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DISTRIBUTION OF ABO GENOTYPES AND ALLELE FREQUENCIES IN A KOREAN POPULATION

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Summary The genotypes of the ABO blood group system were investigated in Korean living in Kangwon-Do area by PCR-RFLP analysis of the seven polymorphic nucleotide positions 261, 467, 526, 646, 703, 796 and 803 of the cDNA from A_1 transferase. In 253 unrelated Korean individuals, 15 genotypes were found and the allele frequencies of A(Pro), A(Leu), B, O(T) and O(A) were 0.022, 0.209, 0.209, 0.360 and 0.200, respectively, with no deviation from Hardy-Weinberg expectations ($\chi^2=2.145$, d.f.$=6$, $0.90<p<0.95$). As for the distribution of allele frequencies, a significant difference was noticed between the Korean and a Japanese ($\chi^2=30.87$, d.f.$=4$, $p<0.001$) and a German ($\chi^2=127.76$, d.f.$=4$, $p<0.001$) populations.

Key Words ABO blood group, genotyping, PCR-RFLP, Korean population

INTRODUCTION

Gene frequencies of the ABO blood group system has been investigated for a large number of populations with serological methods and the varying frequencies of the ABO blood types in different populations has been found (Mourant, 1983; Daniels, 1995). Since the first descriptions of Yamamoto *et al.* (1990a, b), who have cloned and sequenced a complementary DNA (cDNA) encoding the A_1 transferase and both B and O allelic cDNAs, the genetic polymorphisms for the ABO gene have been reported (Yamamoto, 1994; Clausen *et al.*, 1994).

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We studied previously the genetic polymorphisms of the ABO gene in a Japanese (Fukumori *et al.*, 1996) and a German populations (Nishimukai *et al.*, 1996) using a PCR-RFLP method for the analysis of seven nucleotide positions (nts 261, 467, 526, 646, 703, 796 and 803), and divided common A and O alleles into suballeles A(Pro), A(Leu), O(T) and O(A). The A(Leu) suballele was characterized by a nucleotide substitution C467T of the A(Pro) allele. The O(T) and O(A) suballeles have been the same with $O_{(1)}$ and $O_{(2)}$ (Yamamoto, 1994), or O^1 and $O^{1'}$ (Clausen *et al.*, 1994). Besides five nucleotide substitutions (A297G, T646A, G681A, C771T and G829A), the polymorphisms at G106T, G188A, C189T and C220T have been found (Olsson and Chester, 1996) in the O(A) (or $O^{1'}$ or $O_{(2)}$) allele. Recently, a variant O allele designated as O^2 (Grunnet *et al.*, 1994) [or $O_{(3)}$ (Yamamoto, 1994)] has been reported. The nucleotides at nts 261, 703, 796 and 803 of the O^2 allele are the same as those of A^1, whereas the nucleotide at nt 526 is the same as that of B allele.

In this study, we examined the allelic distribution of the ABO gene in a Korean population by the PCR-RFLP method as described previously (Fukumori *et al.*, 1995, 1996), and compared the ABO allele frequencies in the Korean population with those in the Japanese and German populations.

MATERIALS AND METHODS

Blood samples were collected from 253 unrelated healthy Korean donors living in Kangwon-Do area. Prior to DNA analysis, ABO phenotypes of the samples were determined by the conventional serological method. Genomic DNA was prepared from white blood cells according to the method of Ishizawa *et al.* (1991). ABO genotyping was carried out as described previously (Fukumori *et al.*, 1995, 1996). Nts 261, 467, 526, 646, 703, 796 and 803 of the ABO gene were analyzed by PCR with the primers GA16 (5′-AGAAGCTGAGTGGAGTTCCA-GGTG-3′), GA17 (5′-TGATGGCAAACACAGTTAACCC-3′), GA01N (5′-TC-CTGGAGACGGCGGAGAAGCA-3′), GA13 (5′-ACCGACCCCCCGAAGA-ACG-3′) and GA14 (5′-ACCGACCCCCCGAAGAACC-3′), and RFLP with restriction enzymes *Bst*PI, *Kpn*I, *Bss*HII, *Ban*I, *Hap*II, *Alu*I, *Mva*I and *Mbo*I.

