

## HUMAN GENETICS

# Analysis of the Mitochondrial DNA Diversity in Yukaghirs in the Evolutionary Context

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**Abstract**—Based on the mtDNA first hypervariable segment sequence variation data, statistical analysis of the diversity in Yukaghirs in comparison with the other indigenous populations of Siberia, was carried out. The level of the Yukagir mtDNA gene diversity ( $GD$ ) constituted 0.920, which was only slightly different from the corresponding estimate for the other Siberian populations. Integral estimates of the genetic structure of Siberian populations ( $k$ ,  $S$ ,  $\theta_S$ , and  $\pi$ ) are presented. Phylogenetic analysis, performed using the neighbor-joining method, showed that the Siberian populations clustered irrespectively to their language affiliation. Negative  $F_S$  values found in Yukaghirs pointed to the possible influence of adaptive selection.

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## INTRODUCTION

Modern Yukaghirs are the descendants of ancient Mongoloid populations, who by genetic and cultural continuity are tied to prehistoric reindeer and elk hunters of Northern Eurasia [1]. According to archaeological data, direct ancestors of Yukaghirs (pro-Yukaghirs) during many thousand years inhabited tundra zone and northern forests from the Yenisei River to the upper reaches of the Anadyr River [2, 3]. The first historical documents dating back to the mid-17th century showed

that Yukaghirs numbered about 5000 [4], and the whole population was subdivided into 12 to 13 tribes (Fig. 1). After annexation of the Yukagir lands to the Russian state, the population number reduced, primarily because of devastating epidemics of smallpox and measles. By the early 20th century, Yukagir ethnic stratum was represented by only some territorial groups from the interfluvies of Yana and Lower Indigirka rivers, Alazeya River, and lower and upper Kolyma River. The total population number of Yukaghirs, including Yukaghirs–Chuvans from Anadyr, was not more than 1000



**Fig. 1.** Traditional home territory of Yukagir tribes in 17th century [4]. Contemporary settlements, where expeditionary blood samples for the mtDNA analysis were collected are designated by black circles (additional information is presented in [9]).

[5–7]. According to the sites of residence, Yukaghirs are subdivided into tundra reindeer hunters and taiga elk hunters. By now, Yukaghirs are nearly assimilated by Russians, Yakuts, Evens, and Chukchi [8]. For these reasons, blood samples for extraction of mtDNA (mitochondrial DNA) were taken only from those individuals, whose pedigrees contained the data on their belongings to Yukaghir tribe along the maternal lineage [9].

Until recently, mitochondrial gene pool of Yukaghirs remained poorly investigated. Brief data reported by Torroni et al. [10] and Pakendorf et al. [11] were found to be insufficiently informative for phylogenetic reconstructions due small sample sizes and low-resolution techniques used for analysis of mtDNA variation. Exhaustive data on the mtDNA genome variation and evolution in Yukaghirs from Indigirka, Alazeya, Kolyma, and Anadyr were reported by Volodko et al. [9]. In the present study, integral estimates of the genetic structure of Siberian populations, especially of Yukaghirs, are presented with the final goal of identification of possible deviation from standard neutral evolution pattern.

## MATERIALS AND METHODS

Measures of gene diversity ( $GD$ ) [12], the number of haplotypes ( $k$ ) and segregating sites ( $S$ ), the effective population size ( $\theta_s$ ), the mean number of pairwise nucleotide differences ( $\pi$ ), and statistical tests for the model of neutral evolution (Tajima's  $D$  and Fu's  $F_s$ ) [13, 14], and statistical significance of these estimates were computed using the ARLEQUIN 2.000 software program [15]. Genetic distances ( $D_A$ ) were calculated according to [16]. Cluster analysis was performed based on the distances obtained and using the neighbor-joining technique [17] as implemented in the NJBAFD software program [18].

Interpopulation analysis was performed using the frequencies of subhaplogroups characteristic of indigenous populations of Siberia (22 populations). The level of gene diversity was evaluated via analysis of nucleotide sites polymorphism in the first hypervariable segment of mtDNA (from np 16017 to 16390).

