

Nutrigenomics Researchers Replicate Gene Interaction With Saturated Fat

ScienceDaily (Nov. 19, 2009) — Tufts University researchers have identified a gene-diet interaction that appears to influence body weight and have replicated their findings in three independent studies. Men and women carrying the CC genotype demonstrated higher body mass index (BMI) scores and a higher incidence of obesity, but only if they consumed a diet high in saturated fat. These associations were seen in the apolipoprotein A-II gene (*APOA2*) promoter.

"We believe this is the first time a gene-diet interaction influencing BMI and obesity has been replicated in as many as three independent study populations," said corresponding and senior author Jose Ordovas, PhD, director of the Nutrition and Genomics Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging (USDA HNRCA) at Tufts. "Our findings strengthen support for the science of nutrigenomics and are another step toward the goal of individually tailoring dietary recommendations to lower risk of chronic disease or conditions like obesity."

The study, published in the November 9 issue of *Archives of Internal Medicine*, examines gene-diet interactions in the *APOA2* promoter, a region of DNA controlling expression of the *APOA2* gene. Proteins responding to some nutrients in food interact with promoters which dictate how genes behave. There are two variants or alleles of the *APOA2* promoter, T and C. They exist in three genotypes: CC, TT and TC.

Ordovas and colleagues studied these genotypes in 3,462 men and women who participated in the Framingham Offspring Study (FOS), the Genetics of Lipid Lowering Drugs and Diet Network Study (GOLDN) and the Boston-Puerto Rican Centers on Population and Health Disparities Study (Boston-Puerto Rican Study). FOS and GOLDN enrolled Caucasian adults. The Boston-Puerto Rican Study is comprised of Puerto Rican men and women. "We are further encouraged that our findings were replicated in diverse populations," said Ordovas, who is also a professor at the Friedman School of Nutrition Science and Policy at Tufts.

The researchers divided the study population into high and low saturated fat groups. Next, they compared saturated fat intake, BMI and obesity risk across the CC, TT and TC genotypes. High saturated fat intake was defined as 22 grams or more per day. Foods such as fatty cuts of meat and dairy products made with whole or 2 % milk contain saturated fat, which raises cholesterol. CC carriers who consumed high levels of saturated fat were the most susceptible to higher BMI and obesity, Ordovas and colleagues observed.

"Across all three studies, the CC carriers who consumed high-saturated fat diets had the highest BMIs compared to the TT and TC genotypes and, most notably, other CC carriers who reported consuming low-saturated fat diets," said first author Dolores Corella, PhD, Professor at the Valencia University-CIBER Fisiopatología de la Obesidad y Nutrición (Spain), and visiting scientist in the Nutrition and Genomics Laboratory at the USDA HNRCA. "This work is based on a two year-old study finding genotypes influence food preferences, calorie intake and BMI."

In the previous study, Ordovas, Corella and colleagues found men and women with the CC genotype had a statistically significant higher intake of fat than the TT and TC genotype groups. Additionally, CC carriers ate about 200 more calories per day and were about twice as likely to be obese.

The authors saw the same results for obesity prevalence within the CC genotype in the present study. "We

saw a strong association between obesity and high saturated-fat intake, but again, there was no significant association between the two in CC carriers with low saturated-fat intake or in TT or TC carriers," Corella added.

Obesity was defined as BMI of 30 or greater. The researchers calculated BMI as weight in kilograms divided by height in meters squared. Dietary intake was measured by self-reported dietary questionnaires.

As in the general population, the majority of study participants possessed the TT and TC genotypes. Approximately 10 to 15 percent of the United States population is CC carriers, which was reflected in the FOS, GOLDN and Boston Puerto-Rican Study.

"Although CC carriers are only a small portion of the population, we believe the interaction we observed between saturated fat and BMI merits further investigation," Ordovas said. "There is a need to understand the mechanisms behind this particular diet-gene interaction and to find out whether other there are similar interactions in other genes that could factor in obesity prevention."

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Corella D, Peloso G, Arnett DK, Demissie S, Cupples LA, Tucker K, Lai C, Parnell LD, Coltell O, Lee Y and Ordovas JM. *Arch Intern Med* . (Nov. 9, 2009); vol. 169 (20): 1897-1906. "APOA2, Dietary Fat and Body Mass Index."

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