

FADS genotypes and desaturase activity estimated by the ratio of arachidonic acid to linoleic acid are associated with inflammation and coronary artery disease

Martinelli N, Girelli D, Malerba G, Guarini P, Illig T, Trabetti E, Sandri M, Friso S, Pizzolo F, Schaeffer L, Heinrich J, Pignatti PF, Corrocher R, Olivieri O.

Department of Clinical and Experimental Medicine and the Section of Biology and Genetics, University of Verona, Verona, Italy

American Journal of Clinical Nutrition. 2008 88(4):941-949

BACKGROUND: The delta-5 and delta-6 desaturases, encoded by FADS1 and FADS2 genes, are key enzymes in polyunsaturated fatty acid (PUFA) metabolism that catalyze the conversion of linoleic acid (LA) into arachidonic acid (AA) and that of alpha-linolenic acid (ALA) into eicosapentaenoic acid (EPA). Single-nucleotide polymorphisms (SNPs) in FADS1 and FADS2 have been associated with different concentrations of AA and LA, and those associations have possible functional consequences for desaturase activity. **OBJECTIVE:** We aimed to evaluate the possible association among FADS genotypes, desaturase activity, inflammation, and coronary artery disease (CAD). **DESIGN:** Thirteen FADS SNPs and the ratio of AA to LA (AA/LA) on red blood cell (RBC) membranes, a marker of desaturase activity, were evaluated in 876 subjects with (n = 610) or without (n = 266) angiographically documented CAD. **RESULTS:** Both AA/LA and the ratio of EPA to ALA (EPA/ALA) were higher in patients with CAD than in those without CAD, but, in a multiple logistic regression model, only a higher AA/LA resulted an independent risk factor for CAD (odds ratio: 2.55; 95% CI: 1.61, 4.05 for higher compared with lower ratio tertile; P for trend < 0.001). Furthermore, concentrations of high-sensitivity C-reactive protein increased progressively across tertiles of AA/LA. Graded increases in high-sensitivity C-reactive protein concentrations and CAD risk were related to the carriership of FADS haplotypes, including the alleles associated with a higher ratio. **CONCLUSION:** In populations following a Western diet, subjects carrying FADS haplotypes that are associated with higher desaturase activity may be prone to a proinflammatory response favoring atherosclerotic vascular damage.