INTRODUCTION

The West Mexican Mayos form an isolated ethnic Amerindian group, which lives on a flat half desert and half cultivated area, Southern Sonora and North Sinaloa, see Fig. (1). They speak a Nahua/Aztec type language with some dialects that do not hinder mutual understanding. They call themselves Yoremes and probably migrated to the present day location from the North (Colorado River Basin) about 1,000 years ago [1]. They usually get married within their own group [1] which is important for the analyses of our results. Whether the Nahua type language (Mayo) also a sign of Mexica or Aztec relatedness is unknown, since Mexicas imposed their language to other probably non-genetically related Mexican groups [2]. Later, the Spanish conqueror Hernan Cortes arrived to the Mexicas Empire in 1,519 AD which was sized and destroyed by war and invaders’ born-diseases [3].

The present study aims: 1) To relate Mayos group with other Amerindian groups; and 2) To relate Mayos with other worldwide groups, in order to test the uniqueness of all Amerindian groups [4] with respect to their HLA profiles (different loci allele frequencies). This is important for establishing transplant programs in rural areas where some ethnic groups still live, i.e. Mayos, and for studying the epidemiology of HLA linked disorders.

In order to perform this work, a sample of sixty unrelated Mayos has been HLA typed and thereafter the genetic relationship with others Amerindians tested by HLA-A, -B, -DRB1 and -DQB1 DNA typing calculating genetic distances, neighbor-joining dendrograms and correspondence analyses.

MATERIALS AND METHODS

Population Samples

We studied sixty unrelated healthy individuals from the Mayos ethnic group. They were HLA class I and class II typed. They were living at Capomos town, Municipio del Fuerte, in Sinaloa State, northeast Mexico. In the Mayos communities the inbreeding pedigrees are common but we selected only those unrelated individuals for our study. Each individual was born in the Mayos area, their four grandparents had been born in the same area and spoke their own Mayo language. All participants gave their written consent for being included in the present study.

The origin of all other populations used for comparisons is detailed in Table I: 14,896 chromosomes were studied in

Abstract: HLA class I and class II alleles have been studied in 60 unrelated people belonging to Mayos ethnic group, which lives in the Mexican Pacific Sinaloa State. Mayos HLA profile was compared to other Amerindians and worldwide populations' profile. A total of 14,896 chromosomes were used for comparisons. Genetic distances between populations, Neigbour-Joining dendrograms and correspondence analyses were performed to determine the genetic relationship among population. The new specific Mayo HLA haplotypes found are: HLA-A*02-B*35-DRB1*1406-DQB1*0301; HLA-A*02-B*48-DRB1*0404-DQB1*0302; HLA-A*24-B*51-DRB1*0407-DQB1*0302 and HLA-A*02-B*08-DRB1*0407-DQB1*0302. However, the typical Meso American HLA-DRB1*0407 represents a 40% of all DRB1 alleles. While common HLA characteristics are found in Amerindian distant ethnic groups, still new group specific HLA haplotypes are being found, suggesting that a common founder effect (i.e. high DRB1*0407) is noticed. Moreover, new HLA haplotypes are almost certainly appearing along time probably due to specific pathogen (?) selection for diversity. Mayo language is close to the Tarahumara one (another geographically close group); notwithstanding both groups are not genetically close according to our results, showing again the different evolution of genes and languages, which do not correlate. Finally, Sinaloa is one of the Mexican States in which more European genes are found. However, the results presented in this paper, where no European HLA genes are seen in Mayos, should have a bearing in establishing transplant programs and in HLA and disease studies.
total, including populations from different origins (Caucasoids, Orientals, Polynesians, Micronesians, Na-Dene, Eskimos and Amerindians). In particular, the Amerindian group includes tribes from the following linguistic families: Macro-Mixteco (Mixtecs, Zapotecans and Mazatecans), Macro-Maya (Mixe and Mayas), Macro-Yuma (Seris), Andean (Quechua and Aymaras), Chibcha (Arsario, Kogi, Arhuaco and Cayapa), Arawak (Wayu), and Ge Pano Caribe (Xavantes, Mataco and Toba).
HLA Typing and DNA Sequencing

HLA class I (A and B) and class II (DRB1 and DQB1) allele families typing was performed by polymerase chain reaction–sequence specific oligonucleotide (PCR-SSO) reverse dot blot hybridization (Amplicor, Hoffmann La Roche, Basel, Switzerland) (according to IMGT/HLA version 2.6, July 2004). HLA-DRB1 and DQB1 high-resolution typing was done by DNA sequencing in a Perkin Elmer 310 automated DNA sequencer (Foster City, CA, USA). The sequences were analyzed using the IMGT/HLA sequence database (http://www.ebi.ac.uk/imgt/hla/align.html).

