Summary

Background: Cord blood banks are established worldwide as a result of the increased use of umbilical cord blood (UCB) transplantation. The outcomes of this procedure relate to the cell dose of the UCB unit and the UCB collection. The aim of this study was to evaluate whether the differentiation of ethnicity influenced the biological features of the UCB units.

Methods: A total of 1743 UCB units were measured for the biological features, including white blood cell count, red blood cell, Hb, CD34+ and volume of cord blood. Of these, 149 Mainlander, 1367 Hoklo, and 163 Hakka units were selected from the Buddhist Tzu Chi Stem Cell Center.

Results: The three groups were comparable for biological features of the UCB units. No differences were observed between the different ethnic groups in terms of white blood cell count, red blood cell, Hb, and volume of cord blood, except mean CD34+ in univariate analysis. However, the mean CD34+ cells appeared to be lower in Middle Taiwan in trend after adjustment for demographic factors.

Conclusions: This preliminary study showed that ethnic distribution factor appeared to affect CB cell yields in Taiwan.
Microbial Contamination of the Tzu-Chi Cord Blood Bank from 2005 to 2006


Shu-Huey Chen, Ya-Jun Zheng, Shang-Hsien Yang, Kuo-Liang Yang, Ming-Hwang Shyr, Yu-Huai Ho

Background: In total, 4502 units of cord blood (CB) were collected during a 2-year period from 2005 to 2006 by the Buddhist Tzu-Chi Stem Cells Center. The aim of this study was to analyze the incidence of microbial contamination and type of organism present in the cord blood. The clinical impact of microbial contamination on hematopoietic progenitor cell (HPC) grafts used for HPC transplantation is also discussed.

Methods: First and second specimens were obtained for microbial assessment. These were collected in laboratory after cord blood collection and after cord blood unit manipulation, respectively. The samples were cultured and the results reviewed.

Results: The overall incidence of microbiological contamination was 1.8% (82/4502). Three CB units were contaminated with two different organisms. Infectious organisms comprised 9.4% (8/85) of total isolated microbes. These infectious microorganisms were -Streptococci group B, Candida tropicalis and Staphylococcus aureus which were isolated in 6, 1 and 1 of CB units respectively. Escherichia coli, Bacteroides fragilis, Lactobacillus spp., Enterococcus, -Streptococcus Group B, Bacteroides valgatus, Corynebacterium spp., Klebsiella pneumonia and Peptococcus spp. were the most frequently encountered microorganisms. A higher contamination rate of the CB units was noted after vaginal delivery (2.16%) compared to caesarian section (0.85%) (p<0.01).

Conclusions: Extensive training in CB collection, good procedures and good protocols can decrease the rate of microbial contamination. The use of a closed collecting system and an ex utero method have the advantage of a lower contamination rate. In our cord blood bank, we use a closed system but an in utero method. Similar to other studies, most of microorganisms reported here as contaminants are non-pathogenic.

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Cord blood (CB) is considered an alternative resource to bone marrow and peripheral blood stem cells (PBSC) for allogeneic stem cell transplantation. In this study, human leukocyte antigen (HLA)-A, -B, and -DRB1 high-resolution allele types were analyzed from a total of 710 CB units in the Tzu Chi Taiwan Cord Blood Bank. We observed 21 HLA-A alleles, 59 HLA-B alleles, and 28 HLA-DRB1 alleles, whereas 19 unique alleles were present in the CB units of 2,023 individuals selected for confirmatory testing in the Tzu Chi Taiwan Marrow Donor Registry (TCTMDR). The allelic associations between the HLA-A and -B locus were stronger than that of either the HLA-B and -DRB1 loci or the HLA-A and -DRB1 loci. The most common haplotype of CB units in the general Taiwanese population was A*3303-B*5801-DRB1*0301 (6.59%), followed by A*0207-B*4601-DRB1*0901 (3.47%) and then A*1101-B*4001-DRB1*0901 (2.11%). Moreover, two haplotypes, A*2402-B*5201-DRB1*1502 and A*0201-B*1301-DRB1*1202, existed uniquely in the CB units but were not observed in the data of TCTMDR. Although the number of CB units studied for high-resolution of HLA typing in the current study is small, we believe our data should provide useful information to increase the chances of obtaining acceptable HLA-A-, -B-, and -DRB1-matched CB units for patients.
Correlation between characteristics of unrelated bone marrow donor and cell density of total nucleated cell in bone marrow harvest


