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POLYMORPHIC VARIANTS OF THE TLR2 GENE IN SYPHILIS

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ПОЛИМОРФНЫЕ ВАРИАНТЫ ГЕНА TLR2 ПРИ СИФИЛИСЕ

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Immunogenetic studies were performed in 100 people with syphilitic infection of the East Slavic population of the Southern region of Russia. It has been established that genotypic variants of 753 Arg/Gln and 753 Gln/Gln, as well as the presence of Gln/753 allele, are molecular-genetic markers of increased risk of syphilis development.

Keywords: syphilis, gene polymorphism, receptors of innate immunity

Иммуногенетические исследования выполнены у 100 человек с сифилитической инфекцией восточнославянской популяции Южного региона России. Установлено, что молекулярно-генетическими маркерами повышенного риска развития сифилиса являются генотипические варианты 753 Arg/Gln и 753 Gln/Gln, а также наличие аллеля Gln/753.

Ключевые слова: сифилис, генный полиморфизм, рецепторы врожденного иммунитета

An important field of modern medicine is the search for informative biomarkers of persistent infections that can be used to assess the potential risk of developing and realizing its clinical phenotypes [1].

Recent studies have shown that polymorphisms of the genes of the innate immunity receptors (TLR) are associated with the development of gram-positive infections, tuberculosis [3], infective endocarditis [5] and sepsis [4].

It has been established that single-nucleotide mutations (SNP) in the regions responsible for external (LRR) and internal (TIR) domains of receptors, the transformation of structures and functions of which cause defects of signal within the cell, are key among polymorphisms affecting TLR functions [1].

It is known that the violation of expression and function of TLR is manifested in a decrease in the production of cytokines determining the intensity of reactions of congenital and adaptive immunity and promotes the development of persistent infection [2].

The aim of the study was to study the gene polymorphism of the congenital immunity receptor – TLR2 Arg-753Gln (rs5743708) in patients with sero-resistant, early and late latent syphilis.

Material and Methods. Immunogenetic studies were performed in 100 people with a syphilitic infection that were under surveillance in the Regional Clinical Skin and Venereal Dispensary. The group I was formed of 35 patients with early latent syphilis, Group II contained 24 patients with late latent syphilis, Group III – 41 patients with serous-resistant syphilis. The control group consisted of 50 healthy inhabitants of the East Slavic population of the Southern region of Russia, comparable in age and sex.

Typing of SNPs TLR2 TLR6 was performed using the RFLP method (restriction fragment length polymorphism) with the performance of amplification of the corresponding objects and subsequent restriction endonuclease treatment. Diagnostic kits were used in the work to detect polymorphisms in the human genome by the method of polymerase chain reaction «SNP-express» LLC NPF «Litech», Moscow.

Amplification was carried out using a multichannel thermocycler «Terzik» (LLC «DNA-Technology», Russia). Separation of the products of amplification was performed in 3 % agarose gel by horizontal electrophoresis using the BioRad Laboratories equipment set (USA).

For the statistical analysis of the data, the program package «Attestat 10.5.1.», «Statistica SPSS», «Calculator for calculating statistics» (http://www.gen-expert.ru) were used. The reliability of differences in the frequencies of allelic variants and genotypes was evaluated using the criterion χ^2 Pearson, with multiple comparisons – the criterion χ^2 with the Yates correction was used. The degree of risk of events was estimated from the value of the odds ratio (OR) with the calculation of the CI confidence interval.

Results and Discussion. When assessing the distribution of polymorphism alleles 753 Arg Gln (rs5743708) the predominant existence of the wild allele Arg/in the homozygous state was noted both in the patients with syphilis (96 %), and in healthy donors (71 %). At the same time, a significant increase in the frequency of occurrence of a rare allele Gln/753 was marked in patients with syphilis 78/200 (0.39) (OR=20.7, CI: 6.33–67.6).

It should be noted that the homozygous state of the minor allele Gln/753 in the syphilis patients group was 10 times more common than in healthy donors (0.21 and 0.02, $p < 0.01$).

When calculating odds ratios, a significant increase in the risk of syphilis in carriers of homozygous Gln/Gln (OR=13.0, CI: 1.70–90.0) and heterozygous Arg/Gln (OR=4.26, CI: 0.52–35.1) genotypes was observed.

