HLA class II polymorphism in Brazilian populations

Crésio Alves[1]
Thaisa Souza[2]
Sâmia Veiga[2]
Maria Betânia P. Toralles[3]
Denise C. Lemaire[4]

Abstract
The investigation of the distribution and frequency of HLA (*Human Leukocyte Antigen*) genes in presumably healthy populations is important to evaluate the participation of these genes in the susceptibility and protection against diseases, to evaluate the genetic origins of populations and to aid in the practice of transplantations. The advances in molecular biology has allowed a better understanding of this system. In addition, information about the HLA class II molecules, such as their mechanism of action, function, and genetic polymorphism, granted their use as markers for ethnic composition of a population and even of individual distinction. The HLA class II genes appear to be associated with some racial/ethnic groups more than others. By using these genetic characteristics, it may be possible to demonstrate, for example, the degree of admixture of Caucasians, Africans and Amerindians that marks in a significant way the origin of the Brazilian population. It also clarifies some aspects of the ancestry of this population and helps the performance of population studies with the objectives to obtain information related to the history and formation features, migration and composition of theses groups, in conformity with local particularities. The relevance of this theme is the frequency of HLA class II antigens, alleles and haplotypes in the Brazilian populations.

Keywords: HLA - Brazilian population; major histocompatibility complex.

INTRODUCTION

The HLA complex (Human Leukocyte Antigens) is localized in the short arm of the human chromosome six. This system codes for genes involved in the immune response and can be divided in three classes: I, II and III. Four properties of the HLA system are of great interest. The first is the histocompatibility, since the concordance of the HLA of donors and organs recipients is important to a favorable outcome of transplantation procedures (PROBST et al., 2000). The second is the association of some HLA molecules with diseases such as, type 1 diabetes, rheumatoid arthritis, and celiac disease (KLEIN; SATO, 2000b). The third is the identification of individuals in forensic medicine (SOARES-VIEIRA et al., 1999); and the fourth is its use in genetic of populations.

[1] Professor de Pediatria. Faculdade de Medicina. Universidade Federal da Bahia. Salvador - BA
[2] Acadêmico de Medicina da Universidade Federal da Bahia. Salvador - BA
[3] Professora de Genética. Faculdade de Medicina. Universidade Federal da Bahia. Salvador - BA
[4] Professora de Imunologia. Universidade Estadual da Bahia (UNEB). Professora do Curso de Pós-Graduação em Imunologia. UFBA Salvador - BA

Correspondência para / *Correspondence to*:
Crésio Alves
Rua Plínio Moscoso, 222, Apto. 601
40157-190 Salvador – Bahia - Brasil
Tel: (71) 9975-8220
E-mail: cresio.alves@uol.com.br

The HLA genes constitute the most polymorphic genetic system known (PETZL-ERLER et al., 1993). The polymorphism of the HLA genes differs among populations in frequency and presence of particular alleles and haplotypes, making these genes a powerful tool to study the origin of populations and their grade of admixture (PROBST et al., 2000).

Since the frequency of HLA antigens depends on the ethnic composition of the analyzed population (PROBST et al., 2000), studies on the distribution and frequency of HLA class II alleles in Brazil are important to comprehend the formation and ancestry of this nation. The modern Brazilian population reflects the contribution of individuals of many ethnic backgrounds, including Caucasians immigrants mainly from Europe (Portugal, Spain and Italy), Black African populations principally of Niger-Congo in Equatorial Africa and Bantu and native Amerindian populations from the Tupi and Tapuia groups (LOUZADA-JUNIOR et al., 2001; MORAES et al., 1993). The interracial mating between the individuals of these groups originated an admixed population. The individual who descends from the mixture of Indians and Caucasians is called "caboclo"; Africans and Caucasians, "mulato"; and Indians and Africans, "cafuzo". The internal migration between different regions of the nation adds a greater level of complexity to this situation (TRACHTENBERG et al., 1988). All theses features make the Brazilians a unique population, with a high level of admixture, which makes it difficult to define its genetic composition.

The aim of this study is to review the medical literature about the distribution and frequency of the HLA class II antigens, alleles and haplotypes in healthy Brazilians and interpret the results according to the different ethnic/racial categories that compose this population.

