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HLA-A, -B and -DR Allele and Haplotype Frequencies in the European American, African American, and Hispanic Populations in Dallas, Texas: Relatedness to the North American Population

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ABSTRACT

Objective: In the United States of America (USA) population, several studies focusing on frequencies of HLA alleles and their haplotypes have been reported, but HLA data in the USA population living in Dallas, Texas, are reported here for the first time. The aim of this study was to investigate the distribution of HLA in the populations of African American, European American, and Hispanic of Dallas, Texas and its genetic relatedness to the USA populations.

Material and Methods: We present the HLA data available from the Transplant Donor Program database of Southwestern Medical Center at the University of Texas at Dallas. The comparative study of their allele frequencies, characteristic haplotypes, genetic distances with other Americans residing in the USA is complemented by neighbor-joining dendrogram and correspondence analysis.

Results: The results of our study reflect a predominance of European and also Asian rather than African Ancestry for the Hispanic sample, especially those living in South of USA.

Conclusion: As new information, our study results show that the largest genetic distances between all USA groups were those of the African Americans compared with each of the other groups in four major races.

Key Words: African Americans, European Americans, hispanics, haplotype frequency, HLA, Dallas, Texas

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Introduction

Dallas is a county located in the U.S state of Texas within the Dallas-Fort Worth-Arlington metropolitan area in north central Texas. As of July 1, 2006, the historic period in Texas including Dallas is defined by the date of contact between aboriginal groups and the Spanish explorers in the 1500s (1). Historical accounts describe that the Dallas area was inhabited by numerous Indian groups before Anglo pioneers began settling in the 1800s. However, archaeologically, Indian groups cannot be found (2). In 1846, the Republic of Texas was annexed by the U.S and Dallas County was established. Dallas has historically been predominantly European American but its population diversified as it grew in size, and Hispanics outnumbered African-Americans for the first time in the 2000 census as the largest minority group in Dallas. The reason for this may be that Dallas is a major destination for Mexican immigrants seeking opportunities in the U.S, because Texas makes up part of the U.S-Mexico border. The current racial makeup of Dallas is 48.3 percent white, 35.5 percent Hispanic (Hispanics may be of any race, so are also included in applicable race categories), 11.3 percent African American, 3.3 percent Asian, 1.0 percent from two or more races, 0.3 percent Native American (American Indian and Alaska Native), 0.2 percent some other race, and 0.1 percent Native Hawaiian and other Pacific Islander according to the census taken in 2006 (3).

In the U.S population, several studies focusing on frequencies of HLA antigens and/or alleles and their haplotypes have been reported (4-6). However, HLA alleles and haplotypes in the Dallas, Texas (TX) population have not been reported previously. In the present work, it is intended to obtain the distribution of HLA-A, -B, -DR in the populations of African American, European American, and Hispanic of Dallas, Texas for the first time, in order to estimate gene and haplotype frequencies and compare them with the U.S population.

For these purposes, we extracted and presented HLA allele and haplotype frequency data available from the Transplant Donor Program database (TDP) of Southwestern Medical Center at the University of Texas at Dallas from three major U.S. census categories of race and ethnicity. A discriminatory classification of HLA allelic variation on the basis of observed population allele frequencies (very common, common, rare and unseen) based on genotyping for HLA A, B, and DRB1 is introduced. The comparative study of their allele frequencies, characteristic haplotypes and genetic distances with other

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Americans residing in the United States is complemented by a neighbor-joining dendrogram and correspondence analysis.

Materials and Methods

The HLA allele and haplotype frequency data was obtained from volunteer bone marrow donors from the TDP of Southwestern Medical Center at the University of Texas at Dallas. The sample represents a random sample of the entire registry. Informed consent of the donors for making the data publicly available was obtained from all individuals. HLA frequency data are presented on the basis of the three predominant US census categories for categorizing ethnic and racial groups: African Americans, European Americans and Hispanics. These categories from TDP input questionnaires define the self-described ethnic groups. 499 biologically unrelated individuals (195 African Americans, 170 European Americans, and 134 Hispanics) were extracted for presenting HLA frequency data and phylogenetic calculations. Proportionally, Dallas Hispanics samples remain represented lowest, comprising around 26.8% of the total typed samples, but a fall-off in available samples of the three minority groups is not noticeable for haplotypes.

