Lisette Hilton
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Fueled by $32 Million NIA Grant, Hussman Institute to Expand Diverse Data Source for Global Alzheimer's Research

The National Institute on Aging (NIA) has awarded $32.5 million to faculty from the John P. Hussman Institute for Human Genomics at the University of Miami Miller School of Medicine, to increase the diversity of the Alzheimer's Disease Sequencing Project (ADSP).

Margaret Pericak-Vance, Ph.D.

Researchers around the world use the ADSP for genetic studies on Alzheimer's disease, and the Miller School's work will help to ensure that these data sets better mirror the genetic effects of the disease in all the world's populations.

The goal of the "Additional Sequencing for the Alzheimer's Disease Sequencing Project the Follow-Up Study (FUS), The Diverse Population Initiative" study is to add genome sequencing data from about 16,000 individuals, including predominately Hispanic/Latino and Black Americans, according to study contact principal investigator (PI) Margaret A. Pericak-Vance, Ph.D., director of the John P. Hussman Institute for Human Genomics and Professor in the Dr. John T. Macdonald Foundation Department of Human Genetics.

"This is vital for increasing diversity in Alzheimer's research. Genetics data is used to identify possible drug targets and the data need to be representative of all ethnicities and ancestries," Dr. Pericak-Vance said.

Data Pioneers

The Miller School has pioneered the development of genetics data in Alzheimer's disease, including in a paper published in 2019 in *Nature Genetics* analyzing genetics information on more than 94,000 European individuals. The meta-analysis identified five new gene variants that increase Alzheimer's disease risk.

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Brian Kunkle, M.P.H., Ph.D.

“Most genetic studies in Alzheimer’s disease to date have been conducted in populations with European ancestry,” said Brian W. Kunkle, Ph.D., M.P.H., who led the paper in *Nature Genetics* and is a co-PI on the new NIA grant. “The lack of data in other ancestries impacts our ability to find the genetic factors that could influence disease, and ultimately our ability to develop successful therapeutics.”

A lack of diversity also could exacerbate already existing disparities associated with the disease, as Black, Hispanic, and Latino groups are at increased risk for Alzheimer’s disease compared to non-Hispanic white populations, according to Dr. Kunkle, who is an assistant professor in the Dr. John T. Macdonald Foundation Department of Human Genetics and the John P. Hussman Institute for Human Genomics.

“Studies like this will increase the ancestral and ethnic diversity of the Alzheimer’s genetic studies we conduct, with the hope that this will expedite development of prevention strategies and therapeutics that work for everyone,” said Dr. Kunkle.

Leveraging Resources to Overcome Challenges

For this study, Miller School faculty will do genomic sequencing using existing cohorts, according to grant co-PI Anthony J. Griswold, Ph.D., assistant professor of human genetics at the Dr. John T. Macdonald Foundation Department of Human Genetics and the John P. Hussman Institute for Human Genomics.

Anthony J. Griswold, Ph.D.

“Due to the increased recognition of the importance of including individuals of diverse ancestries in studies of Alzheimer’s disease, many large groups have been enrolled in studies collecting clinical data and biological samples,” Dr. Griswold said. “Our grant will leverage these existing resources to perform whole genome sequencing and combine this with other data from the ADSP to identify genetic risk and protective factors for Alzheimer’s disease that may inform potential therapeutic targets.”

Among the challenges of such a project is having the expertise and ability to make sure the diagnoses align among the different ethnic groups.

“Our team includes experts in clinical diagnoses of Alzheimer’s disease, and for every participant in these cohorts, the clinical data is reviewed by a panel and a consensus diagnosis is achieved,” said Dr. Griswold, who was recently elected as a vice chair for the Executive Committee - Cross-Consortium Collaboration Communication Committee (EC-4C) of the ADSP. “Furthermore, the ADSP has established a Phenotype Harmonization Consortium, with the goal of bringing in disparate clinical data and finding overlapping metrics to ensure that these data are generalizable across all participants in the study.”

Miller School faculty are among the leaders in genomics and diversity research in Alzheimer’s disease, according to Dr. Pericak-Vance.

“We are responsible for overseeing the sequencing of existing, diverse ADSP-FUS cohorts and their critical inclusion in genetic studies. The HIHG researchers also work diligently to engage individuals from all groups to participate in research

studies," she said.

Dr. Griswold agrees. "We have years of experience working within the larger ADSP consortium with our collaborators and partners to advance Alzheimer's disease research," he said. "And being in an ancestrally, ethnically, and culturally diverse city like Miami, we recognize the need to expand our genetic research into communities that represent this city and the global population, to ensure that our discoveries will be applicable to all individuals."

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