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Ancillary Study Title: Broad Novartis Diabetes Initiative: JHS Component

Project Overview

To seek a quantitative trait locus (or loci; QTL) for type 2 diabetes by performing whole-genome admixture scanning and mapping of 2,000 African Americans with diabetes and an equal number of African Americans without diabetes. DNA from a total of 2,000 African Americans with type 2 diabetes who are participants in JHS or other large observational studies and from an equal number of "hypernormal" control participants (participants who have risk factors for diabetes, e.g. age >50 and BMI ≥30, but have fasting glucose < 100 mg/dl on no diabetes medications), will be genotyped for 3,072 admixture mapping markers(1). The resulting data will be analyzed to seek chromosomal regions where the proportion of either European or African ancestry is unexpectedly high among participants with diabetes. Such regions are likely to contain the loci of risk alleles for diabetes that were more common in the over-represented ancestral population. An Illumina bead station will be used to genotype a panel of genome wide single nucleotide polymorphisms (SNPs) selected and validated by Dr. Reich to be maximally informative for admixture mapping(1). SNP data will be analyzed for association with type 2 diabetes by statistical methods that have been developed and published by Dr. Reich and colleagues (2). Admixture mapping has only recently become feasible, and available results are limited. However, calculations suggest that it may be as powerful as whole-genome haplotype-based mapping while requiring 200- to 500-fold fewer markers. Although the current proposal will focus on type 2 diabetes, the genotyping data that will be produced can be analyzed subsequently to seek QTLs for any phenotype of interest. Each new analysis will of course be subject to approval by the JHS Ancillary Studies or Publications Committee, as appropriate.