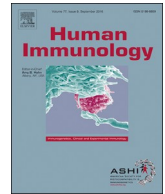




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Genetic diversity of HLA system in four populations from Baja California, Mexico: Mexicali, La Paz, Tijuana and rural Baja California

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ABSTRACT

We studied HLA class I (HLA-A, -B) and class II (HLA-DRB1, -DQB1) alleles by PCR-SSP based typing in 250 Mexicans from the states of Baja California Norte and Baja California Sur living in Mexicali (N = 100), La Paz (N = 75), Tijuana (N = 25) and rural communities (N = 50) to obtain information regarding allelic and haplotypic frequencies. The most frequent haplotypes for the Baja California region include nine Native American and five European haplotypes. Admixture estimates revealed that the main genetic components are European (50.45 ± 1.84% by ML; 42.03% of European haplotypes) and Native American (43.72 ± 2.36% by ML;

Abbreviations: HLA, human leukocyte antigen; MPA, most-probable ancestry; LD, linkage disequilibrium

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40.24% of Native American haplotypes), while the African genetic component was less apparent ($5.83 \pm 0.98\%$ by ML; 9.36% of African haplotypes).

Baja California is located in the northwestern region of Mexico (Fig. 1), bordering on the northwest to the state of Sonora and on the north to the American state of California. Its condition as a peninsula, coupled with its unique demographic history, gives it a special interest when it comes to studying and genetically characterizing its population. At least 10,000 years ago, different human groups started coming to the Peninsula, according to organic settlement evidence accumulated by people who ate shellfish. Radioactive 14 carbon tests on material from Punta Minitas (7020 ± 260 years ago) and San Quintin (6165 ± 250 years ago) is evidence of that early presence [1]. Moreover, lithic utensils found in the middle north of the territory have sufficient affinity to be related with the prehistoric complex of Arizona's southwest or with the third phase of San Dieguito's complex, which is chronologically situated from 7000 to 5000 BC. According to this evidence, different waves of settlement have been suggested in which the oldest population entering the region would have been the first one to reach the southern tip of the peninsula. As mentioned before, there is not sufficient linguistic evidence to support these conclusions and the cultural heritage interpretations have the problem of ubiquity of adaptive constraints because of the lack of options in front of very specific pressures. It can be argued the same about the scientific studies based on craniometrical morphology [2]. Because of the differences of those that we call hyperdolicocephalic groups, there are some statements about different migrations, but the constraints of the different niches can accept an explanation of local adaptive traits. If we consider that Baja California Peninsula has an extension of 143,780 km² with a length over 1200 km and a seashore of 3500 km with a huge desert land, and we think about the lack of big populations, the only strong conclusion is settlements with morphological and cultural stability in multiple isolations and local adaptability. This is why molecular evidence will be needed.

Even though the peninsula's current population exceeds the figure of 3,584,000 inhabitants [3,4], in the middle of 20th century it there were less than 200,000 inhabitants and the majority came from the continental mass [5]. Historical continuity studies of that population in terms of identity have had less attention than other originating Mexican groups. Moreover, except for some native prehispanic languages that belong to the linguistic family Cochimi-Yumana that still exists in the north of Mexico, the rest of the languages actually disappeared in the 18th century when the extinction of the majority of the aboriginal

groups had started. This is why the little is known about groups like the Waycura, the Aripe and the Pericues is thanks to the missionary chronicles, the precarious archaeological evidence and the osteological and molecular studies in some human remains.

Diverse tribes, in constant struggle, occupied the territory, in communities very different to those of Mesoamerican societies and of course European ones [6]. The inhabitants of Baja California at the time of contact with Europeans had no cities, no masonry constructions, no elaborate religion; they virtually did not practice agriculture and lived on the harvesting of fruits (pitahaya was an important part of their diet), hunting and fishing. It is not possible to specify the number of inhabitants that the Peninsula had in the years immediately before the arrival of the Spaniards [6]. The Europeans arrived in Baja California in 1530 and according to their testimony, there found four native groups: Yumanos, Cochimies, Guaycuras and Pericues, distributed from north to south respectively. Most of these groups disappeared or were diluted by the mid-eighteenth century.

In terms of population volumes, which are the first markers of the migration phenomenon (immigration or emigration) possibly from other parts of Mexico and from the expansion of the American Southwest [7], in the case of the Baja California peninsula during the 19th century were about 4508 inhabitants for 1803 to 43,282 inhabitants for the first modern Mexican census in 1895, that is, an increase of more than 900% in 92 years. Still, part of this demographic expansion could be explained from the natural growth of the population (births minus deaths).

