The Gln241His polymorphism in the carbohydrate response element binding protein (MLXIPL) gene is associated with fasting triglyceride concentrations and BMI in a Mediterranean population

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***Abstract**:* In a recent genome-wide association study, we participated in the identification for the first time of a new locus associated with plasma triglyceride concentrations. This loci was at 7q11 near TBL2 (transducin(beta)-like 2) and MLXIPL (MLX interacting protein-like or carbohydrate response element binding protein) genes. Further studies identified a nonsynonymous SNP (rs3812316, G771C, Gln241His) in the MLXIPL gene as the SNP most significantly associated with plasma triglycerides. Moreover, its has been suggested that MLXIPL is a thrifty gene because the wild-type variant may permit more efficient food utilization, fat deposition and rapid weight gain at times of food abundance. Therefore our aims were to study the association between the Gln241His in the MLXIPL gene with fasting triglycerides and obesity-related variables in a high cardiovascular risk Mediterranean population.
We analyzed 1002 high cardiovascular risk individuals from the PREDIMED-Valencia Study. Participants (men and women aged 67y) were free of CVD and had type 2 diabetes (45%), or three or more CVD risk factors. Genetic, clinical, biochemical, anthropometric and life-style data were determined.
Prevalence of the MLXIPL genotypes were: 85.4% CC, 13.7% GC, 0.9% GG (allele frequencies, C=0.923 and G=0.077). Plasma triglyceride concentrations were significantly lower in carriers of the G allele (P=0.012). Interestingly, we found a consistent association of the SNP with lower BMI. In terms of weight, we observed a gene-dosage decreasing effect of this polymorphism: 78+/-13 kg (CC), 75+/-12 kg (CG), 66+/-19 kg (GG); P=0.004. This decrease in body-weight in G-allele carriers was observed in both men and women.