The relationship between the features of bone marrow donor and the quality of marrow harvest has been unclear because most of bone marrow registries have multiple collection centers with somewhat different harvest procedures. We are able to address this issue for Tzu Chi General Hospital is the only collection center affiliated with Tzu Chi Taiwan Bone Marrow Registry. Between November 1997 and March 2002, data of 286 healthy unrelated donors was analyzed to correlate with the cell density of total nucleated cell in bone marrow harvests. The harvest procedure was standardized by single-hole harvest needle under general anesthesia. The operation staffs were restricted within the members of Oncology–Hematology division. The results showed that the cell density of bone marrow harvest was positively correlated with donor body weight and peripheral white blood cell count $P = 0.0475$, $P<0.0001$, but negatively correlated with the total volume of bone marrow harvest $P<0.0001$. We recommend that if multiple human leukocyte antigenmatched donors are available, donor with higher body weight and/or higher white blood cell count be selected for allogeneic bone marrow transplantation.
Successful allogeneic PBSC transplantation depends upon the infusion of an adequate number of CD34+ cells to patients. Granulocyte-colony-stimulating factors (G-CSF) mobilized PBSC were harvested on 5th day after stimulation from donors. When the CD34+ cell target yield was not achieved; secondary apheresis was performed the following day. Before September 2006, 67 donors (Group A) received five doses of G-CSF. After September 2006, a sixth dose of G-CSF was administered to 35 donors (Group B) to improve CD34+ yield. The mean CD34+ cell concentration of the second PBSC harvest was significantly higher in Group B (1,087 × 10^6/l vs. 767 × 10^6/l; P = 0.031). 

Summary

Shu-Huey Chen, Chi-Jui Lu, Shu-Hui Wen, Yo-Jun Zheng, Shang-Hsien Yang, Yu-Chieh Su, Dian-Kun Li

Peripheral blood stem cells (PBSCs) are increasingly used as the source of hematopoietic stem cells, but there are large variations in harvest outcome between individuals mobilized by granulocyte colony-stimulating factor (G-CSF). We examined the effects of donor characteristics and procedure factors on the day 1 CD34+ cell yield in 373 unrelated healthy donors. G-CSF was administered subcutaneously at a planned dose of 8.3 to 11mg/kg daily for 5 days, followed by harvest started on day 5 of G-CSF treatment. Of the 373 donors, 159 (42.6%) had the radial artery as the inlet access for harvest. Poor day 1 cell yield was defined as <10 × 10^6 CD34+ cells/L of processed blood for the first apheresis; 62 donors (16.6%) did not attain this threshold. The male donors had significantly higher yields at harvest compared with the female donors. The female donors had higher CD34+ cell yields if the circulation access was through an artery than if it was through a vein. In a multiple regression analysis, donor age, sex, body mass index (BMI), preharvest white blood cell and circulating immature cell counts, access type, and flow rate correlated with day 1 yield. Female sex, older age, venous access, and a higher flow rate were significantly associated with greater risk for a day 1 poor yield of CD34+ cells (odds ratio = 3.0074, 1.045, 4.3362, and 1.1131, respectively). A higher BMI may decrease the risk (odds ratio = 0.8472). In donors at higher risk for poor CD34+ cell yield, strategies for increasing CD34+ cells must be considered.
Objective: Hematopoietic stem cell transplantation (HSCT) has proved to be an important curative therapy for various hematological disorders. Here we present the first report of adult HSCT at one institution in eastern Taiwan.

