Molecular Genetics, Genomics, Mechanisms of Diseases

AB074. Genetic variation in CYP2U1, CYP4A11 and CYP4F2 involved in the biosynthesis of hydroxyeicosatetraenoic acids and susceptibility to hypertension and atherosclerosis of various locations

Alexey Polonikov[1], Svetlana Sirotina[1], Irina Ponomarenko[1], Yaroslav Shvetsov[1], Marina Bykanova[1], Anna Bocharova[2], Kseniya Vagaytseva[2], Vadim Stepanov[2], Maria Solodilova[1]

[1]Research Institute for Genetic and Molecular Epidemiology, Kursk State Medical University, Kursk, Russian; [2]Tomsk National Medical Research Center, Tomsk, Russian

Background: 20-hydroxyeicosatetraenoic acids (20-HETE), products of arachidonic acid metabolism, possess a wide spectrum of important functions in the cardiovascular system and thereby may contribute to the development of many cardiovascular diseases (CVD). CYP2U1, CYP4A11 and CYP4F2 are important enzymes involved in the biosynthesis of 20-HETE and their genetic polymorphisms became attractive markers for testing of the genetic susceptibility to CVD. The present study investigated association between single nucleotide polymorphisms (SNP) of genes coding CYP2U1 (rs1493131), CYP4A11 (rs3890011, rs9332978, rs9333029), CYP4F2 (rs3093098, rs1558139), enzymes involved in the 20-HETE metabolism, and risk of various CVDs.

Methods: DNA samples from 3,940 unrelated Russian individuals comprising patients with essential hypertension (EH, N=1,410), CAD (N=561), ischemic stroke (IS, N=725), peripheral vascular disease (PVD, N=462) and 782 age- and sex-matched healthy subjects were genotyped for the polymorphisms using by the Mass-ARRAY 4 system.

Results: Polymorphism rs9332978 of the CYP4A11 gene showed a significant association with the risk of several CVD such as EH (OR =1.30, 95% CI: 1.04–1.62, P=0.02), CAD (OR =1.42, 95% CI: 1.14–1.78, P=0.002) and PVD (OR =1.53, 95% CI: 1.10–2.13, P=0.01). In addition, SNP rs3890011 of CYP4A11 was also associated with increased risk of CAD (OR =1.21, 95% CI: 1.02–1.24, P=0.03) and IS (OR =1.36, 95% CI: 1.14–1.64, P=0.001). The associations remained statistically significant after adjustment for sex, age and each CVD. The multifactor dimensionality reduction method identified epistatic gene-gene interactions (mainly between SNPs of CYP4A11 and CYP4F2) specifically associated with the risk of various CVDs.

Conclusions: The study findings demonstrate that pleiotropic effects of these genes may be responsible for the development of hypertension and atherosclerotic lesions of coronary, cerebral and peripheral arteries and the resulted disorders in the biosynthesis of 20-hydroxyicosatetraenoic acids may play an important role in pathogenesis of various CVDs.

Keywords: Cardiovascular diseases (CVD); genetic susceptibility; cytochrome CYP2U1; CYP4A11; CYP4F2; single nucleotide polymorphisms (SNP)

Funding: The study was supported by the Russian Science Foundation (№15-15-10010).

doi: 10.21037/atm.2017.s074

Cite this abstract as: Polonikov A, Sirotina S, Ponomarenko I, Shvetsov Y, Bykanova M, Bocharova A, Vagaytseva K, Stepanov V, Solodilova M. Genetic variation in CYP2U1, CYP4A11 and CYP4F2 involved in the biosynthesis of hydroxyeicosatetraenoic acids and susceptibility to hypertension and atherosclerosis of various locations. Ann Transl Med 2017;5(Suppl 2):AB074. doi: 10.21037/atm.2017.s074

