

Overview of Human Leukocyte Antigen Development at Siriraj Hospital

Dasnayanee Chandanayingyong, M.D.

Department of Transfusion Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

The International Histocompatibility Workshops and Conferences (IHW^C)¹ date back to 1964, when D.B. Amos organized the first workshop. The following workshops were held in 1965, 1967, 1970, 1972, 1975, 1977, 1980, 1984, 1987, 1991 and 1996. These workshops have become a central and unifying forum for research and development in the field of human histocompatibility testing and immunogenetics.

The IHW^C was a unique example of international collaborative research. The endless polymorphisms of Human Leukocyte Antigen (HLA) forces all of us to cooperate. No single investigator could afford to go it alone. The high level of collaboration between the laboratories existed because it was necessary. For serological technique, every laboratory who participates will use the same technique and same HLA antisera set. The results will be analyzed and reported to the meeting by appropriate ones, assigned by the organizer. (Siriraj Med J 2017;69:47-50)

The establishment of the HLA work at Siriraj Hospital was started around the year 1972. During this period, the Royal Thai Government requested and received an aid program under Colombo Plan from New Zealand Government in order to improve the standard practices at the Blood Transfusion Service (BTS) Siriraj Hospital. During this period, the Faculty of Medicine, Siriraj Hospital and Medical School, want to establish “Transplantation Service”. A decision was made for the Blood Bank to take responsibility for performing HLA typing. Prof. Sir JM Staveley, Director of an aid program, helped to establish the HLA work at Siriraj Hospital by:-

- Train personnel of Siriraj Hospital BTS for performing HLA typing
- Donated HLA typing trays (Biotest)
- Funded tissue typing technologist for further training at Auckland BTS, New Zealand.

At this early period, HLA typing results using HLA typing sera (Biotest) from Caucasians were unsatisfactory. The first successful cadaveric kidney transplantation was performed (1973), Patient HLA – HLA A11, -; B-, -; and

Donor HLA – HLA A2, 9; B-, -, with compatible cross-matching.

From this problem, we started screening sera in pregnant Thais women using 5 random donors in order to find HLA antisera from Thai people. At that time, there were no known standard cells. In order to identify antibodies, there must be known standard cells. While to assign unknown antigens, there must be known antisera. We did not have both.

Since the 5th IHW^C (1972), it had been noticed that many populations besides Caucasian had HLA blank when tested with sera from Caucasian origin. Fortunately, on my way back from attending the International Society of Blood Transfusion (ISBT) meeting in Helsinki, Finland (1976), on the plane from Helsinki to Copenhagen, I was seated next to Prof. Rose Payne, world famous HLA expert. I consulted her about our problems. She kindly sent me anti Hsu (B46) to us, so we can assign the first HLA B46 in Thai people. She also informed Prof. Kimiyoshi Tsuji, Professor of Surgery, Transplantation Immunology Center, Tokai University School of Medicine, Japan about our HLA work at Siriraj Hospital.

Correspondence to: Dasnayanee Chandanayingyong

E-mail: dasnayanee.cha@mahidol.ac.th

doi:10.14456/smj.2017.10

Prof. Tsuji, was a workshop chairman, who planned to organize an “Asia Histocompatibility Workshop”. He wrote a letter inviting our BTS to join his workshop. The first Asia and Oceania Histocompatibility Workshop and Conference was held (1978). In this workshop, HLA sera used was mostly from Asian origin. This was the first time, we exchanged sera between countries. After this successful Asia Oceania Histocompatibility Workshop (AOHWC), the 2nd AOWHC was held in Melbourne, Australia (1981)². At this workshop, we found that there were definite problems in the antigen assignment especially HLA-A11 of the A locus and HLA-B15 of the B locus.

At this workshop, only the minority of the Thais HLA-B15 were able to be assigned as HLA-Bw62 (see Reaction pattern of B15 positive of the Thais, 2AOHW)² (Fig 1). It was believed that variation of our results were due to “technical problems”. We decided to repeat study of the HLA B15 which is the most common HLA-B in Thais in the following workshop both regional (AOHW) and international (IHWC). Prof Albert who is the chairman of the 9th IHWC invited every laboratory to participate in the 9th IHWC.

In the 9th IHWC (1984)³ Chandanayingyong, Cambon-Thomsen and Hammond reported that Bw62 was well defined and a number of other Bw6 associated B15s were defined which needed further study (Fig 2).

In the 3rd AOHWC (1986), we used known B15 variants (B62.1, B15S, B15T) of the 9th IHWC to be tested with sera set of the 3rd AOHWC.⁴ We are able to confirm three patterns of B15 variants of the 9th IHWC (Fig 3).

