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Determination of most frequent major histocompatibility complex alleles in Iranian population by immunoinformatic

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Abstract

Background and Objective: Major histocompatibility complex (MHC) is the most polymorphic genes in human genome encoding human leukocyte antigens (HLA) class I and class II. Determination of HLA alleles could help in preparing more efficient vaccines as well as successful organ transplantation in different population of the world. Immunoinformatic uses biologic computational information for modelling and prediction of immune system function in healthiness and diseases. In this study we determined the most frequent MHC alleles in Iranian population by immunoinformatic.

Materials and Methods: Utmost frequent human leukocyte antigens (HLA) alleles in Iranian population were determined using allele frequency net database (AFND, www.allelefrequencies.net).

Results: A total of ten alleles related to HLA Class I (five alleles related to HLA –A [A02 (16%), A03 (12.5%), A11(10%), A24 (13.6%), A26 (10%)], three alleles related to HLA –B [(B35 (13%), B510 (12%), B53(13)%)] and two alleles related to HLA –C [C07 (17.5%), C12 (16%)] and a total of four alleles related to HLA Class II (two alleles related to HLA- DQB1 [DQB1 03 (30.5%), DQB1 05 (22 %)] and two alleles related to HLA-DRB1 [DRB1 04 (17.1%), DRB1 15 (16.1 %)], were utmost frequent alleles in the Iranian population.

Conclusion: In this study most frequent HLA alleles in Iranian population were found by immunoinformatic. These alleles could be very valuable for development of more effective vaccines as well as successful bone marrow transplantation in Iran. Besides these data could have potential implication for finding the best matched un-related donors in Iranian populations.

Keywords: Major histocompatibility complex, Alleles, Iranian, Immunoinformatic

1. Introduction

Major histocompatibility complex (MHC) is the most polymorphic system in human genome encoding human leukocyte antigens (HLA) class I and class II. These genes are strictly interrelated to each other on short arm of human chromosome 6. HLA system encodes for the HLA-A, B and C (class I), and HLA-DR, DQ and DP (class II) antigens (1, 2). Up to now, More than 17000 of MHC alleles have been known (3). Determination of HLA antigens and alleles in distinct ethnic inhabitants is of great value. For example, HLA antigens frequencies could help in finding an appropriate HLA-matched donor for successful organ transplantation (4, 5). Several investigators have studied the HLA polymorphism in varied populations and racial groups (6-9). HLA system is involved in antigen presentation to T lymphocytes (10). Expression of definite HLA class I or II alleles has been associated with a variety of diseases such as infections, autoimmunity or malignancies (11–14). Considering the genetic diversity and inconsistency of HLA alleles in various racial populations, different HLA class I and II alleles may be related to a certain disease in various populations (15). In this regard correlation of definite HLA class I (16) or HLA class II (17) alleles with clinical progress of disease have been shown in different cancers.

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Immunoinformatic (a branch of bioinformatic) uses biologic computational information for modelling and estimation of immune system function in healthiness and diseases Moreover immunoinformatic is helpful in resolving of several immunological problems, faster and more precise diagnosis and therapy of diseases (18, 19).

Bioinformatics uses computer as a workroom, categorizes the experimental facts collected in computer and examines them by computerized software programs (20). Immunoinformatic has nearly been stretched to all parts of immunology and provided advanced occasions for upcoming immunological studies (21, 22).

High Genetic polymorphism of HLA structure causes an extreme variability in induction of immune responses by vaccine and could complicate the choice of vaccine applicants. Thus, high polymorphism of MHC make it necessity to establish related immunoinformatic data particularly in area of preparing more efficient vaccines as well as successful transplantation in different population of the world.

In this study we determined the most frequent MHC alleles in Iranian population by immunoinformatic.