Statistical analysis was performed by the χ^2 test or Fisher's exact probability test.

RESULTS AND DISCUSSION

ABO phenotypes were examined serologically and no rare variant phenotypes were found in the present survey. The phenotype frequencies of the samples (n=253) were 30.4% A (n=77), 26.9% B (n=68), 10.7% AB (n=27) and 32.0% O (n=81). These frequencies were similar to those reported previously (A, 34%; B, 27%; AB, 11%; and O, 28%) (Kim *et al.*, 1993).

Table 1 shows the distribution of genotypes and allele frequencies observed in the present study by using the PCR-RFLP method; 15 genotypes and 5 alleles were found in the Korean population. Two suballeles of A [A(Pro) and A(Leu)], 2 suballeles of O [O(T) and O(A)] and 1 B allele were found but neither O^2 (or $O_{(3)}$) nor other variant allele was detected. In the Korean samples, all of the B and O alleles had cytosine at nt 467 (=proline at amino acid 156), and the A and B alleles, thymine at nt 646 (=tyrosine at amino acid 216). These findings were the same as those in the Japanese samples of our previous report (Fukumori *et al.*, 1996). The observed genotype numbers did not differ significantly from those expected under the assumption of Hardy-Weinberg equilibrium ($\chi^2=2.145$, d.f.=6, $0.90<p<0.95$).

Table 2 compares the ABO allele frequencies of the Korean population with two populations from Japan (Fukumori *et al.*, 1996) and Germany (Nishimukai *et al.*, 1996). There was a statistically significant difference of allele frequency

Table 1. Distribution of ABO genotypes and allele frequencies in the Korean population.

Genotypes	Observed (n=253)		Expected
	n	(%)	n
A(Leu)/A(Leu)	11	(4.3)	11.1
A(Leu)/O(T)	36	(14.2)	38.1
A(Leu)/O(A)	21	(8.3)	21.2
B/B	11	(4.3)	11.1
B/O(T)	38	(15.0)	38.1
B/O(A)	19	(7.5)	21.2
O(T)/O(T)	34	(13.4)	32.8
O(T)/O(A)	34	(13.4)	36.4
O(A)/O(A)	13	(5.2)	10.1
A(Leu)/B	26	(10.3)	22.1
A(Pro)/A(Pro)	1		
A(Pro)/A(Leu)	1		
A(Pro)/O(T)	6 10	(4.0)	10.9
A(Pro)/O(A)	1		
A(Pro)/B	1		

Allele frequencies: $ABO^*A(Pro)=0.022$, $ABO^*A(Leu)=0.209$, $ABO^*B=0.209$, $ABO^*O(T)=0.360$, $ABO^*O(A)=0.200$ ($\chi^2=2.145$, d.f.=6, $0.90<p<0.95$).

Table 2. ABO allele frequencies in Korean, Japanese and German populations.

Population	ABO allele					
	A(Pro)	A(Leu)	B	O(T)	O(A)	O^2
Korean (n=253)	0.022[a,c]	0.209[c]	0.209[c]	0.360[a,e]	0.200[b]	0[d]
Japanese[1] (n=520)	0.071	0.216	0.178	0.273	0.262	0
German[2] (n=169)	0.213	0.077	0.047	0.426	0.216	0.021

[a] Korean *versus* Japanese, $p<0.001$. [b] Korean *versus* Japanese, $p<0.01$. [c] Korean *versus* German, $p<0.001$. [d] Korean *versus* German, $p<0.01$. [e] Korean *versus* German, $p<0.05$ (Fisher's exact probability test).

