

Principal Investigator

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Summary of research:

Hypertension, genetics, public health, blood pressure

Application Lay Summary:

1a: 1. We will study genetic exposures for influence on both the mean values of blood pressure (BP)(systolic BP, diastolic BP, Mean arterial pressure, pulse pressure), and BP variability. We will use resources we have approval and funding to utilize from over 500,000 participants of the MVP and the eMERGE network in a meta-analysis of 1,000,000+ subjects.

2. An exploratory Aim to discover whether it is possible to classify resistant hypertension in UK biobank (BP control with 4+ antihypertensive meds, BP uncontrolled with 3 or fewer antihypertensive meds). If so, we will also evaluate this outcome.

1b: Elevated BP is the leading cause of death and disease worldwide. BP measures also show pronounced racial disparities and the burden of hypertension is very high in African ancestry populations. The consequences of hypertension include stroke, kidney disease, coronary artery disease, and many other major burdens on public health. BP is highly heritable but only a small proportion of variance has been explained to date with genetic studies. Knowledge of the biological basis for hypertension will facilitate drug discovery and disease prediction efforts.

1c: We will use regression models to estimate and conduct statistical tests of the association between inherited exposures and blood pressure measures. We will account for factors such as age and race, as well as antihypertensive medication use. This will allow us to infer what locations in the genome are related to elevated BP and hypertension risk, and may offer insight into novel remedies or risk prediction.

1d: The full cohort of the UK Biobank with measured BP (473,166) and pulse rate measures. We will combine the results from these analyses with results from over 450,000 individuals from the Veteran's Administration Million Veterans Project (also genotyped with a custom Affymetrix UK Biobank array), and up to 100,000 individuals from the NHGRI-funded eMERGE network. If this proposal is approved, the total sample size in the meta-analysis will exceed 1,000,000 subjects.