

Molecular Genetic Studies of Korean Population. 16. Genetic Polymorphism of the Sixth Complement Component (C6)

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The phenotyping of the sixth complement component (C6) was performed on plasma or serum samples from 383 unrelated Korean, by IEF and immunoblotting using anti-human C6 serum. Three common allotypes, C6 A, C6 B and C6 B2 and two rare allotypes, C6 M1 and C6 M11 were observed. The allele frequencies of C6*A, C6*B and C6*B2 were estimated to be 0.4399, 0.5144, 0.0392, respectively. These frequencies are similar to those of the Eastasian populations.

KEY WORDS: Complement C6 allotypes, Korean, Immunoblotting

The sixth complement component (C6) is a single chain glycoprotein with a molecular weight of approximately 124,800 dalton (Podack *et al.*, 1979) and its isoelectric point is between 6.15 and 6.70. The complement C6 is one of the late acting components of complement that participate in the function of the membrane attack. The C6 gene were assigned to 5 chromosome, and functionally related genes C6, C7 and C9 were clustered in the same region (Jeremiah *et al.* 1989, HGM 10).

DiScipio and Hugli (1989) determined the entire primary structure of human complement component C6. The polypeptide chain of C6 consists of 913 amino acids and it has two oligosaccharide groups attached to asparagines located near the amino and carboxyl termini of the molecule. They described that a polymorphism may exist at amino acid position 761 because two separate protein sequence determination of C6 identified both serine and aspartic acid at this site. The poly-

morphism is controlled by codominant alleles at a single autosomal locus. Three common alleles, C6*A, C6*B and C6*B2 and rare variants, C6*A3, C6*A21, C6*B4, C6*B5, C6*B21, C6*M1, C6*M2, C6*M3, C6*M11, C6*M92 have been reported among several populations (Tokunaga *et al.*, 1984; Nishimukai *et al.*, 1985; Kühnl and Kreckel, 1980).

The present paper deals with the distribution of C6 allotypes and allele frequencies in Korean, and the frequencies were compared with those reported for other populations.

Materials and Methods

EDTA-plasma and serum samples were obtained from 383 unrelated Korean in Seoul and stored at -50°C until they are used.

The technique of isoelectricfocusing as described by Whitehouse and Putt (1983) was used with the following modification. The slab gel ($200 \times 130 \times 0.5$) was prepared, using 2.0 ml of acrylamide solution 29.1% (w/v), 2.0 ml of bisac-

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rylamide solution 0.9% (w/v), 12.1% sucrose, 0.8 ml of Ampholine pH 5-8, 0.2 ml of Ampholine pH 3.5-10.0 (LKB), 10 μ l of TEMED, 0.5 ml of ammonium persulfate 1% (w/v) and 9.8 ml of distilled water. The five μ l of each plasma sample absorbed onto pieces of filter paper (Whatman No. 1, 5 \times 5 mm) was applied to the gel 1.5 cm from the anode strip. Nitrocellulose membrane was overlaid on the gel after focusing. Then the sheet was blocked in 3% BSA-PBS overnight at 4°C. The sheet was washed by three times of changes with PBS, and it was incubated with a goat anti-human serum (Cappel) diluted 1:300 with BSA-PBS for 1 hr at 37°C. After the sheet was washed with PBS, it was incubated with a peroxidase conjugated rabbit anti-goat immunoglobulin (ATAB) diluted 1:800 with BSA-PBS for 1 hr at 37°C. After washing with PBS, the sheet was stained with a substrate solution of O-dianisidine/H₂O₂/Tris-HCl for 30 min at room temperature. In this study, the nomenclature used for C6 was followed by Mauff *et al.* (1980) and Tokunaga *et al.* (1983).

Results

Table 1 shows the results of a population study of C6 with 383 unrelated Korean. The two common allotypes are A and B and the third allotype is B2. In addition, two rare allotypes, M1 and M11

are observed. The allele frequencies for C6*A, C6*B, C6*B2 and rare variants are estimated to be 0.4399, 0.5144, 0.0392 and 0.0065, respectively. The observed and expected data are in agreement with the Hardy-Weinberg equilibrium ($\chi^2 = 3.32$, d.f. = 6, $0.75 < P < 0.90$).

The frequencies of C6 allotypes of the different populations are shown in Table 2. The C6*A and C6*B are the most common alleles. Fourteen rare alleles, *A1, *A2, *M, *M1, *M11, *M2, *M3, *M91, *M92, *B1, *B21, *B3, *B4 and *B5 in addition to two common alleles *A and *B have been observed thus far in various populations.