Patients and Methods: Thirteen patients, 7 men and 6 women, underwent HSCT between July 2002 and March 2005. Their median age was 34 years (range: 22-51). Five patients had acute myeloid leukemia, 2 had acute lymphoblastic leukemia, 2 had chronic myeloid leukemia, 2 had severe aplastic anemia, one had non-Hodgkin's lymphoma and one had Hodgkin's disease. Eleven patients received HLA-identical allogeneic transplantations, including two unrelated donor transplantations. Two patients received autologous transplantations. The conditioning regimens were total body irradiation plus busulfan or busulfan plus cyclophosphamide for allogeneic transplantation, and BEAM for autotransplantation. The prevention of graft versus host disease (GVHD) employed standard cyclosporine and methotrexate.

Results: The median numbers of CD34 positive cells obtained were $1.9 \times 10^6$/kg of patient body weight from bone marrow harvest and $6.5 \times 10^6$/kg from peripheral blood stem cell collection. The overall engraftment rate was 100%. The median times to neutrophil and platelet engraftments were 11.4 and 11.2 days, respectively. The one-year event-free and one-year overall survivals were both 90%. Acute GVHD of grade II-IV was seen in 8 out of 11 patients (72.7%) of whom 2 had grade III-IV disease (18.2%). Chronic GVHD developed in 6 out of 10 evaluable patients (60%) with 3 in limited stages and 3 in extensive stages. Eleven patients were alive and free of disease at 124 to 1117 days, with a median survival of 649 days after transplantation. One patient who underwent unrelated transplantation died of CMV pneumonitis on day 67. One patient died of disease relapse on day 485. The median Karnofsky Performance Score of surviving patients was 90%.

Conclusion: The study demonstrates that HSCT in our hospital has achieved promising results and patients can obtain long-term disease-free survival and good social function.
• Summary

Mu-Jung Chen, Cheng-Chung Chu, Ming-Hwang Shyr, Pi-Yu Lin, Kuo-Liang Yang


Here we report the identification and sequence analysis of a new HLA-A11* variant, A*1131 allele, found in a Taiwanese volunteer bone marrow donor. The novel A*11 variant is identical to A*1125 in exon 2 but differs from A*1125 in exon 3 by one nucleotide substitution at position 527 causing an amino acid change at codon 152 E→V (GAG→GTG). In comparison with HLA-A*110101, allele A*1131 has three nucleotide differences in exon 3: 527 C→T, 538 C→T and 539 A→T leading to two amino acid variations at residues 152 A→V and 156 Q→L.

• Summary

Mu-Jung Chen, Cheng-Chung Chu, Ming-Hwang Shyr, Pi-Yu Lin, Kuo-Liang Yang


Human leucocyte antigen (HLA)-B48, an antigen within 7C CREG (cross-reacting group) (Steiner et al., 2001) that cross-reacts frequently with HLA-B40 (i.e. HLA-B60 and -B61) group of antibodies serologically, can be found in Alaskan Natives (Leffell et al., 2002), Amerindians (Martinez-Naves et al., 1997), African Americans, Caucasians, and Oriental ethnicities (Mori et al., 1997; Schipper et al., 1997; Cao et al., 2001; Middleton et al., 2004; Hong et al., 2005; Itoh et al., 2005; Lee et al., 2005; Ogata et al., 2007). Sequencing investigations demonstrated that the common allele encoding the B48 antigen is B*4801 (Belich et al., 1992). To date, there are at least 16 WHO recognized B*48 alleles according to the most recent report from the WHO nomenclature committee (Marsh et al., 2005). Here we report a newly discovered allele B*480102, a variant of B*4801, detected in a 55-year-old Taiwanese patient of Minan origin (southern China).
Summary

The primary function of MHC polymorphism is considered as the foundation of self-defense mechanism of the host in surveillance against countless diverse invading pathogens. However, this biological function can also elicit undesirable immunological responses that jeopardize transplantations when compatibility between donors and recipients is unfavorable.

