



Application number/Title: 34031 - Integrative study of genomic, environmental, and clinical factors for cardio-metabolic diseases

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Keywords provided by the Applicant PI to describe the research project:

cardiometabolic-disease, comorbidity, gene-environment-interaction

Application Lay Summary:

Many genetic loci for cardio-metabolic diseases (CMD) have been identified, but a large proportion of the genetic component remains unknown. Gene-environment (GxE) interaction can improve gene discovery and understanding of the genetic architecture of CMD. In addition to well-defined lifestyle factors, we will employ GxE model to investigate other risk factors and comorbidities interacting with genetics. The UK Biobank provides large sample size to enable genome-wide search for robust GxE interaction associated with CMD. With access to the US-based Million Veteran Program cohort, we will replicate robust GxE findings between these two large biobank studies. This study aims to identify novel disease loci, improve understanding of biological mechanisms, identify new therapeutic targets for innovation, and to develop new prevention strategies of cardio-metabolic diseases by incorporating non-genetic risk factors and comorbidities into genomic analyses. This is in line with UK Biobank's aims to improve the diagnosis, treatment, and prevention of human diseases. This observational study will utilize existing genetic and phenotypic data from the UK Biobank to jointly analyze the genetic, environmental, and clinical factors associated with cardio-metabolic disease traits by employing gene-environment (GxE) interaction models. Lifestyle factors, disease risk factors and comorbidities will be modelled as E in the GxE association analyses. Individual genetic variants and genetic risk scores will be investigated to identify novel genetic loci, and assess the joint GxE effects for cardio-metabolic diseases. We are requesting to use the full cohort of UK Biobank (N~500,000)