[1] Fukumori *et al.*, 1996. [2] Nishimukai *et al.*, 1996.

distribution between the Korean population and the other two populations ($p < 0.001$). The A(Pro) suballele frequency in the Korean population was significantly lower ($p < 0.001$) than that in the Japanese and German populations. The A(Leu) suballele frequency in the present survey was similar to that in the Japanese population but significantly higher ($p < 0.001$) than that in the German population. The Korean population had a significantly lower frequency ($p < 0.05$) of O(T) allele than the German population but a significantly higher frequency ($p < 0.05$) than the Japanese population. The O^2 allele is present with a polymorphic frequency ($ABO^*O^2 = 0.0207$) in the German population, and recently the allele has been reported to occur at a frequency of 3.7% in Danish (Grunnet *et al.*, 1994), 3.3% in Swedish (Olsson and Chester, 1995), 2.6% in whites, 2.0% in blacks and 0% in Amerindians (Franco *et al.*, 1995) in the population samples with O phenotype. However, the O^2 allele was not found in Koreans as well as Japanese, suggesting strongly that this allele does not exist in mongoloid populations.

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REFERENCES

Clausen H, Bennett EP, Grunnet N (1994): Molecular genetics of ABO histo-blood groups. Trans Clin Biol **2**: 79-89

Daniels G (1995): ABO, Hh, and Lewis blood group systems. In: Human blood groups. Blackwell Science Publishing, Oxford, pp 8-120

Franco RE, Simoes BP, Zago MA (1995): Relative frequencies of the two O alleles of the histo-blood ABH system in different racial groups. Vox Sang **69**: 50-52

Fukumori Y, Ohnoki S, Shibata H, Yamaguchi H, Nishimukai H (1995): Genotyping of ABO blood groups by PCR and RFLP analysis of 5 nucleotide positions. Int J Leg Med **107**: 179-182

Fukumori Y, Ohnoki S, Shibata H, Nishimukai H (1996): Suballeles of the ABO blood group system in a Japanese population. Hum Hered **46**: 85-91

Grunnet N, Steffensen R, Bennet EP, Clausen H (1994): Evaluation of histo-blood group ABO genotyping in a Danish population: frequency of a novel O allele defined as O^2. Vox Sang **67**: 210-215

Ishizawa M, Kobayashi Y, Miyamura T, Matsuura S (1991): Simple procedure of DNA isolation from human serum. Nucleic Acids Res **19**: 5792

Kim SI, Han KS, Cho HI (1993): Transfusion medicine. 1st ed. Korea Medical Publishing, Seoul, (in Korean)

Mourant AE (1983) Blood relations. Blood groups and anthoropology. Oxford University Press, Oxford

Nishimukai H, Fukumori Y, Okiura T, Yuasa I, Shinomiya T, Ohnoki S, Shibata H, Vogt U (1996): Genotyping of the ABO blood group system: analysis of nucleotide position 802 by PCR-RFLP and the distribution of ABO genotypes in a German population. Int J Leg Med **109**: 90-93

Olsson ML, Chester MA (1995): A rapid and simple ABO genotype screening method using a novel B/O^2 *versus* A/O^2 discriminating nucleotide substitution at the ABO locus. Vox Sang **69**: 242-247

Olsson ML, Chester MA (1996): Frequent occurrence of a variant O^1 gene at the blood group ABO locus. Vox Sang **70**: 26-30

Yamamoto F, Marken J, Tsuji T, White T, Clausen H, Hakomori S (1990a): Cloning and characterization of DNA complementary to human UDP-GalNAc: Fucα1→2Galα1→3GalNAc transferase (Histo-blood group A transferase) mRNA. J Biol Chem **265**: 1146–1151

Yamamoto F, Clausen H, White T, Marken J, Hakomori S (1990b): Molecular genetic basis of the histo-blood group ABO system. Nature **345**: 229–233

Yamamoto F (1994): Review: recent progress in the molecular genetic study of the histo-blood group ABO system. Immunohematology **10**: 1–7