METHODOLOGY

Scientific articles that approached the association between HLA and Brazilian populations in the last twenty years were searched using the data banks MEDLINE and LILACS-BIREME. The following key-words were used: 1. HLA class II; 2. HLA class II polymorphisms; 3. major histocompatibility complex; 4. Brazil; and 5. Brazilian population.

RESULTS

We found twenty-four articles published between 1980 and 2004 about HLA and Brazilian populations (BELICH et al., 1992; BLACK et al., 1980; CERNA et al., 1993; DONADI; SILVA, 2000; ERLICH et al., 1997; FERNANDEZ-VINA et al., 1991a; FERNANDEZ-VINA et al., 1991b; FERNANDEZ-VINA et al., 1997; GOLDBERG et al., 1998; LÁZARO et al., 1999; LOUZADA-JUNIOR et al., 2001; MACIAG et al., 2000; MACK; ERLICH, 1998; MORAES et al., 1993; MORAES et al., 2004; PANDO et al., 1994; PETZL-ERLER et al., 1993; PETZL-ERLER; MCDEVITT, 1994; PROBST et al., 2000; SOARES-VIEIRA et al., 1999; SOTOMAIOR et al., 1998; TESTA et al., 2004; TRACHTENBERG et al., 1988; TSUNETO et al., 2003). Of the total number of articles, nine didn't fit in the objectives of the present study (BELICH et al., 1992; BLACK et al., 1980; FERNANDEZ-VINA et al., 1991a; FERNANDEZ-VINA et al., 1991b; FERNANDEZ-VINA et al., 1997; GOLDBERG et al., 1998; MORAES et al., 2004; SOARES-VIEIRA et al., 1999; TESTA et al., 2004; TRACHTENBERG et al., 1988). In three of them the focus was the HLA class I molecules (BELICH et al., 1992; BLACK et al., 1980; TRACHTENBERG et al., 1988), six articles, although studying HLA class II antigens, did not specified the ethnic origin of the individuals or separated the results according to race/ethnicity (FERNANDEZ-VINA et al., 1991a; FERNANDEZ-VINA et al., 1991b; FERNANDEZ-VINA et al., 1997; GOLDBERG et al., 1998; MORAES et al. 2004; TESTA et al., 2004).

The frequency and distribution of HLA antigens, alleles and haplotypes in Brazilians,

considering ethnicity/race of the individuals were studied in fourteen papers (CERNA et al., 1993; DONADI; SILVA, 2000; ERLICH et al., 1997; LÁZARO et al., 1999; LOUZADA-JUNIOR et al., 2001; MACIAG et al., 2000; MACK; ERLICH, 1998; MORAES et al., 1993; PANDO et al., 1994; PETZL-ERLER et al., 1993; PETZL-ERLER; MCDEVITT, 1994; PROBST et al., 2000; SOTOMAIOR et al., 1998, TSUNETO et al., 2003). Native Indian tribes were examined by nine articles (CERNA et al., 1993; ERLICH et al., 1997; LÁZARO et al., 1999; MACK; ERLICH, 1998; PANDO et al., 1994; PETZL-ERLER et al., 1993; PETZL-ERLER; MCDEVITT, 1994; SOTOMAIOR et al., 1998, TSUNETO et al., 2003). Black, White and Mulatto populations were analyzed by five articles: Moraes and others (1993) analyzed Blacks and Whites populations living in the city Rio de Janeiro; Probst and others (2000) studied Whites and Mulattos populations residing in the state of Paraná; Donadi and Silva (2000) studied Whites, Blacks and Mulattos samples from the city of São Paulo; Maciag and others (2000) described a novel HLA class II allele in two white individuals from the state of Paraíba and Louzada-Junior and others (2001) examined Whites, Blacks and Mulattos from the state of São Paulo.

For didactic purposes, the data regarding the HLA antigens, alleles and haplotypes were divided in two groups: "Amerindian populations" and "non-Amerindians populations". The "non-Amerindian" group was further divided into Blacks, Mulattos and Whites, based on the classification used by the authors of the original articles.

(I) Amerindian population

The Amerindians are part of the composition of the mixed Brazilian population. Nowadays, these groups are dispersed in different regions, particularly in the north and central-west areas of the country. Few of them are still isolated, keeping cultural, geographic and genetic characteristics that can be distinct from the remaining general population. (CERNA et al., 1993)

Brazilian and South American tribes are of great interest for genetic polymorphism studies because of their isolation from other ethnic groups.

