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Gender Differences in Ancestral Contribution and Admixture in Venezuelan Populations

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Abstract The origin of the contribution of uniparental heritage were analyzed in 615 samples of individuals proceeding from 13 towns classified according to historic differences in their emergence and development as African-derived, European-derived, and admixed/urban. Mitochondrial and Y-chromosome haplogroups were identified by PCR-restriction fragment length polymorphism. The results were compared with previous estimates of admixture made with autosomal markers and with historic aspects. The results show a predominantly indigenous genetic contribution through the female, being more prevalent in urban populations; the African contribution, although dispersed, presents a larger concentration in the African-derived towns, whereas the European contribution is limited to populations with this origin, reflecting isolation and the conservation of the distribution pattern of genes of the Colonial era. With regard to admixture through males, it is almost exclusively of European origin, whereas the African contribution is basically concentrated in the African-derived towns, and the Amerindian lineages are almost nonexistent. The genome of paternal heredity, as opposed to the autosomal and the mitochondrial, shows a homogeneous pattern of admixture that is independent of the origin of the population studied, suggesting that European genes have been introduced into the Venezuelan population through male immigrations, whereas the indigenous contribution has been preserved in the Venezuelan genetic pool through the women. These results provide evidence of the heterogeneity in the genetic origin of the Venezuelan population, which should be taken into account in forensic and epidemiologic genetic studies.

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The conquest of Venezuela began in the early 16th century and produced significant demographic transformations due to the intense admixture that began at an early stage. In the early 19th century, Humboldt and Bonpland estimated that the Venezuelan population was 800,000, classified as follows: whites born in Europe, 12,000; Hispano-American Whites (criollos), 200,000; mixed castes or colored people, 406,000; black slaves, 62,000; and indigenous of pure race, 120,000 (Guerra Cedeño 1996). In 300 years of Spanish presence, half the population was already designated as mixed castes, indicating the intense admixture process in Venezuela.

At the time of contact with the conquerors, Venezuela was populated by indigenous groups of Caribbean linguistic filiations, localized in the north-central and eastern coastal areas, and Arawak groups, which extended basically throughout the entire region west of Caracas (Fundación Polar 1997). There were also Chibchas and groups of other linguistic filiation. Although there are no exact estimations, it has been suggested that the indigenous population was approximately 350,000–500,000 (Sanoja and Vargas 1991).

Conquest and colonization brought about a demographic catastrophe for the indigenous peoples, which justified the abduction of millions of Africans brought as slaves to America. Nevertheless, their presence in Venezuela, though early, was not quantitatively important; it is estimated that 210,000 slaves entered the country legally between the 1500 and 1810. It is estimated that the largest volume entered during the late 17th and 18th centuries, as a consequence of clandestine commerce with the Caribbean and the Antilles (Brito Figueroa 1966). As regards their origin, it has been suggested that they came from Western Africa.

The slave population was distributed in Venezuela following a pattern directly linked to the location of the agricultural plantations, throughout the entire north-central coastal area where they remained till the middle of the 19th century, when they began to migrate to large cities. There are no known important migrations of Africans or their descendants to Venezuela in postcolonial times.

The European contribution, especially of peninsular and insular (Canaries) Spaniards was very important in Venezuelan demographic development, and their geographic distribution was also greatly influenced by economic activity.

During the 19th century and the first decades of the 20th, there was no great Spanish immigration. From 1936 onward and especially between 1945 and 1958, it increased significantly, along with an influx from Portugal and Italy, and, although it declined in more recent years, its contribution has continued to be important (Fundación Polar 1997; Guerra Cedeño 1996).

Colonial activity generated a pattern of population distribution that is still evident and allows identification of areas of African- and Spanish-derived populations, but few of aboriginal survival. Therefore it is possible to classify the Venezuelan population according to its origin, such as African-derived, located in the area of the slave population (the entire coastal area of the country); European-derived, distributed throughout the country; and admixed/urban, those who arose from *mestizo* populations and make up important urban centers today. A similar classification, based on the phenotype, or genetic composition, was suggested

previously for neo-American populations by Sans (2000) and Salzano and Bortolini (2002).

Genetic studies carried out in Venezuela starting with the analysis of blood group and proteins polymorphisms (Bortolini et al. 1992, 1999; Castro de Guerra and Zambrano 2000; Castro de Guerra et al. 1993, 1996, 1997; Rodríguez-Larralde et al. 2001) and most recently with DNA polymorphisms (Acosta Loyo et al. 2004; Martínez et al. 2007; Simmons et al. 2007; Vívenes de Lugo et al. 2003) have revealed that, as in other Latin American countries, the conquest and colonization processes generated very heterogeneous populations. In general, the genetic component that prevails in those studies is Spanish, followed by indigenous, and to a lesser extent, African (see Table 1), but with marked inter- and intra-regional differences.

