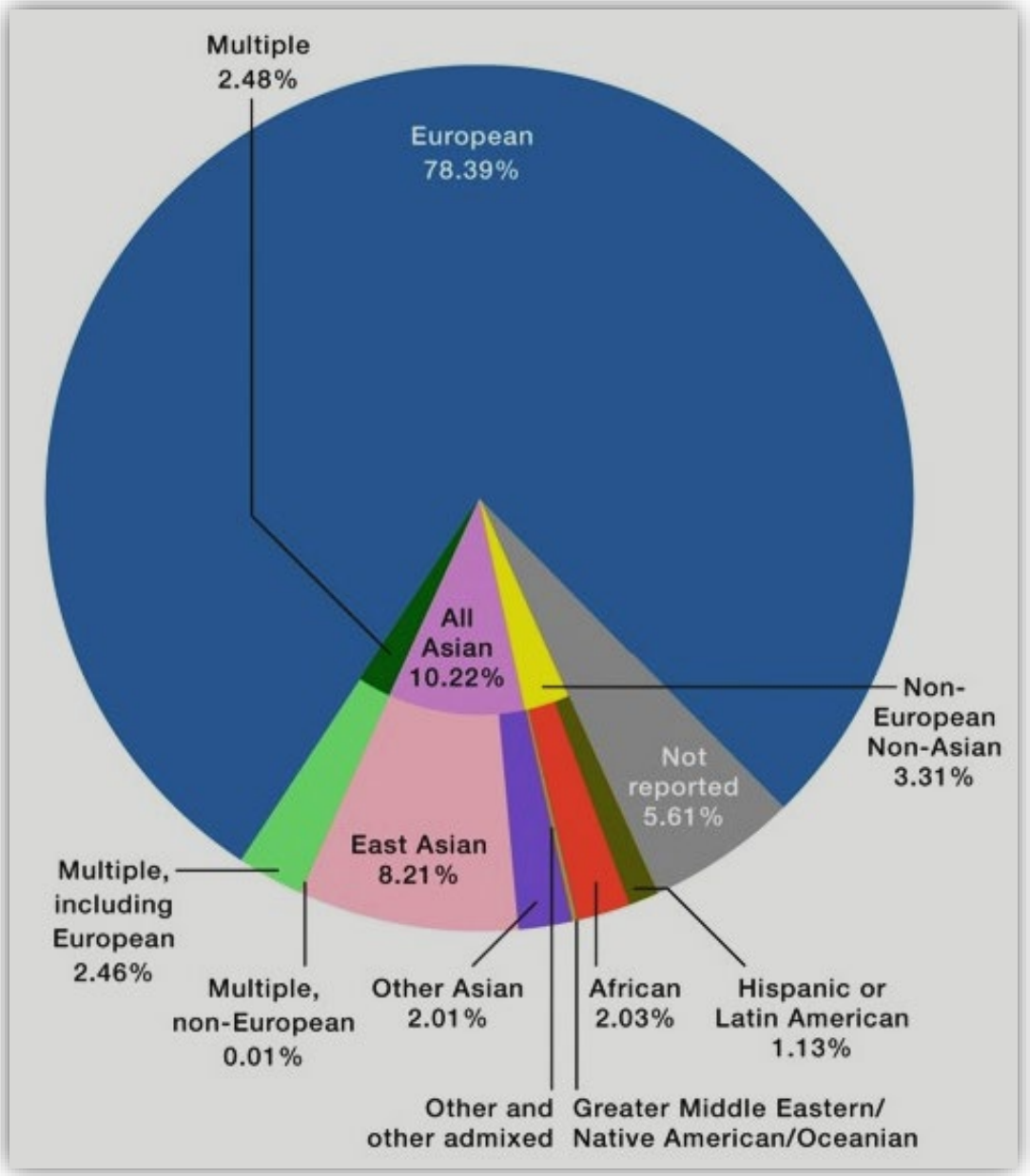
http://www.socialgradient.org/alzheimers-center-aids-african-americans/

http://www.poststat.net/pwp008/pub.49/issue.350/article.528/

Why Study Diverse Groups

- The underrepresentation of ancestrally diverse populations in genetic studies:
  - hinders our ability to fully understand the genetic architecture of disease, and
  - intensify health inequalities.
  - reduce the power of risk prediction
- The translation of genetic research into clinical practice may be dangerously incomplete or, worse, mistaken

Ancestry category distribution of <u>individuals</u> in study catalog



Sirugo, et al, 2019

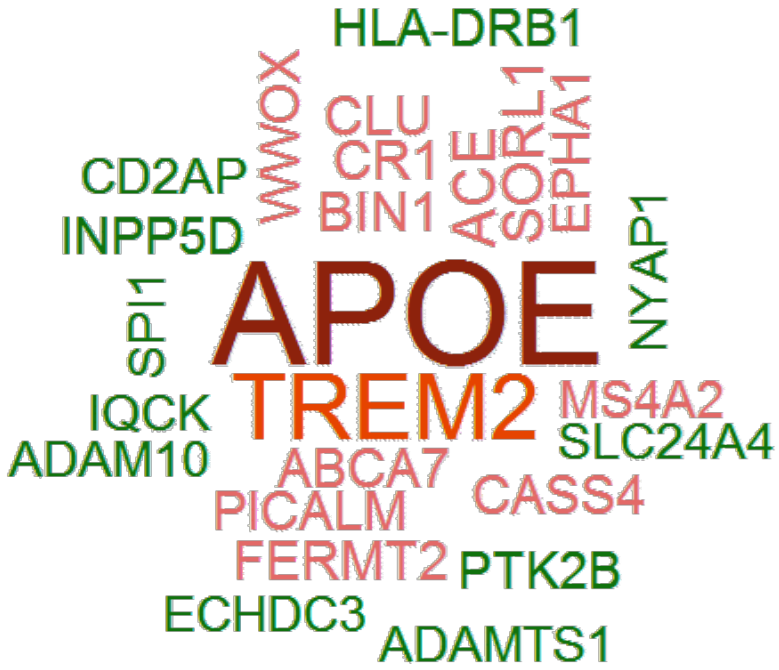
Genetic Studies in Alzheimer Disease

AD GWAS studies

Europeans: N~**93,000** (Kunkle et al. 2019)

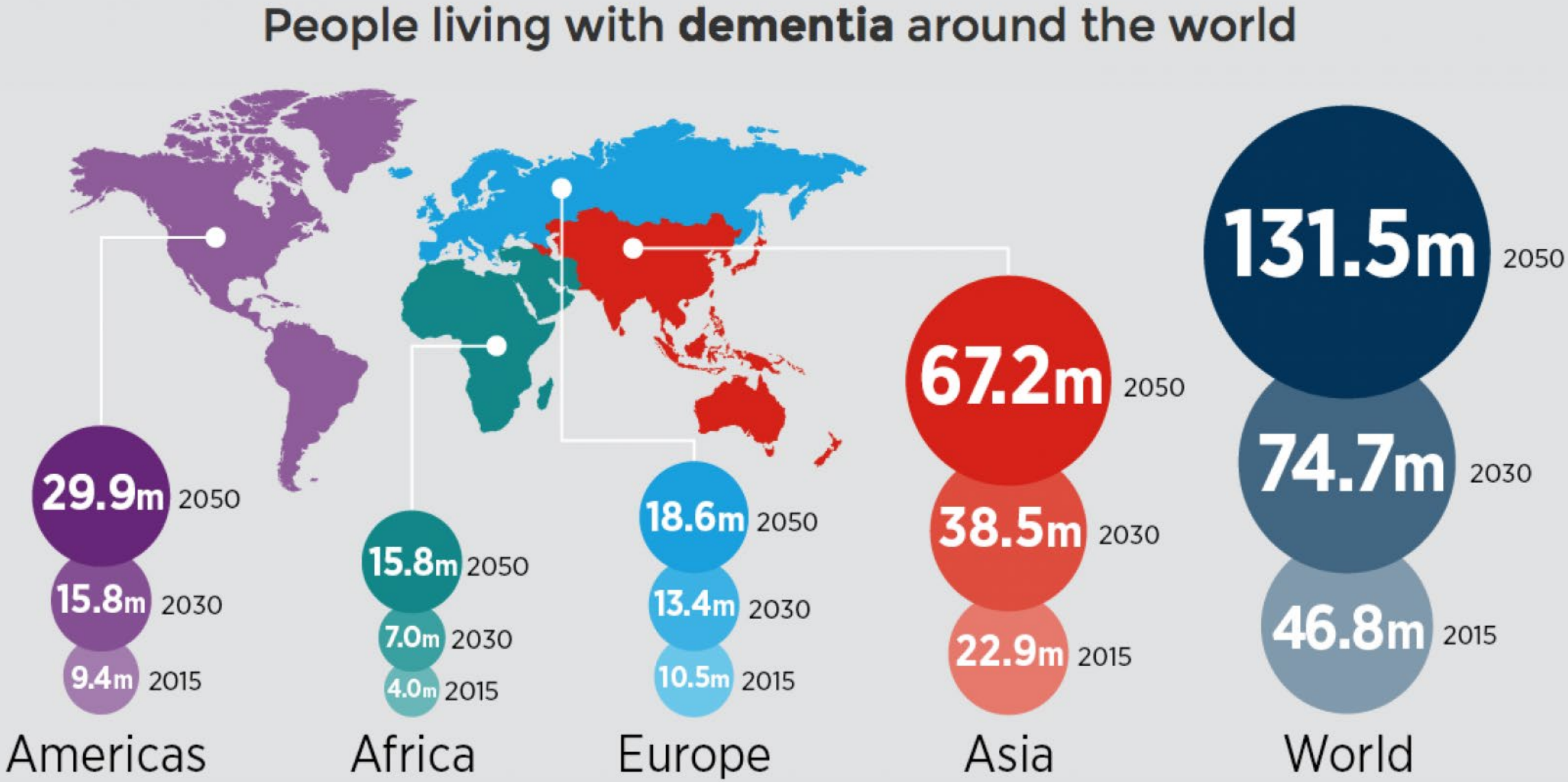
African Americans: N~**8,000** (Kunkle et al. 2020)

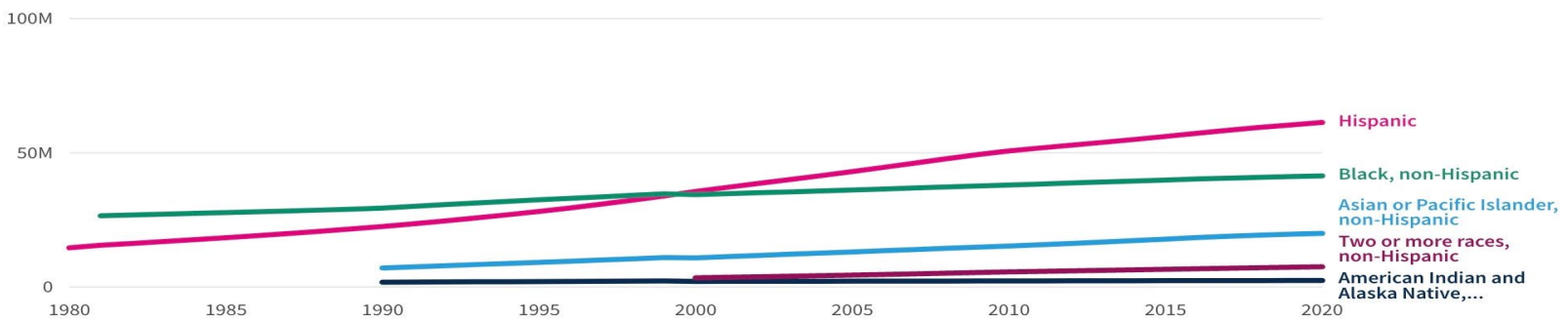
Hispanics: N~**4,500** (Tosto et al., 2015)

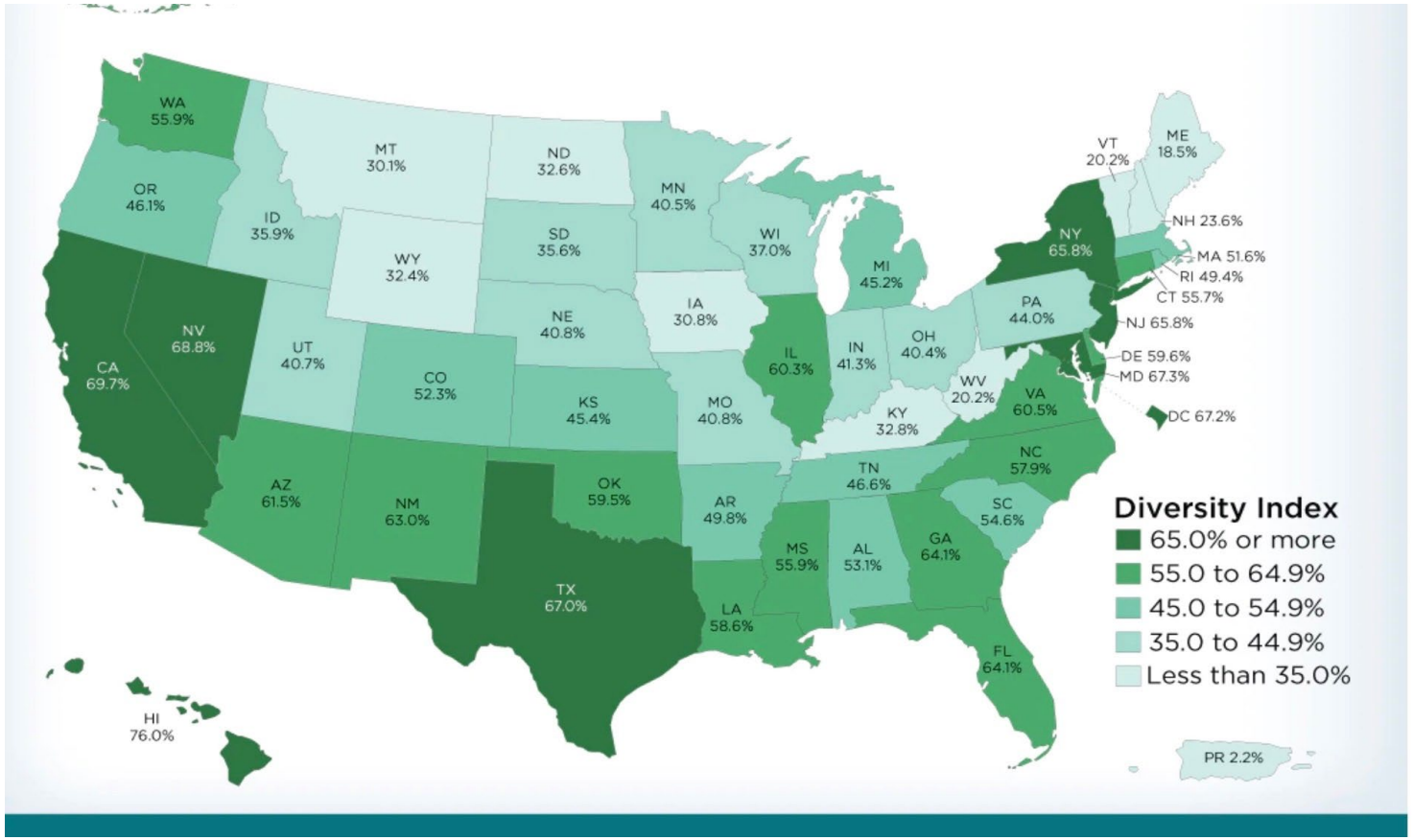


https://all-free-download.com/free-vector/europe-map-transparent-background_sort_by_unpopular.html

