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Genetic Diversity and Population Structure of North Ossetia-Alania Ossetians: Insights from Nuclear DNA Marker Polymorphism in the Context of European and Caucasian Populations of Russia

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ABSTRACT This study aims to characterize the genetic diversity within the Ossetian population of the republic of the North Ossetia-Alania (RNO-Alania) and elucidate its differentiation against the broader genetic landscape of the peoples of the Russian Federation. Allele frequencies for 10 highly polymorphic nuclear DNA markers (CCR5Δ32, ID/ACE, D7S23 (KM19), STR/TH01, STR/FABP2, STR/IVS6aGATT (CFTR), VNTR/PAH, VNTR/DAT1, VNTR/NOS3, VNTR/APOB) were investigated in 370 unrelated Ossetians. Wright's Fst was compared with that for Tatars, Bashkirs, Udmurts, Chuvash, Mari, Karachays, Abazins, Nogais, Circassians, Kumyks, and Russians from Tver, Kirov, and Rostov regions. Within Ossetians, Irons and Digors showed the closest relationship with Kudars exhibiting greater differences from both groups. The Ossetian population formed-a cohesive cluster with other North Caucasus populations, while Kumyks of the RNO-Alania displayed a more significant genetic difference. Comparative analysis with 11 previously studied populations resulted in a dendrogram highlighting two clusters – "Volga–Ural region" and "Caucasian."

INTRODUCTION

The genetic structure of populations can be analyzed in different aspects: anthropological, historical, population genetic, medical and others. In the last nine years, advances in modern genetics have made it possible for researchers to characterize populations by studying the frequencies and relative distribution of hundreds and thousands of different DNA markers in them (Pan and Xu 2020). The study and understanding of genetic variability in human populations provide the key to identifying the genetic basis of rare diseases. The Laboratory of Genetic Epidemiology of the Research Centre for Medical Genetics (RCMG) has devoted more than three decades to the comprehensive study of small populations using a developed protocol that includes: study of a wide range of hereditary diseases (assessment of the burden, diversity, uniformity of distribution of hereditary diseases, accumulation of individual nosological forms, population differentiation), analysis of population structure using standard methods of population statistics and analysis of nuclear genome DNA markers (Zinchenko et al. 2020). The same protocol including population genetic structure study is applied while studying Ossetia population. To date, in the Laboratory of Genetic Epidemiology of the RCMG, considerable material has been accumulated that allows us to analyze phylogenetic relationships between several studied populations – the studies have been conducted in 12 ethnic groups of European Russia, including both populations with predominantly Russian populations and regions with different ethnic compositions. Belonging to an ethnic group can serve as a marker of the historical path passed by the gene pool of a people and a basis for studying phylogenetic ties between different ethnic groups (Balanovskaia and Rychkov Iu 1990; Balanovsky et al. 2011). Thus, it is crucial to characterize the place of Ossetians in neighborhood peoples' landscape as it is made for other populations (Wang et al. 2021).

The present publication is devoted to the study of allele frequencies of 10 polymorphic DNA loci of the nuclear genome in the Ossetian population of the Republic of North Ossetia–Alania (RNO-Alania) and a comparative analy-

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sis of the studied peoples of the Volga-Ural region and the North Caucasus of Russia. Ossetians are an autochthonous Iranian-speaking people of the North Caucasus, living in the Republic of South Ossetia and the RNO-Alania (part of the Russian Federation (RF)). Ossetians have two main sub-ethnic groups: Irons and Digors. A small number of representatives of another sub-ethnic group of Ossetians - Kudars (migrants from South Ossetia from the territory of Georgia), who are ethnogenetically and linguistically close to Irons, live in the territory of the RNO-Alania. The main part of the population is Orthodox Christians, one third of Digors professes Islam. Ethnogenesis of Ossetians is associated with the aboriginal population of the North Caucasus, which assimilated Iranian-speaking aliens, the Scythians in the VIII-VII centuries BC, the Sarmatians in the IV-I centuries BC, with their language and cultural elements, and later, the nomadic Alans (Nasidze et al. 2004). One of the reasons to assess genetic structure is further tracking language and ethnic differences in diverse populations (Atkinson et al. 2022).

Previously, the researchers conducted studies of Ossetians according to the protocol of population survey using standard methods of population statistics: the researchers studied genetic and demographic characteristics and differentiation of the Ossetian population of Ossetians in the RNO-Alania. The method of isonymy (Carrieri et al. 2020) was used to determine the differentiation of sub-ethnic groups of Ossetians: Irons and Digors (El'chinova et al. 2020).

In addition, the Ossetian population was previously studied by biochemical markers and by mitochondrial DNA and Y chromosome markers (Nasidze et al. 2004).

Objectives

This study aimed to characterize the place of Ossetians among other peoples of Russia based on genetic structure, particularly, in comparison of our and other researchers' results.

METHODOLOGY

The methodology of the study is based on two main principals of human genetics. The first one is the lack of discontinuities in genetic distances between human populations, and continuous distribution of clinically neutral genetic markers. The second one is cluster analysis fine resolution capability to differentiate populations based on matrix of markers' frequencies, in other words, on genetics distances (Balanovsky et al. 2021).

Ossetian Cohort

The sample consisted of 370 unrelated individuals belonging to three sub-ethnic groups of the Ossetian ethnos: Irons (N=256), Digors (N=95) and Kudars (N=19), residents of Alagirsky, Kirovsky, Ardonsky, Pravoberezhny, Prigorodny, Irafsky, Digorsky and Mozdoksky districts and the city of Vladikavkaz in RNO-Alania. Ethnicity was determined on the basis of a survey. The study included unrelated individuals who identified themselves as belonging to indigenous ethnic groups up to the third generation. At the time of blood collection, a questionnaire was filled out indicating the places of birth and ethnicity of the subjects and their ancestors up to the third generation (grandparents). The material was collected in 2018-2023 by the staff of the Laboratory of Genetic Epidemiology of the RCMG in the course of a comprehensive genetic and epidemiological study of the population of RNO-Alania.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. They were also approved by the Ethics Committee of the Research Centre for Medical Genetics (Moscow), protocol no. 5 dated December 20, 2010.

Informed consent was obtained from all individual participants involved in the study.

Genetic Analysis

DNA samples were typed at 10 polymorphic loci of the nuclear genome: CCR5Δ32, ID/ACE, D7S23(KM19), STR/TH01, STR/FABP2, STR/IVS6aGATT(CFTR), VNTR/PAH, VNTR/DAT1, VNTR/NOS3, VNTR/APOB, alleles in which are inherited codominantly (69 alleles). The set of

markers is the same in all the population studies performed. When selecting polymorphic loci, the aim of maximum randomization of the set was pursued to achieve an objective characterization of the whole genome and the gene pool as a whole (Rychkov 2000). The set of markers includes both single-nucleotide and insertion-deletion biallelic polymorphisms as well as multiallelic polymorphisms (STR and VNTR) with high heterozygosity. The work on questionnaires, genotyping and analysis of allele and genotype frequencies was carried out according to the previously described methodology (Petrova et al. 2024). The use of the same methodology makes it possible to compare populations correctly.

