

Lipid research

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APOLIPOPROTEIN A1/C3/A5 HAPLOTYPES AND SERUM LIPID LEVELS

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Background and aims Single nucleotide polymorphisms (SNPs) at the apolipoprotein (Apo) A1/C3/A4/A5 gene cluster have been examined in relation to lipid metabolism and cardiovascular disease risk. However, the previous findings are inconsistent. The present study was undertaken to detect the association between ApoA1/C3/A5 haplotypes and serum lipid levels in the general Chinese population.

Methods A total of 1030 unrelated subjects (492 males and 538 females) aged 15–89 were randomly selected from our previous samples. Genotyping of the ApoA1 –75bp G>A, ApoC3 3238C>G, ApoA5 –1131T>C, ApoA5 c.553G>T and ApoA5 c.457G>A was performed by PCR and restriction fragment length polymorphism combined with gel electrophoresis, and then confirmed by direct sequencing. Pair-wise linkage disequilibria (LD) and haplotype analysis among the five SNPs were estimated.

Results The levels of high-density lipoprotein cholesterol (HDL-C) and ApoA1 were lower in males than in females (P A was in LD with the other four SNPs; ApoC3 3238C>G was in LD with ApoA5 –1131T>C; ApoA5 –1131T>C was in LD with c.553G>T and c.457G>A. There was no significant difference in the allelic and genotypic frequencies of the all SNPs except ApoC3 3238C>G between males and females. The levels of triglyceride (TG) in males and HDL-C and the ratio of ApoA1 to ApoB in females were different among the three genotypes of the ApoA1 –75bp G>A (P G (P C (P T (P A (P 1% identified in the cluster in our population. At the global level, the haplotypes comprised of all five SNPs were significantly associated with all seven lipid traits. In particular, haplotype G-A-T-C-G (6%) and G-A-T-C-G (4%) showed consistent association with LDL-C, TC, ApoA1, ApoB and the ratio of ApoA1 to ApoB. In addition, carriers of haplotype G-G-T-C-G (26%) had increased serum concentration of HDL-C and ApoA1, whereas carriers of G-G-C-G-G (15%) had high concentrations of TG, TC and ApoB. The authors also found that haplotypes with five SNPs explain much more serum lipid variation than any single SNP alone, especially for TG (4.4% for haplotype vs 2.4% for –1131T>C max based on R-square) and HDL-C (5.1% for haplotype vs 0.9% for c.553G>T based on R-square). Serum lipid parameters were also correlated with genotypes and several environment factors such as gender, age, weight, body mass index, alcohol consumption, cigarette smoking and blood pressure in the population.

Conclusions Several common SNPs and their haplotypes at the ApoA1/C3/A5 gene cluster are closely associated with modifications of serum lipid parameters in the general Chinese population.