There are few studies regarding the origin of paternal and maternal lineages in Venezuela; some preliminary reports show a European predominance in the paternal contribution in African-derived populations (Bortolini et al. 1999) and its absolute predominance (100%) in European-derived populations (Castro de Guerra et al. 2003). As regards maternal lineages, predominance of Amerindian mitochondrial haplogroups (64%) was reported in the western region of the country, followed by African, a near total European absence (2%) and in 14% of haplogroups whose origin could not be identified (Castro de Guerra et al. 2009). On the other hand, a study carried out in Caracas showed important difference in the type of admixture in two different socioeconomic levels, with a genetic flow via the European man with the indigenous or African woman at both levels (Martínez et al. 2007). These previous results concur with reports on asymmetry in the origin of the ethnic maternal and paternal contribution in Latin American populations (Alves Silva et al. 2000; Carvalho Silva et al. 2001; Martínez-Marignac et al. 2004; Marrero et al. 2005; Mesa et al. 2000; Salzano and Bortolini 2002; Sans 2000; Santos et al. 1999; Seielstad 2000).

To understand the admixture process which gave rise to the present Venezuelan population, the distribution of the mitochondrial DNA and Y-chromosome haplogroups was analyzed for the first time in populations with different historic conditions during their emergence and development. Some of the results presented here correspond to previously studied populations (Castro de Guerra et al. 2003, 2009; Martínez et al. 2007). In such cases, mitochondrial DNA and Y-chromosome haplogroup identification was reevaluated with methods that allow more precise identification of their origin. Information previously published with biparentally inherited polymorphisms was used to make a synthesis of admixture in Venezuela. We examined the origin of uniparental inheritance and discuss these results in the light of the available historical information.

Materials and Methods

Populations and Samples. Samples from 615 and 287 individuals were studied for mtDNA and for the Y-chromosome, respectively, who originated from thirteen populations distributed throughout the northern region of Venezuela (Figure 1) and who were previously studied by our group for estimations of

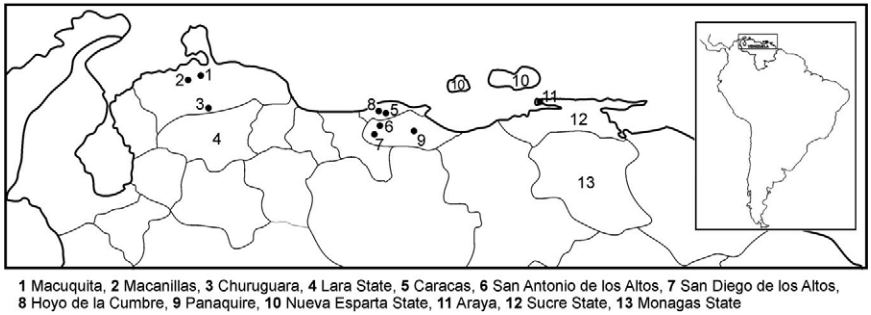

Figure 1. Map of Venezuela showing the location of the populations studied.

biparental admixture (Table 1). The populations were classified according to the historic differences in their emergence: African-derived: Panaquire, $n = 17$ (Castro de Guerra et al. 1996, 1997); Macuquita, $n = 24$ (Quintero et al. 2002); and Macanillas, $n = 29$, for which there are no previous studies; European-derived: San Antonio de Los Altos, $n = 50$; San Diego de Los Altos, $n = 24$; Hoyo de La Cumbre, $n = 42$ (Castro de Guerra and Zambrano 2000); and Araya, $n = 15$, for which there are no previous studies; and admixed/urban: Caracas, was divided into two socioeconomic strata, for reasons previously described (Martínez et al. 2007): high socioeconomic level (Caracas-A), n = 51 and low socioeconomic level (Caracas-M), $n = 50$; Sucre, $n = 84$; Monagas, $n = 41$; Nueva Esparta, $n = 49$ (Vívenes de Lugo et al. 2003); Lara, $n = 81$ (Simmons et al. 2007); and Churuguara, $n = 58$ (Acosta Loyo et al. 2004).

Most of the samples were collected by blood banks, among university students and in health centers in each population. In order to reduce the genetic influence of the recent migratory processes, the sample was collected in adult individuals, not biologically related, and from their four grandparents in the population being studied, thus providing a representation of the genetic pool at the beginning of the 20th Century. In Caracas, due to its history of strong migration, the sample consisted of nonrelated adults, born in the city and neighboring areas and was independent of the origin of their grandparents (Martínez et al. 2007). All the individuals signed an informed consent, approved by the Instituto Venezolano de Investigaciones Científicas (IVIC) Bioethics Committee.

Determination of Haplogroups and Estimation of Uniparental Admixture. DNA was extracted according to the saline method (Lahiri and Nurnberger 1991) and stored in alcohol until used.

