

STUDIES ON THE HUMAN IMMUNOGLOBULIN ALLOTYPES IN FIVE POPULATIONS IN THE USSR

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Summary Serum samples obtained from a total of 664 individuals representing five populations (Koryaks, Northern Buriats, Southern Buriats, Mongols and Uralians) in the USSR were tested for G1m(a,z,x and f) and G3m(b0,b1,b3,b4,b5,s,t,g and u), and Km(l) allotypes. According to Gm patterns, the first four of these populations are characterized by the presence of four haplotypes, namely Gm a,z;g,u, Gm a,z,x;g,u, Gm a,z;b0,b3,b5,s,t and Gm a,f;b0,b1,b3,b4,b5,u which are characteristic of Mongoloid populations, whereas the Uralian population is characterized by three haplotypes, Gm a,z;g,u, Gm a,z,x;g,u, and Gm f;b0,b1,b3,b4,b5,u which are common to Caucasoids as well as the Gm a,z;b0,b3,b5,s,t haplotype typical of northern Mongoloid populations. Results obtained from the four Mongoloid populations in Siberia indicate clear genocline, extending from Kamchatka to Mongol in which the haplotype frequency of Gm a,z;g,u changes from 0.714 to 0.431 and that of the Gm a,f;b0,b1,b3,b4,b5,u haplotype from 0.031 to 0.231. On the other hand, the Gm a,z;b0,b3,b5,s,t haplotype is found in the highest incidence (0.307) among Buriats from north Baikal, a population considered to have the most prominent Mongoloid characters, and indicates a cline from the Baikal to east and to south. In contrast to the Gm system, no significant regional differences in the frequencies of the Km¹ allele were observed among these different populations.

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INTRODUCTION

Inherited structural differences in human immunoglobulins are referred to as allotypes, genetic markers or allotypic markers. So far, genetic markers have been found for the IgG heavy (H) chain (Gm markers), the IgA H chain (Am markers), the IgE H chain (Em marker) recently described by van Loghem *et al.* (1984), and the kappa type light (L) chain (Km markers, formerly called Inv) common to all classes of immunoglobulin.

The first allotype of the H chain of human immunoglobulin was detected in 1956 by Grubb and Laurell. Since then more than 20 allotypes have been described that occur on the H chains of three of the four IgG subclasses, (IgG1, IgG2, and IgG3). The Gm system provides genetic markers which are unique in studies of human genetics, particularly in the characterization of different populations and in studies of genetic drift and gene flow determined by the presence of either a unique haplotype in a particular race or by differences in the frequencies of the same haplotypes in a given ethnic group.

This study of Siberian populations in the USSR forms part of an extensive survey aimed at investigating the distribution of Gm and Km alleles among Mongoloid populations from Southeast Asia through East Asia into South America and results from a collaboration between Japanese and Soviet scientists, and was supported by the Soviet Academy of Sciences in September 1983. Here we report the distributions of Gm and Km allotypes and haplotypes in five distinct populations from Ural and Siberia in the Soviet Union.

MATERIALS AND METHODS

Serum samples from a total of 664 unrelated individuals from five distinct populations in the USSR (65 Koryaks from Kamchatka, 137 from Buriats in north Baikal, Buratskaja, ASSR, 81 from Buriats in south Baikal, Buratskaja, ASSR, 64 from Mongols in Mongolia, ASSR and 317 from Uralian group, Ural, USSR) were tested for G1m(a,z,x and f), G3m(b0,b1,b3,b4,b5,s,t,g,u and c3), and Km(l) allotypes. The reagents used for these tests as well as the numerical and alphabetical nomenclature used are presented in Table 1. The tests were carried out using previously described methods (Matsumoto and Takatsuki, 1968).

RESULTS AND DISCUSSION

Data of Gm phenotypes in five distinct Soviet populations are presented in Table 2, and estimated frequencies of Gm haplotypes are presented in Table 3. Haplotype frequencies and degree of fit with the Hardy-Weinberg distribution were determined using the computer program MAXIM (Kurczynski and Steinberg, 1967).

Of the Gm markers tested, only G1m(a,z,x,f) and G3m(b0,b1,b3,b4,b5,s,t,g,u)

Table 1. Human gammaglobulin allotypes (Gm and Km) used in these studies.