A careful analysis of the HLA system in different ethnic groups can be an important step to better understand its evolution and function. In this context, the study of genetic isolated populations such as Amerindian tribes is rather informative (PETZL-ERLER et al., 1993). The results of these investigations offer significant evidences about the ancestry and patterns of admixture. (CERNA et al., 1993)

Petzl-Erler and others (1993) in the state of Paraná selected two populations: the Guarani and Kaingang Indians (KRC) and only Kaingang Indians (KIV). In Guarani Indians, higher frequencies of the HLA antigens HLA-DR2, -DR4, -DR6, -DR8 and -DQ3 were found. The HLA-DR2, -DR4, -DR6, -DR8 and -DQ3 were the most frequent antigens in the Kaingang. Differences between the two populations concerning DR-DQ haplotypes weren't evident. The combination of HLA-DR and -DQ antigens in the two tribes was the same: HLA-DR2-DQ3; -DR4-DQ3; -DR8-DQ *blank.*

Another paper, from Petzl-Erler and McDevitt (1994), used the same population samples cited above to characterize the HLA-DRB alleles, making a comparison with populations of other studies. The authors reported that the HLA-DR4 antigen from Kaingang Indians is encoded by the *HLA-DRB1*0404* allele, which is also found in non-Amerindian controls. The HLA-DR4 antigen, that belongs to Guarani group, is encoded by *HLA-DRB1*0411*, presenting cross reaction with HLA-DR5 antigen and being in high frequency in Amerindians and Australian aborigines. A new allele, *HLA-DRB1*1413*, was identified in nine individuals of the Guarani tribe. It was the third allele corresponding to the HLA-DR6 antigen noticed in Amerindians (beside *HLA-DRB1*1402* and *-DRB1*1406*). *HLA-DRB1*1402* was observed before in Japanese, Australian aborigines and other ethnic groups, besides Amerindians (PETZL-ERLER; MCDEVITT, 1994). *HLA-DRB1*1406* was detected in Amerindians and in Orientals, but not in Caucasoids or Blacks. (PETZL-ERLER; MCDEVITT, 1994)

The results presented in the works of Cerna and others (1993), Sotomaior and others (1998), and Mack and Erlich (1998) are reported together because they have similar study objects. The allele and gene frequencies are demonstrated in Table 1. Only HLA-DQA1 and -DQB1 alleles's families were presented in the three articles. The HLA-DRB1, -DQA1, -DQB1 and -DPB1 *loci* were analyzed by two groups. (CERNA et al., 1993; MACK; ERLICH., 1998)

Lázaro and others (1999) reported eight DRB1 Amerindian alleles in Terena, a South Central Brazilian tribe. The most frequent were *HLA-DRB1*1602*,*-DRB1*0802*,*-DRB1*1402*, *-DRB1*1406* and *-DRB1*0404*. At the DQB1 locus, *HLA-DQB1*0402*, *-DQB1*0302* and *-DQB1*0301* were prevalent alleles. *HLA-DPB1*0402*, *-DPB1*1301* and *-DPB1*0301* were most frequent alleles in DPB1 locus.

Tsuneto and others (2003) studied seven Amerindian tribes, four of them located in Brazil. In Guarani-M'bya, Guarani-Kaiowá and Guarani-Ñandeva tribes, *HLA-DRB1*1602* was the most frequent HLA-DRB1 allele, *-DQA1*0501* was the most frequent -DQA1 allele and *-DQB1*0301* was the most frequent HLA-DQB1 allele. In Kaingang individuals, *HLA-DRB1*0404* was the most frequent -DRB1 allele, *-DQA1* 0401* was the most frequent -DQA1 allele and *-DQB1*0402* was the most common -DQB1 allele. The alleles *HLA-DRB1*1602*, *-DRB1*0411*, *-DRB1*1402*, *-DRB1*0802*, *-DRB1*090102*, *-DQA1*03*, *-DQA1*0401*, *- DQA1*0501*, *-DQB1*0301*, *-DQB1*0302*,*-DQB1*030302* and *DQB1 *0402* were found in all four tribes. (TSUNETO et al., 2003)

