Human Immunology 80 (2019) 95–96

Contents lists available at ScienceDirect

Human Immunology

journal homepage: www.elsevier.com/locate/humimm

Short population report

6-Locus HLA allele and haplotype frequencies in a population of 1075 Russians from Karelia

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A B S T R A C T

A total of 1075 Russians from the Russian part of Karelia were genotyped at high-resolution for the human leukocyte antigen loci HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 using next generation sequencing methods. The haplotypic and allelic profiles as well as Hardy-Weinberg proportions of this population sample were evaluated. As the most frequent 6-locus haplotype, A*03:01 g ~ B*07:02 g ~ C*07:02 g ~ DRB1*15:01 g ~ DQB1*06:02 g ~ DPB1*04:01 g was identified with an estimated frequency of 3.5%. 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 “Russia Karelia” and the identifier AFN3430.

The Russian Federation is a multiethnic country comprising nearly 200 different ethnic groups [1]. Thereof, Russians are the major ethnic group representing about 80% of the country’s population. Karelia is an area in Northeastern Europe between the Baltic and the White Sea. It is divided between the Russian Federation and Finland. The Russian part includes the Republic of Karelia and Leningrad Oblast, the Finnish part are the regions of South and North Karelia [1,2]. According to the population census in 2010, the population number of the Republic of Karelia is approximately 650,000 with about 260,000 individuals living in its capitcal Petrozavodsk. The population of Leningrad Oblast is about 1,700,000 individuals [3]. The Finnish part of Karelia accounts for about 300,000 inhabitants [4]. In the Republic of Karelia, Russians make up 82% of the population, Karelians 7%, Belarusians 4%, Ukrainians 2%, Finns 1.5%, and others about 3.5% [3]. Russian (Ethnologue three-letter language code *rus*) [5] is the only official language, with additionally Karelian (*krl*), Veps (*vep*) and Finnish (*fin*) as officially recognized and spoken languages.

A number of n = 1075 DNA samples from donors of the “Karelian Registry of Unrelated Donors of Hematopoietic Stem Cells” in Petrozavodsk, Republic of Karelia, Russia was collected via buccal swabs. Informed consent was obtained for sample collection and scientific analyses of anonymized typing data. The samples were gained between 2015 and 2017 from individuals from the Russian part of Karelia. All individuals self-identified their ethnic background as “Russian”. Donors enrolled predominantly lived in urban areas within the Republic of Karelia (≈79%) or Leningrad Oblast (≈17%), for the most part in the Republic of Karelia’s capital city Petrozavodsk (≈56%). The remaining 4% of the donors were from rural areas within the Republic of Karelia.

All DNA samples were typed at high-resolution for the 6 loci HLA-A, -B, -C, -DRB1, -DQB1 and -DPB1 at DKMS Life Science Lab (Dresden, Germany) using next generation sequencing methods [6,7]. Typing results were reported using the “g”notation [8]. In essence, this grouping joins all alleles with an identical nucleotide sequence on exons 2 and 3 with all alleles exhibiting synonymous mutions in this regions. Alleles are part of this group regardless of expression level (ie. null alleles). While in some instances a considerable number of alleles are grouped together by this notation, all alleles expressing an identical antigen recognition domain form one group easing the identification of a suitable, matching donor in the context of hematopoietic stem cell transplantation.

HLA haplotype frequencies of the these loci were computed using our implementation of the EM algorithm, Hapl-o-Mat [9]. Supplementary Table S1 shows the 100 most frequent 6-locus HLA haplotypes. As the three most frequent HLA haplotypes, A*03:01 g ~ B*07:02 g ~ C*07:02 g ~ DRB1*15:01 g ~ DQB1*06:02 g ~ DPB1*04:01 g (3.5%), A*01:01 g ~ B*08:01 g ~ C*07:01 g ~ DRB1*03:01 g ~ DQB1*02:01 g ~ DPB1*01:01 g (2.1%) and A*03:01 g ~ B*35:01 g ~ C*04:01 g ~ DRB1*01:01 g ~ DQB1*05:01 g ~ DPB1*04:02 g (1.9%) could be identified.

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https://doi.org/10.1016/j.humimm.2018.10.017
Received 2 March 2018; Received in revised form 17 October 2018; Accepted 31 October 2018
Available online 02 November 2018

Allele group frequencies were derived from the haplotype frequency distribution via summation. HLA-A*02:01 g (29.6%), HLA-B*07:02 g (13.0%), HLA-C*07:02 g (15.4%), HLA-DRB1*15:01 g (13.6%), HLA-DQB1*03:01 g (17.1%), and HLA-DPB1*04:01 g (39.0%) were identified as most frequent allele groups per locus. A list of all allele group frequencies is given in Supplementary Tables S2–S7.

Departure from Hardy-Weinberg Equilibrium (HWE) was estimated using the chi-squared test implemented in the R-package HWxtest v.1.17 [10]. To handle HLA typing ambiguities, we limited typing results to the first field of the nomenclature for this analysis as no ambiguity occurred on this level. P-values obtained for HLA-A, -B, -C, -DRB1, -DQB1 and -DPB1 are 0.983, 0.003, 0.042, 0.015, 0.345, amd 0.289, respectively. P-values < 0.05 indicate significant deviation from HWE at loci HLA-B, -C, and -DRB1. As data collection is based on self-identified ethnical background, this coud indicate that the notion of being identified as “Russian” is not as homogeneous in the population sample as expected. The effect size statistic W_n [11] was used to express overall degree of deviation in the population sample. Values for the six analyzed loci are 0.0129, 0.0142, 0.0311, 0.0211, 0.0093 and 0.0126, respectively. Supplementary Table S8 illustrates the according results. All haplotype and allele frequency data are available in the Allele Frequencies Net database under the population name “Russia Karelia” and the identifier (AFN3430). Haplotype and allele data is available in “g” notation in the supplementary information accompanying this publication. However thre trailing “g” is omitted on AFND due to AFND format restrictions.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humimm.2018.10.017.

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