

ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #203

1. Title:

Genetic influence on plasma vitamin A concentrations

2. Writing Group:

(lead) E Boerwinkle, AR Sharrett, G Heiss, and W Patsch

3. Timeline:

Data collection and management for the primary dependent and independent variables is already complete. Data analyses can begin immediately.

4. Rationale:

Vitamin A (Retinol) is one of the major fat-soluble vitamins whose primary source is foods containing carotenoids. Vitamin A is involved in numerous metabolic pathways related to vision, growth, and reproduction. There is considerable interest in the relationship between Vitamin A and chronic disease occurrence such as heart disease and cancer. These relationships are likely mediated by the role of vitamin A as an anti-oxidant and mediator of epithelial cell growth. Plasma levels of vitamin A are normally low (approximately 1.5 μM). However, there is considerable interindividual variability in plasma vitamin A levels, possibly contributing to risk of these chronic diseases.

After absorption in the intestine, chylomicron-associated retinol is transported to the liver where it is taken up by an apolipoprotein E-mediated receptor pathway. Apolipoprotein E in humans is polymorphic with three alleles, ϵ 2, ϵ 3, and ϵ 4. In all populations studied thus far, ϵ 3 is the most common allele, with ϵ 2 and ϵ 4 being less frequent. The frequency of the ϵ 4 allele is elevated in hyperlipidemic subjects and the average effect of the ϵ 4 allele is to increase plasma LDL-cholesterol levels. The ϵ 2 allele is associated with type III hyperlipidemia, but the average effect of the ϵ 2 allele in the population-at-large is to decrease plasma LDL-cholesterol levels. The receptor binding defect of the E-2 protein has been well characterized, as has been the pathway in type III hyperlipidemia. We have recently described the role of the common apolipoprotein E polymorphism in determining post-prandial response in the ARIC study.

This study will determine whether fasting plasma vitamin A (retinol) concentrations are influenced by the common apo E polymorphisms.

5. Main Hypotheses/Issues to be Addressed:

*Average fasting plasma retinol palmitate levels are different among the three common apolipoprotein E genotypes, ϵ 2/3, ϵ 3/3, and ϵ 3/4.

*Average fasting plasma retinol palmitate levels after adjusting for fasting LDL-cholesterol, HDL-cholesterol, and triglyceride levels are different among the three common apolipoprotein E genotypes, ϵ 2/3, ϵ 3/3, and ϵ 3/4.