Mitochondrial DNA Haplogroups. A total of 13 restriction sites and one deletion were studied, which allowed the identification, through restriction fragment length polymorphism (RFLP), of the four indigenous haplogroups A, B, C, and D; the African L and the Europeans H, I, J, K, T, U, and V were identified

Table 1. Published Admixture Estimates (%) in Venezuelan Populations Based on Autosomal Markers and Classified According to their Ethnic Origin

	Amerindian	*European*	*Sub-Saharan Africa*	*Genetic Markers*[1]	*References*[2]
African-derived					
Ganga	21	0	79	a	1
Patanemo	11	31	58	a	1
Tapipa	15	21	63	a	2
Panaquire	26	15–19	55–59	a,b	3,4
Curiepe	0–6	23–35	65–70	a,b	4
Birongo	17–25	15–38	46–60	a,b	4
Sotillo	13–22	25–26	54–61	a,b	4
Macuquita	0	43	57	a	5
Several African-derived	2–15	40–49	45–49	a	6
European-derived					
San Antonio	8	88	4	a	7
San Diego	8	78	14	a	7
Hoyo de La Cumbre	0	92	8	a	7
Colonia Tovar	0	100	0	a	8
Several European-derived	12–22	73–78	0–15	a	6
Admixed-urban[3]					
Caracas-A	17	75	8	a,b	9
Caracas-M	40	33	27	a,b	9
RC	24	60	16	a	10
RCN	23–25	38–49	27–38	a,b	11
RCO-1	32	59	9	a	10
RCO-2	21–25	58–69	10–17	a,b	11
RNO	31	54	15	a	10
Churuguara	20	52	28	a,b	12
Coro	41	41	18	a	13
Maracaibo	46	54	0	a	13
RO	33	42	25	a	10
RLA	27	73	0	a	10
Sucre	6	85	9	a	14
Nva. Esparta	5	80	15	a	14
Monagas	23	38	39	a	14
Ciudad Ojeda	39	61	0	a	13
Ciudad Bolívar	46	35	19	a	13
Several mestizo	21–27	52–55	21–24	a	6

1. a, Blood groups and/or proteins; b, STRs.

2. References: 1. Castro de Guerra et al. (1993); 2. Arends et al. (1978); 3. Castro de Guerra et al. (1996); 4. Bortolini et al. (1999); 5. Quintero et al. (2002); 6. Salzano and Bortolini (2002); 7. Castro de Guerra y Zambrano (2000); 8. Weimer et al. (1999); 9. Martínez et al. (2007); 10. Rodríguez-Larralde et al. (2001); 11. Simmons et al. (2007); 12. Acosta Loyo et al. (2004); 13. López-Camelo et al. (1996); 14. Vívenes de Lugo et al. (2008).

3. RC, Central region; RCN, Northern central region; RCO, Western central region; RNO, Northern east region; RO, Eastern region; RLA, Los Andes region.

according to techniques and oligomers previously reported (Baillet et al. 1994; Martínez et al. 2007; Torroni et al. 1995). Those samples that could not be classified through RFLP were sequenced for the HVI region, with oligomers and conditions previously described (Bravi 2005).

Table 2. Observed Values and Percentages (%) of mtDNA Haplogroups in Venezuelan Populations

