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Original Research

Uncommon HLA Alleles Observed in a Population of Istanbul Province

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ABSTRACT

Objective: New polymorphisms are formed in human leucocyte antigen (HLA) genes with point mutations, gene conversions, and duplication, and the diversity continues to increase. Various new HLA alleles have significant roles in transplantation, and epidemiologic and population studies. The aim of our study was to determine the status of HLA alleles in the Turkish population, which is uncommon, well-defined, and non-defined in the world population according to the international ImMunoGeneTics information system® (IMGT) database.

Methods: We performed HLA-A, -B, -C, -DQB1, and DRB1 loci at the four-field resolution level, using Sanger- sequence-based typing (SBT) for 5592 healthy, unrelated bone marrow donor volunteers from Istanbul Province. The uncommon alleles were also confirmed using high-throughput next-generation sequencing (NGS).

Results: Uncommon alleles were determined at five loci as follows: HLA-A*01:155, 02:66, 02:90, 02:110, 02:343, 03:82, 24:28, 24:146, 24:276, 24:356, 31:23,33:33, 68:38; HLA-B *07:240, 18:19, 35:193, 40:303, 51:69, 51:169; HLA-C*04:39, 06:40, 07:93, 12:149, 15:73; HLA-DRB1*11:149, 13:14:02 and HLA-DQB1*03:27. All alleles were arranged according to the common and well-documented (CWD) 3.0.0 catalog.

Conclusion: This is the first study to show uncommon alleles in our population. These reported data increase the knowledge of HLA polymorphisms in the Turkish population and provide a basis for further studies in population genetics. This information may also be useful in determining whether a matched, unrelated donor is unlikely to be found so that a mismatch strategy, an extended family search, or alternate therapy, can be pursued, thus saving time and cost for patients.

Keywords: HLA; uncommon HLA alleles; next-generation sequencing; sequencing-based typing; HLA catalog

INTRODUCTION

Highly polymorphic human leucocyte antigen (HLA) class I and class II molecules are the key molecules for controlling the specificity of antigen presentation. They work with other sets of molecules located within the HLA region to process the antigen into peptides or other fragments [1-4]. HLA typing, such as sequence-specific oligonucleotide probe polymerase chain reaction (PCR-SSOP), sequence-specific primer (PCR-SSP), and sequence-based typing (SBT) are traditional "gold standard" assays are labor-intensive, costly, and relatively low throughput [5-7].

The next-generation sequencing (NGS) used as the routine clinical work of HLAs has led to the development of population-specific HLA typing data pools (Allele Frequency Net Database (AFND)) and better assessment of regional HLA specificity [8]. The introduction of NGS technologies, which provide clonal sequence information and may be used to determine phase over long stretches of DNA, has the potential to overcome many of the limitations of SBT, and 38,909 HLA and related alleles have been described [9].

Significant differences in the frequency of common and well-documented alleles (CWD) recently identified in Europe have been demonstrated. This number continues to increase with the discovery of new HLA alleles. In addition, new polymorphisms are occurring in HLA genes through point mutations, gene transformations, and fragment changes. New alleles may probably be detected at a low frequency in the population. HLA studies associated with viral agents suggest that rare HLA alleles confer a 'selective advantage' to the host against the virus [10,11]. Three catalogs for HLA alleles have been organized to date. The first catalog was prepared by ASHI in 2007 and revised by EFI in 2012 and updated to version 2.0.0. With these updates, alleles have been categorized as CWD. Accordingly, common alleles were defined as alleles with a frequency of over 0.001 observed in a population of at least 1500 individuals. Well-documented alleles are less frequent than common alleles, detected at least five times in the population or three times in a shared haplotype. Apart from these, an allele group is alleles that have been detected 1-3 times in the population after identification. The frequencies of these alleles are extremely low and have been termed non-CWD alleles. The latest updated version of the catalog was published by Hurley et al. It has been updated to version CWD 3.0.0 with the article published in January 2000 [12].

Main Points;

- Uncommon alleles detected in a population of Istanbul Province.
- The NGS technique will bring new changes and alleles.
- All alleles were arranged according to the CWD 3.0.0 catalog.

