Association between TNF-α and Its Receptor TNFRSF1B Polymorphism with Pulmonary Tuberculosis in Tomsk, Russia Federation

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Abstract : Purpose: Tuberculosis (TB), caused by Mycobacterium tuberculosis, is one of the major public health problems worldwide. It is clear that the immune response to M. tuberculosis infection is a relationship between inflammatory and anti-inflammatory responses in which Tumour Necrosis Factor-α (TNF-α) plays key roles as a pro-inflammatory cytokine. TNF-α involved in various cell immune responses via binding to its two types of membrane-bound receptors, TNFRSF1A and TNFRSF1B. Importantly, some variants of the TNFRSF1B gene have been considered as possible markers of host susceptibility to TB. However, the possible impact of such TNF-α and its receptor genes polymorphism on TB cases in Tomsk is missing. Thus, the purpose of our study was to investigate polymorphism of TNF-α (rs1800629) and its receptor TNFRSF1B (rs652625 and rs525891) genes in population of Tomsk and to evaluate their possible association with the development of pulmonary TB. Materials and Methods: The population distribution features of genes polymorphisms were investigated and made case-control study based on group of people from Tomsk. Human blood was collected during routine patients examination at Tomsk Regional TB Dispensary. Altogether, 234 TB-positive patients (80 women, 154 men, average age is 28 years old) and 205 health-controls (153 women, 52 men, average age is 47 years old) were investigated. DNA was extracted from blood plasma by phenol-chloroform method. Genotyping was carried out by a single-nucleotide-specific real-time PCR assay. Results: First, interpopulational comparison was carried out between healthy individuals from Tomsk and available data from the 1000 Genomes project. It was found that polymorphism rs1800629 region demonstrated that Tomsk population was significantly different from Japanese (P = 0.0007), but it was similar with the following Europeans subpopulations: Italians (P = 0.052), Finns (P = 0.124) and British (P = 0.910). Polymorphism rs525891 clear demonstrated that group from Tomsk was significantly different from population of South Africa (P = 0.019). However, rs652625 demonstrated significant differences from Asian population: Chinese (P = 0.03) and Japanese (P = 0.004). Next, we have compared healthy individuals versus patients with TB. It was detected that no association between rs1800629, rs652625 polymorphisms, and positive TB cases. Importantly, AT genotype of polymorphism rs525891 was significantly associated with resistance to TB (odds ratio (OR) = 0.61; 95% confidence interval (CI): 0.41-0.9; P < 0.05). Conclusion: To the best of our knowledge, the polymorphism of TNFRSF1B (rs525891) was associated with TB, while genotype AT is protective [OR = 0.61] in Tomsk population. In contrast, no significant correlation was detected between polymorphism TNF-α (rs1800629) and TNFRSF1B (rs652625) genes and alveolar TB cases among population of Tomsk. In conclusion, our data expands the molecular particularities associated with TB. The study was supported by the grant of the Russia for Basic Research #15-04-05852.

Keywords : polymorphism, tuberculosis, TNF-α, TNFRSF1B gene