Genetic data on other ethnic groups used to determine interpopulation genetic differentiation

The gene pools of several ethnic groups were compared according to 10 loci of DNA markers of the nuclear genome. The studied peoples represent the autochthonous population of some territories of the Volga-Ural region, the North Caucasus and ethnic groups that have developed in these territories and, in addition, the population of the Russian Plain in the form of the most numerous ethnic groups of the Russian Federation, the Russians and Tatars of the Volga region. Previously studied and described populations include: Russians of central Russia (Kirov region (n=274), Tver region (n=126)), Russians of the southern part of the Russian Federation (Rostov region (n=484)), peoples of the Volga-Ural region (Udmurts (n=599), Chuvash (n=396), Mari (n=494), Bashkirs (n=822), Tatars (n=669)) and Karachays (n=485) from the Republic of Karachay-Cherkessia.

This paper is the first to publish data on allele frequencies of 10 DNA markers of the nuclear genome in the populations of the southern territories of the Russian Federation, both Ossetians of the Republic of North Ossetia-Alania (N=370) and 4 other peoples of the North Caucasus: Terek Kumyks living in RNO-Alania (N=82), Abazins (N=118), Nogais (N=142), Circassians (N=136) living in the Republic of Karachay-Cherkessia and studied earlier using the same methodology.

In total, to compare the levels of genetic differentiation and to construct dendrograms, the researchers used both firstly presented and previously published similar data for 12 peoples of the Russian Federation: Ossetians (three subgroups) and Kumyks of RNO-Alania, Karachays, Abazins, Circassians, Nogais of the Republic of Karachay-Cherkessia, Russians of three regions, and Tatars, Bashkirs, Udmurts, Maris, and Chuvashs of the Volga-Ural region (Akhmetova et al. 2006; Bermisheva et al. 2007; Grinberg et al. 2010; Khusnutdinova et al. 2003; Vasilyeva et al. 2013).

Molecular-Genetic Methods

DNA isolation was performed from venous blood using the "Wizard Genomic DNA Purification Kit" from Promega (USA) in accordance with the manufacturer's recommendations.

Polymorphic markers were analyzed by DNA synthesis polymerase chain reaction and restriction fragments length polymorphism (RFLP) analysis using primers and conditions described earlier (Petrova et al. 2024; Salimi et al. 2011). Results were evaluated by performing vertical electrophoresis in 8 percent polyacrylamide gel for VNTR/PAH, VNTR/DAT1, VNTR/NOS3, CCR5Δ32, VNTR/APOB loci, in 12 percent polyacrylamide gel for STR/TH01, STR/FABP2, STR/IVS6aGATT(CFTR) loci, and in 2 percent agarose gel for ID/ACE, D7S23(KM19) loci as previously described (Petrova et al. 2024).

Statistical Analysis

Statistical data processing was performed using GENEPOP software (version 4.7.5) (Rousset 2008) and GeneAlex add-in (v 6.5) (Peakall and Smouse 2012). The researchers calculated allele frequencies, genotypes and differentiation indices of the Ossetian population, observed, expected heterozygosity, fixation index for each of the 10 loci of the nuclear genome, $\chi 2$ test for conformity to the Hardy-Weinberg distribution, Wright's F-statistics (F_{is}, F_{st}) for each locus and in general.

The Wright statistics used to characterize population structure and analyze phylogenetic relationships, especially the F_{st} statistics, reflect microevolutionary processes occurring in the population that affect the structure of genetic

variation within and between populations (Chakraborty and Jin 1993; Holsinger and Weir 2009; Putman and Carbone 2014).

Cluster analysis for the possibility of assessing phylogenetic relationships between peoples was carried out in Statistica 8.0 software by a single-linkage clustering where the distance between the nearest points in two clusters is the distance between the clusters.

RESULTS

The allele frequencies of 10 nuclear genome loci were obtained: CCR5 χ32, ID/ACE, D7S23 (KM19), STR/TH01, STR/FABP2, STR/ IVS6a GATT(CFTR), VNTR/PAH, VNTR/DAT1, VNTR/ NOS3, VNTR/APOB, - in Ossetian populations with regard to subethnic division, heterozygosity values by loci, probability value p(χ2), obtained in the χ2 test for conformity of genotype distribution to the Hardy-Weinberg equilibrium and the fixation index by loci and by subethnicity, which are summarized in Table 1.

Locus CCR5Δ32

The insertion-deletion polymorphism of the CCR5Δ32 diallelic marker of the *CCR5* chemokine receptor gene was studied (Jasinska et al. 2022). A CCR5Δ32 variant (deletion of 32 base pairs) results in impaired adhesive properties of the T cell CCR5 encoded protein, which is a major coreceptor for HIV-1 virus M-tropic chains, and likely prevents the receptor from interacting with HIV-1 virus (Zajac 2018). In Ossetians of RNO-Alania as a whole, the frequency of the rare allele with the *D deletion was 0.041, in subethnic groups of Ossetians (Irons, Digors, and Kudars)-0.037, 0.039, and 0.105, respectively. The distribution of allele frequencies of the CCR5Δ32 locus with the more frequent allele *I in the studied subgroups is similar, and the genotype *I/*I, homozygous for the absence of deletion, prevails.

Locus ID/*ACE*

The *ACE* gene encodes angiotensin-converting enzyme, a protein (carboxypeptidase) circulating in the extracellular space that plays an important role in the regulation of blood pressure and electrolyte balance by catalyzing the cleavage of inactive angiotensin I to active angiotensin II (Tiret et al. 1992). The insertion-deletion (I/D) polymorphism is due to the presence or absence of an Alu repeat insertion of 287 nucleotide pairs in intron 16 of the *ACE* gene (Salimi et al. 2011). The allele with the *D deletion predominates in Ossetian subpopulations (Table 1). Its frequency in Ossetians ranged from 0.521 to 0.553, varying within narrow limits.

Locus D7S23 (KM19)

The KM19 polymorphism (marker D7S23), linked to the *CFTR* gene encoding the cystic fibrosis transmembrane regulator, is a single-nucleotide substitution that can be detected by the presence or loss of the site for *Pst*I restriction endonuclease. The KM19 polymorphism is characterized by the presence of two alleles: allele *A - the absence of a restriction site for the *Pst*I endonuclease, allele *B - the presence of a restriction site (Liechti-Gallati et al. 1990). The most frequent allele in all Ossetians is the *A allele (0.690), the frequency of which varies from 0.632 in Digors to 0.712 in Irons.

