

+294T/C polymorphism in the PPAR- δ gene is associated with risk of coronary artery disease in normolipidemic Tunisians

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ABSTRACT. Peroxisome proliferator-activated receptor delta (PPAR- δ) is a transcription factor implicated in metabolism and inflammation. The +294T/C polymorphism in the PPAR- δ gene is associated with risk of coronary artery disease (CAD) in dyslipidemic women and hypercholesterolemic men. Whether this polymorphism influences the risk of CAD in the absence of dyslipidemia was not known, so we investigated a possible association of this polymorphism with plasma lipid and lipoprotein levels and with risk and outcome of CAD in a normolipidemic Tunisian population. Genotyping was performed by PCR-RFLP in 112 CAD patients and 113 healthy volunteers. The C-allele was significantly more frequent in patients than in controls (0.320 vs 0.189, $P = 0.001$). This association remained significant after adjustment for age, gender, body mass index, smoking, hypertension, and high-density

lipoprotein cholesterol. Subjects carrying either one or two copies of the C-allele had a 2.7-fold higher risk of CAD than subjects homozygous for the T-allele. PPAR- δ genotypes were not associated with lipoprotein concentrations or outcome of CAD. We conclude that PPAR- δ +294T/C polymorphism is an independent risk factor of CAD in normolipidemic Tunisian subjects. The lack of association with lipoprotein concentrations suggests that the effect of the polymorphism on CAD is not mediated through lipoprotein levels in this population and that it may influence the atherosclerotic process through mechanisms involving inflammation.

Key words: PPAR- δ ; Polymorphism; Coronary artery disease; Inflammation