Coll. Antropol. **24** (2000) 2: 303–307
UDC 575.174.015.3(496.5)
Original scientific paper

HLA Class I Polymorphism in the Albanian Population

Z. Grubić[1], V. Kerhin-Brkljačić[1], E. Čečuk-Jeličić[1], S. Kuci[2] and A. Kaštelan[1]

[1] National Referral Organ Transplantation and Tissue Typing Center, University Hospital Center Zagreb, Zagreb, Croatia
[2] Faculty of Medicine Priština, Priština, Kosovo

ABSTRACT

The HLA class I polymorphism was studied in a sample of the Albanian population. Ninety-three unrelated healthy Albanians were typed for HLA-A, -B and -Cw antigens by standard microlyphocytotoxicity test. The antigens with the highest frequencies were: HLA-A2 (34.4%), A3 (14.5%) and A1 (12.4%); B51 (19.3%), B35 (12.4%) and B18 (10.2%); Cw4 (16.2%), Cw7 (16.2%) and Cw6 (10.8%). The HLA haplotypes with high frequency in Albanians included A2-B51 (4.3%), A2-B18 (2.4%), A2-B35 (2.4%), Cw4-B35 (7.6%), and Cw7-B18 (6.5%), which are not significantly different from the other neighboring populations. Low frequency of HLA-A1-B8 haplotype (1.1%) is noted in the Albanian population. The frequency of HLA-B27 antigen (1.1%) is one of the lowest frequencies observed in Caucasians. Such results are important in studies of HLA-A1-B8, HLA-B27 and disease associations. These findings should be also useful in understanding the origin of Albanians, representing a base for future studies about HLA polymorphism in the Albanian population.

The main characteristic of the HLA system is a great polymorphism, which makes it very useful for population studies and for studying the origins of different ethnic groups[1]. It may also be used to single out populations. First, particular alleles are only observed in some populations (e. g., HLA-A36, -A43 in Negroids) or some alleles are very frequent in many populations (e. g., HLA-A2)[2]. Second, the strong linkage disequlibrium between HLA alleles at two or three neighboring loci shows that certain combinations (HLA haplotypes) are characteristic in frequency of one or a large number of populations[3].

Albanians are a very homogenous population, their history suggests that they did not mix with neighboring populations. It is assumed that Albanians have Illyrian origin[4]. The Illyrians are of spe-

Received for publication June 16, 2000.

cial interest because there is no consensus regarding their origin, whether Illyrians were immigrants on the Balkan peninsula or an autochthonous population[4]. Regardless to its origin, Illyrians together with Thracians, are one of the oldest populations which settled the South of Europe. The anthropological diversity of European South and Balkan Peninsula is a result of mixing and massive migration. The presence of Greeks and Romans has been well-established in archeological materials. Goths and Huns invaded the Balkan Peninsula in the 5th century. Later, in the 6th and 7th century Slavs migrated to the Balkan. The territory of Kosovo was under Byzantine and Ottoman domination, respectively.

The purpose of the present study was to obtain information concerning the distribution of HLA class I antigens in the Albanian population from Kosovo and to compare results with other populations from the South of Europe.

Ninety-three unrelated healthy Albanians from Priština were studied, as part of Anthropology Component of XIth International Histocompatibility Workshop[5]. This population should be considered as representative for most of Kosovo since Priština has been an important immigration center after Second World War. It became the main industrial, political and cultural center in Kosovo.

Tissue typing for HLA-A, -B, and -Cw antigens was performed on T+B lymphocyte suspension, according to the standard microlyphocytotoxicity method[6]. The typing sera were obtained from our laboratory and from commercial sources.

Antigen and haplotype frequencies were calculated by the maximum likelihood method. The linkage disequilibrium value (LD) was computed for each two locus haplotype analysis (HLA-A, -B; HLA-B, -Cw) using the formula $Ld_{ij} = HF\text{-}a_i x b_j$ [5]. In this equation, HF is the haplotype frequency, and a_i and b_j represent the frequencies of Ai, and Bj alleles, respectively. The significance of differences in antigen and haplotype frequencies among populations was evaluated using the chi-square, while the Fisher's exact test was used if any value in 2 x 2 table was less than five[7].

The HLA-A, -B, and -Cw frequencies determined in the 93 Albanians are listed in Table 1. No deviation from Hardy-Weinberg equilibrium was observed. The most frequent HLA-A alleles found in the Albanian population were HLA-A2 (34.4%) and -A3 (14.5%), followed by HLA-A1 (12.4), -A24 (10.7%) and -A28 (5.4%). Other alleles had frequencies less than 5%, while HLA-A30 was not been detected in this sample. Comparison of HLA-A frequencies between Albanians and other neighboring populations did not reveal significant difference [8–10]. In this sample we did not observe a high frequency of HLA-A32 antigen as suggested by Cuccia et al[9]. They reported about frequency of 10.4% for HLA-A32 antigen in two Italian villages populated exclusive with Albanians. Southern Albanian people escaping from the Turkish invasion in Europe founded these villages in the fifteenth century and this population is not genetically mixed with Italians.