Statistical Analysis

Statistical analysis was performed with Arlequin v2.0 software kindly provided by Schneider [5]. In summary, this program calculated HLA-A, -B, -DRB1, and –DQB1 allele frequencies, Hardy-Weinberg equilibrium and the linkage disequilibrium (D'; also named LD) [6] and their level of significance (P) for 2X2 comparisons was determined [7] and the 11th International Histocompatibility Workshop methodology [6]. In addition, the most frequent complete haplotypes were deduced from: (1) the 2, 3, and 4 HLA locus haplotype frequencies [8]; (2) the previously described haplotypes in other populations [9]; and (3) haplotypes if they appeared in two or more individuals and if the alternative haplotype was well defined [9]. In order to compare phenotype and haplotype HLA frequencies with other populations, the reference tables of the 11th and 12th International HLA Workshops are used (see also Table 1) [10, 11].

RESULTS

Characteristic HLA Allele Frequencies in the Mayos Population Compared to other Populations

The expected and observed genotype frequency values for HLA-A, -B, and –DQB1 loci were in Hardy-Weinberg equilibrium. Table 2 shows the HLA frequencies found in the Mayos population. HLA-A and –B were typed on 60 individuals. Ten different HLA-A and fifteen different HLA-B alleles were found in the Mayos ethnic group. The most frequent HLA-A alleles were A*02 (allele frequency=0.44) and A*24 (allele frequency=0.36) whereas the most frequent HLA-B alleles were B*35 (allele frequency=0.25), B*39 (allele frequency=0.17) and B*51 (allele frequency= 0.17).

With respect to the HLA class II, 60 individuals were typed. Eighteen different HLA-DRB1 alleles were found, but only two of them had frequencies higher than 0’1 (DRB1*0407 and DRB1*1406), the sum of these two allelic frequencies was more than 0’6. Other three alleles common in Amerindians have been found in this ethnic group with allelic frequencies between 0’05-0’1 (DRB1*0403, DRB1*0404 and DRB1*0802). DQB1 allele frequencies reflect the DRB1 locus allele distribution due to the strong linkage disequilibrium level between these two loci, thus, the most frequent HLA-DQB1 alleles were DQB1*0302 (allele frequency=0.63), DQB1*0301 (allele frequency=0.18) and DQB1*0402 (allele frequency=0.11).

Two types of analysis were done in order to compare Mayos HLA frequencies with other world population’s frequencies: 1) with pooled DRB1 and DQB1 data; and 2) with DRB1 only. It was not possible to carry out a study comparing frequencies of HLA class I and II jointly due to the lack of class I studies in many Amerindian and other populations. The single DRB1 study was carried out in order to compare the American Indian HLA population frequencies with those of Polynesians, Melanesians and Micronesians, who lacked DQB1 analyses, see Table 1, Table 3 and Fig. (2). HLA-DRB1, DQB1 neighbor-joining tree grouped together the Amerindians and separated them from Na-Dene and Eskimo Native American groups and also from the Orientals and Caucasoids, Fig. (3). When the Polynesians, Melanesians and Micronesians were included (see Table 1) the topology of the tree (DRB1 alone) does not change (data not shown), it is also seen in the correspondence analysis, Fig. (2). This effect is more evident when genetic distances are considered (Table 3).

Genetic distances between Mayos and other populations show that Mayos are both close to Meso and South Americans (Table 3). Indeed, Kogi (11.20x10-2, Colombia), Teenek (11.38x10-2, Mexico), Mayans (13.17 x10-2, Guatemala), Arsario (18.13 x10-2, Colombia), Mazatecans (20.44 x10-2, Mexico) and Mixteco (23.20 x10-2, Mexico) show the closest genetic distances to Mayos, followed by Eastern Toba, Arhuaco, Seri, Nahuas and the rest of Amerindian populations. A discontinuity between Amerindians and the other world groups (including Na-Dene and Eskimos) is observed. With respect to Guarani population, we could observe that a more larger genetic distance exists with Mayos; larger than with other non Amerindian population (Athabaskans), this fact may be due to the low number of HLA typings of the Guaraní population or to admixture (Table 3).

HLA-A, -B, -DRB1 and –DQB1 Linkage Disequilibrium Analysis in Mayos Compared to other Populations

Associations between different HLA loci were estimated. The most probable two loci haplotype combinations (A-B, B-DRB1 and DRB1-DQB1) were calculated (data not shown).

The ten most frequent extended haplotypes are depicted in Table 4. Mayos extended HLA haplotypes have been obtained for the first time, allowing their comparison with the previously reported ones in other populations (Table 4 and its footnote).

