Genomic Characterization of Alzheimers Disease Risk in the Puerto Rican Population

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Genomic Characterization of Alzheimers Disease Risk in the Puerto Rican Population

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1

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Alzheimer's disease & other dementias

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Research Abstract

PROJECT SUMMARY To identify new treatment targets, we and others have examined the genomics of Alzheimer's disease (AD). However, genomic successes so far have arisen from studying primarily non-Hispanic White (NHW) participants, and the study of minority populations has been minimal. What few studies have been done in minority populations have suggested that the genetic architectures overlap, but only partially. Thus, studying minority populations not only serves to test generalization of the NHW findings but also provides a unique opportunity for discovery of novel targets and pathways. To begin addressing these issues, we propose here the Puerto Rico Alzheimer Disease and Related Disorders Initiative (PRADI). We will whole-genome sequencing (WGS) Caribbean Hispanic Puerto Rican (CHPR) AD multiplex families to identify novel AD variation in CHPRs, and to generalize existing AD genetic discoveries to this underrepresented population. This initiative will increase our knowledge about genetic variation, particularly for the Caribbean Hispanic population of Puerto Rico (CHPR). The Puerto Rican (PR) population is the 2nd largest Hispanic/Latino population in the continental US. The prevalence of AD in the Caribbean Hispanic population of the island of PR is estimated in 65,000. The PR population is a highly mixed population with average ancestry values of ~64% European, ~21% African, and ~15% Native American. The unique genetic make-up of the PR AD population will be critical in new discovery as well in replication of findings from the Alzheimer Disease Sequencing Consortium (ADSP) CHDR data and the Alzheimer's Disease Genetics Consortium (ADGC) African American (AA) data. Thus, discovery of genetic contributions to AD risk and protective variants in CHPR would have a substantial influence on our understanding of AD and towards our goal of identifying new treatment targets. Through this proposal in response to PAR-15-356 we will address this important issue by conducting genomic studies of AD in PR. Specifically we propose a family-based study in PR that parallels the family-based efforts in the ADSP Discovery phase and that will enhance and extend both current ADSP and ADGC efforts to a broader AD community. We aim to 1) Characterize the genetic epidemiology of AD in PR 2.) Generalize and refine known risk and protective loci in familial PR AD. 3.) Perform variant discovery in our PR AD families and case control data 4.) Leverage multi-ethnic populations (PR, DR and AA) to discover novel AD risk/protective effects by calculation of local ancestry, admixture mapping and bioinformatics analysis and 4.) Perform multi-locus analyses providing insight into functional implications of the risk and protective loci. Our overall goal is to identify targets for therapeutic development that will either prevent or significantly delay the onset of AD.

Lay Summary

PROJECT NARRATIVE To identify new treatment targets, the genomics of Alzheimer's disease (AD) has been examined primarily in non-Hispanic White populations. In response to PAR-15-356, we propose a genomics study of AD in Puerto Ricans. We will whole-genome sequencing Caribbean Hispanic Puerto Rican (CHPR) AD multiplex families to identify novel AD variation in CHPRs, and to generalize existing AD genetic discoveries to this underrepresented population.

Further information available at:

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Investments > €500k

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United States of America

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