Genotyping of HLA-A, B and DR loci was performed by means of the PCR-SSP method using micro SSP kits. This study presents the serologic equivalents of HLA-A, -B, and -DR alleles for a more direct comparison with previous literature. Since the HLA types of our samples were molecularly defined, we used the 2009 HLA Dictionary (the IMGT HLA nomenclature reports-HLADB 2.24.0, January 2009) to determine the serologic equivalents for HLA alleles.

We compared HLA-A-, -B-, and -DR allele frequencies between the Dallas population in our study and the U.S populations in the study of Maiers et al. (6). According to current literature, the recent work of Maiers et al. (2007) appears to be the study reporting the largest database of HLA-A-, -B-, and -DR typed individuals of four major races who reside in the United States: African Americans, Asians, European Americans, and Hispanics (6).

A90, B90 and DR90 were included in the estimation of gene and haplotype frequencies to represent the null alleles and the alleles which have no serologic equivalents based on the WHO assigned type presented in the IMGT HLA database at each of the respective loci. The following alleles were collapsed to A90, B90, DR90 at each of the respective loci: B*8201, B*4008→ B90 in our study; and A*0116N, A*0219, A*0230, A*0253N, A*0260, A*0307, A*2305, A*2425, A*2426, A*2612, A*3010, A*3109, A*3206, A*3403, A*6807, A*6815, A*6825, A*7409, A*7411→ A90, B*0721, B*0805, B*0812, B*1405, B*1540, B*1547, B*1554, B*1561, B*1808, B*3521, B*3522, B*3528, B*3914, B*4008, B*4012, B*4023, B*4040, B*4418, B*5119, B*5137, B*6702, B*8202→ B90, DRB1*0418, DRB1*1115, DRB1*1117, DRB1*1139, DRB1*1208, DRB1*1309, DRB1*1331, DRB1*1425, DRB1*1514→ DR90 in the study of Maiers et al.

Because of the multi-ethnic and multi-racial background of the U.S population, we carried out all the analyses for African Americans, European Americans, and Hispanics separately using an implementation of the expectation-maximization (EM) algorithm (7-9). Statistical analysis and the Hardy-Weinberg equilibrium (HWE) based on the exact test of Guo and Thompson was performed with Arlequin v3.11, a software for population genetics data analysis (Genetics and Biometry Laboratory, University of Geneva, Geneva, Switzerland), (10, 11). A phylogenetic tree (dendrogram) was constructed with the allelic frequencies by using the neighbour-joining (NJ) method (12) with the genetic distances between populations (13), by using the software DISPAN, which contained the programs GNKDST and TREEVIEW (14, 15). Correspondence analysis in three dimensions and its bidimensional representation was carried out by using the SSPS 15.0 for Windows (16).

Results

The frequencies of HLA-A, -B, and -DR alleles in our study population are summarized in Tables 1-3. We determined that all the groups are in HWE at all loci.

Two-loci haplotype frequencies

Table 4 shows the frequencies of the A-B haplotypes occurring at frequencies of more than 1%. We detected 291, 209 and 230 haplotypes in Dallas African Americans, Dallas European Americans, and Dallas Hispanics, respectively, predicted by the EM algorithm.

The strength of association of two alleles from A/B loci was determined by the D' values of the haplotypes (Table 5). Interestingly, the strongest association with the highest D' and Chi-square values in both Dallas African Americans (D'=0.35100, χ^2=37.01100) and Dallas European Americans (D'=0.63520, χ^2=126.88370) was the same: A1-B8, but was different in Dallas Hispanics: A28-B61 (D'=0.40900, χ^2=34.55300). The number of statistically significant A/B combinations identified at frequencies higher than 1% were 6 for Dallas African Americans and 9 for Dallas European Americans and Dallas Hispanics. We found some HLA-A alleles associated with multiple HLA-B in some of our ethnic groups. 3 and 2 statistically significant HLA-A alleles associated with multiple HLA-B were identified at frequencies higher than 1% in Dallas European Americans and Dallas Hispanics, in that order.

Three-locus haplotype frequencies

The overall degree of sharing among HLA haplotypes can be obtained from Table 6. As a reflection of the overall A-B-DR haplotype similarity among the three groups, we present the rank and order of haplotypes from the perspective of the 10 most common haplotypes in each group. For A-B-DR haplotypes, common alleles are defined here as those observed in the 10 most common haplotypes and rare alleles are those not present in the 10 most common haplotypes in each group.

