

THE NATION'S FIRST AFRICAN ANCESTRY NEUROSCIENCE RESEARCH INITIATIVE

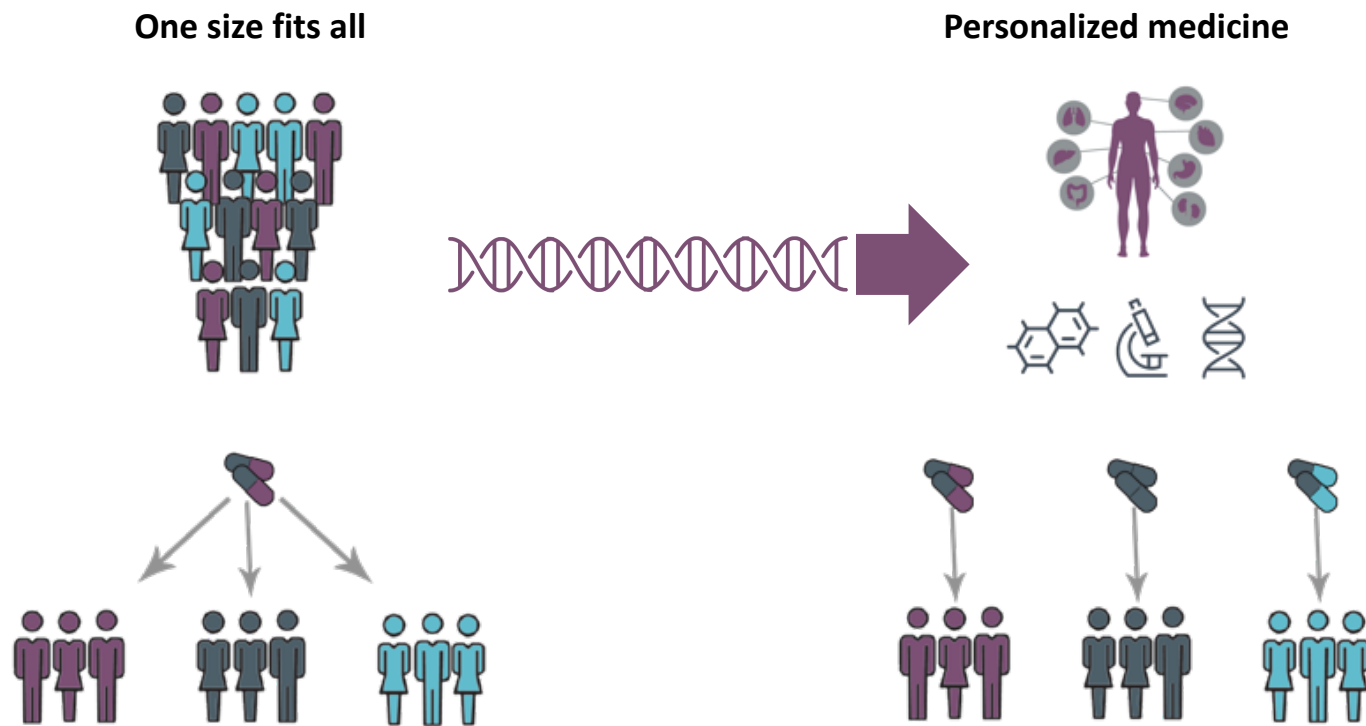
Our Goal:

To reduce health disparities
in brain research in order
to ensure that all people
have equitable access to
new treatments.

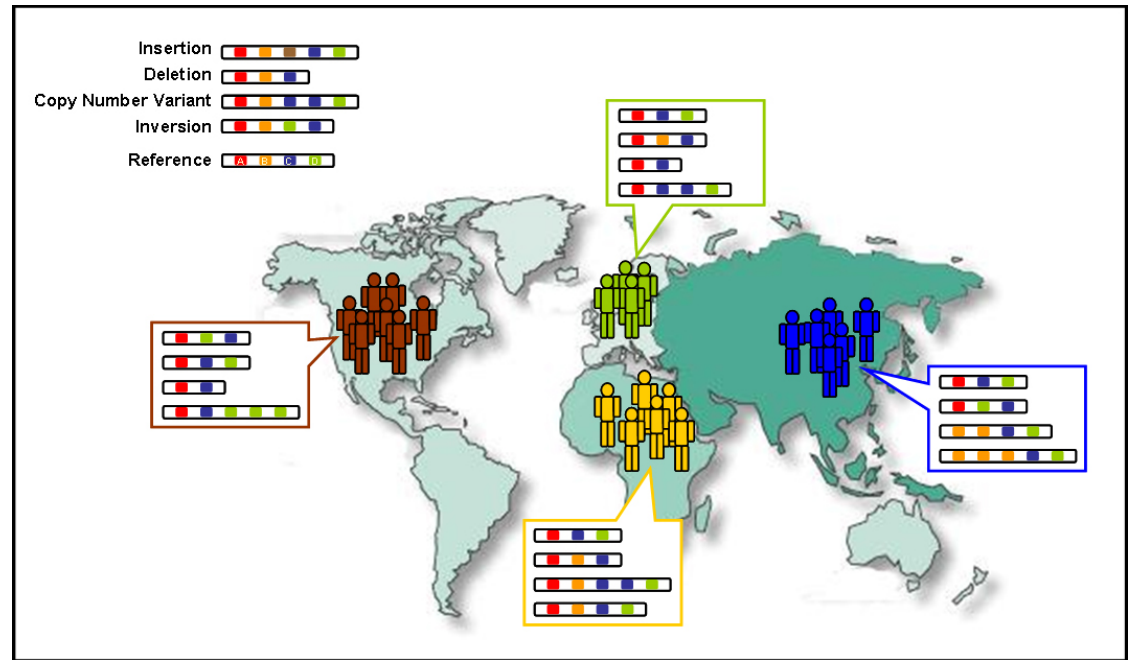
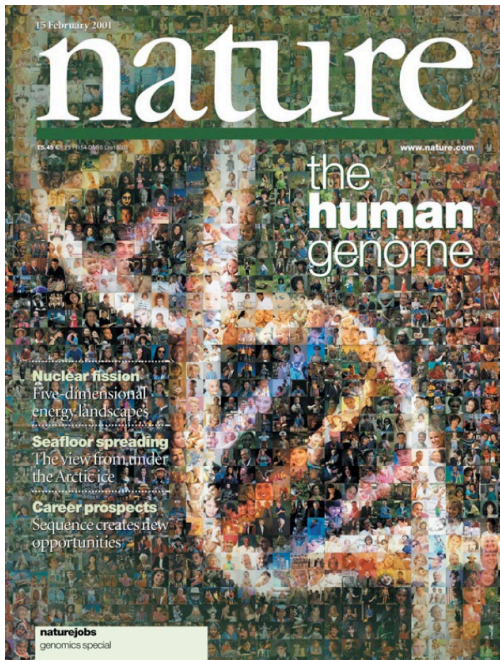