Locus IVS6aGATT*(CFTR)*

The microsatellite locus IVS6aGATT(CFTR) tandemly repeated tetranucleotide GATT sequences in intron 6a of the *CFTR* gene represents an intragenic STR marker (Chehab et al. 1991). Five alleles with four to eight repeats were identified. Two alleles with 6 and 7 repeat units were found in samples of Ossetians from RNO-Alania. The most frequent allele is the allele with 7 repeats (*7) (the frequency was 0.865 in all Ossetians and 0.895 in Kudars).

Locus *HUMFABP2*

The *FABP2* gene encodes a protein that binds fatty acids (Polymeropoulos et al. 1990). The FABP2 protein is found in the epithelium of the small intestine, where it is used to bind fats to form chylomicrons. The microsatellite locus HUMFABP2 is localized in the second intron of the gene, this trinucleotide repeat of ATT, is designated as HUMFABP2 or STR/FABP2 and belongs to the group of short tandem repeats. The name of the alleles corresponds to the number

Table 1: Allele frequencies of 10 investigated DNA markers of the nuclear genome in the studied subpopulations of Ossetians, Ossetians in general and their population characteristics

Locus	*Allele/ Heterozygosity/ Fixation Index*	*Ossetians (N=370)*	*Irons (N=256)*	*Digors (N=95)*	*Kudars (N=19)*	*Fis*	*Fst (by locus)*
CCR5Δ32	*D	0.041	0.037	0.039	0.105	0.230	0.017
	*I	0.959	0.963	0.961	0.895		
	HWE (χ^2)	0.251	0.383	0.149	3.698		
	H_{obs}	0.086	0.075	0.079	0.105		
	H_{exp}	0.112	0.072	0.076	0.188		
	F	0.120	-0.039	-0.041	0.441		
ACE	*D	0.544	0.551	0.521	0.553	0.095	0.001
	*I	0.456	0.449	0.479	0.447		
	HWE (χ^2)	0.917	1.076	0.106	1.235		
	H_{obs}	0.449	0.463	0.568	0.368		
	H_{exp}	0.496	0.495	0.499	0.495		
	F	0.096	0.065	-0.033	0.255		
D7S23(KM19)	*A	0.690	0.712	0.632	0.658	-0.019	0.005
	*B	0.310	0.288	0.368	0.342		
	HWE (χ^2)	0.011	0.070	0.011	0.052		
	H_{obs}	0.450	0.417	0.460	0.474		
	H_{exp}	0.442	0.410	0.465	0.450		
	F	-0.019	-0.017	0.011	-0.052		
CFTR-IVS6a	*6	0.135	0.127	0.163	0.105	-0.146	0.005
	*7	0.865	0.873	0.837	0.895		
	HWE (χ^2)	6.557	3.107	3.61	0.262		
	H_{obs}	0.261	0.246	0.326	0.211		
	H_{exp}	0.228	0.222	0.273	0.189		
	F	-0.141	-0.110	-0.195	-0.118		
HUMFABP2	*9	0.003	0.002	0.006	0.000	0.070	0.016
	*10	0.589	0.573	0.610	0.711		
	*11	0.144	0.153	0.122	0.132		
	*12	0.037	0.034	0.035	0.079		
	*13	0.198	0.212	0.192	0.053		
	*14	0.024	0.022	0.029	0.026		
	*15	0.004	0.004	0.006	0.000		
	HWE (χ^2)	16.296	19.717	11.405	4.223		
	H_{obs}	0.510	0.597	0.512	0.421		
	H_{exp}	0.548	0.602	0.574	0.468		
	F	0.072	0.009	0.108	0.101		
HUMTH01	*6	0.303	0.297	0.319	0.316	-0.005	0.013
	*7	0.160	0.171	0.094	0.289		
	*8	0.109	0.114	0.094	0.105		
	*9	0.181	0.175	0.213	0.132		
	*10	0.239	0.232	0.281	0.158		
	*11	0.004	0.006	0.000	0.000		
	*12	0.001	0.002	0.000	0.000		
	*13	0.001	0.002	0.000	0.000		
	HWE (χ^2)	729.277	533.426	19.407	11.357		
	H_{obs}	0.772	0.772	0.913	0.632		
	H_{exp}	0.768	0.785	0.757	0.763		
	F	-0.006	0.017	-0.206	0.172		
PAH	*3	0.358	0.375	0.322	0.289	0.038	0.009
	*5	0.018	0.018	0.017	0.026		
	*6	0.003	0.002	0.006	0.000		
	*7	0.108	0.117	0.057	0.211		
	*8	0.344	0.337	0.368	0.316		
	*9	0.124	0.107	0.172	0.132		
	*11	0.034	0.042	0.011	0.026		
	*12	0.013	0.002	0.046	0.000		

Table 1: Contd...

Locus	*Allele/ Heterozygosity/ Fixation Index*	*Ossetians (N=370)*	*Irons (N=256)*	*Digors (N=95)*	*Kudars (N=19)*	*Fis*	*Fst (by locus)*
	HWE (χ^2)	24.109	19.970	16.268	10.473		
	H_{obs}	0.705	0.683	0.726	0.754		
	H_{exp}	0.732	0.050	-0.030	0.092		
	F	0.037	0.020	0	0		
DATI	*8	0.014	0.020	0.000	0.000	0.173	0.003
	*9	0.270	0.271	0.259	0.316		
	*10	0.703	0.706	0.707	0.658		
	*11	0.013	0.004	0.034	0.026		
	HWE (χ^2)	36.720	13.457	18.608	1.680		
	H_{obs}	0.366	0.299	0.368	0.133		
	H_{exp}	0.442	0.432	0.467	0.124		
	F	0.171	0.309	0.211	-0.071		
NOS3	*4	0.161	0.186	0.109	0.067	-0.048	0.023
	*5	0.839	0.814	0.891	0.933		
	HWE (χ^2)	0.653	1.071	0.002	0.077		
	H_{obs}	0.217	0.322	0.195	0.133		
	H_{exp}	0.207	0.302	0.195	0.124		
	F	-0.047	-0.066	-0.004	-0.071		
APOB	*25	0.003	0.002	0.006	0.000	0.141	0.011
	*26	0.001	0.002	0.000	0.000		
	*27	0.013	0.010	0.012	0.059		
	*28	0.006	0.008	0.000	0.000		
	*30	0.082	0.002	0.012	0.029		
	*32	0.064	0.080	0.006	0.118		
	*33	0.003	0.004	0.000	0.000		
	*34	0.335	0.345	0.296	0.382		
	*35	0.004	0.006	0.000	0.000		
	*36	0.313	0.295	0.370	0.294		
	*37	0.001	0.002	0.000	0.000		
	*38	0.058	0.063	0.043	0.059		
	*40	0.007	0.006	0.012	0.000		
	*42	0.004	0.004	0.000	0.029		
	*44	0.003	0.004	0.000	0.000		
	*46	0.028	0.025	0.043	0.000		
	*48	0.049	0.050	0.056	0.000		
	*50	0.016	0.019	0.012	0.000		
	*51	0.001	0.002	0.000	0.000		
	HWE (χ^2)	474.405	450.891	116.522	25.831		
	H_{obs}	0.650	0.707	0.654	0.588		
	H_{exp}	0.757	0.775	0.751	0.744		
	F	0.142	0.088	0.128	0.210		
Fst (total)						0.053	0.010
SE						0.036	0.002