The most common haplotype in Dallas African American sample is A2-B35-DR13, which is found in an estimated 0.020532 copies in Dallas African American sample. This haplotype is not seen in either Dallas European American or Dallas Hispanic samples at all. The only one of the ten most common A-B-DR haplotypes present in the Dallas African American sample, A2-B7-DR15, is rarely seen in Dallas His-

Table 1. HLA-A frequencies in the African American, European American, and hispanic populations of Dallas, Texas

	Census Groups					
	African Americans		European Americans		Hispanics	
Rank	Allele	Allele frequencies	Allele	Allele frequencies	Allele	Allele frequencies
1	A2	0.158974	A2	0.308824	A2	0.235075
2	A30	0.125641	A1	0.191176	A24	0.152985
3	A23	0.123077	A3	0.108824	A68	0.093284
4	A68	0.082051	A11	0.091176	A3	0.082090
5	A74	0.076923	A24	0.076471	A11	0.063433
6	A3	0.071795	A29	0.038235	A1	0.059701
7	A33	0.064103	A23	0.032353	A31	0.048507
8	A1	0.058974	A25	0.026471	A29	0.044776
9	A34	0.046154	A31	0.026471	A30	0.041045
10	A29	0.033333	A30	0.020588	A23	0.033582
11	A24	0.028205	A32	0.017647	A33	0.029851
12	A66	0.028205	A26	0.014706	A28	0.026119
13	A28	0.025641	A68	0.014706	A32	0.026119
14	A36	0.025641	A33	0.011765	A26	0.022388
15	A32	0.015385	A28	0.008824	A34	0.014925
16	A80	0.012821	A66	0.005882	A25	0.011194
17	A31	0.010256	A74	0.002941	A74	0.007463
18	A11	0.007692	A80	0.002941	A210	0.003731
19	A26	0.005128			A36	0.003731

panics, at rank 87. The other nine most common Dallas African American haplotypes are absent in Dallas Hispanics. Also, only two of the ten most common A-B-DR haplotypes present in the Dallas African American sample are seen in Dallas European Americans (the common Dallas European American haplotype A2-B7-DR15, the rare Dallas European American haplotype A1-B57-DR17 at rank 72.). The other eight most common Dallas African American haplotypes are absent in the Dallas European Americans.

The most common haplotype in the Dallas European American sample is A1-B8-DR17, which is found in an estimated 0.067150 copies in the Dallas European American sample, and is not seen in other two groups. Seven of the ten most common A-B-DR haplotypes present in the Dallas European American sample are seen in the other two groups. A3-B7-DR15 and A29-B44-DR7 are commonly seen and A2-B44-DR4, A1-B8-DR3, A2-B15-DR4, A2-B7-DR15, and A2-B51-DR13 are rarely seen in Dallas Hispanics. On the other hand, only two of the ten most common A-B-DR haplotypes present in the Dallas European American sample are seen in Dallas African Americans as seen in Table 6 (the common Dallas African American haplotype A2-B7-DR15, the rare Dallas African American haplotype A29-B44-DR7).

The most common haplotype in the Dallas Hispanics sample is A2-B35-DR8, which is found in an estimated 0.040621

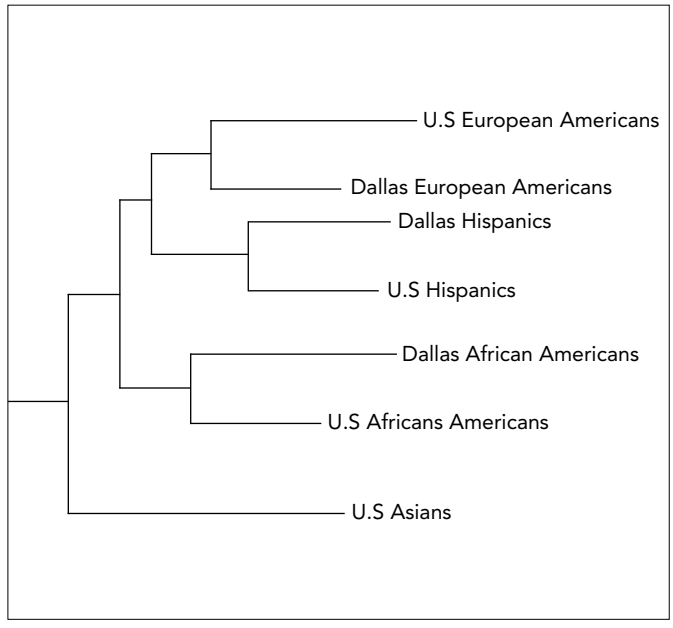

Figure 1. A global view of the relationship among Dallas and U.S populations represented by a neighbor-joining tree. The genetic distances (Da) between populations were calculated by means of HLA A, B, DR allele frequencies. Bootstrap values from 1000 replicates are depicted