GENOMIC INFORMATION IS DRIVING THE PERSONALIZED MEDICINE FRONTIER

Personalized medicine promises delivery of the right intervention to the right patient at the right time.



PERSONALIZED MEDICINE IS BASED ON A REFERENCE GENOME



2001: the first draft of the human genome

- 3 billion “letters” of DNA
- Represents one healthy individual
- The “parts list” that reveals much of human biology
- Can be used to detect causes of inherited disease
- Can be used to map the variation among human populations

MINORITY POPULATIONS ARE SIGNIFICANTLY UNDERREPRESENTED IN GENOMIC RESEARCH

- A recent analysis revealed that the human reference genome, used universally in genetic research to-date, **omits almost 10% of the African genome** (roughly 300 million base pairs).



<16%
of the world is of
European descent, but

81%
of large-scale genomic
datasets are of people
of
European descent

These disparities have tremendous implications for minority populations expecting to benefit from personalized medicine.

RESEARCH LANDSCAPE

4.9+ MILLION

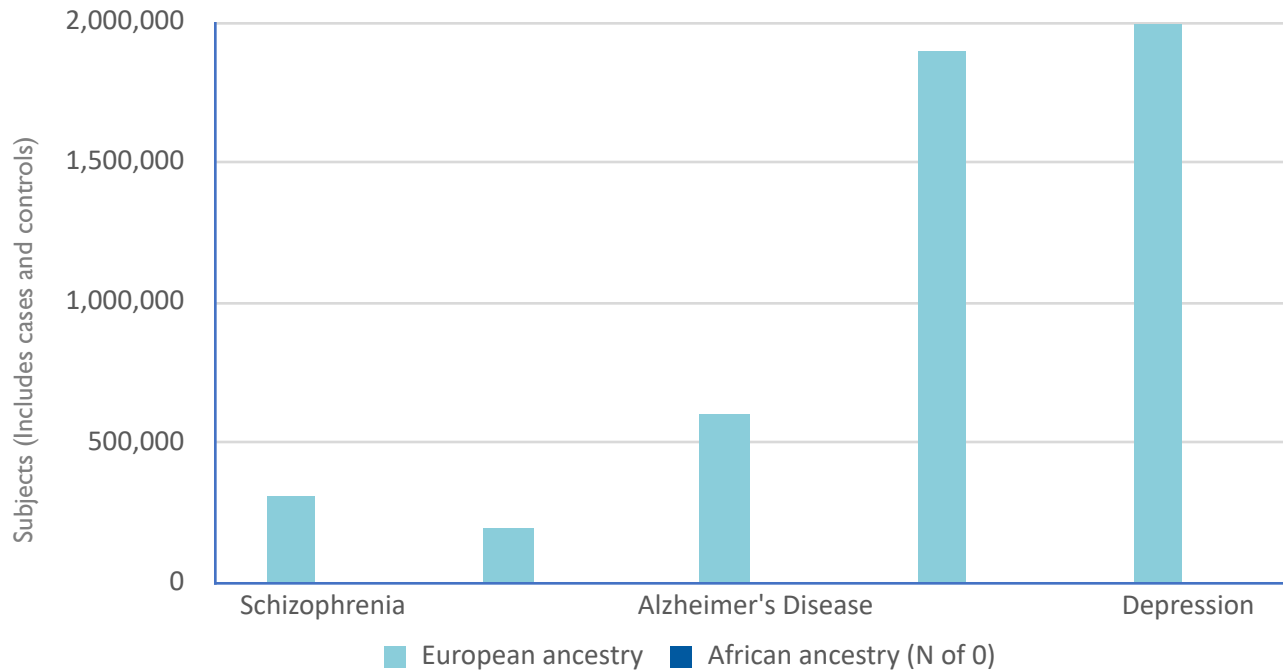
Research subjects

ZERO

Individuals of African ancestry

In the latest genome-wide association studies for Schizophrenia, Autism Spectrum Disorders, Alzheimer's Disease, Parkinson's Disease, and Major Depressive Disorder

Ancestry Representation in Latest GWAS:
African ancestry cohort = N of 0



Weinberger, Dzirasa,
Crompton-Young.
August 5, 2020

SUSCEPTIBILITY TO BRAIN DISORDERS

ALZHEIMER'S DISEASE

- **African Americans** are about **twice as likely** as European Americans to have **Alzheimer's Disease (AD)** and show a different pattern of association with known AD genes (**JAMA 1998**).
- The vast majority of research has focused on the APOE gene, which has a much greater effect in individuals of European ancestry.
- We have known this for **20 years** and we still don't understand why.

