Original Article

JHSMR Journal of Health Science and Medical Research

Human Leukocyte Antigen (HLA) Frequencies and 4-loci HLA Haplotype Frequencies in Southern Thailand

Kantarat Kusolthammarat, M.D.[1], Wanwimon Yindee, M.Sc.[1], Jarin Buakaew, M.Sc.[1], Rassamee Chotipanvithayakul, M.D., Ph.D.[2], Kanoot Jaruthamsophon, M.D., Ph.D.[1]

[1]Department of Pathology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

[2]Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

Received 8 July 2024 ● Revised 30 July 2024 ● Accepted 31 July 2024 ● Published online 10 January 2025

Abstract:

Objective: To determine the antigen and haplotype frequencies of human leukocyte antigen-A (*HLA-A), -B, -DRB1,* and *-DQB1* in southern Thailand.

Material and Methods: We retrospectively analyzed HLA typing data from patients treated at Songklanagarind Hospital between September 2004 and May 2023. In total, 629 patients with HLA-A and -B typing results were included, and HLA-DRB1 and -DQB1 data were available for 529 patients. Haplotype frequencies were determined in 55 patients with complete four-locus HLA typing data from at least two family members.

Results: A total of 66 unique HLA antigens were identified across four loci (16 HLA-A, 30 HLA-B, 13 HLA-DR, and 7 HLA-DQ). The most common HLA-A antigens were A24 (25.4%), A11 (24.3%), and A2 (18.8%). The most common HLA-B antigens were B75 (11.6%), B35 (8.4%), and B58 (8.4%). For HLA class II, the highest frequencies of HLA-DR antigens were found in DR15 (23.6%), DR12 (18.4%), and DR7 (10.9%). HLA-DQ5 (33.9%), DQ7 (21.6%), and DQ6 (14.3%) were the most frequently detected HLA-DQ antigens. The most prevalent four-loci haplotype was A33-B44-DR7-DQ2 (4.6%).

Conclusion: This study provides valuable insights into the HLA antigens and haplotype frequencies in southern Thailand. These findings serve as a foundational basis for future studies on disease associations, support transplantation services, and contribute to personalized medicine.

Keywords: clinical immunology, immune system, pharmacogenetics, population genetics, transplantation

Contact: Kanoot Jaruthamsophon, M.D., Ph.D.
Department of Pathology, Faculty of Medicine, Prince of Songkla University,
Hat Yai, Songkhla 90110, Thailand.
E-mail: jkanoot@medicine.psu.ac.th

J Health Sci Med Res 2025;43(4):e20251141
doi: 10.31584/jhsmr.20251141
www.jhsmr.org

Introduction

Human leukocyte antigens (HLA) are a highly polymorphic family of proteins that play an essential role in both cellular and humoral immune responses. The HLA genes, located on chromosome 6p21.3, are inherited as haplotypes. The HLA molecules are classified into two main types: class I antigens (HLA-A, -B, and-C) that are expressed on nucleated cells and platelets, and class II antigens (HLA-DR, -DQ, and -DP) that are expressed on antigen-presenting cells such as B lymphocytes, monocytes, macrophages, dendritic cells, and early hematopoietic cells. The HLA alleles are grouped into serotype-specific subtypes; for example, HLA-B75 (including *HLA-B*15:02* allele and *HLA-B*15:21*) is an HLA-B serotype. HLAs are strongly associated with transplantation outcomes[1], autoimmune diseases, and drug hypersensitivity reactions[2].

HLA matching is necessary for successful kidney and hematopoietic stem cell transplantation (HSCT). Kidney transplantation is the primary treatment option for end-stage renal disease and is associated with improved quality of life and survival time[3,4]. In Thailand, the minimum resolution of HLA class I and class II typing required for kidney transplantation and allogeneic HSCT from matched sibling donors is an allele group or two-digit level resolution[5–7]. Kidney recipients undergo low-intermediate resolution (two- to four-digit level) *HLA-A*, *-B*, and *-DR* gene typing, with lymphocyte cross-matching against matching donors[7]. HLA disparity between the recipient and donor can lead to sensitization, increased rejection risk, and have a negative impact on graft survival[1,4,8–10]. In contrast to kidney transplantation, HSCT relies almost exclusively on identical HLA gene matching. In HSCT cases, matched sibling donors are the preferred source of allogeneic stem cells, but only approximately 30% of patients have an HLA-identical sibling donor available[11]. Therefore, finding an HLA-identical or near-identical unrelated donor is essential for successful engraftment and reducing the risk of graft-versus-host disease after transplantation[1,11,12].

Understanding HLA frequencies is essential for the study of HLA associations with and susceptibility to various immune disorders. For example, HLA-B27 is associated with ankylosing spondylitis and HLA-B35 with subacute thyroiditis[13–15]. HLA markers also play a role in drug hypersensitivity reactions, particularly in Asian populations. For example, HLA-B75 is associated with an increased risk of carbamazepine-induced severe cutaneous adverse reactions (SCARs)[16–18], *HLA-B*58:01* with allopurinol-induced SCARs[19], and *HLA-B*13:01* with dapsone-induced drug hypersensitivity syndrome[20,21]. Understanding HLA antigens and haplotype frequencies is essential for developing effective organ and stem cell donor recruitment strategies. This allows for an estimation of the probability of identifying a matched unrelated donor within a specific population.

Therefore, in this study, we aimed to determine the antigen and haplotype frequencies of HLA-A, -B, -DR, and -DQ in the southern Thai population. The secondary objective was to compare HLA antigen frequencies between the upper and lower southern Thai populations and to compare the obtained HLA frequencies with those in the Thai Stem Cell Donor Registry (TSCDR)[22].

Material and Methods

Population and data collection

Unrelated patients who underwent *HLA-A* and *HLA-B* genotype testing at Songklanagarind Hospital, Prince of Songkla University, Thailand, between September 2004 and May 2023, were included in this retrospective study. Patient characteristics (sex, age, HLA typing indication, and hometown) were collected from the Hospital Information System. The patients' hometowns were assigned based on their home address and the patients

were categorized into two groups: lower southern Thailand (Songkhla, Yala, Pattani, Narathiwat, Satun, Phatthalung, and Trang provinces) and upper southern Thailand (Nakhon Si Thammarat, Surat Thani, Krabi, Phuket, Phang Nga, Ranong, Chumphon, and Prachuap Khiri Khan provinces). Patients whose addresses were outside southern Thailand were excluded from the study.