Summary

We report here a novel HLA-DRB1 allele, DRB1*0461, discovered in a Taiwanese volunteer marrow donor. The new sequence has nucleotide variation at positions 260 (C→A) and 261 (C→G), i.e. codon 58, as compared to DRB1*0408. Nucleotide change caused an amino acid substitution from alanine to glutamic acid. We believe that the gene conversion took place between DRB1*0405 and DRB1*1101 based on sequence homology and gene frequency in population studies. In comparison to DRB1*0405, DRB1*0461 has two amino acid changes at codons 57 and 58. Amino acid residue substitution at position 57 may affect peptide-binding environment at pocket P9 of the antigen-binding groove of the MHC molecule. This would have potential effect in peptide binding as well as in T-cell recognition, which could have clinical significance in bone marrow and organ transplantations.
Summary

Stem cells are characterized based on two basic characteristics—a capability for self-renewal and a capability to develop into specialized cells. The type of specialization often depends on the cell’s function and location, such as those of acid and protein secreting cells in the stomach or insulin secreting cells in the pancreas. On the other hand, the capability for self-renewal and specialization enables a nerve stem cell, for example, to grow into a mature nerve cell and another self-renewing cell that perpetuates the next cycle of self-replication and specialization. Stem cells can also be categorized into embryonic stem cells and adult stem cells. Pluripotent embryonic stem cells are derived from the inner cell mass of the blastocyst and adult stem cells are undifferentiated cells found in post-embryonic tissues or organs. The primary roles of adult stem cells are to maintain and repair the tissues or organs in which they reside. The pluripotency of embryonic stem cells, which give rise to various cell types, and the ability of adult stem cells to repair tissue damage are the “magic fix” that regeneration medicine is suggesting. Whether the function of stem cells is hematopoietic or non-hematopoietic, researchers all over the world are striving hard to harness the use of stem cells for medicine. As the progress of stem cell research moves steadily forward, let us pause for a minute and pose a question. Are stem cells really going to be the magical medical therapeutic component of the future?
Summary

