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.
Personalized medicine promises delivery of the right intervention to the right patient at the right time.
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.
In the latest genome-wide association studies for Schizophrenia, Autism Spectrum Disorders, Alzheimer’s Disease, Parkinson’s Disease, and Major Depressive Disorder, zero individuals of African ancestry were included in the latest GWAS.
**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

Rev. Dr. Alvin C. Hathaway, Sr.

SUPPORTERS

Abell Foundation

Morgan State University

The State of Maryland

Lieber Institute for Brain Development

Supporters

Brown Capital Management

FOUNDATION PARTNERS

Yasmin Hurd, Ph.D.
Professor, Principal Investigator
Icahn School of Medicine at Mount Sinai

Kafui Dzirasa, M.D., Ph.D.
Principal Investigator, Professor,
Duke University School of Medicine

Steven Salzberg, Ph.D.
Bloomberg Distinguished Professor,
Johns Hopkins University

SCIENTIFIC ADVISORY COMMITTEE
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.
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

“neurotypical” donors

Benjamin et al, Nature Neuroscience 2024
RNA SEQUENCING ANALYSIS IN HUMAN BRAIN

RNA Sequencing

DNA Methylation

Genotyping

Gene

Exons

Expressed Regions

Transcripts

Junctions

Launch COMT Program Q2 2019

IND Submission Q3 2019 Phase 1

TRANSCRIPTOME DATA ANALYSIS

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 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.
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.

African Ancestry Neuroscience Research Initiative