The HLA typing results and test indications were retrieved from the laboratory records of the Blood Bank and Transfusion Medicine Unit, Department of Pathology, Faculty of Medicine, Prince of Songkla University. In total, 629 patients with *HLA-A* and *HLA-B* typing results were included in the HLA class I frequency calculation. Among these 629 cases, 529 with *HLA-DRB1* and *HLA-DQB1* genotypes were included in the HLA class II frequency calculations.

For the HLA haplotype assessments, we included only patients who were tested for both class I and class II HLAs and had two or more family members genotyped for *HLA-A*, *-B*, *-DRB1*, and *-DQB1*. Families with unknown haplotypes were excluded from the analysis. Haplotype frequencies were determined based on the total haplotype of the patients. The study protocol was approved by the Human Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC. 65-136-5-1).

HLA typing and serotype definition

HLA typing of class I (*HLA-A* and *HLA-B*) and class II (*HLA-DRB1* and *HLA-DQB1*) genes was performed by sequence-specific oligonucleotide probes, using INNO-LiPA® kits (Fujirebio Europe, Ghent, Belgium), according to the manufacturer's instructions. All DNA-based typing results were available at low-intermediate resolution and were converted to allele groups or serologically defined split antigens based on the allelic sequences of the HLA system obtained from the IPD-IMGT/HLA database (available from www.ebi.ac.uk/ipd/imgt/hla/; accessed on January 5, 2024)[23]. Patients with a single HLA allele at any locus were considered homozygous and counted twice. The HLA serotype definitions were reassigned and updated based on the IPD-IMGT/HLA database version 3.54 (2023-10)[23].

HLA antigen frequencies, haplotype frequencies, and statistical analysis

The categorical patient characteristics are shown as frequencies and percentages. Ages are shown as medians and ranges. Antigen frequencies were based on direct countings and were calculated as follows:

$$\%\ \text{antigen frequency} = \frac{\text{total count of antigen of interest}}{\text{total count of antigens (2N)}}$$

In patients for whom the HLA genotypes for all four HLA loci were available, the HLA haplotype was assigned based on the HLA typing results of their family members. HLA haplotype frequencies were calculated as follows:

$$\%\ \text{haplotype frequency} = \frac{\text{total count of haplotype of interest}}{\text{total count of haplotypes (2N)}}$$

The HLA frequencies of the upper southern Thai population were compared with those of the lower southern Thai population. The overall HLA frequencies in this study were compared to the HLA frequencies of the TSCDR (n=16,807)[22]. The HLA-A, -B, and -DR antigen frequencies in the TSCDR dataset were based on stem cell donors in central Thailand[22,24]. Statical differences in antigen frequencies between populations were determined by the chi-square test using MedCalc® Statistical Software version 22.021 (MedCalc Software Ltd, Ostend, Belgium). p-values of less than 0.0001 were considered statistically significant. Scatter plots were generated using R software (R Foundation, Austria, available from https://www.r-project.org/). As the TSCDR dataset contained only three HLA loci, a statistical comparison of the haplotype frequencies was not performed.

Results

Demographic data

Of the 629 participants, most (59.5%) were male, with ages ranging from 2 months to 77 years (median, 27 years) (Table 1). Age distribution analysis showed that the largest number of patients were in the less than 20–year–old age group (41.7%), followed by the 21–40–year–old group (31.3%). HSCT was the indication for HLA typing in 55.5% of patients, while kidney transplantation accounted for the remaining 44.5% of patients. Notably, 71.5% of the patients originated from lower southern Thailand.

Table 1 Study patient characteristics (N=629)

Variable	Number (%)
Sex	
Male	374 (59.5)
Female	255 (40.5)
Median age, years (range)	27 (2 months–77 years)
Age group	
Less than 20 years	261 (41.5)
21–40 years	197 (31.3)
41–60 years	167 (26.6)
60–80 years	4 (0.6)
Indication for HLA typing	
Kidney transplantation	280 (44.5)
Hematopoietic stem cell transplantation	349 (55.5)
Hometown	
Lower southern Thailand	450 (71.5)
Songkhla	179 (28.5)
Yala	45 (7.1)
Pattani	47 (7.5)
Narathiwat	38 (6.0)
Satun	24 (3.8)
Phatthalung	69 (11.0)
Trang	48 (7.6)
Upper southern Thailand	179 (28.5)
Nakhon Si Thammarat	91 (14.5)
Surat Thani	19 (3.0)
Krabi	31 (4.9)
Phuket	13 (2.1)
Phang Nga	13 (2.1)
Chumphon	9 (1.4)
Prachuap Khiri Khan	3 (0.5)

HLA=human leukocyte antigen

Class I and class II HLA antigen frequencies

A total of 66 HLA serotype groups were identified, comprising 16 HLA–A, 30 HLA–B, 13 HLA–DR, and 7 HLA–DQ antigens. The most prevalent HLA–A antigens were A24 (25.4%), A11 (24.3%), A2 (18.8%), and A33 (15.5%). The most common HLA–B antigens were B75 (11.6%), B35 (8.4%), B58 (8.4%), and B46 (7.2%) (Table 2).

The most common HLA–DR antigens for HLA class II were DR15 (23.6%), DR12 (18.4%), DR7 (10.9%), and DR4 (8.2%). Among the seven HLA–DQs identified, the most common were DQ5 (33.9%) and DQ7 (21.6%). DQ4 and DQ8 were the least prevalent, with 4.1% and 3.8%, respectively (Table 3).

HLA frequency comparisons

A comparison of antigen frequencies between lower and upper southern Thailand revealed frequency differences (Figure 1, Supplementary Table 1); however, the differences were not statistically significant. A comparison of the HLA frequencies observed in this study with those in the TSCDR dataset revealed statistically significant HLA–A (n=5), HLA–B (n=6), and HLA–DR (n=2) frequency differences between the two datasets (Figure 2, Supplementary Table 2–4). The southern Thai population exhibited higher antigen frequencies of A3, A24, A34, A66, B18, B35, B52, B71, B75, B77, and DR15 compared to the TSCDR. In contrast, the A2, B46, B60, and DR9 frequencies in the southern Thai population were lower than those in the TSCDR.

HLA haplotype frequencies

Among the 529 patients tested for *HLA–A*, *–B*, *–DRB1*, and *–DQB1*, 269 patients had at least two family members with four–loci HLA typing results available, while HLA haplotypes were unknown in 214 families. As a result, four–loci HLA haplotypes were assigned to 55 patients, and 86 different HLA haplotypes were identified. Only seven haplotypes were observed with a frequency of >2% (Table

4, Supplementary Table 5). A33–B44–DR7–DQ2 was the most common four–loci HLA haplotype. The most common two–loci HLA haplotypes were A33–B58 for HLA class I, and HLA–DR12–DQ7 for HLA class II. The haplotype frequencies are listed in Supplementary Table 5.