CellID	A	A	B	B	B	B	5	3	3	3	3	3	3	3	3	3
				w	w	w	0	3	3	4	4	4	4	4	4	2
				4	6	8	8	9	8	7	6	5	4	7	2	8
Chinese																
CHA-042	26	11	w62	w38	w4	w6	1	8	8	8	8	8	8	8	8	1
OBX-064	2	w24	w62	w51	w4	w6	1	8	8	8	8	8	8	8	8	1
Thais																
DCH-059	w24?	w33?	w62	-	w6	w6	1	8	8	8	8	8	8	8	8	1
DCH-048	w24?	11	w62	18	w6	w6	1	8	1	8	8	8	8	8	8	1
DCH-052	2	11	w62	w46	w6	w6	0	8	1	1	8	8	8	8	8	0
DCH-062	w24	11	w62	w60	w6	w6	1	8	1	1	8	8	8	8	8	1
DCH-013	w24?	11	w62	w49?	w4	w6	1	8	1	1	8	8	8	8	8	1
DCH-021	2	w24	w62	-	w6	w6	1	4	8	1	8	8	8	8	8	1
DCH-039	11	-	w62	w60	w6	w6	1	8	1	1	1	1	1	1	1	1
DCH-002	w24?	11	w62?	-	w6	w6	8	8	8	8	8	8	8	8	8	1
DCH-055	w24?	2	w62?	w35	w6	w6	8	1	8	1	8	8	8	8	8	1
DCH-019	w24	11	15	w46	w6	w6	8	1	1	1	8	8	8	8	8	1
DCH-027	w24?	11	15	-	w4	w6	8	1	1	1	8	8	8	8	8	1
DCH-080	w24	11	15	w46	w6	w6	8	1	1	1	8	8	8	8	8	1
DCH-044	2	15	27	w4	w6	w6	8	1	1	1	1	1	1	1	1	1
DCH-030	11	-	15	w46	w6	w6	8	1	1	1	8	8	8	8	8	1
DCH-043	w24	w33?	15	w51	w4	w6	8	1	1	1	1	1	1	1	1	1
DCH-046	w24?	1	15?	w35	w6	w6	8	1	1	1	1	1	1	1	1	1
DCH-086	11	-	15	w46	w6	w6	8	1	1	1	1	1	1	1	1	1
DCH-083	2	11	15?	w46	w4	w6	1	1	1	1	8	6	1	1	1	1
DCH-017	2	28	15?	w35	w6	w6	1	1	1	1	1	1	1	1	1	1
DCH-073	2	11	15	w60	w6	w6	1	1	1	1	1	1	1	1	1	1
DCH-007	1	w24?	15	w37?	w4	w6	1	1	1	1	1	1	1	1	1	1
DCH-025	w24	-	15?	w35	w6	w6	1	1	1	1	1	1	1	1	1	1
DCH-071	11	-	15?	w60	w6	w6	1	1	1	1	1	1	1	1	1	1
DCH-012	w24	-	15?	w46	w6	w6	1	1	1	1	1	1	1	1	1	1
DCH-057	2	w33?	15?	w44	w4	w6	1	1	1	1	1	1	1	1	1	1
DCH-075	2	11	15?	w51	w4	w6	1	1	1	1	1	1	1	1	1	1
CHI-146	2	11	15	18	w6	w6	1	1	1	1	1	1	1	1	1	1
CHI-155	w24	11	15	-	w4	w6	1	1	1	1	1	1	1	1	1	1

Fig 1. Reaction pattern of B15 positive of the Thais (2AOHW)²

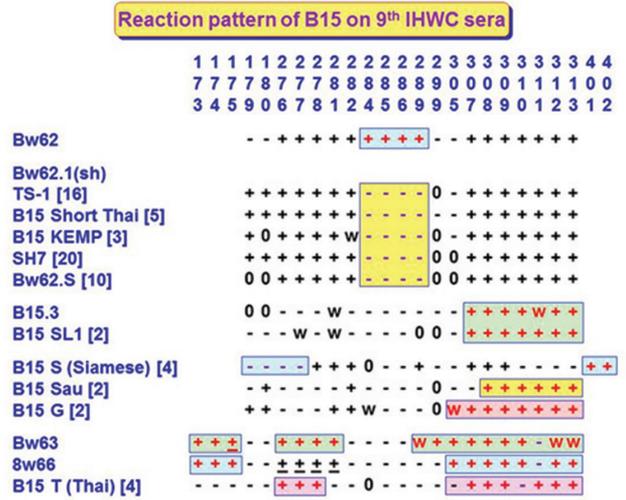


Fig 2. Reaction pattern of B15 on 9th IHWC sera³

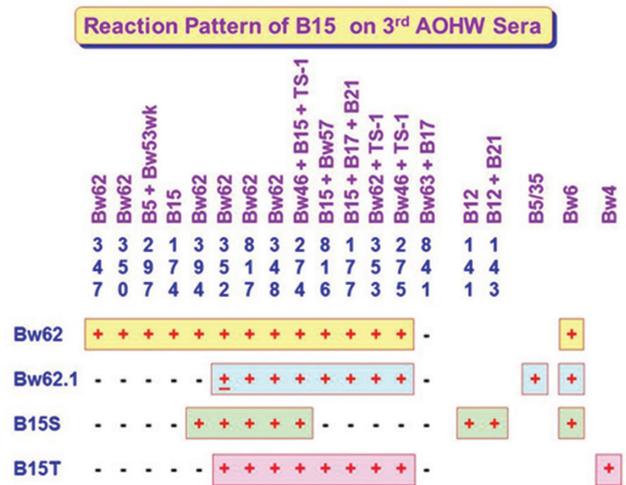


Fig 3. Reaction Pattern of B15 on 3rd AOHW Sera⁴

Following in the 10th IHWC (1987).⁵ Prof. Albert, Chairman of the AHS#9 (Bw46 and subgroup of B15) reported “confirmation of the finding of new Thais variants” (Fig 4).

