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Allele Frequencies of HLA-A, B and DRB1 among People of Fars Ethnicity Living in Tehran

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Abstract

Background: Human leukocyte antigens (HLA) are polymorphic cell surface proteins. Distribution of HLA alleles vary among different racial and ethnic populations in unrelated stem cell registries. Determination of HLA allele frequencies in different ethnic groups is useful for population genetic analyses.

Materials and Methods: Based on data available from the Iranian Stem Cell Donor Registry, HLA-A, B, DRB1 allele frequencies were evaluated from 244 individuals who were recruited as unrelated volunteer donors by PCR-SSP method in people of Fars ethnicity living in Tehran, Iran.

Results: The most frequent alleles found were HLA-A*02(19.8%), HLA-A*03(13%), HLA-A*11 and -24 (12.5%), HLA-B*35(17.7%) HLA-B*51(13.2%), HLA-DRB1*11(20.8%), whereas HLA-A*34 and HLA-A*44 (0.2%), HLA-B*47, B*54, B*56, B*73(0.2%), and HLA-DRB1*09 (0.4%) were the least frequent alleles.

Conclusion: Identifying HLA allele frequencies in different ethnic groups, helps in designing a better plan for development of donor centers in different provinces of a country, and a more precise prediction of donor size in the registry, in addition to finding suitable donors for patients in need of hematopoietic stem cell transplantation.

Keywords: HLA, unrelated donors, ethnic groups, Iran

Introduction

Human Leukocyte Antigen (HLA) genes are one of the most polymorphic loci in the human genome [1], a property which is not only central to their pivotal role in the recognition of self from non-self antigens, but also makes the antigens encoded by these genes important in organ donation and recipients/donor compatibility. HLA typing also provides a useful tool for studies of human population dynamics, migration, and colonization [2]. Anthropological studies, and determination of HLA allele and haplotype frequencies in different ethnic groups, have been found to be a valuable tool in population genetic analyses and the study of genetic relationships among different populations [3]. Furthermore, because of the considerable difference in HLA frequencies, that is known to occur among various populations, knowledge of HLA data at the level of a specific population or ethnic group is particularly important [4]. Because of the wide variability and distribution of HLA alleles among different racial and ethnic groups, unrelated stem cell registries facilitate donor searches[5]. Knowledge of HLA haplotype frequencies, therefore, could provide powerful screening tools for identification of suitable HLA-matched donors for stem cell transplantation as well as a basis for novel registry planning strategies [6, 7]. Although our recently

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established registry of HLA allele frequencies has been of some help in estimation of donor size, complete data of both MHC class I and class II allele frequencies in various Iranian ethnic groups, optimally obtained by molecular methods, are not yet available. The purpose of the present study was to evaluate HLA-A, B, DRB1 frequencies in a population with Fars ethnicity living in Tehran, obtained from the Iranian Stem Cell Donor Registry (ISCDR).

Materials and Methods

A) Source of study subjects

The ISCDR is a national center for recruiting, training and registering of hematopoietic stem cell voluntary donors, and therefore provides a potential source of study subjects, who are willing to donate stem cells, if they are found to be a good match with a patient needing Hematopoietic Stem Cell Transplantation (HSCT). Although the center was established in February 2009 by the Iranian Blood Transfusion Organization (IBTO), the official activity of donor recruitment was initiated on 15 June 2010 (on World Blood Donor Day), and now totals more than 800 unrelated potential donors (all are DNA-based typed for -A, -B, and -DRB1). The ISCDR mission is to provide a repository of HLA-typed donors and to facilitate matching donors among unrelated individuals in Iran. This goal results in a donor pool of several thousand

Table 1: Frequency of HLA-A, -B, DRB1 alleles in individuals originally from Fars ethnicity, Iran.

HLA-A* Alleles	Percent	HLA-B* Alleles	Percent	HLA-DRB1* Alleles	Percent
01	9.0	07	6.5	01	6.2
02	19.8	08	2.6	03	9.8
03	13.0	13	5.0	04	12.6
11	12.5	14	2.6	07	11.1
23	2.0	15	3.0	08	2.9
24	12.5	18	5.4	09	0.4
25	0.7	27	2.2	10	3.5
26	4.0	35	17.7	11	20.8
29	3.7	37	0.9	12	0.7
30	5.7	38	5.0	13	9.3
31	1.3	39	1.1	14	5.1
32	5.9	40	1.9	15	13.5
33	3.5	41	3.2	16	4.0
34	0.2	44	5.0		
44	0.2	45	0.4		
66	1.5	47	0.2		
68	4.0	48	0.4		
74	0.4	49	1.9		
		50	3.7		
		51	13.2		
		52	6.5		
		53	1.7		
		54	0.2		
		55	5.4		
		56	0.2		
		57	2.4		
		58	1.3		
		73	0.2		

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individuals which are anticipated to be recruited.

B) Clinical samples and methods

Data for HLA-A, B, DRB1 allele frequencies were obtained from ISCDR. Peripheral blood samples were collected in EDTA tubes from 244 unrelated healthy people, originally from Fars ethnicity living in Tehran, who were recruited as volunteer donors by the ISCDR from June 2010 to May 2011. Their parents' ethnicity was also questioned and if their parents were not from Fars province the data was excluded from this study. Informed consent was obtained. Physical examination was performed and blood samples were also taken. DNA was extracted from each sample using DNA mini kits (Qiagene). HLA-A, B, DRB1 were typed to two digits by PCR-SSP method using commercial kits (Olerup SSP HLA-A-B-DR Combi Tray), according to the manual's instruction, following which PCR products were analyzed using electrophoresis on a 2.5% agarose gel and staining with ethidium bromide. X2 test was used to compare observed frequency among different groups.

