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LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

A COMBINATION OF SNPS IS ASSOCIATED WITH THE POSTPRANDIAL CHYLOMICRON TRIACYLGLYCEROL RESPONSE IN HEALTHY MALE ADULTS

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The postprandial chylomicron (CM) triacylglycerol (TG) response to dietary fat, which is positively associated with atherosclerosis and cardiovascular disease risk, displays a high inter-individual variability. This is assumed to be due, at least partly, to polymorphisms in genes involved in lipid metabolism. Existing studies have so far focused on single SNPs, resulting in a low explained variability. This study aimed to identify a combination of SNPs that could predict an elevated postprandial CM TG response.

Thirty-four healthy male volunteers were subjected to four standardized fat tolerance test meals and genotyped using whole-genome microarrays. Plasma CM TG were measured at regular interval times after each meal. The association of SNPs, in or near candidate genes (126 genes representing 6099 SNPs), with the high (> mean response + 1 SD) ***vs*** normal postprandial CM TG response (0 to 8 h postprandial AUC averaged for the four test meals) was assessed by partial least squares discriminant analysis, a multivariate statistical approach.

Data obtained allowed us to generate a validated significant model (P=2.6.10^{-7}) that included 28 SNPs in 14 genes (*ABCA1*, *APOB*, *BET1*, *CILP2*, *COBLL1*, *GALNT2*, *IRS1*, *LDLR*, *LIPC*, *MAP3K1*, *MC4R*, *PARK2*, *SLC27A6*, *ZNF664*) and explained 81% of the variance. Univariate analysis revealed several significant (P<0.05) differences in CM TG responses between subjects who bore different genotypes in the abovementioned SNPs.

Our results enable us to propose a genetic score that could suggest whether a subject belongs to the high responder phenotype and hence might be at increased risk of atherosclerosis and cardiovascular diseases.

No conflict of interest