Two novel HLA-DRB1 alleles, HLA-DRB1*1214 and HLA-DRB1*1215, were found in Taiwan using sequence-based typing method. DRB1*1214 differs from DRB1*120101 by two nucleotide substitutions on exon 2, causing amino acid changes at codon 37 (L→F) and codon 38 (L→V). We suggest that DRB1*1214 is the product of a gene conversion between DRB1*120101 and DRB1*140101 or DRB1*1405 and that HLA-DRB1*1215 differs from DRB1*120201 by one single nucleotide transition at exon 2, thereby causing amino acid change at codon 37 (L→F).
We describe here a novel HLA-DRB1* allele, DRB1*0331, observed from a Taiwanese bone marrow donor using DNA sequence-based typing (SBT) method. The ‘new’ allele differs from DRB1*0306 and DRB1*0325 by one nucleotide at positions 196 and 227, respectively. Nucleotide mutations caused amino acid substitutions from N to Y at codon 37 and from F to Y at codon 47, as compared with amino acid sequence encoded by the DRB1*030101 allele. The donor was first typed as DRB1*0403/0406/0439/0441/0446/0451/0452 (NMDP code DRB1*04XX) and DRB1*0304/0323/0325 (NMDP code DRB1*03APDA) by sequence-specific oligonucleotide (SSO) typing kit. Subsequent typing of the donor by high-resolution sequence-specific primer (SSP) protocol indicated DRB1*0403 and DRB1*0306. The anomalous result of DRB1*03 was resolved by SBT and recognized as DRB1*0331. We concluded that SSP or SSO alone may mistype a precedent unrecognized allele and that two different typing techniques or SBT may have to be employed to safe guard true HLA typing when rare alleles are encountered at the first time.
From 120 unrelated Taiwanese marrow stem cell donors with allelic homozygosities at human leucocyte antigen (HLA)-A, -B and -DRB1 loci, we determined 85 distinguishable haplotypes. Using the predetermined haplotype data, we deduced 418 haplotypes from 1903 unrelated individual stem cell donors selected for HLA confirmatory test. Eighteen of the 20 (90%) most frequently observed haplotypes determined in Asian Americans using computer prediction were found in this study. In comparison with haplotypes determined by maximum likelihood algorithm in Korean population, 18 of the 29 (62.07%) Korean haplotypes with a frequency over 0.5% were also among the haplotypes determined in this investigation. Randomized family studies confirmed that over 50% of the haplotypes observed in the families were among the haplotypes deduced based on allelic homozygosity, suggesting that proportionally additional haplotypes can be determined as the number of donors being studied is increased. Haplotypes carrying low incidence allele characteristics of Taiwanese were also observed in this study. This established haplotype information will be beneficial for patients searching for stem cell donors in our registry domestically and internationally.
Minor histocompatibility (H) antigens are allogeneic target molecules having significant roles in alloimmune responses after human leukocyte antigen–matched solid organ and stem cell transplantation (SCT). Minor H antigens are instrumental in the processes of transplant rejection, graft-versus-host disease, and in the curative graft-versus-tumor effect of SCT. The latter characteristic enabled the current application of selected minor H antigens in clinical immunotherapeutic SCT protocols. No information exists on the global phenotypic distribution of the currently identified minor H antigens. Therefore, an estimation of their overall impact in human leukocyte antigen–matched solid organ and SCT in the major ethnic populations is still lacking. For the first time, a worldwide phenotype frequency analysis of ten autosomal minor H antigens was executed by 31 laboratories and comprised 2,685 randomly selected individuals from six major ethnic populations. Significant differences in minor H antigen frequencies were observed between the ethnic populations, some of which appeared to be geographically correlated.
Summary

Using the maximum-likelihood method with the expectation-maximization (EM) algorithm of PYPOP, high-resolution human leukocyte antigen (HLA) three-locus haplotypes (HLA-A, -B, and -C; HLA-A, -B, and -DRB1) and four-locus haplotypes (HLA-A, -B, -C, and -DRB1) were determined. Linkage disequilibrium of high-resolution HLA-B and -C alleles and HLA-DRB1 and -DQB1 alleles was also calculated. Comparison of the Taiwanese haplotypes and haplotypes from donors in the Chinese Han population, the Asia Pacific Islander ethnic category of the NMDP (National Marrow Donor Program), and the Taiwanese cord blood units demonstrated similarities and dissimilarities among the four populations. HLA allele frequencies of our study suggested that the Taiwanese have a relative population relationship with the southern Han Chinese with regard to HLA. Our results also indicated that the Taiwanese population exhibits genetic proximity with Asian Americans with regard to HLA-A and -DRB1 but not HLA-B.

Kuo-Liang Yang, Shee-Ping Chen, Ming-Huang Shyr, Py-Yu Lin

High-resolution human leukocyte antigen (HLA) haplotypes and linkage disequilibrium of HLA-B and -C and HLA-DRB1 and -DQB1 alleles in a Taiwanese population. Human Immunology 70(2009)269-276
A simple and efficient method for generating Nurr1-positive neuronal stem cells from human AQ1 wisdom teeth (tNSC) and the potential of tNSC for stroke therapy. Cytotherapy (2009) (in press)

Background aims: We have isolated human neuronal stem cells from exfoliated third molars (wisdom teeth) using a simple and efficient method. The cultured neuronal stem cells (designated tNSC) expressed embryonic and adult stem cell markers, markers for chemotactic factor and its corresponding ligand, as well as neuron proteins. The tNSC expressed genes of Nurr1, NF-M and nestin. They were used to treat middle cerebral artery occlusion (MCAO) surgery-inflicted SpragueDawley (SD) rats to assess their therapeutic potential for stroke therapy.