STROKE

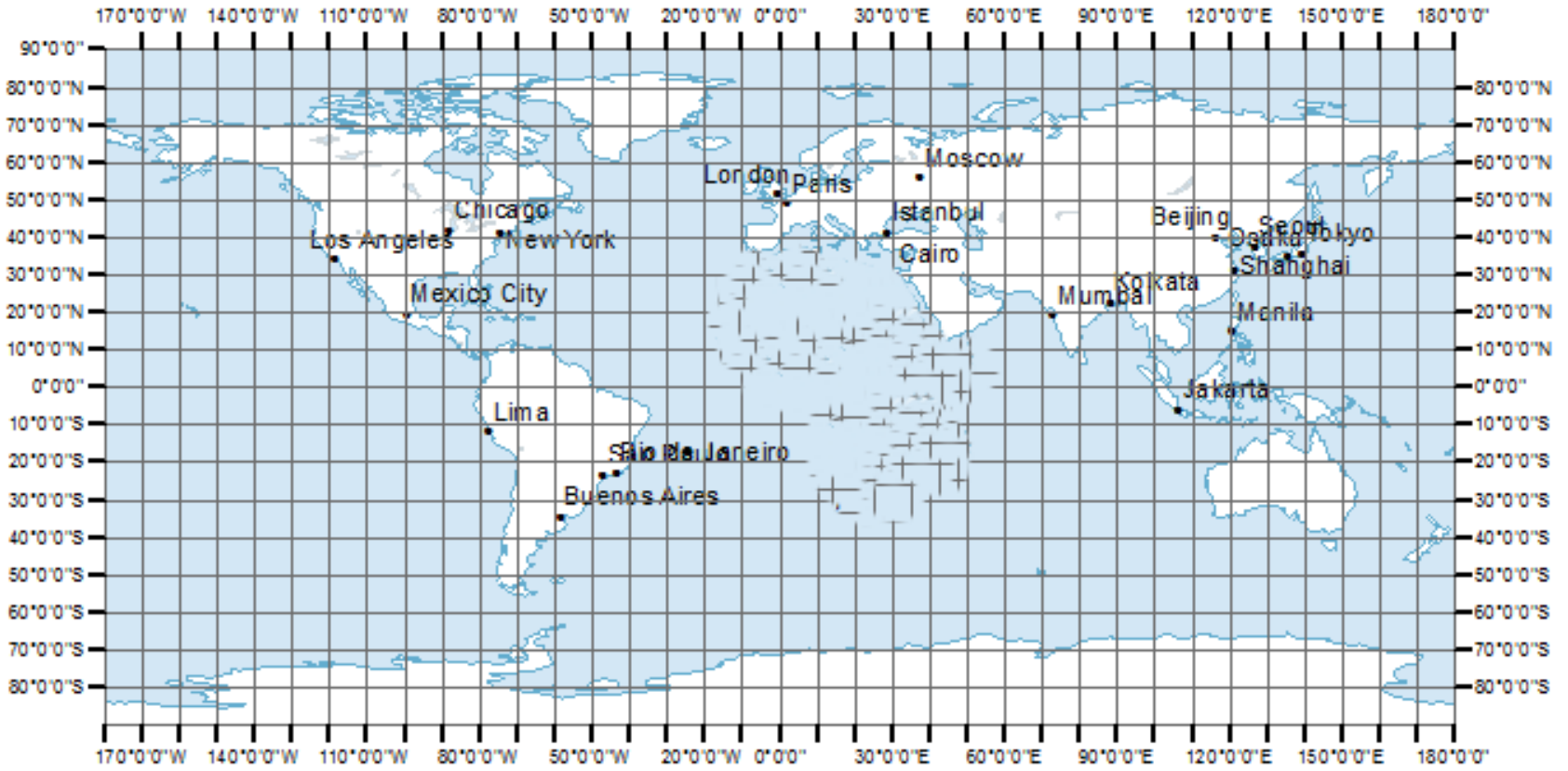
- **African Americans** are **50% more likely** than European Americans to **experience an ischemic stroke**
- **African American** men are **70% more likely to die of an ischemic stroke** than European Americans

PARKINSON'S DISEASE

- **Parkinson's Disease** is **less common** in **African Americans** than in European Americans

HUMAN REFERENCE GENOME

TO FIND ANYTHING ON EARTH (AND IN THE GENOME) YOU NEED THE RIGHT COORDINATES



THE AFRICAN ANCESTRY NEUROSCIENCE RESEARCH INITIATIVE: A PUBLIC-PRIVATE PARTNERSHIP

FOUNDING PARTNERS

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Hathaway, Sr.



Founding Partner &
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THE AFRICAN ANCESTRY NEUROSCIENCE RESEARCH INITIATIVE: A PUBLIC-PRIVATE PARTNERSHIP



AANRI

African Ancestry Neuroscience Research Initiative

Each partner in the AANRI plays a critical and equal role focused on the following **pillars**:

1

Community Engagement

2

Training & development of a diverse research workforce with a focus on individuals of African ancestry

3

Public engagement in scientific research through ongoing communications and advocacy

4

Cutting-edge, high priority scientific research relevant to the biological underpinnings of health disparities

