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:

Recent projects characterizing genomic variation across large numbers of individuals have revealed that somatic mutations driving clonal expansion in hematopoietic cells occur as part of human aging. This phenomenon, is associated with a number of adverse outcomes, including increased mortality, cardiovascular disease risk, and risk of hematological malignancy. The aim of this proposal is to assess what (if any) association clonal hematopoiesis (CH) has with Alzheimer's disease (AD) or Dementia.

We will use the available exome and whole-genome sequencing to look for somatic mutations associated with CH. In general, distinguishing germline mutations from somatic mutations is non-trivial within a single sample. However, somatic and germline variants are expected to differ in their variant allele fraction distributions. Additionally, many somatic mutations associated with CH are thought to cause severe developmental disease when they occur in the germline (e.g., loss of function in DNMT3A is associated with Tatton-Brown-Rahman syndrome). The poor prognosis of affected patients should make germline mutations in these genes rare.

After identifying participants with CH, we will use standard statistical methods (e.g. a fisher test) to determine if CH has any association with AD phenotype. We will also look for sex, race, ethnicity, and APOE specific effects.

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.

Recent projects characterizing genomic variation across large numbers of individuals have revealed that somatic mutations driving clonal expansion in hematopoietic cells occur as part of human aging. This phenomenon, is associated with a number of adverse outcomes, including increased mortality, cardiovascular disease risk, and risk of hematological malignancy. The aim of this proposal is to assess what (if any) association clonal hematopoiesis (CH) has with Alzheimer's disease (AD) or Dementia.