Admixture in Hispanics: Distribution of Ancestral Population Contributions in the Continental United States

BERNARDO BERTONI,[1] BRUCE BUDOWLE,[2] MÓNICA SANS,[3] SARA A. BARTON,[4] AND RANAJIT CHAKRABORTY[5]

Abstract The effect of gene flow on Hispanic populations from different geographic regions of the United States was analyzed using six autosomal DNA markers (*LDLR, GYPA, HBGG, D7S8, GC,* and *HLA-DQA*). By region of sampling, the Hispanic populations showed different ancestry 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). These findings allowed us to define two regional groups, the West and the East. In the former, Native American contributions ranged from 35.58% to 57.87%; in the East region the values ranged from 0% to 21.27%. An African influence was similar in both regions, ranging from 0% to 17.11%, with a tendency of increasing in the East region. These data reflect the different origins of the Hispanic populations that led to the present ones. In the West, Hispanics are mostly of Mexican origin, and in the East, they are predominantly of Cuban and Puerto Rican origin.

Hispanics are a broad and growing community that represents 12% of the United States population (Lapham 1993). The ethnic category, Hispanics, as defined by the Office of Management and Budget (OMB) in 1978, refers to persons or descendants of people from Latin American countries or other Spanish cultures. Under this definition Hispanics are culturally and genetically a heterogeneous group (Chakraborty et al. 1999). In Latin America, each country has its own demographic and genetic structure, with its own distinct migration history between regions. All Hispanics are basically trihybrid, their ancestral populations being European, African, and Native American. However, the proportion of genes Hispanics received from ancestral populations varies greatly (Sans 2000).

[1]Departamento de Genética, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay.
[2]Laboratory Division, Federal Bureau of Investigation Academy, Quantico, VA 20535.
[3]Sección de Antropología Biológica, Facultad de Humanidades y Ciencias de la Educación Magallanes, Montevideo, Uruguay.
[4]Human Genetics Center, School of Public Health, University of Texas, Houston, TX 77225.
[5]Center for Genome Information, Department of Environmental Health, University of Cincinnati, Cincinnati, OH 45267-0056.

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Most efforts to estimate the contribution of each ancestral population in Hispanics have focused on Mexican Americans and have used white and red cell markers only (Chakraborty et al. 1986; Hanis et al. 1986, 1991). One approach has used molecular information such as mitochondrial DNA, which shows differences between nuclear autosomal and uniparental contributions, and has been applied to the Hispanics of Colorado (Merriwether et al. 1997). In contrast, there is little information available for US Hispanic populations where the migrants are from Puerto Rico or Cuba (see, for example, Hanis et al. 1991). The obstacles to developing admixture studies can be ascribed to the limited number of classical or DNA markers analyzed on the relevant parental populations.

With the rapid developments in forensic genetics, more refined information has become available to help in the understanding of gene flow to admixed populations, in this case, to the Hispanic populations. The development and standardization of methodologies in DNA typing and the wide application in paternity and forensic testing allow for the availability of worldwide population data.

Also, in the past two decades there has been an increasing awareness and research focus on Hispanic populations, because they seem to show different disease susceptibility depending on their origin. Obesity, diabetes, and gallbladder diseases have been associated with a Mexican Hispanic heritage (Stern et al. 1981; Hanis et al. 1986; Kieffer 2000), while for Puerto Ricans a major risk of hypertension has been detected (Richardson and Piepho 2000).

These complex heritable characteristics sometimes are not amenable to pedigree analysis, and the admixed populations are a media to map disease genes (Stephens et al. 1994; Kaplan et al. 1998). The method can be simply summarized: when two populations have been isolated for a long period and then there is an exchange of genes, the differences in allele frequencies produce appreciable linkage disequilibrium. The rate at which gametic disequilibrium decays in an admixed population varies depending on whether the alleles are linked or not. The method of mapping by admixture linkage disequilibrium is based on this observation (Chakraborty and Weiss 1988; Stephens et al. 1994; McKeigue 1997; McKeigue 1998).

In the present study we demonstrate the heterogeneity of the Hispanic populations of the Continental United States through an admixture study. Molecular data were used to address three questions: (1) Can molecular data improve the results of admixture studies? (2) What is the distribution of the different parental contributions in Hispanic populations of the United States? (3) Can Hispanic populations be distinguished from each other based on their admixed genetic structure?