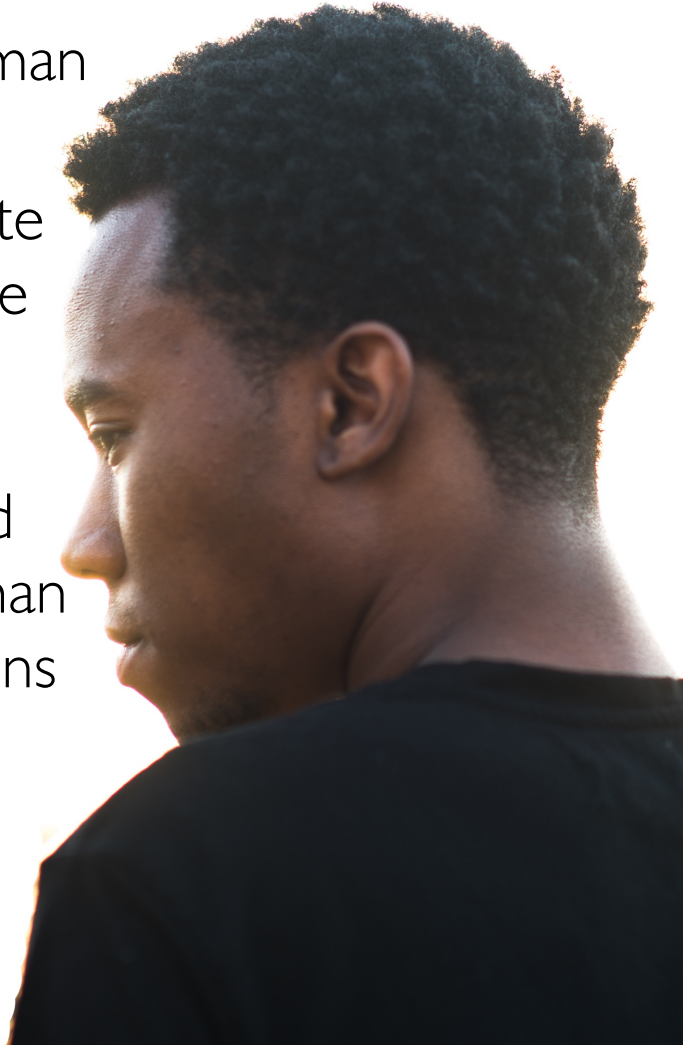
AFRICAN ANCESTRY AND BRAIN ILLNESS: SOME PRINCIPLES

- **Ancestry** is the **story of human history**
- **Human beings are genetically diverse**
- Individuals of “African ancestry” are the most genetically diverse world population
- Genetic variation **influences disease risk and resilience**
- Genetic variation also influences **environmental contributions** to disease risk and resilience

Understanding how African ancestry effects the expression of genes in the brain offers unique opportunities for personalizing medicine for brain disorders.

LIBD BRAIN REPOSITORY

With 4,000+ human brains collected, the Lieber Institute has assembled the largest, most carefully curated and characterized collection of human postmortem brains for study of neuropsychiatric disorders in the world.



Just as Intel's microprocessor ushered in the age of personal computers, LIBD's brain repository is revolutionizing the way we discover and advance breakthroughs in neuroscience.

Postmortem brains are the only way to study the molecular biology of the brain.