Table 2. HLA-B frequencies in the African American, European American, and hispanic populations of Dallas, Texas

	Census Groups					
	African Americans		European Americans		Hispanics	
Rank	Allele	Allele frequencies	Allele	Allele frequencies	Allele	Allele frequencies
1	B53	0.130769	B8	0.179412	B35	0.156716
2	B15	0.089744	B44	0.147059	B39	0.085821
3	B35	0.074359	B7	0.105882	B51	0.067164
4	B44	0.064103	B35	0.076471	B44	0.059701
5	B58	0.061538	B15	0.044118	B14	0.055970
6	B7	0.061538	B51	0.044118	B40	0.052239
7	B42	0.053846	B39	0.038235	B15	0.044776
8	B57	0.046154	B40	0.038235	B18	0.044776
9	B8	0.046154	B18	0.035294	B7	0.041045
10	B70	0.041026	B27	0.035294	B61	0.033582
11	B45	0.038462	B57	0.032353	B48	0.029851
12	B49	0.038462	B14	0.029412	B52	0.029851
13	B81	0.033333	B49	0.020588	B8	0.029851
14	B51	0.028205	B62	0.020588	B57	0.026119
15	B18	0.025641	B13	0.017647	B45	0.022388
16	B39	0.017949	B41	0.017647	B50	0.022388
17	B52	0.017949	B45	0.017647	B13	0.018657
18	B72	0.017949	B38	0.014706	B27	0.018657
19	B14	0.015385	B50	0.014706	B49	0.018657
20	B50	0.015385	B60	0.014706	B38	0.014925
21	B27	0.012821	B61	0.011765	B41	0.014925
22	B55	0.012821	B47	0.005882	B56	0.014925
23	B13	0.007692	B52	0.005882	B58	0.014925
24	B41	0.007692	B53	0.005882	B62	0.014925
25	B63	0.007692	B55	0.005882	B53	0.011194
26	B78	0.007692	B58	0.005882	B37	0.007463
27	B37	0.005128	B70	0.005882	B55	0.007463
28	B40	0.005128	B37	0.002941	B60	0.007463
29	B38	0.002564	B48	0.002941	B65	0.007463
30	B5102	0.002564	B64	0.002941	B4005	0.003731
31	B56	0.002564			B42	0.003731
32	B60	0.002564			B63	0.003731
33	B62	0.002564			B64	0.003731
34	B90	0.002564			B73	0.003731
35					B78	0.003731
36					B90	0.003731

copies in the Dallas Hispanics sample, and is entirely absent in the haplotypes of other two groups. Only one of the ten most common A-B-DR haplotypes presents in the Dallas Hispanics sample, A29-B44-DR7, and is rarely seen in Dallas African Americans. This same haplotype and A3-B7-DR15 is cofigmmonly found in the Dallas European American sample. The dendrogram obtained with the neighbor-joining method is illustrated in Figure 1. These results were confirmed in the correspondence analysis, as illustrated in Figure 2. European Americans, African Americans, Hispanics, and Asians represent genetically distinct groups.