Table 2 HLA class I antigen frequencies of the study (N=629; 2N=1,258)

HLA–A	Count	Antigen frequency (%)	HLA–B	Count	Antigen frequency (%)
1	45	3.6	7	34	2.7
2	236	18.8	8	4	0.3
3	27	2.2	13	89	7.1
11	306	24.3	18	89	7.1
23	2	0.2	27	43	3.4
24	320	25.4	35	106	8.4
26	17	1.4	37	13	1.0
29	5	0.4	38	44	3.5
30	19	1.5	39	22	1.8
31	15	1.2	41	4	0.3
32	5	0.4	44	72	5.7
33	195	15.5	46	90	7.2
34	38	3.0	48	8	0.6
66	2	0.2	50	2	0.2
68	21	1.7	51	66	5.3
74	5	0.4	52	55	4.4
			53	1	0.1
			54	12	1.0
			55	16	1.3
			56	13	1.0
			57	25	2.0
			58	105	8.4
			60	58	4.6
			61	35	2.8
			62	63	5.0
			63	5	0.4
			71	6	0.5
			75	146	11.6
			76	6	0.5
			77	26	2.1
Total	**1,258**		**Total**	**1,258**	

HLA=human leukocyte antigen

Table 3 HLA class II antigen frequencies of the study (N=529; 2N=1,058)

HLA-DR	Count	Antigen frequency (%)	HLA-DQ	Count	Antigen frequency (%)
1	9	0.9	2	148	14.0
4	87	8.2	4	43	4.1
7	115	10.9	5	359	33.9
8	18	1.7	6	151	14.3
9	68	6.4	7	229	21.6
10	27	2.6	8	40	3.8
11	52	4.9	9	88	8.3
12	195	18.4			
13	48	4.5			
14	75	7.1			
15	250	23.6			
16	58	5.5			
17	56	5.3			
Total	**1,058**		**Total**	**1,058**	

HLA=human leukocyte antigen

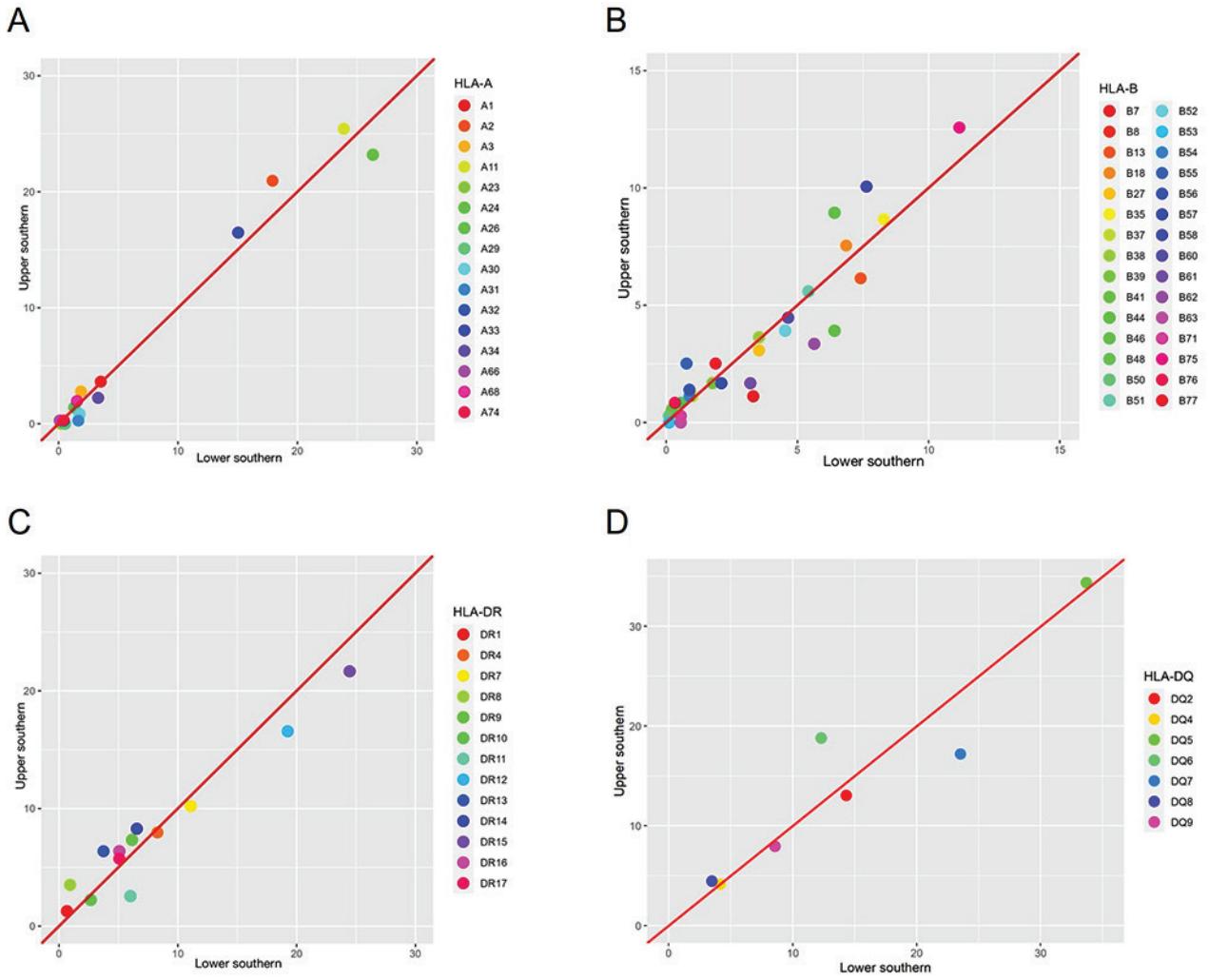
Table 4 HLA class I and II haplotypes with frequency of more than 2% (2N=110)

Haplotype	Count	Haplotype frequency (%)
Four-loci haplotype		
A33-B44-DR7-DQ2	5	4.6
A33-B58-DR13-DQ6	3	2.7
A1-B57-DR7-DQ9	3	2.7
A2-B46-DR9-DQ9	3	2.7
A24-B18-DR12-DQ7	3	2.7
A24-B35-DR12-DQ7	3	2.7
A33-B58-DR17-DQ2	3	2.7
Two-loci HLA class I haplotype		
A33-B58	7	6.4
A33-B44	6	5.5
A11-B13	6	5.5
A11-B75	5	4.6
A2-B46	4	3.6
A1-B57	4	3.6
A24-B35	4	3.6
A24-B46	4	3.6
A11-B46	3	2.7
A11-B62	3	2.7
A24-B18	3	2.7