As of that date, there was an important migration composed of Europeans, *Novohispanos* and continental Native Americans. However, to this demographic reality we must add the presence of African and Asian (mainly from China and Philippines) populations, who worked respectively as stevedores in the ports or as traders in the route of the Manila Galleon that connected commercially the ports of Acapulco and Manila. Baja California is therefore an interesting mixed ancestry population resulting from the anachronistic contribution of different human groups, and recent migration from USA and Canada [8].

For the present work, we analyzed HLA class I (*HLA-A*, *-B*) and class II (*HLA-DRB1*, *-DQB1*) PCR-SSP typings in 250 Mexicans from the region of Baja California [the region of Baja California (includes both Baja California Norte and Baja California Sur) data here analyzed is composed by the following populations: Mexico Baja California, Mexicali,

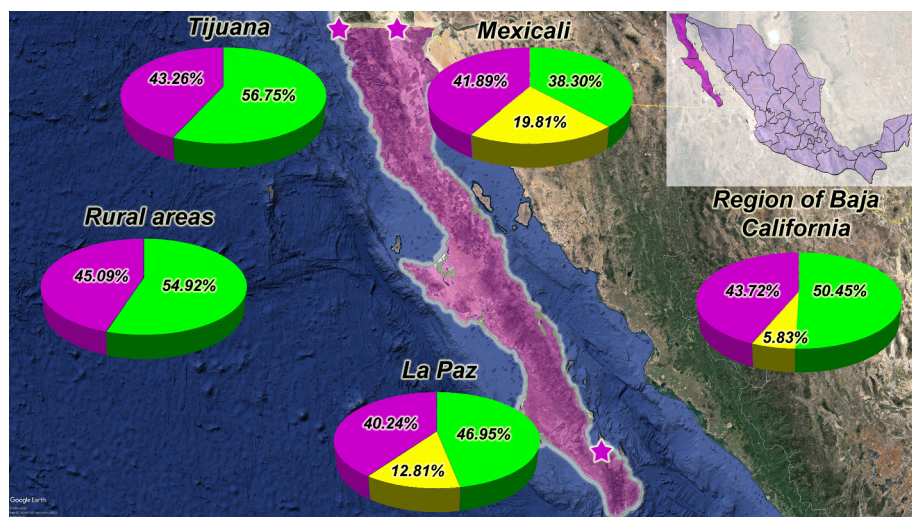


Fig. 1. Geographic situation of the region of Baja California and admixture proportions for the region of Baja California [composed by the following populations: Mexico Baja California, Mexicali, N = 100, Allele Frequencies Net Database Identifier (AFND-ID): 3527; Mexico Baja California, La Paz, N = 75, AFDN-ID: 3526; Mexico Baja California, Tijuana, N = 25, AFDN-ID: 3615; Mexico Baja California Rural, N = 50, AFDN-ID: 3571]. Admixture proportions were estimated by ML using *HLA-A*, *-B* and *-DRB1* frequencies as genetic estimators. Green refers to the proportion of European contribution, purple to Native American contribution and yellow depicts African contribution. Map modified from Google Maps Pro [15].