AANRI

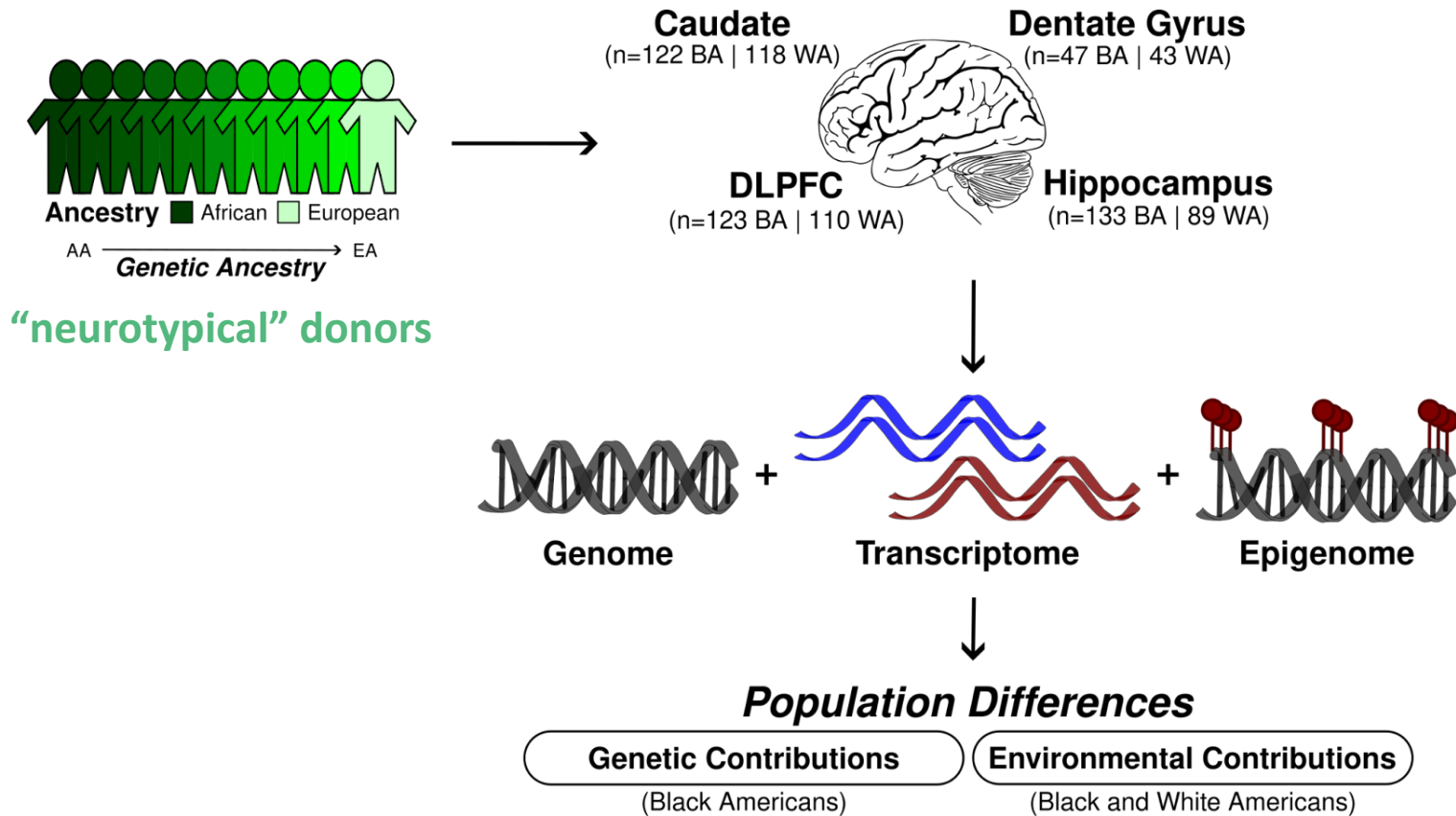
AFRICAN ANCESTRY BRAIN REPOSITORY AT THE LIEBER INSTITUTE

600+

Brain donors are individuals of African ancestry

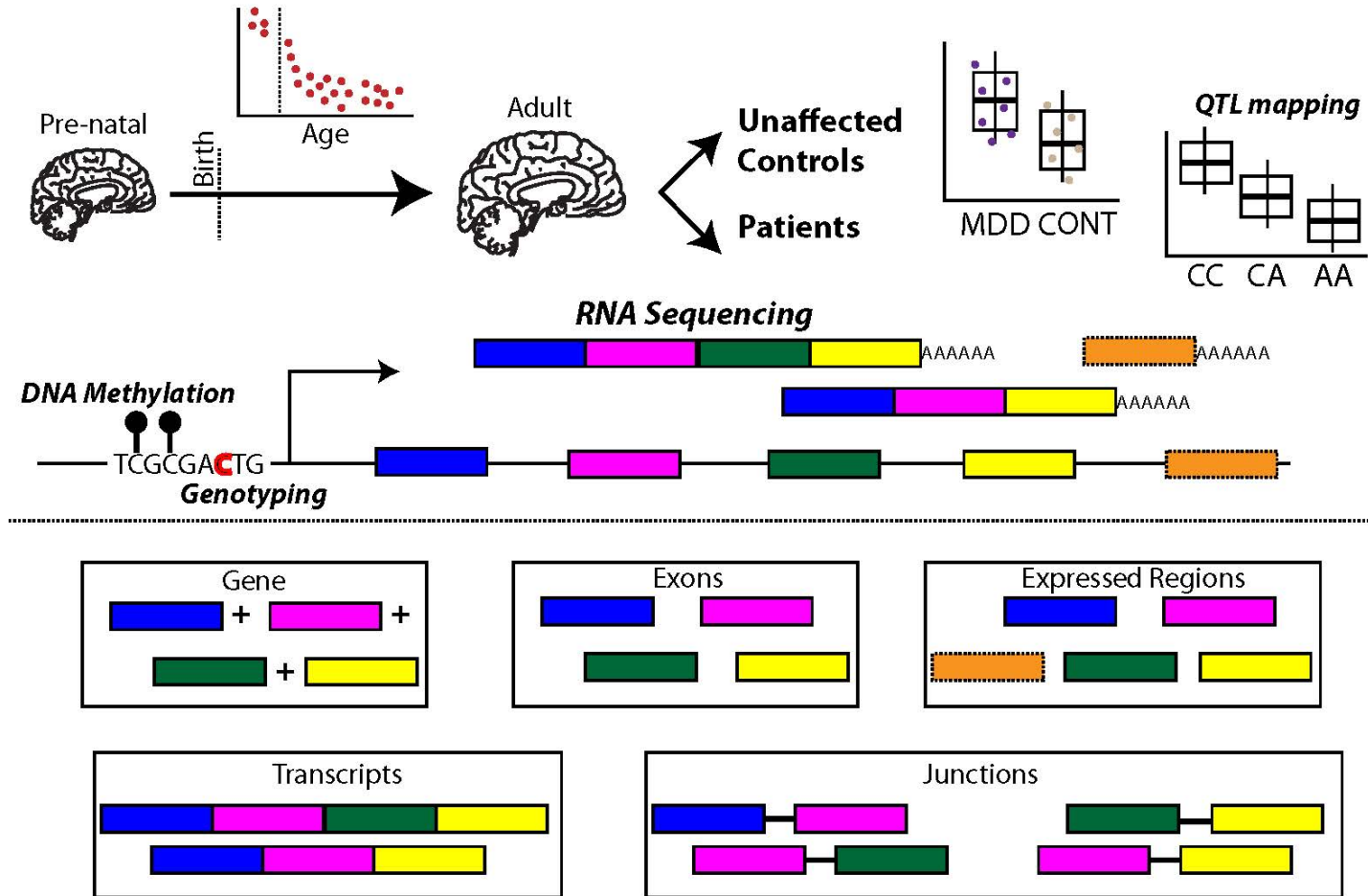
- All donations are consented by next of kin
- African American brain donation rates to LIBD are **60.5%**, higher than all other national brain banks