Methods: For each tNSC cell line, a normal human impacted wisdom tooth was collected from a donor with consent. The tooth was cleaned thoroughly with normal saline. The molar was vigorously shaken or vortexed for 30 min in a 50-mL conical tube with 1520 mL normal saline. The mixture of dental pulp was collected by centrifugation and cultured in a 25-cm2 tissue culture flask with 45 mL Medium 199 supplemented with 510% fetal calf serum. The tNSC harvested from tissue culture, at a concentration of 12105, were suspended in 3 mL saline solution and injected into the right dorsolateral striatum of experimental animals inflicted with MCAO.

Results: Behavioral measurements of the tNSC-treated SD rats showed a significant recovery from neurologic dysfunction after MCAO treatment. In contrast, a sham group of SD rats failed to recover from the surgery. Immunohistochemistry analysis of brain sections of the tNSC-treated SD rats showed survival of the transplanted cells.

Conclusions: These results suggest that adult neuronal stem cells may be procured from third molars, and tNSC thus cultivated have potential for treatment of stroke-inflicted rats.
Since its inception in October 1993, the world-renowned Buddhist Tzu Chi Marrow Donor Registry has facilitated more than 1800 cases of stem cell donations for patients in 27 countries to date. Under the auspices of the Buddhist Tzu Chi Stem Cells Center (BTCSCC), the Registry (>310 000 donors) offers, on average, one case of stem cell donation every day to national or international transplantation community. The accomplishment of the Registry stems from the philosophy and spirit of giving without reward that was inspired by its founder Dharma Master Cheng Yen, the Samaritan devotions of selfless voluntary stem cell donors and the efforts from a dedicated network of volunteer workers. Demographically speaking, slightly less than one third of the donations are provided to domestic patients and the rest to mainland China and countries in Asia, North America, Europe, Middle East, Oceania, and South Africa. While most of the patients belong to the Oriental ethnic group, a few of the patients are non-Oriental. In addition to the Registry, a non-profitable umbilical cord blood (UCB) bank is operating since 2002 to provide a complimentary role for patients unable to identify appropriate bone marrow stem cell donors in the Registry or when time is not favourable. To date, with an inventory of over 12 000 units of UCB cryopreserved in the Tzu Chi Cord Blood Bank, 47 units have been employed in 37 cases of transplantation for both paediatric and adult patients domestically and internationally. The fact that Buddhist Tzu Chi Marrow Donor Registry and Cord Blood Bank are established and operating without governmental financial support is unique and special. To facilitate haematopoietic stem cells to its domestic patients experiencing financial burdens, the BTSCC offers financial aids to the underprivileged for their medical relief. This humanitarian approach and compassion is definitely a role model for many countries in the world.


• **Summary**

K. L. Yang, X. Gao, P.Y. Lin


HLA-A*0248, a rare allele originally found in an individual of Filipino background, was detected in a Chinese donor. We confirmed the novel sequence and analysed its serological reaction pattern. The exon 2 sequence of A*0248 was apparently generated in a gene conversion event with an A2 gene, receiving a sequence segment comprising codons 56 to 74 from an A*24 donor gene. Serological typing showed a clear-cut A2 reaction pattern, indicating that the three amino acid positions 62, 65 and 74, are probably not a critical part of the A2 epitope. Our typing experience also demonstrated that different typing technologies often complement each other in fine HLA typing.

• **Summary**

K. L. Yang, M. L. Schroeder, J. M. Cherng, P.Y. Lin


In a routine HLA antibody screening cross-match test using the complement-mediated lymphocytotoxicity (LCT) assay, we discovered an antibody, in a transfused Caucasian woman, recognizing an Oriental restricted antigen that does not appear to be associated with the human leukocyte antigen (HLA) system. The distribution of this 'novel' antigen in Oriental populations and its frequency in the Taiwanese Chinese population are reported.
Summary

From its DNA sequence, B*5603 is thought to be a product of gene conversion. We present here serological evidence of such an event and further speculate on a possible reciprocal hybrid yet to be identified. In addition, we report the allelic frequency of B*5603 in the Taiwanese population and its association with A*1101, Cw*01 and DRB1*1201.