(II) Non-Amerindian population

- Whites:

The distribution and frequency of HLA class II antigens, alleles and haplotypes in population samples of White individuals were reported in six studies (DONADI; SILVA, 2000; LOUZADA-JUNIOR et al., 2001; MACIAG et al., 2000; MORAES et al., 1993; PROBST

Table 1 - HLA allele frequencies in Amerindian from Brazil and South America

Family	HLA alleles	Articles			
		Mack and Erlich	Cerna et al.	Sotomaior et al.	
		Ticuna (af)	Xavante (gf)	Guarani (f)	Kaingang (f)
-DQA1	*0501	0.280	0.614	0.544	0.204
	*0401	0.270	0.265	0.130	0.514
	*03	0.460	0.154	0.304	0.250
	*0301	--	0.154	0.185	0.190
	*0102	--	0.0	0.011	0.0
	*0101 ou *0104	--	0.0	0.005	0.032
	*0201	--	0.0	0.005	0.0
	*0302	--	--	0.049	0.023
	*03011	--	--	0.158	0.190
-DQB1	*0301	0.280	0.615	0.527	0.204
	*0402	0.270	0.265	0.130	0.514
	*0302	0.380	0.154	0.185	0.219
	*0303	0.071	--	--	--
	*0201	0.010	0.0	0.022	0.0
	*0501	--	0.0	0.005	0.032
	*0602	--	0.0	0.011	0.0
	*03032	--	--	0.049	0.023

Note: (—) Allele was not studied; (af) Allele frequency; (gf) Gene frequency; (f) Allele relative- frequency

et al., 2000; SOARES-VIEIRA et al., 1999). Maciag and others (2000) observed a novel allele, the *HLA-DRB1*1340* in two white individuals of the state of Paraíba.

The articles written by Probst and others (2000) and Donadi and Silva (2000) are compared because they used serologic method to type HLA antigens. Regarding the HLA-DR antigens, Probst and others (2000) detected higher frequencies of HLA-DR5, -DR4 and -DR2, while Donadi and Silva (2000) detected higher frequencies of HLA-DR2, -DR3 and -DR4. Regarding the HLA-DQ antigens, the most common antigens found by Probst and others (2000) were HLA-DQ1, -DQ3 and -DQ2. Donadi and Silva (2000) found higher frequencies of HLA-DQ1 e -DQ3.

Probst and others (2000) reported higher frequencies of the following haplotypes: *HLA-DR5-DQ7*, *-DR11-DQ7*, *-DR2-DQ1*, *-DR4-DQ3* and *-DR7-DQ2*. The haplotypes *HLA-DRB1*0102-DQB1*0501*, *-DRB1*1501-DQB1*0602*, *-DRB1*1101- DQB1*0301*, *-DRB1*1301-DQB1*0603* and *-DRB1*1104-DQB1*0301* were reported by Louzada-Junior and others (2001) and Moraes and others (1993).

-Mullatos:

Individuals labeled as Mulattos were studied in three articles (DONADI; SILVA, 2000; LOUZADA-JUNIOR et al., 2001; PROBST et al., 2000).

Due to similarity in the detection methods of HLA class II antigens, the articles by Probst and others (2000) and Donadi and Silva (2000) were compared. The first group found the following most common HLA antigens in their sample of Brazilian Mulattos population: HLA-DR6, -DR7 ,-DR15, -DQ1, -DQ2 ,-DQ3 and -DQ7. These results suggest that HLA antigen frequency observed in Mulattos are intermediate between the frequencies of European and African populations. Donadi and Silva (2000), noted numbers more expressive for HLA-DR4, -DR2, -DR3 and -DR7. HLA-DR8 and -DR10 antigens were not detected in this sample.

The results obtained Louzada-Junior and others (2001) are shown in Table 2, because they use molecular typing/allele frequency.

According to Louzada-Junior and others (2001), the *HLA-DRB1*07* was the most frequent allele among Mulattos with the *HLA-DRB1*0406* and *-DRB1*1202* alleles appearing as exclusive Mulattos alleles.

Table 2 - HLA –DRB1 and –DQB1 allele frequencies in Mulattos Brazilians.