Table 4 (continued)

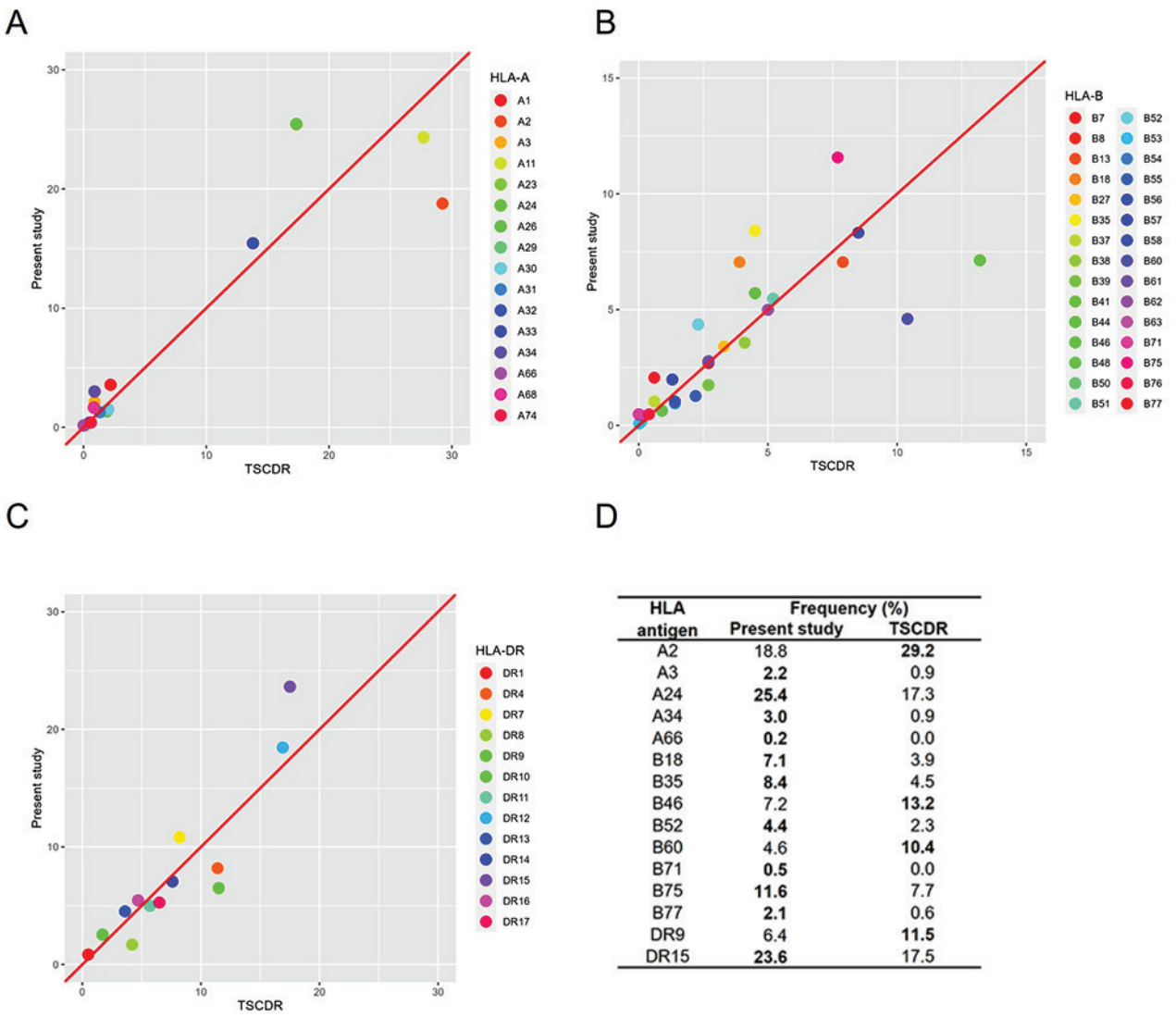
Haplotype	Count	Haplotype frequency (%)
Two-loci HLA class II haplotype		
DR12-DQ7	16	14.6
DR15-DQ5	12	10.9
DR9-DQ9	10	9.1
DR7-DQ2	9	8.2
DR4-DQ4	7	6.4
DR14-DQ5	7	6.4
DR17-DQ2	7	6.4
DR15-DQ6	7	6.4
DR13-DQ6	5	4.6
DR16-DQ5	4	3.6
DR7-DQ9	4	3.6
DR11-DQ7	3	2.7
DR15-DQ7	3	2.7

HLA=human leukocyte antigen



HLA=human leukocyte antigen

Figure 1 Comparison of HLA antigen frequencies between the upper and lower southern Thai populations. The HLA-A (A), HLA-B (B), HLA-DR (C), and HLA-DQ (D) antigen frequencies were compared with x=y line (red line). The x axis represents the antigen frequencies of the lower Southern Thai population. The y axis represents the antigen frequencies of the upper Southern Thai population.



D

HLA antigen	Frequency (%) Present study	TSCDR
A2	18.8	**29.2**
A3	**2.2**	0.9
A24	**25.4**	17.3
A34	**3.0**	0.9
A66	**0.2**	0.0
B18	**7.1**	3.9
B35	**8.4**	4.5
B46	7.2	**13.2**
B52	**4.4**	2.3
B60	4.6	**10.4**
B71	**0.5**	0.0
B75	**11.6**	7.7
B77	**2.1**	0.6
DR9	6.4	**11.5**
DR15	**23.6**	17.5

HLA=human leukocyte antigen, TSCDR=Thai Stem Cell Donor Registry

Figure 2 Comparison of HLA antigen frequencies between the study population and the Thai Stem Cell Donor Registry (TSCDR) dataset. The HLA-A (A), HLA-B (B), and HLA-DR (C) antigen frequencies were compared with a x=y line (red line). The x axis represents the antigen frequencies of the TSCDR. The y axis represents the antigen frequencies of this study. (D) Represents HLA antigens with significant differences (p-value<0.0001) between the two datasets. The populations with higher antigen frequencies are highlighted in bold.

Discussion

This study retrospectively analyzed the frequencies of HLA class I (HLA-A and HLA-B) and class II (HLA-DR and HLA-DQ) antigens and haplotypes in a southern Thai patient population. Our data revealed a predominance of males and a younger age group, reflecting the focus of our setting as a referral center for pediatric hematopoietic transplantation. The HLA antigen profiles exhibited mixed similarities between the Thai and Malaysian populations[22,24–28]. Considering that most of the patients originated from the lower southern region, this study offers valuable information on HLA antigens in this specific population group.

