

## POINT OF VIEW

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## FEATURES OF THE GENE POOL OF THE TUVINIAN ETHNOS BASED ON THE STUDY OF BLOOD GROUP ANTIGENS IN COMPARATIVE PERSPECTIVE

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The indigenous population of the Tuva Republic is characterized by a complex multi-component ethnogenesis, which involved ancient Europoid, northern Samoyedic and Keto-speaking tribes, as well as Turkic and Mongolian-speaking natives of Central Asia. The aim of the study was description of the Tuvinians gene pool in comparison with the modern Siberian populations.

**Materials and methods.** The alleles and haplotypes frequencies of blood groups AB0, MN, Rhesus and Kell in the Kyzyl indigenous population sample (N=502) were determined using the traditional direct hemagglutination method.

**Results.** The high frequency (0.033) of the A2 allele of the AB0 system characterizing the population of Europoid origin was shown. The ratio of the alleles M (0.621) and N (0.379) of the MN system corresponded to the populations of Yakuts, Kazakhs and Mongols. Rhesus Tuvinians showed both Mongoloid features - high frequency cDe (0.318) and rhesus-negative haplotype cde and Cde, which characteristic Europoid populations (total frequency 0.074) on frequencies haplotype systems. The marker of "Europoid" allele K of system Kell was revealed with frequency 0.019. The Tuvinians was clustered with Turkic populations of South Altaians and Yakuts on the map of genetic distances, while the Samoyedic group of Nganasans, Forest and Tundra Nenets formed a separate cluster. The clusters of northern Khanty, Komi-Zyryans and Russians Siberia, including the Old Believers, are also located in a separate cluster. It is shown that alleles and haplotypes of systems MN, Rhesus and Kell, A2 and B on system AB0 made the greatest contribution to differentiation of populations.

**Conclusion.** The present study shown that the Tuvinians of Kyzyl are genetically close to the Yakuts and South Altaians, and the combination of Europoid and Mongoloid genetic markers reflects their complex ethnic history.

**Keywords:** Tuvinians, population frequency of genetic markers of blood groups, AB0, MN, Rhesus, Kell.

**Introduction.** Tuvinians are the indigenous population of the Republic of Tuva, belonging to the Central Asian anthropological type of Mongoloid race. They speak the language of the Uigur group of Turkic languages [2]. Anthropological and serological research indicates heterogeneity of Tuvinians and their unique

position among other groups of Siberia, Central Asia and Kazakhstan. The researches of historians, archeologists, anthropologists have shown that the ancient Europoids, northern Samoyedic and Keto-speaking tribes, and also Turkic and Mongolian-speaking natives from Central Asia took part in the formation of the Tuvinian gene pool [1, 2]. Genetic studies of mitochondrial DNA and Y-chromosomes confirmed these assumptions [22, 24, 27]. A number of anthropometric signs and frequency of genetic markers shows that Tuvinians have more similarity with the South Siberian groups which have been formed with participation of the Europoid component - Altaians and Khakassians, and also with Samoyeds, than with Central Asian peoples - Mongols, Buryats, Kalmyks and Yakuts [2, 22, 27].

Molecular and biological methods of research have been developing rapidly in recent decades. However, serological studies connected to determination of blood group frequencies have not lost their relevance for studying human populations [7, 8, 12, 16]. This is due to the low cost, good reproducibility, independent of subjective evaluation criteria, availability of studies in the field and the possibility of comparison with populations previously studied on a given panel of blood group systems [6, 11, 13, 18, 21, 23, 27].

The aim of the research is to study the allele and haplotype frequencies of blood groups AB0, MN, Rhesus and Kell in a

sample of Tuvinians in the town of Kyzyl and compare them with some Siberian populations belonging to other linguistic groups.

**Material and research methods.** The material was collected during expedition works in September 2019 on the basis of the Republican Center of Medical Prevention of the Kyzyl (Team Leader - M.S. Tabikhanova L.E.) The research was conducted within the framework of agreements between Tuva Research Center, Novosibirsk State University and the Federal Research Center Institute of Cytology and Genetics of The Siberian Branch of the Russian Academy of Sciences (ICG SB RAS). This study was approved by the Bioethical Committee of the ICG SB RAS. It was carried out in accordance with the requirements of the documents "Ethical principles of scientific medical research with human participation" and "Rules of clinical practice in the Russian Federation".