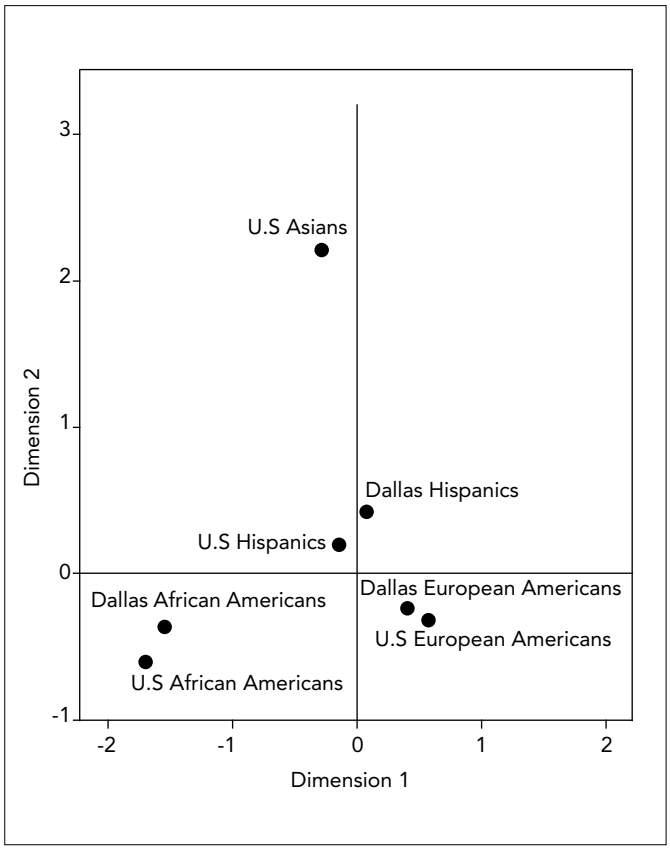

Figure 2. Bi-dimensional representation of correspondence analysis based on HLA A, B and DR allele frequencies, showing the relationship among Dallas and U.S populations

Discussion

The current study is the first to use a sample representative of the European American, African American, and Hispanic populations living in Dallas, TX, stratified by its three main ethnic groups with a depth analysis of the relationship with each other and their ancestries.

To our knowledge, the works of Mori et al. (1975) and Maiers et al. (2007) appear to report the largest database of HLA-A-, -B-, and -DR typed individuals of five major races who reside in the United States: African Americans, Asians, European Americans, Hispanics, and Native Americans, although the study of Maiers et al. does not include Native Americans (5, 6). HLA-A, B and DR alleles, at frequencies of up to 5 percent in the populations in our study and the populations in the previous studies conducted by Mori et al. and Maiers et al. mostly overlap.

It is reported that the Hispanic group in the United States is largely constituted of both Caribbean and Latin American populations, whose ancestries contain distinct contributions of peoples of Native American, European and African origin (6). Concerning the Dallas Hispanics sample, the HLA allele polymorphism supports the historical evidence of a predominantly European ancestry. This is because seven of ten most common HLA-A alleles present in Dallas Hispanics, HLA-A2, A24, A3, A11, A1, A31, and A29 were seen in Dallas European Americans at higher frequencies than in Dallas African Americans and contributed to 83.2% of the population gene pool. In contrast, only three alleles, A68, A30, and A23, were seen in Dallas African Americans at higher frequencies than in Dallas European Americans and contributed to 16.8% of the population

Table 3. HLA-DR frequencies in in the African American, European American, and hispanic populations of Dallas, Texas

	African Americans		European Americans		Hispanics	
Rank	**Allele**	**Allele frequencies**	**Allele**	**Allele frequencies**	**Allele**	**Allele frequencies**
1	DR13	0.176923	DR4	0.188235	DR4	0.264925
2	DR15	0.125641	DR7	0.123529	DR8	0.093284
3	DR11	0.117949	DR17	0.114706	DR14	0.089552
4	DR7	0.107692	DR13	0.108824	DR15	0.085821
5	DR3	0.094872	DR1	0.091176	DR7	0.078358
6	DR8	0.064103	DR15	0.091176	DR1	0.074627
7	DR12	0.051282	DR3	0.079412	DR11	0.070896
8	DR17	0.043590	DR11	0.058824	DR13	0.070896
9	DR4	0.043590	DR8	0.050000	DR3	0.059701
10	DR1	0.041026	DR14	0.026471	DR17	0.037313
11	DR9	0.035897	DR12	0.017647	DR16	0.029851
12	DR14	0.030769	DR9	0.017647	DR12	0.014925
13	DR10	0.025641	DR16	0.011765	DR10	0.011194
14	DR18	0.020513	DR103	0.008824	DR103	0.011194
15	DR16	0.010256	DR10	0.005882	DR90	0.007463
16	DR90	0.010256	DR90	0.005882		

gene pool. The nine of ten most common HLA-B alleles present in Dallas Hispanics were seen in Dallas European Americans at higher frequencies than in Dallas African Americans and contributed to 59.7% of the population gene pool. However, only one allele, B15, is seen in Dallas African Americans at higher frequencies than in European Americans and contributed to 4.47% of the population gene pool. On the DR locus, DR4, which is the most common allele with a frequency of 26.49% in Dallas Hispanics, is also the most frequent allele with a frequency of 18.82% in Dallas European Americans. Moreover, the mean distances of Dallas Hispanics to Dallas European Americans, 0.0110, are smaller than the mean distances to Dallas African Americans, 0.0213, as expected according to the predominance of European rather than African Ancestry for Hispanics.