Nomenclature (W.H.O.)		Anti-allotype	Anti-Rh ₀	
Alphabetical ^a	Numerical			
G1m	a	1	3552	2880
	x	2	2984	2880
	f	3	2871	3097
	z	17	3272	2880
G3m	b ¹	5	7514	3656
	b ⁰	11	0058	3656
	b ³	13	4721	3656
	b ⁴	14	0663	3656
	b ⁵	10	1340	3656
	g	21	1642	3359
	s	15	2624	3068
	t	16	0197	3068
	u	26	1369	2127
	c ³	6	2781	2646
	Km	l	1	5872

^a Alphabetical nomenclature is used in this paper.

Table 2. Gm phenotype frequencies among five Soviet populations.

Phenotype	Koryaks (Kamchatka)		Buriats (North Baikal)		Buriats (South Baikal)		Mongols (Mongolia, ASSR)		Uralian (Ural, USSR)	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
a,z,g,u	33	33.2	30	30.7	20	19.6	13	11.3	30	24.5
a,z,b ⁰ ,b ³ ,b ⁵ ,s,t,g,u	22	18.6	41	39.7	18	21.7	9	12.1	2	5.0
a,z,x,g,u	4	5.3	23	24.6	11	11.2	4	6.0	14	17.3
a,z,f,b ⁰ ,b ¹ ,b ³ ,b ⁴ ,b ⁵ , g,u	1	2.9	9	7.6	12	8.9	14	12.5	102	107.0
a,z,x,b ⁰ ,b ³ ,b ⁵ ,s,t,g,u	0	1.4	14	13.6	6	5.5	3	2.9	3	1.5
a,z,f,b ⁰ ,b ¹ ,b ³ ,b ⁴ ,b ⁵ , s,t,u	0	0.8	3	4.9	4	4.9	8	6.7	13	10.9
a,z,b ⁰ ,b ³ ,b ⁵ ,s,t	2	2.6	13	12.9	8	6.0	4	3.2	0	0.3
a,z,x,f,b ⁰ ,b ¹ ,b ³ ,b ⁴ ,b ⁵ , g,u	3	0.2	4	2.6	2	2.2	5	3.0	35	32.7
a,f,b ⁰ ,b ¹ ,b ³ ,b ⁴ ,b ⁵ ,u	0	0.1	0	0.5	0	1.0	1	3.4	0	0.0
f,b ⁰ ,b ¹ ,b ³ ,b ⁴ ,b ⁵ ,u	0	0.0	0	0.0	0	0.0	0	0.0	117	116.7
Total	65	65.0	137	137.0	81	81.0	61	61.0	316	316.0

Table 3. Gm haplotype frequencies among five Soviet populations.

Gm haplotype	Koryaks (Kamchatka)		Buriats (North Baikal)		Buriats (South Baikal)		Mongols (Mongolia, ASSR)		Uralian (Ural, USSR)	
	Freq.	SE	Freq.	SE	Freq.	SE	Freq.	SE	Freq.	SE
a,z;g,u	.714	.039	.473	.030	.492	.039	.431	.045	.279	.018
a,z,x;g,u	.055	.020	.162	.022	.125	.026	.102	.027	.085	.011
a,z;b ⁰ ,b ³ ,b ⁵ ,s,t	.200	.035	.307	.028	.272	.035	.230	.038	.029	.006
a,f;b ⁰ ,b ¹ ,b ³ ,b ⁴ , b ⁵ ,u	.031	.015	.058	.014	.111	.025	.238	.038	.000	.000
f;b ⁰ ,b ¹ ,b ³ ,b ⁴ ,b ⁵ ,u	.000	.000	.000	.000	.000	.000	.000	.000	.608	.019
χ^2	7.132		1.469		3.663		5.493		5.842	
<i>d.f.</i>	4		4		5		5		4	
<i>P</i> ^a	0.102		0.832		0.598		0.357		0.211	

^a *P* for goodness of fit to Hardy-Weinberg distribution based on haplotype frequencies shown. SE, standard error.

