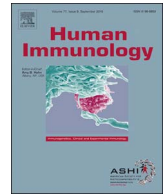




Contents lists available at ScienceDirect

Human Immunology

journal homepage: www.elsevier.com/locate/humimm

Short population report

HLA gene and haplotype frequencies in a Nagaybaks population from the Chelyabinsk Region (Russian South Urals)

T.A. Suslova^{a,b,*}, A.L. Burmistrova^a, M.N. Vavilov^{a,b}, M.S. Chernova^a, E.B. Khromova^a, S.V. Belyaeva^{a,b}, O.N. Zaripova^a, D.S. Stashkevich^{a,b}, A.S. Galkin^{c,d}, C. Darke^e

^a Chelyabinsk State University, Chelyabinsk, Russia

^b Chelyabinsk Regional Blood Transfusion Station, Chelyabinsk, Russia

^c Brain and Mind Research Institute Cornell Medical College, New York, USA

^d School of Biological Sciences, Queens University Belfast, Belfast, UK

^e Welsh Transplantation and Immunogenetics Laboratory, Welsh Blood Service, Wales, UK

ARTICLE INFO

Keywords:

Population studies
HLA
Histocompatibility
Allele frequencies
Population genetics
Nagaybaks
Chelyabinsk Region

ABSTRACT

A total of 112 Nagaybaks, a Turkic ethnoconfessional group living mainly in the Nagaybak district of the Chelyabinsk Region of Russian South Urals, were genotyped for HLA-A, -B, -DRB1, -DQA1 and -DQB1 loci using PCR-SSP (low-resolution) and HLA-A29 (high-resolution). All loci were in Hardy-Weinberg equilibrium (all p values > 0.1 thus showing no locus-level deviations). The genotype data are available in the Allele Frequencies Net Database under the population name “Russia, South Ural, Chelyabinsk Region, Nagaybaks” and the identifier AFND0003397.

1. Introduction

Nagaybaks (Nağaybäks, Nogaybaks, Nogoybaqs) are a Turkic ethnoconfessional group that is close to the Kryashen Tatars. They live mainly in the Nagaybak district of the Chelyabinsk Region. According to the latest census (National Population Census, 2010) some 7679 Nagaybaks, comprising 94.2% of all Nagaybaks in Russia, live in the Chelyabinsk Region.

There are several theories regarding Nagaybak ethnogenesis. The first states that Nagaybaks originated from the Volga region and supposedly are descendants of Nogay and Kipchak peoples, the general population of the Nogai Horde [1]. The Nogai Horde was formed in the 15th/16th Centuries after the collapse of the Golden Horde on the left bank of the lower Volga, the territory of today's Bashkortostan, Chelyabinsk and Orenburg Regions and western and central Kazakhstan. Another version of Nagaybaks' ethnogenesis suggests that ancestors of Nagaybaks came from Kazan Khanate, another state formed after the collapse of the Golden Horde. The Arsk region was a part of Kazan Khanate. A further theory states that the Nagaybaks were Tatarized Finno-Ugric peoples that kept the Kazan Khanate's borders [1].

Early historical records indicate that since ancient times and up until 1736 Nagaybaks lived separately from Bashkirs and Tatars away from Russian cities and villages in Ufa Country (today's Bashkiria).

They spoke a dialect of the Tatar language, professed orthodoxy and paid tribute to the Russian Tsar. In 1736 the Russian tsarist government built a town for them and named it the “Nagaybak's Fortress”. The inhabitants were called “Nagaybaks” and they became Cossacks under the decree of the empress.

In 1773 the Nagaybak population of the Fortress and surrounding 14 villages was about 2000. But among them there were some 200 other nationalities, including Bashkirs and others, notably Persians, Arabs, Arabians, Armenians, Afghans and Turks. Cossack-Nagaybaks, as a military caste, took part in all internal Russian conflicts and foreign campaigns of Russia since the 18th century. In 1864, according to imperial decree, the Nagaybaks were ordered to move to the territory of the modern Nagaybak's districts of the Chelyabinsk Region called Parizh, Cassel and Fershampenuaz. They moved due to changes in the borders of Russia and the establishment of fortresses and Cossack settlements on the “New Orenburg line”. Thus, the majority of Nagaybaks have lived in the Chelyabinsk Region from around 1864 to the present day.

It is clear that the Nagaybaks were in geographic and cultural isolation from their main body of close relatives, the Volga-Urals Tatars. By the beginning of the 20th century Nagaybaks had acquired traits expected of an ethnologically-independent unit and spoke a sub-dialect of the Tatar language [1].

* Corresponding author at: Biology Faculty, Chelyabinsk State University, Br. Kashirinich str, 129, Chelyabinsk 454021, Russia.
E-mail address: tatiana.suslova.hla@gmail.com (T.A. Suslova).

<http://dx.doi.org/10.1016/j.humimm.2017.08.005>

Received 4 August 2017; Received in revised form 15 August 2017; Accepted 21 August 2017

0198-8859/ © 2017 Published by Elsevier Inc. on behalf of American Society for Histocompatibility and Immunogenetics.

Table 1

Distribution of HLA-A, -B, -DRB1, -DQA1 and -DQB1 in the Nagaybaks population of the Chelyabinsk Region (n = 112).