	A	*B*	*C*	*D*	*H*	*I*	*J*	*K*	*T*	*U*	*V*	*X*	*L*	*L3d*	*L3e*	*L3**
African-derived																
Macuquita ($n = 24$)	1 (4)	4 (17)	3 (12)	10 (42)	0	0	0	0	0	0	0	0	5 (21)	0	1 (4)	0
Panaquire ($n = 17$)	2 (12)	0	3 (18)	1 (6)	0	0	0	0	0	0	0	0	9 (53)	1 (6)	1 (6)	0
Macanillas ($n = 29$)	6 (21)	12 (42)	0	1 (3)	0	0	0	0	0	1 (3)	0	0	7 (24)	0	0	2 (7)
Group ($n = 70$)	9 (13)	16 (23)	6 (9)	12 (17)	0	0	0	0	0	1 (1)	0	0	21 (30)	1 (1)	2 (3)	2 (3)
European-derived																
San Antonio ($n = 50$)	5 (10)	2 (4)	2 (4)	1 (2)	24 (48)	0	1 (2)	0	1 (2)	1 (2)	2 (4)	0	8 (16)	0	0	3 (6)
San Diego ($n = 24$)	7 (29)	1 (4)	2 (8)	0	6 (25)	0	3 (13)	0	1 (4)	0	1 (4)	0	3 (13)	0	0	0
Hoyo de La Cumbre ($n = 42$)	1 (2)	0	0	0	21 (50)	0	0	0	2 (5)	9 (22)	1 (2)	2 (5)	3 (7)	0	1 (2)	2 (5)
Araya ($n = 15$)	8 (53)	0	1 (7)	4 (27)	1 (7)	0	0	0	0	1 (6)	0	0	0	0	0	0
Group ($n = 131$)	21 (16)	3 (2)	5 (4)	5 (4)	52 (40)	0	4 (3)	0	4 (3)	11 (8)	4 (3)	2 (1)	14 (11)	0	1 (<1)	5 (4)
Urban/admixed																
Lara ($n = 81$)	18 (22)	29 (37)	5 (6)	8 (10)	0	0	1 (1)	0	0	0	0	0	15 (19)	2 (2)	2 (2)	1 (1)
Churuguara ($n = 58$)	7 (12)	25 (44)	6 (10)	4 (7)	2 (3)	0	0	0	0	1 (2)	0	0	6 (10)	1 (2)	3 (5)	3 (5)
Caracas-A ($n = 51$)	13 (25)	2 (4)	6 (12)	4 (8)	7 (14)	1 (2)	0	2 (4)	1 (2)	2 (4)	1 (2)	1 (2)	6 (11)	1 (2)	2 (4)	2 (4)
Caracas-M ($n = 50$)	19 (38)	8 (16)	9 (18)	3 (6)	3 (6)	0	0	0	0	1 (2)	0	0	4 (8)	0	3 (6)	0
Monagas ($n = 41$)	20 (49)	7 (17)	4 (10)	2 (5)	0	0	0	0	0	3 (7)	0	0	2 (5)	0	2 (5)	1 (2)
Nva Esparta ($n = 49$)	23 (48)	3 (6)	5 (10)	10 (20)	2 (4)	0	0	0	0	1 (2)	0	0	5 (10)	0	0	0
Sucre ($n = 84$)	34 (41)	15 (18)	9 (11)	3 (3)	1 (1)	0	0	0	2 (2)	3 (4)	1 (1)	0	11 (13)	0	3 (4)	2 (2)
Group ($n = 414$)	134 (32)	89 (21)	44 (11)	34 (8)	15 (4)	1 (<1)	1 (<1)	2 (<1)	3 (1)	11 (3)	2 (<1)	1 (<1)	49 (12)	4 (1)	15 (4)	9 (2)
Venezuela ($n = 615$)	164 (27)	108 (18)	55 (9)	51 (8)	67 (11)	1 (<1)	5 (1)	2 (<1)	7 (1)	23 (4)	6 (1)	3 (<1)	84 (14)	5 (1)	18 (3)	16 (2)

Y-Chromosome Haplogroups. Seven biallelic polymorphisms were studied: M168, M1 (YAP), M2, M89, 92R7, M242, and M3, according to methods described by Underhill et al. (2001) and Bortolini et al. (2003), which allowed the identification of African sub-Saharan haplogroups AB and Elbla*, Mediterranean and Indian subcontinent DE, European P*R* (xQ); and Amerindian Q* and Q1a3a*. Those not classified correspond to other infrequent haplogroups mainly of Euro-Asian origin (C, F, G, H, I, J, K, L, M, N, O). The nomenclature used is that suggested by the last Y Chromosome Consortium (Karafet et al. 2008).

The PCR products and digestions were typed using vertical electrophoresis on polyacrylamide gels and silver staining.

Frequencies for the haplogroups were calculated by direct counting, and admixture by the female line was estimated, adding frequencies of haplogroups with equal continental origin. For admixture estimates via males, those due to the nonspecific geographic distribution of the DE haplogroups, and those that were nonclassified, a least-squares method (Long 1991) was used, considering as parental frequencies the averages from the following: the peninsular Spain and Canary Islands as the European (Bosch et al. 2001; Flores et al. 2003); the averages of the populations of Khoisan, Nilo-Saharian, and Niger-Congo languages as the sub-Saharan African (Wood et al. 2005); and as parental Amerindian the averages of Amerindians, as reported by Bortolini et al. (2003) and Marrero et al. (2005). Due to differences in haplogroups resolutions, we reassigned (collapsed) the haplogroups status both for our data and for the populations to be compared, making them into comparable data sets. In both cases, the estimations of the female and male genetic contributions were done for each population, for each ethnic group, and for all Venezuela.

Results

Close to 8% of the mtDNA samples could not be classified by RFLP and were identified through analysis of the HVI (hypervariable region I) sequence. Most of them belonged to haplogroup L3. For the Y-chromosome, the single nucleotide polymorphism (SNP) sites used permitted the unambiguous classification of the African and Amerindian haplogroups. The distribution of female and male lineages detected in the 13 populations studied and classified according to their origin is as follows.

