

# HLA-DR Antigens and HLA-B:DR Haplotypes in Koreans

Se Jong Kim, In Hong Choi and Joo Deuk Kim

*Department of Microbiology, Yonsei University, College of Medicine  
Seoul, Korea*

HLA-DR antigen and gene frequencies were studied in 150 unrelated Koreans in Seoul. HLA-DR4 was the most common DR specificity encountered and HLA-DR1 and -DR3 occurred with the lowest frequencies. The frequency of HLA-DR blank allele was 27.1%. HLA-B:DR haplotypes involving positive delta values differing significantly from zero were DR1:B7, DR2:Bw22, DR3:B17, DR5:Bw35, DRw6:B17, DR7:B12, DR7:B13, and DRw8:Bw16. The supertypic groups (MT1, MT2 and MT3) differ somewhat in frequencies from other populations.

These findings suggested that the Korean population, while having many similarities in HLA-DR antigen frequencies with those of neighboring Orientals, has not only different features in the distribution of HLA-DR antigens but also has unique HLA-B:DR haplotypes.

---

**Key Words:** HLA-DR antigens, HLA-B:DR haplotypes, Korean

The HLA-DR antigens are most probably controlled by multiple alleles at a single locus in the HLA region, which is identical or at least closely linked to the HLA-D locus (Pickbourne *et al.*, 1978; Lamm *et al.*, 1978; Th. Schreuder, 1982). However, the number of loci and the size of the polymorphism in the HLA-DR region of the major histocompatibility complex (MHC) of humans probably have not been fully ascertained. The joint reports of the Eighth International Histocompatibility Workshop (1980) on the serologic and genetic characterization of the

antigens or the HLA-DR locus provided a summary. So far, ten HLA-DR specificities have been defined of which HLA-DR1, DR2, DR3, DR4, DR5, and DR7, are well defined while HLA-DRw6, DRw8, DRw9, and DRw10 are less well characterized and only have provisional status. Definition of one of these antigens, HLA-DRw6, remains unclear. The difficulties in the assignment of HLA-DRw6 is due to the absence of monospecific antisera.

Several investigators have independently reported evidence of the presence of supertypic specificities in the HLA-DR series (Doquesnoy *et al.*, 1979; van Leeuwen *et al.*, 1980; Park *et al.*, 1980). One of the supertypic specifi-

---

Received February 7, 1983

This work was supported by grant from the Faculty Research Grant of YUMC (1981 and 1982).

cities is MT which has six inclusion groups, MT1 through MT6 (Park *et al.*, 1980).

Apart from the Workshop data there is only little information about the gene and antigen frequencies of HLA-DR in more homogenous ethnic groups. It has been considered that Koreans are composed of a relatively homogenous ethnic group. Therefore, we made an attempt to perform the HLA-DR typing with 150 unrelated Koreans. Furthermore, HLA-B:DR haplotype frequencies in Korean population are included to assess the gametic associations between alleles of the HLA-DR locus and alleles of other loci in the HLA region in Koreans.

## MATERIALS AND METHODS

**Population samples:** A total of 150 Koreans in Seoul were included and they were all unrelated.

**Lymphocyte isolation and freezing:** Blood samples were collected and mixed immediately with equal volumes of RPMI 1640 with heparin (20 units/ml) and either processed immediately or held at room temperature overnight. Using sterile technique throughout the procedures, peripheral blood lymphocytes (PBL) were separated by layering on Ficoll-Hypaque (SG=1.07) according to the method of Böyum (Böyum, 1968). PBLs were resuspended in RPMI 1640 containing 20% fetal calf serum (FCS), 10% dimethylsulfoxide (DMSO), penicillin (100 units/ml), and streptomycin (100 ug/ml). After making one ml aliquots ( $10 \times 10^6$  cells/Nunc), cells were cooled to  $-70^\circ\text{C}$  and stored in the vapor phase of liquid nitrogen.

**HLA-DR typing:** Cryopreserved PBLs were thawed rapidly at  $37^\circ\text{C}$  in a water bath (Kim *et al.* 1980) and two ml of RPMI 1640 was added with 50% FCS and five ml of RPMI 1640 drop by drop. After washing the cells with Hanks', the PBLs were resuspended in RPMI

1640 containing 15% FCS and incubated in 60 mm plastic petri dishes for 30 minutes at  $37^\circ\text{C}$  in a 5%  $\text{CO}_2$  humidified incubator to remove monocytes. Nonadherent cells were resuspended in 0.5 ml of McCoy's medium with 25% FCS and incubated for 45 minutes at  $37^\circ\text{C}$  after applying the cell suspension on nylon wool in a  $5 \times 0.6\text{cm}$  plastic straw (Danilovs *et al.*, 1980). B lymphocytes were eluted from the nylon wool by squeezing the nylon wool column after eluting nonadherent T lymphocytes by applying 15ml of McCoy's medium with 25% FCS. HLA-DR typing was performed on B lymphocytes by a complement dependent microcytotoxicity test (van Rood *et al.*, 1975).

