ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #417

1. a. Full Title: Plasma Fatty Acid Composition and 6-Year Incidence of Non-Isulin Dependent Diabetes Mellitus (NIDDM) in Middle-Aged Adults.
b. Abbreviated Title : Plasma FA COmDOSitiOn and Incident DM

2. Writing Group:

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3. Timeline: This is based on ancillary Minneapolis data. Analyses are expected to be completed within 4 weeks; a draft manuscript can be presented to the writing group within 1 month after the completion of the analysis.

4. Rationale:

Fatty acid (FA) intake and metabolism may play an important role in the etiology of non-insulin dependent diabetes mellitus (NIDDM). In animal models, low carbohydrate and high fat feeding produces insulin resistance by a mechanism which may involve increased free fatty acid levels. Epidemiologic studies have found that high dietary fat intake and FA composition of adipose tissue, serum/plasma cholesterol esters and phospholipids are associated with fasting hyperinsulinemia, reduced insulin sensitivity, impaired glucose tolerance, and NIDDM.

A recent prospective study of 50 year old men who were normoglycemic at baseline, found that serum cholesterol ester FA composition was associated with the risk of NIDDM during 10-year follow up. Individuals who developed NIDDM had higher proportions of saturated fatty acids and palmitoleic acids (16:ln7), higher proportions of γ-linolenic (18:3n6) and dihomo-γ-linolenic (20:3n6) acids, and a lower proportion of linoleic acid (18:2n6) in the serum cholesterol esters. After adjustment for BMI, glucose,

insulin, systolic and diastolic blood pressures, and triglycerides, only dihomo-*gamma*-linolenic (20:3n6) acid was statistically significantly associated with the risk of NIDDM.

We measured the FA composition of plasma cholesterol esters and phospholipids at the Minneapolis Field Center during the ARIC baseline examination. During 6 years of follow up (up to visit 3), approximately 160 Minneapolis participants have developed diabetes.

5. Main Hypotheses:
1) Higher levels of saturated fatty acids and monounsaturated fatty acids in plasma cholesterol esters and phospholipids are associated with increased risks of diabetes mellitus; 2) Higher levels of polyunsaturated FAs and higher P/S ratio are associated with lower risks of diabetes mellitus.

6. Data:

ARIC baseline, visit 2, and visit 3 data from Minneapolis will be used for analyses. Incident NIDDM is defined as fasting glucose > or = 140 mg/dl, non-fasting glucose > or = 200 mg/dl, or history of, diabetes, at the visit 2 or visit 3 examinations, but without evidence of NIDDM at the baseline visit. The main variables include baseline status of diabetes, visit 3 status of diabetes, baseline FA composition of plasma cholesterol esters and phospholipids. Other variables include age, gender, baseline levels of glucose, insulin, triglycerides, fibrinogen, body-mass index, waist-hip ratio, baseline cigarette smoking status, education, alcohol consumption, physical activity (leisure and sport indeces), and family history of diabetes mellitus.