Allele family ^a	Number positive	Carriage freq.	Gene freq.	SE of gf ^b	Hom ^c
A*01	21	0.188	0.094	0.020	0
A*02	41	0.366	0.219	0.029	8
A*03	25	0.223	0.121	0.022	2
A*11	17	0.152	0.080	0.018	1
A*23	5	0.045	0.022	0.010	0
A*24	33	0.295	0.161	0.026	3
A*25	16	0.143	0.080	0.018	2
A*26	7	0.063	0.031	0.012	0
A*29	9	0.080	0.040	0.013	0
A*30	5	0.045	0.022	0.010	0
A*31	2	0.018	0.009	0.006	0
A*32	13	0.116	0.063	0.016	1
A*33	9	0.080	0.040	0.013	0
A*68	4	0.036	0.018	0.009	0
B*07	18	0.161	0.080	0.019	0
B*08	18	0.161	0.089	0.019	2
B*13	20	0.179	0.089	0.020	0
B*14	5	0.045	0.022	0.010	0
B*15	4	0.036	0.018	0.009	0
B*18	18	0.161	0.080	0.019	0
B*27	9	0.080	0.045	0.013	1
B*35	28	0.250	0.134	0.024	2
B*37	3	0.027	0.013	0.008	0
B*38	2	0.018	0.009	0.006	0
B*39	5	0.045	0.022	0.010	0
B*40	3	0.027	0.013	0.008	0
B*41	5	0.045	0.022	0.010	0
B*44	13	0.116	0.063	0.016	1
B*45	3	0.027	0.013	0.008	0
B*46	6	0.054	0.027	0.011	0
B*48	11	0.098	0.049	0.015	0
B*49	6	0.054	0.027	0.011	0
B*50	12	0.107	0.054	0.015	0
B*51	14	0.125	0.067	0.017	1
B*52	2	0.018	0.009	0.006	0
B*54	2	0.018	0.009	0.006	0
B*56	1	0.009	0.004	0.004	0
B*57	8	0.071	0.036	0.013	0
B*58	1	0.009	0.004	0.004	0
DRB1*01	35	0.313	0.179	0.026	5
DRB1*03	21	0.188	0.103	0.020	2
DRB1*04	19	0.170	0.098	0.019	3
DRB1*07	39	0.348	0.174	0.028	0
DRB1*08	9	0.080	0.040	0.013	0
DRB1*09	10	0.089	0.049	0.014	1
DRB1*10	4	0.036	0.022	0.009	1
DRB1*11	18	0.161	0.085	0.019	1
DRB1*12	9	0.080	0.040	0.013	0
DRB1*13	20	0.179	0.094	0.020	1
DRB1*14	4	0.036	0.018	0.009	0
DRB1*15	17	0.152	0.076	0.018	0
DRB1*16	5	0.045	0.022	0.010	0
DQA1*01:01	39	0.348	0.214	0.028	9
DQA1*01:02	19	0.170	0.085	0.019	0
DQA1*01:03	16	0.143	0.076	0.018	1
DQA1*02	36	0.321	0.161	0.027	0
DQA1*03	32	0.286	0.161	0.025	4
DQA1*04	5	0.045	0.022	0.010	0
DQA1*05	55	0.491	0.281	0.033	8
DQB1*02:01	21	0.187	0.103	0.020	2
DQB1*02:02	33	0.294	0.147	0.024	0
DQB1*03:01	45	0.402	0.223	0.030	5
DQB1*03:02	12	0.107	0.063	0.016	1
DQB1*03:03	13	0.116	0.063	0.016	1
DQB1*04:02	6	0.054	0.031	0.011	1
DQB1*05:01	38	0.339	0.196	0.028	6
DQB1*05:02/04	9	0.080	0.040	0.013	0
DQB1*05:03	2	0.018	0.009	0.006	0
DQB1*06:01	8	0.071	0.036	0.012	0

Table 1 (continued)

Allele family ^a	Number positive	Carriage freq.	Gene freq.	SE of gf ^b	Hom ^c
DQB1*06:02	10	0.089	0.045	0.014	0
DQB1*06:03	8	0.071	0.040	0.013	1
DQB1*06:04	3	0.027	0.013	0.008	0

^a No examples of the allele families: A*34, A*36, A*43, A*69, A*74, A*80, B*42, B*59, B*67, B*78, B*81, B*82, B*83 were found.

^b Standard error of the gene frequency.

^c Number of likely homozygous individuals identified.

All subjects were normal, healthy unrelated blood donors, of between 18 and 55 years of age, living in the Chelyabinsk Region (South Urals, Russia). Their ethnic origin was determined by a comprehensive questionnaire. Only subjects with a Nagaybaks origin spanning at least three generations were included in the study. All 112 Nagaybaks (54 men and 58 women) were Russian language speakers and some 95% spoke the Nagaybaks language (a dialect of the Tatar language). One hundred and nine lived in the Nagaybak's districts of the Chelyabinsk Region (38 from Kassel'skij, 31 from Fershampenuaz, 19 from Parizh, 16 from Ostrolenka and 5 from Nagajbaskij) (Supplementary Fig. 1). The remaining 3 came from other cities of the Region. DNA was obtained from EDTA-anticoagulated peripheral blood using AxyPrep spin columns (AxyPrep_Blood Genomic DNA Miniprep Kit; Axygen Biosciences, Union City, CA, USA) according to the manufacturer's protocol.