African-derived Populations. Table 2 shows the distribution of the mitochondrial haplogroups, with the most frequent in these three populations being the African L haplotype (L1L2). L3, also African, is scarce with a slight predominance of L3e. The Amerindian haplogroups A, B, C, and D differ in distribution among the three populations. There is a predominance of the B group in Macanillas, of C and A in Panaquire, and of D in Macuquita. Haplogroups of European origin were not detected, with the exception of U in Macanillas that was present in one individual, although the possibility of being of African origin (U6) cannot discounted.

Table 3. Observed Values and Percentages (%) of Y-Chromosome Haplogroups in Venezuela and Its Parental Populations

Populations	*AB*	*DE*	*E1b1a**	*P*R*(xQ)*	*Q**	*Q1a3a**	*Others*
African-derived							
Macuquita ($n = 8$)	0	1 (13)	2 (25)	3 (37)	0	0	2 (25)
Panaquire ($n = 22$)	0	3 (14)	2 (9)	10 (46)	0	0	7 (31)
Macanillas ($n = 17$)	0	0	2(12)	11 (65)	1 (6)	0	3 (17)
Group ($n = 47$)		4 (9)	6 (13)	24 (51)	1 (2)	0	12 (25)
European-derived							
San Antonio ($n = 21$)	0	4 (19)	0	14 (67)	0	0	3 (14)
San Diego ($n = 13$)	0	0	0	10 (77)	0	0	3 (23)
Hoyo de La Cumbre ($n = 19$)	0	1(5)	0	10(53)	0	0	8 (42)
Araya ($n = 13$)	0	1 (8)	1 (8)	8 (61)	0	0	3 (23)
Group ($n = 66$)		6 (9)	1 (2)	42 (64)	0	0	17 (25)
Urban/admixed							
Lara ($n = 28$)	0	1 (4)	1 (4)	19 (67)	0	1 (4)	6 (21)
Churuguara ($n = 15$)	0	0	3 (20)	8 (53)	0	0	4 (27)
Caracas-A ($n = 29$)	0	4 (14)	1 (3)	14 (48)	0	0	10 (35)
Caracas-M ($n = 29$)	0	1 (3)	2 (7)	18 (62)	0	2 (7)	6 (21)
Monagas ($n = 19$)	0	2 (11)	1 (4)	9 (48)	0	0	7 (37)
Nva Esparta ($n = 16$)	0	1 (6)	0	12 (75)	0	0	3 (19)
Sucre ($n = 38$)	1 (2)	1 (2)	4 (11)	22 (58)	0	1 (3)	9 (24)
Group ($n = 174$)	1 (<1)	10 (6)	12 (7)	102 (58)	0	4 (2)	45 (26)
Venezuela ($n = 287$)	1 (<1)	20 (7)	19 (7)	168 (59)	1 (<1)	4 (1)	74 (26)
Parental populations	AB	DE	E1b1a*	P*R*(xQ)	Q*	Q1a3a*	Others
European ($n = 749$)	0	73 (9.7)	4 (0.5)	493 (66)	0	0	178 (23.8)
Sub-Saharan Africa ($n = 895$)	362 (40)	149 (16.6)	367 (41)	13 (1)	0	0	4 (0.4)
Amerindian ($n = 438$)	0	0	0	0	71 (16)	368 (84)	0

Y-chromosome haplogroups and the parental frequencies used for admixture estimations through males are shown in Table 3. There is a predominance of the category that includes European haplogroups P*R* (xQ), with a minimum value of 37% in Macuquita; the Elbla* African shows a higher frequency in the same population (25%). The nonclassified haplogroups with nonassigned geographic origin have an average frequency of 25%, but we assume that they probably have been introduced by Europeans because of their importance as a parental population of the Venezuelan gene pool (Castro de Guerra et al. 1996). Amerindian haplogroups are almost nonexistent, with the exception of Q* in Macanillas.

Table 4 shows the proportions of uniparental admixture. The female contribution is predominantly Amerindian, with an average of 62%, in these African-derived populations; African mitochondria predominate only in Panaquire (65%). In Macuquita and Macanillas the most frequent are Amerindians, with 75% and 66%, respectively. The nearly nonexistence of European mitochondria (<3%) is evident.

Estimates for admixture through the male lineage indicate a predominance of the European contribution, at 69–89%, with the African contribution also

Table 4. Estimates of Admixture (%) for Venezuelan Populations Using mtDNA and Y-Chromosome

	European		*African*		*Native American*	
	mtDNA	*Y-Chromosome*	*mtDNA*	*Y-Chromosome*	*mtDNA*	*Y-Chromosome*
African-derived						
Macuquita	0	69	25	31	75	0
Panaquire	0	89	65	11	36	0
Macanillas	3	82	31	12	66	6
Group	1	83	37	15	62	2
European-derived						
San Antonio	58	100	22	0	20	0
San Diego	46	100	13	0	41	0
Hoyo de la Cumbre	84	100	14	0	2	0
Araya	13	92	0	8	87	0
Group	59	100	15	0	26	0
Admixed/urban						
Lara	1	92	24	4	75	4
Churuguara	5	80	22	20	73	0
Caracas-A	30	97	21	3	49	0
Caracas-M	8	85	14	8	78	7
Monagas	7	96	12	4	81	0
Nva Esparta	6	100	10	0	84	0
Sucre	8	84	19	13	73	3
Group	9	90	19	8	72	2
Venezuela[a]	19 ± 1.5	89 ± 2.4	20 ± 3.6	8 ± 2.1	61 ± 1.9	3 ± 1.1

a. Values are mean ± SE, expressed as percentages.

being prominent at 11–31%. An Amerindian contribution is found only in Macanillas (6%).