Alzheimer Disease



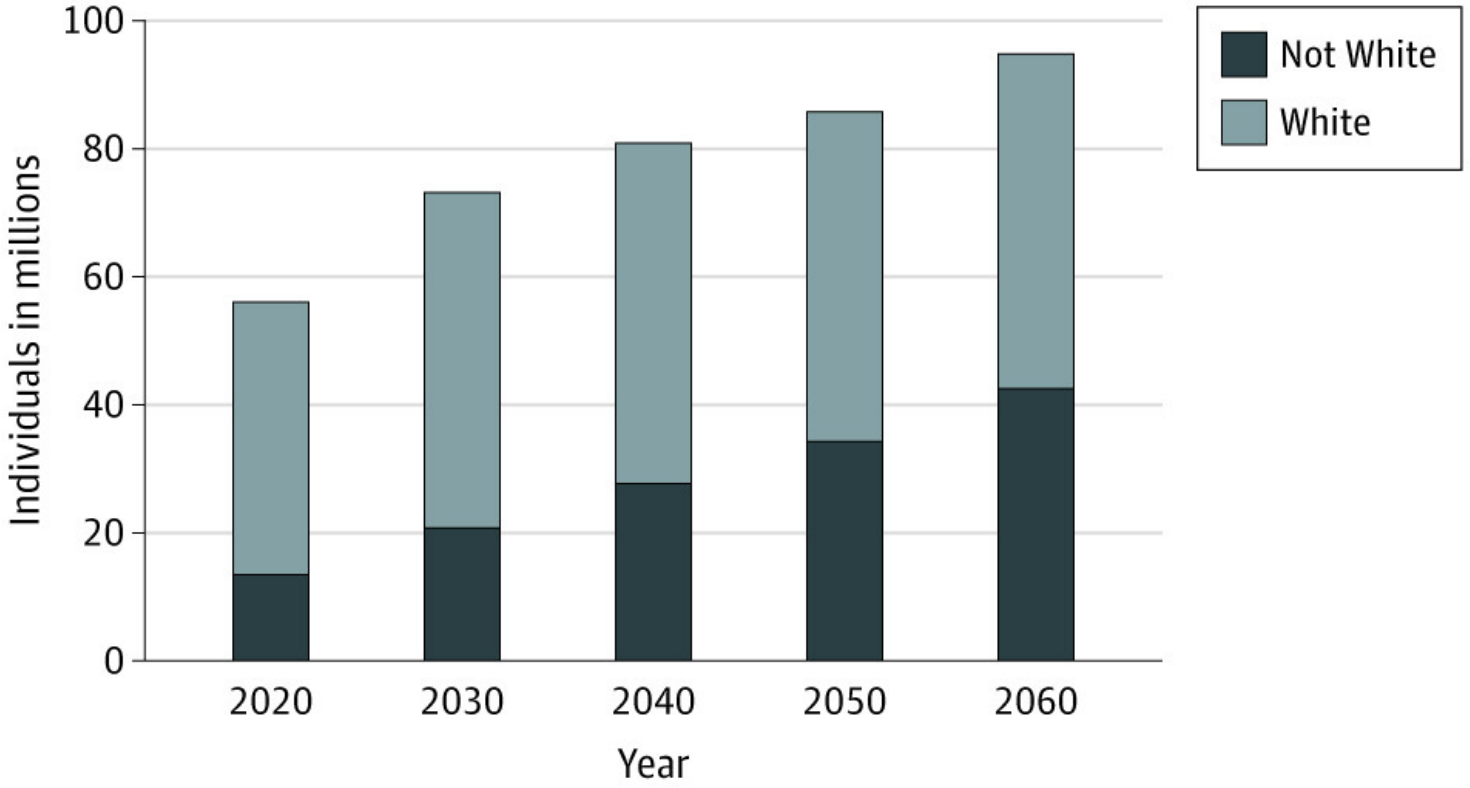




US Populations Diversity and Growth*

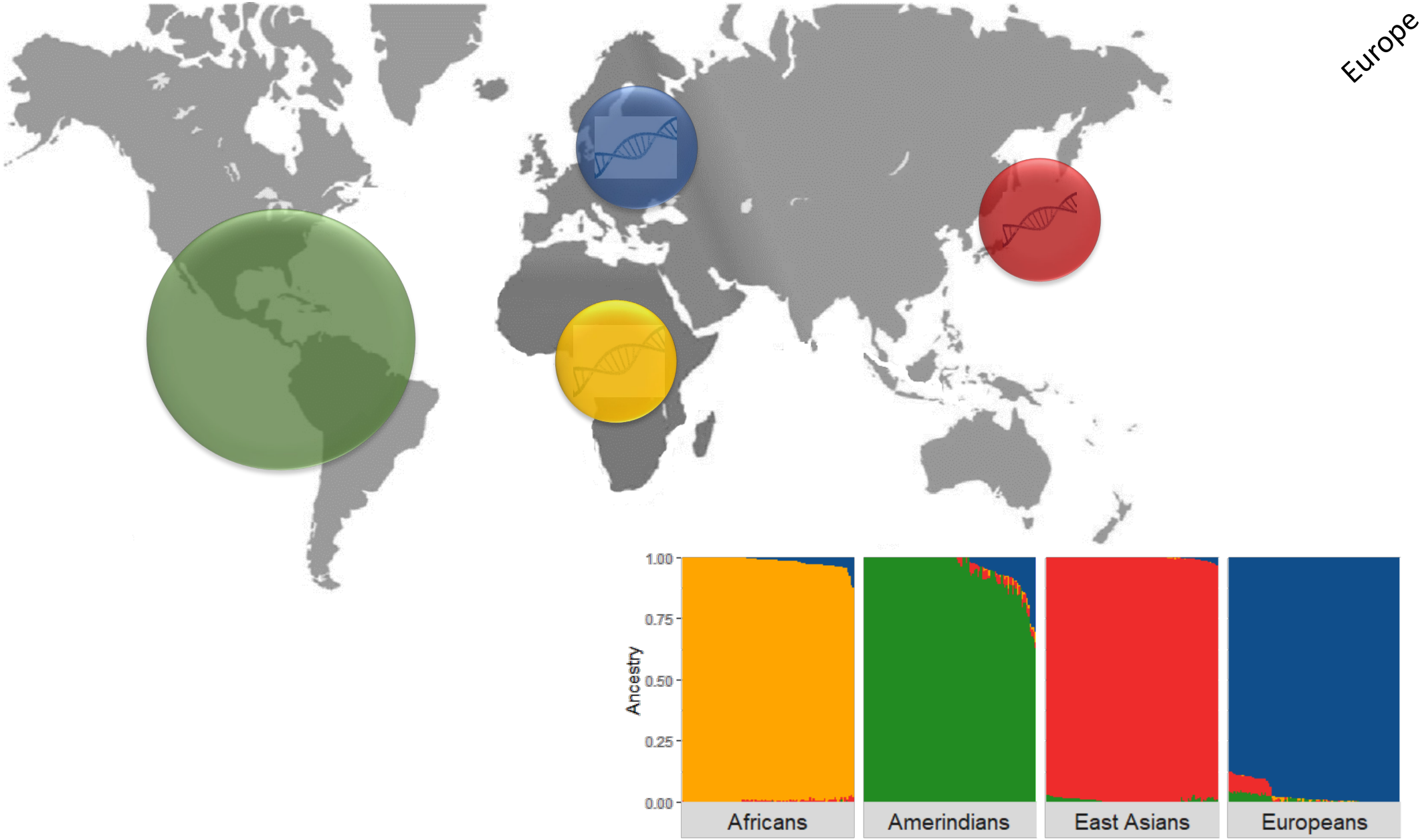
*2020 US Census

Aging Population 65 yrs and older in the US

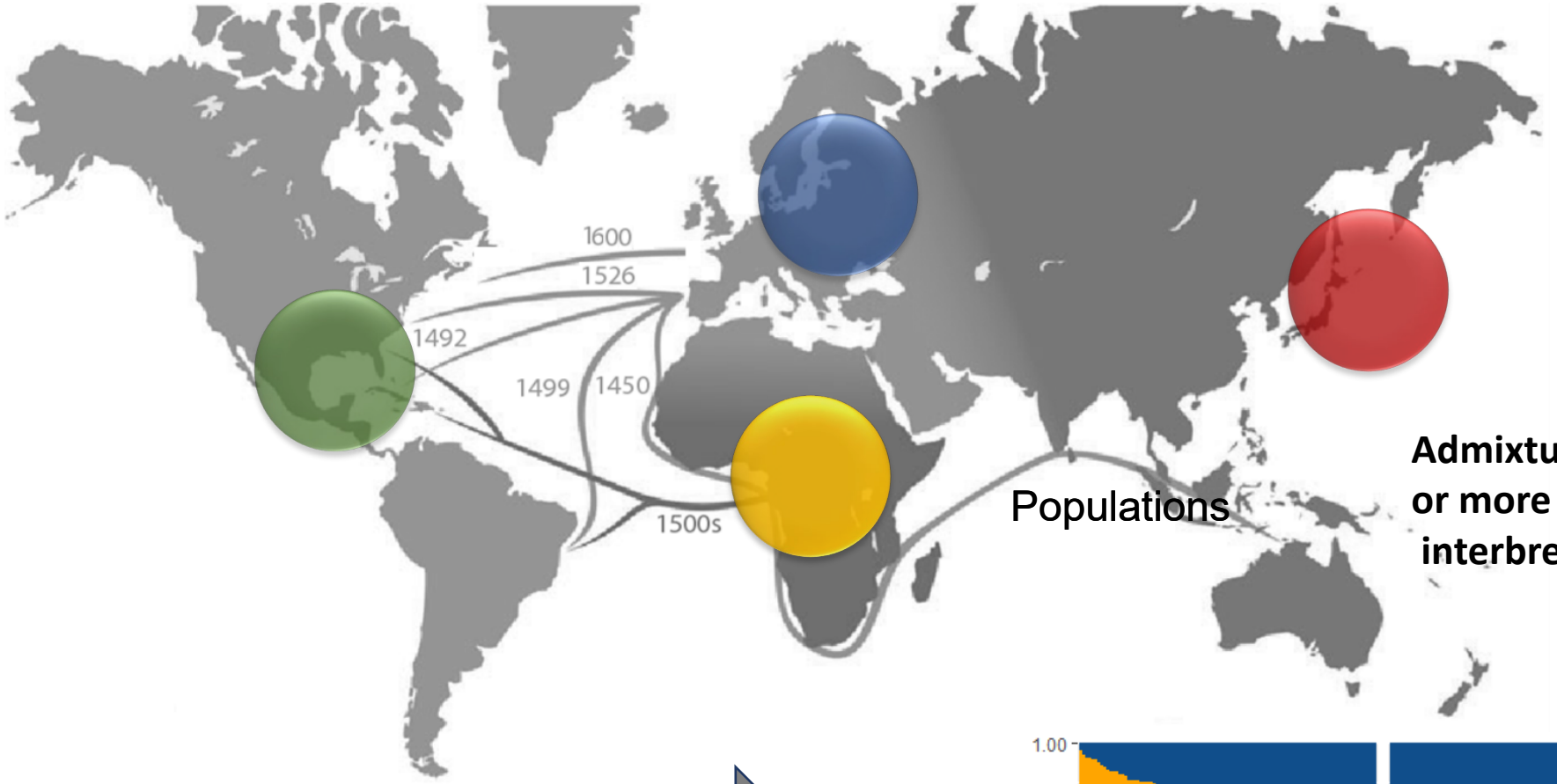


From Kawas CH et al
JAMA 78(6): 650, 2021

Global Ancestry: Continental Populations



Global Ancestry and Admixture



Europe

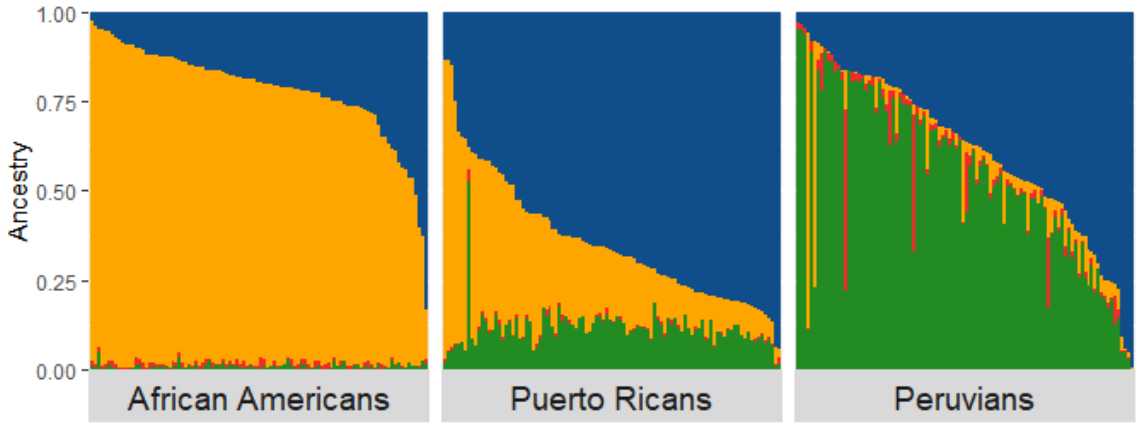
Africa

East Asia

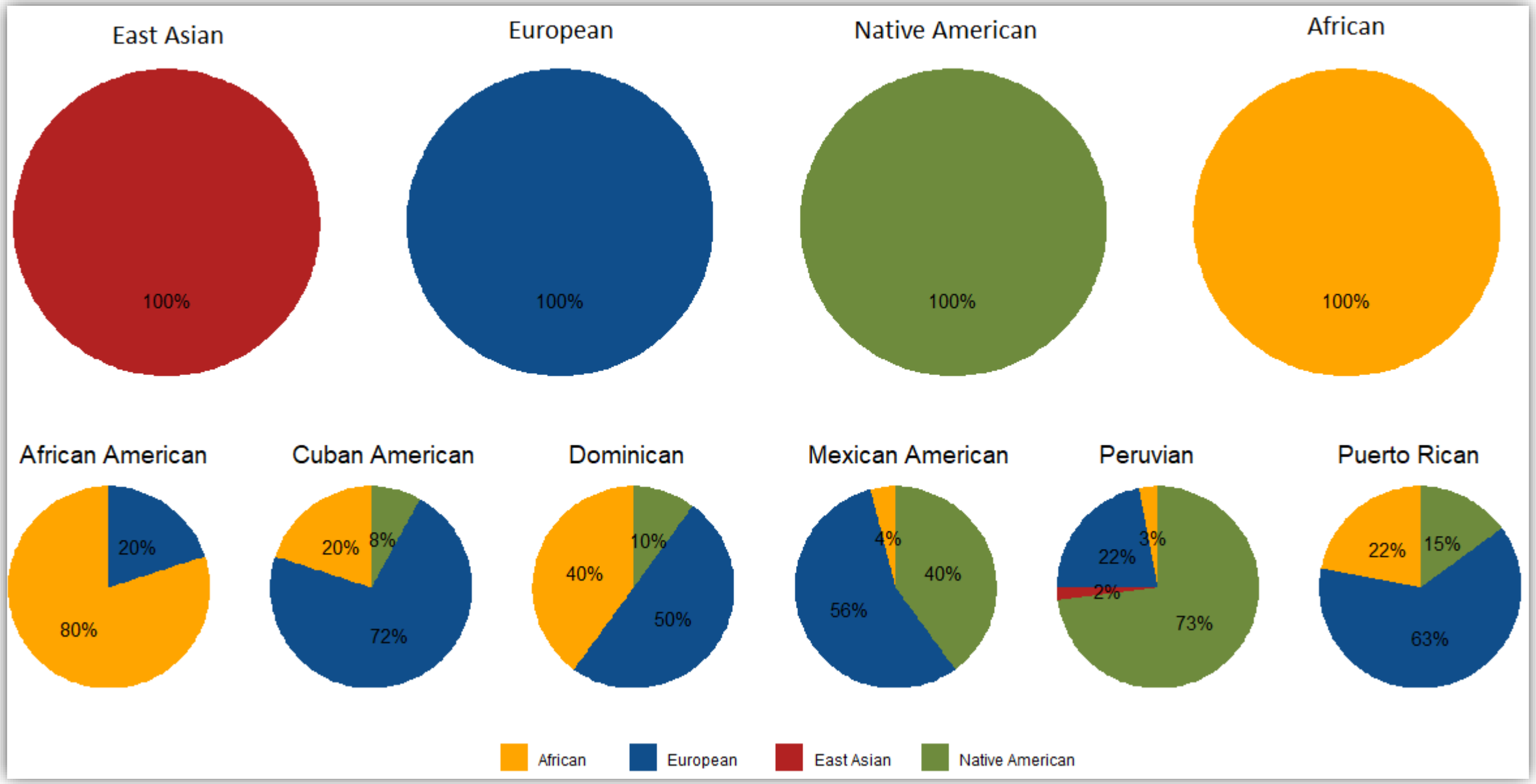
Populations

Admixture happens when individuals from two or more genetically distinct populations are interbreeding