Türkiye has a genetically diverse population due to its geographic location and historical migration routes. However, comprehensive and high-resolution data on how this diversity is reflected in HLA allele distribution are limited. In this study, we aimed to identify rare HLA alleles in the Turkish population classified as uncommon, well-defined, and non-defined in the world population according to the international ImMunoGeneTics information system® (IMGT) database. Also, to provide detailed information on the frequency, genetic variation, and potential clinical significance of these alleles. An important lesson learnt from genetic studies in HIV is that viral replication is significantly inhibited by the immune system with less common or even rare HLA alleles.

The study was conducted retrospectively and included the typing results of 3 consecutive years (2016-2019). The data of different groups in the Turkish population : the first group used as a data source were unrelated volunteer donors from the Istanbul Bone Marrow Donor Registry and the second group was the healthy individuals.

The study includes the following objectives:
HLA allele diversity: To determine the diversity and frequency of rare HLA alleles belonging to HLA-A, HLA-B, HLA-C, HLA-DRB1 and HLA-DQB1 loci in the Turkish population.
Genetic Analysis: To perform comparative genetic analysis of the obtained HLA sequences with other known HLA alleles worldwide and to examine the genetic similarities and differences of the HLA profile of the Turkish population with other populations.
Creating a Database: In light of the data obtained, to create a database containing HLA alleles specific to the Turkish population and integrate these data into global HLA databases.

MATERIALS AND METHODS

Participants and Sample Collection
healthy individuals (n=5592) who voluntarily participated in

Istanbul University Istanbul Faculty of Medicine between 2016-2019 and gave informed consent were included in the study. Genomic DNA was isolated from blood samples obtained from the participants. DNA isolation was performed using a Qiagen EZ1 Advanced XL instrument and the isolated DNA samples were stored at -20°C.

HLA Typing

Sanger sequencing-based typing (Sanger-SBT) was used to determine HLA alleles. HLA typing was performed in the tissue typing laboratory at Istanbul Medical Faculty. This laboratory is accredited by the European Federation of Immunogenetics (EFI) for clinical HLA typing. The HLA loci and exons typed were as follows: HLA-A and HLA-B: Exons 1-5, HLA-C: Exon 1-7, HLA-DR Exon 2-3, HLA-DQ Exon 2-3.

Allele Detection and Data Analysis

In total, 11,184 HLA alleles were detected. Twenty-seven of these alleles were detected for the first time in the Turkish population. These rare alleles were evaluated using the IMGT database (version 3.55.0, 2024-01).

Verification with NGS

Confirmation of rare alleles was performed using NGS methods. Multiple long-range PCR primers were designed to amplify HLA-A, HLA-B, HLA-C, DRB1, and DQB1 genes from the promoter region to the 3'-UTR region for NGS typing. Omixon Holotype HLA™ kit was used for NGS and the One Lambda Secore Locus Sequencing Kit was used for Sanger sequencing.

Statistical Analysis

Descriptive statistics are given as mean±standard deviation for numerical variables and number for categorical variables. The SPSS for Windows version 21.0 package software was used for statistical analysis. The IMGT-HLA database system was used for the detection of uncommon alleles.

The uncommon alleles detected were analyzed in the IMGT database, aligned to the closest available allele sequence. This database enables the validation of newly identified HLA alleles by aligning them with the closest allele sequences already known and catalogued. This alignment is done to confirm the accuracy of the identified alleles and understand the genetic variation of the new alleles. In this way, it is indicated that the rare HLA alleles obtained in the study have been compared and validated against the closest similar allele sequences in the IMGT database.

RESULTS

Five thousand five hundred ninety-two volunteers were included in our study (F/M: 3256/2336; age range; 19-46 years; mean age 37.79 ± 9.2 years). Among the 11,184 alleles detected, the uncommon, well-defined, and non-CWD allele distributions were as follows: HLA-A*01:155, 02:66, 02:90, 02:110, 02:343, 03:82, 24:28, 24:146, 24:276, 24:356, 31:23,33:33, 68:38; HLA-B *07:240, 18:19, 35:193, 40:303, 51:69, 51:169; HLA-C*04:39, 06:40, 07:93, 12:149, 15:73; HLA-DRB1*11:149, 13:14:02, and HLA-DQB1*03:27.