**Statistical analysis:** The HLA-DR gene frequencies were calculated by the formula  $gf = 1 - \sqrt{1 - pf}$ , where  $gf$  denotes the gene frequencies and  $pf$  denotes the frequency of the corresponding phenotypes. And the haplotype frequencies for two-locus, HLA-B:DR, were estimated from the phenotypes of random individuals (Mattiuz *et al.*, 1970).

## RESULTS AND DISCUSSIONS

HLA-DR antigen and gene frequencies were determined from the phenotypes of 150 unrelated Korean individuals.

Table 1 compares the antigen frequencies of Koreans with data obtained from the Eighth International Histocompatibility Workshop population studies (Baur and Danilovs, 1980) on Japanese and Caucasians and the data on Chinese-American families (Colombe *et al.*, 1982). HLA-DR4 was the most common DR specificity encountered in the Koreans. HLA-DR1 and DR3 are less frequent, not only in the Koreans, but also in Oriental populations than in Caucasians. Several antigens appear to have different frequencies in Koreans, Japanese

Table 1. Frequencies of HLA-DR specificities in comparison with other populations

Specificities	Korean (150)		japanese* (884)		Chinese <sup>+</sup> (60)		American Caucasian* (1145)	
	gf	pf	gf	pf	gf <sup>++</sup>	pf	gf	pf
DR1	3.4	6.7	6.3	12.2	0	1.7	10.6	20.0
DR2	9.1	17.3	20.0	36.0	20.5	41.4	13.6	25.3
DR3	2.7	5.3	1.6	3.2	2.6	6.9	11.8	22.2
DR4	26.5	46.0	23.5	41.1	18.0	27.6	14.8	22.2
DR5	5.5	10.7	2.2	4.3	9.0	13.8	10.2	19.4
DRw6	9.4	18.0	4.6	9.1	18.0	34.5(w6Y)	3.7	7.2
DR7	8.0	15.3	0.5	1.0	2.6	10.3	12.6	23.6
DRw8	8.3	16.0	6.5	12.6	2.6	3.4	2.7	5.3
DRw9	NT	NT	12.2	23.0	11.5	20.7	1.5	3.0
DRw10	NT	NT	0.6	1.2	2.6	3.4	0.6	1.2
DRx	27.1		22.0		12.8		18.0	

\* From the Histocompatibility Testing 1980

+ From Colombe et al. (1982)

++ Gene frequencies was identified in 17 Chinese-American families

gf: Gene frequency

pf: Phenotype frequency

Table 2. Associations of HLA-DR blank with MT1 and MT2 in Koreans

Cell No.*	DR	MT
KC#022	5, -**	1,2,4
KC#035	5, -	1,2
KC#125	(4), -	1,2,4
KC#130	-, -	1,2,3
KC#133	8, -	1,2
HA#020	8, -	1,2
HA#038	8, -	1,2,3

\* Cells typed HLA-DR blank but reactive with MT1 and MT2 sera.

\*\* Assignment of HLA-DR blank allele in this study is provisional since family study has not been done.

and Chinese; HLA-DR2 is quite frequent in Japanese and Chinese, whereas the frequency of this antigen in Koreans is low and close to that of Caucasians. The frequencies of HLA-DR5 is intermediate between that of Japanese

and Chinese. As there are no sera monospecific for HLA-DRw6, the assignment of DRw6 is more difficult than any other HLA-DR antigens. The Koreans studied show 18% of DRw6 antigen frequency which is higher than in the Japanese or in Caucasians, whereas DRw6 was not detected in Chinese (Colombe *et al*, 1982). However, the Chinese showed a high frequency of HLA-DRw6Y. Even though our study cannot give the antigen frequency of HLA-DRw6Y in Koreans, we may attempt to mention that DRw6Y antigen is not infrequent in Koreans since seven individuals among HLA-DR blank individuals have been typed as MT1 and MT2 in our study (Table 2). According to the Eighth Workshop definition of HLA-DRw6Y, only cells positive with MT1 and MT2 antisera but negative with DR3+DRw6 antisera, were assigned DRw6Y (Sekiguchi *et al*, 1980).

From the gene frequencies of the Koreans, the frequency of the blank at the HLA-DR

**Table 3. Supertypic DR groups in Koreans in comparison with other populations**

Groups	Frequencies (%)		
	Korean	Japanese*	Caucasian*
MT1	54	72	64
MT2	49	48	64
MT3	65	48	40

\* Park et al (1980)

**Table 4. HLA-B:DR haplotype frequencies and delta values in Koreans**

Haplotype	Hf (x10 <sup>4</sup> )	$\Delta$ (x10 <sup>4</sup> )
DR1:B7	179	163***
DR2:Bw22	214	139*
DR3:B17	102	86**
DR5:Bw35	267	203**
DRw6:B17	190	135*
DR7:B12	331	244**
DR7:B13	205	170***
DRw8:Bw16	98	76*

\*: P&lt;0.05, \*\*: P&lt;0.01, \*\*\*: P&lt;0.001

locus was estimated to be 27.1%. The high frequencies of DR blank allele might be caused assuming that not only our study did not include DRw9 and DRw10 antisera, but also weak serum reactions were common in the typing of Korean cells.

