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FUT2 gene polymorphism in samples of Tuvinians and Russians of Eastern Siberia

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Motivation and Aim: The *FUT2* gene encodes α-1,2-fucosyl-transferase, an enzyme that modifies oligosaccharides in the intestine, which are a substrate for microflora. The state of the *G772A rs602662* polymorphic locus affects FUT2 enzyme activity: the -*772G* variant is secretory, while the -*772A* allele is non-secretory. FUT2 secretory status differentially affects susceptibility to a number of infections: the FUT2 "secretor" phenotype (allele -*772G*) is associated with susceptibility to viral infections, including influenza, Epstein-Barr virus, SARS-COV 2, and *Helicobacter pylori* [1]. "Nonsecretory" FUT2 phenotype (allele -*772A*) is associated with susceptibility to bacterial pathogens, including *Streptococcus pneumoniae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus infl uenzae*, and *Salmonella typhimurium*. [2]. These differences are reflected in susceptibility to multifactorial diseases. For example, chronic pancreatitis is associated with a nonsecretory phenotype [3]. Approximately 20 % of the global population carries the non-functional -*772A* allele, and there are interpopulation differences. In East Asia, less than 2 % of the population has -*772A* in their genotype, while in European countries the proportion is 30-50 % [4]. In the literature, we have not encountered data on the frequencies of polymorphic variants of the *FUT2* gene in indigenous populations of Siberia, so research in this area remains relevant.

Methods and Algorithms: Two Siberian samples served as the material for the present research. Persons of Tuvinian nationality having no ancestors with foreign ethnic backgrounds and living in the city of Kyzyl of Tuva Republic were included in the Tuvinian group (N = 308). Russians from Eastern Siberia, whose ancestors lived in the settlements of Zabaykalsky Krai and the Irkutsk Region for several generations, were included in the second sample (N=153).

The frequencies of polymorphic variants due to the single nucleotide substitution *G772A (rs602662)* of the *FUT2* gene were determined by the real-time polymerase chain reaction method. Population allele frequencies of polymorphic variants were determined based on the observed genotype frequencies. The match between the empirically observed genotype frequency distribution and the expected theoretical distribution in Hardy-Weinberg equilibrium was examined using $\chi 2$ Pearson test (the equilibrium holds at $p>0.05$). Significance of differences in allele frequencies between the studied samples was determined using $\chi 2$ test with Yates's correction for continuity; the results were considered statistically significant at $p<0.05$. The obtained parameters were compared with those in the literature.

Results: Genotype distribution for polymorphic locus of the *FUT2 G772A (rs602662)* in samples of Tuvinians and Russians from Eastern Siberia is presented in Table 1.

Table 1. Genotype distribution for *FUT2 G772A (rs602662)* in samples of Tuvinians and Russians from Eastern Siberia

Population			Tuvinians	Russians from Eastern Siberia
–772G/A, rs602662	Genotype distribution *n*	*G/G*	237	66
		G/A	61	70
		A/A	10	17
	N, ppl		308	153
	p (H–W)		0.581	0.808

Note. *N* is the sample size, *p (H-W)* is the probability of deviation from the Hardy–Weinberg equilibrium.

Genotype distribution matched the Hardy-Weinberg equilibrium for both polymorphic loci. The frequency of the non-secretory allele *-772A* in the sample of Russians from Eastern Siberia (34 %) corresponds to the data for Caucasoids. The frequency of allele in the sample of Tuvinians were statistically significantly lower than in samples of Russians from Eastern Siberia and Caucasoid groups described in the literature [4]. On the other hand, frequencies of the *-772A* variant in Tuvinian sample significantly increased if compared to a number of East Asian groups. In accordance with the general geographical gradient of the distribution of this variant, its frequency in the Tuvinian sample is in an intermediate position between Caucasoid and East Asian populations. The same trend was revealed by us earlier in studies of polymorphisms of other functionally important genes [5].

Conclusion: Thus, the allele frequencies of the polymorphic locus *FUT2 G772A (rs602662)* in Tuvinians and Russians of Eastern Siberia were determined for the first time. It was shown that in the Russian sample the frequency of the non-secretory allele *-772A* is within the frequency range for other Caucasoid populations. The frequency of *-772A* in the Tuvinian sample is in an intermediate position between Caucasoids and East Asian populations. The statistically significantly reduced frequency of the non-secretory allele *-772A* of the *FUT2* gene in the Tuvinian population may indicate an increased risk of gastrointestinal pathologies in case of *H. pylori* infection, compared to the Russians. At the same time, the Tuvinian population probably has a reduced risk of chronic pancreatitis. However, to test this hypothesis, additional medical genetic studies are needed in various populations with a large sample size, as well as the study of the frequencies of allelic variants, not only of *FUT2*, but also of other functionally significant genes.

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