**Application number/Title:** 19416 - A genome-wide and Pheno-wide association study of common diseases on 900,000 individuals from US and UK.

**Applicant PI**: Professor Christopher O'Donnell

**Applicant institution:** VA Boston Healthcare System, Medicine, Cardiology Section, 1400 VFW Parkway, West Roxbury, Boston MA 02132, United States.

**Lead Collaborators:**

1) Dr Abbas Dehghan
2) Dr Alanna Morrison

**Collaborating Institutions and Addresses:**

1) Imperial College London, Epidemiology and Biostatistics, Faculty of Medicine Building, St Mary's Campus, Norfolk Place, Paddington, London W2 1PG, United Kingdom.
2) University of Texas (UT Health), Human Genetics Center, 1200 Pressler Street, Suite 453E, Houston TX 77030, United States

**Funding body:** VA Boston Healthcare System

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

Common diseases, GWAS, PheWAS, multiple races

**Application Lay Summary:**

1a: The US Million Veteran Program (MVP) partners with Veterans to study how genes affect health, by safely collecting blood samples and health information from up to one million Veteran volunteers. So far, four beta projects were approved and funded to study Cardiovascular risk factors, Multi-substance use, pharmacogenomics of kidney disease, and Metabolic conditions. Here, we aim to use the genotype and phenotype data from UK

biobank to replicate novel findings from MVP, to become a genetic study with unprecedented power for discovery and replication.

1b: The goal of MVP is to better understand how genes affect health and illness in order to improve health care for Veterans. This is well in line with the UK Biobank's aim to improve the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses. The research participants of MVP are US Veterans volunteers, their motivation is to help transform health care, not only for themselves, but for future generations of veterans and the general population.

1c: We propose to: (1). Use the MVP data as a discovery for genome-wide and pheno-wide analysis to discover novel associations with the four group of traits mentioned above (with a plan to extend to more traits including cancer and neurodegenerative traits); (2). Follow up the novel findings in the UK Biobank data, where we use the same protocol for statistical analyses; (3). Explore the combination of two largest cohorts (MVP in US and UK Biobank in UK) to further characterize the genetic architecture of complex traits with an unprecedented statistical power.

1d: MVP will be the single largest cohort with a rich collection of clinical records over two decades. Also, the MVP used the same Affymetrix Axiom genotype array as UK Biobank, which made synergizing these two studies a natural choice. We are requesting to use the full cohort of UK Biobank.