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:

The primary objective of the proposed research is identifying mutations in novel genes that may cause Parkinson's disease and other Parkinsonism disorders by assessing case-control sample differences.

Study Design:

Individual genotype control data from NIAGADS will serve as a replication cohort, in combination with individual genotype data generated in-house, for existing research efforts being undertaken by Prof Huw Morris and his collaborators. We have generated candidate genes from whole exome analysis of familial and early onset Parkinson's and Parkinsonism samples and wish to use the NIAGADS data to explore background ("control") variant and genotype frequency data.

Analysis Plan:

Variant data from PD candidate genes (up to 200) will be extracted from the NIAGADS data. Individual variant frequency comparisons will be performed to assess whether individual variants are associated with disease. Under gene based analyses, recessive and/or dominant modes of inheritance will be modelled and carrier frequencies will be compared to determine whether if candidate genes are involved in disease aetiology.

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.

Clear evidence for a genetic component to Parkinson's disease (and other Parkinsonism disorders) comes from the fact that relatives of patients have an increased chance of getting the disease themselves. However, few cases have an identified "spelling mistake" mutation in known disease genes. We think that there are further disease-causing genes to be identified. Next generation sequencing technology now allows us to analyse all the protein coding regions of an individual's genome in a single experiment (called exome sequencing). By usingLxome sequencing, we aim to identify novel genes/mutations that cause disease. Using the control data will allow us to more accurately determine if newly-identified mutations/genes are involved in the disease process. New mutations identified would help lead to a better understanding of the genetic makeup and disease mechanisms of diseases, which could lead to the development of more appropriate strategies to combat them.