Note: HWE (χ^2) — χ^2-test for Hardy-Weinberg Equilibrium, H_{obs} = Observed Heterozygosity = No. of Hets / N, H_{exp} = Expected Heterozygosity = 1 - Sum p_i^2, where pi is the frequency of the i-th allele for the population & Sum p_i^2 is the sum of the squared population allele frequencies, F = Fixation Index = (H_{exp} - H_{obs}) / H_{exp} = 1 - (H_{obs} / H_{exp}), Fis = (Mean H_{exp} - Mean H_{obs}) / Mean H_{exp} , Fst = (Ht - Mean H_{exp}) / Ht

of trinucleotide repeats. Eight alleles of this locus have been described with the number of repeats ranging from 8 to 16. The high heterozygosity value of the HUMFABP2 locus makes it reasonable to use the marker in population genetic studies (Polymeropoulos et al. 1990). Seven alleles of the STR/FABP2 locus were identified in Ossetians. The most frequent were alleles *10 (frequency from 0.573 to 0.711), *11 (frequency from 0.122 to 0.153) and *13 (frequency from 0.053 to 0.212). Alleles *9 and *15 are rare in the studied samples and were detected in Irons

and Digors with frequencies of 0.003 and 0.004, respectively (Table 1).

Locus *HUMTH01*

The HUMTH01 locus (or STR/TH01) represents another locus of short tandem repeats. The human tyrosine hydroxylase (*TH*) gene contains an AATG repeat locus in intron 1 (van Oorschot et al. 1994). The name of alleles of the HUMTH01 locus corresponds to the number of repeats. In some alleles, one nucleotide disappears from the tetranucleotide sequence; such alleles are designated as n.3, where n is the number of core repeats (for example, 9.3). This polymorphic locus has a high level of heterozygosity and is actively used in population genetics and in the identification of individuals (van Oorschot et al. 1994). Eight alleles of the STR/TH01 locus were detected in Ossetians of RNO-Alania; the most frequent were alleles *6, *7, *8, *9, and *10, which were found with frequencies of 0.303, 0.160, 0.109, 0.181, and 0.239, respectively (Table 1). Alleles *11, *12, and *13 are rare (<1%), and allele *13 was found only in Irons.

Locus *VNTR/PAH*

The VNTR/PAH minisatellite marker represents a highly polymorphic 30-bp AT-rich repetitive sequence region localized at the 32 -end of the *PAH* phenylalanine hydroxylase gene (Hoang et al. 1996). Nine alleles of the VNTR/PAH locus with the number of repeats of the core unit from 1 to 12 (alleles with the 4 repeats were not detected) were identified in Ossetians. The highest number of alleles at the VNTR/PAH locus was noted for Irons (all 9 alleles). In all subpopulations, the most frequent alleles were *3 (from 0.289 in Kudars to 0.375 in Irons) and *8 (from 0.316 in Kudars to 0.368 in Digors), as well as a noticeable frequency of allele *9 (0.124 in all Ossetians).

Locus *VNTR/DAT1*

SLC6A3 gene (formerly called *DAT1*), encodes a dopamine transporter that belongs to the family of Na^+,CI^--dependent neurotransmitter transporters and limits dopaminergic activity at synapses by reversing neurotransmitter uptake into presynaptic terminals, which plays an important role in dopaminergic neurotransmission (Sano et al. 1993). In the *SLC6A3* gene, a locus of variable tandem repeats (VNTR) was found in the 32 -untranslated region with the number of copies from 3 to 11 (the length of a repeat copy is 40 bp). In samples of Ossetians from RNO-Alania, 4 alleles were detected in the VNTR/DAT1 locus. The most frequent allele is the allele with 10 repeat units. The maximum frequency of allele *10 was detected in Digors (0.707), the minimum in Kudars (0.658). The second most frequent allele is allele *9, the highest frequency of which was found in Kudars (0.316), the lowest in Digors (0.259) (Table 1). The distribution of allele frequencies of the VNTR/DAT1 locus among Ossetians of RNO-Alania is characterized by the rare occurrence of alleles with 8 repeats and 11 repeats <1 percent.

Locus *VNTR/NOS3*

The *NOS3* gene encodes a constitutive endothelial nitric oxide synthase enzyme involved in the formation of nitric oxide, one of the most important secondary messengers in the human body (Mustafina et al. 2001). The polymorphism of the minisatellite repeat in intron 4 is due to a varying number of 27 bp tandem sequences (Reshetnikov et al. 2019). Two alleles *A and *B, with the number of repeating units 4 and 5, were detected in the Ossetian population. The frequency of the *B allele of the VNTR/NOS3 gene in Ossetians of RNO-Alania is much higher, it amounted to 0.839, the frequency of the *A allele - 0.161 (Table 1).

Locus *VNTR/APOB*

The VNTR/APOB locus is a repetitive AT-rich sequence of 14-16 bp in length, localized in the 3'-untranslated region of the apolipoprotein B gene. Usually, 12 alleles of this locus are segregated in populations with the number of repeats ranging from 28 to 52 (Yalin et al. 2007). In Ossetians of RNO-Alania, 9 alleles with a frequency of more than 1 percent were found, with 27-50 repeats. The most frequent were alleles with 34 (frequency 0.335) and 36 (frequency 0.313) repeats. There were two more alleles with a frequency of about 1 percent: *30 and *38 (frequencies of 0.082 and 0.058, respectively).

Genetic Structure of Ossetian Population

A total of 69 alleles were determined in 10 polymorphic DNA loci of the nuclear genome in Ossetians of RNO-Alania.

Wright's F statistics values were obtained for the loci of 10 DNA markers in the Ossetian population. Fis and Fst coefficients for each marker and in the population as a whole are given in Table 1.

The average Fis coefficient, characterizing the difference between the observed frequency of heterozygous carriers and the expected frequency and deviation from panmixia in the population, was Fis=0.053.

The average Fst coefficient for all loci was 0.010, the largest differences were found for the loci NOS3 (Fst=0.023), CCR5Δ32, (Fst=0.017) FABP2 (Fst=0.016) the smallest for the locus ACE (Fst=0.001).

The average value of Fst, which characterizes the subdivision of the population, indicates the existing differentiation of different Ossetian subethnic groups that make up the Ossetian population of RNO-Alania.