2. Materials and Methods

Most abundant MHC alleles in Iranian population were determined using allele frequency net database (AFND, www.allelefrequencies.net) (23). AFND is a virtual web-based storehouse (24) offers a freely accessible source for storing of frequency information (alleles, haplotypes, …) correlated to human leukocyte antigens (HLA), major histocompatibility complex related genes (MHC), killer-cell immunoglobulin-like receptors (KIR) and a numeral cytokine gene polymorphism in global citizens. In recent years, due to current rise of genotyping information, AFND has got widespread medical and scientific usage. In this regard, an easy-to-use desktop application for HLA genotype/public information submissions has been established. Furthermore, sorting of current and new information into 'gold-silver-bronze' norms, permitting operators to mesh and enquiry reliant on their requests has been developed. Besides, this expertise has been expanded to other fields such as on HLA associations with adverse drug reactions (23). Today, AFND covers >1784 inhabitants from >14 million healthy people from 129 countries, making AFND a valued source for study of some utmost polymorphic areas in human genome (24).

Also, over recent years AFND has combined genotype fresh data from 85,000 persons from 39 countries. Additionally, extra residents’ data groups having next generation sequencing documents overpass >3 million persons have been supplemented. This reservoir has been broadly used in a different set including immunology, epitope prediction for population analysis in vaccine production, histocompatibility, pharmacogenetics, epidemiology, people genetics, and others (24).

3. Results

The most frequent MHC alleles (HLA class 1 and 2) in the Iranian population were determined using the allele frequency net database. The HLA alleles with a frequency of more than 10% in the Iranian population were selected. The results for the most frequent HLA class I and HLA class II alleles in the Iranian population are shown in tables 1 and 2, respectively.

Table 1. Most frequent HLA class I alleles in Iranian population

HLA allele no	**Frequency (%) ***
HLA-A 02	16
HLA-A 03	12.5
HLA-A 11	10
HLA-A 24	13.6
HLA-A 26	10
HLA-B 35	13
HLA-B 51	12
HLA-B 53	13
HLA-C 07	17.5
HLA-C 12	16

* Frequency more than 10%

Table 2: Most frequent HLA class II alleles in Iranian population

HLA allele no	Frequency (%) *
HLA- DQB1 03	30.5
HLA- DQB1 05	22
HLA- DRB1 04	17.1
HLA- DRB1 15	16.1

* Frequency more than 10%

4. Discussion

Studies carried out by other investigators in the field of allele frequency net database (AFND) application, encouraged us to study and identify of most frequent HLA alleles (class I and II) in the Iranian population. These HLA alleles had a frequency of more than 10% in the Iranian people. According to the results of present study, five alleles related to HLA –A [A02 (16%), A03 (12.5%), A11(10%), A24 (13.6%), A26(10%)], three alleles related to HLA –B [(B35 (13%), B510 (12%), B53(13) %)] and two alleles related to HLA –C [(C07 (17.5%), C12 (16%)] (totally ten alleles related to HLA class I), were the most frequent alleles. Also two alleles related to HLA-DQB1 [DQB1 03 (30.5%), DQB1 05 (22 %)] and two alleles related to HLA- DRB1 [DRB1 04 (17.1%), DRB1 15 (16.1%)] (totally four alleles related to HLA class II were the utmost frequent alleles.

Owing to HLA high polymorphism, distribution of its alleles in different populations has been investigated by several studies. Nevertheless, limited studies are performed with HLA allele frequencies in Iranian people and generally have done about HLA class II loci polymorphism (25, 26) and allelic linkage with diseases (27). HLA-A typing in Iranian population has been done by Hadadianpour et.al study (28). In Hadadianpour et.al study (28), only two alleles related to HLA –A [A*02:01 (13%) and A*24:02 (12%)] were the most frequent alleles while in our study, five alleles related to HLA –A [A02 (16%), A03 (12.5%), A11 (10%), A24 (13.6%), A26 (10%)], were the most frequent alleles. The discrepancy between Hadadianpour et.al study (28) and us may be partly due to that Hadadianpour et.al used sequence-based typing method whereas we used immunoinformatic method.