The DRB1*0407-DQB1*0302 was associated with A*24-B*39, A*02-B*35, A*24-B*35, A*02-B*40, A*24-B*51, A*02-B*39 and A*02-B*08, meanwhile DRB1*
Table 1. Populations Included in the Analysis. A Total of 14,896 Chromosomes were Analyzed. Geographical Locations are Represented in [26]

| ID | Populations       | N  | Ref. | ID | Populations       | N  | Ref.          |
|----|-------------------|----|------|----|-------------------|----|--------------|
| 1  | Mayos             | 60 | -    | 38 | Buyi              | 70 | [9]          |
| 2  | Nahuaas           | 85 | [2]  | 39 | Manchu            | 50 | [33]         |
| 3  | Aymaras           | 102| [21] | 40 | Koreans           | 100| [9]          |
| 4  | Quechuans         | 80 | [22] | 41 | Japanese          | 493| [9]          |
| 5  | Mazatecans        | 89 | [4]  | 42 | Khalk Mongolians  | 202| [34]         |
| 6  | Mayans            | 132| [26] | 43 | Tuvanians         | 197| [35]         |
| 7  | Seri              | 100| [17] | 44 | Khoton Mongolians | 85 | [34]         |
| 8  | Mixe              | 55 | [17] | 45 | Germans           | 295| [9]          |
| 9  | Mixtecans         | 103| [17] | 46 | Sardinians        | 91 | [9]          |
| 10 | Zapotecans        | 75 | [17] | 47 | Italians          | 284| [9]          |
| 11 | Mexican Mestizos  | 99 | Unpublished | 48 | French           | 179| [9]          |
| 12 | Wayu              | 112| [27] | 49 | Spaniards         | 176| [36]         |
| 13 | Arhuaco           | 123| [27] | 50 | Spanish Basques   | 80 | [36]         |
| 14 | Kogi              | 67 | [27] | 51 | Algerians         | 102| [8]          |
| 15 | Arsario           | 20 | [27] | 52 | Berbers (Souss)   | 98 | [37]         |
| 16 | Cayapa            | 100| [28] | 53 | Moroccans         | 98 | [38]         |
| 17 | Xavantes          | 74 | [29] | 54 | Macedonians       | 172| [39]         |
| 18 | Guarani           | 32 | [17] | 55 | Cretans           | 135| [40]         |
| 19 | Toba Pilaga       | 19 | [29] | 56 | Ashkenazi Jews    | 80 | [41]         |
| 20 | Mataco Wichi      | 49 | [29] | 57 | Non Ashkenazi Jews| 80 | [41]         |
| 21 | Eastern Toba      | 135| [29] | 58 | Lebanese NS       | 59 | [11]         |
| 22 | Jaidukama         | 39 | Unpublished | 59 | Lebanese KZ       | 93 | [11]         |
| 23 | Teenek            | 55 | [19] | 60 | Moroccan Jews     | 94 | [42]         |
| 24 | Lakota Sioux      | 302| [30] | 61 | Danish            | 124| [9]          |
| 25 | Terena Indians    | 60 | [31] | 62 | Chuvashians       | 82 | [43]         |
| 26 | Tarahumaras       | 44 | [18] | 63 | Russians          | 200| [44]         |
| 27 | Lamas             | 83 | [23] | 64 | Western Samoa     | 102| [45]         |
| 28 | Eskimos           | 35 | [32] | 65 | Madag            | 65 | [46]         |
| 29 | Athabaskans       | 124| [24] | 66 | Rabaul           | 60 | [46]         |
| 30 | Tlingit           | 53 | [9]  | 67 | New Caledonia     | 65 | [46]         |
| 31 | Nivkhs            | 32 | [32] | 68 | Fidji             | 57 | [46]         |
| 32 | Udegeys           | 23 | [32] | 69 | Papua New Guinea  | 57 | [46]         |
| 33 | Koryaks           | 92 | [32] | 70 | Central Desert    | 152| [47]         |
| 34 | Chukchi           | 59 | [32] | 71 | Ainu              | 50 | [48]         |
| 35 | Kets              | 22 | [32] | 72 | Yuendumu          | 119| [47]         |
| 36 | Evenks            | 35 | [32] | 73 | Cape York         | 80 | [49]         |
| 37 | Singapore Chinese | 71 | [9]  | 74 | Kimberley         | 82 | [49]         |
Table 2. HLA-A, -B, -DRB1 and -DQB1 Allele Frequencies in the Studied Mayos Population

| Alleles | %  | Alleles | %  | Alleles | %  |
|---------|----|---------|----|---------|----|
| HLA-A*  |    |         |    |         |    |
| 0106    | 0.8| 0107    | 1.7| 0201    | 0.8|
| 02      | 44.2| 0202    | 4.2| 0203    | 5.8|
| 03      | 1.7| 0204    | 7.5| 0301    | 0.8|
| 11      | 1.7| 0205    | 0.8| 0302    | 62.6|
| 23      | 2.5| 0206    | 50.1| 0401    | 0.8|
| 24      | 35.8| 0207    | 50.1| 0402    | 10.8|
| 26      | 2.5| 0208    | 0.8| 0501    | 0.8|
| 31      | 2.5| 0209    | 3.3| 0601    | 0.8|
| 32      | 0.8| 0210    | 0.8| 0602    | 9.3|
| 35      | 25.0| 0211    | 0.8| 0603    | 3.3|

