

## ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #203

1. Title:

Genetic influence on plasma vitamin A concentrations

2. Writing Group:

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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  $\mu\text{M}$ ). 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,  $[\sigma]2$ ,  $[\sigma]3$ , and  $[\sigma]4$ . In all populations studied thus far,  $[\sigma]3$  is the most common allele, with  $[\sigma]2$  and  $[\sigma]4$  being less frequent. The frequency of the  $[\sigma]4$  allele is elevated in hyperlipidemic subjects and the average effect of the  $[\sigma]4$  allele is to increase plasma LDL-cholesterol levels. The  $[\sigma]2$  allele is associated with type III hyperlipidemia, but the average effect of the  $[\sigma]2$  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,  $[\sigma]2/3$ ,  $[\sigma]3/3$ , and  $[\sigma]3/4$ .

\*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,  $[\sigma]2/3$ ,  $[\sigma]3/3$ , and  $[\sigma]3/4$ .