The obtained ratio of genotypes at the loci of TH01, DAT1 and APOB markers differed significantly from the Hardy-Weinberg equilibrium; this deviation can be explained by high heterozygosity of these polymorphic loci and a large number of alleles in them. In other loci, deviations from the Hardy-Weinberg equilibrium were statistically insignificant.

DISCUSSION

A sample of 370 healthy unrelated individuals belonging to the Ossetian ethnic group from seven districts and the city of Vladikavkaz in RNO-Alania was genotyped according to loci of ten polymorphic DNA markers of the nuclear genome. The obtained allele frequencies of the studied markers and their ratios in the Ossetian populations are within the range of variation established for other populations and have a number of characteristic features.

In the CCR5"32 locus in the Ossetian sample of RNO-Alania, the frequency of the allele with deletion was 4.1 percent (0.041), which corresponds to low European values. The frequency of the CCR5"32 variant in European populations averages 10 percent, varying from a maximum value in the Finnish and Mordovian populations (16%) to a minimum value in Greece (4%) (Novembre et al. 2005). Among previously conducted similar studies of populations of the Volga-Ural region, the maximum frequency of the *D allele was observed in the populations of Udmurts and Russians (0.126 and 0.138), the minimum - in Bashkirs and Chuvashians (0.034) (Akhmetova et al. 2006; Bermisheva et al. 2007; Grinberg et al. 2010; Khusnutdinova et al. 2003; Vasilyeva et al. 2013) (see Supplementary File).

Among the previously studied peoples of the North Caucasus, namely, the peoples of the Republic of Karachay-Cherkessia, a similar distribution of allele frequencies with and without deletion and a similar frequency of the allele with deletion were observed: for Karachais it amounted to 0.054, Circassians - 0.027, Abazins - 0.053 and Nogais - 0.032 (Petrova et al. 2024).

At the ID/ACE locus, the *D allele predominates in Ossetian subpopulations. The deletion allele *D is more frequent in European populations than in Asian populations (Prasad et al. 1994). The populations of the Volga-Ural region by frequencies of *D/*D genotype occupy an intermediate position between the peoples of Europe and Asia (Evans et al. 1994). It is also assumed that Turkic peoples differ from the Finno-Ugric group of peoples by a lower frequency of the *D/*D genotype (Vasilyeva et al. 2013). In Kumyks, a Turkic-speaking ethnic group of RNO-Alania, the frequency of the allele with deletion is 0.443 (in Ossetians - 0.544) (Table 1) The frequency of the allele *D in Ossetians is slightly higher than in previously studied populations: in Russians - 0.538, in Chuvash - 0.525, Udmurts - 0.505, Mari - 0.452, Tatars - 0.513, Bashkirs - 0.423 (see Supplementary File). In Karachay-Cherkessia, the frequency of the *D allele was 0.476 in Karachais, 0.517 in Circassians and Abazins, and 0.500 in Nogais (Petrova et al. 2024) (see also Supplementary File).

The most frequent allele in the D7S23 (KM19) locus in the Ossetian subethnic groups of RNO-Alania is the *A allele (0.632 - 0.712). A similar distribution of allele and genotype frequencies of the D7S23 (KM19) locus is characteristic of other populations (see Supplementary File).

Two alleles with 6 and 7 repeats were found in the IVS6aGATT(CFTR) locus in Ossetians;

the predominant allele is *7 with a frequency of 0.865. The frequency of these two alleles in European populations, on average, is 0.25 and 0.75, respectively (Chehab et al. 1991). In general, in terms of allele frequency distribution of the IVS6aGATT locus, the Ossetian populations of RNO-Alania differ from the studied populations of the Volga-Ural region, which are characterized by lower frequencies of the *7 allele (0.590 - 0.707) (see Supplementary File), and are similar to the previously studied populations of the North Caucasus (with a variation from 0.789 in Karachais to 0.887 in Circassians) (Petrova et al. 2024) (see also Supplementary File).

Eight alleles with repeat numbers ranging from 8 to 16 have been described at the HUMFABP2 locus (Polymeropoulos et al. 1990). In Ossetians, the most frequent three alleles are *10 (frequency 0.573 - 0.711), *11 (frequency 0.122 - 0.153), and *13 (frequency 0.053 - 0.212). The distribution where the three alleles, *10, *11, and *13, are the most frequent is described in the previously studied peoples of the Volga-Ural region and Karachay-Cherkessia (Petrova et al. 2024) (see also Supplementary File). In a small sample of Kudars from RNO-Alania, the frequency of the frequent allele *10 was maximal (0.711), and the frequency of the allele *13 was minimal (0.053).

Five frequent (*6, *7, *8, *9, and *10) and three rare (*11, *12, *13) alleles were detected at the HUMTH01 locus in Ossetians. The distribution of frequencies of frequent alleles *6/*7 in Ossetians resembles the European one, with the *6 allele prevailing (0.3/0.16 and 0.21/0.15) (Perez-Lezaun et al. 1997; van Oorschot et al. 1994). In general, the distribution is similar to that obtained in the peoples of Karachay-Cherkessia and is characterized, for example, by a more uniform ratio of frequencies determined for alleles *9 and *10 than in the peoples of the Volga-Ural region (Petrova et al. 2024) (see also Supplementary File).

In the VNTR/PAH locus, 9 allelic variants containing different numbers of repeats have been identified in European populations (Hoang et al. 1996). In Ossetians the allele *3 was found with a frequency ranging from 0.289 to 0.375. In Europe, the frequency of allele *3 is approximately the same (0.280) as in Ossetians, while in China it is much higher (0.820) than in Ossetians. The frequency of the second frequent allele *8 in Ossetians was 0.316 - 0.368, in Europe it is higher (0.450). Thus, in the total sample of Ossetians the frequencies of alleles *3 and *8 do not differ significantly: 0.358 for the *3 allele and 0.344 for the *8 allele. The same smoothed difference was observed among the peoples of Karachay-Cherkessia, with frequencies ranging from 0.340 to 0.441 for the *3 allele and from 0.269 to 0.378 for the *8 allele (Petrova et al. 2024) (see also Supplementary File). In addition, a rather high frequency of the *9 allele (0.124) was found in Ossetians, which is probably a peculiarity of all North Caucasian populations studied; a similar distribution was observed in Karachay-Cherkessia. Another allele was frequent in the studied populations of the North Caucasus - the *7 allele, which was found with frequencies at the level of the *9 allele. It should be noted that in the previously studied Russian populations (see Supplementary File), the frequency of the *3 allele significantly prevailed over the frequencies of all other alleles, including the frequency of the *8 allele.