Blood was taken with disposable needles from the elbow vein from individuals who expressed their willingness to participate in the research and voluntary signed an informed consent. Preliminarily, each of the subjects filled in a specially designed questionnaire that indicated the nationality of their ancestors up to 2-3 generations. In the course of the study, a sample of ethnic Tuvinians (N=502) was formed from natives, mainly from the western and central regions of Tuva, who did not indicate ancestors of other

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nationalities in their lineage. 18% of the sample consists of adolescents aged 16-18 years, persons aged 19-39 years - 37%, 40-59 years - 33%, 12% are 60-70 years old. The female part of the sample is 73 per cent, while the male part is 27 per cent.

"Hematologist" Ltd. (EritroTestM-Coloclon anti -A, -A1, -B, -M, -N, -C, -Cw, -c, -D, -E, -e and anti-Kell) determined blood group affiliation in the field laboratory by direct hemagglutination method using sets of diagnostic reagents for typing human blood groups. Frequencies of alleles and haplotypes of systems AB0, Rhesus and Kell were calculated by a method of the maximum plausibility with use of the computer program developed by the employee of ICG SB RAS Kirichenko A.V. Allele frequencies *M* and *N* were defined on the basis of observed frequencies of phenotypes of system MN. For construction of maps of genetic distances between populations, and also for revealing the contribution of alleles and haplotypes in differentiation processes was used A.V. Kirichenko's program, that developed on the basis of Harpending and Jenkins's method [25].

**Results and discussion.** The quantities and frequencies (%) of blood group phenotypes in the Tuvanian sample are shown in Table 1, and the allele and haplotype frequencies of blood groups are shown in Table 2.

The frequency distribution of alleles of the AB0 system in the Tuvanian samples is characterized by a high occurrence of allele *O* (0.670), which is typical for indigenous Siberian populations [4, 6, 10, 13, 15, 18, 20, 27]. The frequency of allele *B* in the studied samples corresponds to the frequency interval described in the literature for Tuvanian populations (0.103-0.210) [2, 3, 10]. According to the literature, zones with the opposite ratio of AB0 system genes frequencies are distinguished in the Tuva territory [2]. The group of Tuvinians of Kyzyl, which, according to the survey data, consists of 90% of natives of the western and central regions, demonstrates increase in the frequency *A*, characteristic for this geographical localization, compared with *B*. In the southern and eastern regions the opposite trend is observed, indicating increase in the Mongoloid component [2, 3]. The frequency of the marker "Europoid" allele *A2* (0.033) is significant, and falls into the range corresponding to the Russian samples 0.024-0.070 [21].

The maximum frequency of the allele *N* of the MN system from Siberian populations was found in the Nganasan (0.713) [20], followed by a decrease in the allele

*N* of the MN system, up to 0.206-0.233 in the northern Altaians [4]. Yakuts also demonstrate a low frequency of this allele (0.234-0.255) [13], which is associated with their southern origin. Russian populations are characterized by an average frequency *N* in the range of 0.449-0.469 [21]. A low allele frequency *N* (0.379) was observed in Tuvinians of Kyzyl city; it is statistically significantly lower than that in the Shinaan population of eastern Tuva

(0.491) [3]. The low frequency allele *N* is typical for Kazakhs (0.357) [9], Mongols (0.413) [5] and Tuvinians of the Tojin group in the north-east of Tuva (0.363-0.417) [3, 10].

Tuvinians in Kyzyl demonstrate the highest possible frequency of haplotype *CDe* of Rhesus system (0.569). At the majority of the South Siberian (South and North Altaians) [4, 18], Central Asian populations (Mongols and Yakuts) [5, 13], and also Tundra Nenets [27], this indicator is raised (0.522-0.549) in comparison with Russians [21] and inhabitants of the North of Siberia - Komi, Khanty, Nganasans (0.253-0.432) [6, 20]. The Rhesus *cDe* haplotype is considered a marker for northern Mongoloids. Its maximal value is found at Nganasans of the Taimyr Peninsula (0.622) [20], and minimal - at Russians of Siberia (0.162) [21]. The intermediate value of frequency haplotype *cDe* at Tuvinians (0.318) makes them similar to Mongols, a population of Yakuts of Nurbinsky ulus and South Altaians [5, 13, 18]. Two individuals with rhesus-negative phenotype were found, which was not registered in the previous works on Tuvinians [3, 10]. Total frequency haplotype *cde* and *Cde*, causing "Europoid" rhesus-negative phenotype at Tuvinians is equal 0.074. Such value of frequency rhesus-negative haplotype characterizes also Forest (0.069) and Tundra (0.096) Nenets and North Altaians Kumans (0.094) [4, 15, 27]. No marker allele *C<sup>w</sup>* for Europoid populations was found in the studied sample of Tuvinians. It is fixed with considerable frequency 0.038 presence "ancient" haplotype *cDe*.