In another study conducted by Aminikhah et.al, distribution of HLA class I and class II genes in Sistanis population in Iran were determined (29). In Aminikhah et.al study (29), the highest frequently observed alleles were A02:01, B35:01, C12:03, C06:02, DRB1 11, DQA105:05 and DQB1*03:01. Accordingly, in Aminikhah et.al study (29), four alleles related to HLA class I (A02:01, B35:01, C12:03, C06:02) and three alleles related to HLA class II (DRB1 11, DQA1 05:05, DQB1 03:01), were the most frequent alleles in Sistanis population in Iran. Also in Aminikhah et.al study (29), one allele related to HLA –A (A02:01), one allele related to HLA –B (B35:01) and two allele related to HLA –C, were the most frequent alleles while in our study, five alleles related to HLA –A [A02 (16%), A03 (12.5%), A11 (10%), A24 (13.6%), A26 (10%)], three alleles related to HLA –B [(B35 (13%), B510 (12%), B53 (13 %)] and two alleles related to HLA –C [(C07 (17.5%), C12 (16%)] (a total 10 alleles related to HLA Class I), were the most frequent alleles. Therefore only three of most frequent alleles related to HLA class I in Aminikhah et.al study (29), were similar with our most frequent alleles related to HLA Class I. Also, in Aminikhah et.al study (29), one allele related to HLA – DRB1 (DRB1 11), one allele related to HLA – DQA1 (DQA1 05:05) and one allele related to HLA – DQB1 (DQB1 03:01) were the most frequent alleles related to HLA Class II while in our study, two alleles related to HLA- DQB1 [DQB1 03 (30.5%), DQB1 05 (22 %)] and two alleles related to HLA- DRB1 [DRB1 04 (17.1%), DRB1 15 (16.1 %)], (totally 4 alleles related to HLA Class II) were the utmost frequent alleles. Thus only one most frequent allele related to HLA Class II, in Aminikhah et.al study (29), was similar to our most frequent alleles related to HLA Class II. The inconsistency between Aminikhah et.al study results (29) and us may be somewhat due to that different population and methods were used. In Aminikhah et. al study, polymerase chain reaction (PCR) using sequence-specific primers (PCR-SSP) method in Sistani's population of Iran was used while we utilized immunoinformatic method in whole Iranian population.

Most of information presented in above mentioned and similar studies was attained by HLA typing techniques such as PCR-SSP (28, 29). Another similar research has indicated A*24:02 (17.6%) and A*02:01 (12.5%) as most frequent HLA class I alleles in Kurd people (30). In another comparable research , A*02:11 (20.2%) and A*11:11 (14.6%), were introduced as most frequent alleles of HLA class I in Baloch population using molecular HLA typing technique (31). Additionally, in a HLA allele typing of Iranian healthy residents from Yazd region conducted by Nikbin et. al., A*02:01, B*51:01 and C*12:03

were the three greatest frequent alleles of HLA class I (32).

Similarly, in a study done on Korean people (33), A*02 (29%) and A*24 (22.4%) were the utmost frequent alleles of HLA class I. Also in a study were accomplished in six diverse Chinese populations (34), HLA-A*02 (15.45- 30.65%), -A*11 (16.66-30.72%), and -A*24 (11.03- 17.07%) were the first three frequent alleles of HLA-A locus.

Nonetheless, this is the first report which determined the most frequent HLA (class I and class II) alleles in Iranian population by immunoinformatic. These data can probably cover a big percentage of Iranian people. Moreover, data of present study is very valuable for development of more effective vaccines as well as successful bone marrow transplantation in Iran. Furthermore, these types of investigation directing on allele frequencies in Iranian people could have potential implication for finding the best matched un-related donors in Iranian populations.

Conclusion

In the present study, the most frequent HLA (class I and class II) alleles in Iranian population were determined by immunoinformatic. These HLA alleles can probably cover a big percentage of Iranian people and are very valuable for development of more effective vaccines as well as successful bone marrow transplantation in Iran. Furthermore, these most frequent HLA alleles in Iranian people could have potential implication for finding the best matched un-related donors in Iranian populations.

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Conflict of interest

The authors have no conflict of interest in this study.

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