Research Use Statement for Application for Genomic Data from NIAGADS

Please limit to 2,200 characters max. The statement should include the following components:

- Objectives of the proposed research;
- Study design;
- Analysis plan, including the phenotypic characteristics that will be evaluated in association with genetic variants

Research Use Statement:

Growing evidence suggests that vascular traumas contribute to dementia, wherefore vascular and neurodegenerative pathologies commonly coexist. Vascular dementia (VaD) is currently considered the second most common cause of dementia after Alzheimer's disease (AD). Still, its diagnostic criteria have varied due to historical changes in the concept, the overlap with other neurodegenerative pathologies leading to a variety of criteria proposed by different groups. For the last decades, a direct consequence of the heterogeneity of VaD definition has been the difficulty of identifying genetic loci associated with this pathology, due to the large sample size required to reach genome-wide significance. But, with the development of big consortia, this goal is now achievable and we will leverage data from the Cohort for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium to attempt to identify new genetic loci associated with “all-cause” dementia (combination of all dementia subtypes) and VaD. These efforts are critically important as identifying new genetic variants may provide new insights into the pathophysiological mechanisms of these diseases as well as the potential differences in prevention strategies, diagnosis, and treatment effectiveness.

The Objective of this proposal is to meta-analyze GWAS to identify new genetic loci with effects across all dementia subtypes and to study the subtype defined as VaD. Given our role in the neurology working group of the CHARGE consortium, we are in a unique position to achieve this goal, through the following two aims:

Aim 1: Discovery and replication of new genetic loci associated with “all-cause” dementia and VaD. Leveraging infrastructure from CHARGE consortium, we will attempt to identify novel genetic loci associated with “all-cause” dementia and VaD, in a meta-analysis of GWAS, followed by a replication on samples from other studies.

Aim 2: Fine mapping and functional analysis of genome-wide significant and suggestive loci. We will use publicly available bioinformatics tools and databases to determine the mechanistic and functional consequences of inherited risk variants identified through all-cause and vascular dementias GWASs.

Non-Technical Summary for Application for Genomic Data from NIAGADS

Investigators will provide a non-technical summary of their proposed research. If the project is approved, this statement will be publicly available for lay audiences to read the purpose and objectives of the research. Please limit to 1,100 characters.

Vascular dementia is currently the second most common cause of dementia after

Alzheimer's disease. But the heterogeneity of its definition has hindered the discovery of genetic loci associated with the pathology. The goal of this proposal is to meta-analyze genome-wide associations studies of all-cause and vascular dementia, with the goal of identifying new genetic loci. We will leverage the infrastructure created by the Cohort for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium