HLA Class II Allele Frequencies in Northern Thais (Kamphaeng Phet)

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Abstract

The polymorphism of HLA class II genes (HLA-DRB1, -DQA1, -DQB1 and -DPB1) was investigated in 97 normal Northern Thais (NT) from Kamphaeng Phet province using PCR-SSO typing. Allele frequencies (AF) have been determined. DRB1*1202 (17.5%), DRB1*1502 (16.5%), DQA1*0101 (25.8%), DQA1*0102 (21.7%), DQB1*0502 (22.7%), DPB1*0501 (23.2%) and DPB1*1301 (22.7%) showed the highest frequencies in each locus. These results were more similar to those observed in Present-day Thais (PDT) and Central Thais (CT) than Northern Thais from Chiang Mai (CM) and Dai Lue (DL). However, the data presented in this population study should be useful in many fields, such as anthropology, organ transplantation, disease susceptibility and evolutionary genetics.

Kamphaeng Phet province located at the lower part of Northern Thailand. Kamphaeng Phet is an old city in the history of Thailand of more than 700 years, which is some 8,607.5 square kilometres in area. The polymorphism of the HLA system and the differences in HLA allele frequencies in various ethnic groups make these immunological molecules good markers for studies of inheritance, ancestral, origin, migration of populations and disease association. The Thais, Dai or Tai people, have proliferated throughout SE Asia, S China, and the NE Indian subcontinent(1). The Thai Ethnics are distinct by their languages, cultures, architecture, religions and agricultural practices. Conversely, migration and assimilation of Chinese peoples, have contributed to the many ethnic admixtures to recreate modern Thai Ethnics. Recently, over 200 HLA class II alleles have been officially named(2) and almost all of them can be genotyped with oligonucleotide probes. In Thailand, HLA class II has been studied in Central Thais(3-5), Northeastern Thais(5), upper part of Northern Thais(4,6) and Southern Thais(7) but has not yet been studied in the lower part of Northern

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Thais. In this study, we have analyzed the allele frequencies for the HLA class II in normal healthy Northern Thais (NT). Such analysis has enabled us, to comprehensively compare genetic class II polymorphism of NT with other Thai groups(3-7).

MATERIAL AND METHOD

Ninety-seven random healthy NT from Kamphaeng Phet province were studied for HLA class II polymorphism. The HLA-DRB1, -DQA1, -DQB1 and -DPB1 loci were typed by PCR-SSO according to the 11th IHW protocol(8). The primers and oligonucleotide probes for HLA-DRB1, -DQA1, -DQB1 and -DPB1 loci were used from 11th IHW.

Analysis of the results was carried out by the conventional method. Allele frequencies (AF) of the HLA class II loci were obtained by direct counting. AF were calculated from the following formula: AF (%) = [(the sum of the allele) / 2N x 100], where N is the sum of the individuals analyzed.

RESULTS

Twenty-three DRB1 alleles were detected in NT (Table 1). DRB1*1202, an allele of DR5, was the most frequent allele with AF=17.5 per cent. The second most common allele was DRB1 *1502, an allele of DR2 with AF=16.5 per cent. The third most common allele was DRB1*0901 (12.4%). Eight DQA1 alleles and 12 DQB1 alleles were detected in NT (Table 1). DQA1*0101 and DQA1*0102 were the most two common alleles of DQA1 (25.8% and 21.7%, respectively). DQB1*0502 was the highest frequent allele of DQB1 (22.7%), whereas the second most frequent allele was DQB1*0301 (16.0%). Finally, 18 alleles of DPB1 were detected (Table 1). Two highest frequent alleles were DPB1*0501 (23.2%) and DPB1*1301 (22.7%).

DISCUSSION

The HLA class II alleles can be determined with greater accuracy than the past by using

Table 1. DRB1, DQA1 and DPB1 allele frequencies (AF) in Northern Thais (Kamphaeng Phet) (N = 97).

DRB1*	n	AF(%)	DQA1*	n	AF(%)	DQB1*	n	AF(%)	DPB1*	n	AF(%)
01	1	0.5	0101	50	25.8	0201	21	10.8	0101	1	0.5
0301	12	6.2	0102	42	21.7	0301	31	16.0	0201	15	7.7
0401	1	0.5	0103	7	3.6	0302	7	3.6	0202	15	7.7
0403	2	1.0	0201	13	6.7	03032	27	13.9	0301	12	6.2
0404	2	1.0	0301	40	20.6	0401	5	2.6	0401	20	10.3
0405	10	5.1	0401	1	0.5	0402	4	2.1	0402	8	4.1
0406	1	0.5	0501	20	10.3	0501	26	13.4	0501	45	23.2
0701	13	6.7	0601	19	9.8	0502	44	22.7	0901	1	0.5
0802	1	0.5	Blank		1.0	05031	10	5.1	1001	2	1.0
08032	3	1.6				0601	17	8.8	1301	44	22.7
0901	24	12.4				0602	1	0.5	1401	10	5.2
1001	1	0.5				0603	1	0.5	1601	3	1.6
1101	5	2.6				Blank		0.0	1701	6	3.1
1104	1	0.5							1901	1	0.5
1110	4	2.1							2101	7	3.7
1202	34	17.5							2801	1	0.5
1301	1	0.5							3101	1	0.5
1401	11	5.7							3601	2	1.0
1404	6	3.1							Blank		0.0
1405	3	1.6									
1501	13	6.7									
1502	32	16.5									
1602	13	6.7									
Blank		0.0									

