Polymorphic Markers in Apolipoprotein C-III Gene Flanking Regions and Hypertriglyceridemia


Elevated circulating blood triglycerides (a fat) and cholesterol lipids are very common in Americans, but are associated with coronary artery disease and premature death. The proteins called apolipoproteins (apo) are involved with the metabolism and transport of triglycerides and lipids through the blood. We hypothesized that genetic differences in apo genes may cause people to have differences in triglyceride and cholesterol levels and, by extension, heart disease.

In this study we investigated three apo genes, A-I, C-III, and A-IV, which are located very close to each other on a chromosome. We genotyped (measured) six genetic polymorphisms in these genes in a large sample of people from the Atherosclerosis Risk in Communities Study (ARIC). The ARIC study population has been measured for numerous traits related to heart disease and health, including cholesterol and triglyceride levels. We determined that one particular polymorphism, called Sst I, was significantly associated with elevated triglycerides, but not other cardiac-related traits such as carotid artery wall thickness, plasma apo C-III levels, or elevated cholesterol. We found significant linkage disequilibrium (LD), lack of independence, between the alleles of the six polymorphisms we genotyped, but the strongest evidence for association with triglyceride levels was with the Sst I polymorphism (odds ratio, 4.0; P < .0001).

This study suggested that the Sst I polymorphism had a significant effect on triglyceride levels and that the gene it was located closest to, apo C-III, is very important for triglyceride transport or metabolism.

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