

## Genetic Susceptibility to Obesity-Related Dyslipidemia in African Americans, or the GOLD-A (Genetics of Lipid Disorders) Study.

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Principal Investigator: Ronald Krauss, MD

### Synopsis:

Obesity is often associated with insulin resistance and an atherogenic dyslipidemia that is characterized by elevated triglyceride, decreased HDL cholesterol and increased small, dense LDL particles. Genetic factors play a role in determining susceptibility to this dyslipidemia. We have recently identified a single nucleotide polymorphism (SNP) in the angiotensin receptor 1 (AGTR1) gene that was associated with protection from obesity-related dyslipidemia. Interestingly, the SNP occurs more frequently in African Americans than Caucasians.

Genetic association studies require replication before an observation can be considered "true". This pilot study seeks to: 1) confirm the protective association of the AGTR1 polymorphism on dyslipidemia in an independent cohort of generally healthy African Americans, and 2) build on existing programs of community outreach to local Oakland/Berkeley minority communities as well as develop an infrastructure for community participation in clinical research from traditionally underrepresented minority and ethnic groups

The AGTR1 polymorphism occurs with greater frequency in African Americans and has been associated with protection from atherogenic dyslipidemia, even in persons who are overweight and/or obese. To be eligible for this study, participants must be of African American ancestry as defined by having at least three grandparents of African American descent, be older than 18 years, and have a waist circumference  $> 101.6\text{cm}$ . Given the financial limitations of this pilot study, we have restricted participant enrollment to African Americans in the upper tertile of waist circumference in order to maximize statistical power and allow for the greatest likelihood of determining whether the AGTR1 polymorphism has a protective effect on obesity-associated dyslipidemia.

Persons with a history of diabetes or CVD and/or who are on lipid lowering medications will be excluded. Eligible and interested persons will be asked to provide a fasting blood specimen either at our clinic, the Cholesterol Research Center at 3101 Telegraph Avenue, Berkeley, or at other sites in collaboration with other investigators at CHORI and/or under the umbrella of the Clinical Translational Science Institute (CTSI). Details of our recruitment plans are given below. Plasma will be isolated for the determination of glucose, triglycerides, total cholesterol, LDL and HDL cholesterol, LDL subclass pattern and LDL peak particle size. DNA isolated from mononucleated blood cells from the same blood sample will be assayed for the AGTR1 SNP\_0019387 polymorphism using a Taqman assay-on-demand reagent available from Applied Biosystems (Santa Clara, CA).