The majority of the HLA antigen frequencies observed in the study of southern Thai patients were consistent with those observed in previous studies performed in other regions of Thailand (central, northeastern, and northern regions), which were tested using serological and molecular methods[25,26,28]. In the present study, the most common antigens were HLA-A24, B75, DR15, and DQ5. For HLA-A, A24 was the most common, followed by A11 and A2, findings which are consistent with data from a southern Thai-Muslim population studied in Nakhon Si Thammarat province[28] and the Malaysian Marrow Donor Registry[27]. While these alleles were also prominent in the TSCDR (primarily the central Thailand population) and a northeastern Thailand study, their frequencies differed between populations[22,25]. Notably, HLA-B46 and B60 (commonly attributed to alleles *HLA-B*46:01* and *HLA-B*40:01*, respectively) were prevalent in the TSCDR but were less common in southern Thailand. In contrast, the B77 (assigned from allele *HLA-B*15:13*), B35, and B18 frequencies were higher than those in the TSCDR and as reported in a previous study also relatively more common in Malaysian populations[27]. For HLA class II, the antigen frequencies were largely concordant with TSCDR, with significant differences only observed for DR9 and DR15.

Based on the larger and broader HLA frequency data, it may be more appropriate to suggest which populations have a higher likelihood of carrying specific HLA antigens or haplotypes. However, recruiting perfectly matched unrelated donors for HSCT remains difficult. Even the most common haplotypes identified in this study, A33-B44-DR7-DQ2, had a frequency of <5%. In the context of kidney transplantation in Thailand, factors influencing the transplantation score include the ABO blood group, HLA mismatches, donor-specific anti-HLA antibodies, waiting time, and age[5,29]. Understanding HLA frequencies can help identify donors with potentially favorable transplant scores and improve our understanding of antibody-mediated rejection, which is often caused by anti-HLA antibodies. Acute antibody-mediated rejection remains a significant challenge in kidney transplantation, affecting 20–50% of cases, while chronic rejection occurs in 50–80%[4,30].

Interestingly, our study found that some of the common HLA-B antigens are clinically important markers. HLA-B75 (primarily *HLA-B*15:02* and *HLA-B*15:21*) was the most common antigen in the southern Thai population, a marker which has been associated with an increased risk of carbamazepine-induced SCARs[16–18]. This significantly higher frequency of the HLA-B75 marker observed in this study indicated a particularly higher risk in the population[31], and further studies are required to elucidate the clinical implications of this HLA marker. Other HLA markers linked to SCARs, including HLA-B13 and HLA-B58, were also prevalent in the southern Thai cohort, mirroring other observations across Thailand[26]. *HLA-B*13:01* (identified by the HLA-B13 serotype) has been reported to increase the risk of dapsone-induced DRESS[20,21] and cotrimoxazole-induced SCARs[32–34]. However, *HLA-B*13:01* screening before dapsone prescriptions had not been implemented as a national policy in Thailand at the time of these earlier studies. A case report in 2024 also described a non-leprosy

patient with dapsone-induced hypersensitivity in southern Thailand which could have been prevented by *HLA-B*13:01* screening[35]. Importantly, *HLA-B*58:01* (identified by the B58 serotype) is a well-established risk factor for allopurinol-induced SCARs[19]. These findings highlight the importance of HLA screening for improving drug safety in populations. In addition, this study found that HLA antigens were associated with certain common autoimmune diseases. HLA-B35, which is associated with subacute thyroiditis[14,15], was found to be relatively more common in the southern Thai population than in other Thai populations. Further investigations into the potential environmental and genetic factors that contribute to the prevalence of these diseases in this specific population are required.

As this was a retrospective study that analyzed a hospital cohort, three main limitations were identified. First, the patients' origins were determined by their home addresses that were logged in the hospital information system, which may not accurately reflect the geographic origin of their ancestry. Second, this study employed low-to-intermediate-resolution HLA typing, which is commonly used for kidney transplant candidates, kidney donors, HSCT patients, and their sibling donors, thus these results may not directly translate to the probability of finding a matched unrelated donor for HSCT in a stem cell registry, which typically requires high-resolution HLA typing (four-digit level). To predict the matching probability, further calculations to determine allele frequencies within the serotype groups may be required. Finally, owing to the limited data availability, the analysis of HLA haplotype frequencies was severely restricted. The number of cases eligible for HLA haplotype analysis (55 out of 529) was limited because of the limited HLA typing results in the patients' family members and unassignable HLA haplotypes. In addition, the comparison of HLA haplotype frequencies across populations was constrained by the lack of complete HLA haplotype data for both the Thai and Malaysian populations. Theoretically, further analyses of other Southeast Asian populations could provide valuable insights into the anthropological aspects of HLA distribution in the region.

Conclusion

In this study, we determined the frequency of HLA antigens and haplotypes in southern Thai patients. The observed antigen frequencies were consistent with previous findings in larger Thai populations, and we found that the observed antigen frequencies were somewhat comparable to those in the Malaysian populations. The study findings serve as an updated population-specific resource for HLA typing in transplantation and pharmacogenetic services.

Acknowledgement

The authors thank Mrs. Prapaporn Jitpakdee for her long devotion to the Blood Bank at Songklanagarind Hospital. We thank Ms. Sarinna Rahad and Ms. Jirawan Jayuphan for their suggestions on the statistical analysis.

Funding sources

This research received no specific grants from any funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare no conflicts of interest regarding the content of this article.

References

1. Liwski R, Ryan Pena J. The HLA system. In: Cohn CS, Delaney M, Johnson ST, Katz LM, Schwartz J, editors. Technical manual. 21st ed. Bethesda, Maryland: American Association of Blood Banks; 2023;p.503–28.
2. Jaruthamsophon K, Thomson PJ, Sukasem C, Naisbitt DJ, Pirmohamed M. HLA allele-restricted immune-mediated adverse drug reactions: framework for genetic prediction. Annu Rev Pharmacol Toxicol 2022;62:509–29.
3. Naik RH, Shawar SH. Renal transplantation rejection. In:

StatPearls [homepage on Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Jun 3]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK553074/

