

## ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #357 REVISED

1. Title:

Diabetes Genes in African Americans I: Case-Control Studies

2. Writing Group:

(lead) Brancati, Boerwinkle, Sharrett, Szklo, Kao, Lei, Shuldiner, Watson

Correspondence:      Fred Brancati, MD, MHS  
                          Johns Hopkins Medical Institution  
                          Welch Center  
                          2024 E. Monument St., Suite 2-600  
                          Baltimore, MD 21205-2223  
Phone:                (410) 614-2410  
Fax:                  (410) 955-0476  
E-mail:               fbrancat@welchlink.welch.jhu.edu

3. Timeline:

Depends on technical aspects of DNA processing and analysis (1-2 years)

4. Rationale:

Previous studies have identified mutations in a variety of candidate genes which appear to be associated with obesity, insulin resistance, and/or non-insulin-dependent diabetes mellitus. Such candidate genes include those coding for the beta-3 adrenergic receptor, the insulin promoter, fatty acid binding protein 2, the glucagon receptor, glucose transporter 2, and mitochondrial tRNA. Previous studies of these genes have been limited by highly selected populations, small samples sizes, lack of data concerning known behavioral risk factors for obesity and NIDDM such as diet and physical activity, and few data on African Americans, a group at high risk for NIDDM and its complications. The identification of genotypes that confer risk for obesity, insulin resistance, and NIDDM in larger populations would represent an important advance in our understanding of the pathophysiology of these conditions. These genotypes would also have immediate applications as prognostic markers in observational and interventional studies of persons at risk for NIDDM.

5. Main Hypothesis:

Mutations in the aforementioned genes are associated with the presence of obesity, hyperinsulinemia, and NIDDM in African Americans.

6. Design:

Case-control studies stratified by race, with three distinct case groups and a single comparison group

Case #1: Diabetes mellitus (ARIC definition, including undiagnosed cases)

Case #2: Severe obesity (Top decile of body-mass index)

Case #3: Hyperinsulinemia without diabetes (Top decile in non-diabetics)

Control: Random sample of all non-cases

7. Data:

Case-control status: Diabetes, body-mass index; fasting glucose and insulin

Exposure status: Diabetes susceptibility genotypes to be determined from DNA extracted from existing frozen buffy coat

Covariates: Age, race, gender, education, physical activity indices, dietary energy intake, parental history of diabetes, smoking

8. Sample Size:

270 in each of the three case groups and 1,080 in the one control group, comprising a total of 1,803 distinct individuals. [See attachment\* for power calculations; note that case definitions partially overlap].

\*Note: For a copy of the manuscript with the attachment, please contact the ARIC Student Assistant at Collaborative Studies Coordinating Center, Department of Biostatistics, UNC-Chapel Hill. Contact by phone: (919) 962-3268 or fax: (919) 962-3265.