European-derived Populations. In Table 2 we see that the most frequent mitochondrial haplogroup is H (European) in San Antonio (48%) and Hoyo de la Cumbre (50%), whereas in San Diego (29%) and Araya (53%), the A (Amerindian) haplotype is more frequent. The frequency of J in San Diego stands out (13%) as well as U in Hoyo de la Cumbre (22%), which may be due to the Italian contribution and that of the Canary Islands, respectively (Flores et al. 2001; Morelli et al. 2000). In general, there is a marked predominance of European mitochondrial lineages, between 46% and 84%, with the exception of Araya, which has a frequency of 13% (Table 4).

The indigenous female contribution among these populations is not low (Table 4), especially in Araya, where it reaches 87%, and in all of them the frequency of haplogroup A stands out. African lineages are present and are almost exclusively L (L1+L2). Due to the presence of African female lineages in Spain (peninsula and the Canary Islands), it cannot be ignored that the ancestors of these Europe-derived populations could be carriers of the African lineages, especially in San Antonio, where an African female contribution of 22% was recorded.

In relation to the Y-chromosome haplogroups (Table 3), there is a predominance of the category that includes European haplogroups P*R*, from 53% to 77%, with only Araya reporting the presence of African haplogroup Elbla*.

In general the most important maternal contribution in these populations is European (58%), whereas through males, it is absolute (100%), with the exception of Araya, where the African contribution is 8% (Table 4).

Admixed/Urban Populations. The frequencies of Amerindian and African mitochondrial lineages show a large variability in these populations (Table 2). In all of them, the four Amerindian haplogroups are present and are the most frequent, with predominance of B only in Lara (37%) and Churuguara (44%), whereas in the rest, A predominates (25%–49%). As regards the Africans, the most frequent is L (L1+L2) and the presence of L3* (neither L3d nor L3e) stands out in almost all the populations; the most frequent European haplogroup is H, with an average frequency of 4%, followed by U (3%).

In relation to the paternal contribution (Table 3), a predominance of the category that includes the P*R* European haplogroup is observed, with frequencies greater than 48%. Of the African haplogroups, only Elbla* appears in most of the populations, albeit with lower frequencies, less than 11%, with the exception of Churuguara, where it reaches 20%. The presence of African haplogroup AB in Sucre is noticeable. Indigenous haplogroups were found only in Lara and lower socioeconomic level in Caracas and in Sucre.

The maternal admixture in these populations highlights the predominance of an Amerindian contribution (Table 4), with values between 49% (Caracas-A) and 84% (Nueva Esparta), followed by the African and a low European contribution (less than 9%), except for the higher socioeconomic level in Caracas, where European lineages reach 30% and show a diverse representation. As regards the paternal admixture, a predominating European contribution is observed in this group, with an average value of 90%, followed by African (8%) and an almost nonexistent Amerindian contribution. The low indigenous contribution at the autosomal level previously detected in Sucre and Nueva Esparta (Table 1) may be partially explained because of the limitations of the systems used in this estimation, the ABO and Rh blood groups, as mentioned in Castro de Guerra and Zambrano (2000).

We can sum up that for all the populations studied, in mitochondrial lineages there is a predominance of the indigenous component at a national level (Table 4). Amerindian and African contributions are distributed throughout the populations, regardless of their origin, although Africans have a larger presence in African-derived populations; the Europeans component is concentrated in European-derived populations. As regards the male contribution, it is almost entirely European in all the populations studied, with some African presence, especially in Afro-descendant populations. The indigenous contribution is almost nonexistent.

Discussion and Conclusions

The data published on admixture in Venezuela (Table 1) refers to populations located in different geographic regions of the country, most of them being included in this study. They show different historic backgrounds in their emergence, manifested in the origin of their ethnic composition. The information reported is based on different types of autosomal polymorphisms (classic and molecular), and different methods for admixture estimation were used.

The first approximation of admixture estimates of the general Venezuelan population (Rodríguez-Larralde et al. 2001) revealed the predominance of the European genetic component (59%), followed by the Amerindian (28%) and to a lesser extent, the African (13%), with important interregional differences. This first approach does not provide information on the genetic diversity within each region (e.g., the central region where coexist populations of Spaniards/Canaries with African descent); thus, the classification criteria by geographic region is occasionally not the most adequate, and it may be more suitable to consider common historic aspects, such as ethnic origin.