Discussion

The result of this study is the same as those obtained previously and also the C6*A frequency for Korean is very similar to those for other East Asian populations (Park *et al.*, 1988; Kim, 1989; Tokunaga *et al.*, 1984; Nakamura *et al.*, 1984; Zeng *et al.*, 1986).

In contrast to Caucasian data, the C6*B is more common than the C6*A in East Asian populations (Tokunaga *et al.*, 1983; Washio *et al.*, 1986; Olving *et al.*, 1979; Kühnl and Kreckel, 1980). The C6*B2 which designated as 'Nauru' by Ransford and coworker observed in third allele in East Asian, Melanesian, Polynesian and Micronesian, but has not been reported in Caucasian (Park *et*

Table 1. The distribution of C6 phenotypes and allele frequencies in a Korean population.

Phenotypes	No. observed	Percent	No. expected	Allele frequencies
A	77	20.1	74.1	C6*A = 0.4399 ± 0.179
B	101	26.4	101.3	C6*B = 0.5144 ± 0.0181
AB	171	44.6	173.3	C6*B2 = 0.0392 ± 0.0070
AB2	9	2.3	13.2	C6*R = 0.0065 ± 0.0029
BB2	19	5.0	15.4	
B2	1	0.3	0.6	
AM1	3	0.8	2.2	
BM11	2	0.5	2.6	
Others	0	0.0	0.3	
Total	383	100.0	383.0	

C6*R: *M1 + *M11, $\chi^2 = 3.32$, d.f. = 6, $0.75 < P < 0.90$.

Table 2. Comparison of C6 allele frequencies in East Asian and Caucasian populations.

Populations (place)	No. samples	C6 alleles				Authors
		C6*A	C6*B	C6*B2	Others	
Korean						
Seoul	383	0.440	0.524	0.039	0.007	(M1, M11) Present study
„	522	0.467	0.502	0.026	0.005	(M) Kim, 1989
„	490	0.433	0.523	0.039	0.005	(M2, M11, M91, M92) Park <i>et al.</i> , 1988
Japanese						
Iwate	495	0.423	0.510	0.062	0.005	(M11, M91, B4, B5) Tokunaga <i>et al.</i> , 1984
Tokyo	288	0.427	0.483	0.076	0.014	(A3, A21, M1, M2, M3, B4) Tokunaga <i>et al.</i> , 1983
Fukuigen	340	0.478	0.464	0.052	0.006	(A1, M2) Kishi <i>et al.</i> , 1988
Western	135	0.467	0.481	0.037	0.015	(B3) Nishimukai <i>et al.</i> , 1985
	565	0.432	0.503	0.060	0.005	(M) Nakamura <i>et al.</i> , 1984
Eastern	351	0.450	0.477	0.064	0.009	(M2, M11, M92, B4) Washio <i>et al.</i> , 1986
Chinese						
Beijing	155	0.416	0.532	0.042	0.010	(A21, M91, B3) Zeng <i>et al.</i> , 1986
Guangzhou	255	0.445	0.518	0.033	0.004	(B21) Zeng <i>et al.</i> , 1986
Micronesian	186	0.447	0.452	0.068	0.003	Ranford <i>et al.</i> , 1982
Naura						
Polynesian	459	0.637	0.354	0.006	0.003	Ranfold <i>et al.</i> , 1982
W. Samoa,						
Rarotonga						
New Caledonia						
Melanesian	388	0.665	0.326	0.009	0.000	Ranfold <i>et al.</i> , 1982
New Caledonia						
Uvea, Fiji						
German						
Hessen	254	0.646	0.346	0.000	0.008	(A1, B2) Kühnl & Kreckel, 1980
Westren	709	0.601	0.388	0.003	0.008	(A1, M, B1) Kunstmann <i>et al.</i> , 1980
Norwegian						
Lappos	167	0.533	0.467	0.000	0.000	Olving <i>et al.</i> , 1980
Caucasian	1.623	0.587	0.409	0.000	0.004	Olving <i>et al.</i> , 1980
Sweden	218	0.642	0.358			Rudduck <i>et al.</i> , 1985

al., 1988; Kishi *et al.*, 1988; Ranford *et al.*, 1982; Olving *et al.*, 1980).

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한국인 집단의 유전학적 연구.

16. Complement Component 6의 유전적 다형

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한국인 383명의 Complement Component 6(C6)의 유전적 다형성을 등전점 전기영동과 immunoblotting으로 조사하였다. 5가지 allotypes, C6 A, C6 B, C6 B2, C6 M1, C6 M11이 나타났고, 이들의 대립유전인자 빈도는 $C6^*A = 0.4399$, $C6^*B = 0.5144$, $C6^*B2 = 0.0392$ 로 산출되어 이는 동아시아인과 비슷하였다.