BACKGROUND AND AIMS: Several genes have been shown to individually affect plasma lipoprotein metabolism in humans. Studies on gene-gene interactions could offer more insight into how genes affect lipid metabolism and may be useful in predicting lipid concentrations. We tested for gene-gene interactions between TaqIB SNP in the cholesterol ester transfer protein (CETP) and three novel single nucleotide polymorphisms (SNPs), namely rs11774572, rs7819412 and rs6995374 for their effect on metabolic syndrome (MetS) components and related traits.

METHODS AND RESULTS: The aforementioned SNPs were genotyped in 1002 subjects who participated in the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study. Lipids were measured by standard procedures and lipoprotein subfractions, by proton nuclear magnetic resonance spectroscopy. Polymorphism rs11774572 was significantly associated with MetS (P=0.020), mainly driven by the association of the C allele with lower HDL-C (P=0.043) and higher triglycerides (P=0.049) and insulin...
(P=0.040) concentrations than TT subjects. A significant interaction between SNPs rs11774572 and CETP-TaqIB SNPs was found for HDL-C concentrations (P=0.006) and for HDL (P=0.008) and LDL particle sizes (P=0.009), small LDL (P=0.004), and VLDL concentrations (P=0.021), in which TT homozygotes displayed higher HDL-C concentrations and for HDL and LDL particle sizes, and lower small LDL and VLDL concentrations than C carriers, if they were CETP B2 allele carriers (P values ranging from <0.001 to 0.001).

**CONCLUSIONS:** The rs11774572 polymorphism may play a role in the dyslipidemia that characterizes MetS. The interaction between rs11774572 and CETP-TaqIB SNPs on HDL-C concentrations provides some insights into the underlying mechanisms.