Materials and Methods

Samples from nine Hispanic populations from different regions of the United States were analyzed in this study. Table 1 provides information about the ori-

Table 1. Population Origin, Number of Individuals, Symbols, and References for the Samples Used in the Study

Population	*No.*	*Symbol*	*Reference*
Hispanics			
California	155	HI_CA	TWGDAM data, Peterson et al. 2000
California II	200	HI_CA2	Product Brochure, Peterson et al. 2000
Florida	100	HI_FL	Peterson et al. 2000
New Jersey	128	HI_NJ	Peterson et al. 2000
Nevada	100	HI_NV	Peterson et al. 2000
Pennsylvania	100	HI_PA	Peterson et al. 2000
Southeast	94	HI_SE	Peterson et al. 2000
Southwest	96	HI_SW	Peterson et al. 2000
Virginia	102	HI_VA	Peterson et al. 2000
Parentals			
European			
Dutch	157		Peterson et al. 2000
Denmark	104		Peterson et al. 2000
Madrid (Spain)	202		Bell et al. 1997
Minnesota	100		Peterson et al. 2000
Pirineos (Spain)	106		Bell et al. 1997
Teruel (Spain)	99		Bell et al. 1997
Native American			
Navajo	81		Scholl et al. 1996
Pueblo	103		Scholl et al. 1996
Sioux	64		Scholl et al. 1996
African			
Nigeria	67		Peterson et al. 2000
Zimbabwe	108		Peterson et al. 2000

gin, number of individuals sampled, and reference populations. The population samples chosen for this analysis are part of the population databases from the Continental United States used in DNA Forensics and Parentage Testing, created and organized by the Technical Working Group of DNA Analysis Methods (TWGDAM), currently renamed as the Scientific Working Group of DNA Analysis Methods (SWGDAM).

For the admixture analysis, two African, three Native American, and six European populations were selected as parental populations. The European parental populations include a collection of European samples and a Caucasian American sample, because it is likely that Hispanics not only received Spanish genes during their history but also Caucasian American genes; these include persons of Germanic and Anglo origins as well (Panunzio 1941; Mittelbach and Moore 1968; Murguia and Frisbie 1977). The parental populations are also listed in Table 1.

Six loci were used in the admixture analysis: a group of loci named polymarkers (PM), commonly typed by using the commercial kit, AmpliType® PM + DQA1 amplification and typing kit (Applied Biosystems, Foster City, CA, 2000).

The loci included in this typing kit are: low density lipoprotein receptor (*LDLR*), glycophorin A (*GYPA*), hemoglobin G gamma globulin (*HBGG*), *D7S8*, a group of specific components (*GC*), and an HLA locus, *HLA-DQA1*. The allele frequency data for each Hispanic population used in the present analysis were reported earlier in Peterson et al. (2000). However, for a ready reference they are reproduced in Table 2, together with those in the parental populations used in the present analysis. The allele frequencies in the parental populations, in this context, refer to the weighted average of frequencies of all populations listed in Table 1 for each major ancestral group (i.e., European, African, and Native American).

The software DISPAN (Ota 1993) was used to compute Nei's standard genetic distance (Nei 1972) among the different Hispanic populations. The neighbor-joining method (NJ) was used to display the matrix of pairwise distance (Saitou and Nei 1987), and the bootstrap method was used to test the significance of population clusters in the dendrogram (Felsenstein 1985). An analysis of molecular variance (AMOVA) (Excoffier et al. 1992) was applied to determine the statistical significance of the East-West groupings of the Hispanic populations, for which computations were performed using the program ARLEQUIN 1.1 (Schneider et al. 1997). The admixture proportions of the Hispanic populations were estimated by the gene identity method (Chakraborty 1985).

Results

Using six autosomal loci, Nei's pairwise distance matrix among the nine Hispanic samples was constructed. Figure 1 shows the NJ tree relating the samples. Two clusters can be defined with a 77% value for a bootstrap with 1000 permutations. The East region cluster includes samples from Florida, Southeast, New Jersey, Pennsylvania, and Virginia, and the West region cluster includes California II, Southwest, California I, and Nevada samples. Table 3 shows the results of AMOVA tests of these clusters. With 1000 permutations the test was significant for all three sources of variation; the among groups (i.e., East versus West) variation indicates the relevance of the cluster found in the NJ tree ($p = 0.004$).