When the whole HLA gene was amplified, we also detected nucleotide positions (Table 1). All alleles were arranged according to the CWD 3.0.0 catalog. When these alleles were also checked against the HLA-IMGT database, we found that most were confirmed by only one laboratory. The table contains the IMGT/HLA accession numbers, version number, the most closely matched allele information and nucleotide change, and exon numbers in which the change was detected for these alleles. All this information was obtained using the IMGT-HLA database (Table 1).

In our study, among the HLA alleles detected using Sanger and NGS methods, we identified alleles that were rarely detected in the Turkish population and in most populations. Although the separation force of some tools is more limited in Sanger sequencing, the allele can be precisely distinguished using NGS. According to the IMGT database, the ethnic groups of 10 alleles were determined, but nine were not determined (Table 2).

The characteristics of variation in HLA class I loci, possibly caused by single point mutations, are described in detail based on the sequences of alleles submitted to the IPD-IMGT/HLA database. We know that the frequency of HLA alleles in different populations reflects the evolutionary history of the population, and this effect is manifested in CWD allele frequencies.

The comparison of the 27 alleles we identified in our population with the information in the IMGT-HLA database showed that the well-defined alleles were generally identified in the Middle East and North Africa (MENA) and/or European (EURO) populations. Other alleles were those that have not been observed in other populations since they were first identified (Table 2). The name A*01:155 was officially assigned by the World Health Organization (WHO) Nomenclature Committee for Factors of the HLA System in March 2014. This follows the agreed policy that,

subject to the conditions stated in the most recent Nomenclature Report, names will be assigned to new sequences as they are identified. In August 2023, our Confirmatory HLA sequence (delivery number HWS10061798) was officially named by the WHO Nomenclature Committee for factors of the HLA System.

Table 1. IMGT/HLA accession numbers, version number, the most closely matched allele information and nucleotide change, exon numbers

	IMGT/HLA	IMGT/HLA 3.45.0			
Locus	**IPD Accession**	**Alel name**	**Closest match**	**Position/Base change**	**Exon**
A	HLA11389	A*01:155	A*01:01:01:01/ A*01:155	810 G>A	4
	HLA01781	A*02:66	A*02:01:01:01 / A*02:66	750 C>T	4
	HLA02374	A*02:90	A*02:01:01:01 / A*02:90	292 C>G	2
	HLA02776	A*02:110	A*02:01:01:01 / A*02:110	355 G>A	3
				362 G>T	3
				368 A>T	3
	HLA04893	A*02:243	A*02:01:01:01 / A*02:243	97 T>C	2
				98 T>C	2
	HLA05359	A*03:82	A*03:01:01:01 / A*03:82	411 C>T	3
				412 C>G	3
				413 G>A	3
				414 G>A	3
				418 G>C	3
				527 A>T	3
				538 T>C	3
				539 T>A	3
	HLA01268	A*24:28	A*24:02:01:01 / A*24:28	292 G>C	2
				299 A>G	2
				301 A>G	2
				307 C>G	2
				311 T>C	2
				313 G>C	2
				314 C>T	2
				317 T>G	2
				319 C>G	2
	HLA05673	A*24:146	A*24:02:01:01 / A*24:146	411 C>T	3
				412 C>A	3
	HLA10976	A*24:276	A*24:02:01:01 / A*24:276	209 A>G	2
	HLA15818	A*24:356	A*24:02:01:01 / A*24:356	349 C>T	3
	HLA03417	A*31:23	A*31:01:02:01 / A*31:23	811 G>A	4
	HLA05633	A*33:33	A*33:01:01:01 / A*33:33	463 C>A	3
				468 T>C	3