Study	Family	Alleles	Frequenc y (%)
Louzada Jr. et al.	-DRB1	*07	10,7
		*0301	8,9
		*1301	8,9
		*1501	7,1
		*1503	5,4
		*1101	5,4
		*0102	3,6
		*0402	3,6
		*0101	1,8
		*0401	1,8
	-DQB1	*0201	19,6
		*0301	16,1
		*0602	16,1
		*0401	10,7
		*0402	10,7
		*0603	8,9
		*0302	8,9
		*0501	7,1
		*0604	5,4
		*0503	3,6
		*0303	3,6

Note: (%) Allele frequency in percentage

Regarding haplotypes, Probst and others (2000) reported a high frequency of *HLA-DR5-DQ7* and *DR11-DQ7* and these authors suggest that the Mulattos have haplotypes usually present in European and African populations. Louzada-Junior and others (2001) reported a higher frequency of the *HLA-DRB1*0301-*

*DQB1*02*, *-DRB1*1301-DQB1*0603* and *-DRB1*1401-DQB1*0503* haplotypes in a sample of Mullatos from the northeast of the state of São Paulo.

- Blacks:

Donadi and Silva (2000), Louzada- Junior and others (2001), and Moraes and others (1993) described the frequency of HLA class II alleles and haplotypes in Black Brazilian population.

Donadi and Silva (2000) studied HLA-DR and –DQ antigens and found higher frequencies of -DR52, -DR53, -DR1, -DR2, -DQ1, -DQ3 and -DQ6. The HLA-DR5, -DR6, -DR7 and -DQ2 antigens appeared less frequently.

Louzada-Junior and others (2001) and Moraes and others (1993) reported similar HLA-DRB1 and -DQB1 *loci* frequencies in these Black Brazilian populations.

The HLA-DQA1 and -DPB1 families were examined only by Moraes and others (1993). The *HLA-DQA1*0102*, *-DPB1*0101* and *-DPB1*0402* were the most frequent alleles.

As for the haplotypes, *HLA-DRB1*1503-DQB1*0602* and *HLA-DRB1*0301-DQB1*02* were the most frequent combinations (LOUZADA- JUNIOR et al., 2001; MORAES et al., 1993).

(III) Comparison of Black, White end Mullato population

Moraes and others (1993) noticed great differences among the distribution of HLA-DRB1 alleles in Blacks and Whites. As showed in Table 3, some HLA-DRB1 alleles were found only in Whites (*-DRB1*0404*) and others only in Blacks (*-DRB1*1503*, *-DRB1*0302*). Among Whites, the HLA class II genes were more polymorphic than in Blacks. This finding is atypical and contradictory with others articles comparing White and Black groups and the authors recognized that there might be some bias in their sample (MORAES et al., 1993). The haplotypes were the most distinct and elucidative element between Whites and Blacks in this article, because some of them were found only in the Blacks (*HLA-DRB1*1503-DQA1*0102-DQB1*0602*, *-DRB1*1101-DQA1*0102-DQB1*0602*, *-DRB1*1102-DQA1*0501-DQB1*0301* and *-DRB1*0901-DQA1*03-DQB1*0201*).

According Louzada-Junior and others (2001), the *HLA-DRB1*0103*, *-DRB1*0405* and *-DRB1*1103* alleles were observed only in Whites, while the *-DRB1*0406* and *-DRB1*1202* alleles were identified only in Mulattos. As for haplotypes the *HLA-DRB1*0401-DQB1*0302* and *-DRB1*0404-DQB1*0301* were reported only in Whites, and the *-DRB1*0406-DQB1*04* and *-DRB1*1202-DQB1*0602* only in Mulattos.

Probst and others (2000), found differen-

Table 3. HLA –DRB1 allele frequencies in Black Brazilians.

