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Genetic structure of Mexican Mestizos with type 2 diabetes mellitus based on three STR loci

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ABSTRACT

Background: The aims of this population genetics study were: 1) to ascertain whether Mexicans with type 2 diabetes mellitus (DM) were genetically homogeneous and 2) to compare the genetic structure of this selected population with the previously reported data of four random populations (Nuevo León, Hispanics, Chihuahua, and Central Region of Mexico).
Methods: A sample of 103 unrelated individuals with DM and whose 4 grandparents were born in five zones of Mexico was interviewed in 32 Medical Units in the Mexican Institute of Social Security (IMSS). The non-coding STRs D16S539, D7S820, and D13S317 were analyzed.
Results: Genotype distribution was in agreement with Hardy–Weinberg expectations for all three markers. Allele frequencies were found to be similar between the selected population and the four random populations. Gene diversity analysis suggested that more than 99.57% of the total gene diversity could be attributed to variation between individuals within the population and 0.43% between the populations.
Conclusions: According to the present and previous studies using molecular and non-molecular nuclear DNA markers not associated with any disease, the Mexican Mestizo population is found to be genetically homogeneous and therefore the genetic causes of DM are less heterogeneous, thereby simplifying genetic epidemiological studies as has been found in a previous study with the same design in Mexican women with breast cancer.
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1. Introduction

In Mexico, there are 112,322,757 inhabitants, 51.22% women and 48.78% men (Censo de Población y Vivienda, 2010).

In previous studies using non-molecular nuclear DNA markers, we showed that populations of Northeastern Mexico (grouped by birthplace of the four grandparents and birth year) are similar in terms of the contribution of Spanish and Native American genes. More than 96% of the total genetic diversity (G_{ST}) could be attributed to individual variation within the populations defined by birthplaces and/or birth year. There was no nonrandom association of alleles among the genetic marker systems despite the Mestizo origin of the study population (Cerda-Flores and Garza-Chapa, 1989; Cerda-Flores et al., 1987, 1991).

Also, Cerda-Flores et al. (2002a, 2002b) compared genetic polymorphisms at the D1S80 and HLA-DQA1 loci in three unrelated and

Abbreviations: CHIH., Chihuahua; CRMx, Central Region of Mexico; DF, Degree of freedom; DM, Type 2 diabetes mellitus; Exp., Expected; Gst, Total genetic diversity; Ht, Total average gene diversity; HWE, Hardy–Weinberg expectations; IMSS, Mexican Institute of Social Security; LRT, Likelihood ratio test; N.L., Nuevo León; NEGST, Nested gene diversity; Obs., Observed; P, Probability value; PC1, Principal component 1; PC2, Principal component 2; PCR, Polymerase chain reaction; STR, Short tandem repeats; TFA, Fast technology for analysis of nucleic acids; X^2, Chi squared test; CI, Coefficient interval.

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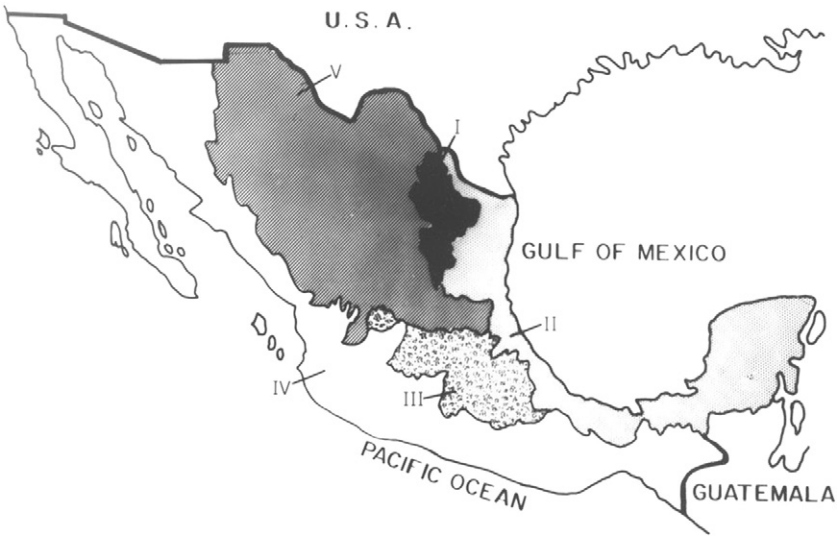

Fig. 1. The location of the five zones of Mexico where the grandparents were born.

healthy Mexican Mestizo populations from three large states (Nuevo León, Jalisco, and the Federal District). Allele frequencies were relatively homogeneous in the three samples. In terms of genetic composition, these Mestizo populations showed evidence of admixture with predominantly Spanish (50–60%) and Native American (37%–49%) contributions; the African contribution (1–3%) was minor.

