Research Use Statement for Application for Genomic Data from NIAGADS

Secondary Analysis Plan for data derived from NIAGADS data.

Research Use Statement:

Objectives of the proposed research:
        In this proposal, we aim to elucidate the molecular mechanisms underlying the associations of depression and psychological well-being with clinical Alzheimer's disease (AD), AD pathology, and cognitive decline. We also aim to uncover new genetic risk variants for Alzheimer's disease.

Study design
        We will perform a case-control analysis of AD using clinical and pathologic definitions of AD. We will combine those analyses with our analysis of deep-brain proteomes to weight variants and associations identified in the case-control analysis to identify genes and networks that are associated with AD. We will repeat the aforementioned approach using depressive symptoms as the outcome instead of AD and identify genes and networks that appear to overlap the genetic associations between depression and AD. We plan to publish our findings so they are shared with the scientific community.

Analysis plan.
        Outcomes that will be tested include: (1) clinical disease status, (2) pathologic characterization (e.g., measures of beta-amylodi, tau, etc.), and (3) cognitive decline. For sequencing data, we will extract raw sequencing reads from BAM (or equivalent encrypted files) and re-map those to hg38 build of the human genome using PEMapper. Bascalling will be performed using PECaller using default settings. Variant annotation will be performed using Bystro and quality control will follow Wingo et al., 2017. For rare variants, we will use SKAT and burden-based tests to estimate association between variants and outcome for each gene in the genome. For common variants from genotyping (after imputation to 1000G), we plan to test for differences in allele frequencies using maximum likelihood tests after excluding poorly behaving samples and genotypes. For all analyses, we plan to control for population structure deriving principal components from the underlying sequencing or genotyping data.

        In keeping with our agreement to the NIA Sharing Policy/NIA AD Genetics Sharing Plan, and the NIAGADS Data Distribution Agreement, we plan to provide data derived from our study to NIAGADS.

NIAGADS

RESEARCH USE STATEMENT
AND NON-TECHNICAL SUMMARY

Non-Technical Summary for Application for Genomic Data from NIAGADS

Our aim is to identify genetic variants that are associated with Alzheimer's Disease (AD) either using genomic data (from NIAGADS or from Emory University) or brain protein sequencing data (from Emory University) as a starting point. We will perform an integrated analysis to uncover new genetic risk for AD and shared risk between AD and depression. The goal of this work is to identify novel mechanisms of AD pathogenesis that could inform design of new treatment and models for AD.