HLA *locus*	Frequency %		
	Alleles	Moraes et al. (N= 72)	Louzada Jr et al. (N= 47)
DRB1	0101	4,1	6,4
	0102	2,7	5,6
	1503	20,8	7,4
	0301	18	7,4
	0302	11,1	6,4
	0407	1,3	0
	1101	15,2	5,6
	1102	11,1	3,2
	1201	9,7	1,1
	1301	12,5	7,4
	1303	4,1	1,1
	07	18	11,7
DQB1	0501	26,4	10,1
	0602	34,7	13,8
	0601	0	1,1
	0201	41,6	21,3
	0301	33,3	12,8
	0302	8,3	4,3
	0303	2,7	0
	0401	0	9,6

Note: N = number of subjects.

ces among antigen frequencies in Whites and Mulattos. The HLA-DR18 antigen was found in Mulattos, but not in Whites, and the -DR12 antigen was found only in Whites. Regarding haplotypes, *HLA-DR5-DQ7* and *-DR2-DQ1* were typed in Whites but not in Mulattos.

Differences were observed in regard to the HLA-DR7 antigen (present in 12% of Whites, 22% of Mulattos and 5% of Blacks), -DR8 and -DR13 (2% in Whites and absent in Blacks and Mulattos), -DR9 (15% in Whites, 13% in Mulattos and absent in Blacks) and -DR14 (present in 4% of Whites, 4% of Mulattos and 17% of Blacks).

DISCUSSION

(I) Population samples

Among articles that used race/ethnic concepts to divide the population sample in Whites, Blacks and Mulattos, only one, by Probst and others (2000), specified the criteria utilized to include individuals in a determinate group. They admitted, for example, that among White sample, there were individuals with known Black or Amerindian ancestry and that people with Black phenotype feature may be included in Mulatto group. The fact that most authors didn't specify their racial classification criteria made it difficult to analyze the data reported in the literature.

Articles about HLA class II that used urban population samples of Brazilian North, Northeast and West-Center weren't found, so it wasn't possible to obtain a representative population group of Brazilian people. This fact makes it difficult the extern validation or the extrapolation of these results to individuals living in areas yet not studied.

(II) Methods

The methods used to detect the HLA were not uniform. Some typed the alleles based on DNA molecular analysis, while others used the detection of antigens expressed in surface of cell membranes (linfocitotoxicity method).

The HLA typing with classic serologic techniques is still widely used in the whole world although adequate results with this technique are difficult to be obtained due to strong cross reaction among different antigens (FERNANDES et al., 2003). Although DNA-based typing methods also have pitfalls similar to those of serology (e.g., "cross-reaction" of oligonucleotide probes) they have the advantage of typing alleles.

The possibility of wrong typing or biologic sample switch should always be considered when unexpected haplotypes combinations are seen. The unusual haplotypes can only be ruled out or confirmed after comparison with anterior molecular and serologic typing, after a new sample typing and after family segregation analysis.

(III) Brazilians Amerindians and non-Amerindians

The South American tribes reveal a notable grade of HLA polymorphism restriction when compared to other continental populations. This restriction is characteristic of all Native Americans, including those of North America. The isolation of the analyzed tribes doesn't completely explain this finding, because in other parts of the world, like Australia, tribes are as isolated as those and don't present this pattern of restriction (CERNA et al., 1993). Some possible reasons are suggested to explicate this finding: the tribes could be originated from small number of founders and it is also feasible that the homogeneity of the alleles occur as a result of a great population bottleneck because of diseases and a hostile environment. This could be associated with the predominance of certain alleles that may confer a selection advantage. Finally, a random genetic drift in the gene pool occurring in isolated tribes could lead to this state of restricted polymorphism. (CERNA et al., 1993)

The diversity of HLA-DQ alleles and haplotypes is greater in Asian, European and African populations than in Native Americans (SOTOMAIOR et al., 1998). The conservation of haplotypes in populations of different continents could indicate that they are evolving together under the effect of natural selection (SOTOMAIOR et al., 1998). Combinations of HLA-DRB1-DQ are more variable than those

with -DQA1-DQB1, therefore they are probably less susceptible to restrictions from natural selection. Its strong conservation among South and North Americans propose a great role for founder effect and the random genetic deriver in the formation of the class II HLA haplotypes diversity in Native Americans (SOTOMAIOR et al., 1998). The HLA-DQ alleles show smaller level of polymorphism than -B, -DPB1 and -DRB1 in the same Amerindian populations. This isn't different from what is seen in other populations. The antigens detected in the Guarani and Kaingang groups are well known because they can be found in other South-American Indians (PETZL-ERLER et al., 1993). The HLA-DR4 antigens of both tribes diverge and a detailed analysis showed that -DR is more heterogeneous than it was previously reported (PETZL-ERLER et al., 1993). The HLA-DR11 antigens weren't found in non-mixed South-American Indian populations. This may be considered as a genetic marker of admixture in new Brazilians (PETZL-ERLER et al., 1993). No specific Amerindian class II antigen was found in high frequency in Kaingang tribe, and many alleles that suggest admixture with new Brazilians were encountered in Guarani individuals (PETZL-ERLER et al., 1993). In spite all of this estimative suggests that more than 90% of the genetic ancestral contribution of this tribe was conserved. (PETZL-ERLER et al., 1993)