ADMIXTURE

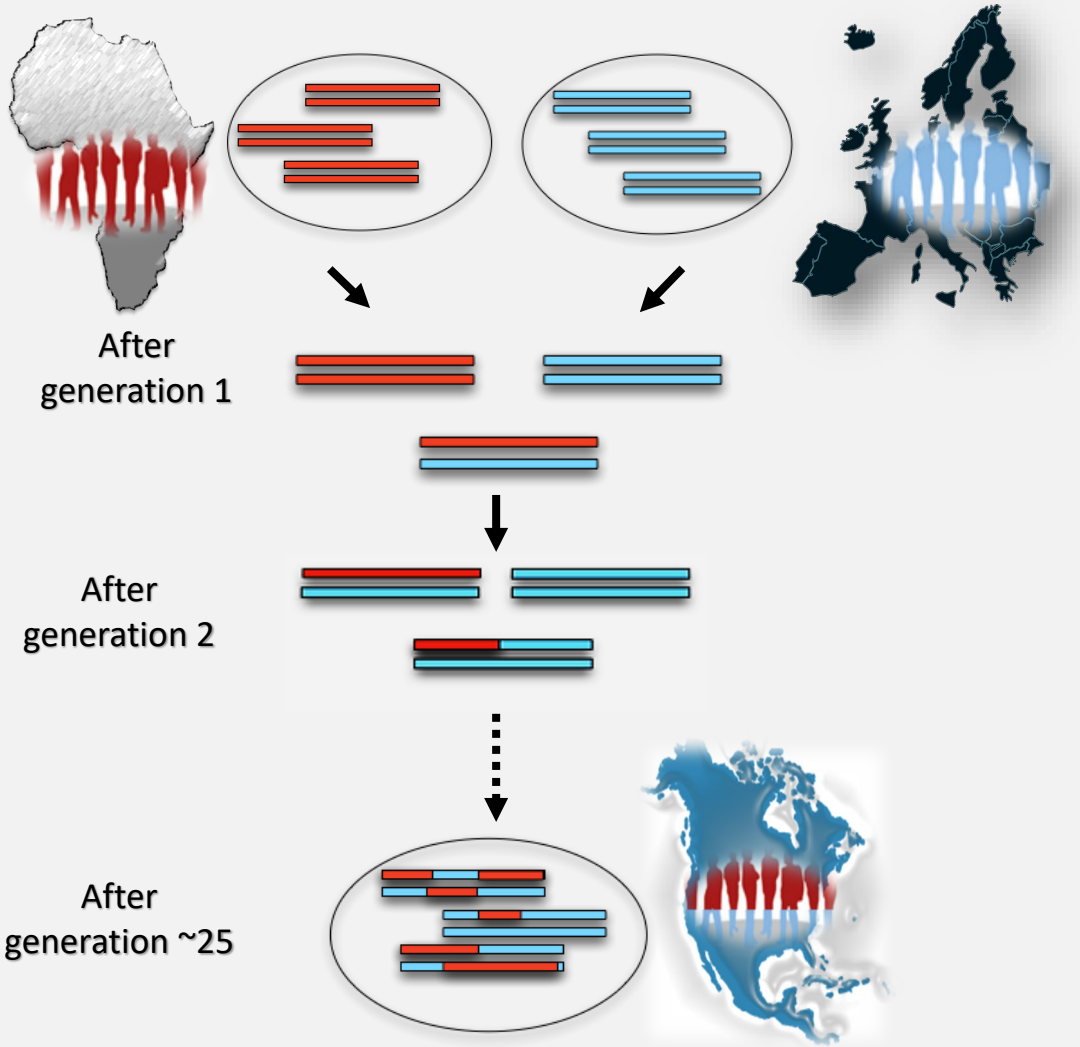


Average Ancestral Proportions in Hispanic Populations and African Americans

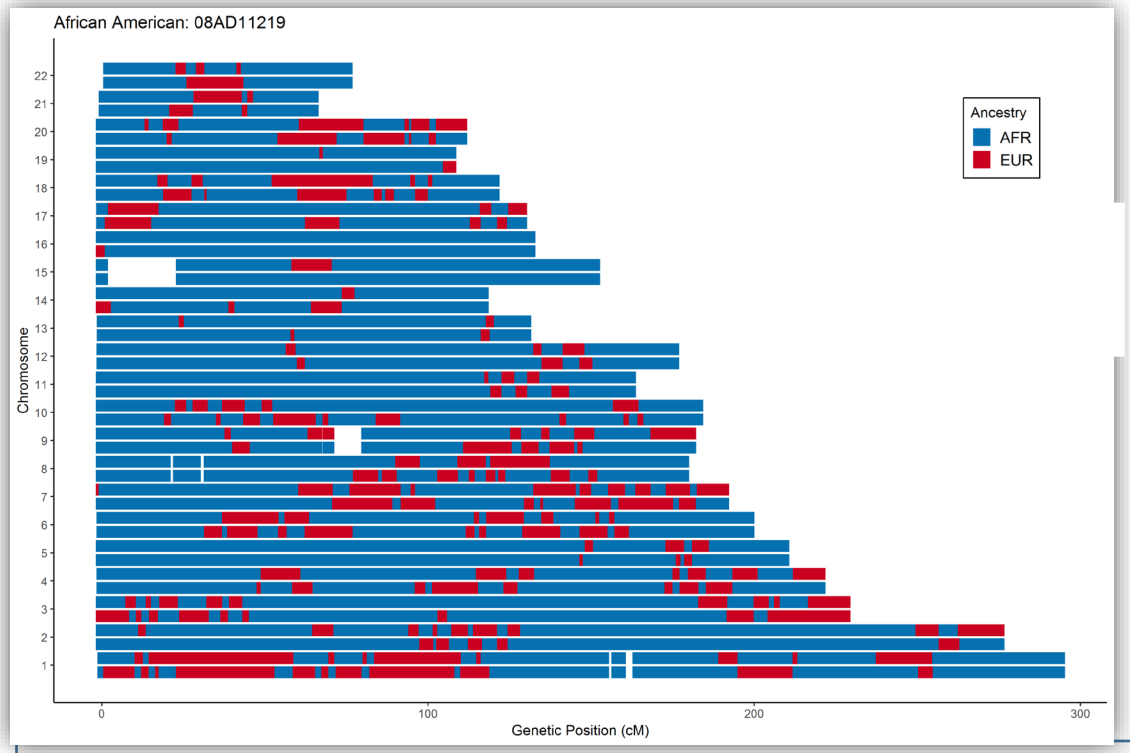


Admixture and **Local Ancestry**

- AA population is an admixed population



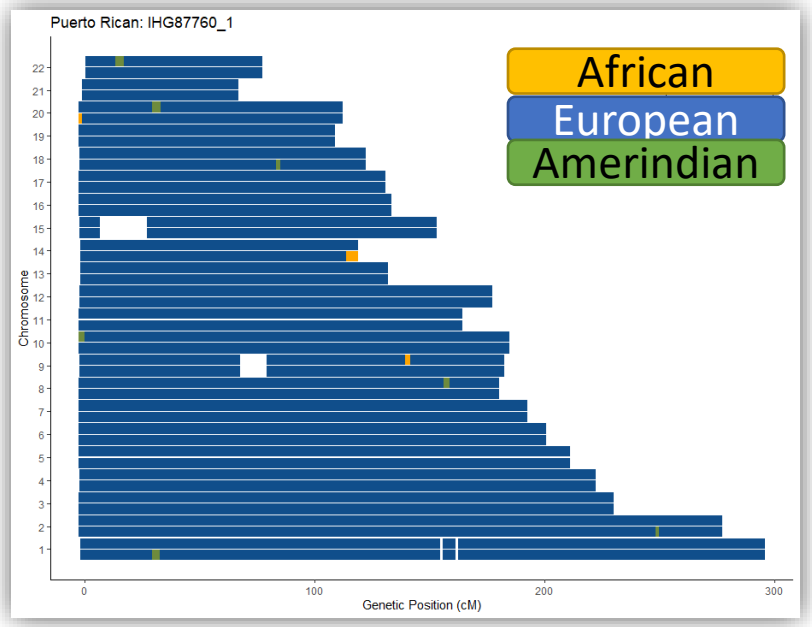
- Local ancestry estimates of a Black American individual



The US Black population is a two-way admixed population with genetic ancestry from African and European ancestors.

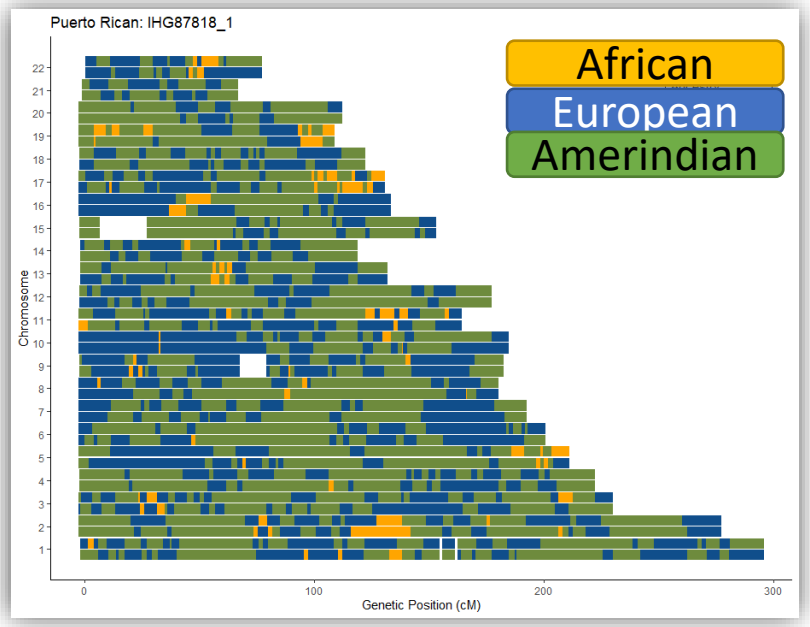
Local Ancestry in Puerto Ricans

Puerto Rican 1



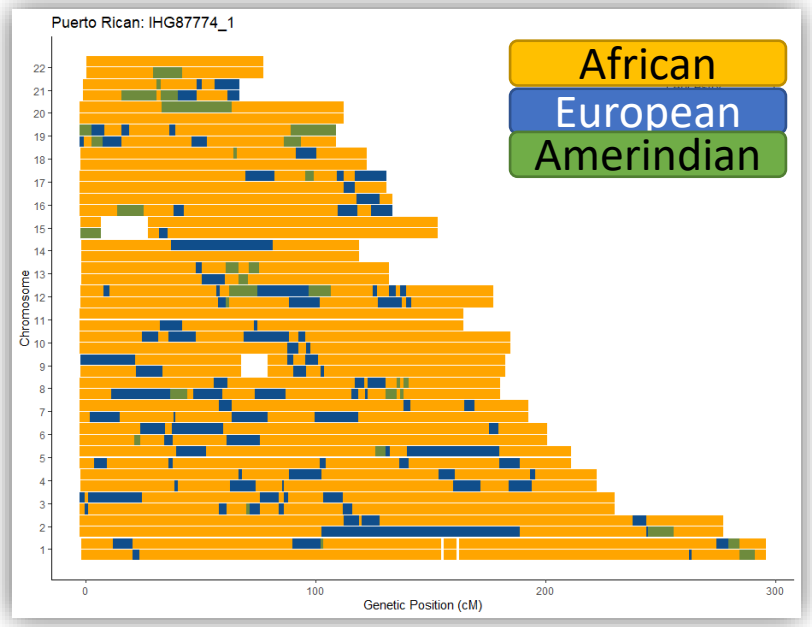
99.7%

Puerto Rican 2



39% 4 57%

Puerto Rican 3

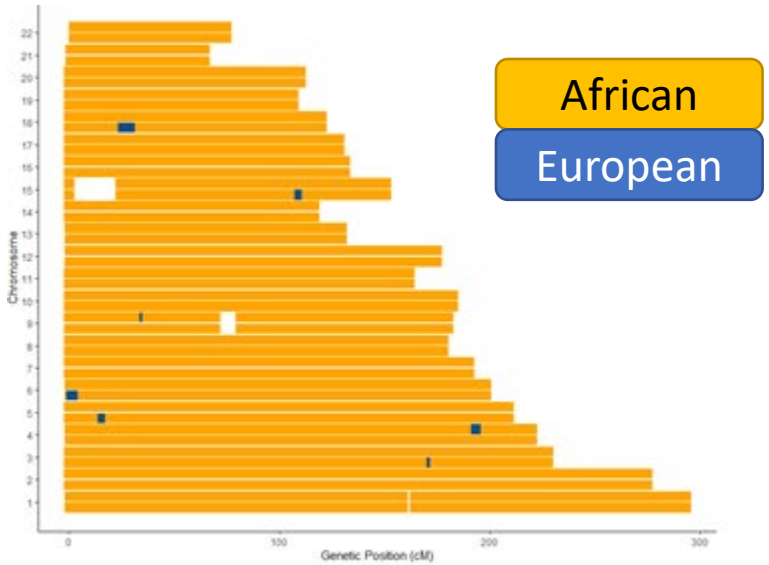


13 84% 3

Race versus Ancestry

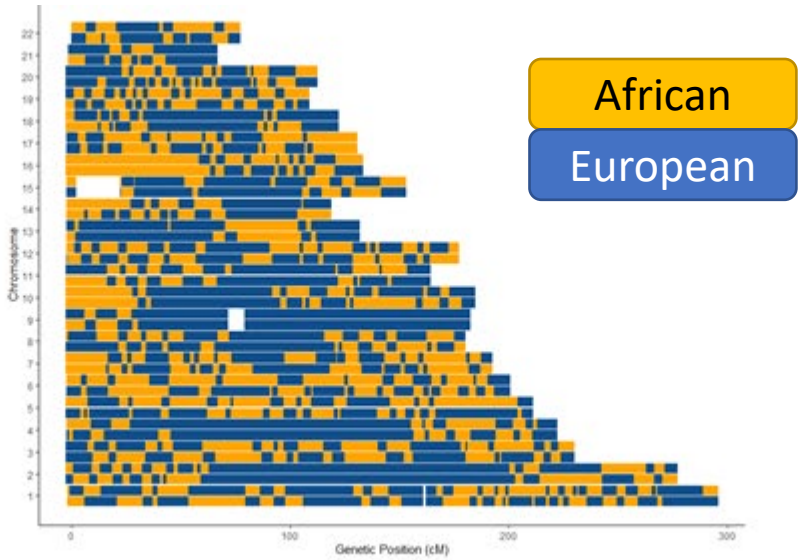
- Ancestry is biological and is about the history of genetic variation and the origin of one's population
- Race, itself is not biological, but is often self-ascribed or socially-ascribed by others
- As I have shown populations used to live in isolation with each geographic region having its own genetic map (Continental Populations)
- Populations today particularly in the US are admixed (multiple ancestries) with individuals of European, African, Amerindian and Asian ancestry.

Ancestry versus Race



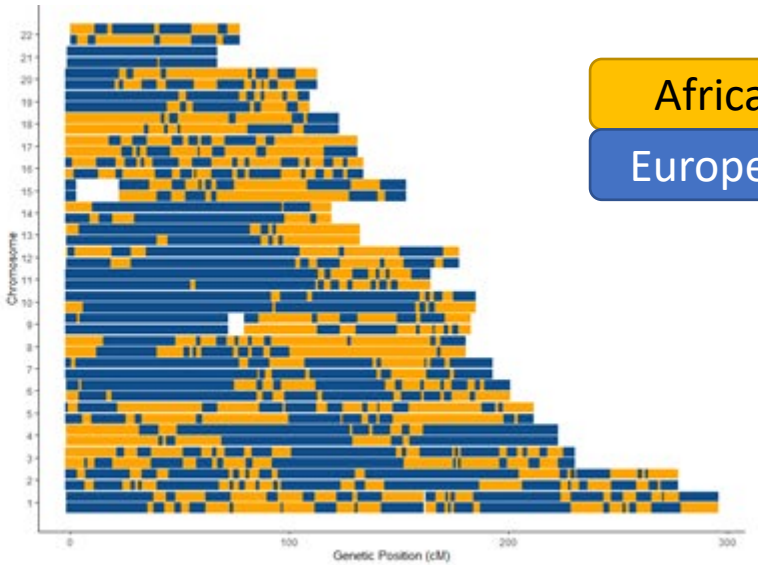
African
European

99%



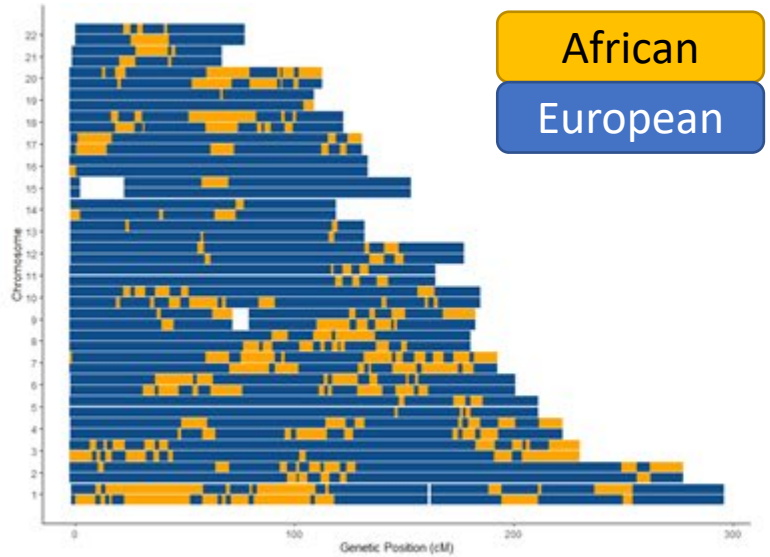
African
European

61%
39%



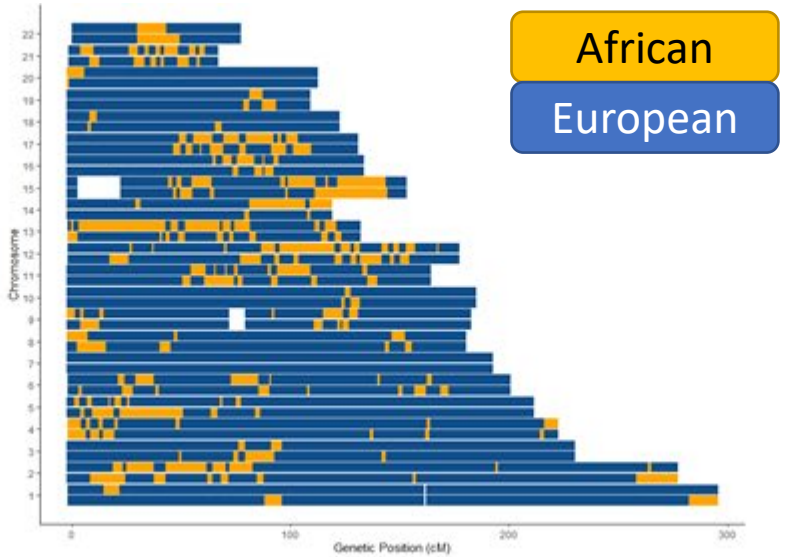
African
European

62%
38%



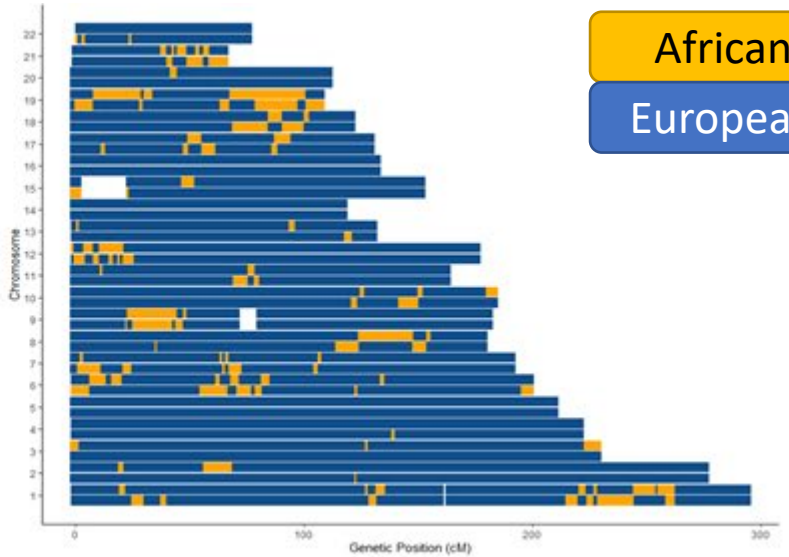
African
European

82%
18%



African
European

86%
14%



African
European

93%
7

Admixture – Local Ancestry – *APOE*

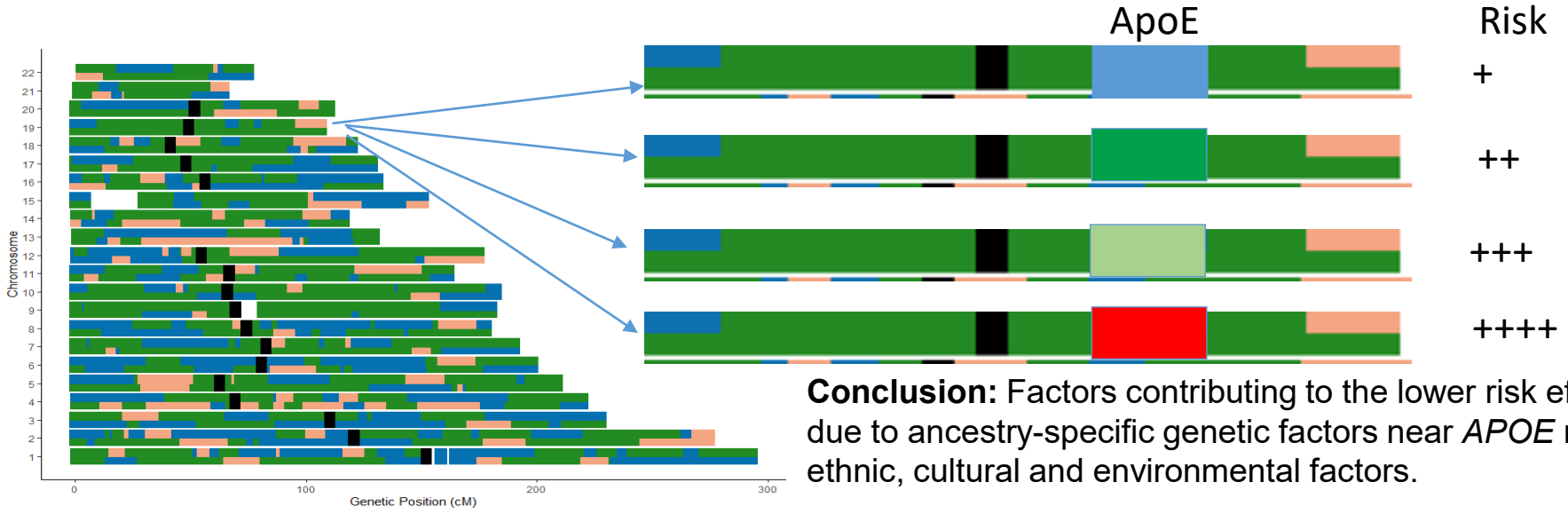
Plos Genetics 2018

RESEARCH ARTICLE

Ancestral origin of *ApoE ε4* Alzheimer disease risk in Puerto Rican and African American populations