Table 4 presents the estimated contributions of admixture based on the six loci. The Hispanics conform to a trihybrid model with European, Native American, and African contributions, with three exceptions. Negative estimates and high standard errors are observed in the Southwest, Pennsylvania, and Southeast samples when the trihybrid model is applied, and in those cases the dihybrid model of admixture fitted almost equally well (by the criteria of multiple correlation coefficient R^2, of observed allele frequencies, and of the ones predicted under the admixture model). The specifics are different in those dihybrid populations; the Southwestern Hispanic sample is composed of European and Native American contributions, while the samples from Pennsylvania and Southeast exhibited European and African contributions alone. For the samples of trihybrid origin, the Native American contribution is higher in the West region, with values ranging

Table 2. Allele Frequencies (%) in the Hispanic Populations and Weighted Averages for the Three Major Parental Populations

	Hispanics									*Parental*		
	California	*California II*	*Florida*	*New Jersey*	*Nevada*	*Pennsylvania*	*Southeast*	*Southwest*	*Virginia*	*European*	*African*	*Native American*
LDLR												
A	47.10	48.50	43.50	46.88	47.50	48.00	41.50	56.25	46.08	44.80	18.21	56.85
B	52.90	51.50	56.50	53.12	52.50	52.00	58.50	43.75	53.92	55.20	81.79	43.15
GYPA												
A	66.13	61.50	55.00	57.42	71.00	56.50	53.19	65.63	58.82	53.62	50.87	73.99
B	33.87	38.50	45.00	42.58	29.00	43.50	46.81	34.37	41.18	46.38	49.13	26.01
HBGG												
A	37.10	37.50	44.50	41.41	30.50	38.00	42.55	34.38	39.22	49.23	38.15	30.24
B	60.32	58.00	52.50	50.78	65.50	48.00	54.79	60.94	52.94	49.89	21.97	69.36
C	2.58	4.50	3.00	7.81	4.00	14.00	2.66	4.69	7.84	0.88	39.88	0.40
D7S8												
A	56.13	62.25	60.50	52.34	55.50	63.00	58.51	68.23	59.31	58.01	67.34	52.62
B	43.87	37.75	39.50	47.66	44.50	37.00	41.49	31.77	40.69	41.99	32.66	47.38
GC												
A	23.23	20.25	22.50	23.05	17.50	26.00	27.66	27.08	20.59	29.69	8.67	9.88
B	32.58	33.50	25.00	25.78	31.50	32.50	22.34	20.83	31.86	15.20	84.39	32.66
C	44.19	46.25	52.50	51.17	51.00	41.50	50.00	52.08	47.55	55.10	6.94	57.46
HLA-DQA1												
1.1	9.68	10.50	14.50	15.35	10.00	15.00	18.09	14.06	12.11	14.75	13.01	6.08
1.2	12.58	13.00	11.00	14.57	12.50	16.00	15.43	13.54	19.47	18.73	37.28	2.28
1.3	4.52	5.25	7.00	5.91	3.00	6.50	7.98	3.13	3.68	7.28	8.67	1.14
20	8.39	11.50	11.50	12.21	8.50	11.00	15.96	9.37	9.47	13.17	9.83	1.90
30	26.45	21.75	21.00	21.26	26.00	26.00	19.15	22.92	24.74	15.47	5.20	25.10
40	38.39	38.00	35.00	30.71	40.00	25.00	23.40	36.98	30.53	30.60	26.01	63.50

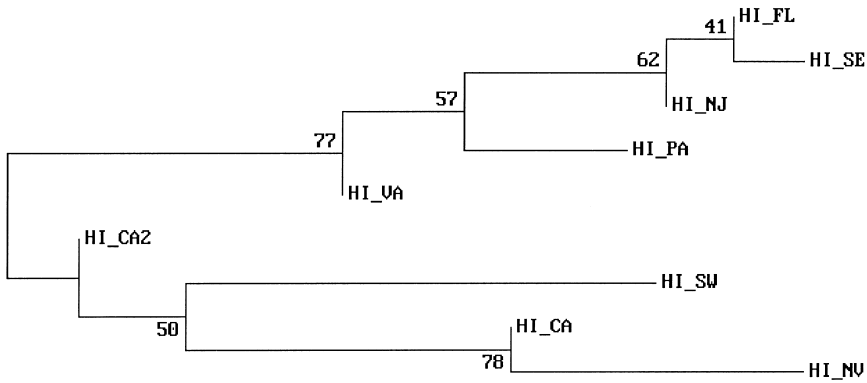

Figure 1. Neighbor-joining tree for the Hispanic samples constructed from the Nei's standard distances. Numbers represent the bootstrap values; symbols are explained in Table 1.

