Application number>Title: 47429 - The genetic basis of postoperative atrial fibrillation after cardiac surgery

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Keywords provided by the Applicant PI to describe the research project: atrial fibrillation, cardiac, cardiac surgery, genetics/genotyping, pharmacogenomics, risk-prediction

Application Lay Summary:
Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting about 3 million individuals in the US, with a $26 billion health care cost that is expected to double in the next 25 years. Postoperative AF (poAF) is the most common complication after cardiac surgery with an incidence of 30-50%, and it is associated with increased postoperative intensive care unit and hospital lengths of stay, increased morbidity and mortality and increased healthcare utilization.

There is a substantial heritable component to AF as evidenced by family studies, linkage analysis, and most recently, by genome-wide association studies (GWAS), which are studies that examine the entire human genetic code for alterations. However, despite increased elucidation of genetic associations with AF, the exact biological mechanisms underlying the development of AF are not well established. In the cardiac operating room, we have the opportunity to study poAF in patients who present for surgery in normal sinus rhythm but in whom the stress of surgery evokes poAF in over 30% of these patients. Therefore, we propose to examine DNA variants in patients undergoing cardiac surgery to identify an association with poAF. The close temporal relationship between the insult (cardiac surgery) and the event (poAF) and the high incidence of the poAF outcome make a well phenotyped cardiac surgical cohort an ideal patient group for AF research.

We will therefore perform a GWAS to test for an association between common and rare variants and poAF. Furthermore, we will perform a heritability analysis to understand how much a person's genetic make-up contributes to poAF. And finally, we will construct a risk score using all the genetic information in the UK Biobank to determine how genetic variants, with and without clinical risk factors, can predict poAF. We will do these analyses while adjusting for variables that
could also contribute to poAF.

By performing these studies, we will provide new insights into the mechanisms and pathways that initiate AF. These insights may facilitate the development of novel therapeutic strategies to alleviate the burden of AF in the community, notably in the aging population.