In the analysis of individual clinical forms, a significant decrease in the frequency of the major allele (Arg/753) and an increase in the prevalence of the mutant allele (Gln/753) are established, both with sero-resistant and with latent forms of syphilis. The risk of disease development in residents of Gln/753 with early latent syphilis was 8.1 (CI: 2.23–29.4), with late latent – 7.46 (CI: 1.92–23.0), with sero-resistant it increased dozens of times – 65.8 (CI: 19.1–227.1).

Patients of all groups showed a decrease in the frequency of occurrence of the homozygous genotype by the dominant allele (Arg/Arg). Whilst, only in the group with serous-resistant syphilis a significant increase in the prevalence of the homozygous variant of the genotype by a rare allele (Gln/Gln) was determined.

The relative risk of disease development in residents of the homozygous genotype of the polymorphism TLR2 – 753Arg/Arg (rs5743708) was extremely low. In carriers of the heterozygous genotype Arg/Gln with early latent syphilis was 2.97 (CI: 0.26–34.1), with late latent syphilis – 2.13 (95 % CI: 0.13–35.6), with sero-resistant – 6.81 (95 % CI: 0.76–60.8). The highest probability of a syphilitic process development was in homozygotes by a mutant allele Gln/Gln. With early latent syphilis, the odds ratio was 10.2 (95 % CI: 1.16–88.5), with late latent – OR=9.8 (95 % CI: 1.03–93.2), with sero-resistant – OR=17.9 (95 % CI: 1.21–146.3).

Conclusions. Thus, it can be assumed that the carriage of the minor allele Gln/753, as well as the heterozygous (Arg/Gln) and homozygous (Gln/Gln) by a rare allele of genotypes, have predictive properties for the development of syphilitic infection. The highest degree of association of the genotypes 753 Arg/Gln and 753 Gln/Gln is determined with the development of sero-resistant syphilis.

References

1. Petruccioli E., Scriba J. T., Petrone L., Hatherill M., Cirillo D. M. [et al.] Correlates of tuberculosis risk: predictive biomarkers for progression to active tuberculosis. *European Respiratory Journal*. 2016;48:1751-1763. doi: 10.1183/13993003.01012-2016
2. Medvedev A. E. Receptor Polymorphisms, Inflammatory and Infectious Diseases, Allergies, and Cancer *J. Interferon Cytokine Res.* 2013;33(9):467-484. doi: 10.1089/jir.2012.0140
3. Biyikli O. O., Baysak A., Ece G., Oz A. T., Ozhan M. H. [et al.] Role of Toll-Like Receptors in Tuberculosis Infection. *Jundishapur J. Microbiol.* 2016;9(10):e20224. Published: Oct 2016. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5136443/. doi: 10.5812/jjm.20224
4. Ahmad-Nejad P., Denz C., Zimmer W., Wacker J., Bugert P. [et al.] The presence of functionally relevant toll-like receptor polymorphisms does not significantly correlate with development or outcome of sepsis. *Genet. Test Mol. Biomarkers.* 2011;15:645-651. doi: 10.1089/gtmb.2010.0258
5. Bustamante J., Tamayo E., Flórez S., Telleria J. J., Bustamante E. [et al.] Toll-like receptor 2 R753Q polymorphisms are associated with an increased risk of infective endocarditis. *Rev. Esp. Cardiol.* 2011;64(11):1056-1059. doi: 10.1016/j.rec.2011.02.027

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THE PLACE OF EVALUATION VASCULAR RIGIDITY IN PROCESS OF STUDENT'S HEALTH SCREENING

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МЕСТО ОЦЕНКИ СОСУДИСТОЙ РИГИДНОСТИ В ПРОЦЕССЕ СКРИНИНГА СТУДЕНЧЕСКОГО ЗДОРОВЬЯ

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Cardio-ankle vascular index (CAVI) has a high prognostic significance for development of cardiovascular events. However, its values in the young population are quite vague still. In 149 students (55 boys, 94 girls) from 17 to 22 years old were assessed the vascular wall by indicators of CAVI using the device Vasera VS-1500 (Fukuda Denshi, Japan). Percentile analysis showed that the 95th percentile for boys at R-CAVI and L-CAVI was 7.1 and 7.2, and for