HLA-DRB1*  

| Alleles | %  | Alleles | %  | Alleles | %  |
|---------|----|---------|----|---------|----|
| 0101    | 0.8| 0102    | 2.5| 0201    | 5.8|
| 0301    | 1.7| 0302    | 62.6| 0401    | 0.8|
| 0403    | 5.8| 0404    | 7.5| 0402    | 10.8|
| 0407    | 50.1| 0408    | 0.8| 0501    | 0.8|
| 0701    | 0.8| 0702    | 0.8| 0603    | 3.3|
| 0801    | 0.8| 0802    | 9.3| 0609    | 0.8|
| 1301    | 2.5|         |    |         |    |

HLA-DQB1*  

| Alleles | %  | Alleles | %  | Alleles | %  |
|---------|----|---------|----|---------|----|
| 0101    | 0.8| 0102    | 2.5| 0201    | 5.8|
| 0301    | 1.7| 0302    | 62.6| 0401    | 0.8|
| 0403    | 5.8| 0404    | 7.5| 0402    | 10.8|
| 0407    | 50.1| 0408    | 0.8| 0501    | 0.8|
| 0701    | 0.8| 0702    | 0.8| 0603    | 3.3|
| 0801    | 0.8| 0802    | 9.3| 0609    | 0.8|
| 1301    | 2.5|         |    |         |    |

Fig. (2). Correspondence analysis showing a global view of the relationship among Amerindian, Na-Dene, Eskimo, Asian, European and Polynesian populations according to HLA-DRB1 allele frequencies in n dimensions (bi-dimensional representation). Grey intensity represents an approximate grouping of populations.
### Table 3. Genetic Distances (DA) between Mayos and other Populations (x 100) Obtained by Using HLA-DRB1 Allele Frequencies

| Population         | DA | Population          | DA | Population | DA |
|--------------------|----|---------------------|----|------------|----|
| Kogi               | 11.20 | Athabaskan         | 63.46 | Algerians | 78.77 |
| Teenek             | 11.38 | Tuvinians           | 65.05 | Chukchi   | 78.96 |
| Mayans             | 13.17 | Russians            | 65.59 | Moroccan Jews | 80.02 |
| Arsario            | 18.13 | French              | 66.09 | Ashkenazi Jews | 80.61 |
| Mazatecan          | 20.44 | Lebanese-KZ        | 68.86 | Udegeys   | 80.69 |
| Mixteco            | 23.20 | Khalk-Mongolian     | 69.24 | Eskimos   | 80.88 |
| Eastern-Toba       | 23.32 | Germans             | 69.39 | Western Samoa | 83.37 |
| Arhuaco            | 24.22 | Ainu                | 69.96 | Fidji     | 84.19 |
| Seri               | 26.73 | Japanese            | 69.96 | Kets      | 84.27 |
| Nahuas             | 27.33 | Koreans             | 70.74 | Sardinians | 84.48 |
| Zapotocans         | 29.37 | Spaniards           | 70.95 | Manchu    | 84.87 |
| Lakota Sioux       | 30.05 | Danish              | 71.23 | Evenks    | 86.05 |
| Wayu               | 30.45 | Guaraní             | 71.62 | Singapore-Chinese | 86.72 |
| Toba-Pilaga        | 30.72 | Italians            | 72.40 | New Caledonia | 90.12 |
| Mixe               | 30.98 | Tlingit             | 72.73 | Buyi      | 90.25 |
| Quechuas           | 31.47 | Moroccans           | 73.03 | Nivkh    | 90.63 |
| Mexican Mestizos   | 33.93 | Khorton-Mongolian   | 74.60 | Rabaul    | 91.81 |
| Cayapa             | 37.40 | Lebanese-NS         | 75.36 | Cape-York | 95.58 |
| Tarahumaras        | 37.96 | Cretans             | 75.58 | Central-Desert | 95.74 |
| Lamas              | 40.49 | Berber-Souss        | 75.59 | Madang    | 97.04 |
| Mataco-Wichi       | 41.29 | Macedonians         | 77.33 | Yuendumu  | 98.45 |
| Jaidukama          | 41.50 | Chuvashians         | 77.66 | Papua New Guinea | 99.24 |
| Aymara             | 42.45 | Non Ashkenazi Jews  | 77.77 | Kimberley | 100 |
| Terena Indians     | 43.08 | Spanish Basques     | 78.15 |          |    |
| Xavantes           | 52.25 | Koryaks             | 78.34 |          |    |

1406-DQB1*0301 was associated with A*2-B*35; DRB1*0404-DQB1*0302 was associated with A*02-B*48 and DRB1*0802-DQB1*0402 was associated with A*02-B*35.