HLA-A, -B, -DRB1 and -DQB1 typing was performed by PCR using sequence-specific primers (SSP). The primers and primer mixtures used were essentially those of Downing et al. [2]. HLA-DQA1 typing to the 2nd field and HLA-A*29 typing, to the 2nd field, was undertaken using commercial kits (One Lambda, Canoga Park, CA, USA) (Tables 1–5).

Population genetics analysis was performed as described by Schipper et al. [3]. The validity of Hardy–Weinberg equilibrium and homozygosity was tested for each locus. Carriage frequencies and gene frequencies were determined by direct counting and maximum likelihood, respectively. Two- and three-locus haplotype frequency (HF) estimates were calculated by maximum likelihood. The linkage disequilibrium (LD) parameter (Δ), the relative magnitude of the delta value (Δ_{rel}) and the significance of delta values for two- and three-locus haplotypes were determined as previously described [4].

HLA-A, -B and -DRB1 frequency data were used for the construction of a dendrogram using the maximum likelihood method (PHYLIP version 3.68) [5]. Thus, the Nagaybak population was compared with populations of Russians, Tatars and Bashkirs of the Chelyabinsk Region [6] and with 18 other populations [6,7,8,9,10]. The findings of the Hardy–Weinberg and homozygosity analyses for HLA-A, -B, -DRB1, -DQA1 and -DQB1 all showed an acceptable goodness-of-fit for both phenotype distribution and the number of likely homozygotes identified (all p values > 0.1). Allele family frequencies are presented in Supplementary Table 1, 2-loci HF and LD data in Supplementary Table 2, 3-loci HF and LD data in Supplementary Table 3, and 5-loci HF data in Supplementary Table 4. Supplementary Table 5 shows the findings of HLA-A*29 typing to the 2nd field. Prior to taking blood samples full informed consent for the collection and use of specimens was given by all donors. All obtained data are publicly available at Allele Frequencies Net Database AFND0003397.

A dendrogram, comparing the Nagaybak population with other populations of the Chelyabinsk Region and populations worldwide, is presented in Supplementary Fig. 2.

This study was supported by the Russian Foundation for Basic Research 15-04-05176 and by MRC Grant MR/L007339/1.

Table 2

HLA-A-B, HLA-B-DRB1, HLA-DRB1-DQB1 and HLA-DQA1-DQB1 2-locus haplotypes with significantly positive (uncorrected $p < 0.05$) Δ values in the Nagaybaks population of the Chelyabinsk Region.