The supertypic groups (MT1, MT2 and MT3) differ somewhat in frequency from other populations: MT3 is the most common supertypic group in the Koreans, but MT1 is the most common one in the Japanese (Table 3).

Haplotype frequencies and delta values in the Koreans are shown in Table 4 for the HLA-B:DR haplotypes involving positive delta values differing significantly from zero. It appears that the pattern of significantly encountered HLA-B:DR haplotypes in the Korean popula-

tion is quite different from that in other populations. The haplotypes B13:DR7, B12:DR7, and B17:DRw6, which are very rare in Japanese (Baur and Danilovs, 1980), showed significantly strong association in the Koreans. More interestingly, the haplotypes B13:DR7 and B12:DR7, are also relatively common in Caucasoids (Jakobsen *et al.*, 1981).

## REFERENCES

- Baur MP and Danilovs JA: *Population analysis of HLA-A, B, C, DR, and other genetic markers. In Terasaki PI (Ed.) Histocompatibility Testing 1980 pp. 955-1210, ULCA Press, Los Angeles, 1980*
- Böyum A: *Separation of leukocytes from blood and bone marrow. Scand J Clin Lab Invest 21 (Suppl. 97):1-109, 1968*
- Colombe B, Pask S, Cann H and Payne R: *HLA-DR antigens in Chinese-American families. Human Immunol 4:229-238, 1982*
- Danilovs JA, Ayoub G and Terasaki Pi: *Joint report: B lymphocytes isolation by thrombin-nylon wool. In Terasaki PI (Ed.) Histocompatibility Testing 1980 pp. 287-288, UCLA Press, Los Angeles, 1980*
- Duquesnoy RJ, Marriri M and Annen K: *Identification of an HLA-DR associated system of B cell alloantigens. Transplant Proc 11: 1757-1760, 1979*
- Jakobsen BK, Morling N, Platz P, Ryder LP, Thomsen M, and Svejgaard A: *HLA-DR phenotype and HLA-B, DR haplotype frequencies in 704 unrelated Danes. Tissue Antigens 18:270-275, 1981*
- Kim SJ, Christiansen FT, Gosar I, Silver DM, Pollack MS and Dupont B: *Frequency of alloantibodies reacting with PHA-activated T lymphocytes, unexplainable by known HLA-activities. Human Immunol 1:347-355,*

1980

- Lamm LU, Kristensen T, Jorgensen F and Kissmeyer-Nielsen F: *Serological and cellular HLA-determinants. A panel study. Tissue Antigens* 10:138, 1978
- Mattiuz OL, Ihde D, Piazza A, Ceppellini R and Bodmer WF: *New approaches to the population genetics and segregation analysis of the HL-A system. In Terasaki PI (Ed.) Histocompatibility Testing 1970. pp. 193-205, Munsgaard, Copenhagen, 1970*
- Park MS, Terasaki PI, Bernoco D and Iwaki Y: *Evidence for a second B-cell locus separate from the DR locus. Transplant Proc* 10:823-828, 1978
- Park MS, Terasaki PI and Bernoco D: *Relationship between MT and DR antigens, In Terasaki PI (Ed.) Histocompatibility Testing 1980 pp. 572-573, UCLA Press, Los Angeles, 1980*
- Park MS, Terasaki PI, Nakada S and Aoki D: *Supertypic DR groups: MT1, MT2, and MT3. In Terasaki PI (Ed.) Histocompatibility Testing 1980 pp. 854-857, UCLA Press, Los Angeles, 1980*
- Pickbourne P, Piazza A and Bodmer WF: *Population analysis. In Bodmer WF, Batchelor JR, Bodmer JG, Festenstein H and Morris PJ (Eds.), Histocompatibility Testing 1978 pp. 259-278, Munsgaard, Copenhagen, 1978*
- Sekiguchi S, Kreisler M, Omori K, Nakada S, Park MS and Jeannet M: *8WDRW6Y (6.3, seb. In Terasaki PI (Ed.) Histocompatibility Testing 1980 pp. 530-531, UCLA Press, Los Angeles, 1980*
- Th. Schreuder GM, van Leeuwen A, Termijtelen A, Parlevliet J, D'Amaro J and van Rood JJ: *Cell membrane polymorphisms coded for in the HLA-D/DR region. I. Relation between D and DR. Human Immunol* 4:301-312, 1982
- van Leeuwen A, Festenstein H, Amaro J, Navarette CH, Awad J and van Rood JJ: *A new B cell locus defined by a recombinant family. In Terasaki PI (Ed.) Histocompatibility Testing 1980 p. 853, UCLA press, Los Angeles, 1980*
- van Rood JJ, van Leeuwen A, Keunig JJ, Blusse van Oud and Alblas A: *The serological recognition of the human MLC determinants using a modified cytotoxicity technique. Tissue Antigens* 5:73-79, 1975