4. Alelign T, Ahmed MM, Bobosha K, Tadesse Y, Howe R, Petros B. Kidney transplantation: the challenge of human leukocyte antigen and its therapeutic strategies. J Immunol Res 2018; 2018:1–18.
5. Kupatawintu P, Tatawatorn A, Phiencharoen S, Choketaweesak N, Nathalang O, Attajarusit Y, et al. Allocation criteria to increase chances of kidney transplantation for highly HLA-sensitized patients. J Hematol Transfus Med 2014;24:103–9.
6. National Blood Centre, Thai Red Cross Society. Standard for blood bank and transfusion services. 5th ed. Bangkok: Udomsuksa; 2024.
7. Srisuddee A, Tupmongkol T, Thongpaknam S, Phiancharoen SP, Kupatawintu P, Nathalang O, et al. HLA mismatch between deceased donors and kidney transplant recipients: a retrospective study from January 2019 to December 2021. J Hematol Transfus Med 2022;32:193–200.
8. Hafeez MS, Awais SB, Razvi M, Bangash MH, Hsiou DA, Malik TH, et al. HLA mismatch is important for 20-year graft survival in kidney transplant patients. Transpl Immunol 2023;80:101861.
9. Tambur AR, Kosmoliaptsis V, Claas FHJ, Mannon RB, Nickerson P, Naesens M. Significance of HLA-DQ in kidney transplantation: time to reevaluate human leukocyte antigen–matching priorities to improve transplant outcomes? An expert review and recommendations. Kidney Int 2021;100:1012–22.
10. Williams RC, Opelz G, McGarvey CJ, Weil EJ, Chakkera HA. The risk of transplant failure with HLA mismatch in first adult kidney allografts from deceased donors. Transplantation 2016;100:1094–102.
11. Tiercy JM. How to select the best available related or unrelated donor of hematopoietic stem cells? Haematologica 2016;101:680–7.
12. Little AM, Akbarzad-Yousefi A, Anand A, Diaz Burlinson N, Dunn PPJ, Evseeva I, et al. BSHI guideline: HLA matching and donor selection for haematopoietic progenitor cell transplantation. Int J Immunogenet 2021;48:75–109.
13. Braun J, Sieper J. Fifty years after the discovery of the association of HLA B27 with ankylosing spondylitis. RMD Open 2023;9:e003102.
14. Bartalena L, Bogazzi F, Pecori F, Martino E. Graves' disease occurring after subacute thyroiditis: report of a case and review of the literature. Thyroid 1996;6:345–8.
15. Kramer AB, Roozendaal C, Dullaart RPF. Familial occurrence of subacute thyroiditis associated with human leukocyte antigen-B35. Thyroid 2004;14:544–7.
16. Jaruthamsophon K, Tipmanee V, Sangiemchoey A, Sukasem C, Limprasert P. HLA-B*15:21 and carbamazepine-induced Stevens-Johnson syndrome: pooled-data and in silico analysis. Sci Rep 2017;7:45553.
17. Sukasem C, Chaichan C, Nakkrut T, Satapornpong P, Jaruthamsophon K, Jantararoungtong T, et al. Association between HLA-B alleles and carbamazepine-induced maculopapular exanthema and severe cutaneous reactions in Thai patients. J Immunol Res 2018;2018:2780272.
18. Sukasem C, Sririttha S, Chaichan C, Nakkrut T, Satapornpong P, Jaruthamsophon K, et al. Spectrum of cutaneous adverse reactions to aromatic antiepileptic drugs and human leukocyte antigen genotypes in Thai patients and meta-analysis. Pharmacogenomics J 2021;21:682–90.
19. Tassaneeyakul W, Jantararoungtong T, Chen P, Lin PY, Tiamkao S, Khunarkornsiri U, et al. Strong association between HLA-B*5801 and allopurinol-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in a Thai population. Pharmacogenet Genomics 2009;19:704–9.
20. Tempark T, Satapornpong P, Rerknimitr P, Nakkam N, Saksit N, Wattanakrai P, et al. Dapsone-induced severe cutaneous adverse drug reactions are strongly linked with HLA-B*13:01 allele in the Thai population. Pharmacogenet Genomics 2017;27:429–37.
21. Satapornpong P, Pratoomwun J, Rerknimitr P, Klaewsongkram J, Nakkam N, Rungrotmongkol T, et al. HLA-B*13:01 is a predictive marker of dapsone-induced severe cutaneous adverse reactions in Thai patients. Front Immunol 2021;12:661135.
22. Kupatawintu P, Pheancharoen S, Srisuddee A, Tanaka H, Tadokoro K, Nathalang O. HLA-A, -B, -DR haplotype frequencies in the Thai Stem Cell Donor Registry. Tissue Antigens 2010;75:730–6.
23. Robinson J, Barker DJ, Georgiou X, Cooper MA, Flicek P, Marsh SGE. IPD-IMGT/HLA database. Nucleic Acids Res 2020;48:D948–55.
24. Ounjai S, Ponraweethitikorn P, Kanunthong S, Srisuddee A, Phiencharoen S, Kupatawintu P, et al. HLA-A, -B, and -DR

frequencies in deceased kidney donors of the Organ Donation Centre, Thai Red Cross Society. J Hematol Transfus Med 2019;29:175–81.

25. Romphruk AV, Romphruk A, Kongmaroeng C, Klumkrathok K, Paupairoj C, Leelayuwat C. HLA class I and II alleles and haplotypes in ethnic northeast Thais. Tissue Antigens 2010;75:701–11.
26. Satapornpong P, Jinda P, Jantararoungtong T, Koomdee N, Chaichan C, Pratoomwun J, et al. Genetic diversity of HLA class I and class II alleles in Thai populations: contribution to genotype-guided therapeutics. Front Pharmacol 2020;11:78.
27. Dhaliwal JS, Shahnaz M, Too CL, Azrena A, Maiselamah L, Lee YY, et al. HLA-A, -B and -DR allele and haplo- type frequencies in Malays. Asian Pac J Allergy Immunol 2007;25:47–51.
28. Chiewsilp P, Mongkolsuk T, Sujirachato K, Junpong S, Rattanasombat K, Uden C. HLA in southern Thai-Muslims. J Med Assoc Thai 1997;80(Suppl 1):S30-7.
29. Regulation of the Organ Donation Centre, Thai Red Cross Society. Bangkok: Thai Red Cross Society; 2002.
30. Thammanichanond D. Human leukocyte antigen matching in kidney transplantation. J Hematol Transfus Med 2014;24:99–102.
31. Jaruthamsophon K, Sangmanee P, Plong-On O, Charalsawadi C, Sukasem C, Hnoonual A. Molecular identification of HLA-B75 serotype markers by qPCR: A more inclusive pharmacogenetic approach before carbamazepine prescription. Clin Transl Sci 2024;17:e13867.
32. Pratoomwun J, Thomson P, Jaruthamsophon K, Tiyasirichokchai R, Jinda P, Rerkpattanapipat T, et al. Characterization of T-Cell responses to SMX and SMX-NO in co-trimoxazole hypersensitivity patients expressing HLA-B*13:01. Front Immunol 2021;12:658593.
33. Wang CW, Tassaneeyakul W, Chen CB, Chen WT, Teng YC, Huang CY, et al. Whole genome sequencing identifies genetic variants associated with co-trimoxazole hypersensitivity in Asians. J Allergy Clin Immunol 2021;147:1402–12.
34. Wu PC, Chen WT, Huang IH, Chen CB, Wang CW, Tai CC, et al. Human leukocyte antigens and sulfamethoxazole/cotrimoxazole-induced severe cutaneous adverse reactions: a systematic review and meta-analysis. JAMA Dermatol 2024;160:525–34.
35. Thungthienthong M, Tongsengkee N, Intapiboon P. Sulfone syndrome: a unique delayed type of drug hypersensitivity from dapsone. J Health Sci Med Res 2024;42:e20241054. doi: 10.3158/jhsmr.20241054.