				583 C>T	3
	HLA02859	A*68:38	A*68:01:01:01 / A*68:38	102 C>T	2
				376 G>A	3
B	HLA12761	B*07:240	B*07:02:01:01 / B*07:240	301 A>G	2
				302 G>A	2
	HLA01782	B*18:19	B*18:01:01:01 / B*08:19	527 T>A	3
				538 C>T	3
				539 T>G	3
	HLA07692	B*35:193	B*35:01:01:01 / B*35:193	134 G>C	2
				419 C>T	3
	HLA13250	B*40:303	B*40:01:02:01 / B*40:303	103 G>T	2
				106 A>G	2
				363 G>C	3
				499 T>A	3
				512 T>G	3
				603 C>G	3
				605 A>C	3
				610 G>C	3
				618 T>G	3
				693 T>C	4
				959 T>C	5
				1008 T>C	5
	HLA03716	B*51:69	B*51:01:01:01 / B*51:69	475 G>A	3
	HLA11052	B*51:169	B*51:01:01:01 / B*51:169	670 A>T	4
C	HLA03735	C*04:39	C*04:01:01:01 / C*04:39	568 G>C	3
	HLA05184	C*06:40	C*06:02:01:01 / C*06:40	544 G>A	3
	HLA04399	C*07:93	C*07:01:01:01 / C*07:93	445 G>A	3
				912 C>T	5
	HLA13043	C*12:149	C*12:03:01:01/ C*12:149	173 T>C	2
		C*15:73	C*15:02:01:01 / C*15:73	454 G>C	3
DRB1	HLA10205	DRB1*11:149	DRB1*11:01:01:01 / DRB1*11:149	181 T>C	2
				189 A>G	2
				197 A>T	2
				429 C>G	3
	HLA01154	DRB1*13:14:02	DRB1*13:01:01:01/DRB1*13:14:02	181 C>T	2
				189 G>A	2
				196 A>T	2
				258 T>C	2
				261 C>T	2
				286 A>T	2

				298 G>A	2
				299 A>G	2
				344 T>G	3
				345 G>T	3
DQB1		DQB1*03:27	DQB1*03:01:01:01 / DQB1*03:27	343 T>C	3

Table 2. According to IMGT database alleles etnic group.

A*01:155	
A*02:66	
A*02:90	WD (NOT MENA)
A*02:110	WD (MENA, EURO)
A*02:243	
A*03:82	NONE
A*24:28	WD (EURO, HIS)
A*24:146	WD (MENA)
A*24:276	NONE
A*24:356	NONE
A*31:23	
A*33:33	WD (MENA)
A*68:38	WD (MENA)
B*07:240	NONE
B*18:19	WD (EURO,MENA)
B*35:193	WD (MENA)
B*40:303	NONE
B*51:69	WD (EURO, MENA)
B*51:169	NONE
C*04:39	WD (MENA)
C*06:40	NONE
C*07:93	WD (EURO, MENA)
C*12:149	WD (NOT MENA)
C*15:73	
DRB1*11:149	NONE
DRB1*13:14:02	WD
DQB1*03:27	NONE

MENA: Middle east and North Africa, EURO: Europian Population, HIS: Hispanic

DISCUSSION

The literature related to this subject give us an idea about how NGS will bring new changes and alleles to the field of HLA typing. Our data show that the diversity of HLA alleles and haplotypes is a result of the mixing of different populations in Türkiye. The coexistence of people from different populations will further increase the diversity of HLA alleles and haplotypes in the Turkish population in the coming years. As a result, it will be difficult to find suitable donors for human stem cell, tissue, and solid organ transplantation. Therefore, continuous updating of allele and haplotype frequency information will increase the accuracy and reliability of information about the immunogenic profile of the population. Thus, suitable donors can be found quickly, waiting lists for transplants can be shortened, and survival rates among recipients may be increased.

Today, using molecular methods, it has been shown to be possible to identify hundreds of different HLA alleles that differ in one or more nucleotides. Even single amino acid differences are known to cause immunological responses to donor antigens after haematopoietic stem cell transplantation. [12]. In our population, we found 27 well-defined and non CWD allele such as HLA-A*01:155, 02:66, 02:90, 02:110, 02:343, 03:82, 24:28, 24:146, 24:276, 24:356, 31:23, 33:33, 68:38; HLA-B *07:240, 18:19, 35:193, 40:303, 51:69, 51:169; HLA-C*04:39, 06:40, 07:93, 12:149, 15:73; HLA-DRB1*11:149, 13:14:02 and HLA-DQB1*03:27.

Kamenaric et al. identified six new HLA alleles (HLA-A*01:200, A*02:836, A*11:01:01:44, B*08:251, B*18:169 and C*05:46:01:02 and very rare (HLA-B*08:78, DRB1*12:39, DRB1*13:23:02 and DQB1*06:09:04) or rare (HLA-A*24:41, B*39:40:01N, B*51:78:01, DRB1*01:31 and DRB1*14: 111) in the Croatian population [13]. In another study conducted in the Croatian population, it was reported that eight HLA alleles from the ‘rare’ and ‘very rare’ categories were in the process of being sent to the rare allele database; A*02:11, one of these alleles, was also present among the rare alleles identified in our study. In a study conducted with donors registered in the DKMS (Deutsche Knochenmarkspenderdatei) database, it was reported that the 02:11 allele was also observed in Romanian, Bosnian,

Polish, Greek, Croatian, Turkish, and United States Hispanic populations [14]. The alleles A*02:11, A*68:38, B*18:19, B*51:69, C*04:39, C*07:93, C*15:73, DRB1*13:14, which were reported to be detected in Turkish donors in the allele frequency analysis of the same study, were similar to the rare alleles detected in our study [14].