- Cases include disease areas such as major depression, schizophrenia, substance abuse disorder, post-traumatic stress disorder, bipolar disorder, suicide, and those with no known psychiatric disorders (“so-called, neurotypicals”)
- Mean age: 44

GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO ANCESTRY DIFFERENCES IN GENE EXPRESSION IN BRAIN



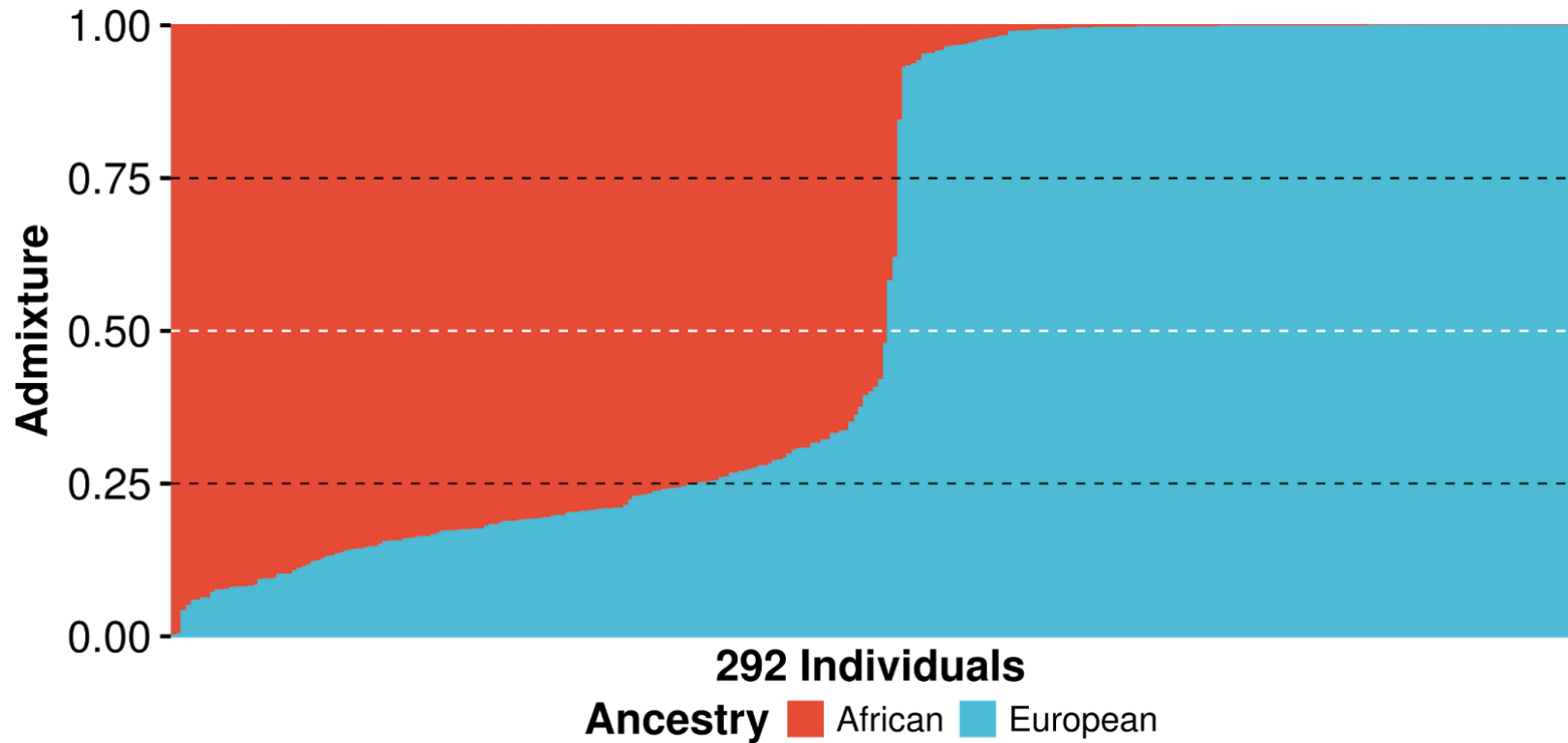
Benjamin et al *Nature Neuroscience* 2024