Like other Native Americans, the Ticuna tribe presents a reduction in the diversity of the HLA class II genes. This population was one the first to be detected as having the *HLA-DRB1*0807* allele (MACK; ERLICH, 1998). Subsequently, several Amerindian populations were shown to have this allele which differs from *HLA-DRB1*0802* in only one amino acid in the position 57 and is probably originated by a punctual mutation in the allele *-DRB1*0802*, which is the most common *-DRB1*08* allele in America (MACK; ERLICH, 1998). This mutation occurred in the end of the gene, responsible for codification HLA molecule peptide binding sites (ERLICH et al., 1997; MACK; ERLICH, 1998). The HLA-DRB1*0807 allele, associated with -B*3913, was observed only in South-American populations (ERLICH et al., 1997), and it is likely that this association collaborates with the immune response to local pathogens and functional adaptation and might have clinical applications in the selection of bone marrow transplantation. (MORAES et al., 2004)

The presence of some alleles and haplotypes in low frequencies, like HLA-DRB1*0801 and -DPB1*0101, in Ticuna tribe may suggest that there is a certain grade of African and Caucasian admixture in this population. (ERLICH et al., 1997; MACK; ERLICH, 1998)

Another new allele founded in Guarani's, HLA-DRB1*1413, is similar to -DRB1*1402 (PANDO et al., 1994). This allele seems to be originated from a segment switch between two alleles, HLA-DRB1*1402 e -DRB1*0411. It was the only HLA-DR6 allele found in this tribe and differs from -DRB1*1402 in the HLA molecule peptide binding site. (PANDO et al., 1994)

As observed in Brazilian and South-American Indian tribes, the HLA-DQ alleles, in Black, White and Mulatto populations, demonstrated smaller level of polymorphism than -DRB1 locus. (LOUZADA-JUNIOR et al., 2001)

CONCLUSION

The HLA system is an important tool to assess the history of human populations and to study the structure of populations recently formed, such as the Brazilian populations analyzed here. These results in Blacks, Whites and Mulattos, which comprise most of the Brazilian population, illustrate the heterogeneous composition of this population with many individuals exhibiting a mixture of HLA alleles and haplotypes that are typical of Caucasian, Black and native Amerindian populations. Besides, they reinforce the concept that the HLA system is an important tool to access the history of human populations.

Polimorfismo do HLA de classe II em populações brasileiras

Resumo

A investigação da distribuição e freqüência dos genes HLA (Human Leukocyte Antigens) em populações presumivelmente saudáveis é importante para avaliar a participação desses genes na susceptibilidade e proteção a doenças, para avaliar a origem genética das populações e para auxiliar na realização de transplantes. Os avanços na biologia molecular têm permitido um melhor entendimento desse sistema. Além disso, informações sobre as moléculas HLA de classe II, tais como seu mecanismo de ação, função e polimorfismo genético têm colocado esse sistema como marcador da composição das populações. Os genes HLA de classe II parecem ser associados a alguns grupos étnico-raciais mais que a outros. Usando essas características genéticas, é possível demonstrar, por exemplo, o grau de mistura de caucasianos, africanos e ameríndios que contribuem, de modo significante, para a origem da população brasileira, bem como esclarecer alguns aspectos da ancestralidade dessas populações, o que ajuda na realização de estudos populacionais com o objetivo de obter informações sobre a história, formação, migração e composição de grupos populacionais de acordo com suas peculiaridades locais. Esse tema assume relevância em virtude da freqüência dos antígenos, alelos e haplótipos HLA de classe II na população brasileira.

***Palavras-chave**: HLA; população brasileira; complexo principal de histocompatibilidade.*

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