The A*68:38 and DRB1*13:14 alleles detected in a study conducted with HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQB1 and HLA-DPB1 allele frequencies of Saudi stem cell donors were similar to the rare alleles detected in our study [15]. Analysis of the Buddhist Tzu Chi Stem Cell Center's (BTCSCC) HLA database of 291,677 bone marrow volunteer donors from 1993 to 2008, showed that 27 rare alleles were identified and six new alleles were discovered in Taiwan population. Rare alleles were confirmed using an SSP typing protocol and/or an SBT method [16]. The rare alleles detected in these studies have differences from the alleles detected in our study. Creating such databases by uncovering new/rare HLA alleles and haplotypes in each population will facilitate donor search and speed up the turnaround time of the procedure, as well as help transplant centers to quickly decide whether to search for an HLA-matched unrelated donor or cord blood unit or to proceed with a haploidentical donor [17]. In our study, we identified 11,184 alleles from 5592 volunteer donors. Of these alleles, we identified 13 HLA-A, six HLA-B, five HLA-C, three HLA-DR, and one HLA-DQ allele as well-defined or not yet categorized according to the IMGT database and CWD3.0.0 catalog.

Limitations

The characteristic of the study population, which is restricted to only the Marmara region, is the most important limitation.

CONCLUSIONS

Similar studies based on next-generation sequencing techniques, as in our study, are important in terms of documenting and recording possible new and rare alleles. These reported data increase the knowledge of HLA polymorphisms in the Turkish population and provide a basis for further studies in population genetics. This information may also be useful in determining that a matched unrelated donor is unlikely to be found so that a mismatch strategy, an extended family search or alternate therapy, can be pursued thus saving time and cost for the patient. The results of this study will contribute to a better understanding of the genetic structure of the Turkish population and the development of personalized medicine practices by providing important information in terms of both scientific and clinical applications. Furthermore, the identification of uncommon HLA alleles may significantly guide future genetic research and transplantation medicine.

Conflict of Interest: The authors report no conflicts of interest related to this study.

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Ethical Approval: This study was approved by the Ethics Committee of the Istanbul University Faculty of Medicine (Ethics no: 470) and in accordance with the standards of the Declaration of Helsinki.

Author Contributions: Yeliz Ogret provided technical support and materials and interpretation of the data, drafting of the paper. Suleyman Rustu Oguz provided the concept, design, interpretation of the data, drafting of the paper, and gave final approval. Hayriye Senturk Ciftci contributed to the concept and design, assembled the data, and helped with the data analysis. Sedat Karadeniz provided the data and statistical input. Demet Kivanc help with assembly of data with technical support. Fatma Savran Oğuz provided the concept drafting of the paper, and gave final approval.

REFERENCES

[1] Kelly A, Trowsdale J (2019) Genetics of antigen processing and presentation. Immunogenetics. 71:161-170. https://doi.org/10.1007/s00251-018-1082-2

[2] Robinson J, Halliwell JA, Hayhurst JD, Flicek P, Parham P, Marsh SGE (2015). The IPD and IMGT/HLA database: allele variant databases. Nucleic Acids Res. 43:423–31. https://doi.org/10.1093/nar/gku1161

[3] Daly AK (2013). Pharmacogenomics of adverse drug reactions. Genome Med. 5:5. https://doi.org/10.1186/gm409

[4] Gough SCL, Simmonds MJ (2007). The HLA region and autoimmune disease: associations and mechanisms of action. Curr Genomics. 8:453–65. https://doi.org/10.2174/138920207783591690

[5] Erlich H (2012). HLA DNA, typing: past, present, and future. Tissue Antigens 80:1–11. https://doi.org/10.1111/

j.1399-0039.2012.01881.x

[6] Dunn PPJ (2011). Human leucocyte antigen typing: techniques and technology, a critical appraisal. Int J Immunogenet. 38:463–73. https://doi.org/10.1111/j.1744-313X.2011.01040.x