Farid Rajabli[1☯], Briseida E. Feliciano[2], Katrina Celis[1], Kara L. Hamilton-Nelson[1], Patrice L. Whitehead[1], Larry D. Adams[1], Parker L. Bussies[1], Clara P. Manrique[1], Alejandra Rodriguez[2], Vanessa Rodriguez[1], Takiyah Starks[3], Grace E. Byfield[3], Carolina B. Sierra Lopez[2], Jacob L. McCauley[1], Heriberto Acosta[4], Angel Chinea[2], Brian W. Kunkle[1], Christiane Reitz[5], Lindsay A. Farrer[6], Gerard D. Schellenberg[7], Badri N. Vardarajan[5], Jeffery M. Vance[1,8], Michael L. Cuccaro[1,8], Eden R. Martin[1,8], Jonathan L. Haines[9], Goldie S. Byrd[3], Gary W. Beecham[1,8☯], Margaret A. Pericak-Vance[1,8☯*]

Ancestry
- African
- European
- Amerindian
- Asian

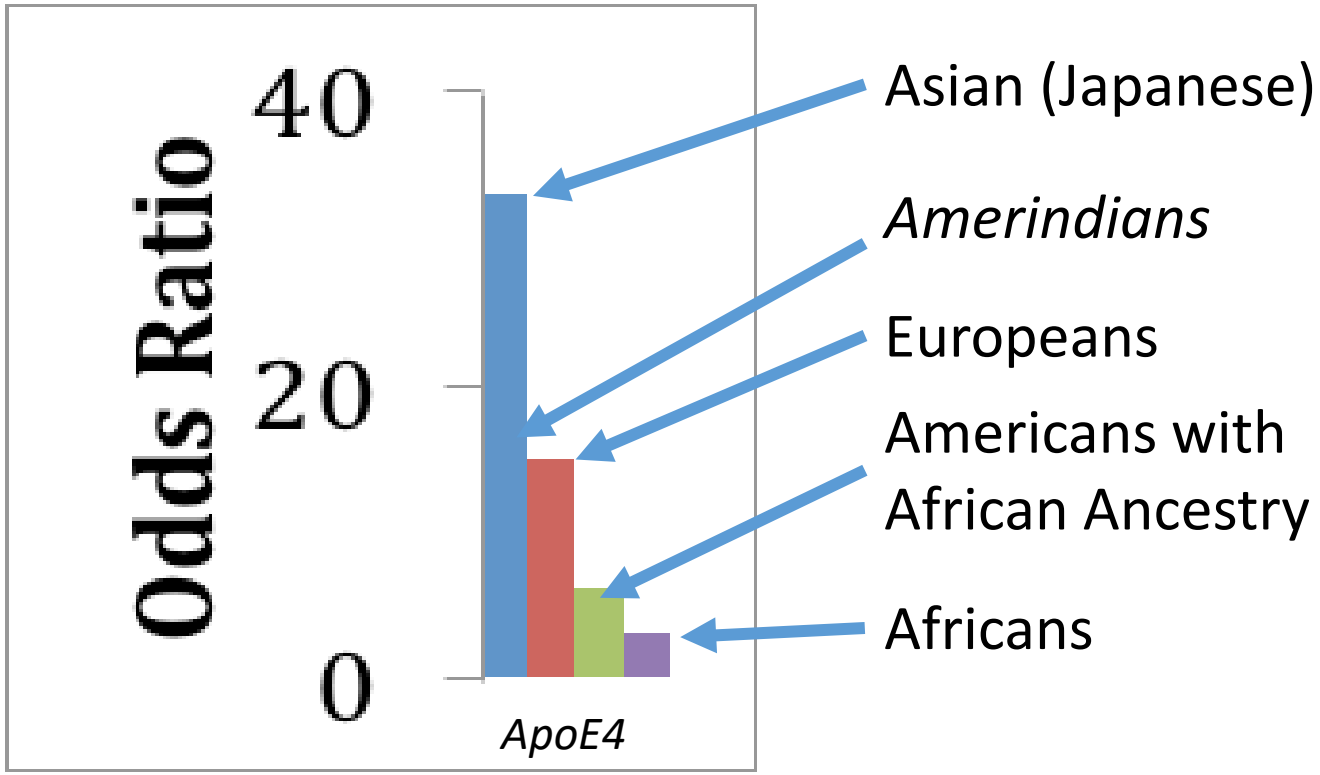


Conclusion: Factors contributing to the lower risk effect in the *APOE* are due to ancestry-specific genetic factors near *APOE* rather than non-genetic ethnic, cultural and environmental factors.

The Risk to Develop Alzheimer Disease (AD) *for ApoEe4/4* carriers (compared to *ApoEe3/3* carriers) is <u>different across ancestral groups</u>

Odds Ratios:

2= twice the risk
3= three times the risk
Etc.



alzheimer's association | Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

FEATURED ARTICLE | Full Access

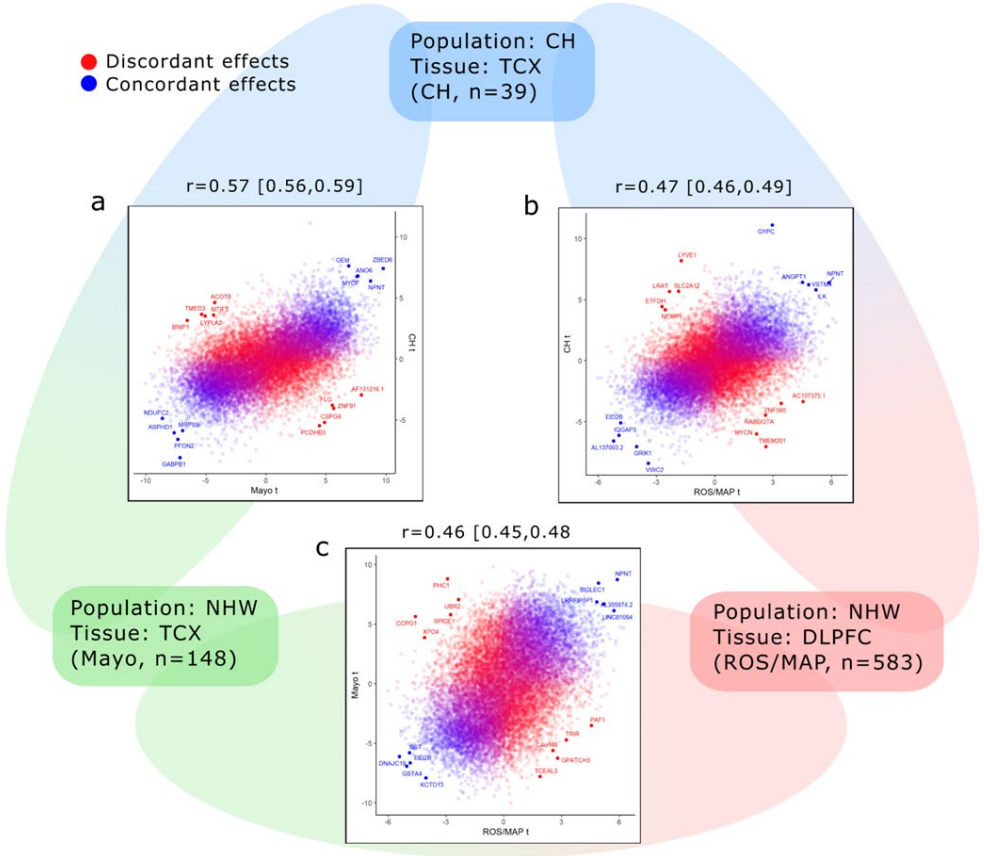
Increased *APOE* ε4 expression is associated with the difference in Alzheimer's disease risk from diverse ancestral backgrounds

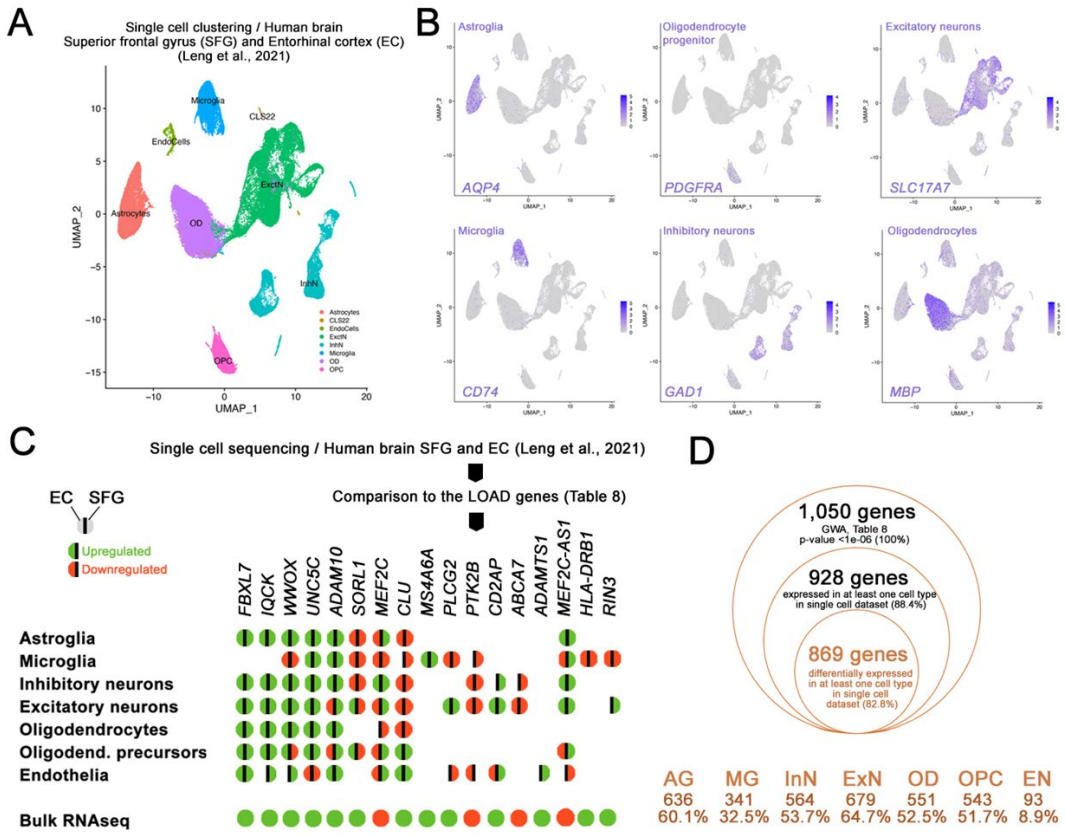
Anthony J. Griswold, Katrina Celis, Parker L. Bussies, Farid Rajabli, Patrice L. Whitehead, Kara L. Hamilton-Nelson, Gary W. Beecham, Derek M. Dykxhoorn, Karen Nuytemans, Liyong Wang, Olivia K. Gardner, Daniel A. Dorfsman, Eileen H. Bigio, Marek Marsel Mesulam, Sandra Weintraub, Changiz Geula, Marla Gearing, Elisa McGrath-Martinez, Clifton L. Dalgard, William K. Scott, Jonathan L. Haines, Margaret A. Pericak-Vance, Juan I. Young, Jeffery M. Vance ... See fewer authors

First published: 01 February 2021 | https://doi.org/10.1002/alz.12287 |

Anthony J. Griswold, Katrina Celis, Juan I. Young, and Jeffery M. Vance contributed equally to this study.

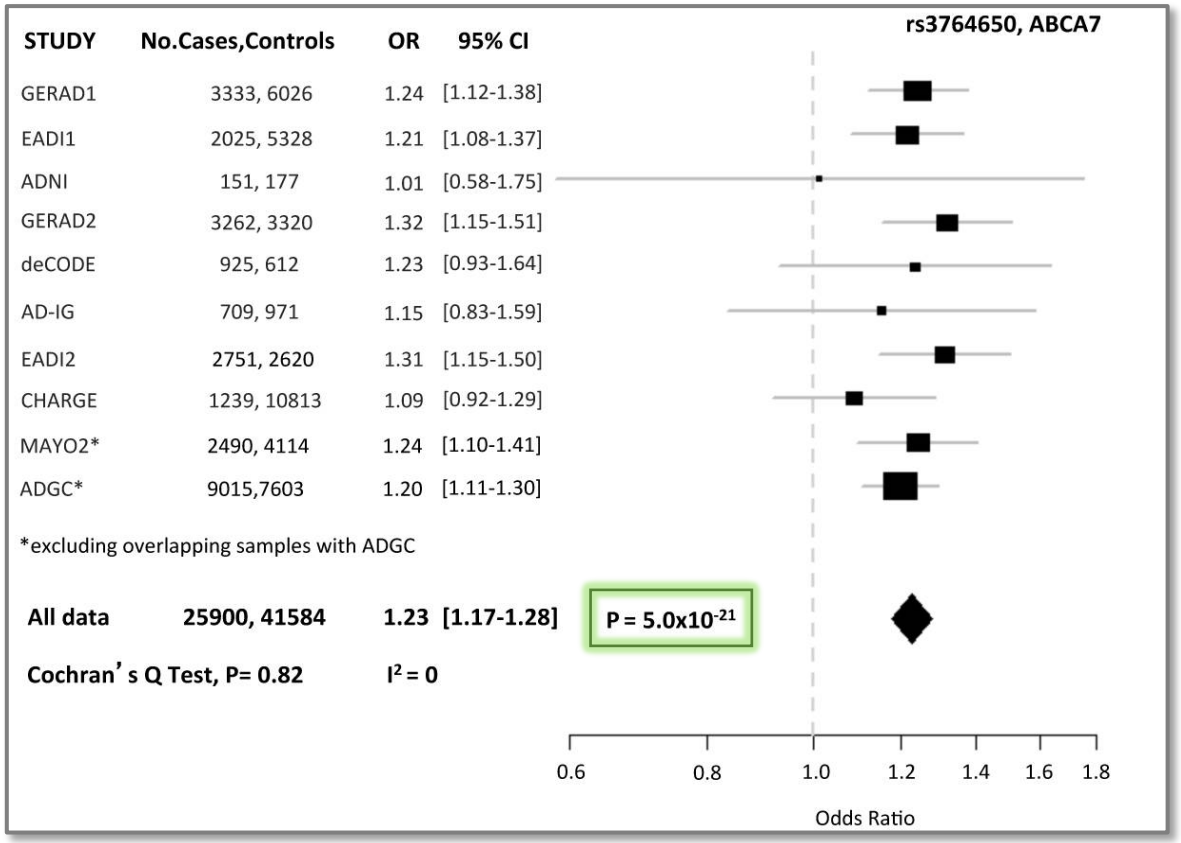
The Caribbean-Hispanic Alzheimer's Brain Transcriptome Reveals Ancestry-Specific Disease Mechanisms – *in press*

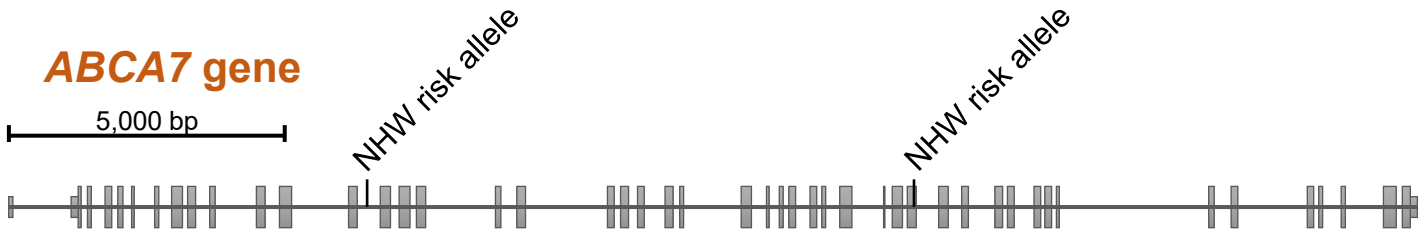




ABCA7 first implicated in AD risk in Europeans

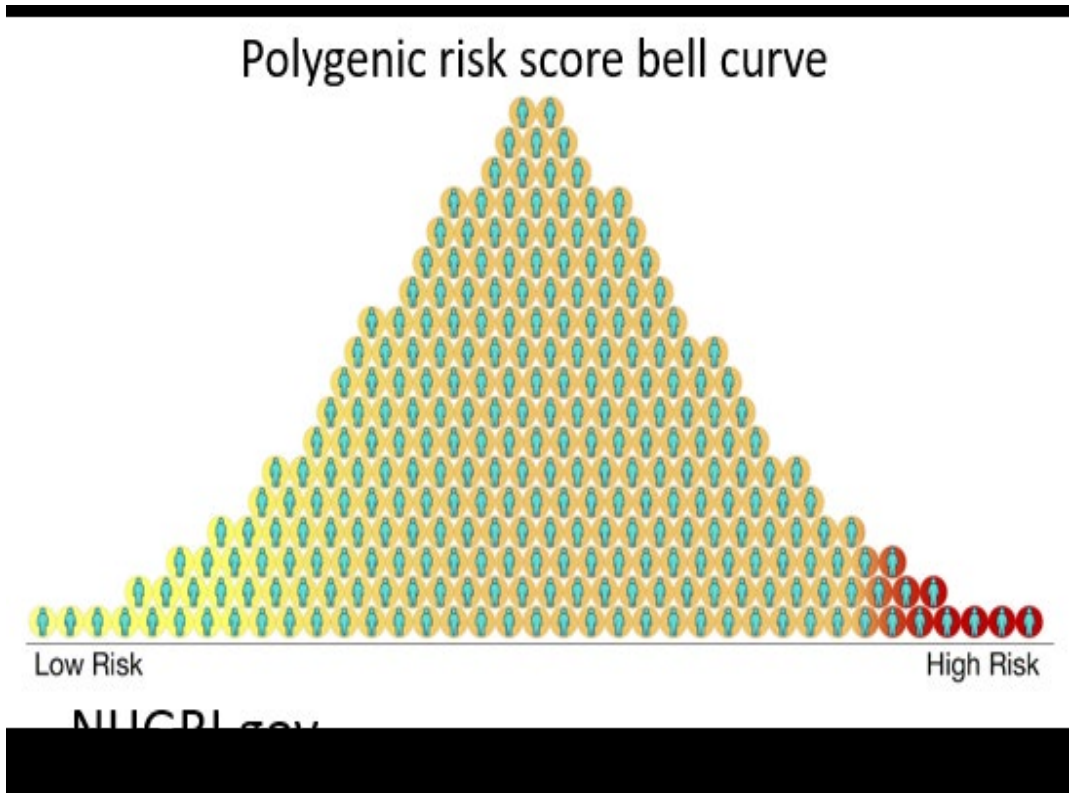
- *ABCA7: ATP-binding cassette, sub-family A (ABC1), member 7*
  - ABC transporters are a large gene superfamily involved in the movement of molecules across cellular membranes
- Two distinct studies identified single nucleotide polymorphisms (SNPs) in *ABCA7* significantly associated with AD risk
- Both studies were performed with large cohorts of AD patients and controls with European ancestry (non-Hispanic white/NWH).