Supplementary Table 1 Antigen frequencies of HLA-A, -B, -DR, -DQ in the patients from lower southern Thailand and upper southern Thailand

HLA	Lower southern Thailand		Upper southern Thailand		p-value
	count	%	count	%	
HLA-A (n=629)					
1	32	3.56	13	3.63	p=0.9519
2	161	17.89	75	20.95	p=0.2099
3	17	1.89	10	2.79	p=0.3205
11	215	23.89	91	25.42	p=0.5684
23	2	0.22	0	0.00	p=0.3746
24	237	26.33	83	23.18	p=0.2472
26	12	1.33	5	1.40	p=0.9227
29	5	0.56	0	0.00	p=0.1561
30	16	1.78	3	0.84	p=0.2179
31	14	1.56	1	0.28	p=0.0596
32	4	0.44	1	0.28	p=0.6830
33	136	15.11	59	16.48	p=0.5448
34	30	3.33	8	2.23	p=0.3036
66	1	0.11	1	0.28	p=0.4940
68	14	1.56	7	1.96	p=0.6179
74	4	0.44	1	0.28	p=0.6830
HLA-B (n=629)					
7	30	3.33	4	1.12	p=0.0292
8	2	0.22	2	0.56	p=0.3331
13	67	7.44	22	6.15	p=0.4208
18	62	6.89	27	7.54	p=0.6851
27	32	3.56	11	3.07	p=0.6663
35	75	8.33	31	8.66	p=0.8493
37	9	1.00	4	1.12	p=0.8495
38	31	3.44	13	3.63	p=0.8685
39	16	1.78	6	1.68	p=0.9029
41	2	0.22	2	0.56	p=0.3331
44	58	6.44	14	3.91	p=0.0814
46	58	6.44	32	8.94	p=0.1235
48	5	0.56	3	0.84	p=0.5742
50	1	0.11	1	0.28	p=0.4940
51	46	5.11	20	5.59	p=0.7306
52	41	4.56	14	3.91	p=0.6112
53	1	0.11	0	0.00	p=0.5303
54	8	0.89	4	1.12	p=0.7053
55	7	0.78	9	2.51	p=0.0135
56	8	0.89	5	1.40	p=0.4202
57	19	2.11	6	1.68	p=0.6221
58	69	7.67	36	10.06	p=0.1669
60	42	4.67	16	4.47	p=0.8788
61	29	3.22	6	1.68	p=0.1341
62	51	5.67	12	3.35	p=0.0889
63	5	0.56	0	0.00	p=0.1561
71	5	0.56	1	0.28	p=0.5171
75	101	11.22	45	12.57	p=0.5001
76	3	0.33	3	0.84	p=0.2354
77	17	1.89	9	2.51	p=0.4857

Supplementary Table 1 (continued)

HLA	Lower southern Thailand		Upper southern Thailand		p-value
	count	%	count	%	
HLA-DR (n=529)					
1	5	0.67	4	1.27	p=0.3311
4	62	8.33	25	7.96	p=0.8414
7	83	11.16	32	10.19	p=0.6435
8	7	0.94	11	3.50	p=0.0033
9	45	6.05	23	7.32	p=0.4418
10	20	2.69	7	2.23	p=0.6649
11	44	5.91	8	2.55	p=0.0209
12	143	19.22	52	16.56	p=0.3082
13	28	3.76	20	6.37	p=0.0624
14	49	6.59	26	8.28	p=0.3281
15	182	24.46	68	21.66	p=0.3276
16	38	5.11	20	6.37	p=0.4111
17	38	5.11	18	5.73	p=0.6809
HLA-DQ (n=529)					
2	107	14.38	41	13.06	p=0.5719
4	30	4.03	13	4.14	p=0.9340
5	251	33.74	108	34.39	p=0.8384
6	92	12.37	59	18.79	p=0.0064
7	175	23.52	54	17.20	p=0.0226
8	26	3.49	14	4.46	p=0.4499
9	63	8.47	25	7.96	p=0.7839

Supplementary Table 2 HLA-A antigen frequencies in this study compared to the Thai Stem Cell Donor Registry

HLA-A	Present study (N=629)	TSCDR (N=16,807)	p-value
1	3.58%	2.20%	p=0.0012
2	18.76%	29.24%	p<0.0001
3	2.15%	0.90%	p<0.0001
11	24.32%	27.70%	p=0.0084
23	0.16%	0.10%	p=0.5131
24	25.44%	17.34%	p<0.0001
26	1.35%	1.90%	p=0.1585
29	0.40%	0.60%	p=0.3643
30	1.51%	2.00%	p=0.2209
31	1.19%	1.34%	p=0.6490
32	0.40%	0.50%	p=0.6203
33	15.50%	13.80%	p=0.0867
34	3.02%	0.90%	p<0.0001
66	0.16%	0.01%	p<0.0001
68	1.67%	0.84%	p=0.0019
74	0.40%	0.60%	p=0.3643

TSCDR=Thai Stem Cell Donor Registry

Supplementary Table 3 HLA–B antigen frequencies in this study compared to the Thai Stem Cell Donor Registry