[7] Seyhun Y, Kekik C, Karahan G, Oguz SF, Carin MN (2008). Undetected HLA-A,B Antigens by serological method and application of molecular methods. Gaziantep Med. Journal. 14:41-45. https://doi.org/10.58600/eurjther.2008-14-1-1357-arch

[8] Gonzalez-Galarza FF, McCabe A, Melo Dos Santos EJ, Takeshita L, Ghattaoraya G, Jones AR, Middleton D (2018). Allele Frequency Net Database.Methods Mol Biol. 1802:49-62. https://doi.org/10.1007/978-1-4939-8546-3_4.

[9] Robinson J, Barker DJ, Georgiou X, Cooper MA, Flicek P, Marsh SGE (2020). IPD-IMGT/HLA Database. Nucleic Acids Res. 8:948-955. https://doi.org/10.1093/nar/gkz950

[10] Kaur G, Mehra N. (2009). Genetic determinants of HIV-1 infection and progression to AIDS: immune response genes. Review Tissue Antigens.74:373-85.https://doi.org/10.1111/j.1399-0039.2009.01337.x

[11] Hurley CK, Kempenich J, Wadsworth K, Sauter J, Hofmann JA, Schefzyk D, Schmidt AH, Galarza P, Cardozo MBR, Dudkiewicz M, Houdova L, Jindra P, Sorensen BS, Jagannathan L, Mathur A, Linjama T, Torosian T, Freudenberger R, Manolis A, Mavrommatis J, Cereb N, Manor S, Shriki N, Sacchi N, Ameen R, Fisher R, Dunckley H, Andersen I, Alaskar A, Alzahrani M, Hajeer A, Jawdat D, Nicoloso G, Kupatawintu P, Cho L, Kaur A, Bengtsson M, Dehn J (2020). Common, intermediate and well-documented HLA alleles in world populations: CIWD version 3.0.0. HLA. 95:516-531. https://doi.org/10.1111/tan.13811

[12] Schreuder GM, Hurley CK, Marsh SG, Lau M, Fernandez-Vina M, Noreen HJ, et al. (2005). World Marrow Donor Associations Quality Assurance and IT Working Groups; WHO Nomenclature Committee for Factors of the HLA system; 13th International Histocompatibility Workshop Serology Component; International Cell Exchange, UCLA; US National Marrow Donor Program. The HLA Dictionary 2004: a summary of HLA-A, -B, -C, -DRB1/3/4/5 and -DQB1 alleles and their association with serologically defined HLA-A, -B, -C, -DR and -DQ antigens. Tissue Antigens. 65:1-55. https://doi.org/10.1111/j.1399-0039.2005.00350.x

[13] Burek Kamenaric M, Maskalan M, Grubic Z, Stingl Jankovic K, Zunec R (2020). Detection of novel and confirmation of very rare and rare HLA alleles by next generation sequencing in Croatia. HLA. 96:70-75. https://doi.org/10.1111/tan.13905

[14] Pingel J, Solloch UV, Hofmann JA, Lange V, Ehninger G, Schmidt AH. (2013). High-resolution HLA haplotype frequencies of stem cell donors in Germany with foreign parentage: how can they be used to improve unrelated donor searches? Hum Immunol. 74:330-40. https://doi.org/10.1016/j.humimm.2012.10.029

[15] Jawdat D, Uyar FA, Alaskar A, Müller CR, Hajeer A. (2020). HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 Allele and Haplotype Frequencies of 28,927 Saudi Stem Cell Donors Typed by Next-Generation Sequencing. Front Immunol. 22:11:544768. https://doi.org/10.3389/fimmu.2020.544768

[16] Yang KL, Chen MJ, Shyr MH, Lin CL, Lin PY. (2011). Rare HLA alleles and their predicted haplotypes in Tzu Chi Taiwanese marrow donor registry. Int J Immunogenet. 38(3):263-7. https://doi.org/10.1111/j.1744-313X.2010.00992.x

[17] Petersdorf EW (2013). The major histocompatibility complex: a model for understanding graft-versus-host disease. Blood. 12;122:1863-72. https://doi.org/10.1182/blood-2013-05-355982

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