Some additional information about the high diversity and the interethnic admixture of our population can be inferred from the haplotype data analysis. The 162, 121, and 129 A/B combinations were identified at frequencies higher than 1% in Dallas African American, European Americans and Hispanic populations, in that order. About half of HLA-A-B haplotypes are shared between all the groups (Table 4). The statistically significant HLA-A-B haplotypes in each group are shown in Table 5. Concerning the statistically significant HLA-A-B haplotypes shared between all the groups, A1-B8 is shared between all the groups. Additionally, two statistically significant HLA-A-B haplotypes, A3-B7 and A24-B39, are shared between Dallas European Americans and Dallas Hispanics. Our results confirm the well-known fact that the distributions of haplotypes varies among races, and they also reveal that certain common haplotypes are shared among all racial groups and represent an opportunity for well-matched transplants between donors and recipients of different races (17).

As mentioned in the Results section, when we evaluated the A-B-DR haplotypes shared between groups from the perspective of the 10 most common haplotypes in each group, we saw that at least one of the ten most common A-B-DR haplotypes present in any group is commonly seen in at least one of the other two groups (Table 6). Two of the ten most common A-B-DR haplotypes present in Dallas African Americans are seen in Dallas European Americans, while seven of the ten

Table 4. The frequencies of all (statistical significant and non-significant) the A-B haplotypes occurring at frequencies of more than 1% in the African American, European American, and Hispanic populations of Dallas, Texas

	Dallas racical/ethnic groups					
	African Americans		European Americans		Hispanics	
Rank	Allele	Allele frequencies	Allele	Allele frequencies	Allele	Allele frequencies
1	A2 B35	0.031	A1 B8	0.1265	A2 B35	0.0746
2	A23 B15	0.023	A2 B7	0.0441	A24 B39	0.0299
3	A30 B42	0.023	A2 B44	0.0412	A68 B39	0.0224
4	A2 B53	0.021	A2 B15	0.0353	A24 B35	0.0224
5	A1 B8	0.018	A2 B51	0.0294	A2 B39	0.0224
6	A74 B53	0.018	A3 B7	0.0294	A3 B7	0.0187
7	A23 B7	0.015	A2 B35	0.0235	A2 B15	0.0187
8	A2 B7	0.013	A2 B8	0.0206	A2 B40	0.0187
9	A2 B42	0.013	A3 B35	0.0206	A2 B14	0.0187
10	A3 B53	0.013	A11 B44	0.0176	A68 B35	0.0187
11	A30 B15	0.013	A11 B7	0.0147	A3 B18	0.0187
12	A2 B15	0.013	A29 B44	0.0147	A11 B51	0.0149
13	A66 B58	0.013	A1 B7	0.0147	A1 B8	0.0149
14	A36 B53	0.013	A24 B39	0.0118	A24 B40	0.0149
15			A3 B44	0.0118	A68 B48	0.0112
16			A1 B44	0.0118	A2 B44	0.0112
17			A2 B14	0.0118	A2 B18	0.0112
18			A24 B44	0.0118	A2 B8	0.0112
19			A11 B35	0.0118	A3 B35	0.0112
20			A2 B27	0.0118	A24 B15	0.0112
21					A28 B61	0.0112
22					A29 B50	0.0112

Table 5. The statistically significant HLA-A and -B combinations identified at frequencies higher than 1% in Dallas racial groups, with highest relative linkage disequlibrium, Chi-square and p values

