Principal Investigator: James G. Wilson

Institution Affiliation: University of Mississippi Medical Center

Ancillary Study Title: A challenge grant to develop methods for imputations and CNV analysis in genetic studies in African Americans and the Jackson Heart Study

Project Overview: In relatively homogeneous populations, correlations among different genetic variants along each chromosome make it possible to predict the genotypes of untyped single nucleotide polymorphisms (SNPs) based on data from SNPs that have been typed. Robust methods for this process, called imputation, have been established. Further, methods to detect copy number variation (CNVs) across the genome have now been developed, offering the possibility of genotyping CNVs and imputing untyped CNVs. In genetically admixed persons, however, each chromosome is a mosaic of segments that are derived from, and typical of, each of the continental populations of each person's ancestors. Thus, relationships among variants differ depending on the ancestral origin of each chromosomal segment, complicating attempts at accurate imputation. The objectives of the current project are to produce a high-quality, genome wide map of common and less common CNVs in African Americans using quantitative probe hybridization and direct sequence analysis; to develop statistical methods to perform local ancestry inference and imputation of SNPs and CNVs jointly, so that imputation in each chromosomal segment can be based on the appropriate ancestral population; and finally, to validate genotype-phenotype associations of imputed variants, detected *in silico* in the CARe cohort, by direct genotyping and analysis in the JHS cohort. These studies will provide mapping data and statistical methods that will serve as an important foundation for future genetic association studies in African Americans.