Table 3. AMOVA Results Considering Two Groups: West (California, California II, Nevada, and Southwest) and East (Florida, New Jersey, Pennsylvania, Southeast, and Virginia)

Source Variation	*df*	*Sum of Squares*	*Variance Components*	*Percentage of Variation*	*Significance Test**
Among groups	1	12.446	0.00948	0.56	0.0039
Among populations within groups	7	15.139	0.00208	0.12	0.0000
Within populations	2151	3602.743	1.67492	99.31	0.0000
Total	2159	3630.327	1.67492		

**p* estimated with 1000 permutations.

between 57.87% in Nevada to 35.58% in the Southwest, while in the East region the maximum Native American contribution (21.27%) was observed in the Virginia sample. The African contributions are similar between regions, with a maximum of 17.11% for the Pennsylvania sample and a minimum of 6.38% for the New Jersey sample. The fit to the admixture model, as measured by the multiple correlation coefficient R^2, was high for all the samples, with values ranging between 0.999 and 0.992.

Discussion

The nine Hispanic populations from different geographic areas in the United States delineate into two defined regions, the West and the East. Whereas the AMOVA shows that the intergroup variances account for only 0.56% of the total

Table 4. Admixture Coefficients with the Gene Identity Method (Chakraborty 1985), Percentage Contributions, Standard Errors (SE), and Model Fitting (R^2)

Region	*European % (SE)*	*Native American % (SE)*	*African % (SE)*	R^2
West				
California	46.26 (2.60)	42.96 (2.06)	10.78 (0.96)	0.999
California II	48.39 (1.16)	38.20 (0.92)	13.41 (0.43)	0.999
Nevada	33.95 (1.99)	57.87 (1.58)	8.19 (0.73)	0.999
Southwest	64.42 (1.67)	35.58 (1.67)		0.995
	66.80 (3.72)	34.43 (2.95)	–1.22 (1.37)	0.999
East				
Florida	71.98 (0.73)	19.91 (0.58)	8.12 (0.27)	0.999
New Jersey	84.49 (7.44)	9.14 (5.90)	6.38 (2.74)	0.997
Pennsylvania	82.89 (2.97)		17.11 (2.97)	0.992
	82.88 (9.94)	0.23 (7.88)	16.89 (3.87)	0.994
Southeast	93.28 (0.78)		6.72 (0.78)	0.999
	95.51 (2.50)	–2.17 (1.98)	6.66 (0.92)	0.999
Virginia	63.83 (3.05)	21.27 (2.42)	14.90 (1.13)	0.999

variance (although significant, $p = 0.004$), the admixture analysis clearly defines the two regions.

The Mexican migration area traditionally extended from Arizona, California, Colorado, New Mexico, and Texas (Cardoso 1980). As can be seen from the 1990 census data (Table 5), the relative weight of the Mexican immigration is greater in the West (68%–90%) than in the East (<19%) populations (Lapham 1993).

In the continental United States most of the genetic admixture studies on Hispanics are from the western region of the country. In previous studies (Table

Table 5. Hispanic Census Data in the States Sampled in the Study: Hispanic Proportion in the Total Population and Mexican and non-Mexican Origin Proportion among the Hispanic Populations (from 1990 US Census in Lapham 1993)

State	*Hispanic Proportion (%)*	*Percentage of Mexican Origin (%)*	*Percentage of Non-Mexican Origin (%)*
West			
California	25.8	80.0	20.0
Nevada	10.4	68.0	32.0
Southwest (Texas)	25.5	90.0	10.0
East			
Florida	12.2	10.0	90.0
New Jersey	9.6	4.0	96.0
Pennsylvania	2.0	10.0	90.0
Virginia	2.6	19.0	81.0

Table 6. Admixture Coefficient and Standard Errors (SE) for Hispanics Analyzed in Previous Studies

Population (Loci Applied)	*European (SE)*	*Native American (SE)*	*African (SE)*	*Reference*
Arizona (red cell)	68.3 (4.6)	29.2 (4.0)	2.5 (2.2)	Long et al. 1991
California (HLA)	83.4 (6.3)	16.6 (6.3)		Long et al. 1991
West-Southwest (KM-GM)	57.5 (4.3)	39.0 (4.2)	3.5 (1.4)	Tseng et al. 1998
Texas (red cell)	62.3 (1.2)	30.5 (1.0)	7.2 (1.0)	Cerda-Flores et al. 1992
Texas[a] (red cell)				Chakraborty et al. 1986
Barrio	56.2	43.8		
Transitional	70.0	30.0		
Suburb	81.3	18.7		

a. Barrio, transitional, and suburb represent low-, middle-, and high-income neighborhoods.