The WHO nomenclature for factors of the HLA system met after the 10th IHWC, and approved designation and specificities for the new serological specificities, B15 short Thai (Bw75), B15 S stands for Siamese (Bw76), B15 T, stand for Thai (Bw77).

In 1991, the 11th IHWC in Japan⁶, they agreed that the HLA B15 antigens officially recognized were HLA-B62, -B63, -B76 and -B77.

In the 12th IHWC (1996) in Paris⁷, I was honored to take part in the workshop as chairman of the AHS#8 (B15, B17, B46 and B70 antigens). The objective was to concentrate on cross-linking information serology, biochemistry, ID-IEF, DNA typing and sequence base

typing. We also reported the new B15 variant *HLA-B*1532 in the Thais in GenBank upon introducing molecular technique to perform HLA typing of more than 395 alleles of HLA-B*15 which were recognized (2014). The workshop organizer awarded the best antigen society report to Prof. Dr. Dasnayanee Chandanayingyong (Fig 5). Our laboratory is also known as one of the best serology laboratories in the world.

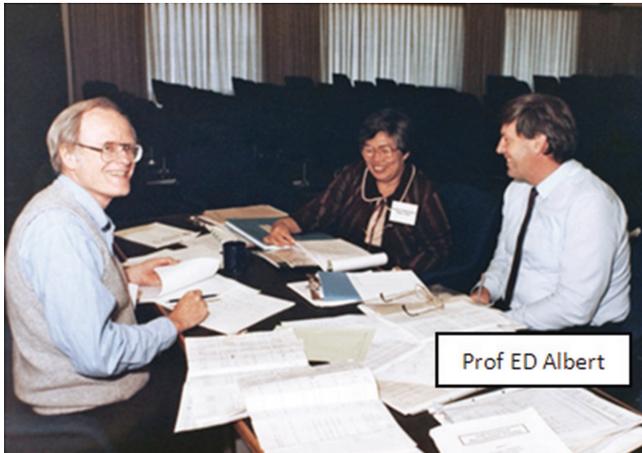


Fig 4. 10th IHWC in 1987, Prof ED Albert, Chairman of the AHS # 9 (Bw46 and Subgroup of B15) reported “confirm the finding of new Thais variants”.



Fig 5. The workshop organizer awarded the best antigen society report to Prof. Dr. Dasnayanee Chandanayingyong.

As for the study at DNA level we introduce RFLP technique during the 10th IHWC, PCR-SSO technique during the 11th IHWC HLA Class I DNA typing and sequencing during the 12th IHWC. We performed the test according to the workshop protocol.

It is also important to mention that co-operation between a private organization which was a program of exchange sera against equipments with One Lambda Inc, had resulted in much progress in our HLA work.

I would like to take this opportunity to express my personal gratitude to Prof. P.I. Terasaki for his kind thoughtfulness.

It seems right to end the history of HLA work in Thailand during the year 1992-1997. The IHWC had been an invaluable resource for stimulating immunogenetics research and facilitating rapid translation of new technology and knowledge to patient care. It is time for the young generation to solve the more complex problem in the character and significance of the polymorphism. Finally, I would like to thank all of my colleagues especially from the laboratory THA-DCH who gave so much of their energy to our HLA work.

Acknowledgment: Special thanks go to Associated Professor Sasitorn Bejrachandra, Assistant Prof. Parichart Permpikul, Associated Professor Sasijit Vejbaesya and staff members at the HLA and DNA laboratories especially Ms. S. Udee, Ms. R. Klaythong, Ms. K. Koktathong, Ms. M. Sirikong, Mr. E. Rungroung, Mrs. K. Apisawes, Mr. R. Thongpradit, Mr. W. Bintaprasit, Mr. S. Lekmak, Ms. S. Ngamthawornwong, Mrs. R. Chantangpol, Mrs. P. Luangtrakool and Dr. K. Luangtrakool who gave so much of their energy to our HLA work.

Finally thanks must go to all the blood donors at Siriraj including their families who donated their blood to our studies.

Besides HLA work, Prof. Dr. Dasnayanee Chandanayingyong had also reported an important work in immunohematology. The studies of Miltenberger complex frequency in Thai population including other related articles were reported in 1975. Since then, the significance of this red cell antigen in blood transfusion among Southeast Asian population has been documented. At present, it is essential for every blood bank and transfusion service to screen for antibody to this antigen in both the patient and donated blood, in order to provide safe transfusion for every patient. Additionally, this finding lead to the discovery of more satellite antigens to Mi^a (Miltenberger), and there are 11 subclasses of Mi^a at present which can be detected by serologic and molecular techniques.

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