Cerda-Flores et al. (2002a, 2002b) did not find significant differences when they made a comparison of the genetic admixture among the 143 Mestizos from Northeastern Mexico with the data on previously reported molecular markers, D1S80 and HLA-DQA1 (Spanish 60%, Amerindian 37%, and African 3%) versus 13 short tandem repeat (STR) loci (Spanish 55%, Amerindian 40%, and African 5%).

Type 2 diabetes mellitus (DM) is one of the most common metabolic and endocrinal disorders in developed countries. The prevalence of DM varies widely in populations around the world, with polygenic inheritance and environmental factors contributing to its clinical expression (Bennett and Stern, 1991).

In Mexico, during the 1970s it was the seventh highest, in the 1980s it was the third highest, and in the 1990s it has been considered the highest of all non-communicable diseases (Vazquez-Robles and Escobedo-de la Peña, 1990).

Table 1
Demographic distribution of the zone of birth of the four grandparents of the Mexicans with type 2 diabetes mellitus.

Zone of birth[a]	Maternal		Paternal		Total (%)
	Grandfather	Grandmother	Grandfather	Grandmother	
I	21	22	15	16	74 (19.07)
II	4	5	5	4	18 (4.64)
III	7	7	9	8	31 (7.99)
IV	5	5	5	4	19 (4.90)
V	61	58	63	64	246 (63.40)
Total	98	97	97	96	388
Probability (R × C)	0.9932				

Zone II. Tamaulipas, Veracruz, Yucatán, Campeche, Tabasco, Quintana Roo.
Zone III. Guanajuato, Federal District, Aguascalientes, Puebla, Querétaro, Hidalgo, Tlaxcala, Morelos, Mexico State.
Zone IV. Jalisco, Michoacán, Oaxaca, Nayarit, Guerrero, Colima, Sinaloa, Sonora, Chiapas, Baja California (North and South).
Zone V. San Luís Potosí, Coahuila, Zacatecas, Durango, Chihuahua.
[a] Zone I. Nuevo Leon.

In a previous population genetics study we showed that 115 Mexican women with breast cancer (BC) were genetically homogeneous. The genetic structure of this selected population was similar to four random populations [Nuevo León, Hispanics, Chihuahua, and Central Region of Mexico (CRMx)]. The Spanish and Native American contribution were 40.08 ± 6.17% and 59.92 ± 6.17%, respectively. The design and genetic markers of this previous study was similar to the present study (Calderón-Garcidueñas et al., 2008).

The aims of this population genetics study using the non-coding STRs D16S539, D7S820, and D13S317 that are not associated with DM were: 1) to study the genetic variation in Mexicans with DM; 2) to compute the total contribution of the ancestral populations to this selected population; 3) to evaluate whether there is a residual effect of population admixture on the nonrandom association of alleles; and 4) to compare the observed distribution of the number of heterozygous loci in this population with the data reported in the literature for four random populations [Nuevo León, Hispanics, Chihuahua, and Central Region of Mexico (CRMx)].

2. Materials and methods

Genetic data from this population were collected as part of a larger investigation of the genetic structure of the Mexican Mestizo and Indigenous populations using nuclear DNA, mitochondrial DNA, and Y-chromosome markers.

A sample of 103 unrelated Mexicans with DM (48 men and 65 women), recently diagnosed, was interviewed in 32 Medical Units of the Mexican Institute of Social Security (IMSS) in 2002. Each one of the IMSS Medical Units correspond to each one of the 31 States (capitols) and one Federal District in the entire Mexico.

The study was explained to the patients who were requested to sign an informed consent. The sampled population was interviewed using a structured questionnaire that asked for age, sex, total number of pregnancies, years of education, weight status, civil stage, and place of birth of four grandparents. This study was approved by the Ethical Committee of the IMSS and the Universidad Autonoma de Nuevo Leon.

The data were subgrouped in accordance to the zone of Mexico where the grandparents were born. The country was divided into five zones as is shown in Fig. 1 and Table 1:

I. All in the State of Nuevo León.
II. At least one in the States of Tamaulipas, Veracruz, Yucatan, Campeche or Tabasco.