Among the 19 different antigens at the HLA-B locus detected in the Albanian population, the most frequent were HLA-B51 (19.3%), -B35 (12.4%) and -B18 (10.2%). The HLA-B51 was found with higher frequency (but not significantly different) than in other South European populations (Italians, Greeks, Romanians, Croatians)[11,13]. Other HLA-B antigens had frequencies less than 10%. One of the characteristics of the Albanian population is the very low frequency of HLA-B27 (1.1%). This finding is in agreement with data from the two Italian villages with Albanians and it is important

to mention for further studies about association between HLA and diseases. Namely, this gene serves for the identification of high-risk patients for ankylosing spondylitis (AS) and may also identify patients sufficiently early in the case of not clear clinical picture. A low frequency of this antigen perhaps instructs on low incidence of AS in Albanians or on other HLA-B antigen associated with disease[13,14]. Unfortunately, there are no published data about prevalence of AS in the Albanian population or distribution of HLA antigens among AS patients from Kosovo.

Among the nine HLA-Cw antigens determined in this sample, the most frequent were HLA-Cw4 and -Cw7 with equal frequencies (16.2% each). The high frequency of HLA-Cw7 antigen is in concordance with other Europeans[5], whereas HLA-Cw7 was reported to be prevalence antigen.

Two-locus haplotype analysis between HLA-A, -B and HLA-Cw, -B loci was also performed (Table 2). The most frequent HLA-A, -B haplotype was HLA-A2, -B51 (4.3%) like in Greeks (5.0%), Romanians (4.5%) and Portuguese (5.3%). The HLA-A1, -B8 haplotype is less frequent than in some neighboring populations (1.1% compared to Greeks -2.3%, Italians -4.2%, Romanians -4.4%, and Croatians -6.0%)[5,15,16]. The low frequency of this haplotype may be significant to future epidemiological studies about autoimmune diseases in this population. Namely, it is well established that HLA-A1, -B8, -DR3 haplotype is associated with many autoimmune diseases (e. g., Systemic Lupus Erythematosus)[17,18]. Its low frequency also suggests a low admixture between Albanians and other populations. It would be interesting to study citizens of one Kosovo village (Janjevo) populated with Croatians as an example of isolated population, and to compare those results

TABLE 1
THE DISTRIBUTION OF HLA CLASS I ANTIGENS IN A SAMPLE (N=93) OF ALBANIAN POPULATION

HLA-A	Albanians (n=93) %	HLA-B	Albanians (n=93) %	HLA-Cw	Albanians (n=37) %
A1	12.4	B7	5.9	Cw1	5.4
A2	34.4	B8	4.3	Cw2	4.1
A3	14.5	B13	1.6	Cw4	16.2
A11	3.7	B14	0.5	Cw5	1
A23	3.2	B15	2.7	Cw6	10.8
A24	10.7	B17	4.8	Cw7	16.2
A25	1.1	B18	10.2	Cw8	1
A26	2.2	B22	1.6	Cw9	4.1
A28	5.4	B27	1.1	Cw10	5.4
A29	0.5	B35	12.4	blank	35.1
A30	0	B37	2.7		
A31	1.1	B38	5.4		
A32	3.2	B39	0.5		
A33	1.1	B40	5.4		
blank	5.4	B41	2.2		
		B44	8.1		
		B45	1.6		
		B51	19.3		
		B52	2.7		
		blank	4.3		

n-total number of individuals

TABLE 2
THE DISTRIBUTION OF TWO-LOCUS HAPLOTYPES HLA-A, -B AND HLA-CW, -B WITH FREQUENCIES 1.1 IN A SAMPLE (N=93) OF ALBANIAN POPULATION

HAPLOTYPE	HF × 100	LD × 100	HAPLOTYPE	HF × 100	LD × 100
A2, B51	4.3	4.0	Cw4, B35	7.6	6.1
A2, B18	2.4	2.2	Cw7, B18	6.5	4.9
A2, B35	2.4	2.3	Cw7, B7	6.2	4.8
A2, B44	1.6	1.3	Cw7, B51	3.4	3.3
A24, B44	1.6	1.4	Cw4, B44	3.1	1.6
A3, B5	1.6	1.4	Cw2, B44	1.7	1.1
A28, B18	1.3	1.2			
A28, B5	1.1	1.0			
A1, B8	1.1	1.0			

HF-haplotype frequency; LD × 100-linkage disequlibrium × 100

with present data and Croatian population data.

Since complete studies of the HLA polymorphism have not been reported yet for most of populations from South-Eastern Europe, as well as more data from other populations from Near East, definitive conclusion of Albanians origin is not possible to make. Our preliminary data suggest that the Albanian population shows some characteristic HLA class I haplotypes and thus an extended study, including DR and DQ DNA analysis and characteristic extended HLA haplotypes, with molecular typing methods would be justified.

