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Ancillary Study Title: Variation in cardiac sodium channel gene SCN5A as a predictor of baseline ECG features and CV outcomes in the Jackson Heart Study

Project Overview

Variation in cardiac sodium channel gene SCN5A as a predictor of baseline ECG features and CV outcomes in the Jackson Heart Study

Activation of the cardiac sodium channel is the initiating event in the cardiac cycle and the major determinant of the speed of conduction velocity in the heart. Slow conduction predisposes to reentrant excitation, the cause of serious arrhythmias such as ventricular fibrillation (VF), the major cause of sudden cardiac death (SCD). Reduced sodium current, by loss of function mutations in *SCN5A*, the gene encoding the cardiac sodium channel protein, or by treatment with sodium channel blocking drugs, increases the risk of SCD due to VF. A single nucleotide polymorphism resulting in S1102Y has a high minor allele frequency (13%) in African-Americans, modulates channel activity *in vitro*, and has been linked to a high propensity to arrhythmias in a small association study. Further studies have defined *SCN5A* haplotype structure and have demonstrated that promoter variants modulate regulatory activity *in vitro*, and the duration of the QRS complex – a surface electrocardiographic marker of cardiac conduction – in patient cohorts. Taken together, these data support the hypothesis that genomic variants regulate cardiac sodium channel function or expression, are detectable by analysis of surface electrocardiograms, and are predictors of cardiovascular outcome. Accordingly, this ancillary study will have three Specific Aims: (1) to determine haplotype and genotype frequencies within *SCN5A* in the Jackson Heart Study cohort; (2) to study the association between genomic variants and variability in the surface electrocardiogram; and (3) to identify polymorphisms that predict SCD or other arrhythmia outcomes in the cohort.