

Principal Investigator/Program Director (Last, First, Middle): Mitchell, Braxton D.

DESCRIPTION: See instructions. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the mission of the agency). Describe concisely the research design and methods for achieving these goals. Describe the rationale and techniques you will use to pursue these goals.

In addition, in two or three sentences, describe in plain, lay language the relevance of this research to public health. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

Stroke is a leading cause of cardiovascular-related mortality and morbidity in the United States, and a substantial genetic contribution to this disease is widely accepted. We propose to identify genes whose effects are modified in the presence of smoking. We will focus on young-onset stroke (i.e., stroke onset before age 56), in whom genetic factors and smoking-associated risk may play an even larger role. A two-stage approach will be used, beginning with a genome-wide association study in 929 young-onset stroke cases and 936 controls accrued from population-based case-control studies at University of Maryland over the past 20 years. The 1% most strongly associated SNPs will then be genotyped in the Stage 2 replication set, which will utilize 1,853 young-onset cases and 1,199 controls contributed by 9 participating sites from the International Stroke Genetics Consortium. In addition to its focus on young-onset stroke, our study has the strength of including both women and men, and African-Americans and Whites. The proposed study will complement studies of older stroke patients and will be a continuing resource for understanding the genetic basis of stroke risk and how this risk is modified by smoking.

Lay summary: Stroke, defined as acute vascular disease of the brain, is the third leading cause of death and the leading cause of major disability. The long-range goal of our research is to characterize the genetic and environmental basis for stroke susceptibility in order to develop more effective prevention and treatment strategies.

PERFORMANCE SITE(S) (organization, city, state)

University of Maryland at Baltimore (UMAB), Baltimore, Maryland