Manuscript #600 DEFERRED

1. Title: Frequencies of Genetic polymorphisms of glutathione S-transferase M1 (GSTM1) and glutathione S-transferase T1 (GSTT1) in the ARIC cohort
   Abbreviated Title: FREQUENCIES OF GSTM1 & GSTT1

2. Writing Group (list individual with lead responsibility first):
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3. Timeline:
   Analyses will be completed in two months after approval by the Publications Committee and completion of genotype assays. Draft manuscript will be done within 2-3 months after completion of the analysis.

4. Rationale:
   Smoking is strongly associated with atherosclerosis and cardiovascular disease. Similar genetic polymorphisms of GSTs and atherosclerosis susceptibility given exposure to carcinogens in tobacco has been studied in animal models and tissue or cell cultures in vitro. No population-based study has addressed genetic susceptibilities to CHD given exposure to cigarette smoking.

   The enzymes encoded by GSTM1 and GSTT1 have been found to detoxify promutagens/mutagens in cigarette smoke in studies of cancer end-points. Monoclonal origin or arterial smooth muscle proliferation was proposed to be similar to tumor regionalism. In addition, GSTM1 is thought to be involved in the inflammatory pathology, and GSTT1 has been found to detoxify oxidized lipids. Thus, individuals with a homozygous deletion of GSTM1 and GSTT1 may be more likely to have a higher risk of atherosclerosis given exposure to intrinsic and environmental promutagens/mutagens.

   There is NOT reliable population-based GST prevalence data for US blacks and whites. The specific aim of this study is to detect the frequencies of homozygous deleted genotype of glutathione S-transferase M1 (GSTM1 0/0) and glutathione S-transferase T1 (GSTT1 0/0) in the ARIC cohort, a community-based biracial population.

5. Main Hypotheses:
   Frequencies of GSTM1 0/0 and GSTT1 0/0 are not significantly different between African-Americans and whites.
6. Data (variables, time window, source, inclusions/exclusions):
GSTM1 and GSTT1 of cohort random sample, and of phantoms (for reproducibility assessment); age, race, gender, and centers in visit 1.

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