Among Tuvinians we found carriers of allele *K* (0.019) of the **Kell** system, which is absent in many Siberian populations (Nganasans, Yakuts, Forest Nenets and South Altaians) [13, 15, 18, 20], and is registered with statistically significantly lower frequency in North Khanty (0.001) and Tundra Nenets (0.003) [6, 27]. Among the North Altaians this marker Europoid allele was found with a frequency of 0.012-0.040, while in the Russians (0.031-0.074) and Komi (0.076) this index is statistically significantly higher [4, 6, 21].

Figure 1 presents a map of genetic distances between 16 populations of indigenous peoples of Northern Eurasia, built on 15 alleles and haplotypes (*O*, *A1*, *A2*, *B*, *K*, *M*, *N*, *CDe*, *cDe*, *cde*, *CDE*, *C<sup>w</sup>De*) 4 genetic blood systems (AB0, MN, Rhesus and Kell) by the Harpending and Jenkins method. It shows the mutual location of the populations of Russians, Komi, Khanty, Samoyedic (Nganasans, Forest and Tundra

Table 1

**Quantities of blood group phenotypes in the studied sample of Tuvinians of Kyzyl (N=502).**

Blood group system	Phenotype	quantity (n)	Frequency (%)
AB0	0(I)	229	45.6
	A1(II)	102	20.3
	A2(II)	20	4.0
	B(III)	119	23.7
	A1B(IV)	24	4.8
	A2B(IV)	8	1.6
MN	MM	201	40.0
	NN	80	15.9
	MN	221	44.1
Rhesus	CCDee	179	35.6
	CcDEe	174	34.7
	CcDee	53	10.6
	ccDEE	54	10.7
	ccDEe	38	7.6
	ccDee	2	0.4
	ccdee	1	0.2
	CCDEe	1	0.2
	Ccdee	1	0.2
Kell	K	19	3.8
	kk	483	96.2

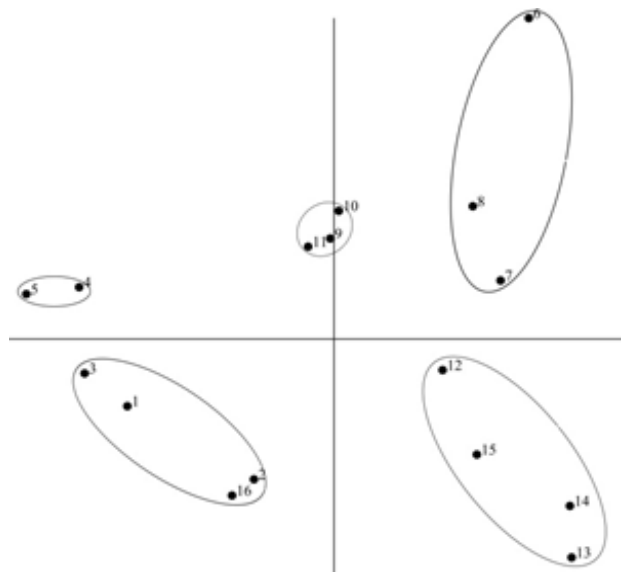
Table 2

**Frequencies of alleles and haplotypes blood groups in the studied sample of Tuvinians.**

Blood group system	Allele, haplotype	Frequency
AB0	<i>O</i>	0.670
	<i>A1</i>	0.134
	<i>A2</i>	0.033
	<i>B</i>	0.163
MN	<i>M</i>	0.621
	<i>N</i>	0.379
Rhesus	<i>CDe</i>	0.569
	<i>cDE</i>	0.318
	<i>cDe</i>	0.038
	<i>cde</i>	0.060
	<i>Cde</i>	0.014
	<i>CDE</i>	0.001
Kell	<i>K</i>	0.019
	<i>k</i>	0.981