Haplotype	+ / + ^a	HF ^b	SE of HF ^c	Δ -value	Δ rel	χ^2	P value	P corr ^d
A*03 – B*35	12	0.053	0.015	0.037	0.357	9.7	0.002298	ns ^e
A*01 – B*08	11	0.049	0.014	0.040	0.497	20.7	0.000057	0.002489
A*02 – B*44	10	0.048	0.014	0.035	0.710	10.4	0.001735	ns
A*25 – B*18	9	0.040	0.013	0.034	0.466	18.0	0.000121	0.005299
A*25 – B*13	7	0.030	0.011	0.023	0.323	6.7	0.009657	ns
A*29 – B*14	5	0.022	0.010	0.021	1.000	38.3	0.000002	0.000078
A*32 – B*48	5	0.022	0.010	0.019	0.417	9.0	0.0031	ns
A*30 – B*50	4	0.018	0.009	0.017	0.789	15.1	0.0003	0.013125
A*33 – B*46	3	0.013	0.008	0.012	0.479	6.9	0.008773	ns
A*29 – B*45	3	0.013	0.008	0.013	1.000	15.5	0.000262	0.011462
A*26 – B*27	3	0.013	0.008	0.012	0.402	4.9	0.025069	ns
A*23 – B*49	3	0.013	0.008	0.013	0.589	13.7	0.000485	0.02111
B*08 – DRB1*03	16	0.075	0.018	0.066	0.819	57.2	< 0.000001	0.000008
B*35 – DRB1*01	17	0.074	0.017	0.050	0.456	14.1	0.000417	0.019821
B*13 – DRB1*07	16	0.071	0.017	0.055	0.749	24.7	0.000022	0.001045
B*50 – DRB1*07	10	0.044	0.014	0.035	0.785	14.1	0.000419	0.019899
B*48 – DRB1*12	6	0.027	0.011	0.025	0.649	25.8	0.000017	0.000825
B*14 – DRB1*01	5	0.021	0.010	0.018	0.953	6.1	0.013282	ns
B*48 – DRB1*09	4	0.018	0.009	0.016	0.345	6.5	0.010511	ns
B*39 – DRB1*04	4	0.018	0.009	0.016	0.779	7.6	0.006092	ns
B*51 – DRB1*10	3	0.013	0.008	0.012	0.662	5.4	0.018915	ns
B*46 – DRB1*09	3	0.013	0.008	0.012	0.475	5.6	0.017237	ns
B*37 – DRB1*11	3	0.013	0.008	0.012	1.000	6.7	0.009341	ns
DRB1*01 – DQB1*05:01	34	0.168	0.025	0.134	0.950	84.0	< 0.000001	< 0.000001
DRB1*07 – DQB1*02:02	33	0.147	0.024	0.104	0.793	41.3	0.000001	0.000024
DRB1*03 – DQB1*02:01	21	0.099	0.020	0.074	0.975	31.9	0.000005	0.000107
DRB1*11 – DQB1*03:01	18	0.083	0.018	0.065	0.992	30.8	0.000006	0.000131
DRB1*04 – DQB1*03:02	12	0.056	0.015	0.050	0.981	51.1	< 0.000001	0.000007
DRB1*13 – DQB1*06:03/04	12	0.052	0.015	0.043	0.510	22.1	0.00004	0.000833
DRB1*09 – DQB1*03:03	10	0.046	0.014	0.044	0.980	66.2	< 0.000001	0.000001
DRB1*15 – DQB1*06:02	10	0.045	0.014	0.037	0.544	19.6	0.000077	0.001611
DRB1*12 – DQB1*03:01	9	0.040	0.013	0.031	1.000	12.2	0.000835	0.017391
DRB1*15 – DQB1*06:01	7	0.031	0.012	0.029	0.865	26.9	0.000014	0.000284
DRB1*16 – DQB1*05:02/04	5	0.022	0.010	0.022	1.000	43.4	0.000001	0.000018
DRB1*08 – DQB1*04:02	5	0.022	0.010	0.021	0.742	26.9	0.000013	0.00028
DRB1*10 – DQB1*05:01	4	0.019	0.009	0.016	0.985	4.6	0.029989	ns
DRB1*14 – DQB1*05:03	2	0.009	0.006	0.009	1.000	13.4	0.000538	0.011229
DQA1*01:01 – DQB1*05:01	38	0.193	0.026	0.151	0.998	92.3	< 0.000001	< 0.000001
DQA1*05 – DQB1*03:01	38	0.177	0.025	0.115	0.723	39.2	0.000002	0.000026
DQA1*02 – DQB1*02:02	33	0.147	0.024	0.108	0.889	47.4	0.000001	0.000009
DQA1*01:02 – DQB1*06:02/04	15	0.058	0.016	0.050	0.650	33.8	0.000004	0.000062
DQA1*03 – DQB1*03:02	12	0.056	0.015	0.047	0.999	28.7	0.000009	0.000158
DQA1*03 – DQB1*03:03	10	0.048	0.014	0.038	0.738	16.1	0.000213	0.003615
DQA1*01:03 – DQB1*06:03	8	0.039	0.013	0.032	0.463	13.5	0.000515	0.008721
DQA1*01:03 – DQB1*06:01	8	0.036	0.012	0.033	1.000	37.8	0.000002	0.000032
DQA1*01:02 – DQB1*05:02/04	7	0.027	0.011	0.024	0.727	15.6	0.000252	0.004276
DQA1*04 – DQB1*04:02	5	0.022	0.010	0.022	1.000	54.0	< 0.000001	0.000004

^a Number of subjects possessing alleles.

^b Haplotype frequency.

^c Standard error of the haplotype frequency.

^d Corrected p-values.

^e ns = non-significant – $p > 0.05$.

Table 3

Twenty most frequent HLA-A-B-DRB1 and DRB1-DQA1-DQB1 three-locus haplotypes with significantly positive (uncorrected $p < 0.05$) Δ values in the Nagaybaks population of the Chelyabinsk Region.