The most frequent extended HLA haplotypes have Amerindian characteristics and it has been found in other Amerindian populations. The most frequent extended HLA haplotype A*24-B*39-DRB1*0407-DQB1*0302 (8.2%) has also been found only in Mazatecan Amerindian population. Six of the ten most frequent Mayos haplotypes have been found in other Amerindians populations, mainly in other Meso-American populations as Mazatecan, Seri, Mixe, Teeneks, Mixtecs, Mayans, Nahuas and Zapotecans. Four of them have not been found in any other worldwide ethnic group, these haplotypes seem to be specific for this Mexican ethnic group (Table 4 and its footnote).

### DISCUSSION

#### Mayos and Mexican Populations

We studied an isolated population from Northeast Mexico (Mayos) which confirmed the limited HLA polymorphism found in other isolated tribes from Meso and South America. We detected only ten HLA-A alleles and fifteen HLA-B different alleles in this population. Only two (A*02 and A*24) HLA-A alleles and three (B*35, B*40 and B*51) HLA-B alleles had frequencies higher than 0.1. With respect to HLA class II genes, only two (DRB1*0407 and DRB1*1406) HLA-DRB1 alleles and three (DQB1*0302, DQB1*0301 and DQB1*0402) HLA-DQB1 alleles had frequencies higher than 0.1. All of these HLA class I and II alleles have already been described in other Mexican populations [2, 4, 17, 18, 19].
Neighbour-Joining dendrogram and correspondence analyses correlate Mayos tribe together with Mexican populations like Teeneks and Tarahumaras, Fig. (3), and also with Nahuas ethnic group, Fig. (2). Regarding the genetic distances (a bidimensional parameter), Kogi from Colombia, and Mayans from Guatemala are the populations most related to Mayos (Table 3).

We can deduce from HLA genetic results (allele frequencies and extended haplotypes) that our Mayos sample has not had any contact with European people, because it would be clearly shown by using these particular HLA genetic markers [20].

Mayos and South American Populations

The results of HLA genetic typing in Mayos population confirm that they belong to Amerindian HLA genetic profile.

The presence of HLA-B*48 allele in this population is remarkable (allele frequency= 0.05, Table 2) as it is lacking in all Mexican populations so far except in Andean populations like Aymaras, Quechus and Lamas [21-23].
HLA-B*48 is relatively common in Na-Dene and Asian populations [9, 24]. The presence of this allele (together with DRB1*0901) in a few Amerindian populations is the only evidence that could strictly support the three wave model of peopling America including Meso and South America [25] because these two alleles would be shared with southern Asian populations.

All Amerindian ethnic groups bearing HLA-B*48 allele in its HLA profile are living in the Pacific Coast (Mayos and Andean Populations). This might mean the existence of southern Asian migrations to coastal Meso and South America.

Amerindian Languages

Again, while Mayos seem to be genetically related with South American populations [Kogi, Table 1; Terena and Aymaras, Fig. (3); and Wayu and Quechua, Fig. (2)], languages spoken by these groups are disparate and belong to far related linguistic branches.

It is also remarkable that Tarahumara ethnic group, which speaks a similar language to Mayos and is geographically very close to it, genetically shows relatively distant, Table 2, Fig. (2) and Fig. (3). This is a general phenomenon in Amerindians: genes and languages do not correlate.

Finally, Mayos ethnic group lives in Sinaloa Mexican State and at least in our sample European HLA genes and haplotypes are not found; this occurs in spite of that Sinaloa is one of the Mexican States where more European HLA alleles are found [20].

These facts may be taken into account when setting up transplantation programs and also for studying HLA and disease associations.

ACKNOWLEDGEMENTS

This work was supported in part by three grants from the Fundacion Mutua Madrileña Automovilista (2004, 2005, 2006) and Ministerio de Sanidad (PI-051039).

