Hussman Institute Awarded $26M NIH Grant to Study, Identify Genetic Risk Factors for Alzheimer’s Disease in Families with African Ancestry

There are essentially two main approaches for finding new genetic targets for Alzheimer’s disease prevention and treatment. One is to study large populations of people with and without Alzheimer’s disease; another is the family approach, in which researchers study families that have multiple members with Alzheimer’s disease. The family approach has been used in many families of European ancestry to identify genes for Alzheimer’s disease.
Researchers at the John P. Hussman Institute for Human Genomics (HIHG) at the University of Miami Miller School of Medicine are tackling both approaches, along with continuing to expand diversity in Alzheimer’s disease research, with the institute’s newest grant—$26 million in funding from the National Institutes of Health titled “The Origins of Alzheimer Disease in African Americans”—focused on the family approach. The Miller School will be joined by collaborators from Case Western Reserve University, Wake Forest University and Columbia University.

“Our aim is to include African American families in this research who have several members with Alzheimer’s disease,”
said the grant’s contact principal investigator Margaret A. Pericak-Vance, Ph.D., director of the HIHG and Dr. John T. Macdonald Foundation Professor of Human Genetics at the Miller School. “We will look at DNA, blood biomarkers, and more in family members with and without symptoms of the disease, to try and uncover rare genetic variants that could be clustered in families that increase family members’ risk for getting Alzheimer’s disease.”

There are many variants that convey risk for Alzheimer’s disease that are relatively common in the general population. One example is Dr. Pericak-Vance’s discovery of the APOE 4 gene and its contribution to risk of getting Alzheimer’s disease, which transformed the field.

It is critical to look at families that might harbor these genetic traits, because Alzheimer’s disease is not one gene or one change. It’s much more complex, according to Dr. Pericak-Vance.

This latest grant brings the total funding since June 2022 for HIHG’s Alzheimer’s research program to about $104 million, which includes a $32.5 million grant from the National Institute on Aging (NIA) to increase the diversity of the Alzheimer’s Disease Sequencing Project (ADSP) and a $46 million NIA grant to build a resource that significantly expands Alzheimer's disease genetic studies in underrepresented Latino/Hispanic and African ancestry groups. In total, the HIHG has over $226 million in active Alzheimer’s disease and related disorders research funding.

“The funding we’ve received this year to study Alzheimer’s shows the strength of our genomics program at the Miller School. It shows the excellence and experience of our team and
how we are regarded nationally and internationally. It also highlights our major focus on diversity in research—an area that is finally being recognized and is vital for finding treatments and potential cures for all patients threatened by this disease,” Dr. Pericak-Vance said.

So Much to Learn

Research on Alzheimer’s disease in African American families is particularly important because the data on African Americans is lacking. The Miller School has the largest database in the world of African American families with high rates of Alzheimer’s disease, with about 100 families.

“It’s a resource that we share with all our collaborators that is unparalleled and will help us to learn about the disease for everyone, but especially those in the Black community,” Dr. Pericak-Vance said.

As part of this grant, HIHG researchers and collaborators will enrich the existing DNA data by retesting family members who were part of the original data gathering for any signs of disease progression. Researchers will also measure blood biomarkers, which have become important indicators of dementia.

Biomarkers that have come onto the market in the last few years are much less intrusive and less expensive than imaging and other studies sometimes used in genetic research, according to grant co-PI Gary W. Beecham, Ph.D., director of the Division of Research Informatics in the Center for Genetic Epidemiology and Statistical Genetics at the HIHG.

“These biomarkers can be done off a simple blood draw, but their utility is still unclear,” Dr. Beecham said.
This grant will allow researchers to test the utility of blood biomarkers as they follow participants at risk for Alzheimer’s for five to 10 years, to understand if there are things that make people at greater or lesser risk for the disease.

“That’s critical down the road when treatments become available,” Dr. Beecham said.

Collaboration with Nigeria, Ghana

An aspect of this grant that has not yet been done, according to Dr. Pericak-Vance, is that HIHG researchers are collaborating with investigators in Nigeria and Ghana, where a high proportion of the U.S. Black population originated. They plan to add more than 100 families from the African countries to the U.S. data. Studying families from Nigeria and Ghana will enable the researchers to follow the origin of Alzheimer’s, as it is known that African Americans have on average 80% African ancestry, she said.

“That’s incredibly important because we could find a variant that doesn’t occur at all in European populations but occurs in the African American population,” she said.

And to better understand how the genetic findings translate to brain changes and symptoms, HIHG researchers hope to encourage more African American Alzheimer’s patients and families to learn about and possibly become involved in brain donation programs.

“Researchers have access to autopsy tissue from non-Hispanic whites, but very few samples from African American patients,” Dr. Pericak-Vance said. “With this grant, we hope to learn more about why African American patients are hesitant about autopsy, and address their concerns and some of the myths as
well as explain the importance of brain donation programs in identifying eventual treatments.”

Autopsy studies are particularly relevant for Alzheimer’s disease because it is a neurodegenerative disease and there are many variations in how the disease looks clinically, according to Dr. Beecham.

“We’ve found in autopsy studies that many patients and even their doctors might not detect Alzheimer’s disease because the patients didn’t complain of memory problems or symptoms of dementia, yet their autopsies revealed Alzheimer’s disease pathology,” Dr. Beecham said. “What’s going on in the brain is much more complicated and varied than the clinical symptoms often show, making it important to get people participating in autopsy.

“For the African American community, this means there is a lot we just don’t know because there are so few African American participants in autopsy programs. This lack of participation translates to a lag in the research. Studies that yield important information in whites would be difficult and underpowered in African Americans.”

Joining Drs. Pericak-Vance and Beecham as multiple principal investigators are Jonathan Haines, Ph.D., and Scott Williams, Ph.D., from Case Western Reserve University; Goldie Byrd, Ph.D., and Alison Caban-Holt, Ph.D., from Wake Forest University; Christiane Reitz, M.D., Ph.D., from Columbia University; and Rufus Akinyemi, Ph.D., MSc., from the University of Ibadan. Other members of the Miller School team include Michael Cuccaro, Ph.D.; Jeffery Vance, M.D., Ph.D.; Anthony Griswold, Ph.D.; Juan Young, Ph.D.; Derek Dykxhoorn, Ph.D.; Azizi Seixas, Ph.D.; and William K. Scott, Ph.D.
This grant will help researchers close those gaps and determine genetic variants and possible targets for the early treatment or prevention of Alzheimer’s disease in Black families greatly impacted by the disease, according to Dr. Pericak-Vance.