n = number of positive alleles
N = number of individuals analyzed

Table 2. HLA class II alleles in Northern Thais (Kamphaeng Phet), compared with other Thai groups.

HLA allele	NT	PDT	CT	DL	CM	STM	D	NET	Thai-Khmer
DRB1*0701	Present	Present	Present	Rare	Low	Present	ND	ND	ND
DRB1*0404	Present	Absent	Absent	Absent	Absent	Absent	ND	ND	ND
DRB1*0802	Present	Absent	Present	Absent	Absent	Absent	ND	ND	ND
DRB1*1104	Present	Present	Absent	Absent	Absent	Absent	ND	ND	ND
DRB1*1602	Low	Low	Low	High	High	Low	ND	ND	ND
DQA1*0103	Present	Present	Present	Absent	ND	Present	ND	ND	ND
DQA1*0201	Present	Present	Present	Rare	ND	Present	ND	ND	ND
DQB1*05032	Absent	Absent	ND	Present	ND	Absent	ND	ND	ND
DPB1*0901	Present	Present	ND	Absent	ND	Absent	Absent	Present	Present
DPB1*1001	Present	Present	ND	Absent	ND	Absent	Absent	Absent	Present
DPB1*1701	Present	Present	ND	Absent	ND	Absent	Present	Present	Present
DPB1*1901	Present	Present	ND	Present	ND	Present	Absent	Absent	Absent
DPB1*2301	Absent	Absent	ND	Absent	ND	Present	Absent	Absent	Absent
DPB1*2801	Low	Low	ND	Rare	ND	Low	Absent	Low	High

NT = Northern Thais (Kamphaeng Phet), PDT = Present-day Thais (Bangkok, data from Chandanayingyong D, et al in press), CT = Central Thais (Bangkok,data from Sujirachato K, et al 1994)

DL = Dai Lue (N Thailand and Burma, DQA1 and DQB1 from Chandanayingyong D, et al. in press while DPB1 from Chandanayingyong D, et al. 1994)

CM = Chiang Mai (data from Kunachiwa W. 1995), D = Dai (Yunnan and S China, data from Chandanayingyong D, et al 1994),

NET = Northeastern Thais (Thailand and Laos, data from Chandanayingyong D, et al. 1994), Thai-Khmer = Eastern Thais and Cambodia (data from Chandanayingyong D, et al. 1994)

STM = Southern Thai-Muslim (data from Chiewslip P, et al. in press), ND = Molecular HLA typing was not done

PCR-SSO method. Allele frequencies of HLA class II have been observed in other Thai groups (3-7). From Table 2, the interesting finding was DRB1*0404 was present in NT but was absent in other Thai groups (Present-day Thais, PDT; Central Thais, CT; Dai Lue, DL; Chiang Mai, CM; Southern Thai-Muslim, STM; Dai, D; Northeastern Thais, NET; and Thai-Khmer). The presence of HLA-DRB1*0404 was also observed in Brazilian white(9), Japanese(10), Colombian Amerindian Population(11) and Bulgarians(12). DRB1 *1602 was present with higher frequency in DL and CM but low in NT, PDT, CT and STM. DQA1*0103 was present in NT, CT, STM and other Thai groups but was absent in DL while DQB1*05032 was absent in NT, PDT and STM but was present in DL. DPB1*2301 was absent in NT and other Thai groups but was predominate in STM. In addition, DPB1*2801 was predominate in Thai-Khmer, whereas, it was low in NT, PDT, CT, DL, STM and NET.

SUMMARY

In our study, the allele frequencies observed in NT have revealed more interesting similarities to PDT(4,5) and CT(3) than CM(6) and DL(4,5) who are the people from the upper part of Northern Thailand and Burma. The migration and intermarriage among NT and CT (from Bangkok) may contribute to the many ethnic admixtures to recreate modern Thai Ethnics and account for these findings. However, the data presented in this population study should be useful in many fields, such as anthropology, organ transplantation, disease susceptibility and evolutionary genetics.

ACKNOWLEDGEMENT

This work was partially supported by Mahidol University Research Grant #1994.