African-derived populations have a predominance of the African genetic contribution; in some, such as Ganga (Miranda State), the scarce admixture is with Amerindians (Castro de Guerra et al. 1993), but in Macuquita the European contribution is important. In others, such as Panaquire, Curiepe, Birongo, and Sotillo (Bortolini et al. 1999), about 40% of the genes are of Amerindian and/or European origin, with interpopulation differences related to specific conditions of their emergence and socio-historic development. Similar levels of African contribution and diversity of admixture to our African Venezuelan towns have been reported for other Latin American African-derived populations (Salzano and Bortolini 2002), showing less African ancestral than North American African-derived origins (Parra et al. 1998).

Biparental estimates of admixture published by us for European-derived populations, such as San Antonio, San Diego, and Hoyo de La Cumbre (Table 1), although preserving an almost exclusive proportion of European genes, register an indigenous and African contribution (Castro de Guerra and Zambrano 2000). The admixed/urban populations, without precise ethnic origin, are important urban centers with significant gene flow from other towns in the same geographical area, such as Churuguara and Lara, from the northwest of the country, and those of Monagas, Nueva Esparta, and Sucre, from the northeast. However Caracas, Venezuela′s capital has attracted its population from all over the country. In all of the admixed/urban populations, a genetic predominance of European origin followed by an indigenous contribution is observed, with internal heterogeneity in Caracas, which has a predominance of the European contribution of almost 54%, but presents differences when the individuals of the sample are classified according to their socio-economic level, with a higher indigenous contribution in the lower (40%) and European in the higher (75%) levels (Martínez et al. 2007). The level of European contribution in urban

Venezuelan populations resembles the tendencies reported for Argentina, Uruguay and the southern part of Brazil (Salzano and Bortolini 2002).

Polymorphisms of uniparental heritage offer another image of the admixture process and reveal the way in which men and women of different ethnic origins intercrossed to conform the present Venezuelan population. We found a predominantly female indigenous contribution, which is more important in urban populations. The African and European contributions, although scattered throughout the admixed/urban populations, naturally are more evident in the African and European-derived populations respectively. Both cases reflect the importance of isolations and inbreeding for geographical or cultural reasons, in limiting gene flow and preserving the gene distribution pattern of the colonial era. The distribution of the African and European female contributions in Venezuela presents some differences in relation to other South American countries. For example, in African-derived populations in Brazil, Uruguay, and Colombia (Bortolini et al. 1999; Ribeiro-dos-Santos et al. 2002; Rodas et al. 2003; Sans et al. 2002), the proportion of African haplogroups is greater than in Venezuela, and presents a varied European and indigenous proportion, whereas in those Venezuelan African-derived groups studied, no European mitochondria were detected. In populations with this origin, the results obtained in Macuquita are of particular interest because the indigenous contribution detected for autosomal markers was absent, whereas 75% of their mitochondrial lineages were Amerindians. The estimation of autosomal admixture was based solely on information from the ABO and Rh blood groups, and the limitation on the information provided by these systems may be an explanation of this difference. However, Macuquita is a small town founded by runaway slaves from Curacao and the western Venezuelan region, in addition to some indigenous natives, which explain its female Indian ancestry. Founder effect, which is more intense for uniparental markers, plus gene flow limited due to isolation and matrilocality (Castro de Guerra et al. 2009), may also be considered. In admixed/urban populations, in addition to indigenous predominance, there is meager presence of European haplogroups, which are concentrated in the higher socioeconomic level of Caracas.

In general, the mtDNA results suggest that (1) the arrival of European women in Venezuela in the colonial era was limited, (2) that the number of African slaves must have been low in relation to other Latin American countries, and (3) that the immigration of European women in the 20th century occurred preferentially to urban centers, with a greater predominance in the higher socioeconomic strata (Martínez et al. 2007; Suárez and Torrealba 1979).

It is difficult to establish through RFLP, the precise ethnic origin of the female genetic contribution; nonetheless, some tendencies may be proposed. The most frequent Amerindian haplogroups in northern Venezuela are A and B, as is reported for Colombia and populations of Central and North America (Keyeux et al. 2002). However, the highest B frequency in Macanillas, Macuquita, Lara, and Churuguara draws our attention. All of these are located in the western region of

Venezuela, whereas in the rest of the central and eastern populations, there is a predominance of A. Haplogrupos C and D are also more frequent in mid-eastern populations, with the exception of Macuquita, located in the West, where the high frequency of the D haplogroup is explained by specific historic causes (Castro de Guerra et al. 2009). These differences, between the West and the Mid-East, may be a reflection of the settlement patterns in the preconquest era, specifically, the presence of Arawacs in the West and the Caribes in the Mid-East. These results demonstrate that the present Venezuelan population is an important reservoir of Amerindian mtDNA, which allows us to make genetic inferences on already extinct populations.

