

## VARIATION IN THE MINICHROMOSOME MAINTENANCE COMPLEX COMPONENT 6 GENE, DAIRY INTAKE AND CARDIOVASCULAR RISK

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**Objectives and Background:** Single nucleotide polymorphisms (SNPs) in the minichromosome maintenance complex component 6 (MCM6) gene are associated with differential transcriptional activation of the promoter of the neighboring lactase (LCT) gene and, thereby, influence lactase persistence (LP) in adulthood. The rs4988235 SNP, located at -13910 bp upstream from the LCT gene (-13910C>T) within intron 13 of the MCM6 has been the most studied SNP in relation to LP, dairy intake and obesity-related diseases. However, other SNPs may be more relevant. Although currently there is an intense debate regarding the association between dairy intake and cardiovascular diseases (CVD), few studies have integrated the genetic variation in these analyses. Our objectives were to select the most relevant SNPs in the MCM6 gene and to study their association with dairy intake and CVD risk.

**Methods:** We carried out a bioinformatic analysis for the selection of the most relevant MCM6 SNPs (700K Illumina microarray) and studied their associations with dairy intake and CVD incidence in the PREDIMED study (n=7,187 participants with a median follow-up of 4.8 years).

**Results:** We selected the rs375468 (A>G) SNP within intron 15 of the MCM6 as the most relevant variant. It was strongly associated with total dairy intake: 359+/-210 g/d in lactase non persistent (LNP) AA subjects; 386+/-225 g/d in AG (LP) and 400+/-229 g/d in GG (LP); P=0.00000006. This association remained significant after adjustment for sex, age, field center, diabetes and total energy intake (P=0.00002). When we applied the Mendelian randomization approach, using the MCM6 genotype as a proxy for dairy intake to explore the association between the SNP and incidence of total CVD, no significant results were found in the population as a whole (P=0.357).

**Conclusions:** Despite the strong association between the rs375468 SNP and dairy intake, no such association with CVD incidence was observed.