AB026. Genetic variation in CYP2C8, CYP2C9 and CYP2C19 and the risk of coronary artery disease

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Background: Genetic diversity of cytochrome P450 2C subfamily metabolizing epoxyeicosatrienoic acids, vasoactive substances with a wide range of biological actions in the cardiovascular system, contributes to the molecular basis of coronary artery disease (CAD). Association between genetic polymorphisms of CYP2C8, CYP2C9 and CYP2C19 and CAD risk has been extensively investigated in Chinese, Japanese, Korean and other Asian populations whereas a few studies have been done in Europeans. The present study investigated whether common single nucleotide polymorphisms (SNPs) of CYP2C8, CYP2C9 and CYP2C19 genes are important risk factors of CAD in a Russian population.

Methods: DNA samples from 1,255 unrelated subjects comprising 561 patients with angiographically diagnosed CAD and 694 age- and sex-matched healthy subjects were genotyped for six SNPs such as rs7909236, rs1934953 of CYP2C8, rs9332242, rs4918758 and rs61886769 of CYP2C9 and rs4244285 of CYP2C19 using by the Mass-ARRAY 4 system.

Results: SNP rs4918758 of CYP2C9 was associated with decreased risk of CAD with odds ratio 0.61 adjusted for sex and age (codominant genetic model, 95% CI: 0.41–0.92, P=0.038, Q =0.20). Log-likelihood ratio test pointed out epistatic interactions between SNPs rs9332242 and rs61886769 of CYP2C9 at a codominant genetic model (Pinteraction =0.02). Moreover, SNP rs9332242 of CYP2C9 showed a trend towards association with increased CAD risk in cigarette smokers (P=0.049, Q =0.29). Bioinformatic analysis using the SNP prediction tool revealed a regulatory potential for all SNPs associated with CAD.

Conclusions: To our knowledge, the present study is the first to show that polymorphisms rs4918758 and rs9332242 of CYP2C9 represent significant genetic markers of CAD susceptibility in Europeans. A validation of genetic markers associated with CAD risk in different races and ethnicities may cut corners between discovery and clinical qualification of such markers for the purposes of translational medicine. The study was supported by the Russian Science Foundation.

Keywords: Coronary artery disease (CAD); disease susceptibility; cytochrome P450 2C subfamily; single nucleotide polymorphisms (SNPs); epoxyeicosatrienoic acids

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