RNA SEQUENCING ANALYSIS IN HUMAN BRAIN

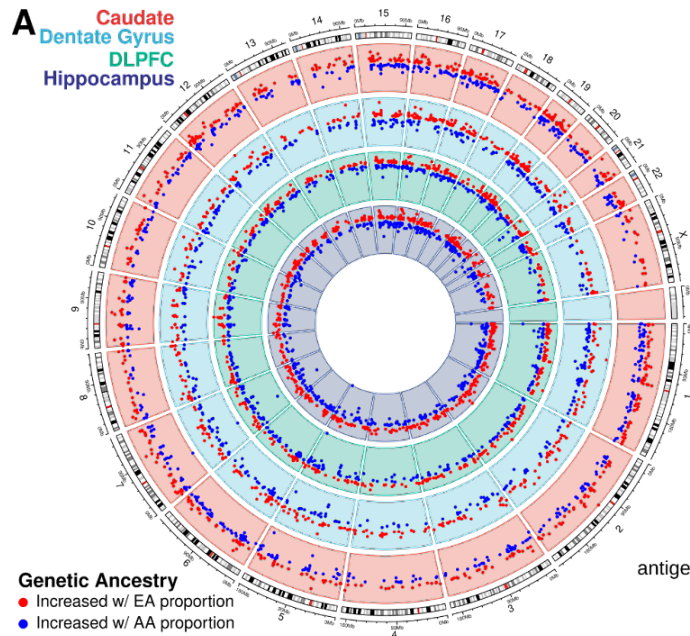


<http://eqtl.brainseq.org/phase1/>

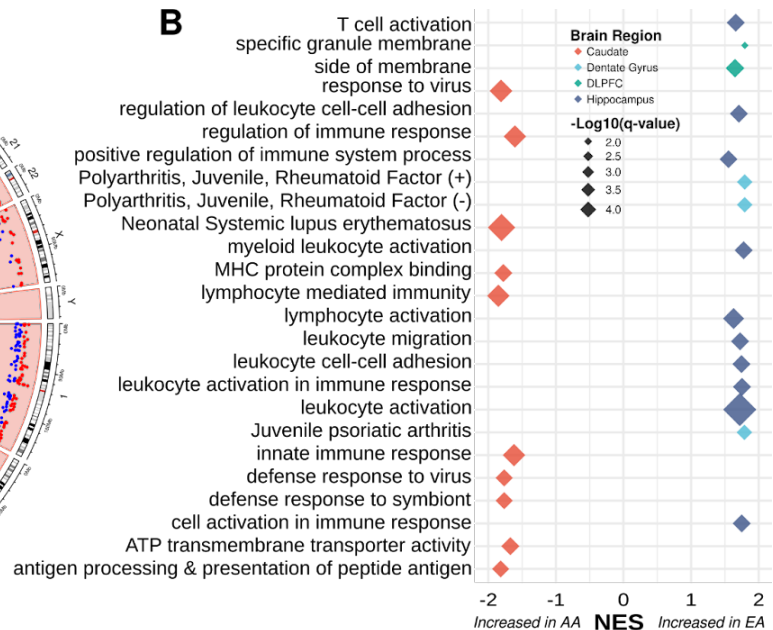
ON AVERAGE, 20% OF AFRICAN AMERICAN GENETIC BACKGROUND IS EUROPEAN



>2500 UNIQUE DIFFERENTIALLY EXPRESSED GENES (DEGS)
BASED ON “GLOBAL” ANCESTRY VARIATION

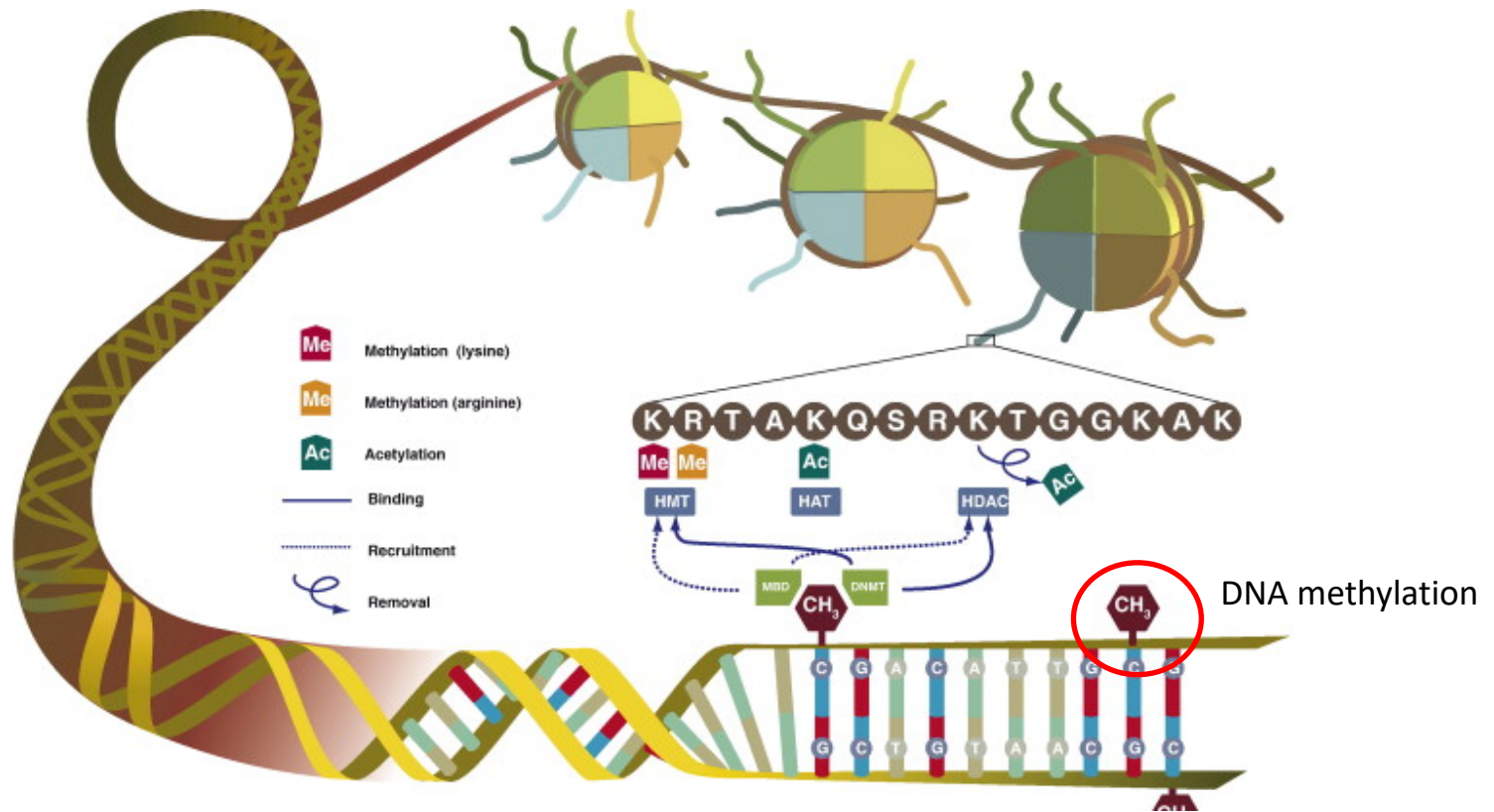


Enriched for immune function

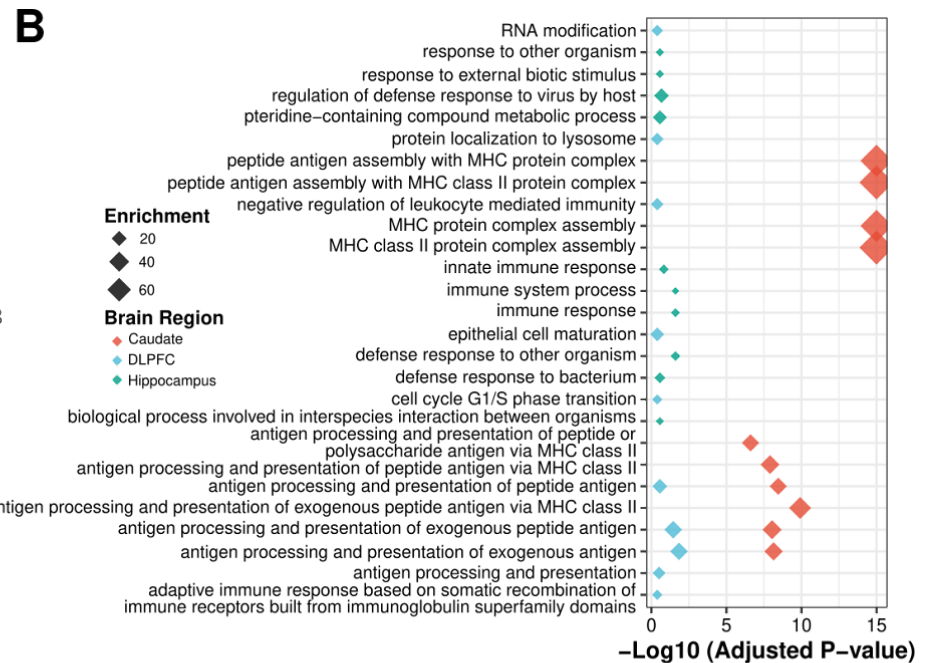
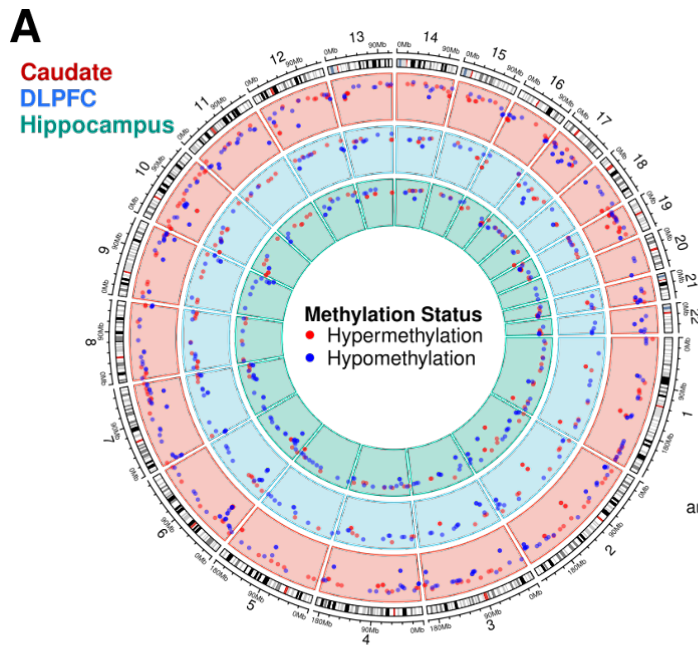