ABBREVIATIONS

HLA = Human leukocyte antigen
NJ = Neighbor-joining

REFERENCES

[1] Scheffler, L. Los indigenas Mexicanos. Panorama, Mexico DF, 1992.
[2] Vargas-Alarcon, G., Moscoso, J., Martinez-Laso, J., Rodriguez-Perez, J.M., Flores-Dominguez, C., Serrano-Vela, J.I., Moreno, A., Granados, J., Arnaiz-Villena, A. Origin of Mexican Nahuas (Aztecs) according to HLA genes and their relationships with worldwide populations. Mol. Immunol. 2007, 44: 747-755.
[3] Lopez-Lujan, L. Los Mexicanos, últimos señores de Mesoamerica. In: Gran Enciclopedia de España y América. Espasa-Calpe/Argantiano, Madrid, 1983.
[4] Arnaiz-Villena, A., Vargas-Alarcon, G., Granados, J., Gomez-Casado, E., Longas, J., Gonzalez-Hevilia, M., Zuniga, J., Salgado, N., Hernandez-Pacheco, G., Guileen, J., Martinez-Laso, J. HLA genes in Mexican Mazatecans, the peopling of the Americas and the uniqueness of Amerindians. Tissue Antigens 2000, 56: 405-416.
[5] Schneider, S., Roessler, D., Excoffier, L. ARLEQUIN: a software for population genetics database analysis. (2.0). Genetics and Biometry Laboratories, Department of Anthropology, University of Geneva, 2000.

Table 4. The Ten Most Frequent HLA-A, -B, -DRB1 and -DQB1 Extended Haplotypes in the Mayos Population. HF: Haplotype Frequency

| Haplotypes | HF (%) | Possible Origin |
|------------|--------|----------------|
| HLA-A*24-B*39-DRB1*0407-DQB1*0302 | 8.2 | Amerindian |
| HLA-A*02-B*35-DRB1*0407-DQB1*0302 | 7.3 | Amerindian |
| HLA-A*24-B*35-DRB1*0407-DQB1*0302 | 6.0 | Amerindian |
| HLA-A*02-B*35-DRB1*1406-DQB1*0301 | 4.2 | New |
| HLA-A*02-B*40-DRB1*0407-DQB1*0302 | 4.2 | Amerindian |
| HLA-A*02-B*48-DRB1*0404-DQB1*0302 | 3.3 | New |
| HLA-A*24-B*51-DRB1*0407-DQB1*0302 | 3.3 | New |
| HLA-A*02-B*39-DRB1*0407-DQB1*0302 | 2.7 | Amerindian |
| HLA-A*02-B*08-DRB1*0407-DQB1*0302 | 2.5 | New |
| HLA-A*02-B*35-DRB1*0802-DQB1*0402 | 2.5 | Amerindian |

Table 4 footnote: *Only found in Mazatecans (3.3%). † Found in Seri (18.2%); Teeneks (15.5%); Mayans (10.6%); Mixtecos (3%); Mazatecans (2.5%); Aymaras (1.7%); Peruvian Indians (1.7%). ‡ Found in Mayans (5%); Teeneks (3.7%); Seris (2.3%); Lakota-Sioux (2.2%); Aymaras (2.1%); Quechua (1.4%). § Not found in any other ethnic groups. ¶ Found in Aymaras (2.3%) and Mayans (0.7%). δ Found in Mazatecans (10.8%); Mixe (9%); Mayans (4.2%); Teeneks (3.7%); and Terena Indians (2.3%). ι Found in Aymaras (10.4%); Peruvian Indians (9.6%); Mayans (8.4%); Nahuas (6.1%); Mixtecos (6%); Seri (4.5%); Zapotecans (3%); and Mixe (1.5%).

Other haplotypes found are: HLA-A*02-B*15-DRB1*0802-DQB1*0402 (1.7%); HLA-A*02-B*39-DRB1*0403-DQB1*0302 (1.7%); HLA-A*02-B*39-DRB1*1406-DQB1*0402 (1.7%); HLA-A*02-B*48-DRB1*0407-DQB1*0302 (1.7%); HLA-A*02-B*51-DRB1*1301-DQB1*0603 (1.7%); HLA-A*03-B*51-DRB1*0407-DQB1*0302 (1.7%); HLA-A*24-B*07-DRB1*0802-DQB1*0402 (1.7%); HLA-A*24-B*15-DRB1*0407-DQB1*0302 (1.7%); HLA-A*24-B*40-DRB1*0407-DQB1*0302 (1.7%); HLA-A*24-B*40-DRB1*0802-DQB1*0402 (1.7%); HLA-A*24-B*51-DRB1*1406-DQB1*0301 (1.7%); HLA-A*68-B*40-DRB1*0407-DQB1*0302 (1.7%).

References: [4, 17, 21, 22, 26, 30, 31, 50].
[6] Imanishi, T., Akaza, T., Kimura, A., Tokunaga, K., Gojobori, T. Estimation of allele and haplotype frequencies for HLA and complement loci. In: Tsuji, K., Aizawa, M., Sasazuki, T. (Eds.), HLA 1991. Oxford University Press. Oxford, 1992, pp. 76-79.