Nenets) and Turkic-speaking groups (South Altaians, Yakuts, and Tuvians), which differ in linguistic identity, in the space of two main components deriving 74% of the total variability. We can see that Tuvians are clustered with other Turkic-speaking populations of South Altaians and Yakuts. Genetic closeness of Yakuts to Tuvians and Altai was shown earlier at the analysis of mtDNA lines [17, 19, 26], and also by the results of full genomic analysis [19]. Separately located is the Samoyedic group of Nganasans, Forest and Tundra Nenets, as well as clusters of North Khanty, Komi-Zyryans and Russians of Siberia, including the Old Believers. The maximum distance separates the sample of the indigenous population of Kyzyl from the Komi, Nganasans, and also from the North Khanty, whose gene pool obviously contains other ethnic components.

Figure 2 shows the graphical location of genetic markers used to build a map of genetic distances (Fig. 1). It can be noted that the greatest contribution to differentiation of populations is made by the alleles and haplotypes most removed from a point of intersection of axes of coordinates: "Europoid" markers (*cde*, *K* and *C<sup>w</sup>*), alleles *M* and *N* of system MN, haplotypes *cDE* and *CDe* of system Rhesus. The ABO system is informative for the *A2* and *B* alleles.



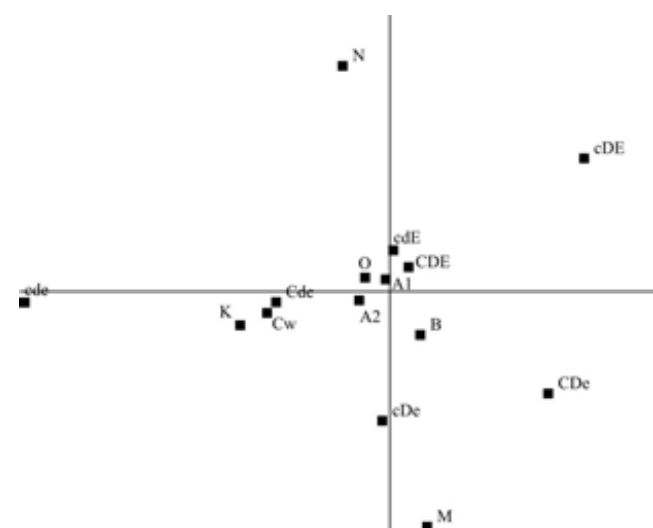
**Fig. 1.** Map of genetic distances between 16 Siberian populations, constructed on 15 alleles and haplotypes of 4 genetic systems of blood by Harpending and Jenkins method. Note: 1 - Russians Old Believers of Isetsk area, 2 - Russian Old Believers of settlement Burnyi, 3 - Russians of the Tyumenskaya oblast [21], 4 - Komi-Zyryans of settlement Gorki and Pitlyar, 5 - Komi-Zyryans of s. Vosyakhovo, Ovgort, p. Muzhi and Shuryshkary [6], 6 - Nganasans, 7 - Forest Nenets [9], 8 - Tundra Nenets [27], 9 - Khanty of s. Lopkhari, 10 - Khanty of s. Ovgort [6], 11 - Khanty of s. Lopkhari, 12 - South Altaians [18], 13 - Yakuts of Nyurbinsk ulus, 14 - Yakuts of Ust-Aldan ulus [13], 15 - Tuvians of Kyzyl, 16 - Russians of Kyzyl (N=23) [own data].

## Conclusion.

Thus, the present study shows that among the studied 16 Siberian populations Tuvian Kyzyl are genetically closest to the Yakuts and South Altaians in terms of allele and haplotype frequencies of blood groups ABO, MN, Resus and Kell. It was found out that Tuvians are characterized by a combination of Europoid and Mongoloid features, which reflects their complex ethnogenesis.

## The results of the research presented

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**Fig. 2.** The arrangement of 15 alleles and haplotype 4 genetic systems of blood in space of two main components concerning 16 populations of Siberia, presented on fig. 1.

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