N = 100, Allele Frequencies Net Database Identifier (AFND-ID): 3527; Mexico Baja California, La Paz, N = 75, AFDN-ID: 3526; Mexico Baja California, Tijuana, N = 25, AFDN-ID: 3615; Mexico Baja California Rural, N = 50, AFND-ID: 3571]. In addition to the individual populations we also show data for these combined populations. This latter data is not held on AFND to prevent duplication of data. Maximum-likelihood (ML) frequencies for alleles and four-locus haplotypes were estimated using an Expectation-Maximization algorithm. For a comprehensive review on the methods, such as sample collection, HLA typing and statistical analyses, please refer to Ref. [9] in this same issue. For the frequencies of *HLA-A*, *-B*, *-DRB1* and *-DQB1* and haplotypic data for the sample sets of the region of Baja California please refer to the [Supplementary Information: Supplementary Tables 1–9](#). For data on Hardy-Weinberg equilibrium (HWE) please see [Supplementary Information: Supplementary Table 10](#) of this work and [Supplementary Information: Supplementary Table 9](#) in Ref. [9] in this same issue. The most frequent haplotypes for the state (haplotypic frequency, H.F. $\geq 1.0\%$, arbitrarily; [Supplementary Table 5](#)) include nine Native American MPA (HLA-A*02~B*35 ~ DRB1*04 ~ DQB1*03:02, A*02 ~ B*35 ~ DRB1*08 ~ DQB1*04, A*02 ~ B*39 ~ DRB1*04 ~ DQB1*03:02, A*68 ~ B*40:02 ~ DRB1*04 ~ DQB1*03:02, A*02 ~ B*40:02 ~ DRB1*08 ~ DQB1*04, A*24 ~ B*39 ~ DRB1*04 ~ DQB1*03:02, A*02 ~ B*40:02 ~ DRB1*04 ~ DQB1*03:02, A*02 ~ B*39 ~ DRB1*08 ~ DQB1*04 and A*31 ~ B*35 ~ DRB1*04 ~ DQB1*03:02) and five European MPA haplotypes (HLA-A*29 ~ B*44 ~ DRB1*07 ~ DQB1*02, A*33 ~ B*14:02 ~ DRB1*01 ~ DQB1*05, A*02 ~ B*18 ~ DRB1*03:01 ~ DQB1*02, A*03 ~ B*07 ~ DRB1*15 ~ DQB1*06 and A*11 ~ B*18 ~ DRB1*11 ~ DQB1*03:01). Admixture estimates ([Fig. 1](#)) revealed that the main genetic components are European ($50.45 \pm 1.84\%$ by the ML method and 42.03% by estimating the proportion of European haplotypes) and Native American ($43.72 \pm 2.36\%$ the ML method and 40.24% by estimating the proportion of Native American haplotypes), while the African genetic component was less apparent ($5.83 \pm 0.98\%$ by the ML method and 9.36% by estimating the proportion of African haplotypes). Proportions vary among the different datasets from the region. The city of La Paz shows roughly the same amount of European ($46.95 \pm 6.77\%$ by ML and 40.00% of European haplotypes) and Native American ($40.24 \pm 5.08\%$ by ML and 38.00% of Native American haplotypes) components, with a prominent African contribution ($12.81 \pm 9.65\%$ by ML and 12.67% of African haplotypes). Even though Mexicali is very far away from La Paz, it exhibits very similar results: virtually equal European ($38.03 \pm 3.85\%$ by ML and 44.50% of European haplotypes) and Native American ($41.89 \pm 2.99\%$ by ML and 44.00% of Native American haplotypes) components, with an important African contribution ($19.81 \pm 5.64\%$ by ML and 8.50% of African haplotypes). Surprisingly, Tijuana and the rural communities show a similar, and somewhat unexpected, profile: due to their classification as migration attractors [10], we expected them to bear a higher Native American and probably African components. Instead, they show a higher European component (Tijuana: $56.75 \pm 6.63\%$ by ML and 44.00% of European haplotypes; rural areas: $54.92 \pm 2.25\%$ by ML and 39.00% of European haplotypes) than the Native American one (Tijuana: $43.25 \pm 1.04\%$ by ML and 42.00% of Native American haplotypes; rural areas: $45.09 \pm 6.34\%$ by ML and 44.00% of Native American haplotypes), and a low African contribution (Tijuana: $0.00 \pm 6.30\%$ by ML and 6.00% of African haplotypes; rural areas: $0.00 \pm 4.52\%$ by ML and 8.00% of African haplotypes). This profile,

contrasting with previous reports [11], may be explained by the important amount of foreign immigrants born in USA moving into the Mexican side of the border zone [8].

The presence of Asian haplotypes in the region (Baja California region: 5.98% ; La Paz: 8.00% ; Mexicali: 4.00% ; Tijuana: 6.00% ; rural areas: 8.00%) can be explained by the immigration of Asians escaping from California by the end of the 19th century and the beginning of the 20th century and settling in northern Mexico before the violence held against them during the first decades of the last century in Mexico [12], but also by immigrants arriving into the region from the Philippines, China and East Asia in general, using the transpacific commercial route known as the Manila Galleon during the Colonial period [13]. The admixture estimates and the presence of Native American, European and Asian haplotypes can be explained by the aforementioned historical events that shaped the demographic traits of the present-day region of Baja California, but also exhibit some specific traits that could help shape questions arising from historical and archaeological contexts. All data from our sample sets, both frequencies and individual genotypes, can be found at The Allele Frequency Net Database website (www.allelefrequencies.net) [14].

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.humimm.2019.06.007>.

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