were found and all samples were negative for G3m(c3) as would be predicted. Among the four Siberian populations (Koryaks from Kamchatka, Buriats in north Baikal, Buriats in south Baikal and Mongols in Mongolia), nine phenotypes were observed which are explained by the presence of four haplotypes (Gm a,z;g,u, Gm a,z,x;g,u, Gm a,z;b⁰,b³,b⁵,s,t and Gm a,f;b⁰,b¹,b³,b⁴,b⁵,u) characteristic of Mongoloid populations. On the other hand, 8 phenotypes determined by the presence of three haplotypes, (Gm a,z;g,u, Gm a,z,x;g,u, and Gm f;b⁰,b¹,b³,b⁴,b⁵,u) characteristic of Caucasoids, in addition to the Gm a,z;b⁰,b³,b⁵,s,t haplotype which occurs in northern Mongoloids (Matsumoto, 1977; Matsumoto *et al.*, 1982) were observed in the Uralian group. Agreement was obtained for all five populations between the observed and the expected frequencies on the basis of the Hardy-Weinberg equilibrium of phenotypes.

To determine if significant heterogeneity in haplotypic distributions exists among the four Siberian populations, haplotype frequencies were analysed using a contingency chi-square test according to the methods of Snedecor (Snedecor, 1956). A test for heterogeneity of each of four haplotypes in the four populations are given in Table 4. Homogeneity was found between Buriats from northern Baikal and southern Baikal ($\chi_3^2=5.79$, $p=0.12$), except for the haplotype Gm a,f;b⁰,b¹,b³,b⁴,b⁵,u ($\chi_1^2=3.94$; significant at the 5% level). The results show most highly significant heterogeneity between Koryaks and Mongols ($\chi_3^2=46.63$, $p=0.000$), notably for the Gm a,z;g,u haplotype ($\chi_1^2=20.69$, $p=0.000$) and for the Gm a,f;b⁰,b¹,b³,b⁴,b⁵,u haplotype ($\chi_1^2=23.68$, $p=0.000$). Heterogeneity can also be seen between Koryaks and Buriats from both southern and northern Baikal ($\chi_3^2=27.56$, $p=0.000$; and $\chi_3^2=36.26$, $p=0.000$, respectively), particularly with re-

Table 4. Heterogeneity in Gm haplotypic distributions among four Siberian populations.

	Buriats (South Baikal)	Buriats (North Baikal)	Koryaks (Kamchatka)	
Buriats (N. Baikal)	ag	$\chi^2_{(1)} = 0.151, p=0.697$	$\chi^2_{(1)} = 20.715, p=0.000$	
	axg	$\chi^2_{(1)} = 1.102, p=0.294$	$\chi^2_{(1)} = 9.059, p=0.002$	
	ab ³ st	$\chi^2_{(1)} = 0.600, p=0.438$	$\chi^2_{(1)} = 5.054, p=0.024$	
	afb ¹ b ³	$\chi^2_{(1)} = 3.935, p=0.047$	$\chi^2_{(1)} = 1.430, p=0.231$	
	Total	$\chi^2_{(3)} = 5.788, p=0.122$	$\chi^2_{(3)} = 36.258, p=0.000$	
Buriats (S. Baikal)	ag		$\chi^2_{(1)} = 14.692, p=0.000$	
	axg		$\chi^2_{(1)} = 4.151, p=0.041$	
	ab ³ st		$\chi^2_{(1)} = 2.029, p=0.154$	
	afb ¹ b ³		$\chi^2_{(1)} = 6.683, p=0.009$	
	Total		$\chi^2_{(3)} = 27.555, p=0.000$	
Mongols (Mongolia)	ag	$\chi^2_{(1)} = 1.054, p=0.384$	$\chi^2_{(1)} = 0.604, p=0.437$	$\chi^2_{(1)} = 20.694, p=0.000$
	axg	$\chi^2_{(1)} = 0.365, p=0.545$	$\chi^2_{(1)} = 2.480, p=0.115$	$\chi^2_{(1)} = 1.928, p=0.165$
	ab ³ st	$\chi^2_{(1)} = 0.652, p=0.419$	$\chi^2_{(1)} = 2.471, p=0.116$	$\chi^2_{(1)} = 0.325, p=0.568$
	afb ¹ b ³	$\chi^2_{(1)} = 8.076, p=0.004$	$\chi^2_{(1)} = 26.946, p=0.000$	$\chi^2_{(1)} = 23.682, p=0.000$
	Total	$\chi^2_{(3)} = 10.146, p=0.017$	$\chi^2_{(3)} = 32.502, p=0.000$	$\chi^2_{(3)} = 46.629, p=0.000$