6), the Native American estimations based on red cell or GM and KM markers show no large differences with our estimations. The African contribution was detected by us in California, California II, and Nevada. However, the Southwest sample shows a better fit to a dihybrid model (since the African contribution was negative for the trihybrid model, and R^2 for the dihybrid model still remained high, $R^2 = 0.995$). This apparently contradicts the previous findings in Southwest region populations such as Arizona, Colorado, New Mexico, and Texas, described as trihybrid (Long et al. 1991; Cerda Flores et al. 1992; Tseng et al. 1998). Our findings are not surprising if we consider that, for Long et al. (1991) and Tseng et al. (1998), the African estimates range from 2.5 to 3.5% and the standard errors are high. Long et al. (1991) justified that fact due to the presence of the African *Fy* null allele in the sample. On the other hand, Cerda Flores et al. (1992) estimated a 7% African contribution among Mexican Americans in a sample from Starr County, Texas, while Chakraborty et al. (1986) stated no African contribution for a San Antonio sample from the same state. North Mexican populations also present low or no African contribution when serological markers or mitochondrial DNA haplogroups are considered (Cerda-Flores and Garza-Chapa 1989; Green et al. 2000).

A previous study in California showed a dihybrid pattern with Native American and European contributions (Long et al. 1991). Our results show a trihybrid pattern and a greater Native American contribution compared with the previous study. The coherence between the results for the two independent California samples in the present study implies that the differences found with Long et al. (1991) can be ascribed to the markers chosen. In that previous work, estimations were based on the HLA loci, and selective forces could be acting upon these loci (Chakraborty 1986; Long et al. 1991). The Nevada sample has the highest

Native American contribution in the West region, and its value is closer to Mestizo samples in Mexico as reported by Lisker et al. (1996).

The greater European contribution in the East rather than in the West region is in agreement with the high similarity found between Caucasian Americans and Southeastern populations for hypervariable DNA markers that depict copy number variations of minisatellite loci (Devlin and Risch 1992; Chakraborty et al. 1995). An African contribution is present in all the East region samples, reflecting the weight of Cuban Americans and Puerto Ricans in this area. A previous serological study showed that African gene admixture in these groups is greater than the observed admixture in Mexican Americans (Hanis et al. 1991).

The Southeast and Pennsylvania samples we analyzed conformed better to a dihybrid model composed of European and African contributions. With respect to the Southeast sample, the census information demonstrates that the Cuban origin (40%) is the main source in this community (Lapham 1993). A study on admixture in Cuba indicated a low or a zero Native American contribution, while the African parental contribution is 8% for Cuban Caucasians (Hidalgo 1998). These findings explain the dihybrid structure found in the Southeast sample. However, the Native American contribution found in the Florida sample shows heterogeneity inside the Southeast region. The New Jersey, Pennsylvania, and Virginia samples have higher standard errors than the other samples; this can be due to diverse factors, for example, a not very accurate selection of parental populations. In summary, two different areas can be defined for the American Hispanics as shown by the Native American contribution to the populations.

This study illustrates the genetic heterogeneity present in Hispanics. The distinctiveness of the migration histories and marital behaviors in different areas of the United States can account for the variation observed in the admixture proportions. The term *Hispanic* comprises Spanish-speaking populations with different ancestries; it is necessary to identify these populations for a better understanding of admixture in the United States. On the other hand, Hispanics show an increase of out-group marriages directly correlated with the number of generations following the event of initial immigration, so gene flow would be occurring and will vary between regions (Panunzio 1941; Fitzpatrick 1966; Murguia and Frisbie 1977). For that reason, in the context of genetic epidemiology, the observed heterogeneity must be considered to avoid spurious relationships in studies related to disease risk factors. As was suggested by Chakraborty et al. (1999), future studies will need to address a research design that subdivides the group using genetic parameters.

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