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Short population report

HLA-A, -B, -C, -DRB1 and -DQB1 allele and haplotype frequencies of 1463 umbilical cord blood units typed in high resolution from Bogotá, Colombia

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ABSTRACT

Allele and haplotype frequencies were calculated from 1463 umbilical cord blood (UCB) units, from Bogotá (Colombia) donors, HLA-typed in high resolution. This is the first report using allele-level typed colombian samples of five HLA loci related to hematopoietic stem cell transplantation (HLA-A, -B, -C, -DRB1 and -DQB1). The most frequent haplotype found in our sample was A*24:02g ~ B*35:43g ~ C*01:02g ~ DRB1*04:07g ~ DQB1*03:02g (4.14%). Our data are available at the Allele Frequencies Net Database under the code AFND3604.

Colombia is a South American country with an approximate population of 41.5 million people according to the latest official report and its population is divided into four main groups of heritage: Mestizo or non-Native American (defined as a racial mixture among Native American, African and European; 35 million, 84.16%), Native American (1.4 million, 3.36%), Afro-colombian (4.3 million, 10.40%) and Romani (c.a. 5000, 0.01%) [1]. The most spoken language in Colombia is Spanish, however there are at least 87 different ethnic groups (including three Afro-colombian and one Romani) which represent 70 linguistic groups [2]. Several genetic composition studies show that Colombian population has an European, Native American and African ancestry which changes according to the geographic location [3]. This admixture results from the Spanish colonization and African slave trade. Bogotá is located at the andean area of the country and is the capital of Colombia. People living in Bogotá belong to different ethnic groups: Native American (0.22%), Afro-colombian (1.44%), Romanies (0.01%) and Mestizo or non-Native American (98.33%). Almost 6.8 million people (16.35%) live in the city from which 40.51% were born in different regions [1]. Violence and armed conflict in the country from 1950s, 1990s and early 2000s is associated with a high internal migration mainly to the capital. Also, the Ministry of Foreign Affairs has reported over 200 thousand migrants from Venezuela currently living in Bogotá [4].

A total of 1463 UCB units available for hematopoietic stem cell transplantation were analyzed in this study and donors were classified as Mestizo (98.43%) and Afro-colombian (1.57%). All UCB units were collected between 2014 and 2018 in public and private hospitals in Bogotá, Colombia. Cryopreserved UCB units are stored at Instituto Distrital de Ciencia, Biotecnología e Innovación en Salud – IDCBIS (Bogotá, Colombia). All donors signed the informed consent form reviewed by the Ethical Committee of the District Secretary of Health and fulfilled the previously reported eligibility criteria for clinical use in our bank [5]. Only half of our cord blood donor parents were born in Bogotá (51.45%).

All UCB units for clinical purposes were typed in high-resolution for HLA-A, -B, -C, -DRB1 and -DQB1 loci. Next-generation high-throughput sequence (NGS) typing was performed at the sequencing laboratory accredited by ASHI, Histogenetics Inc. In HLA class I genes, exons 2 and 3 were typed, while only exon 2 was typed in HLA class II genes [6]. Allele coding classification was performed directly by Histogenetics using the updated IMGT/HLA database when HLA typing was carried out, and typing results were reported with six digits (including null alleles). We reduced allele-coding to g groups, leading all typing in a four-digit format considering null alleles by the open-source software Hapl-o-Mat [7].

Allele frequencies were calculated by direct count and haplotype frequencies were calculated with an EM algorithm, using a $\varepsilon = 10^{-7}$ threshold to stop the algorithm with Hapl-o-Mat [7]. Haplotype frequencies below 10^{-6} were not reported. The Hardy-Weinberg equilibrium (HWE) test was assessed using five repetitions in the Arlequin software package [8]. Input parameters for HWE test were 10^6 Markov chain steps and 10^5 dememorization steps.

Allelic and haplotype frequencies are given in Supplementary Tables S1–2 and they are available at the Allele Frequencies Net Database (AFND) [9] under the identifier code AFND3604 named "Colombia Bogotá Cord Blood" (http://www.allelefrequencies.net/population.asp?pop_id=3604). Because AFND cannot take g-group alleles, data were reported in a 2-field format. For example, the A*01:01 allele reported in AFND is actually an A*01:01g allele (Tables S1–2).

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The allele distribution in our sample is at HW equilibrium except for HLA-B. We found 51 HLA-A, 98 HLA-B, 36 HLA-C, 51 HLA-DRB1 and 18 HLA-DQB1 alleles in our sample. The two most common alleles for each locus were A*24:02g (20.81%), A*02:01g (16.13%), B*35:43g (8.65%), B*40:02g (8.44%), C*04:01g (14.90%), C*01:02g (11.38%), DRB1*04:07g (12.27%), DRB1*07:01g (9.40%), DQB1*03:02 g (22.45%) and DQB1*03:01g (19.07%). In our sample, which represents the 0.003% of the total Colombian population, we identified three new alleles: HLA-DRB1*14:183, HLA-C*08:162, and HLA-C*03:296:02 [10,11] confirming that new alleles will be found along with the sample size increase.

A total of 1439 different haplotypes were calculated including the previously mentioned five loci. The 217 most frequent haplotypes represent about 50% of the whole estimated haplotype number. Five estimated haplotypes had frequencies greater than 1% and the top predicted haplotype was A*24:02g ~ B*35:43g ~ C*01:02g ~ DRB1*04:07g ~ DQB1*03:02g (4.14%). To our knowledge this is the first report and analysis performed with this sample size using five loci at high resolution level in Colombia, which could be the first assess to build up our national registry and our own donor search algorithms.

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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.2019.03.006.

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