## RESULTS AND DISCUSSION

### *Integral Estimates of Genetic Structure*

Measures of gene diversity ( $GD$ ) obtained in Yukaghirs in comparison with the other indigenous populations of Siberia are presented in the table. It was demonstrated that tundra Yukaghirs were characterized by rather low diversity (0.837), caused by nonrandom distribution of mtDNA haplotypes. Although the whole population contained 23 haplotypes, only one of these (C2a) was found with unusually high frequency (41.5%) [9]. It was suggested that the main reason of the evident gene drift, was a dramatic decrease of the Yukaghir number due to the epidemics, which occurred

particularly often in the 19th century, and subsequent geographic isolation of Tundra Yukaghirs from lower Indigirka, Kolyma, and Alazeya [6]. Minimum genetic diversity was found in Udegeis and Nivkhs (0.860 and 0.849, respectively), while maximum diversity was observed in Mansi, Tuvinians, and Yakuts (0.972, 0.972, and 0.964, respectively). These differences are probably explained by different demographic histories, specifically, in the gene flow between the neighboring demes [19]. Minimum  $\theta_s$  values were observed in the populations of Nganasans, Tofalars, Udegeis, Nivkhs, and Chaun Chukchi, while maximum values were detected in Tuvinians and Yakuts. Yukaghirs were characterized by intermediate values of this index. It should be noted in this respect that the  $\theta_s$  index depends on the cumulative effect of many factors, including effective population size, drift, selection, and the sample size [20].

Interpopulation comparison of the mean numbers of pairwise nucleotide differences showed that Tofalars were distinguished from the other populations examined by a rather high value of this parameter ( $\pi = 6.598$ ). This may result from the high frequency of one from 11 haplotypes (21%), while the frequencies of the remaining ten haplotypes varied in the range from 4.5 to 15% [19].

### *Evaluation of the Degree of Similarity and Differences*

Differentiations of Siberian populations was evaluated using neighbor-joining method [12]. Figure 2 shows that Siberian populations clustered with no respect to their language affiliation. At least one of the two clusters was composed of the populations belonging to the Altai or Uralic language family. As it was expected based on recent historic events, Forest and Tundra Yukaghirs formed one cluster with Nganasans and Evenks. In the second cluster, special attention is attracted by the pairwise similarities of the geographically close neighbors, Koryaks and Itel'mens, Chuvans and Chaun Chukchi, and Ulchi and Nivkhs.

### *The Role of Natural Selection in Human Colonization of the Arctic and Subarctic*

In recent studies, there is an increasing discussion on the possible role of adaptive selection in shaping the mtDNA gene pool of the populations of modern humans, as they moved northwards [21–26]. It is suggested that some mutations in the mtDNA molecule provide uncoupling of oxidative phosphorylation, thereby increasing generation of heat and imparting selective advantages to one haplotypes at the expense of the others. Finally, the carriers of a small number of mtDNA variants become important for human adaptation to cold stress and further expansion.

The role of natural selection in shaping the mtDNA gene pool of Yukaghirs was evaluated using the tests of Tajima and Fu (table). It was demonstrated that the  $D$  values favoring the influence of negative selection were

## Estimates of mtDNA diversity in Yukaghirs and other indigenous populations of Siberia

Population	<i>n</i>	<i>GD</i> (SD)	<i>k</i>	<i>S</i>	$\theta_S$ (SD)	$\pi$ (SD)	Tajima's <i>D</i>	Fu's <i>F<sub>S</sub></i>
Yukaghirs	155	0.920 (0.015)	37	43	7.646 (2.043)	5.180 (2.791)	-0.969	-12.993*
Tundra	82	0.873 (0.027)	23	32	6.413 (1.933)	4.147 (2.309)	-1.106	-6.513*
Forest	18	0.936 (0.032)	11	25	7.153 (2.776)	5.918 (3.303)	-0.676	-1.341
Chuvans	32	0.915 (0.026)	14	22	5.463 (1.983)	5.694 (3.116)	0.147	-1.588
Yukaghirs/Evens	23	0.913 (0.039)	13	28	7.498 (2.756)	6.246 (3.426)	-0.626	-1.711
Nganasans	39	0.891 (0.023)	12	22	5.204 (1.838)	4.534 (2.532)	-0.432	-0.545
Vadeyev	17	0.853 (0.047)	6	12	3.550 (1.567)	3.912 (2.309)	0.383	1.339
Avam	22	0.887 (0.043)	10	20	5.486 (2.139)	4.810 (2.724)	-0.459	-0.662
Mansi	98	0.972 (0.006)	44	59	11.441 (3.110)	6.261 (3.320)	-1.457	-24.028**
Tubalars	72	0.942 (0.011)	25	54	11.141 (3.195)	6.081 (3.246)	-1.504	-5.317
Tuvinians	96	0.972 (0.008)	51	64	12.266 (3.320)	5.871 (3.134)	-1.698*	-25.231**
Tofalars	46	0.899 (0.020)	11	30	6.826 (2.246)	6.598 (3.524)	-0.112	2.277
Yakuts	178	0.964 (0.006)	65	67	11.640 (2.883)	6.329 (3.337)	-1.398	-24.859**
Buryats	25	0.940 (0.026)	14	33	8.740 (3.131)	5.727 (3.162)	-1.298	-2.747
Ulchis	87	0.920 (0.023)	36	38	7.544 (2.202)	5.801 (3.104)	-0.730	-16.351**
Evens	64	0.952 (0.013)	28	37	7.825 (2.388)	6.138 (3.279)	-0.706	-9.159*
Evenks	71	0.948 (0.011)	29	37	7.656 (2.304)	4.963 (2.708)	-1.137	-12.262**
Negidals	33	0.898 (0.030)	13	26	6.406 (2.258)	6.371 (3.445)	-0.019	-0.329
Udegeis	46	0.860 (0.032)	12	22	5.006 (1.730)	3.991 (2.257)	-0.662	-0.638
Itel'mens	46	0.921 (0.022)	17	22	5.006 (1.730)	4.338 (2.426)	-0.436	-3.812*
Koryaks	147	0.922 (0.011)	36	39	7.009 (1.914)	5.587 (2.987)	-0.608	-11.094*
Chaun Chukchi	40	0.937 (0.017)	17	21	4.937 (1.752)	5.903 (3.197)	0.650	-2.600
Nivkhs	56	0.849 (0.028)	14	20	4.354 (1.496)	4.455 (2.472)	0.072	-0.868
Kets	38	0.882 (0.029)	13	31	7.378 (2.486)	6.694 (3.587)	-0.323	0.363