60% OF DEGS ARE RELATED TO VARIATION IN DNA
These DEGs are not enriched for neurons or neuronal function

GENE X ENVIRONMENT = SEQUENCE X EPIGENETIC STATE

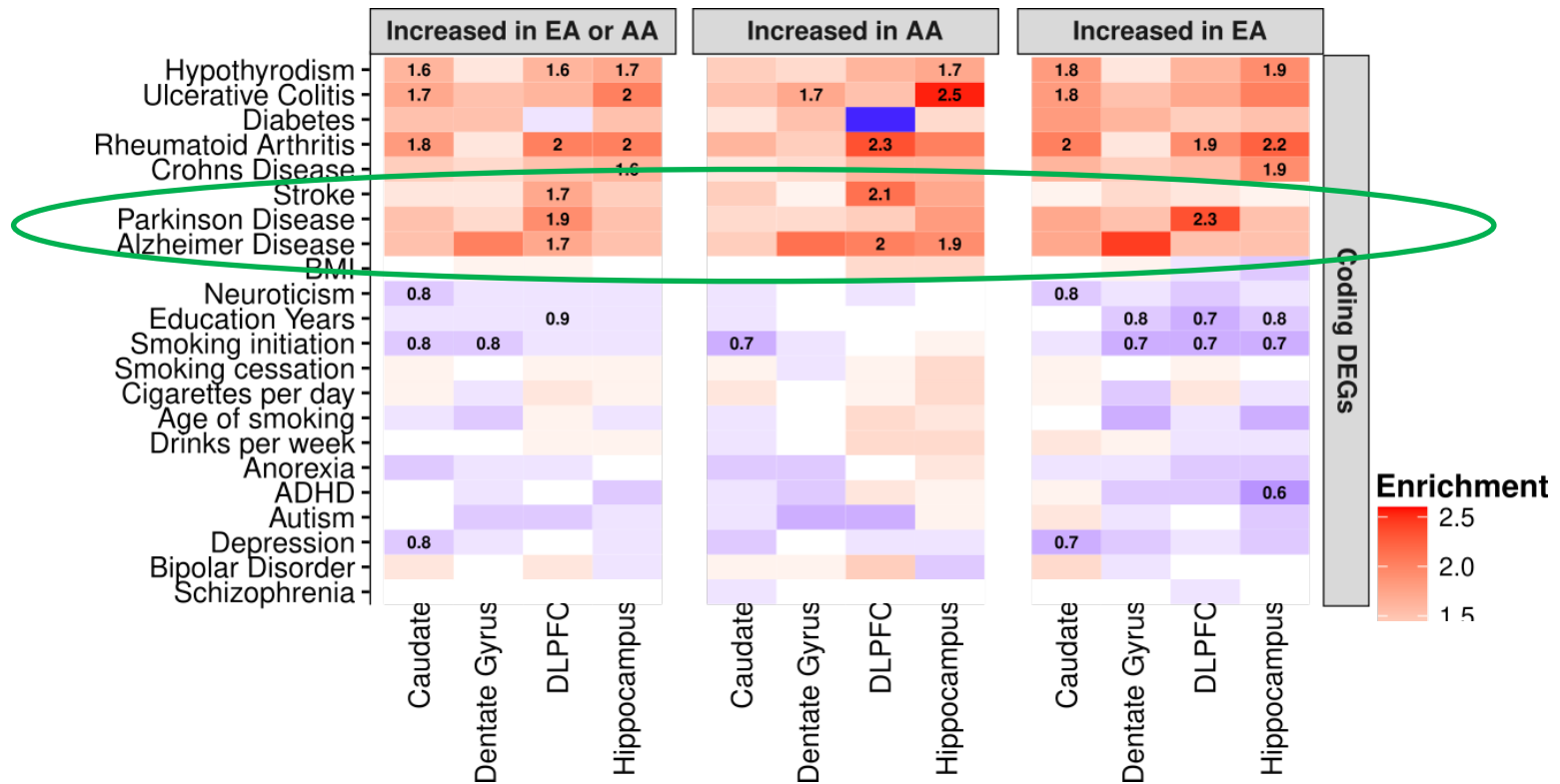


15% OF ANCESTRY DEGS ARE RELATED TO THE ENVIRONMENT



DNA methylation variation based on proportion of African ancestry

ANCESTRY DEGS PREDICT HERITABILITY FOR IMMUNE AND FOR NEUROLOGIC DISORDERS CONSISTENT WITH PUBLIC HEALTH DATA



DEGs in proportion to AA predict 26% heritability for **ischemic stroke**

DEGs in proportion to AA predict 30% heritability for **Alzheimer's Disease**

DEGS in proportion to EA predict 27% heritability for **Parkinson's Disease**

AFRICAN ANCESTRY AND BRAIN ILLNESS: TAKE HOME MESSAGE

- Thousands of genes and transcripts are differentially expressed in brain based on proportions of African v. European ancestry in African Americans
- The differentially expressed genes involve immune function and blood vessel cells but ***not neurons***
- The majority of **ancestry associated gene expression is driven by DNA sequence variation**
- **Minor role for the environment** on gene expression, independent of ancestry
- The prevalence of various diseases in African Americans is based in part on genetic ancestry

PIONEERING TREATMENTS

We are relentlessly pushing the scientific frontier to discover ways to prevent, treat and ultimately cure brain disorders.

JOIN US.



AANRI

African Ancestry Neuroscience
Research Initiative

