ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #559

1. Full Title: Associations of total serum sialic acid and related acute phase proteins with incident diabetes.
   Abbreviated Title (length 26): Sialic acid and diabetes

2. Writing Group (list individual with lead responsibility first):
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3. Timeline:
   2/98 - 5/98

4. Rationale:
   The concept of type-2 diabetes as a disorder involving acute-phase reactants has been recently proposed by Pickup et al (1) from studies on prevalent cases of type 2 diabetes. This raises the question as to whether activation of the innate immune system plays a role in the causation of type 2 diabetes or is merely a consequence of it.

   Inflammatory markers have been noted as risk factors for CVD. The multiple metabolic syndrome, a cluster of risk factors that overlap in the causal pathways of type 2 diabetes and CVD, has also been related to cytokines and acute phase reactants (1; 2). Thus, it is reasonable to propose that markers of these inflammatory processes are risk factors also for type 2 diabetes.

   Sialic acid, and the three acute phase proteins, orosomucoid, haptoglobin and alpha 1 antitrypsin, which account for 70% of its variability, were measured in a sub-sample of ARIC participants at Visit 2. Sialic acid associates cross-sectionally with Atherosclerosis and prospectively with incident CHD (3; 4).

   The objective of this proposal is to study the association of serum total sialic acid and the related acute phase proteins with incident diabetes in the ARIC (Atherosclerosis case control) sub-study.

REFERENCES:
1) Pickup JC, Mattock MB, Chusney GD, Burt D. NIDDM as a disease of the innate
2) Yudkin JS. Is insulin vasculotoxic? Diabetologia. 1997;40:S140-S146

5. Main Hypotheses:
1) Serum total sialic acid, alpha l anti-trypsin, haptoglobin and orosomucoid are associated with incident diabetes.
2) Serum total sialic acid, alpha l anti-trypsin, haptoglobin and orosomucoid are associated with prevalent diabetes.

6. Data (variables, time window, source, inclusions/exclusions):
Participants of the atherosclerosis case-control subsample with valid sialic acid measurements. Data from visits 14.
Variables to define diabetes (fastO802, medication use, physician history, glucos0l, and visit 2-4 equivalents)
Exposure variables: Sialic acid, orosomucoid, haptoglobin, alpha l antitrypsin
Covariates: Gender, age, ethnicity, BMI, WS, physical activity, blood pressure, lipids, glycated hemoglobin (V2 only), fasting insulin, family history of diabetes, smoking status and pack-years of smoking, antidiabetes medication use.