Dallas racical/ethnic groups	Haplotypes	HF	SD	D	D′	χ^2	p
African Americans	A2 B35	0.031	0.009	0.01900	0.30300	15.21500	0.00000
	A23 B15	0.023	0.008	0.01200	0.15300	6.40300	0.01100
	A30 B42	0.023	0.008	0.01600	0.34600	18.54100	0.00000
	A1 B8	0.018	0.007	0.01500	0.35100	37.01100	0.00000
	A66 B58	0.013	0.006	0.01100	0.41900	30.27300	0.00000
	A36 B53	0.013	0.006	0.00900	0.42500	12.30900	0.00000
European Americans	A1 B8	0.1265	0.0181	0.09220	0.63520	126.88370	0.00000
	A2 B15	0.0353	0.0100	0.02170	0.71060	17.73630	0.00000
	A2 B51	0.0294	0.0092	0.01580	0.51770	9.41400	0.00220
	A3 B7	0.0294	0.0092	0.01790	0.18960	11.85110	0.00060
	A2 B8	0.0206	0.0077	-0.03480	-0.62840	13.11650	0.00030
	A3 B35	0.0206	0.0077	0.01230	0.18000	7.46940	0.00630
	A29 B44	0.0147	0.0065	0.00910	0.27850	6.08130	0.01370
	A24 B39	0.0118	0.0059	0.00880	0.25040	10.23260	0.00140
	A1 B44	0.0118	0.0059	-0.01630	-0.58150	4.68590	0.03040
Hispanics	A2 B35	0.0746	0.0161	0.03800	0.31500	16.10300	0.00000
	A24 B39	0.0299	0.0104	0.01700	0.23000	7.37100	0.00000
	A68 B39	0.0224	0.0091	0.01400	0.18500	8.35400	0.00400
	A3 B7	0.0187	0.0083	0.01500	0.40600	21.11800	0.00000
	A3 B18	0.0187	0.0083	0.01500	0.36400	18.66300	0.00000
	A1 B8	0.0149	0.0074	0.01300	0.46800	28.47700	0.00000
	A68 B48	0.0112	0.0064	0.00800	0.31100	7.73700	0.00500
	A28 B61	0.0112	0.0064	0.01000	0.40900	34.55300	0.00000
	A29 B50	0.0112	0.0064	0.01000	0.47700	29.73600	0.00000

HF: Haplotype frequencies, SD: Standard deviation, D: Linkage disequilibrium, D′: Relative linkage disequilibrium, χ^2: Chi-square, $p<0.05$

most common A-B-DR haplotypes present in Dallas European American sample are seen in Dallas Hispanics. These results again support the historical evidence of a predominantly European ancestry for Dallas Hispanics sample and represent an opportunity for well-matched transplants between donors and recipients of different races. Nine of the ten most frequent haplotypes in the Dallas African American sample are not found in the ten most frequent haplotypes reported by Maiers et al. in the U.S African Americans. However, Dallas African Americans showed the closest genetic distance values with the U.S African Americans.

Bertoni et al. investigated the effect of gene flow on Hispanic populations from different geographic regions of the United States, using six autosomal DNA markers (LDLR, GYPA, HBGG, D7S8, GC, and HLA-DQA). They concluded that the U.S Hispanic populations showed different ancestral contributions, from a trihybrid structure with European, Native American, and African contributions (California, Nevada, Florida, New Jersey, and Virginia) to a dihybrid structure with European and American contributions (Southwest population) or European and African contributions (Pennsylvania and Southeast population), according to the region of sampling (18). Our data analysis reflects a predominance of European and Asian rather than African Ancestry for the Hispanic sample, especially those living in the Southern region of the U.S because the Hispanic sample from Dallas, TX is closer to the U.S Asian than to the U.S Hispanics group. The HLA dendrogram (Fig. 1) and correspondence analysis (Fig. 2) show how close Hispanics are genetically to Europeans, and also to Asian rather than African Americans.

Our study has several limitations. The first of the major limitations of our study is the reduction to broad serologic types. It was explained in the 2009 HLA Dictionary (the IMGT HLA nomenclature reports-HLADB 2.24.0, January 2009), for example, how broad types and serologic splits. Second, our study populations did not include other ethnic groups. For example, if the "Hispanic" population sample had been compared to Amerindian populations, the conclusion may have been that the ancestry is predominantly European and Amerindian. However, these limitations could not rule out our find-

Table 6. Occurrences of the first 10 A-B-DR frequency-ranked haplotypes for each census group in each of the other two groups for A-B-DR haplotypes, common alleles are defined here as those observed in the 10 most common haplotypes and rare alleles are not those present in the 10 most common haplotypes in each group in the text