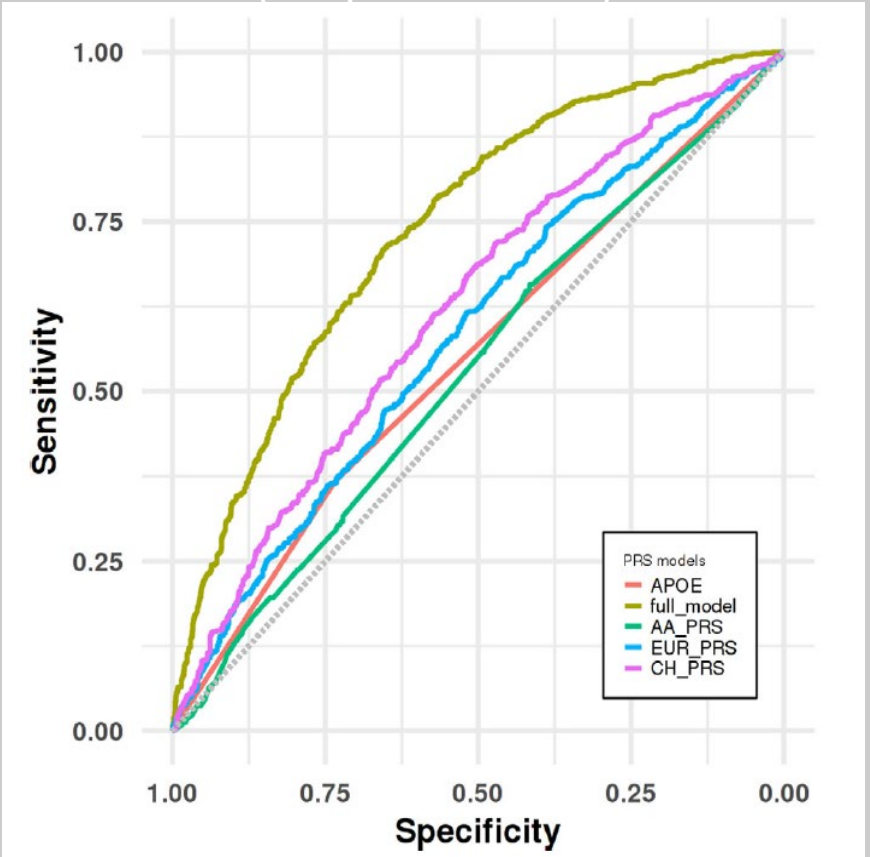


Hollingworth, et al, *Nat Genet.*, 2011
Naj, et al, *Nat Genet.*, 2011

Risk Prediction may not be accurate



Alzheimer's Disease in Hispanic Ancestry
(Sariya et al. 2021)



Critical variants may be missed

- Low frequency variants/variants absent in European populations may be missed
- Rare variants are more likely to be population specific

Rare variants in *AKAP9*

- African Americans (Logue et al. 2014)
- Hispanic families in ADSP (Vardarajan et al. 2016)

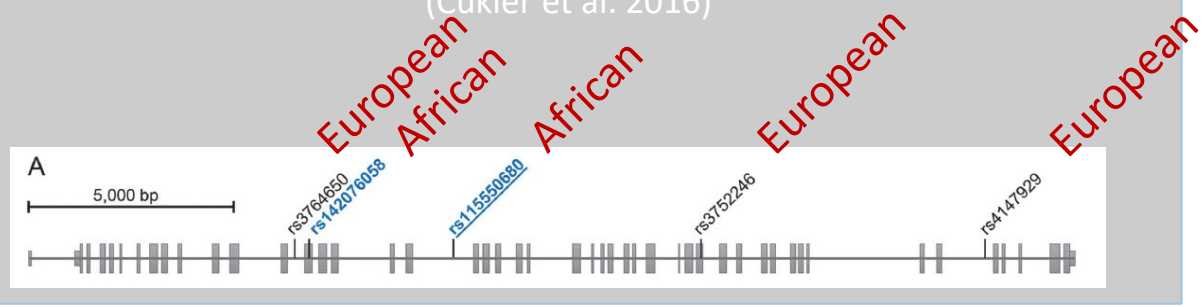
ANNALS of Clinical and Translational Neurology
Open Access
RESEARCH ARTICLE

Whole genome sequencing of Caribbean Hispanic families with late-onset Alzheimer's disease

Badri N. Vardarajan[1,2,3], Sandra Barral[1,2,4], James Jaworski[5], Gary W. Beecham[5], Elizabeth Blue[6], Giuseppe Tosto[1,2], Dolly Reyes-Dumeyer[1,2], Martin Medrano[7], Rafael Lantigua[1,8], Adam Naj[9], Timothy Thornton[10], Anita DeStefano[11], Eden Martin[5], Li-San Wang[9], Lisa Brown[10], William Bush[12], Cornelia van Duijn[13], Allison Goate[14], Lindsay Farrer[11], Jonathan L. Haines[12], Eric Boerwinkle[15], Gerard Schellenberg[9], Ellen Wijsman[6,10], Margaret A. Pericak-Vance[5] & Richard Mayeux[1,2,3,16,17] for The Alzheimer's Disease Sequencing Project[a]

***ABCA7* in European and African Ancestries**

(Cukier et al. 2016)



Novel Rare Loci in African American GWAS

(Kunkle et al. 2020)

IGFIR: chr15q26

AP15: chr11p12

RBFOX1: chr16p13

Genetic Summary

1. **Genetic risk factors for AD can be different defending on your ancestral background**
2. **The mechanisms (pathways) between ancestries appear to be similar, but some pathways may be more important in some ancestries than others**
3. ***ABCA7* is much stronger risk factor for AD in African Ancestry than European**
4. ***ApoE4* is a much weaker risk factor for AD in African Ancestry than European**
5. **The ancestry your patient inherited their *ApoE4* allele from determines their risk for AD from *ApoE4*.**
6. **Different ancestral risks suggest different therapies maybe needed for different ancestries**

Some Recent Studies Applying Ancestry to Genetic Studies.

ADMIXTURE MAPPING

Molecular Psychiatry www.nature.com/mp

ARTICLE

Admixture Mapping of Alzheimer's disease in Caribbean Hispanics identifies a new locus on 22q13.1

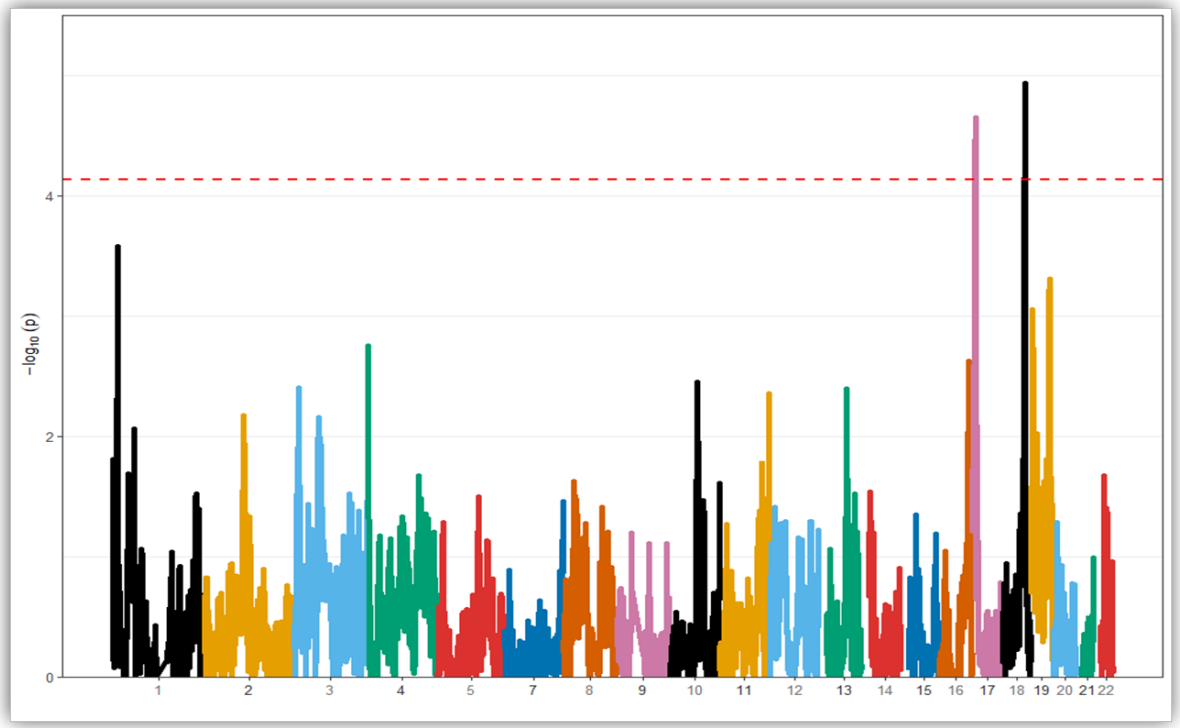
Caghan Kizil[1,2,3,12], Sanjeev Sariya[1,2,4,12], Yoon A. Kim[1,5], Farid Rajabli[6], Eden Martin[6,7], Dolly Reyes-Dumeyer[1,2,4], Badri Vardarajan[1,2,4], Aleyda Maldonado[8], Jonathan L. Haines[9], Richard Mayeux[1,2,4,10,11], Ivonne Z. Jiménez-Velázquez[8], Ismael Santa-Maria[1,5] and Giuseppe Tosto[1,2,4]✉

Late-onset Alzheimer's disease (LOAD) is significantly more frequent in Hispanics than in non-Hispanic Whites. Ancestry may explain these differences across ethnic groups. To this end, we studied a large cohort of Caribbean Hispanics (CH, $N = 8813$) and tested the association between Local Ancestry (LA) and LOAD ("admixture mapping") to identify LOAD-associated ancestral blocks, separately for ancestral components (European [EUR], African [AFR], Native American[NA]) and jointly (AFR + NA). Ancestral blocks significant after permutation were fine-mapped employing multi-ethnic whole-exome sequencing (WES) to identify rare variants associated with LOAD (SKAT-O) and replicated in the UK Biobank WES dataset. Candidate genes were validated studying (A) protein expression in human LOAD and control brains; (B) two animal AD models, Drosophila and Zebrafish. In the joint AFR + NA model, we identified four significant ancestral blocks located on chromosomes 1 (p value = 8.94E-05), 6 (p value = 8.63E-05), 21 (p value = 4.64E-05) and 22 (p value = 1.77E-05). Fine-mapping prioritized the *GCAT* gene on chromosome 22 (SKAT-O p value = 3.45E-05) and replicated in the UK Biobank (SKAT-O p value = 0.05). In LOAD brains, a decrease of 28% in GCAT protein expression was observed (p value = 0.038), and GCAT knockdown in Amyloid-β_{42} Drosophila exacerbated rough eye phenotype (68% increase, p value = 4.84E-09). In zebrafish, *gcat* expression increased after acute amyloidosis (34%, p value = 0.0049), and decreased upon anti-inflammatory Interleukin-4 (39%, p value = 2.3E-05). Admixture mapping uncovered genomic regions harboring new LOAD-associated loci that might explain the observed different frequency of LOAD across ethnic groups. Our results suggest that the inflammation-related activity of *GCAT* is a response to amyloid toxicity, and reduced *GCAT* expression exacerbates AD pathology.

Molecular Psychiatry; https://doi.org/10.1038/s41380-022-01526-6

Admixture mapping identifies novel Alzheimer disease risk regions in African Americans.

Farid Rajabli[1], Giuseppe Tosto[2], Kara L. Hamilton-Nelson[1], Brian W. Kunkle[1], Badri N. Vardarajan[2], Adam Naj[3], Patrice G. Whitehead[1], Olivia K. Gardner[1], William S. Bush[4], Sanjeev Sariya[2], Richard P. Mayeux[2], Lindsay A. Farrer[5], Michael L. Cuccaro[1,6], Jeffrey M. Vance[1,6], Anthony J. Griswold[1,6], Gerard D. Schellenberg[3] , Jonathan L. Haines[4], Goldie S. Byrd[7], Christiane Reitz[2], Gary W. Beecham[1,6], Margaret A. Pericak-Vance[1,6], Eden R. Martin[1,6*], for the Alzheimer's Disease Genetics Consortium (ADGC), Collaboration on Alzheimer's Disease Research (CADRE) and Alzheimer's Disease Sequencing Project (ADSP) (***IN PRESS, ALZ DIS & DEMENTIA)***



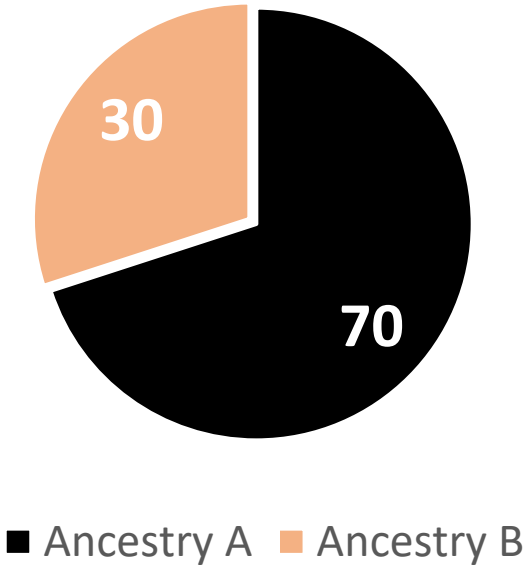
Why Admixture Mapping ?

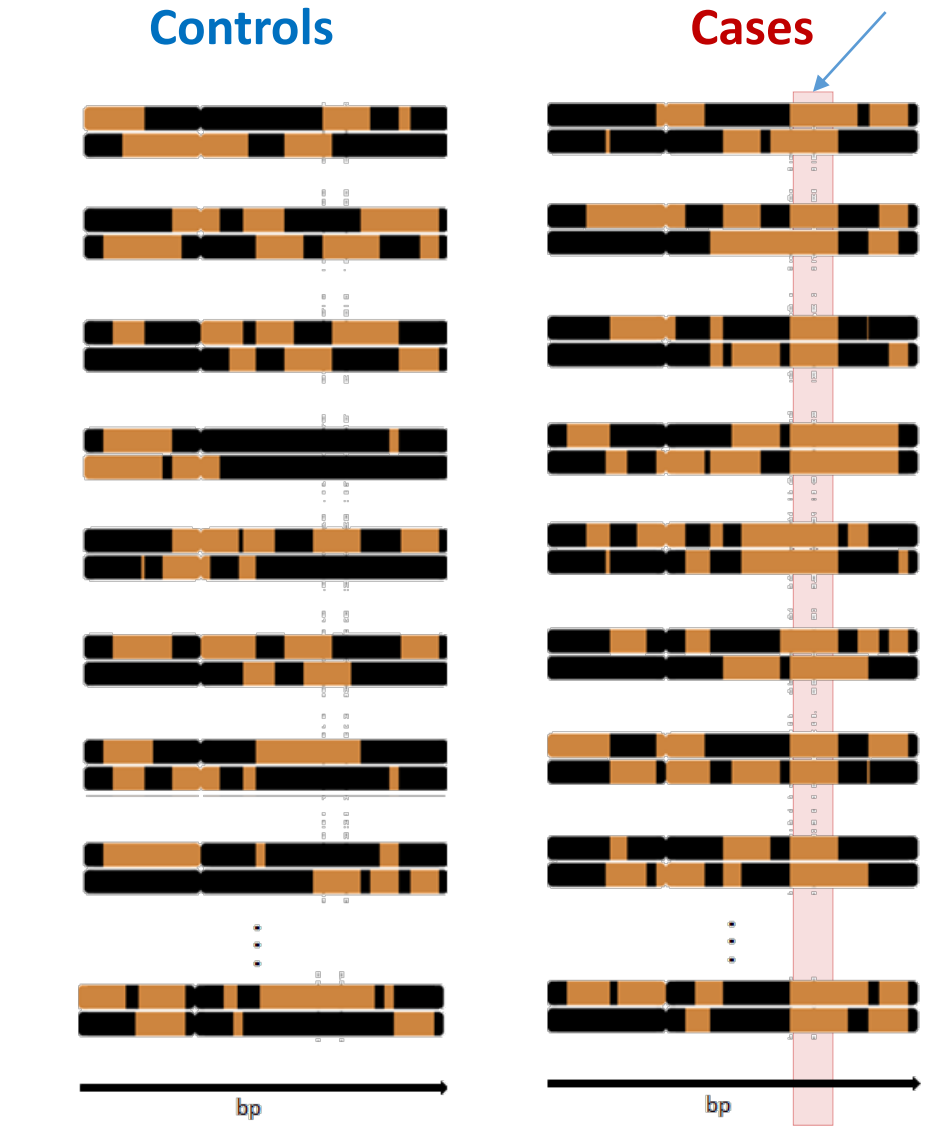
- The admixture mapping has a lower multiple testing burden than SNP-based GWAS studies