At the VNTR/DAT1 locus, alleles with 9 and 10 repeats are the most frequent (identified in more than 90 percent of Europeans and Americans of European and African descent) (Sano et al. 1993). The predominant frequency of the allele with 10 repeat units in the VNTR/DAT1 locus, which is frequent in many other populations, was also determined in Ossetians (see Supplementary File). The distribution of allele frequencies of the VNTR/DAT1 locus among Ossetians resembles the ratio obtained earlier in Karachay-Cherkessia (Petrova et al. 2024) (see also Supplementary File). The frequency of the *10 allele ranged from 0.658 in Kudars to 0.707 in Digors in RNO-Alania and from 0.622 in Circassians to 0.818 in Abazins, and the frequency of the *9 allele ranged from 0.316 in Kudars to 0.259 in Digors in RNO-Alania, and from 0.344 in Circassians to 0.612 in Abazins in Karachay-Cherkessia. Kumyks in RNO-Alania differed from Ossetians in the ratio of frequent alleles *10 and *9, which amounted to 0.908/0.092, and more resembled the previously obtained proportion for Bashkirs of 0.864/0.110. In general, in the populations of the Volga-Ural region, the frequency of the *10 allele is higher than in the North Caucasus (0.799 - 0.864 vs. 0.622 - 0.818), and the frequency of the

*9 allele is lower (0.110 - 0.186 vs. 0.112 - 0.361) (Petrova et al. 2024) (see also Supplementary File).

In Ossetians of RNO-Alania, the frequency of the *B allele with 5 repeat units at the VNTR/NOS3 locus significantly exceeds the frequency of the *A allele (Table 1.). This corresponds to the distribution of locus allele frequencies in many populations (Mustafina et al. 2001; Petrova et al. 2024) (see also Supplementary File).

Typically, 12 alleles of the VNTR/APOB locus with repeat counts ranging from 28 to 52 are segregated in populations (Yalin et al. 2007). Ossetians have 9 alleles, the most frequent with 34 (frequency 0.335) and 36 (frequency 0.313) repeats, such distribution corresponds to the literature data on frequency distribution in other studied populations) (Petrova et al. 2024) (see also Supplementary File). As before, two other frequent alleles, with 30 and 38 repeats, were encountered in Karachay-Cherkessia (Petrova et al. 2024) (see also Supplementary File).

The analysis of observed heterozygosity levels for the studied markers for Ossetian subpopulations showed that the highest level of observed heterozygosity in the biallelic system was found for the KM19 and ACE loci (0.450 and 0.449), and in the multiallelic system - for the TH01 (0.772), PAH (0.705), APOB (0.650), and FABP2 (0.510) loci.

Differentiation of Ossetians of RNO-Alania within the Ethnic Group

The parameters Fis and Fst were used to analyze the differentiation of the studied populations. Fis can express both the mean deviation from the expected Hardy-Weinberg equilibrium distribution and the proportion of alleles of the same origin in individuals of the same population. Fst can express both the degree of genetic differentiation due to differences in allele frequencies in different populations and the proportion of alleles of the same origin within populations relative to a group of populations (random inbreeding) (Holsinger and Weir 2009; Lavanchy et al. 2024). In this paper, Wright's statistics are used mainly in the first value of the indicators of deviation from panmixia and differentiation of populations; in the study of genetic closeness of the Kudar subethnic group to the Irons and Digors, Fst characterizes pairwise inbreeding coefficients between subpopulations of Ossetians (Bryant and Huson 2023).

To assess genetic differences between the studied Ossetian subpopulations, the researchers calculated pairwise random inbreeding coefficients Fst, which we have given in Table 2.

Table 2: Pairwise Fst Values. Pairwise Population Matrix of Fst Values for Total. Fst values below the diagonal. Probability, P(rand >= data) based on 999 permutations is shown above diagonal

p-value / *Fst*	*Irons*	*Digors*	*Kudars*
Irons	***	0.017	0.415
Digors	0.004	***	0.300
Kudars	0.008	0.010	***

Pairwise inbreeding coefficients between Ossetian subethnic groups indicate genetic closeness of Irons and Digors and closer kinship of Kudars with Irons than with Digors, which confirms the data of linguists and ethnographers. Earlier analysis of mitochondrial DNA in several subgroups of Ossetians also indicated their common ancestry (Nasidze et al. 2004).

Genetic diversity of Ossetians of RNO-Alania, estimated by the average variant of allele frequencies of 10 DNA markers of the nuclear genome, amounted to Fst=0.010. This estimate corresponds to the data obtained earlier on the basis of the analysis of quasi-genetic markers. When analyzing the prevalence of surnames among Ossetian-Irons and Ossetian-Digors, the coefficient Fst=0.001 was obtained (El'chinova et al. 2020).

The ratio of Fst statistics calculated by the two different methods is as expected; estimates of the statistics may differ by an order of magnitude because such a quasi-genetic marker as surnames can be considered as only one multiallelic parameter of population.

Ossetians of RNO-Alania and Their Place in the Genetic Landscape of the Studied Ethnic Groups of Russia

The established population differentiation of Ossetians (Fst=0.010) is slightly higher than that established for other populations: for Mari Fst=0.0024; Udmurts Fst=0.0048; Chuvash

Fst=0.006, Tatars Fst=0.0075, Bashkirs Fst=0.008, Karachais Fst=0.007.

The assessment of assortativity, or deviation from the expected Hardy-Weinberg equilibrium distribution (Fis) turned out to be both positive and negative at different loci of the nuclear genome, which, to a large extent, may be due to stochastic processes of gene drift (Table 1) (Li et al. 2017). The small positive average estimate of Ossetian assortativity (Fis=0.053, Table 1), which may indicate deviation from the panmictic population and deficiency of heterozygotes, is consistent with the previously calculated low average ethnic mating assortativity of the Ossetians (El'Chinova et al. 2019; El'chinova et al. 2020).

When comparing Ossetians as a whole ethnic group with previously studied populations of the Volga-Ural region and the North Caucasus, which were genotyped using the same DNA markers, the genetic closeness of Ossetians to other peoples of the North Caucasus, Circassians, Abazins, Nogais, Karachays was revealed, which is reflected in Figure 1.