Haplotype	+ / + / + ^a	HF	SE of HF ^b	Δ -value	Δ rel	χ^2	P value	P corr ^c
A*03 – B*35 – DRB1*01	11	0.049	0.014	0.046	0.397	154.8	< 0.000001	< 0.000001
A*01 – B*08 – DRB1*03	10	0.044	0.014	0.043	0.471	453.9	< 0.000001	< 0.000001
A*25 – – B*13 – DRB1*07	7	0.031	0.012	0.030	0.385	143.8	< 0.000001	< 0.000001
A*02 – B*44 – DRB1*01	5	0.025	0.011	0.023	0.379	49.5	< 0.000001	0.000019
A*24 – B*35 – DRB1*13	5	0.022	0.010	0.020	0.223	42.1	0.000001	0.00005
A*30 – B*50 – DRB1*07	4	0.018	0.009	0.018	0.798	364.3	< 0.000001	< 0.000001
A*24 – B*48 – DRB1*12	4	0.018	0.009	0.018	0.440	240.0	< 0.000001	< 0.000001
A*02 – B*44 – DRB1*07	6	0.018	0.009	0.015	0.250	21.8	0.000044	0.002133
A*29 – B*14 – DRB1*01	5	0.018	0.009	0.017	0.785	431.8	< 0.000001	< 0.000001
A*25 – B*18 – DRB1*13	4	0.017	0.009	0.016	0.213	104.4	< 0.000001	< 0.000001
A*03 – B*08 – DRB1*03	4	0.014	0.008	0.013	0.137	32.1	0.000005	0.000241
A*11 – B*27 – DRB1*01	4	0.013	0.008	0.013	0.290	58.6	< 0.000001	0.000007
A*32 – B*48 – DRB1*09	3	0.013	0.008	0.013	0.296	324.8	< 0.000001	< 0.000001
A*25 – B*18 – DRB1*15	3	0.013	0.008	0.013	0.171	81.6	< 0.000001	0.000001
A*24 – B*39 – DRB1*04	3	0.013	0.008	0.013	0.509	96.5	< 0.000001	< 0.000001
A*02 – B*07 – DRB1*11	4	0.013	0.008	0.012	0.144	19.4	0.000082	0.004004
A*02 – B*51 – DRB1*12	3	0.013	0.008	0.013	0.323	62.5	< 0.000001	0.000005
A*02 – B*13 – DRB1*07	10	0.013	0.008	0.009	0.096	5.1	0.022655	ns
A*01 – B*35 – DRB1*01	5	0.012	0.008	0.010	0.100	8.3	0.004387	ns
A*03 – B*07 – DRB1*15	3	0.011	0.008	0.011	0.148	34.7	0.000003	0.000154
DRB1*01 – DQA1*01:01 – DQB1*05:01	34	0.171	0.025	0.163	0.886	749.3	< 0.000001	< 0.000001
DRB1*07 – DQA1*02 – DQB1*02:02	33	0.147	0.024	0.140	0.913	637.4	< 0.000001	< 0.000001
DRB1*03 – DQA1*05 – DQB1*02:01	21	0.100	0.020	0.092	0.853	234.5	< 0.000001	< 0.000001
DRB1*11 – DQA1*05 – DQB1*03:01	18	0.070	0.017	0.066	0.980	219.0	< 0.000001	< 0.000001
DRB1*04 – DQA1*03 – DQB1*03:02	12	0.056	0.015	0.055	0.997	774.4	< 0.000001	< 0.000001
DRB1*09 – DQA1*03 – DQB1*03:03	10	0.047	0.014	0.047	0.969	1027.4	< 0.000001	< 0.000001
DRB1*15 – DQA1*01:02 – DQB1*06:02	10	0.045	0.014	0.044	0.585	694.0	< 0.000001	< 0.000001
DRB1*13 – DQA1*05 – DQB1*03:01	10	0.040	0.013	0.034	0.388	45.1	0.000001	0.000015
DRB1*12 – DQA1*05 – DQB1*03:01	9	0.040	0.013	0.037	1.000	126.0	< 0.000001	< 0.000001
DRB1*13 – DQA1*01:03 – DQB1*06:03	8	0.039	0.013	0.038	0.509	472.2	< 0.000001	< 0.000001
DRB1*15 – DQA1*01:03 – DQB1*06:01	7	0.031	0.012	0.031	0.874	1049.5	< 0.000001	< 0.000001
DRB1*04 – DQA1*03 – DQB1*03:01	8	0.031	0.012	0.027	0.289	48.1	< 0.000001	0.00001
DRB1*08 – DQA1*04 – DQB1*04:02	5	0.022	0.010	0.022	1.000	4344.6	< 0.000001	< 0.000001
DRB1*16 – DQA1*01:02 – DQB1*05:02/04	5	0.022	0.010	0.022	1.000	1640.5	< 0.000001	< 0.000001
DRB1*10 – DQA1*01:01 – DQB1*05:01	4	0.021	0.010	0.020	0.971	101.3	< 0.000001	< 0.000001
DRB1*07 – DQA1*02 – DQB1*03:03	5	0.013	0.006	0.012	0.198	18.8	0.000096	0.002112
DRB1*13 – DQA1*01:02 – DQB1*06:04	3	0.013	0.006	0.012	0.151	48.0	< 0.000001	0.000011
DRB1*08 – DQA1*05 – DQB1*03:01	4	0.013	0.008	0.010	0.276	8.9	0.003322	ns
DRB1*07 – DQA1*03 – DQB1*03:01	3	0.013	0.007	0.007	0.042	1.5	0.211943	ns
DRB1*01 – DQA1*01:02 – DQB1*05:02/04	2	0.009	0.007	0.007	0.219	9.0	0.003202	ns
DRB1*04 – DQA1*03 – DQB1*04:02	2	0.006	0.006	0.006	0.208	16.7	0.000180	0.003961

ns – not significant (p -value > 0.05).

^a Number of subjects possessing alleles.

^b Standard error of the haplotype frequency.

^c Corrected p -values.

Table 4

The HLA-A-B-DRB1-DQA1-DQB1 five-locus haplotypes in the Nagaybaks population of the Chelyabinsk Region.