- Identifies wide genomic regions that might harbor multiple risk loci

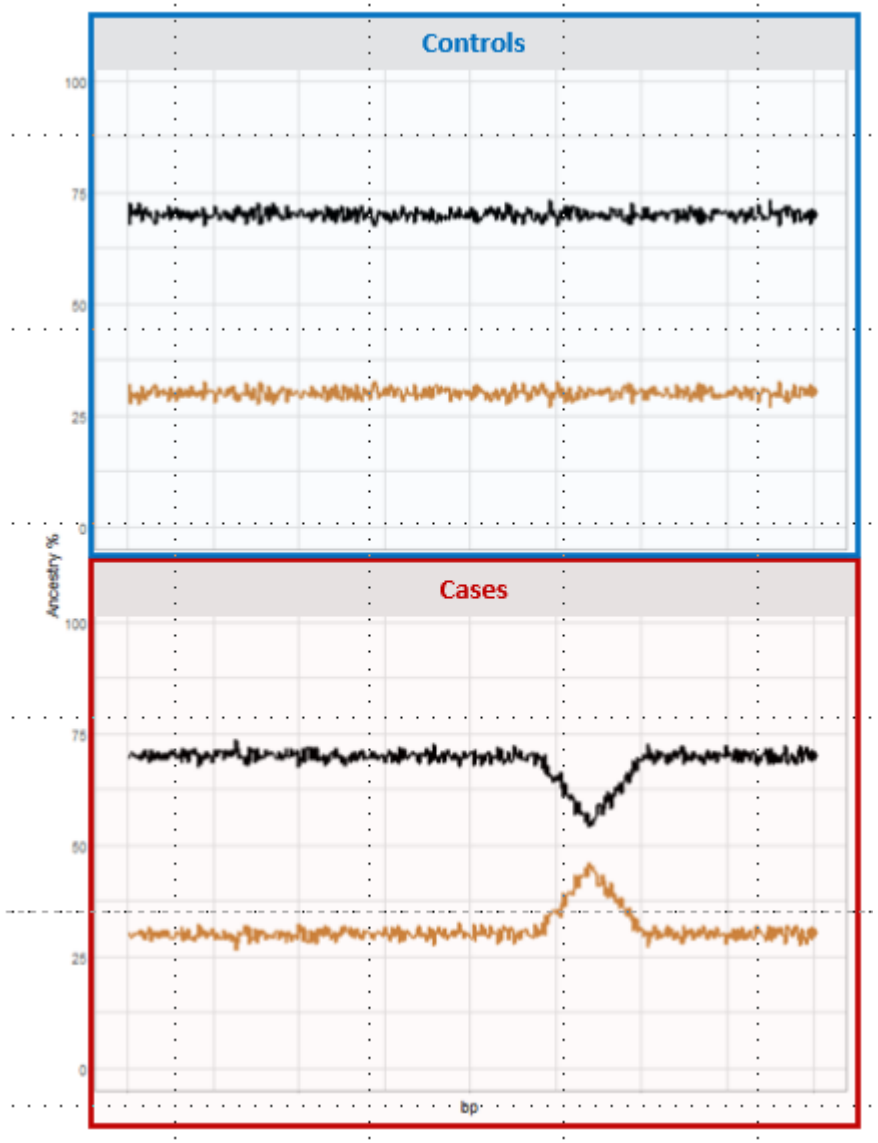
Admixture Mapping

Admixed Population X

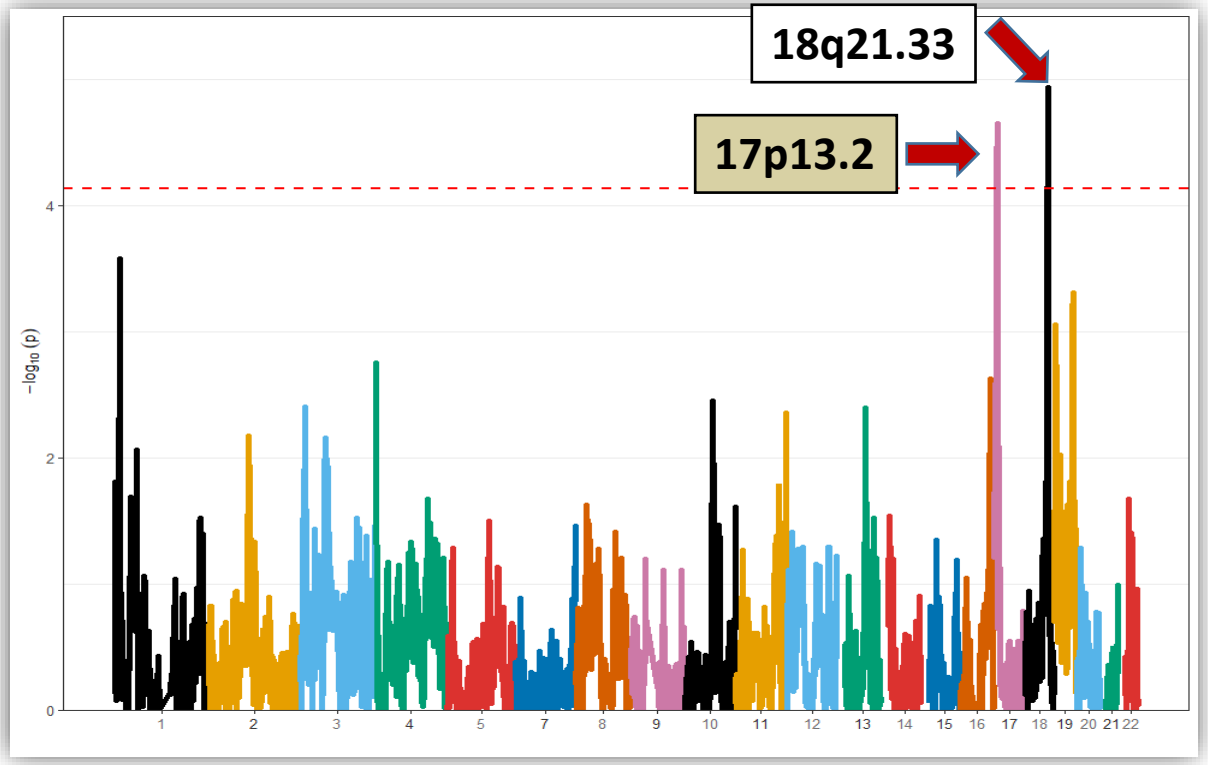




Risk locus; $MAF_B \gg MAF_A$

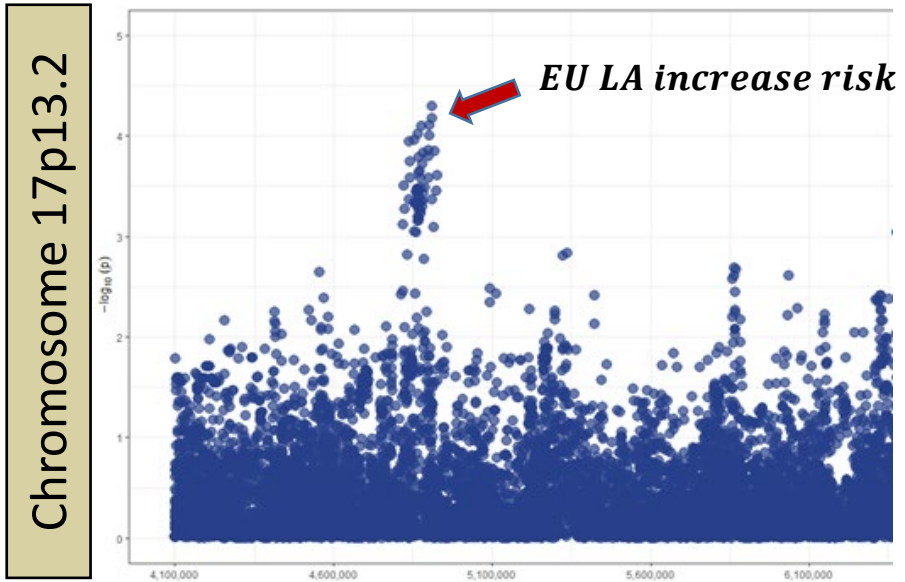


Admixture Mapping Results



Fine-Mapping

(i) Ancestry-aware regression analysis



(ii) Differential Gene-expression Analysis

Significant differential gene-expression results of peripheral blood and post-mortem brain tissues studies*

LOCUS	GENE NAME
Chr.17p13.2	GP1BA
	SLC25A11
	MINK1
Chr. 18q21.33	BCL2

(*) Griswold et al, 2019; ROSMAP, MSBB, Mayo

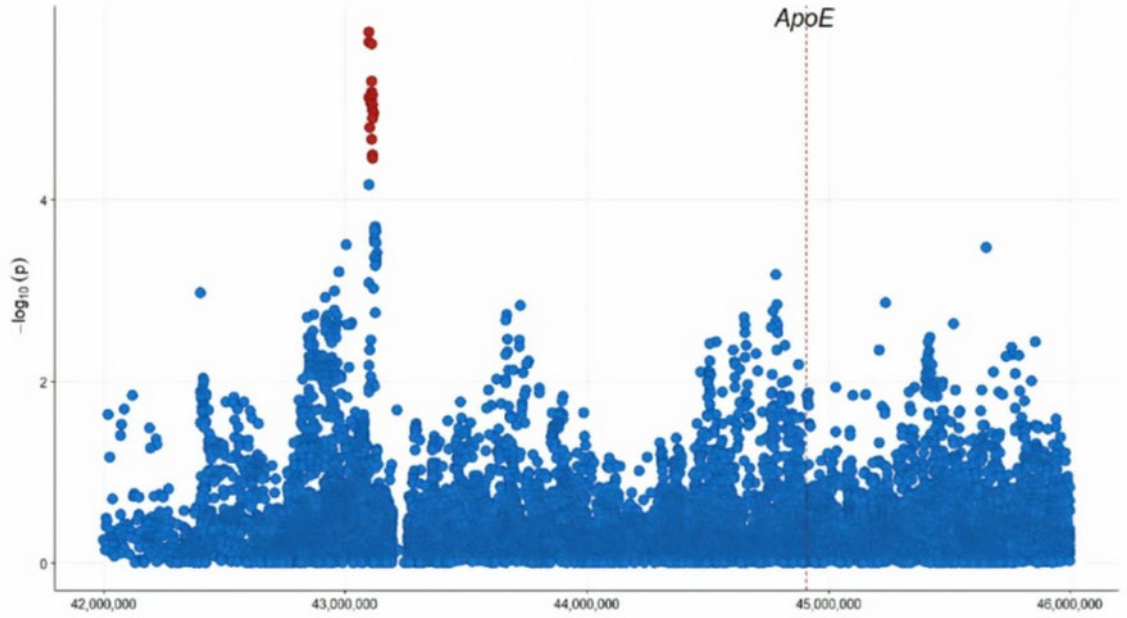
Summary

- We identified two novel genome-wide significant admixture mapping signals in AA population:
  - on chromosomes **17p13.2** and **18q21.33**
- Our study **generalized** the European genetic AD risk locus (17p13.2) to the AA population.
- Our ancestry-aware analysis showed that AA individuals **have a lower risk of AD** if they inherited African ancestry at the **17p13.2 locus**
- Our fine-mapping revealed several interesting candidate genes, some of which were implicated to contribute to AD risk such as ***SLC25A11***, ***MINK1*** and ***BCL2***.

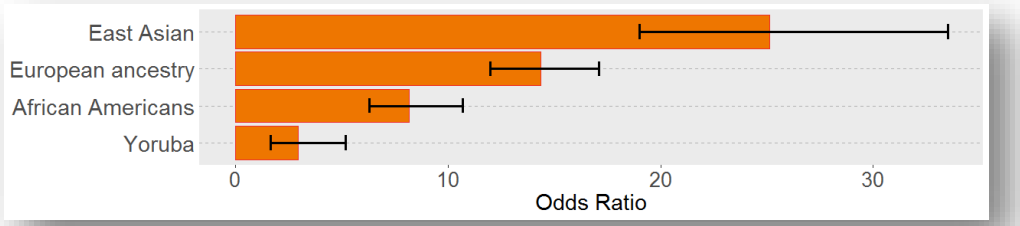
IDENTIFYING THE APOE PROTECTIVE EFFECT

A locus at 19q13.31 significantly reduces the *ApoE* ε4 risk for Alzheimer's Disease in African Ancestry *PLOS GENETICS, 2022)*

Farid Rajabli[1], Gary W. Beecham[1,2], Hugh C. Hendrie[3], Olusegun Baiyewu[4], Adesola Ogunniyi[4], Sujuan Gao[5], Nicholas A. Kushch[1], Marina Lipkin-Vasquez[1], Kara L. Hamilton-Nelson[1], Juan I. Young[1,2], Derek M. Dykxhoorn[1,2], Karen Nuytemans[1,2], Brian W. Kunkle[1,2], Liyong Wang[1,2], Fulai Jin[6], Xiaoxiao Liu[6], Briseida E. Feliciano-Astacio[7], Alzheimer's Disease Sequencing Project, Alzheimer's Disease Genetic Consortium, Gerard D. Schellenberg[8], Clifton L. Dalgard[9], Anthony J. Griswold[1,2], Goldie S. Byrd[10], Christiane Reitz[11], Michael L. Cuccaro[1,2], Jonathan L. Haines[12], Margaret A. Pericak-Vance[1,2], Jeffery M. Vance[1,2]*



Identifying the Protective effect of the African genome for ApoE4

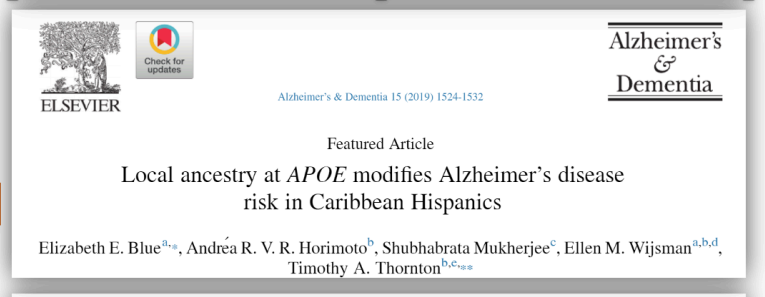


Risk for AD from ApoE4


PLOS GENETICS

RESEARCH ARTICLE

Ancestral origin of *ApoE ε4* Alzheimer disease risk in Puerto Rican and African American populations

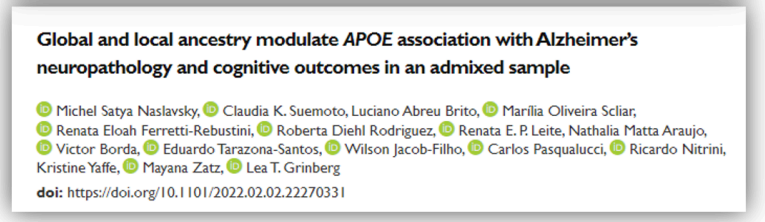

ELSEVIER

Alzheimer's & Dementia 15 (2019) 1524-1532

Alzheimer's & Dementia

Featured Article

Local ancestry at *APOE* modifies Alzheimer's disease risk in Caribbean Hispanics


Global and local ancestry modulate *APOE* association with Alzheimer's neuropathology and cognitive outcomes in an admixed sample

Due to local ancestry surrounding ApoE

Autopsy studies in different LA

Single nuclei RNAseq, ATACseq, HiC

Sequence differences in LA region

Interaction with ApoE4 and differences In function due to sequence

Inducible Pluripotent Stem Cell studies

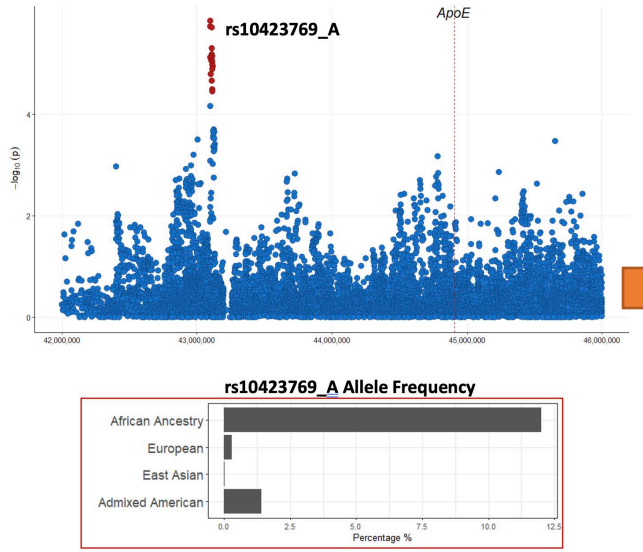
African and European LA

CRISPR

Potential Protective Variant RF1AG059018-Vance

New protective locus for ApoE4 (Rajabli et al 2022)

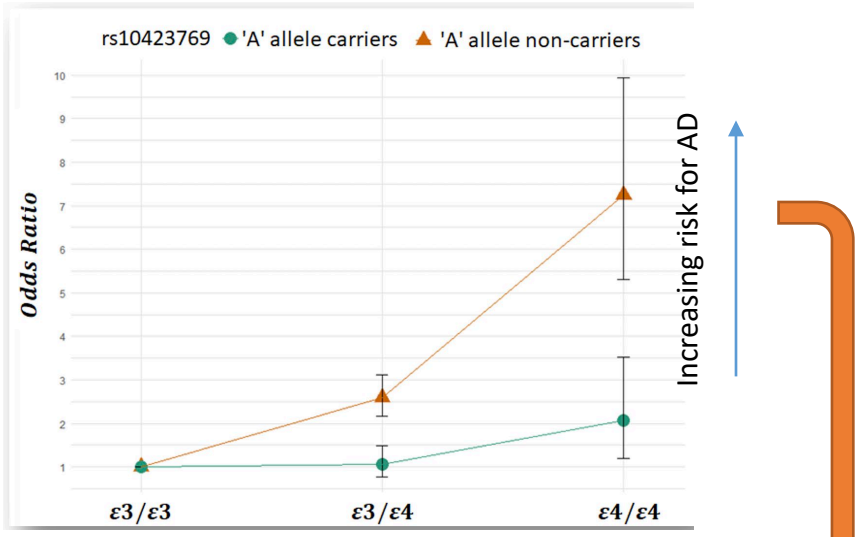
Interaction with ApoE4 in 6,500 African Americans