The Ossetian population is at the closest genetic distance with other studied populations of the North Caucasus, forming a single cluster with them. This cluster is sister to the so called Volga-Ural cluster forming by peoples of Turkic and Finno-Ugric ethnic groups (Tatars, Bashkirs, Udmurts, Mari, Chuvashes). The Kumyks of RNO-Alania are far from both Ossetians and other previously studied peoples of the North Caucasus. The Kumyks (Terek Kumyks) are a Turkic people of the North Caucasus, who only in 1944 (three generations ago) as a result of the change in the administrative composition of the Russian Federation with the transfer of the Mozdok district to the RNO-Alania found themselves on this territory. The Kumyks on the dendrogram are represented by a separate clade. Russians are equally distant from the peoples of the North Caucasus and Volga-Ural region. Rychkov et al. analyzed two dozen of biochemical markers and obtained similar results. The authors concluded the closeness of the Ossetian people and other peoples of the Caucasus and the unity of the Caucasian cluster of popula-

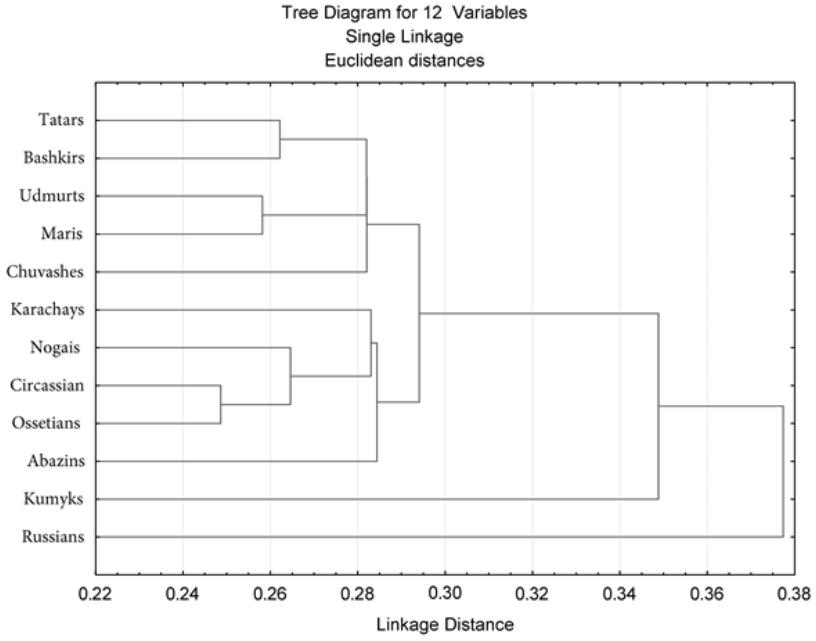

Fig. 1. Dendrogram of genetic relationships between the Ossetians of RNO-Alania and other peoples of the Russian Federation based on polymorphism data of 10 DNA loci of the nuclear genome. The single linkage method was used

tions (Rychkov et al. 1996). Geography influencing the pattern of genetic variation through several mechanisms could explain expected and observed Caucasian populations similarity (Taravella Oill et al. 2022).

CONCLUSION

The data on the distribution of frequencies of 69 alleles of 10 polymorphic markers of the nuclear genome were used to characterize the structure of the gene pool of the population of RNO-Alania (a total of 370 Ossetians from seven districts and the city of Vladikavkaz). The genetic variability of the population of RNO-Alania (Fst =0.010) is small on the Russian genetic scale, although it slightly exceeds the genetic diversity of the previously studied peoples of Russia.

Ossetians of RNO-Alania are differentiated into two clusters Irons and Digors, with Ossetian-Kudars are at a closer genetic distance to Ossetian-Irons than to Ossetian-Digors, which corresponds to ethnographic and linguistic data.

A comparative analysis of 12 ethnic groups of the Russian Federation was carried out: Russians of the central and southern territories, five peoples of the central part of the Russian Federation - Volga-Ural region (Tatars, Bashkirs, Mariis, Udmurts and Chuvash) and six ethnic groups of the North Caucasus (Terek Kumyks, Ossetians, Abazins, Nogais, Ossetians, Abazins, Nogais, Circassians and Karachais) allowed us to characterize the peoples according to the studied markers, to show the genetic proximity of Ossetians to other peoples of the North Caucasus and to demonstrate differences with the peoples of the Volga-Ural region, Russians and Terek Kumyks.

The data obtained in this study expand the understanding of allele frequencies of 10 loci of the nuclear genome in 12 ethnic groups of the Russian Federation and make a certain contribution to genetic variability in human populations and ethnic genetics.

Ossetians of RNO-Alania have minimal genetic distances to the populations of the North Caucasus and are genetically distant from the populations of the Volga-Ural region.

RECOMMENDATIONS

Further study of Kudars who was little presented in the study is recommended, though there are few Kudar residents in the RNO-Alania, they mostly live in the South Ossetia. To elucidate Kumyks relationships to other ethnic groups and peoples further study of Dagestan's Kumyks is also needed as the most part of them resident in the republic.

CONFLICT OF INTEREST STATEMENT

Nil

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REFERENCES

Akhmetova VL, Khusainova RI, Yuryev EB et al. 2006. Analysis of polymorphism at nine nuclear genome DNA loci in Maris. *Russ J Genet+*, 42: 192-207.

Atkinson EG, Dalvie S, Pichkar Y et al. 2022. Genetic structure correlates with ethnolinguistic diversity in eastern and southern Africa. *American Journal of Human Genetics*, 109: 1667-1679.

Balanovskaia EV, Rychkov Iu G 1990. Ethnogenetics: Adaptive structure of the gene pool of the mankind from the data on human polymorphic genetic markers. *Genetika*, 26: 739-748.

Balanovsky O, Dibirova K, Dybo A et al. 2011. Parallel evolution of genes and languages in the Caucasus region. *Molecular Biology and Evolution*, 28: 2905-2920.

Balanovsky O, Petrushenko V, Mirzaev K et al. 2021. Variation of genomic sites associated with severe Covid-19 across populations: Global and national patterns. *Pharmgenomics Pers Med*, 14: 1391-1402.

Bermisheva MA, Petrova NV, Zinchenko RA et al. 2007. Population study of the Udmurt population: Analysis of ten polymorphic DNA loci of the nuclear genome. *Russ J Genet+*, 43: 563-578.

Bryant D, Huson DH 2023. NeighborNet: Improved algorithms and implementation. *Front Bioinform*, 3: 1178600.

Carrieri A, Sans M, Dipierri JE et al. 2020. The structure and migration patterns of the population of Uruguay through isonymy. *J Biosoc Sci*, 52: 300-314.

Chakraborty R, Jin L 1993. A unified approach to study hyper-variable polymorphisms: statistical considerations of determining relatedness and population distances. *EXS*, 67: 153-175.

Chehab FF, Johnson J, Louie E et al. 1991. A dimorphic 4-bp repeat in the cystic fibrosis gene is in absolute linkage disequilibrium with the delta F508 mutation: Implications for prenatal diagnosis and mutation origin. *American Journal of Human Genetics,* 48: 223-226.

El'Chinova GI, Getoevà ZK, Kadyshev VV et al. 2019. Endogamy, the intensity of assortative intra-ethnic marriage of ossets (the end of XX century). *Medical Genetics,* 18: 51-53. (In Russ.).

El'chinova GI, Kadyshev VV, Getoeva ZK et al. 2020. Cartographic analysis of random inbreeding and surname structure of the population of North Ossetia. *Russ J Genet+,* 56: 996–999.