HLA–B	Present study (N=629)	TSCDR (N=16,807)	p–value
7	2.70%	2.70%	p=1.0000
8	0.32%	0.10%	p=0.0196
13	7.07%	7.90%	p=0.2831
18	7.07%	3.90%	p<0.0001
27	3.42%	3.30%	p=0.8152
35	8.43%	4.50%	p<0.0001
37	1.03%	0.60%	p=0.0556
38	3.50%	4.10%	p=0.2908
39	1.75%	2.70%	p=0.0400
41	0.32%	0.10%	p=0.0196
44	5.72%	4.50%	p=0.0414
46	7.15%	13.20%	p<0.0001
48	0.64%	0.90%	p=0.3352
50	0.16%	0.10%	p=0.5131
51	5.25%	5.20%	p=0.9375
52	4.37%	2.30%	p<0.0001
53	0.08%	0.02%	p=0.1605
54	0.95%	1.40%	p=0.1798
55	1.27%	2.20%	p=0.0261
56	1.03%	1.40%	p=0.2705
57	1.99%	1.30%	p=0.0356
58	8.35%	8.50%	p=0.8514
60	4.61%	10.40%	p<0.0001
61	2.78%	2.70%	p=0.8636
62	5.01%	5.00%	p=0.9873
63	0.40%	0.20%	p=0.1256
71	0.48%	0.00%	p<0.0001
75	11.61%	7.70%	p<0.0001
76	0.48%	0.40%	p=0.6601
77	2.07%	0.60%	p<0.0001

TSCDR=Thai Stem Cell Donor Registry

Supplementary Table 4 HLA–DQ antigen frequencies in this study compared to the Thai Stem Cell Donor Registry

HLA–DR	Present study (N=529)	TSCDR (N=16,807)	p–value
1	0.85%	0.50%	p=0.1158
4	8.22%	11.40%	p=0.0013
7	10.87%	8.20%	p=0.0019
8	1.70%	4.20%	p=0.0001
9	6.43%	11.50%	p<0.0001
10	2.55%	1.70%	p=0.0366
11	4.91%	5.70%	p=0.2742
12	18.43%	16.90%	p=0.1915
13	4.54%	3.60%	p=0.1074
14	7.09%	7.60%	p=0.5373
15	23.63%	17.50%	p<0.0001
16	5.48%	4.70%	p=0.2390
17	5.29%	6.50%	p=0.1150

TSCDR=Thai Stem Cell Donor Registry

Supplementary Table 5 Haplotype frequencies (N=55; 2N=110)

Haplotype	Count	%
A33–B44–DR7–DQ2	5	4.55
A33–B58–DR13–DQ6	3	2.73
A1–B57–DR7–DQ9	3	2.73
A2–B46–DR9–DQ9	3	2.73
A24–B18–DR12–DQ7	3	2.73
A24–B35–DR12–DQ7	3	2.73
A33–B58–DR17–DQ2	3	2.73
A2–B13–DR15–DQ5	2	1.82
A11–B13–DR16–DQ5	2	1.82
A11–B35–DR13–DQ6	2	1.82
A3–B35–DR17–DQ2	2	1.82
A11–B46–DR9–DQ9	2	1.82
A11–B75–DR12–DQ7	2	1.82
A24–B60–DR15–DQ5	2	1.82
A34–B75–DR15–DQ6	2	1.82
A1–B57–DR10–DQ5	1	0.91
A2–B41–DR17–DQ2	1	0.91
A2–B46–DR14–DQ5	1	0.91
A2–B55–DR17–DQ2	1	0.91
A3–B7–DR15–DQ6	1	0.91
A11–B7–DR4–DQ4	1	0.91
A11–B7–DR10–DQ5	1	0.91
A11–B13–DR14–DQ5	1	0.91
A11–B13–DR15–DQ6	1	0.91
A11–B18–DR15–DQ5	1	0.91
A11–B54–DR14–DQ5	1	0.91
A11–B56–DR12–DQ5	1	0.91
A24–B13–DR15–DQ6	1	0.91
A24–B27–DR1–DQ5	1	0.91
A24–B27–DR11–DQ6	1	0.91
A24–B35–DR7–DQ2	1	0.91
A24–B38–DR15–DQ5	1	0.91
A24–B46–DR14–DQ5	1	0.91
A24–B48–DR15–DQ5	1	0.91
A24–B51–DR4–DQ4	1	0.91
A24–B54–DR14–DQ5	1	0.91
A24–B58–DR4–DQ4	1	0.91
A26–B44–DR7–DQ2	1	0.91
A26–B54–DR4–DQ4	1	0.91
A30–B13–DR7–DQ2	1	0.91
A31–B51–DR15–DQ5	1	0.91
A33–B44–DR11–DQ2	1	0.91
A33–B58–DR4–DQ4	1	0.91

Supplementary Table 5 (continued)

Haplotype	Count	%
A34–B38–DR15–DQ5	1	0.91
A34–B51–DR15–DQ6	1	0.91
A2–B41–DR17–DQ6	1	0.91
A2–B55–DR15–DQ7	1	0.91
A2–B60–DR12–DQ7	1	0.91
A2–B60–DR16–DQ5	1	0.91
A2–B61–DR12–DQ7	1	0.91
A2–B75–DR11–DQ5	1	0.91
A2–B75–DR14–DQ5	1	0.91
A2–B77–DR12–DQ7	1	0.91
A2–B77–DR12–DQ8	1	0.91
A11–B13–DR11–DQ7	1	0.91
A11–B13–DR12–DQ7	1	0.91
A11–B18–DR4–DQ7	1	0.91
A11–B27–DR9–DQ9	1	0.91
A11–B39–DR12–DQ7	1	0.91
A11–B46–DR4–DQ8	1	0.91
A11–B61–DR11–DQ7	1	0.91
A11–B62–DR7–DQ2	1	0.91
A11–B62–DR15–DQ5	1	0.91
A11–B62–DR16–DQ5	1	0.91
A11–B71–DR14–DQ7	1	0.91
A11–B75–DR4–DQ4	1	0.91
A11–B75–DR8–DQ7	1	0.91
A11–B75–DR15–DQ6	1	0.91
A24–B7–DR15–DQ7	1	0.91
A24–B46–DR9–DQ9	1	0.91
A24–B46–DR11–DQ7	1	0.91
A24–B46–DR12–DQ7	1	0.91
A24–B51–DR4–DQ8	1	0.91
A24–B55–DR9–DQ9	1	0.91
A24–B57–DR7–DQ9	1	0.91
A24–B62–DR4–DQ4	1	0.91
A24–B62–DR15–DQ5	1	0.91
A24–B75–DR11–DQ5	1	0.91
A24–B75–DR12–DQ7	1	0.91
A24–B76–DR15–DQ7	1	0.91
A24–B77–DR15–DQ5	1	0.91
A26–B51–DR12–DQ7	1	0.91
A33–B60–DR8–DQ8	1	0.91
A33–B61–DR9–DQ9	1	0.91
A33–B75–DR14–DQ5	1	0.91
A34–B13–DR9–DQ9	1	0.91