Note: *GD*, gene diversity; *k*, number of haplotypes; *S*, number of segregating sites;  $\theta_S$ ,  $\theta$  estimate, based on the number segregating sites;  $\pi$ , mean number of pairwise nucleotide differences. The HVSI sequences used in comparative analysis (from np 16017 to 16390) were examined in our laboratory and elsewhere (Yukaghirs/Evens, Mazunin et al., unpublished results; Avam Nganasans [9, 27]; Mansi [28]; Kets [27]; Tubalars, Tuvinians, Tofalars, Buryats, Ulchis, Evenks, Negidals, Udegeis, and Nivkhs [19]; Chaun Chukchi [9]; Evens [29]; Itel'mens and Koryaks [30]; Yakuts [11]).

\**P* < 0.05.

\*\**P* < 0.01.

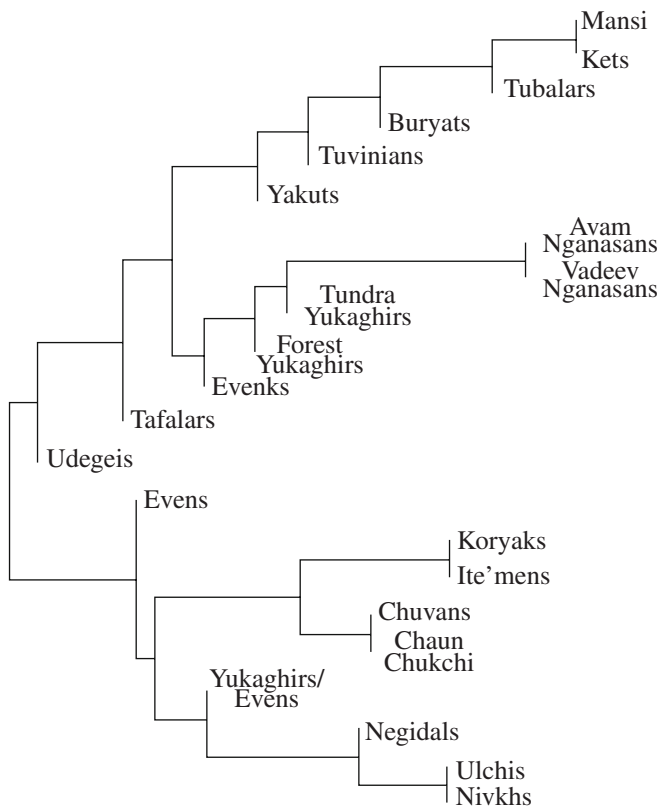


Fig. 2. Phylogenetic tree of Siberian populations constructed using the neighbor-joining technique.

typical of most of the populations. However, statistically significant  $D$  values were obtained only for Tuvinians. At the same time, in case of the application of  $F_S$  statistics, negative values were obtained for all populations, except Kets and Tofalars. Moreover, maximum  $F_S$  values were observed in Tuvinians and Yakuts, while minimum values were characteristic of Nganasans.

Statistically significant  $F_S$  values observed in Yukaghirs pointed to the effect of natural selection. However, it should be taken into consideration that negative  $F_S$  values can also reflect recent population growth. The latter event remains hypothetical, since the population of Yukaghirs rather substantially reduced in size, than increased [4].

As far as the neutrality test statistics strongly depend on population dynamics, the methods based on comparative analysis of nonsynonymous and synonymous sites variation in total mtDNA genomes [25, 26] seem to be more promising for elucidation of the role of natural selection in shaping of the mtDNA gene pool of the indigenous populations of Siberia.

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