Evans AE, Poirier O, Kee F et al. 1994. Polymorphisms of the angiotensin-converting-enzyme gene in subjects who die from coronary heart disease. *Q J Med,* 87: 211-214.

Grinberg YI, Grinberg ER, Akhmetova VL et al. 2010. Medical genetic study of Bashkortostan Republic population. Report VI: Population genetic study of ethnogeographic bashkir groups (analysis of 10 autosomal DNA markers). *Medical Genetics,* 9: 12-29. (In Russ.).

Hoang L, Byck S, Prevost L et al. 1996. PAH mutation analysis consortium database: A database for disease-producing and other allelic variation at the human PAH locus. *Nucleic Acids Res.* 24: 127-131.

Holsinger KE, Weir BS 2009. Genetics in geographically structured populations: Defining, estimating and interpreting F(ST). *Nat Rev Genet,* 10: 639-650.

Jasinska AJ, Pandrea I, Apetrei C 2022. CCRΔ532 as a Coreceptor for human immunodeficiency virus and simian immunodeficiency viruses: A prototypic love-hate affair. *Front Immunol,* 13: 835994.

Khusnutdinova EK, Victorova TV, Akhmetova VL et al. 2003. Population-genetic structure of Chuvash populations inferred from the data on eight DNA loci of the nuclear genome. *Russ J Genet+,* 39: 1313-1325.

Lavanchy E, Weir BS, Goudet J 2024. Detecting inbreeding depression in structured populations. *Proc Natl Acad Sci U S A,* 121: e2315780121.

Li X, Redline S, Zhang X et al. 2017. Height associated variants demonstrate assortative mating in human populations. *Scientific Reports,* 7: 15689.

Liechti-Gallati S, Niederer BU, Schneider V et al. 1990. Haplotype analysis for CF-linked DNA polymorphisms in Switzerland. *Clinical Genetics,* 37: 442-449.

Mustafina OE, Shagisultanova EI, Nasybullin TR et al. 2001. Endothelial nitric oxide synthase gene minisatellite polymorphism in populations of the Volga–Ural Region and analysis of its association with myocardial infarction and essential hypertension. *Russ J Genet+,* 37: 546-552.

Nasidze I, Quinque D, Dupanloup I et al. 2004. Genetic evidence concerning the origins of South and North Ossetians. *Annals of Human Genetics,* 68: 588-599.

Novembre J, Galvani AP, Slatkin M 2005. The geographic spread of the CCR5 Delta32 HIV-resistance allele. *PLoS Biol,* 3: e339.

Pan Z, Xu S 2020. Population genomics of East Asian ethnic groups. *Hereditas,* 157: 49.

Peakall R, Smouse PE 2012. GenAlEx 6.5: Genetic analysis in Excel. Population genetic software for teaching and research-an update. *Bioinformatics,* 28: 2537-2539.

Perez-Lezaun A, Calafell F, Mateu E et al. 1997. Allele frequencies for 20 microsatellites in a worldwide population survey. *Hum Hered,* 47: 189-196.

Petrova NV, Marakhonov AV, Balinova NV et al. 2024. Study of the Karachay population based on the analysis of ten polymorphic DNA loci. *Russ J Genet+,* 60: 180-191.

Polymeropoulos MH, Rath DS, Xiao H et al. 1990. Trinucleotide repeat polymorphism at the human intestinal fatty acid binding protein gene (FABP2). *Nucleic Acids Res,* 18: 7198.

Prasad N, O'Kane KP, Johnstone HA et al. 1994. The relationship between blood pressure and left ventricular mass in essential hypertension is observed only in the presence of the angiotensin-converting enzyme gene deletion allele. *QJM,* 87: 659-662.

Putman AI, Carbone I 2014. Challenges in analysis and interpretation of microsatellite data for population genetic studies. *Ecol Evol,* 4: 4399-4428.

Reshetnikov E, Ponomarenko I, Golovchenko O et al. 2019. The VNTR polymorphism of the endothelial nitric oxide synthase gene and blood pressure in women at the end of pregnancy. *Taiwan J Obstet Gynecol,* 58: 390-395.

Rousset F 2008. GENEPOP'007: A complete re-implementation of the GENEPOP software for Windows and Linux. *Molecular Ecology Resources,* 8: 103-106.

Rychkov YG 2000. *Gene Pool and Genogeography of Populations: Gene Pool of the Populations of Russia and Neighboring Countries* (In Russ.). Moscow: Nauka.

Rychkov YG, Balanovskaya EV, Zhukova OE et al. 1996. Gene pool, genegeography, and morbidity of population (based on data of North Ossetia). In: YuG Rychkov, YuP Altukhov (Eds.): *Advances in Modern Genetics*. Nauka: Moscow, pp. 113-174. (In Russ.).

Salimi S, Mokhtari M, Yaghmaei M et al. 2011. Association of angiotensin-converting enzyme intron 16 insertion/deletion and angiotensin II type 1 receptor A1166C gene polymorphisms with preeclampsia in South East of Iran. *J Biomed Biotechnol,* 2011: 941515.

Sano A, Kondoh K, Kakimoto Y et al. 1993. A 40-nucleotide repeat polymorphism in the human dopamine transporter gene. *Human Genetics,* 91: 405-406.

Taravella Oill AM, Handley C, Howell EK et al. 2022. Genomic analysis reveals geography rather than culture as the predominant factor shaping genetic variation in northern Kenyan human populations. *Am J Biol Anthropol,* 178: 488-503.

Tiret L, Rigat B, Visvikis S et al. 1992. Evidence, from combined segregation and linkage analysis, that a variant of the angiotensin I-converting enzyme (ACE) gene controls plasma ACE levels. *American Journal of Human Genetics,* 51: 197-205.

van Oorschot RA, Gutowski SJ, Robinson SL 1994. HUMTH01: Amplification, species specificity, population genetics and forensic applications. *Int J Legal Med,* 107: 121-126.

Vasilyeva TA, Petrova NV, Timkovskaya EE, et al. 2013. Medical Genetic Study of population of Tatrstan Re-

public. Report VI. Population Genetic study of ethnogeographic Tatar groups (analysis of 9 autosomal DNA markers). *Medical Genetics*, 12: 3-20. (In Russ.).
Wang HY, Hu YH, Cao YY et al. 2021. AI-SNPs screening based on the whole genome data and research on genetic structure differences of subcontinent populations. *Yi Chuan*, 43: 938-948.
Yalin E, Attila G, Yalin S et al. 2007. Allele frequency distributions of Apo B VNTR locus in Cukurova, Turkey. *Cell Biochem Funct*, 25: 665-668.
Zajac V 2018. Evolutionary view of the AIDS process. *The Journal of International Medical Research*, 46: 4032-4038.
Zinchenko RA, Makaov AK, Marakhonov AV et al. 2020. Epidemiology of hereditary diseases in the Karachay-Cherkess Republic. *Int J Mol Sci*, 21.

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