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**Key words:** *Helicobacter pylori, chronic hepatitis, oxidative stress*

DOI: 10.29256/v.03.01.2019.escbm25

## ASSOCIATION OF GENE POLYMORPHISMS WITH RISK OF SPORADIC PAPILLARY THYROID CARCINOMA

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Thyroid cancer represents approximately 1% of newly diagnosed cancers and is the most common endocrine malignancy. Papillary thyroid carcinoma (PTC) is the main form of nonmedullary thyroid carcinoma, accounting for approximately 80% of all thyroid cancers. PTC is mostly sporadic, whereas 5 to 10% are familial. The incidence of PTC is increasing in recent decades, but this may be due to improved diagnostics [1]. Although the etiology of PTC is not well characterized, it is clearly influenced by both genetic and environmental factors. Genetic predisposition plays a major role, as evidenced by case control studies [2]. In the virtual absence of high-penetrance Mendelian-type causative genes, the genetic factors can likely be attributed to many low-penetrance DNA variants in the human genome [3]. Recently, significant advances have been made in searching for DNA variants predisposing to PTC through genome-wide association studies (GWAS) and target gene studies in European populations, and replication studies in Japanese and Korean, and two-step candidate-gene association study in Spanish population groups have demonstrated that rs965513 (chromosome 9q22.33) and rs944289 (chromosome 14q13.3) display the strongest association with the risk for PTC. Aim of the study was to identify the association of the single nucleotide polymorphisms of the FOXE1 (rs 965513) and NKX2-1 (rs 944289) genes and papillary thyroid cancer among the Kazakh population.

**Materials and Methods.** Association of the NKX2-1 (rs944289) and FOXE1 (rs 965513) genes with papillary thyroid cancer in the Kazakh population was assessed retrospectively. Each of the study participants gave written informed consent to participate in the study, including blood sampling for genetic research. The study protocol was approved by the local Ethical Committee of the Semey State Medical University No. 2 dated March 18, 2015. The research work is performed in accordance with the principles of the Helsinki Declaration.

**Results.** Association of these SNPs in Kazakh population in a sample of 485 sporadic PTCs (90.3% females, mean age  $54.78 \pm 13.3$  y.o., 18 – 87 y.o., range) and 1008 controls (78.7% females, mean age  $39.02.1 \pm 15.8$  y.o., 15 – 83 y.o., range) was assessed. The next significant associations were identified in the multiplicative model of inheritance adjusted for age and sex: rs965513 ( $p=1.34E-16$ ; OR=2.252, 95% CI 1.858 to 2.730) and rs944289 ( $4.55E-05$ ; OR=1.444, 95% 1.210 to 1.724). Results demonstrated that the frequency of risk alleles of rs965513 and rs944289 in Kazakh population was intermediate between typical Asian and European populations.

**Conclusion.** Existence of genetic determinants of susceptibility to PTC in Kazakh population was confirmed.

Perspectives of future research. Development of genetic map of associations between thyroid gland's cancer-specific markers of in Kazakh population.

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**Key words:** thyroid gland cancer, biomarkers, single nucleotide polymorphisms

DOI: 10.29256/v.03.01.2019.escbm26

## ROLE OF THE IL-6 / TNF RATIO IN DIAGNOSTICS OF PERINATAL INFECTIONS

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Sporadic miscarriage is mostly associated with infectious causes. Infectious agents on the background of the gestational immunomodulation realize the pathogenic effect by direct damaging effect and through the cytokine system. In this case, it is relevant to study the functioning of the immune system in pregnant women. Given the interaction of cytokines in the development of the inflammatory reaction and the wide variability of their concentrations in the venous and umbilical cord blood of patients. Ratio of IL-6 to TNF $\alpha$  (IL-6v / TNF $\alpha$ v) in venous blood for infection-related gestational pathology and similar coefficient for cord blood cytokines was studied.

**Materials and Methods.** The case group has consisted of patients with diagnosis of spontaneous preterm birth (before 37 weeks' gestation). Healthy women with the term labor ( $\geq 37$  weeks) were included into the control group. All participants were at least 18 years old at enrollment. All patients in the preterm group had spontaneous delivery between 27+1 and 36 + 6 weeks of gestation. Maternal plasma levels of IL-6 and TNF $\alpha$  different stages of pregnancy were quantified with enzyme linked immunosorbent assay. Mann-Whitney U test was used to compare two independent groups. Odds ratio events in the one group to the chances of the same event in another (OR) and 95% confidence interval for them (95% CI) were calculated. Method of constructing a ROC-curves with the calculation of the area under the curve (AUC), sensitivity (Se) and specificity (Sp) obtained models were used for diagnostically significant indicators of quantitative traits. Significance was established as  $p < 0.05$ . Statistical analysis was performed using the program «MedCalc 10.2.0.0» (MedCalc, Mariakerke, Belgium).

**Results.** Ratio of IL-6 / TNF $\alpha$  in the venous and umbilical cord blood in preterm and term labor was as follows (table 1).

Table 1. - The ratio of IL-6 to TNF in venous and cord blood in preterm and term labor, n; Me (25; 75)

Ratio IL-6 / TNF $\alpha$	Case group (N = 47)	The control group (N = 50)	Significance level
Venous blood	46; 2,50 (1,41; 46,40)	50; 37,15 (7,74; 232,75)	U=650, p=0,0002
Cord blood	46; 1,51 (0,10; 15,80)	50; 1,55 (0,36; 30,22)	U=1006, p=0,4

IL-6 / TNF $\alpha$  ratio in women in the main group who did not have the effect of the injection of tocolytics was lower 3.37 (0.78; 36.92), in comparison with patients whose pregnancy was prolonged 86.29 (4.97; 453.59); U = 77, p = 0,02.