**TARGETED SCREENING OF THE ASSOCIATIONS BETWEEN CANDIDATE GENES AND ALCOHOL CONSUMPTION IN A HIGH CARDIOVASCULAR RISK POPULATION**

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**Background**: Moderate alcohol intake has been controversially associated with cardiovascular risk. Several unmeasured confounders may influence such association. Therefore, Mendelian randomization, using a genetic proxy as a more objective marker for intake has been used. There are some polymorphisms in candidate genes associated with alcohol intake in several populations, however, the validity of these markers may vary depending on the population characteristics (age, gender, disease status, cultural factors, etc. Our aim is to analyze whether polymorphisms in candidate genes for alcohol intake such as the ADH (alcohol deshidrogenase) cluster (chromosome 4) and the aldehyde deshidrogenase gene (ALDH2) in a high cardiovascular risk population.

**Methods**: We have carried out an observational study at baseline in high cardiovascular risk subjects from a Mediterranean population, including (n=1040) men and women aged 67+/-7 y. with type-2 diabetes or three or more cardiovascular risk factors. Alcohol intake was measured by a validated questionnaire and genotyping and carried out by the Human OmniExpress Array.

**Results and conclusions**: We tested several genes and polymorphisms in this population as follows: ADH1A: 14 SNPs; ADH1B: 16 SNPs; ADH1C: 15 SNPs; ADH4:48 SNPs; ADH5:26 SNPs; ADH6:24 SNPs; and ADH7:26 SNPs. For the ALDH2, we tested 22 SNPs. We observed several statistically significant associations between alcohol consumption and the analyzed SNPs. The top-ranked SNPs was the rs3819197, in the ADH1A gene. The minor allele (MAF: 0.4) was associated with higher alcohol consumption (B=1.83 +/-0.48 g/d; P=0.00017). The second top-ranked SNPs was the rs2075633 in the ADH1B gene. The minor allele (MAF: 0.36) was also associated with higher alcohol consumption (B=1.66+/-0.49 g/d; P=0.00079). Other SNPs in the different genes analyzed within the ADH cluster having statistically significant associations (P<0.05) were: rs1229966, rs13133908, rs9995799, rs10008281, rs4147531, rs4147532, rs971074, rs1353621 and rs4147545. These results indicate that even in a high cardiovascular risk population, the genetic influence in determining alcohol consumption is statistically significant.