John P. Hussman Institute to Lead International Genetic Study of Alzheimer's Disease in People of Hispanic and African Ancestry

To build a resource that greatly expands Alzheimer's disease genetic studies in the currently underrepresented African ancestry populations and Hispanic/Latinx groups, the John P. Hussman Institute for Human Genomics (HIHG) at the University of Miami Miller School of Medicine will lead a major five-year, international, multi-site initiative with Case Western Reserve University, Columbia University, Wake Forest University, the University of Pennsylvania, and the University of Ibadan, which is the lead institution for the African Dementia Consortium (AfDC).

The new initiative is funded by a $46 million grant awarded to the HIHG by the National Institute on Aging, part of the National Institutes of Health. Margaret A. Pericak-Vance, Ph.D., director of the HIHG and Dr. John T. Macdonald Foundation Professor of Human Genetics, will oversee the overall efforts of the principal investigators across several domestic and international sites. She is joined by co-PIs Drs. Brian Kunkle and Jeffery Vance (HIHG); Drs. Jonathan Haines and William Bush of Case Western Reserve; Dr. Goldie Byrd of Wake Forest; and Drs. Christiane Reitz and Giuseppe Tosto of Columbia.

Margaret Pericak-Vance, Ph.D.

"We recognized early on the need to advance community-based participatory efforts to increase understanding of Alzheimer's disease," said Dr. Pericak-Vance. "Only by being inclusive in our approach and including all groups will we be able to develop targeted drug therapies, which would be universally beneficial."

Alzheimer's is a complex disease with a pronounced genetic component; its estimated heritability is 60% to 80%. Though the disease can affect individuals of almost all ethnic and ancestral backgrounds, efforts for genetic studies have not historically been well diversified. Most genetic-based studies in Alzheimer's disease have been performed in non-Hispanic white populations of European ancestry, with communities of Hispanic and African ancestries largely ignored.

"We know risk due to genetic factors varies greatly across

ancestral groups," said Brian Kunkle, Ph.D., M.P.H., assistant professor of human genetics, HIHG. "However, research on groups with primarily African, Hispanic, and Latinx ancestry is limited. Expanding studies in these populations will be vital for developing prevention and treatment strategies that work for everyone."

Creating a Genetic Data Resource

The new multi-site enterprise will help to bridge the research disparities that have historically existed in diverse communities. Through the recruitment, assessment, and genetic analysis of a significantly large cohort of participants of Hispanic/Latinx and African ancestries, clinical, phenotypic, and genetic data, along with social determinants of health factors, will be collected to create a large genomic study resource.

The cohort will include 5,000 individuals from various African countries, 4,000 African Americans, and 4,000 Hispanic/Latinx individuals. Data collected from participants will be added to existing databases of harmonized data from other ongoing studies as part of the Alzheimer's Disease Sequencing Project (ADSP).

Jeffery M. Vance, M.D., Ph.D.

Recruitment in Africa will be done under the umbrella of the AfDC. Led by Rufus Akinyemi, M.B., B.S., Ph.D., F.M.C.P., and Adesola Ogunniyi, M.B., Ch.B., F.M.C.P., the AfDC is a coalition of African dementia researchers in a multidisciplinary framework, working together with the aim of generating clinical, cognitive, socioeconomic, neuroimaging, genomic, and biomarker data to improve the phenotypic characterization of dementia, particularly Alzheimer's, in Africa. The AfDC's goals include the translation of scientific evidence to health policy and clinical practice, lessening the burden of dementia among Africans and ultimately contributing to the reduction of the global burden of dementia.

Currently the AfDC includes researchers from nine African countries, including Nigeria, Ghana, Uganda, Benin, Cameroon, Kenya, Mozambique, Tanzania, and Ethiopia.

Higher Risk Requires Focused Study

This new initiative is particularly significant because members of African American and Hispanic/Latinx communities have one of the highest risks of developing Alzheimer's disease. Thus, identifying the ancestral differences in causes of Alzheimer's is critical to treating all individuals.

"These studies will accelerate our understanding of the genetic factors contributing to Alzheimer's disease, especially in the multi-ancestral population of the United States as well as populations around the world," said Jeffery Vance, M.D., Ph.D., professor of human genetics and neurology, HIHG.

Studies show that people differ genetically based on their ancestral backgrounds when it comes to Alzheimer's risk. Therefore, the participation of the African American and Hispanic/Latinx communities is essential in the search for possible causes, treatments, and solutions specific to these groups and more broadly applicable to all people with Alzheimer's.

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

Through the participation of individuals, the initiative will be able to help address inequalities and medical disparities in Alzheimer's treatment and prevention. The study is also one of the first to examine the interaction between ancestry and the social determinants of health. Both factors can contribute to the risk and age of onset of Alzheimer's disease, and studying both types of risk factors will help researchers understand how they interact in the development of Alzheimer's.

Study Sites Across Africa

The collaborative group includes the five U.S. sites listed above and 11 sites across Africa — University of Ibadan; University of Ghana College of Health Sciences; Korle-Bu Teaching Hospital; Kwame Nkrumah University of Science and Technology; Makerere University; University of Parakou; University of Yaounde; University of Nairobi; Eduardo Mondlane

University; Kilimanjaro Christian Medical College; and Addis Ababa University.

In addition to Drs. Pericak-Vance, Kunkle, and Vance, the University of Miami study team includes co-investigators Gary Beecham, Ph.D., Susan Blanton, Ph.D., Michael Cuccaro, Ph.D., Anthony Griswold, Ph.D., Katalina McInerney, Ph.D., Farid Rajabli, Ph.D., and Azizi Seixas, Ph.D.

For more information, or to participate in the study, please contact study coordinators at (877) 582-8788, or visit www.READD-ADSP.org (live August 1, 2022).

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