N E W S
OF THE NATIONAL ACADEMY OF SCIENCES OF THE REPUBLIC OF KAZAKHSTAN
SERIES OF BIOLOGICAL AND MEDICAL
ISSN 2224-5308
Volume 2, Number 326 (2018), 74 – 83

UDC 577.21 – 616.1

L. A. Skvortsova[1], A. V. Perfilyeva[1], E. M. Khussainova[1], A. T. Mansharipova[2], B. O. Bekmanov[1], L. B. Djansugurova[1]

[1]«Institute of General Genetics and Cytology» CS MES RK, Almaty, Kazakhstan,
[2]Kazakh-Russian Medical University, Almaty, Kazakhstan.
E-mail: lilia_555@rambler.ru khussainova@mail.ru nastyaper2009@mail.r bobekman@rambler.ru dralma@mail.ru leylad@mail.ru

ASSOCIATION OF GCG REPEAT POLYMORPHISM OF THE *GPX1* GENE CODING SELENIUM DEPENDENT ANTIOXIDANT ENZYME WITH ISCHEMIC HEART DISEASE DEVELOPMENT IN KAZAKHSTAN POPULATION

Abstract. Human selenium dependent antioxidant protein GPX1 has been shown having a strong protective role in cardiovascular disorders. The *GPX1* gene has a unique GCG repeat polymorphism from four to six, resulting in the protein with 5, 6 or 7 numbers of alanine repeats and has been noted in associations with various disorders in different populations. The aim of this study was to evaluate whether this polymorphism is associated with ischemic heart disease (IHD) development in population from Kazakhstan. We evaluated 360 patients with IHD and 341 control volunteers. For detection of GCG repeats a real-time based, high resolution melting (HRM) analysis was applied. Multiple logistic regression analysis was applied to assess the risk for different genotypes obtained. There were no statistically significant associations of *GPX1Ala 5-7* alleles and IHD development for general ethnically mixed group. Separate analysis of the main ethnic sub-groups showed that the presence of *Ala5* allele significantly increased the risk of IHD among Kazakhs (OR=1.73; 95% CI=1.31-2.29; $\chi 2$ = 17.248, p = 0.005). For Russian ethnic subgroup statistically significant associations for *Ala 5-7* alleles were not observed. But there is a higher risk tendency for *GPX1Ala7* allele (OR=1.37) and less for *Ala6* (OR=1.20). The presence of at least one *Ala5* allele of *GPX1* gene in genotype is associated with an increased tendency of IHD among Kazakhs.

Key words: oxidative stress, antioxidant system, glutathione peroxidase, Ischemic heart disease.

Inflammation accompanying all stages of ischemic heart disease development is characterized by the formation of an excessive amount of reactive oxygen species (ROS). Having a high reactivity and generated in a large amount, they can potentially interact with molecules that are not participants of vital signaling pathways and lead to destruction of cell components. Human glutathione peroxidase 1 (*hgpx1*) catalyzes the reduction of hydrogen peroxide and lipid hydroperoxides molecules which take place at high levels in the IHD conditions[1]. Low levels of red-cell GPX1 protein were observed as an independent risk factor for cardiovascular events [2]. Studies in mice show significant destruction of endothelial, vascular and cardiac tissue structure in heterozygous *GPX1*(+/-) carriers [3], [4], [5]. Regulation of *GPX1* expression and its protein activity is complex and many outer and inner gene factors can potentially be involved. In the *GPX1* gene protein coding region, it was identified several polymorphisms affecting GPX1 protein activity individually or in linkage disequilibrium [6]. Specific GCG repeat polymorphism located in the exon1 region has been noted to change the GPX1 activity and shown in associations with various disorders in different populations.

In this study we examined the hypothesis that *GPX1* in-frame GCG repeat polymorphism, resulting in the GPX1 protein with 5, 6 or 7 numbers of alanine repeats, may play a role in the pathogenesis of IHD in Kazakhstan population.