Replicated in

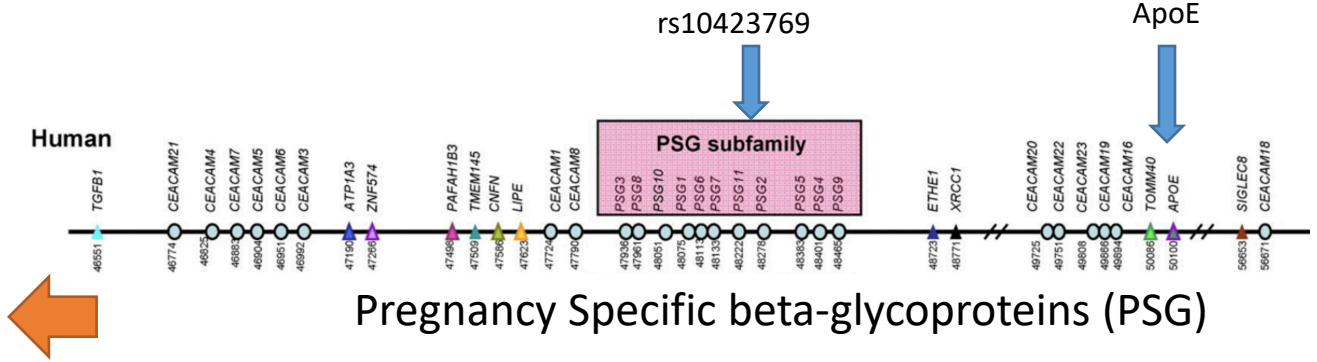
Ibadan/Nigeria N~ 700

Puerto Ricans N~ 550



ApoE genotypes

- This study identified a new African ancestry-specific haplotype that reduces the AD risk effect of *APOE* ε4 homozygotes in African ancestry by approximately 75%.
- 2 mB from ApoE and lack of known AD genes surrounding rs10423769 suggests novel mechanism of protection
- Located in area of high segmental DNA duplications
- Rs10423769 is a splicing qTL for TMEM145, expressed in brain, highest in cerebellum



Pregnancy Specific beta-glycoproteins (PSG)

2 megabases

adsp
Alzheimer's Disease Sequencing Project

HOME | ABOUT | DATA ACCESS | STUDY INFO | CONTACT US | LINKS | ADSP SITE LOGIN

Welcome to the **Alzheimer's Disease Sequencing Project**

The overarching goals of the ADSP are to:

1. Identify new genomic variants contributing to increased risk of developing Late-Onset Alzheimer's Disease (LOAD)
2. Identify new genomic variants contributing to protection against developing Alzheimer's Disease (AD)
3. Provide insight as to why individuals with known risk factor variants escape from developing AD
4. Examine these factors in multi-ethnic populations as applicable in order to identify new pathways for disease prevention

Study Design
Learn about study design, sample selection, and data generation procedures

Apply for Data
Instructions on how to apply for ADSP data

Access Data
Log into NIAGADS DSS

News

- Wednesday, March 3, 2021 - 09:15
  NIAGADS DSS Releases Additional 17K Whole Genomes
- Wednesday, February 19, 2020 - 15:30
  NIAGADS DSS Releases 20K Whole Exomes
- Monday, November 5, 2018 - 20:30
  Additional ADSP Data Released on NIAGADS DSS
- Friday, September 7, 2018 - 19:15
  NIAGADS Data Sharing Service Now Accepting Applications
- Friday, April 13, 2018 - 18:15
  Genetic variation paper published in Dementia and Geriatric Cognitive Disorders

Home | About | Data Access | Study Info | Contacts | Links |

NIAGADS

Funded by:
National Institute For Aging

https://www.niagads.org/adsp/content/home

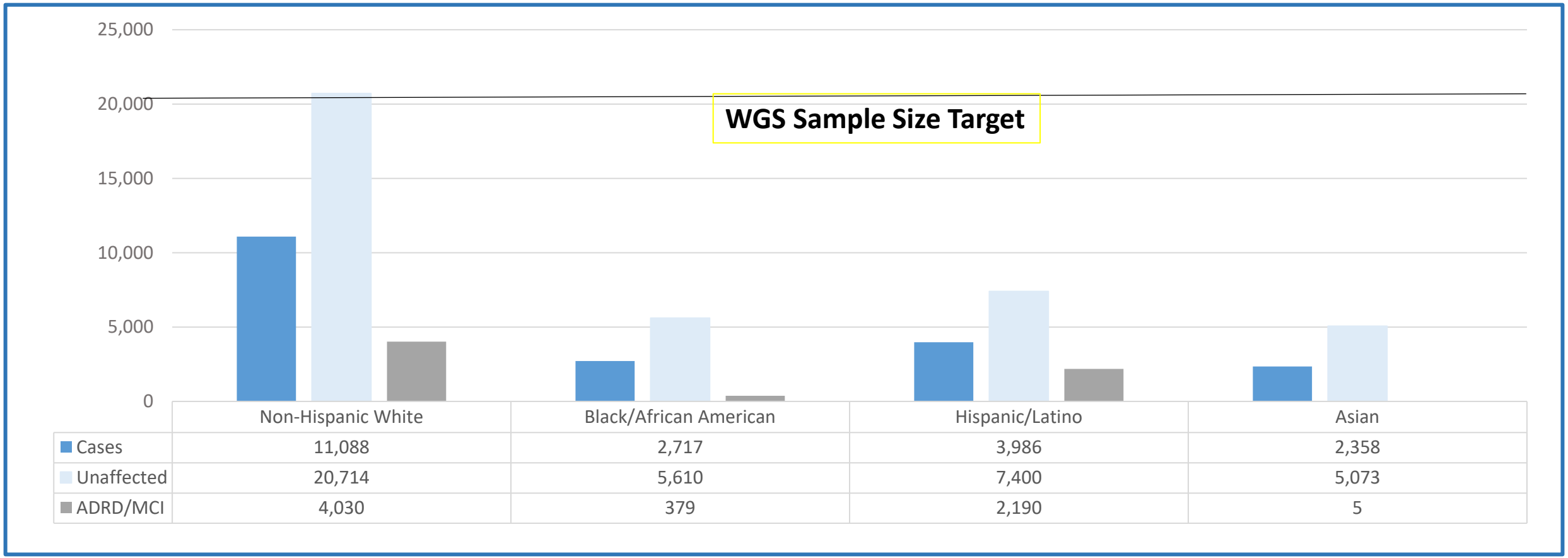
Alzheimer's Disease
Sequencing Project Follow-up Study (ADSP-FUS)*

Global Effort to Generate Whole Genome Sequencing in Alzheimer's Disease

Identify new genomic variants contributing to increased risk of developing and protection against Alzheimer's Disease (AD)

Examine these factors in multi-ethnic populations as applicable in order to identify new pathways for disease prevention

**https://www.niagads.org/adsp/content/home*



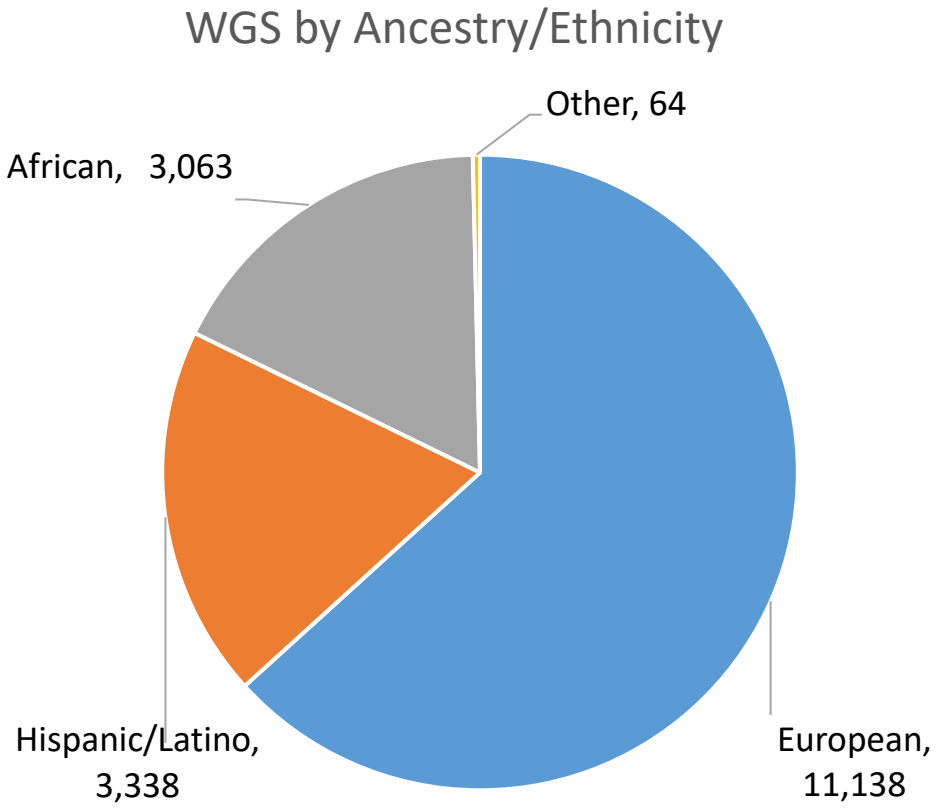
	Non-Hispanic White	Black/African American	Hispanic/Latino	Asian
Cases	11,088	2,717	3,986	2,358
Unaffected	20,714	5,610	7,400	5,073
ADRD/MCI	4,030	379	2,190	5

Cases

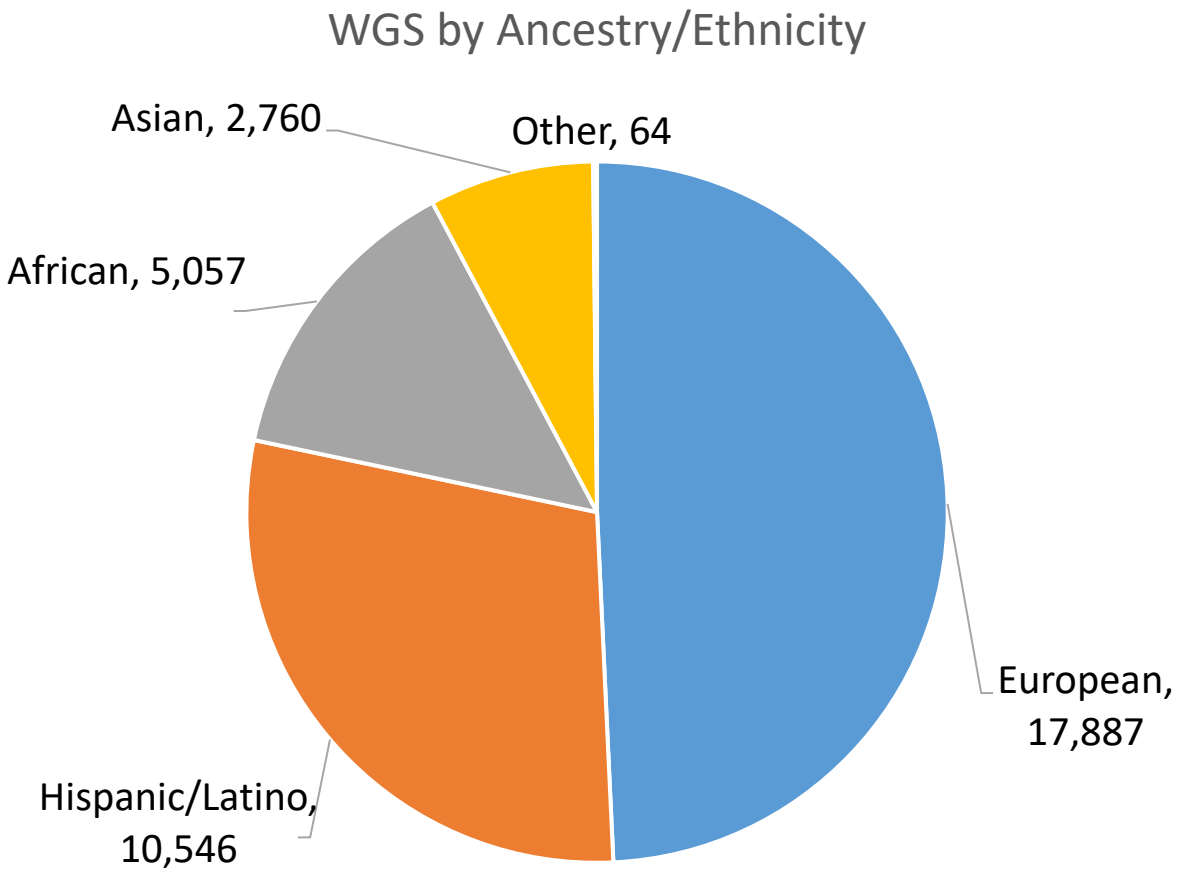
Unaffected

ADRD/
Mild Cognitive Impairment (MCI)/
PSP

r3 (17k) release 2021



r4 (36k) initial release Fall 2022



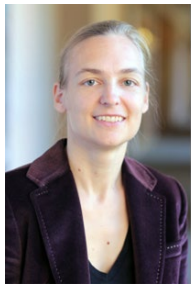
Recruitment and Retention for AD Diversity Genetic Cohorts in the ADSP (READD-ADSP)

University of Miami
Margaret Pericak-Vance
Brian Kunkle
Jeffery Vance



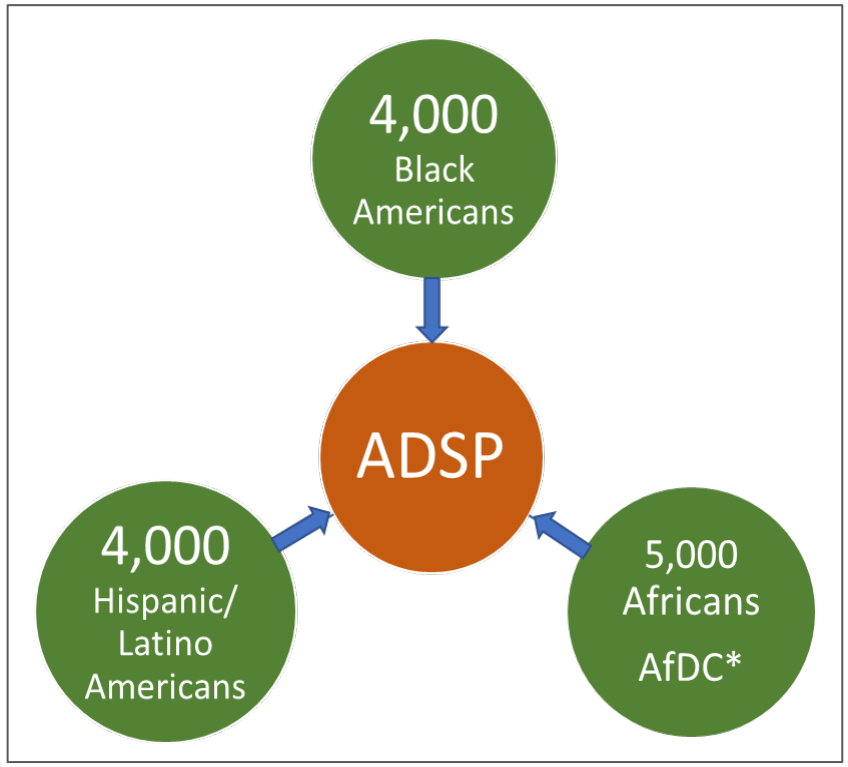
Wake Forest University
Goldie Byrd

Columbia University
Giuseppe Tosto
Christiane Reitz

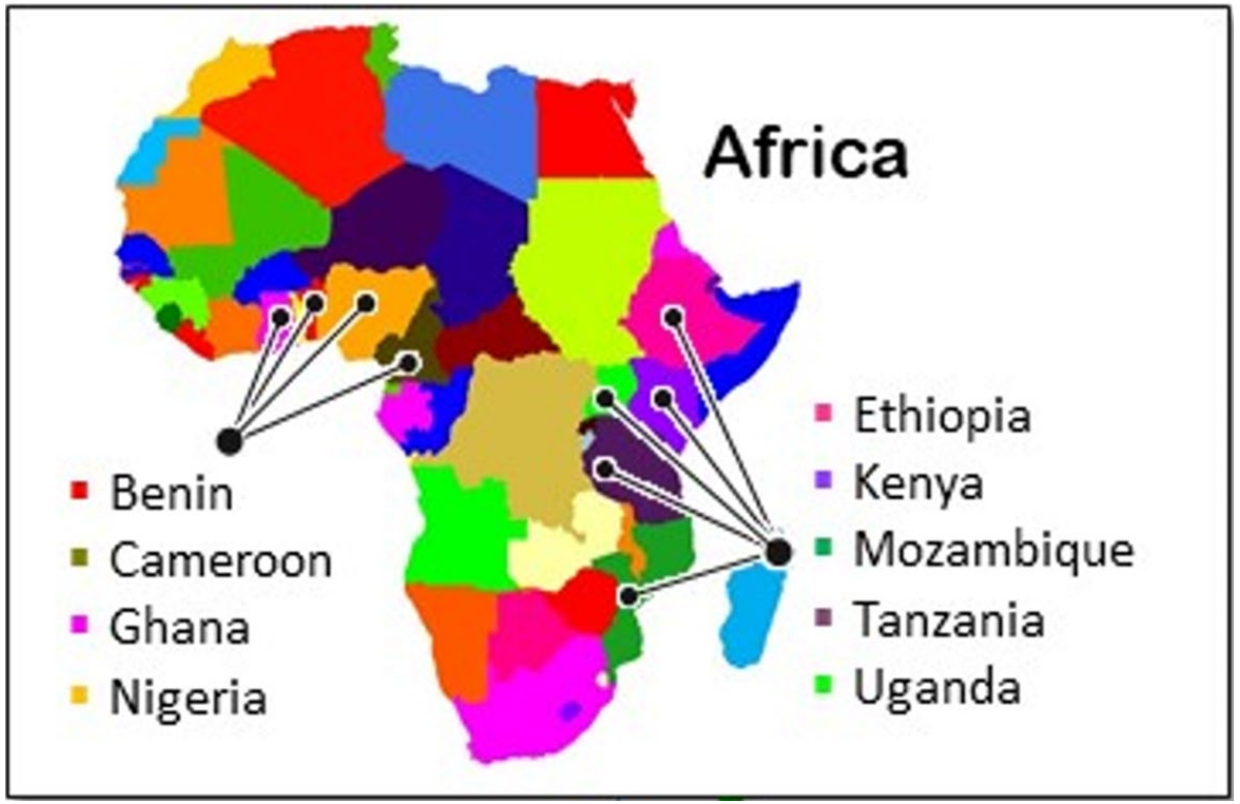



University of Ibadan
Rufus Akinyemi
Adesola Ogunniyi


Case Western Reserve University
Jonathan Haines
Will Bush

*AfDC; African Dementia Consortium



READ-ADSP GOALS

- DNA, RNA, Plasma Biomarkers and CVD markers and extensive phenotyping
- Whole Genome Sequencing
- Social Determinants of Health (SDOH) also influence AD risk, but studies collecting both biological and SDOH data are rare. *Collecting SDOH data provides a basis for the integrative studies of biological and social risks of AD.*

Dr. Azizi Seixas (U of Miami)

Dr. Joshua Akinyemi (University of Ibadan, Nigeria)