[7] Mattiaz, P.L., Hede, D., Piazza, A., Ceppelini, R., Wodmer, W.F. New approaches to the population genetics and segregation analysis of the HLA system. In: Histocompatibility testing, 1970. Munksgaard, Copenhagen, 1970, pp. 193-206.

[8] Arnarz-Villena, A., Martinez-Laso, J., Gomez-Casado, E., Dominguez-Carpio, N., Mercado-Bustamante, R. Genetic relationships among various human populations indicated by MHC polymorphisms. Immunogenetics 1997; 47: 37-43.

[9] Imanishi, T., Akaza, T., Kimura, A., Tokunaga, K., Gojobori, T. Allele and haplotype frequencies for HLA and complement loci in various ethnic groups. In: Tsuji K, Aizawa M, Sasazuki T (Eds.), HLA 1991. Oxford University Press. Oxford, 1992, pp. 627-632.

[10] Clayton, J., Lonjou, C. Allele and Haplotype frequencies for HLA loci in various ethnic groups. In: Charon D (Ed.), Genetic diversity of HLA. Functional and medical implications. EDK, Paris, 1997, pp. 665-820.

[11] Saitou, N., Nei, M. The neighbor-joining method: a new method for reconstructing phylogenetic trees. Mol. Biol. Evol. 1987; 4: 406-425.

[12] Nei, M. Genetic distances between populations. Am. Nat. 1972; 106: 283.

[13] Nei, M. Analysis of gene diversity in subdivided populations. Proc. Natl. Acad. Sci. USA 1973; 70: 3321-3323.

[14] Nei, M., Tajima, F., Tateno, Y. Accuracy of estimated phylogenetic trees from molecular data. II. Gene frequency data. J. Mol. Evol. 1983; 19: 153-170.

[15] Young, F.W., Bann, C.M. A visual statistics system. In: Stine RA, Kao C (Eds.), Human genetics: current methods and applications. Sage Publications, London, 1996, pp. 207-236.

[16] Petzl-Erler, M.L., Gorodezky, C., Layrisse, Z. Anthropology report for the Latin American region: Amerindian and admixture populations. In: Charon D (Ed.), Genetic diversity of HLA. Functional and medical implications. EDK, Paris, 1997, pp. 337-345.

[17] Garcia-Ortiz, J.E., Sandoval-Ramirez, L., Rangel-Villalobos, H., Maldonado-Torres, H., Cox, S., Garcia-Sepulveda, C.A., Figueroa, F., Takahata, N., Klein, J. Polymorphism of the HLA class II loci in Siberian populations. Hum. Immunol 1993; 37: 213-222.

[18] Leffell, M.S., Fallin, M.D., Hildebrandt, W.H., Cavett, J.W., Iglehart, B.A., Zachary, A.A. HLA alleles and haplotypes among the Lakota Sioux: report of the ASHI minority workshops, part III. Hum. Immunol. 2004; 65: 78-89.

[19] Lazoar, A.M., Moraes, M.E., Marcos, C.Y., Moraes, J.R., Fernandez-Vina, M.A., Stastny, P. Evolution of HLA class I compared to HLA class II polymorphism in the Tarahumara Amerindians. Immunogenetics 1999; 50: 1138-1149.

[20] Grabovac, B., Sukernik, R.I., O'Uiginn, C., Zaleska-Rutczynska, Z., Blagitko, N., Ruldruga, O., Kosutic, T., Satta, Y., Figueroa, F., Takahata, N., Klein, J. Genetic diversity of HLA class II loci in the basal populations of Europe. Hum. Immunol 1999; 60: 1138-1149.

[21] Martinez-Laso, J., Sartakova, M., Allende, L., Konenkov, V., Moscoso, J., Silvera-Redondo, C., Pacho, A., Trapaga, J., Gomez-Casado, E., Arnaiz-Villena, A. HLA class II alleles in the sub-Saharan origin of the Greeks. Immunogenetics 2003; 55: 124-134.

[22] Cerna, M., Falco, M., Friedman, H., Macagno, A., Fernandez-Vina, M., Stastny, P. HLA and class II in the Basque, Portuguese, Spaniards, and Algerians studied by HLA allelic frequencies and haplotypes. Immunogenetics 1996; 45: 473-489.

[23] Mensalve, M.V., Edin, G., Devine, D.V. Analysis of HLA class I and class II in Na-Dene and Amerindian populations from British Columbia, Canada. Hum. Immunol. 1998; 59: 48-55.

[24] Greenberg, J.H., Turner, C.G., Zegura, S.L. The settlement of the Americas: a comparison of the linguistic, dental and genetic evidence. Curr. Anthrop. 1996; 37: 477-498.