Number	Haplotype	Haplotype frequency (%)
1	A*03-B*35-DRB1*01-DQA1*01:01-DQB1*05:01	4.88
2	A*01-B*08-DRB1*03-DQA1*05-DQB1*02:01	4.43
3	A*25-B*13-DRB1*07-DQA1*02-DQB1*02:02	3.12
4	A*02-B*44-DRB1*01-DQA1*01:01-DQB1*05:01	2.54
5	A*24-B*35-DRB1*13-DQA1*05-DQB1*03:01	1.79
6	A*24-B*48-DRB1*12-DQA1*05-DQB1*03:01	1.79
7	A*30-B*50-DRB1*07-DQA1*02-DQB1*02:02	1.79
8	A*29:10-B*14-DRB1*01-DQA1*01:01-DQB1*05:01	1.76
9	A*03-B*08-DRB1*03-DQA1*05-DQB1*02:01	1.37
10	A*02-B*07-DRB1*11-DQA1*05-DQB1*03:01	1.34
11	A*02-B*50-DRB1*07-DQA1*02-DQB1*02:02	1.34
12	A*02-B*51-DRB1*12-DQA1*05-DQB1*03:01	1.34
13	A*11-B*27-DRB1*01-DQA1*01:01-DQB1*05:01	1.34
14	A*24-B*13-DRB1*07-DQA1*02-DQB1*02:02	1.34
15	A*24-B*39-DRB1*04-DQA1*03-DQB1*03:02	1.34
16	A*25-B*18-DRB1*13-DQA1*01:03-DQB1*06:03	1.34
17	A*25-B*18-DRB1*15-DQA1*01:02-DQB1*06:02	1.34
18	A*32-B*48-DRB1*09-DQA1*03-DQB1*03:03	1.34
19	A*02-B*13-DRB1*07-DQA1*03-DQB1*03:01	1.31
20	A*01-B*35-DRB1*01-DQA1*01:01-DQB1*05:01	1.22
21	A*03-B*07-DRB1*15-DQA1*01:02-DQB1*06:02	1.19
22	A*02-B*57-DRB1*15-DQA1*01:03-DQB1*06:01	0.91
23	A*01-B*37-DRB1*11-DQA1*05-DQB1*03:01	0.89
24	A*02-B*18-DRB1*11-DQA1*05-DQB1*03:01	0.89
25	A*02-B*18-DRB1*16-DQA1*01:02-DQB1*05:02	0.89
26	A*02-B*35-DRB1*01-DQA1*01:01-DQB1*05:01	0.89
27	A*02-B*35-DRB1*13-DQA1*05-DQB1*03:01	0.89
28	A*02-B*41-DRB1*13-DQA1*05-DQB1*03:01	0.89
29	A*02-B*44-DRB1*07-DQA1*02-DQB1*02:02	0.89
30	A*03-B*07-DRB1*13-DQA1*01:03-DQB1*06:03	0.89
31	A*03-B*18-DRB1*11-DQA1*05-DQB1*03:01	0.89
32	A*11-B*13-DRB1*15-DQA1*01:02-DQB1*06:02	0.89
33	A*11-B*27-DRB1*07-DQA1*02-DQB1*02:02	0.89
34	A*23-B*49-DRB1*11-DQA1*05-DQB1*03:01	0.89
35	A*24-B*35-DRB1*08-DQA1*04-DQB1*04	0.89
36	A*24-B*57-DRB1*07-DQA1*02-DQB1*03:03	0.89
37	A*26-B*27-DRB1*01-DQA1*01:01-DQB1*05:01	0.89
38	A*29:02-B*45-DRB1*08-DQA1*05-DQB1*03:01	0.89
39	A*29:02-B*46-DRB1*09-DQA1*03-DQB1*03:03	0.89
40	A*32-B*07-DRB1*04-DQA1*03-DQB1*03:01	0.89
41	A*32-B*08-DRB1*03-DQA1*05-DQB1*02:01	0.89
42	A*32-B*39-DRB1*08-DQA1*04-DQB1*04	0.89
43	A*32-B*48-DRB1*12-DQA1*05-DQB1*03:01	0.89
44	A*68-B*51-DRB1*10-DQA1*01:01-DQB1*05:01	0.89
45	A*02-B*07-DRB1*07-DQA1*02-DQB1*02:02	0.86
46	A*02-B*51-DRB1*13-DQA1*01:03-DQB1*06:03	0.86
47	A*26-B*49-DRB1*01-DQA1*01:02-DQB1*05:04	0.86
48	A*02-B*35-DRB1*04-DQA1*03-DQB1*04	0.78
49	A*24-B*15-DRB1*04-DQA1*03-DQB1*03:02	0.78
50	A*01-B*08-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
51	A*01-B*38-DRB1*03-DQA1*05-DQB1*02:01	0.44
52	A*01-B*40-DRB1*15-DQA1*01:03-DQB1*06:01	0.44
53	A*01-B*41-DRB1*13-DQA1*05-DQB1*03:01	0.44
54	A*01-B*57-DRB1*07-DQA1*02-DQB1*02:02	0.44
55	A*02-B*07-DRB1*15-DQA1*01:02-DQB1*06:02	0.44
56	A*02-B*13-DRB1*07-DQA1*02-DQB1*02:02	0.44
57	A*02-B*13-DRB1*10-DQA1*01:01-DQB1*05:01	0.44
58	A*02-B*18-DRB1*04-DQA1*03-DQB1*03:02	0.44
59	A*02-B*18-DRB1*16-DQA1*01:02-DQB1*05:04	0.44
60	A*02-B*40-DRB1*04-DQA1*03-DQB1*03:02	0.44
61	A*02-B*41-DRB1*04-DQA1*03-DQB1*03:02	0.44
62	A*02-B*44-DRB1*03-DQA1*05-DQB1*02:01	0.44
63	A*02-B*44-DRB1*11-DQA1*05-DQB1*03:01	0.44
64	A*02-B*44-DRB1*16-DQA1*01:02-DQB1*05:02	0.44
65	A*02-B*46-DRB1*08-DQA1*01:03-DQB1*06:01	0.44
66	A*02-B*46-DRB1*09-DQA1*03-DQB1*03:03	0.44
67	A*02-B*48-DRB1*09-DQA1*03-DQB1*03:03	0.44
68	A*02-B*51-DRB1*09-DQA1*03-DQB1*03:03	0.44
69	A*03-B*07-DRB1*07-DQA1*02-DQB1*02:02	0.44
70	A*03-B*18-DRB1*15-DQA1*01:02-DQB1*06:02	0.44
71	A*03-B*27-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
72	A*03-B*27-DRB1*09-DQA1*03-DQB1*03:03	0.44
73	A*03-B*35-DRB1*08-DQA1*04-DQB1*04	0.44
74	A*03-B*51-DRB1*04-DQA1*03-DQB1*03:01	0.44

