Complex Genetic Disorders, Genetic Susceptibility to Infections

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.

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

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