Application number/Title: 41910 - Genetics of complex diseases, comorbidities, and other traits in multi-ethnic samples

Applicant PI: Dr Hang Zhou

Application Institution: Yale University, New Haven, Connecticut, USA

Keywords provided by the Applicant PI to describe the research project:
GWAS, comorbidities, complex traits, multi-ethnic study, polygenic risk score, psychiatric disorders

Application Lay Summary:
Genetics of complex diseases, comorbidities, and other traits in multi-ethnic samples

1a: According to the Global Burden of Disease Study 2016, many genetically complex diseases, including psychiatric disorders, are among the top diseases that cause morbidity and mortality. Genetic factors contribute substantial risks to the etiology of those diseases, and the genetic heritability was estimated to be moderate to high for many of these deleterious traits. Genetic studies, including genome-wide association studies, have identified risk genes in global populations, but mostly in European populations. However, considerable work still needs to be done, and the availability of very large datasets is greatly increasing opportunities to do this work. Some of the most important work requires us to address the lack of study in populations except Europeans. Many traits may share, to some extent, risk variants and biological pathways. Only a few studies investigated the shared genetic factors for comorbid diseases. There is much more to do to improve our understanding of the complex genetic architecture of different disorders and the comorbidity in different populations.

1b: The purpose of the proposal is to map novel genetic risk variants to diseases and traits, identify brain areas that mediate the genetic risk, and detect differential brain connectivity patterns by investigating the UK Biobank data, and by meta-analyzing the UK Biobank data with other resources to increase power, in different populations.
1c: We will conduct genome-wide association studies using genetic data collected from UK Biobank, our datasets, and other publicly available resources, to identify genetic variants associated with each relevant disease or trait in different populations. Then we will meta-analyze all the available datasets to improve power. Brain image data will be used to map the brain neural activities, connectivity, and structural regions associated with the genetic profiles for some diseases, especially psychiatric ones. Polygenic risk scores will be used to predict genetic risks for related diseases. The heritability of diseases in different populations will be estimated, and genetic correlations with other traits will be analyzed. Functional enrichments for the genetic variants will also be investigated.

1d: This study will extend our understanding of the genetic etiology of many diseases and comorbid diseases, as well as other complex traits, which will benefit the downstream intervention or treatments.