

CETP Genetic Variation Modulates Effects of Weight-loss Diets on Lipid Profile in Two Independent 2-Year Diet Intervention Studies: The Pounds Lost and DIRECT Trails

Ronen Durst¹, Qibin Qi³, Dan Schwarzfuchs^{2,5}, Eran Leitersdorf¹, Shoshi Shpitzen¹, Meir J. Stampfer^{3,4}, Frank M. Sacks³, Lu Qi^{3,4}, Iris Shai²

¹*Cardiology Department, Hadassah Hebrew University Medical Center, Israel*

²*Department of Public Health, Ben Gurion University of the Negev, Israel*

³*Department of Nutrition, Harvard School of Public Health, USA*

⁴*Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, USA*

⁵*The Nuclear Research Center, The Nuclear Research Center, Israel*

Background:

Cholesterol ester transfer protein (CETP) plays a key role in the transport of cholesteryl esters and triglycerides between the lipoproteins; and genetic variation in CETP gene has been related to blood lipids levels. It remains unclear whether CETP genetic variation may modulate effects of dietary intervention on lipid profiles.

Methods

We have genotyped a CETP genetic variant rs3764261 in 732 adults with overweight from the Pounds Lost Trial and Dietary Intervention Randomized Controlled Trial. We compared the effects of high and low fat diets on HDL and triglycerides according to the genotypes of rs3764261 at 6 months and over the 2-year intervention.

Results

At baseline, the C allele of rs3764261 was significantly associated with low HDL cholesterol levels in participants from both trials. In the Pounds Lost trial, there were significant interactions between the genotype and diet intervention on changes in HDL cholesterol (P for interaction = 0.05) and triglycerides (P for interaction = 0.002). Among participants with CC genotype, the high-fat diet had greater effects on increases in HDL cholesterol (P = 0.001) and decrease in triglycerides (P = 0.007) than the low-fat diet at 6 months, while no significant difference between the 2 diet groups was observed among participants with CA/AA genotype. The findings were replicated in the DIRECT trial (both P ≤ 0.0005; Figure 1). Generalized estimating equation analysis further indicated that the high-fat diet was more effective in improvement of HDL cholesterol (P = 0.007 and 0.0001 in the Pounds Lost and DIRECT, respectively) and triglycerides levels (P = 0.06 and 0.003, respectively) than the low-fat diet among participants with CC genotype over the 2-year intervention.

Conclusions

Our data from two independent dietary intervention trials suggest that individuals with the CETP rs3764261 CC genotype might obtain more benefits in improvement of lipid profile by choosing a high-fat weight-loss diet compared with a low-fat diet.