Results

HLA-A, B, DRB1 allele frequencies in 244 unrelated normal individuals studied are shown in table 1. It can be seen that eighteen alleles for the locus HLA-A, twenty-eight for the HLA-B locus and thirteen for HLA-DR were detected in this population, indicating that polymorphism of these antigens was not very high. The most frequently founded alleles were HLA-A*02(19.8%), HLA-A*03(13%), HLA-A*11 and HLA-A*-24 (12.5%), HLA-B*35 (17.7%) HLA-B*51(13.2%), HLA-DRB1*11(20.8%), whereas HLA-A*34 and HLA-A*44 (0.2%), HLA-B*47, -B*54, B*56, -B*73(0.2%), and HLA-DRB1*09 (0.4%) were the least frequently encountered alleles. Linkages between some alleles are shown in Table 2, with simultaneous prevalence of observed alleles counted by ISCDR data software.

Discussion

Our data shows both MHC class I and class II allele frequencies among individuals originally from Fars ethnicity and recruited as unrelated volunteer donors by ISCDR.

Although complete ethnicity or population based data are not available for both MHC class I and class II allele frequencies among Iranian ethnic groups, there are several studies in which the polymorphism of the HLA class II genes in different ethnic groups or different diseases have been studied [1, 10-16].

Khazaei et al. (5,16) serologically typed both MHC class I and class II allele frequencies in 71 healthy unrelated individuals (52 males and 19 females), from Baloch and Zaboli populations, and reported HLA-DR11(43.66%) and HLA-DR4 (30.99%), (a HLA-DR serotype that recognizes the DRB1*04 gene products), as frequently occurring alleles. The most frequent alleles of HLA class I in Balloch and Zaboli populations obtained by serologic method were: HLA-B05 (63.38%), HLA-A02 (46.48%) and HLA-A01(42.25%), followed by HLA-A11(25.35%), HLA-A24 (22.54%) and HLA-B16 (21.13%). Allele frequencies reported in these studies showed higher frequencies than our study and HLA-B05 and B16 were not found in our population, which might be due to ethnic differences. There were not any HLA-B05 and –B16 among our population. HLA-A02, -A01, -A11, -A24, DR11 (-DRB1*11) and DR04 (-DRB1*04), typed by serologic method, were statistically (p=0.025) different among individuals

Table2: Simultaneous prevalence of observed alleles

Linkages	Percent
HLA-A*01 & HLA-B*08	0.68
HLA-A*02 & HLA-B*18	4.76
HLA-A*03 & HLA-B*07	3.06
HLA-DRB1*01 & HLA-B*14	2.72
HLA-A*01 & HLA-B*08& HLA-DRB1*03	0.35
HLA-A*02 & HLA-B*44& HLA-DRB1*04	0.34
HLA-A*03 & HLA-B*07& HLA-DRB1*01	2.8

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with Fars ethnicity living in Tehran and Zabolis and Baloches.

We also found HLA-DRB1*11(20.8%) as the most common allele in our population, which is in agreement with the previous reports [6, 8]. The polymorphism of the HLA class II genes, in individuals from Fars province in South Iran, has been studied using molecular methods in two other studies [8, 15]. Amirzargar et al. [10] reported DRB1*11(25%), DRB1*15(14.5%), and DRB1*04(10.5%) as the most common DRB1 alleles in 72 people from Fars province. Farjadian et al. [15] also reported DRB1*11 as the most frequent allele in 100 people from Fars province. While Farjadian et al. did not report HLA-DRB1*12 in Fars province, but Amirzargar [10] reported this allele with a frequency of 1.5%, and 0.7% of our population also showed this allele. The Frequency of HLA-DRB1*15 (13.5%) in our study were similar to reported frequency by Amirzargar et al. (14.5%), while Frajadian et al. reported HLA-DRB1*15 frequency of 10.4% for HLA-DRB1*1501, 1502 and 1503 genes. In general, Farjadian et al.[15] found a close genetic relationship among the ethnic groups of Iran, but they believed that there were some genetic differences in HLA class II allele distribution among Iranians.

Yari et al. [6] also reported DRB1*11 as the most frequent allele. Apparently all individuals in their study were ascertained to be of Iranian origin, not specifically from Fars province, but all observed frequencies for HLA-DRB1 alleles in their study seem to be in agreement with our findings. Mohyuddin et al. [17] analyzed the HLA-B, -C, -DRB1 and -DQB1 loci using PCR-SSP in the Parsi (Zoroastrian) population in Pakistan, who had migrated from India to Karachi in Pakistan. They are assumed to be descendants of Zoroastrians from Iran who migrated to Gujarat in India after the Arab invasion in 900 AD. HLA-B*35(15.9%), and HLA-DRB1*11(23.0%) were the most common alleles in their study, which is also in agreement with our findings.

Conclusions

Identifying HLA allele frequencies in different ethnic groups, helps in designing a better plan for development of donor centers in different provinces of a country, and a more precise prediction of donor size in the registry, in addition to finding suitable donors for patients in need of hematopoietic stem cell transplantation.

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