Conclusions about the specific ethnic origins of the maternal African and European contributions are difficult due to their limited representation in the sample studied. However, the presence of haplogroups L3e and L3* in most of the populations leads us to assume the importance of contribution from west-central Africa in Venezuela. In that respect, some previous approximations with other genetic systems show results that suggest a contribution of groups of the Bantú language (Arends et al. 2007; Bortolini et al. 1995; Vívenes de Lugo et al. 2003). As regards the European contribution, haplogroup H is the most frequent, as in Western Europe, although the ample distribution of haplogroup U may reflect the importance of the original contribution from the Canary Islands. A sequence analysis would clarify this situation.

In relation to the origin of the male contribution, the seven investigated SNPs do not permit conclusions regarding the geographical origin of 25% of the Y-chromosomes analyzed. However, admixture estimates suggest that Y-chromosomes are predominantly European in origin and that the inclusion of other SNPs markers would identify the specific origin as that of subhaplogroups of the R* clade.

The African lineages are concentrated basically in the African-derived populations, whereas Amerindian lineages are almost nonexistent. The proportion of African lineages present, even in the African-derived populations, is one of the lowest in South America; the absence of AB and the presence of Elbla* suggests a contribution from Western Africa. In addition to the low number of African slaves brought to Venezuela, it is very probable that those who entered illegally from the Caribbean and the Antilles were descendants of the unions of African women with European men and thus were carriers of the European Y-chromosome.

In Venezuela the genome of paternal heredity, unlike the autosomic and mitochondrial, shows an homogeneous admixture pattern that is independent of the ethnic origin of the population. In conclusion, African and Amerindian Y-chromosomes were almost all substituted by the Europeans, in a phenomenon that we have previously designated as transplanted male genomes (Castro de Guerra et al. 2003). These results corroborate the tendency found in preliminary studies carried out in the Venezuelan population (Bortolini et al. 1999; Castro de Guerra et al. 2003, 2009; Martínez et al. 2007) and in other American

populations, in relation to a marked asymmetry in sexual unions that occurred predominantly between European men and indigenous or African women.

In general, our data suggest heterogeneity in relation to the origin of the different genomes in Venezuela. The autosomic is predominantly European with an important Amerindian contribution; the mtDNA is mainly Amerindian, whereas the Y-chromosome is European. Thus European genes have entered the Venezuelan population through male immigrations, whereas the indigenous contribution has been preserved in the genetic pool of Venezuela through the women.

Our results support the colonial census data that suggest that the admixture process in Venezuela was intense and began early. Furthermore, the existence of 50% mixed castes at the beginning of the 19th century (Guerra Cedeño 1996) suggest that the individuals classified in this category were mostly descendants from indigenous women.

The predominance of unions between men and indigenous women in post-conquest times is well documented and is justified by diverse reasons such as the scarcity of Spanish women during the first years of colonization and factors of prestige that favored the descendants of unions between indigenous women with Spanish males. In that respect, the laws of the Indies allowed mixed marriages between Hispanics and Indians, but not between Spanish or Indians with Africans (Troconis Veracochea 1969); thus Spanish/indigenous genetic exchange was favored. Other types of unions (African/Spanish or African/indigenous) occurred illegally.

After colonial times, European migrations, especially of males, were favored by the immigration laws. During the mid-20th century abundant Spanish, Italian, and Portuguese immigration occurred in Venezuela. The European genetic flow was favored continuously from colonial times to the present, whereas African immigrations were limited only to the colonial period.

The economic and socio-cultural factors favored the relative isolation of Venezuelan populations in postcolonial times. For these reasons the African genetic contribution, although disperse, still remains concentrated in colonial areas of black population, and those of indigenous and European origin are disperse in most of the country.

Summing up, the Venezuelan genetic pool is a product of a complex admixture process conditioned by different historic events, where economic variables played a fundamental role in the geographic distribution of inhabitants in the colonial era, marking the distribution of genes with different ethnic origins around the territory. This distribution persists today. The data on uniparental and biparental admixtures, sustain the classification of these populations according to their ethnic/historic origin.

The results obtained demonstrate the intra- and interpopulation heterogeneity in Venezuelan populations, which should be taken into account in forensic and genetic epidemiologic studies. For example, the European-derived populations studied, due to the homogeneity of their genetic origin, are good candidates

for association studies, whereas African-derived and admixed/urban populations require a more careful approach, considering the origin of the chromosomal regions of the genes in question, according to the chromosomal maps of linkage disequilibrium (Bedoya et al. 2006; Price et al. 2007; Wang et al. 2008).

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