

**POPULATION FREQUENCIES AND ASSESSMENT OF THE CONTRIBUTION
OF THE RS1800469 POLYMORPHISM OF THE *TGFB1* GENE TO THE
PATHOGENETIC MECHANISM OF MYOPIA AMONG THE POPULATION OF
THE FERGANA VALLEY**

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Relevance of the problem. In Western and East-West Asia, there is an increase in axial hyperopia among the young population in the last three decades. Which is caused by hereditary factors or pregnancy defects.

The genetic determination of myopia was noted in the three-factor theory of Avetisov E.S. (1995), according to which refractive anomalies are formed with the participation of environmental factors, conditions of visual activity and hereditary factors. Various studies have shown that myopia can be inherited in both autosomal dominant and autosomal recessive patterns. In the former case, the disease manifests itself mainly in adolescence with a milder clinical course. In the autosomal recessive pattern of inheritance, myopia often develops at an early age and tends to progress with complications.

Numerous scientific works by ophthalmologists have proven that myopia develops in the case of a number of genetic diseases accompanied by connective tissue dysplasia, such as Marfan syndrome, Ehlers-Danlos syndrome, Cohen syndrome, Knobloch syndrome, etc. And also, in addition to connective tissue pathology, there are a large number of genetic determinants that determine the predisposition to the development of myopia. For example, changes in the *ACTC1* gene, involved in the formation of contractile cells - scleral myofibroblasts, the *GJD2* gene associated with the regulation of eyeball growth, the *GRIA4* gene associated with retinoic acid metabolism, the decrease in *MMP - 2* expression observed in myopia significantly suppresses the decrease in the accumulation of the Ia1 collagen chain in the sclera [Markosyan G.A., Tarutta E.P., 2016; Zhao F, Zhou Q, 2018; Sun Y, Sha Y, 2024] etc. Currently, the search for decisive genetic factors that determine hereditary predisposition to myopia continues to be a pressing scientific task.

It is known that the formation of biologically active molecules is controlled by genetic mechanisms underlying the regulation of the expression of the genes encoding them. Gene expression occurs in the process of implementing the information encoded in the DNA structure with the formation of an mRNA molecule, then an amino acid sequence of a protein molecule that performs its intended function.

In this research, to assess the contribution of genetic predisposition to the development and course of myopia, we studied Population frequencies and assessment of the contribution of the rs1800469 polymorphism of the *TGFB1* gene to the pathogenetic mechanism of myopia among the population of the Fergana Valley.

The data obtained in the study on the frequency of occurrence of alleles and genotypes of the rs 1800469 (C 509 T) polymorphism of the *TGFB 1* gene, as well as their distribution among patients with myopia of varying degrees and among conditionally healthy individuals of the population sample (control) are presented in the table we compiled.

Table of frequencies of alleles and genotypes of polymorphism

rs 1800469 (C 509 T) of the *TGFB 1* gene in the groups of patients with myopia and controls

No.	Group	Allele frequency				Genotype frequency					
		C		T		C/C		C/T		T/T	
		n	%	n	%	n	%	n	%	n	%
1	Main group (n = 130)	189	72.69	71	27.31	71	54.62	47	36.15	12	9.23
2	Mild myopia (n = 30)	46	76.67	14	23.33	18	60	10	33,33	2	6.67
3	Moderate myopia (n = 34)	50	73.53	18	26.47	19	55.88	12	35.29	3	8.82
4	High myopia (n = 66)	93	70.45	39	29.55	34	51,52	25	37.88	7	10.61
5	Control (n=110)	177	80.45	43	19.55	73	66.36	31	28.18	6	5.45

It is known that the frequency of occurrence of polymorphic variants of genes has population differences [Abdulfattah SY, Salman Alagely H, 2024; Kumar P, Kumar A, 2016]. According to some researchers, the heterozygous genotype "T/C" of the rs1800469 (C509T) polymorphism of the *TGFB* gene occurs in 43% of the subjects, and the homozygous genotype "T/T" - in 8% [Grossberg AJ, Lei X, 2018], according to others, the frequency of the genotypes "C/T" and "T/T" is 47.8% and 19.9%, respectively [Cao H, Zhou Q, 2014].

We have shown that the population frequency of occurrence of variant genotypes “C/ T ” (28.2%) and “T/T” (5.5%) of the rs1800469 (C 509 T) polymorphism of the *TGFB* gene in the Uzbek population is lower than existing estimates of its prevalence among individuals of Asian and other populations .

Our study showed that the frequency of occurrence of the “wild” allele “C” of the rs1800469 (C 509 T) polymorphism of the *TGFB* gene among the population of the Fergana Valley without vision pathology was 80.5% , and the frequency of the mutant allele " T " was 19.5%. In the main group of patients with myopia, the frequency of the mutant allele "T" was 27.3% and significantly exceeded the control indicator ($\chi^2 = 4.0$; $P = 0.05$; $OR = 1.5$). The intergroup difference in the frequency of the "wild" allele "C" was also reliable (main group - 72.7%; control group - 80.5%; $\chi^2 = 4.0$; $P = 0.05$). (*Appendix 3.1. A*) .

When assessing the frequency of occurrence of the “T” allele among patients with different clinical variants of myopia, it was found that in the subgroup of patients with high myopia, the variant allele was more common (29.5%) than in mild (23.3%) and moderate myopia (26.5%), but the difference between the subgroups was insignificant (subgroups A and B – $\chi^2 = 0.2$; $P = 0.7$; $OR = 0.8$; subgroups A and B – $\chi^2 = 0.8$; $P = 0.4$; $OR = 0.7$; subgroups B and C – $\chi^2 = 0.2$; $P = 0.7$; $OR = 0.9$) (Tables 3.4, 3.5, 3.6) . The frequency of the “T” allele in the subgroups of patients with mild and moderate myopia also did not have a reliable difference with the control group (subgroup A and control – $\chi^2 = 0.4$; $P = 0.6$; subgroup B and control – $\chi^2 = 1.5$; $P = 0.3$), whereas in the subgroup of patients with severe myopia and the control, a reliable difference in the studied indicator was revealed – $\chi^2 = 4.6$; $P = 0.05$; $OR = 1.7$).

Thus, the data from the study of the frequency of occurrence of the variant allele of the polymorphic *TGFB* gene (C 509 T) in samples of patients with visual impairment and conditionally healthy individuals indicate an association of the functionally unfavorable allele “T” with the risk of developing high myopia.

Analysis of the distribution of genotypic variants of the rs1800469 (C 509 T) polymorphism of the *TGFB* gene revealed the prevalence of the “C/C” genotype both in the population control sample (66.4%) and in the group of patients with myopia (54.6%). The frequency of the “C/C” genotype in the group of patients with myopia was lower than the control value, but the reliability of this difference was at the trend level ($\chi^2 = 3.4$; $P = 0.1$; $OR = 0.6$).

An indeterminate difference in the frequency of the genotype "C/C" was found between subgroups of patients with myopia of varying degrees (subgroup A and B – 60.0% and 55.9%; $\chi^2 = 0.1$; $P = 0.8$; $OR = 1.2$; subgroup A and B – 60.0% and 51.5%; $\chi^2 = 0.6$; $P = 0.5$; $OR = 1.2$; subgroup B and B – 55.9% and 51.5%; $\chi^2 = 0.2$; $P = 0.7$; $OR = 1.1$).

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