ag = a,z;g,u, axg = a,z;x;g,u, ab³st = a,z;b⁰,b³,b⁵,s,t and afb¹b³ = a,f;b⁰,b¹,b³,b⁴,b⁵,u.

spect to the Gm a,z;g,u haplotype ($\chi_1^2 = 14.69, p=0.000$; and $\chi_1^2 = 20.72, p=0.000$, respectively), and also between Mongols and Buriats from northern Baikal ($\chi_3^2 = 32.50, p=0.000$), notably for the Gm a,f;b⁰,b¹,b³,b⁴,b⁵,u haplotype ($\chi_1^2 = 26.95, p=0.000$). The results of these significant differences observed among haplotype frequencies between the four Siberian populations confirm the anthropological observations which would indicate considerable local genetic differences among them. In general, however, the Gm patterns of the four Siberian populations are characterized by a high frequency of the Gm a,z;g,u haplotype and a very low frequency of the Gm a,f;b⁰,b¹,b³,b⁴,b⁵,u haplotype, which is similar to that observed previously in northern Mongoloids (Matsumoto, *et al.*, 1982). Furthermore, as seen in the Table 3, there is a regular increase from south to north in the frequency of the Gm a,z;g,u haplotype and a regular decrease in the frequency of the Gm a,f;b⁰,b¹,b³,b⁴,b⁵,u haplotype. In contrast to these results, the Gm a,z;b⁰,b³,b⁵,s,t haplotype was observed in the highest incidence in Buriats from northern Baikal but decreases in a gentle cline both to the north and south of this population.

On the other hand, the Uralian population is considered to be Caucasoid in origin based on a high incidence of the Gm f;b⁰,b¹,b³,b⁴,b⁵,u haplotype, but is

Table 5. Km phenotype and allele frequencies among five Soviet populations.

Population	No. Tested	Km(1)	Km ¹	
			Frequency	SE
Koryaks (Kamchatka)	65	16	0.13	0.03
Buriats (North Baikal)	137	9	0.03	0.01
Buriats (South Baikal)	81	17	0.11	0.02
Mongols (Mongolia, ASSR)	61	8	0.07	0.02
Uralian	316	46	0.08	0.01

SE, standard error.

admixed with Mongoloids in a relatively high proportion. Considering the Uralian population in terms of this Mongoloid admixture, the Gm a,f;b0,b1,b3,b4,b5,u haplotype which is considered to be a southern gene defining Mongoloid populations, was not found. The Gm a,z;b0,b3,b5,s,t haplotype, which is a marker of northern Mongoloid populations, was, however, observed at a relatively high frequency. Therefore, the Uralian population is basically Caucasoid in origin but with considerably high Mongoloid admixture.

The Km data is shown in Table 5. The Km¹ allele frequency was estimated by the square root of the Km(1—). In contrast to the significant variation observed in Gm haplotypes, the Km data does not reveal any significant variation among the five Soviet populations studied.

Four sera (3 from Mongols and 1 from Uralian) excluded from a total of 664 serum samples tested, possessed uncommon phenotypes which could not be explained by the presence of the four commonly occurring Gm haplotypes. From all sera tested, two unusual phenotypes were encountered. In Mongols, the Gm a,z,f,b0,b1,b3,b4,b5,s,t,g,u type, which is identical to the variant described in Chinese and Koreans by Schanfield *et al.* (1972a, 1972b) was observed on three occasions. In the Uralian group, the Gm (a,z,x,b0,b1,b3,b4,b5,g,u) variant identical to that reported by Schanfield *et al.* (1972a, 1972b) was found in one individual. It was not possible to define the unusual Gm haplotype which contributed to the genesis of these phenotypes, because family data were not available.

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