(Received for publication on July 11, 1997)

REFERENCES

1. Chandanayingyong D, Kunmatini S, Udee S, et al. W5.21 HLA in Thais, Thai / Chinese Vietnamese, Javanese and Timorese. In : HLA 1991, Proceeding of the Eleventh International Histocompatibility Workshop and Conference Vol 1 Anthropology component Tsuji K, Aizawa M and Sasazuki T (eds). Oxford, New York, Tokyo, Oxford University Press 1992: 681-3.
2. Bodmer JG, Marsh SGE, Albert ED, et al. Nomenclature for factors of the HLA system, 1994. Tissue Antigens 1994; 44: 1-18.
3. Sujirachato K, Chiewsilp P, Tsuji K, et al. HLA class II polymorphism in Thais detected by PCR-SSO and PCR-RFLP. Tissue Antigens 1994; 43: 224-8.
4. Chandanayingyong D, Stephens HAF, Klaythong R, et al. HLA-A,-B,-DRB1,-DQA1 and DQB1 polymorphism in Thais. Hum Immunol 1997 (in press).
5. Chandanayingyong D, Stephens HAF, Fan L, et al. HLA-DPB1 Polymorphism in the Thais of Southeast Asia. Hum Immunol 1994; 40: 20-4.
6. Kunachiwa W. HLA class II in Leprosy patients in Northern Thailand. Thesis, Mahidol University 1995; 59.
7. Chiewsilp P, Mongkolsuk T, Sujirachato K, Junpong S, Rattanasombat K, Uden C. HLA in Southern Thai-Muslim. J Med Assoc Thai 1997; 80: (Suppl. 1) 30-7.
8. Kimura A, Sasazuki T. W3.3 Eleventh International Histocompatibility Workshop reference protocol for the HLA DNA-typing technique. In HLA 1991, Proceeding of the 11 th International Histocompatibility Workshop and Conference Vol 1 DNA component Tsuji K, Aizawa M and Sasazuki T(eds). Oxford, New York, Tokyo, Oxford University Press 1992: 397-419.
9. Moraes ME, Frenandez-Vina M, Salatiel I, Tsai S, Moraes JR, Stastny P. HLA class II DNA typing in two Brazilian populations. Tissue Antigens 1993; 41: 238-42.
10. Hashimoto M, Kinoshita T, Yamasaki M, et al. Gene frequencies and haplotypic associations within the HLA region in 916 unrelated Japanese individuals. Tissue Antigens 1994; 44: 166-73.
11. Trachtenberg EA, Keyeux G, Bernal JE, Rhodas MC, Erlich HA. Results of Expedicion Humana. I. Analysis of HLA class II (DRB1-DQA1-DQB1-DPB1) alleles and DR-DQ haplotypes in nine Amerindian populations from Colombia. Tissue Antigens 1996; 48: 174-81.
12. Ivanova R, Naoumova E, Lepage V, et al. HLA-DRB1, DQA1,DQB1 DNA polymorphism in the Bulgarian population. Tissue Antigens 1996; 47: 122-6.

การศึกษา เอช แอล เอ คลาส สอง อัลลีล ในคนไทยภาคเหนือ (จังหวัด กำแพงเพชร)

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ได้ทำการศึกษาความหลากหลายของ เอช แอล เอ คลาสสองทั้ง 4 โลไค (DRB1, DQA1, DQB1 และ DPB1) ในประชากรจังหวัดกำแพงเพชร จำนวน 97 ราย ด้วยวิธีการใช้เทคนิค PCR–SSO. โดยทำการตรวจสอบ allele frequencies (AF) ของยีน เอช แอล เอ คลาสสอง ผลจากการศึกษาพบว่า DRB1*1202 (17.5%) DRB1*1502 (16.5%) DQA1*0101 (25.8%) DQA1*0102 (21.7%) DQB1*0502 (22.7%) DPB1*0501 (23.2%) และ DPB1*1301 (22.7%) เป็นอัลลีลที่พบมากที่สุดในแต่ละโลคัส จากการศึกษาพบว่าความหลากหลายทางพันธุกรรมของคนไทยภาคเหนือจากจังหวัดกำแพงเพชรใกล้เคียงกับคนไทยภาคกลาง (CT, PDT) มากกว่าคนไทยภาคเหนือจากจังหวัดเชียงใหม่ และคนไทยลื้อ (DL) ข้อมูลที่ได้จากการศึกษานี้สามารถนำไปใช้ประโยชน์ในการศึกษาด้านมนุษยวิทยา, ด้านการเปลี่ยนถ่ายอวัยวะ, ด้านความสัมพันธ์ระหว่าง HLA กับการเกิดโรค และด้านวิวัฒนาการทางพันธุกรรม

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