



First report of SR-B1 mutation in man influencing HDL cholesterol levels

Researchers from the Academic Medical Center, Amsterdam, The Netherlands reported on the first evidence of a scavenger receptor class B1 (SR-B1) mutation in man.¹ SR-B1 is a hepatic receptor for high-density lipoprotein (HDL). SR-B1 promotes selective uptake and removal of HDL from the plasma, and is therefore important in protecting against atherosclerosis. Experimental studies have previously shown that mice with attenuated SR-B1 expression have very high levels of HDL cholesterol.

Genetic sequencing of the SR-B1 gene in 90 unrelated subjects with hyperalphalipoproteinaemia (defined as plasma HDL cholesterol levels > 95th percentile for age and gender) identified one subject who was heterozygous for a point mutation (substitution of proline for a serine residue at position 297 [P297S] in the extracellular domain of SR-B1).

Genetic studies of 96 members of this subject's family identified a further 14 P297S carriers (n=14). This mutation had a significant effect on HDL cholesterol levels, even when data were adjusted for sex, age, body mass index, smoking habits and alcohol use (p=0.0034). Notably, the P297S carriers had 37% increased HDL cholesterol levels (p=0.003) and a 17% increase in apolipoprotein A-1 levels (p=0.042), compared with non-carrier family members who were matched for age and sex. There were no significant effects on total cholesterol, low-density lipoprotein cholesterol, triglycerides, apolipoprotein B and apolipoprotein E levels.

The researchers concluded that the study suggests that SR-B1 may be as important as other enzymes involved in HDL metabolism for controlling HDL cholesterol levels in humans.

Reference

1. Vergeer M, Kuivenhoven JA. Heterozygosity for a mutation in the extracellular domain of SR-B1 is associated with high HDL cholesterol levels in a family of Caucasian descent. Presented at the American Heart Association Scientific Sessions 2006, Abstract 1340.