(continued on next page)

Table 4 (continued)

Number	Haplotype	Haplotype frequency (%)
75	A*03-B*51-DRB1*11-DQA1*05-DQB1*03:01	0.44
76	A*03-B*51-DRB1*14-DQA1*01:01-DQB1*05:03	0.44
77	A*11-B*07-DRB1*04-DQA1*03-DQB1*03:01	0.44
78	A*11-B*08-DRB1*03-DQA1*05-DQB1*02:01	0.44
79	A*11-B*08-DRB1*11-DQA1*05-DQB1*03:01	0.44
80	A*11-B*08-DRB1*13-DQA1*01:02-DQB1*06:04	0.44
81	A*11-B*13-DRB1*07-DQA1*02-DQB1*02:02	0.44
82	A*11-B*13-DRB1*09-DQA1*03-DQB1*03:03	0.44
83	A*11-B*35-DRB1*07-DQA1*02-DQB1*03:03	0.44
84	A*11-B*51-DRB1*04-DQA1*03-DQB1*03:02	0.44
85	A*11-B*51-DRB1*11-DQA1*05-DQB1*03:01	0.44
86	A*11-B*52-DRB1*15-DQA1*01:03-DQB1*06:01	0.44
87	A*11-B*57-DRB1*15-DQA1*01:03-DQB1*06:01	0.44
88	A*23-B*49-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
89	A*23-B*50-DRB1*07-DQA1*02-DQB1*02:02	0.44
90	A*23-B*51-DRB1*10-DQA1*01:01-DQB1*05:01	0.44
91	A*24-B*07-DRB1*07-DQA1*02-DQB1*02:02	0.44
92	A*24-B*07-DRB1*15-DQA1*01:02-DQB1*06:02	0.44
93	A*24-B*15-DRB1*10-DQA1*01:01-DQB1*05:01	0.44
94	A*24-B*27-DRB1*09-DQA1*03-DQB1*03:03	0.44
95	A*24-B*35-DRB1*13-DQA1*01:03-DQB1*06:03	0.44
96	A*24-B*40-DRB1*11-DQA1*05-DQB1*03:01	0.44
97	A*24-B*48-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
98	A*24-B*50-DRB1*04-DQA1*03-DQB1*03:01	0.44
99	A*24-B*50-DRB1*07-DQA1*02-DQB1*02:02	0.44
100	A*24-B*54-DRB1*04-DQA1*03-DQB1*03:02	0.44
101	A*24-B*56-DRB1*07-DQA1*02-DQB1*02:02	0.44
102	A*24-B*57-DRB1*04-DQA1*03-DQB1*03:02	0.44
103	A*24-B*57-DRB1*15-DQA1*01:03-DQB1*06:01	0.44
104	A*24-B*58-DRB1*03-DQA1*05-DQB1*02:01	0.44
105	A*25-B*07-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
106	A*25-B*15-DRB1*13-DQA1*01:02-DQB1*06:04	0.44
107	A*25-B*18-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
108	A*25-B*18-DRB1*03-DQA1*05-DQB1*02:01	0.44
109	A*25-B*18-DRB1*04-DQA1*03-DQB1*03:02	0.44
110	A*26-B*08-DRB1*03-DQA1*05-DQB1*02:01	0.44
111	A*26-B*27-DRB1*13-DQA1*01:03-DQB1*06:03	0.44
112	A*26-B*44-DRB1*16-DQA1*01:02-DQB1*05:02	0.44
113	A*29:02-B*45-DRB1*09-DQA1*03-DQB1*03:03	0.44
114	A*30-B*49-DRB1*13-DQA1*01:02-DQB1*06:04	0.44
115	A*31-B*51-DRB1*11-DQA1*05-DQB1*03:01	0.44
116	A*31-B*52-DRB1*15-DQA1*01:03-DQB1*06:01	0.44
117	A*32-B*35-DRB1*14-DQA1*01:01-DQB1*05:02	0.44
118	A*32-B*44-DRB1*04-DQA1*03-DQB1*03:01	0.44
119	A*32-B*50-DRB1*04-DQA1*03-DQB1*03:01	0.44
120	A*33-B*07-DRB1*01-DQA1*01:01-DQB1*05:01	0.44
121	A*33-B*37-DRB1*11-DQA1*05-DQB1*03:01	0.44
122	A*33-B*38-DRB1*07-DQA1*02-DQB1*02:02	0.44
123	A*33-B*46-DRB1*08-DQA1*05-DQB1*03:01	0.44
124	A*33-B*46-DRB1*14-DQA1*01:01-DQB1*05:02	0.44
125	A*33-B*46-DRB1*14-DQA1*01:01-DQB1*05:03	0.44
126	A*33-B*50-DRB1*07-DQA1*02-DQB1*02:02	0.44
127	A*33-B*51-DRB1*13-DQA1*01:03-DQB1*06:03	0.44
128	A*33-B*54-DRB1*04-DQA1*03-DQB1*03:02	0.44
129	A*68-B*35-DRB1*03-DQA1*05-DQB1*02:01	0.44
130	A*68-B*44-DRB1*03-DQA1*05-DQB1*02:01	0.44

