## 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:

**Objectives**

Post-transcriptional modification of RNA molecules can generate many different transcript isoforms from the same genes and thus increase the complexity of transcriptome and then that of the proteome. Two of the most frequent modifications are alternative splicing (AS) and RNA editing. Both types of modifications have been shown to play a crucial role in embryonic development, the central nervous system, normal brain functions, and many neuropathological disorders.

**Study design**

On the basis of the transcriptome data of Alzheimer's Disease (AD) samples, we can identify potentially AD-associated events. We apply our recently developed tools, ExonFinder (BMC Plant Biology, 15:39, 2015) and NCLscan (Nucleic Acid Research, 44 (3), e29, 2016) to identify potentially disease-specific collinear and non-col-linear (circular; trans-splicing and fusion) AS transcripts in AD brains. We further apply our newly developed tools, ICARES (Genome Biology and Evolution, 10(2), 521-537, 2018), to detect A-to-I editing sites. Some RNA editing events might play an essential role of recruiting such AS transcripts. Our study will help uncover AS transcripts for AD and thus increase our understanding of AD-associated molecular pathology.

**Analysis plan**

This study aims to identify AD-associated AS transcripts (including co-linear and no-co-linear transcripts, circular RNAs; trans-splicing RNAs; fusions) and RNA editing events. Our study will help uncover novel AS transcripts for AD and thus increase our understanding of molecular pathology of this disease.

## 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.

Our study aims to identify AD-associated AS transcripts (including co-linear and no-co-linear transcripts, circular RNAs; trans-splicing RNAs; fusions) and RNA editing events. This study will help uncover novel AS transcripts for AD and thus increase our understanding of molecular pathology of this disease.