REFERENCES

1. SO, A., In: LECHLER, R. (Ed.): Genetics, polymorphism and regulation of HLA region genes. (Academic Press Limited, London, 1994). — 2. ERLICH, H. A., In: BROWING, M., A. MC MICHAEL (Eds.): HLA and MHC genes, molecules and function. (BIOS Scientific Publishers, Oxford, 1996). — 3. KRAUSA, P., M. BROWING, In: BROWING, M., A. MC MICHAEL (Eds.): HLA and MHC genes, molecules and function. (BIOS Scientific Publishers, Oxford, 1996). — 4. MIRDITA, Z. Encyklopaedia Moderna, 13 (1970) 30. — 5. IMANISHI, T., T. AKAZA, A. KIMURA, K. TOKUNAGA, T. GOJOBORI, In: TSUJI, K., M. AIZAWA, T. SASAZUKI (Eds.): Proceedings of the Eleventh International Histocompatibility Workshop and Conference. (Oxford University Press, Oxford, 1991). — 6. AMOS, D. B., H. BASHIR, W. BOYLE, et al., Transplantation, 7 (1969) 220. — 7. FISHER, R. A.: Statistical methods for research workers. (Hafner Publishing Company, New York, 1973). — 8. KAŠTELAN, A., V. KERHIN-BRKLJAČIĆ, J. HORS, LJ. BRKLJAČIĆ, P. MACAŠEVIĆ, Tissue Antigens, 4 (1974) 69. — 9. CUCCIA, M., P. ASTOLFI, E. GYODI, et al., In: TSUJI, K., M. AIZAWA, T. SASAZUKI (Eds.): Proceedings of the Eleventh International Histocompatibility Workshop and Conference. (Oxford University Press, Oxford, 1991). — 10. PIAZZA, A., R. FAUCHET, P. RICHIARDI, C. CARACASSI, L. CONTU, et al., In: TSUJI, K., M. AIZAWA, T. SASAZUKI, (Eds): Proceedings of the Eleventh International Histocompatibility Workshop and Conference. (Oxford University Press, Oxford, 1991). — 11. IVANOVA, R., E. NAOMOVA, V. LEPAGE, S. DJOULAH, Y. YORDANOV, M. N. LOSTE, D. CHARRON, Tissue Antigens, 47 (1996) 122. — 12. CERNA, M., M. FERNANDEZ-VINA, E. IVASKOVA, P. STASTNY, Tissue Antigens, 39 (1992) 111. — 13. GONZALES-ROCES S., M. V. ALVAREZ, S. GONZALES, et al., Tissue Antigens, 49 (1997) 116. — 14. ROBINSON, W. P., S. M. VAN DER LINDEN, M. A. KHAN, et al., Arthritis and Rheumatism, 32 (1989) 1135. — 15. IVANOVA, M., A. MICHAILOVA, A. NEDIALKOVA, E. NAUMOVA, Human Immunology, 61 (2000) 124. — 16. GRUBIĆ, Z., R. ŽUNEC, E. ČEČUK-JELIČIĆ, V. KERHIN-BRKLJAČIĆ, A. KAŠTELAN, European Journal of Immunogenetics, 27 (2000) 47. — 17. MAEDA, H., C. BRAUTBAR, A. AMOROSA, S. BATTAT, W. B. BIAS, et al., In: CHARRON, D. (Ed.): Genetic diversity of HLA. Functional and medical Implication. (EDK Medical and Scientific International Publisher, Paris, 1997). — 18. REED, E., E. HO, F. LUPU, Tissue Antigens, 39 (1992) 8.

Z. Grubić

National Referral Organ Transplantation and Tissue Typing Center, University Hospital Center Zagreb, Kišpatićeva 12, 10000 Zagreb, Croatia

RAZNOVRSNOST ANTIGENA »HLA RAZREDA I« U POPULACIJI KOSOVA

S A Ž E T A K

Raznovrsnost antigena HLA razreda I istraživana je među 93 nesrodna zdrava stanovnika Prištine (Kosovo, SR Jugoslavija). Najzastupljeniji antigeni na lokusu HLA-A bili su: HLA-A2 (34,4%), A3 (14,5%) i A1 (12,4%), tri najčešća antigena lokusa HLA-B su: B51 (19,3%), B35 (12,4%) i B18 (10,2%), dok su na lokusu HLA-C najveću učestalost pokazali antigeni: Cw4 (16,2%), Cw7 (16,2%) i Cw6 (10,8%). Unutar albanske populacije najveću učestalost pokazali su slijedeći haplotipovi: HLA-A2-B51 (4,3%), A2-B18 (2,4%), A2-B35 (2,4%), Cw4-B35 (7,6%) i Cw7-B18 (6,5%), međutim njihova učestalost nije statistički značajno različita od njihovih učestalosti u susjednim populacijama. Osobitosti albanske populacije su smanjena zastupljenost haplotipa HLA-A1-B8 (1,6%), te niska učestalost antigena HLA-B27 (1,1%). Ovi nalazi su važan temelj za sva daljnja istraživanja povezanosti sustava HLA i bolesti među stanovništvom Kosova, kao i za bolje shvaćanje podrijetla Albanaca.