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Short population report

4-Locus high-resolution HLA allele and haplotype frequencies in Costa Ricans from African-Caribbean descent

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ABSTRACT

A total of 102 Costa Ricans of African-Caribbean descent were genotyped at high-resolution for the human leukocyte antigen loci HLA-A, -B, -C, and -DRB1 using sequence-based typing methods. The respective allele and extended haplotype frequencies, as well as Hardy-Weinberg proportions were calculated. The most frequent extended haplotype identified was A*01:01:01-B*08:01:01-C*07:01:01-DRB1*03:01:01G, with an estimated frequency of 1.96%. No deviation from Hardy-Weinberg Equilibrium was detected at any of the loci studied. The HLA genotypic data of the population sample reported here are available publicly in the Allele Frequencies Net Database under the population name “Costa Rica African-Caribbeans” and the identifier AFN3607.

Costa Rica is a Central American country with an area of 51,000 km^2 and a population of approximately 5 million inhabitants. Its African-descendant population, namely Costa Ricans of African-Caribbean descent (CRAC), represents approximately 2% (8% if Mulattoes are included) of the general population. This population arose relatively recently as it is constituted mostly by descendants from migrant workers from Jamaica and other Caribbean islands who arrived to Costa Rica’s Caribbean coast during the second half of the 19th century to participate in the building of the Caribbean Railway and later worked in the cocoa and banana plantations. In stark contrast to the Mestizo populations of this country, most of them carry English or Scottish surnames, and in many cases retain their English-based creole. Despite nowadays inhabiting other regions of the country too, a large proportion of these Costa Ricans of African-Caribbean descent still reside along the Caribbean coast of the country, with the highest agglomeration located in the provincial capital city of Limón. The CRAC population has been a focus of interest for research in glucose-6-phosphate dehydrogenase deficiency [1–3] and hemoglobinopathies [4–7] in Costa Rica.

A total of 102 saliva samples from unrelated healthy volunteer donors were included in this study. All individuals included self-identified as Costa Ricans of African-Caribbean descent and had two parents who were also of African-Caribbean descent. All samples were collected in the city of Limón as part of the DNA biobank at the University of Costa Rica’s Centre for Research in Hematology and Related Disorders (Centro de Investigaciones en Hematología y Trastornos Afines, CIHATA), which continuously collects samples for the characterization of genetic variation across the country and its association with medically-relevant traits. DNA was extracted from blood or saliva by routine methods. All participants gave informed written consent as per CIHATA’s DNA biobank standard procedures. Sample collection under CIHATA’s biobank and this study were approved by the local ethics

Abbreviations: AFND, Allele Frequencies Net database; CRAC, Costa Ricans of African-Caribbean descent; EM, expectation-maximization; HWE, Hardy-Weinberg equilibrium

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committee at the University of Costa Rica.

High-resolution HLA typing was performed at Anthony Nolan by in house sequence-based typing methods, with generic amplification of exons 2, 3 and 4 for HLA-A, HLA-B, HLA-C. For HLA class II, exon 2 of the HLA-DRB1 gene was amplified using in-house allele group-specific primer pairs. Amplicons were purified and each exon was sequenced on an ABI 3730xL DNA Analyzer with specific forward and reverse primers using the Big Dye® Terminator v3.1 Cycle Sequencing Kit (Applied Biosystems). Sequence analysis was done with Assign-SBT software (version 3.6+, Conexio Genomics, Freemantle, Australia) using IPD-IMGT/HLA database release 3.9.0 [8]. Ambiguities were further solved using allele-group- (HLA class I) or codon-86-specific (HLA class II) primer combinations and sequencing of the allelic products. For HLA class I, alleles with identical sequences at codons 2, 3, and 4 could not be distinguished, and were assigned the third-field name of the allele with the lowest numerically ordered name (which is usually the more common one). Hence, HLA class I allele frequencies given may in many cases represent the frequency of a group of alleles sharing sequences at these exons. Allele groups (G) were assigned to HLA class II alleles according to IPD-IMGT/HLA database specifications. All homozygous samples were confirmed by at least two determinations and using different techniques. Allele frequencies and compliance with Hardy-Weinberg equilibrium (HWE) were computed using the online tools available from the HLA-net platform (http://hla-net.eu/tools/) [9]. Haplotype frequencies were estimated by an in house implementation of the expectation-maximization (EM) algorithm [10].

All samples were successfully typed for HLA-A, HLA-B, HLA-C, and HLA-DRB1. A total of 31, 43, 25, and 34 alleles were identified for HLA-A, -B, -C, and -DRB1, respectively. Compliance with HWE was confirmed for all loci ($p > 0.5$). The five most common alleles per locus were A*30:01:01 (10.8%), A*23:01:01 (10.3%), A*03:01:01 (8.8%), A*74:01 (8.8%), A*02:01:01 (8.3%); B*53:01:01 (13.7%), B*15:03:01 (9.3%), B*35:01:01 (6.7%), B*42:01:01 (6.4%), B*07:02:01 (5.9%); C*04:01:01 (23.5%), C*02:10 (9.3%), C*17:01:01 (8.8%), C*06:02:01 (8.3%), C*07:01:01 (7.8%); DRB1*15:03:01G (14.7%), DRB1*03:01:01G (10.3%), DRB1*07:01:01G (9.8%), DRB1*11:01:02 (8.8%), DRB1*13:02:01 (7.8%). The complete lists of alleles for each locus are given in Supplementary Table 1.

Based on the results for HLA typing, 4-locus haplotype frequency estimations based on the expectation-maximization algorithm were generated. The number of the extended haplotypes with an estimated frequency > 1/2N was 173. Six extended haplotypes have estimated frequencies of > 1%, the most common being A*01:01:01-B*08:01:01-C*07:01:01-DRB1*03:01:01G (1.96%), A*23:01:01-B*53:01:01-C*04:01:01-DRB1*11:01:02 (1.96%), A*02:02-B*53:01:01-C*04:01:01-DRB1*15:03:01G (1.96%), A*74:01-B*44:03:01-C*04:01:01-DRB1*15:03:01G (1.47%), and A*01:01:01-B*35:01:01-C*04:01:01-DRB1*03:01:01G (1.47%). A complete list of estimated extended haplotypes is given in Supplementary Table 2. The HLA profiles of CRAC show great similarity to other populations of Sub-Saharan African descent, especially those native to Western Africa and other African-descendant populations in the Americas [11]. However, gene flow from other continental groups can also be appreciated via our HLA data. This is demonstrated by the presence of alleles common in Amerindians (B*35:43:01, C*03:05), as well as the 8.1 haplotype (A1 ~ B8 ~ DR3). Gene flow in African-Caribbeans from Costa Rica, as well as evidence for genetic drift as a result of isolation in Costa Rica has also been reported by others [12]. All genotype, as well as haplotype and allele frequency data are available in the Allele Frequencies Net database (AFND) [13] under the population name “Costa Rica African-Caribbeans” and the identifier (AFN3607). Haplotype and HLA class II allele data are available in “G” notation in the supplementary information accompanying this publication. However, the notation “G” is omitted in AFND due to format restrictions, and second-field level resolution is shown for the relevant alleles instead.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humimm.2019.05.007.

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