Table 5
HLA-A*29 alleles and A*29-bearing haplotypes in four populations from the Chelyabinsk Region.

Population (n)	A*29 allele	Number found	% carriage freq.	Allele freq.	A*29-bearing haplotypes	+ / + / + ^a	HF	SE of HF ^b	Δ -value	Δ_{rel}	χ^2	P value	P corr ^c
Nagaybaks (112)	A*29:02	4	3.571	0.018	A*29:02-B*45-DRB1*08	2	0.009	0.006	0.009	0.666	766.1	< 0.00001	< 0.00001
					A*29:02-B*46-DRB1*09	2	0.009	0.006	0.009	0.395	386.0	< 0.00001	< 0.00001
	A*29:10	5	4.464	0.022	A*29:10-B*14-DRB1*01	5	0.017	0.009	0.017	0.783	401.1	< 0.00001	< 0.00001
Russians (207) ^d	A*29:02	4	1.932	0.010	A*29:02-B*44-DRB1*07	3	0.002	0.005	0.002	0.381	332.6	< 0.00001	< 0.00001
Tatars (1 3 5) ^d	A*29:01	2	1.482	0.007	A*29:01-B*07-DRB1*04	2	0.007	0.005	0.007	1.000	205.5	< 0.00001	< 0.00001
Bashkirs (146) ^d	None												

^a Number of subjects possessing alleles.

^b Standard error of the haplotype frequency.

^c Corrected p-values.

^d Suslova et al. [6].

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.humimm.2017.08.005>.

References

- [1] I.R. Atnagulov, Material culture and subsistence Verkhneursalsk, Cossack, Nagaybaks, second half of XIX - early XX centuries (PhD thesis), Institute of Archaeology and Ethnography of the Siberian Branch of the Russian Academy of Sciences, Novosibirsk, 2002.
- [2] J. Downing, M.G. Guttridge, J. Thompson, C. Darke, Five-locus HLA typing of hematopoietic stem cell donor volunteers using PCR sequence specific primers, *Genet. Testing*. 8 (2004) 301–312.
- [3] R.F. Schipper, J. D'Amato, J.T. Bakker, J. Bakker, J.J. van Rood, M. Oudshoorn, HLA gene haplotype frequencies in bone marrow donors worldwide registries, *Hum. Immunol.* 52 (1997) 54–71.
- [4] C. Darke, M.G. Guttridge, J. Thompson, S. McNamara, J. Street, M. Thomas, HLA class I (A, B) and II (DR, DQ) gene and haplotype frequencies in blood donors from Wales, *Exp. Clin. Immunogenet.* 15 (1998) 69–83.
- [5] J. Felsenstein, PHYLIP (Phylogeny Inference Package). Version 3.68. Distributed by the author. Department of Genome Sciences, University of Washington, Seattle, WA. Available from: <http://evolution.gs.washington.edu/phylip> 2008 (accessed 08.06.2017).
- [6] T.A. Suslova, A.L. Burmistrova, M.S. Chernova, E.B. Khromova, E.I. Lupal, S.V. Timofeeva, et al., HLA gene and haplotype frequencies in Russians, Bashkirs and Tatars, living in the Chelyabinsk Region (Russian South Urals), *Int. J. Immunogenet.* 39 (2012) 394–408.
- [7] F.F. Gonzalez-Galarza, L.Y. Takeshita, E.J. Santos, F. Kempson, M.H. Maia, A.L. da Silva, et al., Allelefrequency net 2015 update: new features for HLA epitopes, KIR and disease and HLA adverse drug reaction associations, *Nucleic Acids Res.* 43 (2015) D784–8, <http://dx.doi.org/10.1093/nar/gku1166>.
- [8] M.H. Park, H.S. Kim, S.J. Kang, HLA-A,-B,-DRB1 allele and haplotype frequencies in 510 Koreans, *Tissue Antigens* 53 (1999) 386–390.
- [9] A. Wennerström, E. Vlachopoulou, L.E. Lahtela, R. Paakkanen, K.T. Eronen, M. Seppänen, M.L. Lokki, Diversity of extended HLA-DRB1 haplotypes in the Finnish population, *PLoS One*. 8 (2013) e79690.
- [10] A. Johansson, M. Ingman, S.J. Mack, H. Erlich, U. Gyllensten, Genetic origin of the Swedish Sami inferred from HLA class I and class II allele frequencies, *Eur. J. Hum. Genet.* 16 (2008) 1341–1349.