	Dallas racical/ethnic groups									
Dallas racical/ ethnic groups	Haplotype			African Americans		European Americans		Hispanics	
	Rank	A	B	DR	Rank	Count	Rank	Count	Rank	Count
Dallas African Americans	1	A2	B35	DR13	1	0.020532	none	0	none	0
	2	A2	B53	DR8	2	0.017949	none	0	none	0
	3	A23	B15	DR15	3	0.012821	none	0	none	0
	4	A34	B44	DR15	4	0.012821	none	0	none	0
	5	A74	B53	DR13	5	0.012821	none	0	none	0
	6	A1	B57	DR17	6	0.010256	72	0.002941	none	0
	7	A2	B7	DR15	7	0.010256	6	0.019376	87	0.003731
	8	A30	B42	DR11	8	0.010256	none	0	none	0
	9	A68	B15	DR3	9	0.010256	none	0	none	0
	10	A2	B53	DR3	10	0.010237	none	0	none	0
Dallas European Americans	1	A1	B8	DR17	none	0	1	0.067150	none	0
	2	A2	B44	DR4	none	0	2	0.040175	24	0.007463
	3	A1	B8	DR3	none	0	3	0.038235	17	0.007463
	4	A3	B7	DR15	none	0	4	0.026471	9	0.014925
	5	A2	B15	DR4	none	0	5	0.023529	11	0.011194
	6	A2	B7	DR15	7	0.010256	6	0.019376	87	0.003731
	7	A1	B44	DR15	none	0	7	0.014706	none	0
	8	A2	B51	DR13	none	0	8	0.014706	26	0.007463
	9	A29	B44	DR7	16	0.007692	9	0.014706	4	0.018657
	10	A2	B44	DR1	none	0	10	0.012495	none	0
Dallas Hispanics	1	A2	B35	DR8	none	0	none	0	1	0.040621
	2	A2	B39	DR4	none	0	none	0	2	0.026119
	3	A24	B35	DR4	none	0	none	0	3	0.022811
	4	A29	B44	DR7	16	0.007692	9	0.014706	4	0.018657
	5	A3	B18	DR4	none	0	none	0	5	0.018657
	6	A24	B40	DR4	none	0	none	0	6	0.018233
	7	A24	B39	DR14	none	0	none	0	7	0.014925
	8	A24	B39	DR4	none	0	none	0	8	0.014925
	9	A3	B7	DR15	none	0	4	0.026471	9	0.014925
	10	A68	B39	DR4	none	0	none	0	10	0.014925

ing suggesting that Hispanics are genetically closer to Asians than African Americans.

As new information, our results show that the largest genetic distances between all U.S. groups were those of the African Americans compared with each of the other groups in the four major races (African Americans, Asians, European Americans, Hispanics) who reside in the United States. In contrast to this finding, Cao et al. reported that the largest genetic distances to all U.S. groups were those of the Asians compared with each of the other groups in their study of a large database of HLA-A, -B, and -C typed individuals of the five major races of U.S: African Americans, Asians, European Americans, Hispanics, and Native Americans (4). Mori et al., in their study with the largest population size, also found that Asians are the most genetically distinct group of all U.S. groups including Native Americans (4). This finding was reported as the one of the major conclusions in both studies. It could be argued that HLA information obtained at low resolution level and from a local area in our study has very limited use in biomedical or anthropological studies. However, it should be considered that

HLA data in the study of Mori et al. were also obtained at a low resolution level. Morever, HLA information in the study with the largest population size of Maiers et al. supporting our finding were obtained at a high resolution level and not from a local area. For this reason, our finding also reflects the importance of local area studies in population genetics. Local area studies could provide different findings regarding well-known facts, even previous studies that were applied in a larger area, population size, and resolution level. It could be explained that allele and haplotype distribution in the HLA system differ from one ethnic group to another or between the members of the same ethnic group living in different geographic areas, as shown in previous studies (19).

The present study is the first investigation of the HLA status of the European American, African American, and Hispanic populations in Dallas, TX. All the groups shared the most common haplotypes, many of them frequently. These results support the concept that substantial gene flow has taken place among the four major U.S. census categories of race and ethnicity: African Americans, European Americans, Asians and Hispanics, now all comprising constituents of the United States population as a whole, as previously reported (6), or similarities can be explained by the common origin of human beings.

This knowledge will be useful in biomedical and anthropological studies and will contribute to correct interpretations of variations in HLA associations among the main ethnic groups at the population level.

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Conflict of Interest

No conflict of interest was declared by the authors.

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