[25] Gomez-Casado, E., Martinez-Laso, J., Moscoso, J., Zamora, J., Martin-Vila, M., Perez-Blas, M., Lopez-Santalla, M., Lucas, G.P., Silvera, C., Lowy, E., Arnaiz-Villena, A. Origin of Mayans according to HLA genes and the uniqueness of Amerindians. Tissue Antigens 2003; 61: 425-436.

[26] Yunis, J.J., Ossa, H., Salazar, M., Delgado, M.B., Deulofeu, R., de la C., Bing, D.H., Ramos, O., Yunis, E.J., Yunis, E.J. Major histocompatibility complex class II alleles and haplotypes and blood groups of four Amerindian tribes of northern Columbia. Hum. Immunol. 1994; 41: 248-258.

[27] Titus-Trachtenberg, E.A., Rickards, O., De Stefano, G.F., Ehrich, H.A. Analysis of HLA class II haplotypes in the Cayapa Indians of Ecuador: a novel DRB1 allele reveals evidence for convergent evolution and balancing selection at position 86. Am. J. Hum. Genet. 1994; 55: 160-167.

[28] Cerna, M., Falco, M., Friedman, H., Raimondi, E., Maccagno, A., Fernandez-Vina, M., Stastny, P. Differences in HLA class II alleles of isolated South American Indian populations from Brazil and Argentina. Hum. Immunol. 1993; 37: 213-222.

[29] Graf, L., Imanishi, T., Tokunaga, K., Zhu, D., Mizuki, N., Xu, S., Geng, Z., Gojobori, T., Tsuji, K., Inoko, H. Determination of amino acid alleles in the NKp44 gene in the Manchu population. In: Charron D (Ed.), Genetic diversity of HLA. Functional and medical implications. EDK, Paris, 1997, pp. 665-820.

[30] Martinez-Laso, J., Gazit, E., Gomez-Casado, E., Morales, P., Martinez-Quiles, N., Alvarez, M., Martin-Villa, J.M., Fernandez, V., Arnaiz-Villena et al.
Arnaiz-Villena, A. HLA DR and DQ polymorphism in Ashkenazi and non-Ashkenazi Jews: comparison with other Mediterraneans. Tissue Antigens 1996, 47: 63-71.

[42] Roitberg-Tambur, A., Witt, C.S., Friedmann, A., Safirman, C., Sherman, L., Battat, S., Nelken, D., Brautbar, C. Comparative analysis of HLA polymorphism at the serologic and molecular level in Moroccan and Ashkenazi Jews. Tissue Antigens 1995, 46: 104-110.

[43] Arnaiz-Villena, A., Martinez-Laso, J., Moscoso, J., Livshits, G., Zamora, J., Gomez-Casado, E., Silvera-Redondo, C., Melvin, K., Crawford, M.H. HLA genes in the Chuvashian population from European Russia: admixture of Central European and Mediterranean populations. Hum. Biol. 2003, 75: 375-392.

[44] Kapustin, S., Lyshchov, A., Alexandrova, J., Imyanitov, E., Blinov, M. HLA class II molecular polymorphisms in healthy Slavic individuals from North-Western Russia. Tissue Antigens 1999, 54: 517-520.

[45] Gao, X., Veale, A., Serjeantson, S.W. HLA class II diversity in Australian aborigines: unusual HLA-DRB1 alleles. Immunogenetics 1992, 36: 333-337.

[46] Gao, X., Bhatia, K., Trent, R.J., Serjeantson, S.W. HLA-DR,DQ nucleotide sequence polymorphisms in five Melanesian populations. Tissue Antigens 1992, 40: 31-37.

[47] Lester, S., Cassidy, S., Humphreys, I., Bennett, G., Hurley, C.K., Boettcher, B., McCluskey, J. Evolution in HLA-DRB1 and major histocompatibility complex class II haplotypes of Australian aborigines. Definition of a new DRB1 allele and distribution of DRB1 gene frequencies. Hum. Immunol. 1995, 42: 154-160.

[48] Bannai, M., Tokunaga, K., Imanishi, T., Harithara, S., Fujisawa, K., Juji, T., Omoto, K. HLA class II alleles in Ainu living in Hidaka District, Hokkaido, northern Japan. Am. J. Phys. Anthropol. 1996, 101: 1-9.

[49] Gao, X., Zimmet, P., Serjeantson, S.W. HLA-DR,DQ sequence polymorphisms in Polynesians, Micronesians, and Javanese. Hum. Immunol. 1992, 34: 153-161.

[50] de Pablo, R., Beraun, Y., Nieto, A., Calzada, J.E., Rementeria, M.C., Sanz, L., Lopez-Nevot, M.A., Martin, J. HLA class I and class II allele distribution in the Peruvian population. Tissue Antigens 2000, 56: 507-514.