ADSP FOREIGN COHORTS

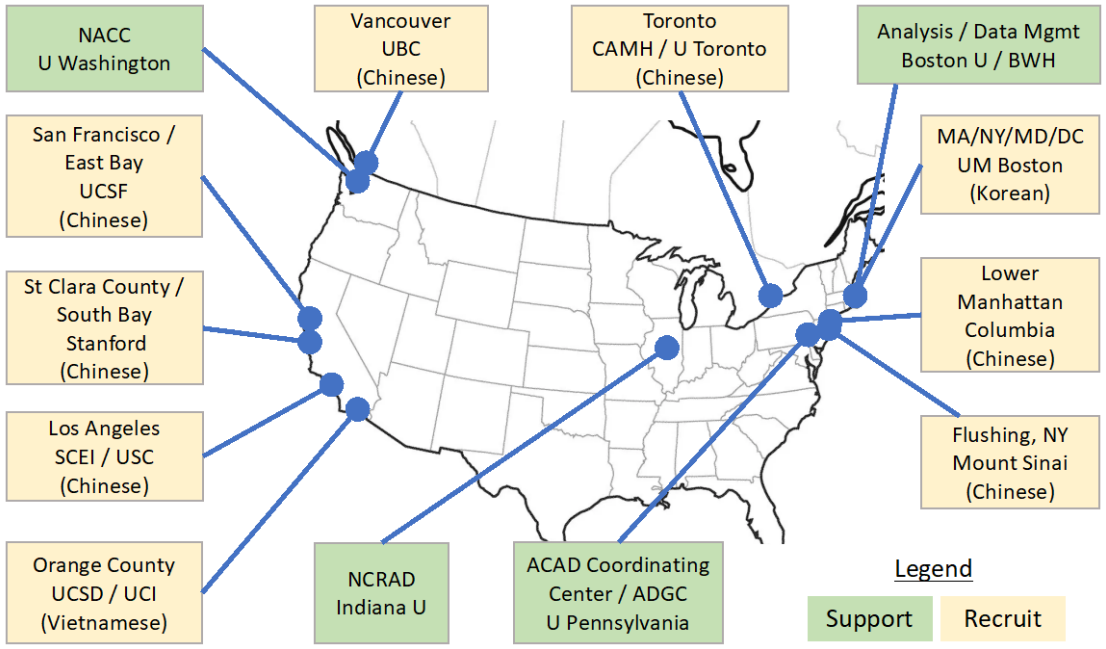
- **Gwangju Alzheimer's & Related Dementias (GARD) Study – Korea**
  - PI: Lindsay Farrer (Boston University)
  - Korea site PI: Kunho Lee (Chosun University)
- **Aspirin in Reducing Events in the Elderly (ASPREE) Trial cohort – Australia**
  - PI: Paul Lacaze (Monash University)
- **Interaction between SARS-CoV-2 Infection and Ancestral genomic Variations in the Risk of Alzheimer's Disease and Related Disorders (ISAVRAD) - Argentina**
  - PI: Gabriel De Erausquin (UT San Antonio)
- **Longitudinal Aging Study in India – Diagnostic Assessment of Dementia (LASI-DAD) – India**
  - PI: Jincook Li (University of Southern California)





Asian Cohort for Alzheimer's Disease

ACAD
Asian Cohort for Alzheimer's Disease



- **R56 phase: 1,000 Chinese in US and Canada**, additional pilots for Vietnamese and Korean Americans at two sites
- Eventually 5,000 participants in 5 years: Chinese / Korean / Vietnamese Ancestry in US and Canada
- Culturally appropriate recruitment and assessment
- DNA for genetics and plasma for blood-based biomarkers

Li-San Wang (王立三)
University of Pennsylvania, PI

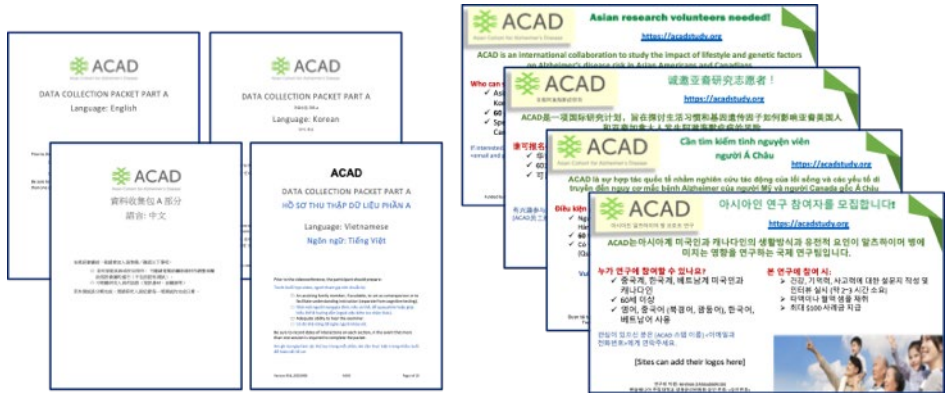
Helena Chui
University of Southern California, PI

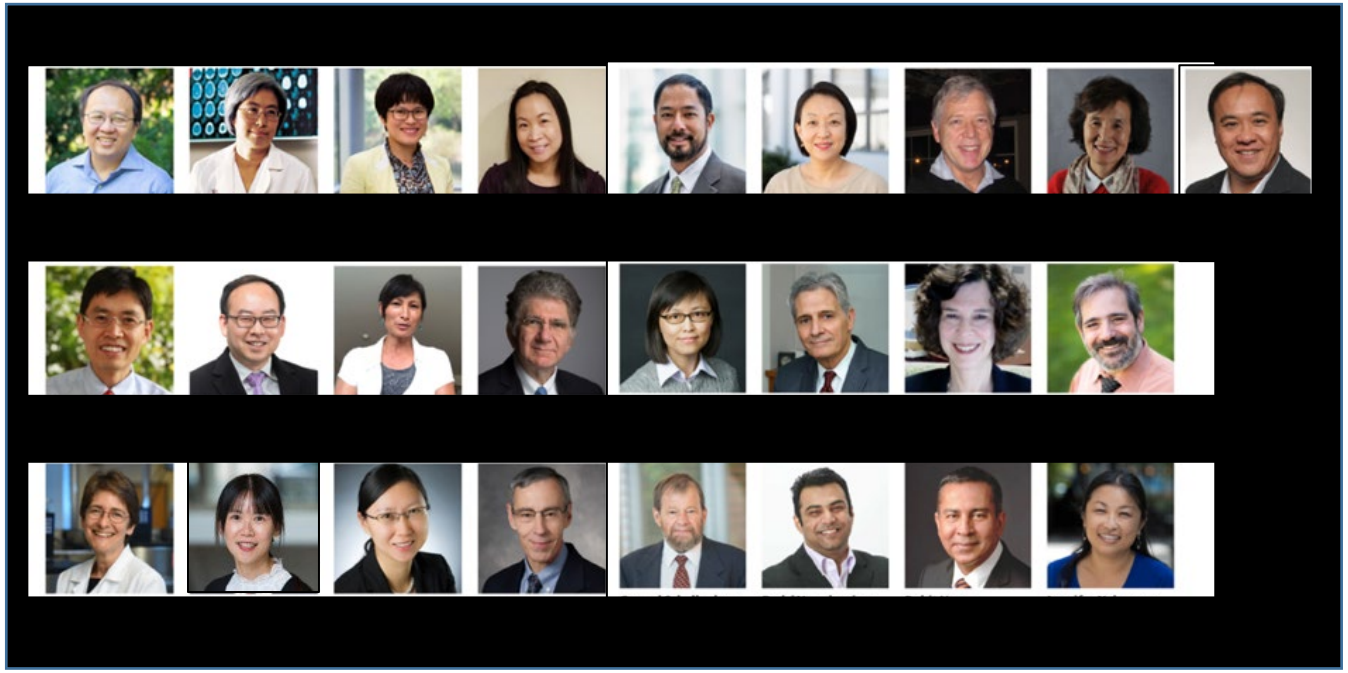
Gyungah Jun (전,경아)
Boston University, PI

Van Park (Tạ Mỹ Vân)
University of California San Francisco, PI

ACAD Strategy

- 3-Part Data Collection Packet based on NACC UDS; translated into Chinese, Vietnamese, Korean
- Translated validated cognitive test instruments
- Training/outreach material and REDCap data capture
- Recruitment started in September 2021; >1000 signed up, ~500 completed assessment
- Community-Based Participatory Research (CBPR)
- Interdisciplinary team/international collaboration





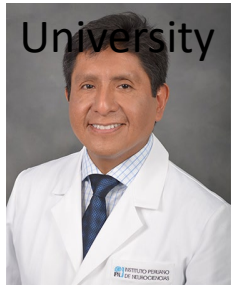
Studies in Amerindian populations in South America

Principal Investigators

Giuseppe Tosto
Columbia University

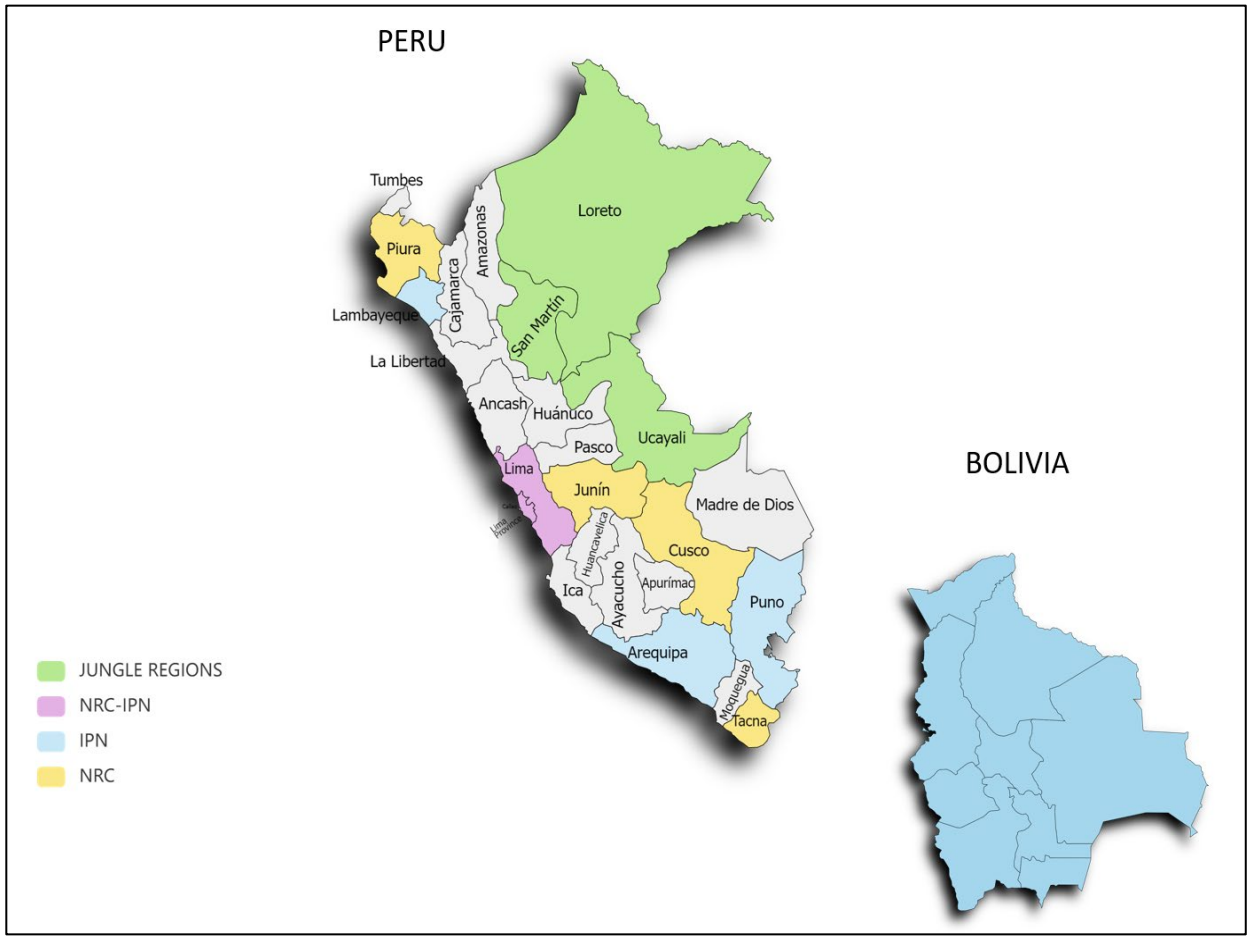
Mario Cornejo-Olivas
San Marcos Foundation and Instituto Nacional de Ciencias Neurologicas (NRC)

Eden R. Martin
University of Miami



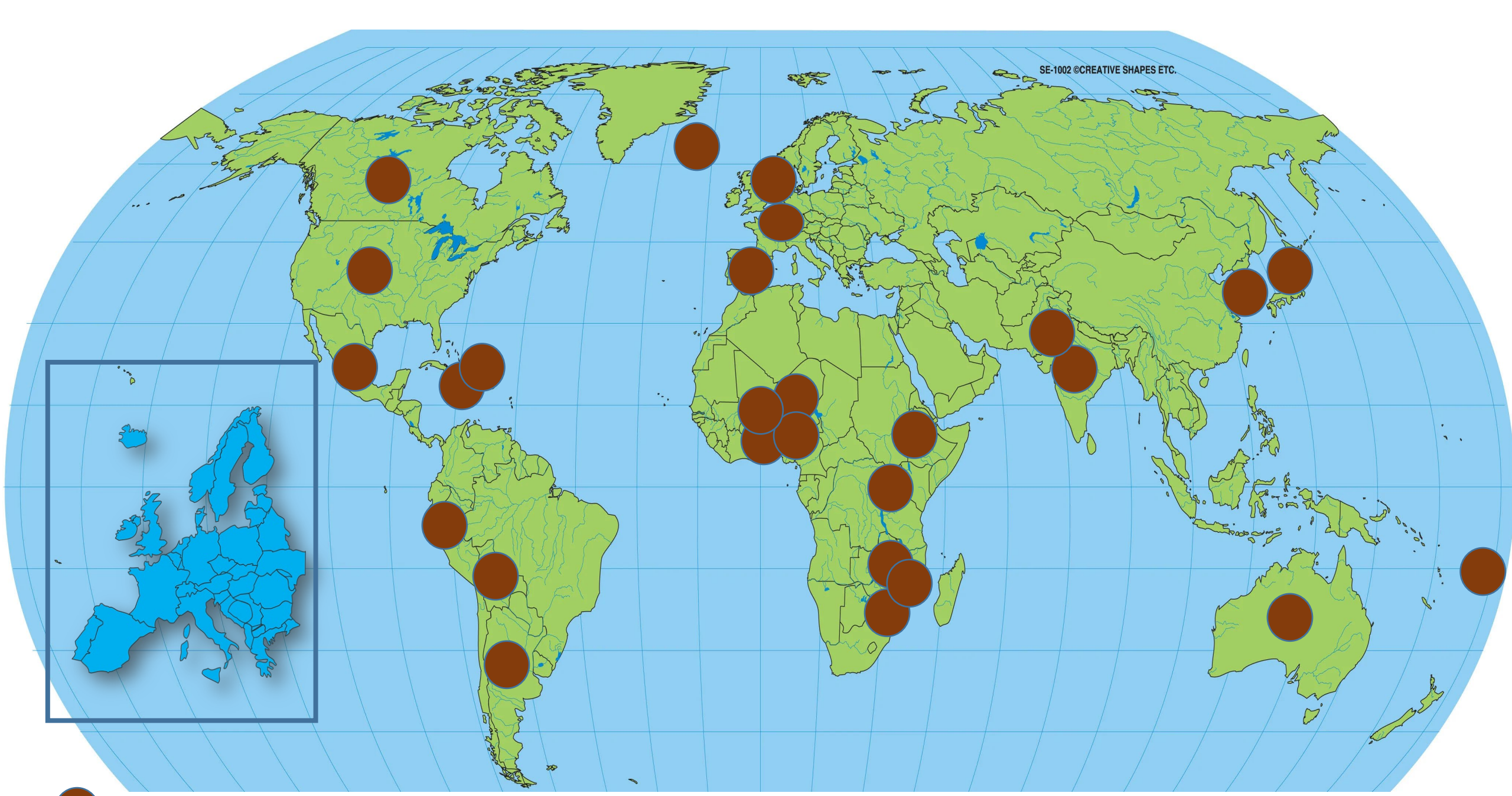
Nilton Custodio
Instituto Peruano de Neurociencias

Margaret Pericak-Vance
University of Miami



Enrollment

- 1,700 dementia cases and 1,850 healthy controls
  - 7 sites in Peru
  - 1 site in Bolivia



International Expansion: ADSP and Collaborators

- Genetic risk factors for AD can be different depending on your ancestral background
- The mechanisms (pathways) between ancestries appear to be similar, but some genes/pathways may be more important in some ancestries than others
- Investigating the relationship between genetic ancestry, SDOH and disease may inform precision medicine initiatives, risk assessment, and development of ancestry-specific therapeutics and prevention strategies
- ADSP FUS focused on increasing Asian, African and Hispanic/Latino Ancestry Participants

Critical need to significantly increase diversity in genomic analyses to truly achieve the ability to conduct cross-ancestry comparisons and clarify differences in genetic etiology and potential molecular therapeutic targets

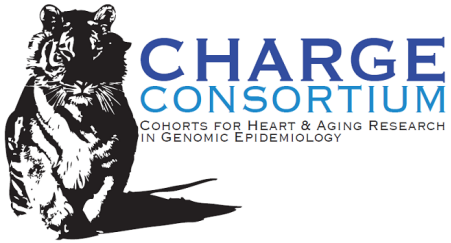
Acknowledgments

Members of the Alzheimer's Disease Sequencing Project (ADSP) Follow-Up Study Implementation Team

University of Miami	Columbia University	NCRAD	USUHS	University of Pennsylvania
Margaret Pericak-Vance	Richard Mayeux	Tatiana Faroud	Clifton Dalgard	Jerry Schellenberg
Brian Kunkle	Giuseppe Tosto	Kelley Faber		Li-San Wang
Jeffery M Vance	Badri Vardarajan	Kelly Nudelman		Adam Naj
Michael Cuccaro	Dolly Reyes			Fanny Leung
Eden Martin				
Anthony Griswold				
Pedro Mena				
Larry Adams				
Patrice Whitehead				
Jovita Inciute				

Thanks to all the researchers and collaborators who have contributed cohorts and to all the patients who have participated in the studies

NIH National Institute on Aging



ADGC Alzheimer's Disease Genetics Consortium

Marilyn Miller **Alison Yao**

Damali Martin