Summary

The presence of HLA-B27 in patients affected with ankylosing spondylitis (AS) was well established prior to the advent of DNA typing of various genes within the major histocompatibility complex (MHC) in humans. However, molecular typing of the MHC genes revealed that B27 comprises a motley assortment of alleles, some of which are strongly positively associated with the disease and some of which are negatively associated with the disease. B*2706 was reported to have a negative association with AS in the Thai population and in Chinese Singaporeans. We report here our finding of an absence of B*2706 in 184 Taiwanese AS patients.
Absence of CCR5-Δ32 Mutation in Healthy and HIV-1-Infected Aborigines in Eastern Taiwan.
Tzu Chi Med J 2002; 14:353-357

Objective: Human immunodeficiency virus type 1 requires coreceptor CCR5 to enter into host cells. Homozygous deletion of 32 nucleotides (CCR5-Δ32) of CCR5 results in a severely truncated molecule and near-complete protection against HIV-1 infection. This deletion mutation is commonly found in Caucasians. However, no such a mutation has yet been found in Hong Kong and Taiwan. Furthermore, most current data in Taiwan were collected from non-aborigines. Therefore, we investigated whether CCR5-Δ2 mutation occurs in aborigines in eastern Taiwan.

Materials and Methods: Genomic DNA was extracted from healthy aborigines (n=1433) and HIV-1 infected aboriginal patients (n=11) in eastern Taiwan. Genotyping was performed using polymerase chain reaction (PCR) amplification of a portion of the CCR5 gene and analyzed with agarose gel electrophoresis. Results: All samples contained the wild-type CCR5 gene structure and no single deleted form of the CCR5 gene was found.

Conclusion: Although some Taiwan aborigines are believed to have European and other ancestors as well as mainland Chinese ancestors, Taiwan aborigines have a CCR5 gene construction similar to non-aboriginal Taiwanese.
Graves' disease has been associated with different human leukocyte antigen (HLA) genes in different races. To evaluate the association of HLA type in Taiwanese with Graves' disease, the HLA-A, -B, and -DRB1 alleles in a total of 236 Taiwanese adults with Graves' disease and 533 racially matched normal control subjects were examined using the PCR-SSOP (sequence specific oligonucleotide probe) technique. The prevalence of HLA-A*0207, -B*2704, -B*4601, and -DRB1*0901 among patients with Graves' disease was found to be increased, with odds ratios (OR) of 2.21, 3.82, 1.76 and 1.62, respectively. However, after correction for multiple comparisons, the relative risk of HLA-A*0207 susceptibility to Graves' disease remained statistically significant and the haplotype HLA-A*3303 -B*5801 -DRB1*0301 had a significantly protective effect. None of the other 2- or 3-locus haplotypes showed any significantly increased risk. Although HLA-DRB1*1405 showed an increased relative risk in patients with GO (Graves' ophthalmopathy) (OR 4.61) when compared with patients without GO, the relative risk after adjusting for the number of comparisons was not significant. Taiwanese patients with Graves' disease have HLA-associated susceptibility genes which are similar to those found in Chinese patients in Hong Kong and Singapore. However, the finding in this study of a higher frequency of HLA-A*0207 in Taiwanese with Graves' disease has not been documented in any other ethnic group.

Summary

The association of HLA-A, -B, and -DRB1 genotypes with Graves' disease in Taiwanese people.

Tissue Antigens 2003: 61: 154-158

S. M. Huang, T. J. Wu, T. D. Lee, K. L. Yang, C. K. Shaw, C. C. Yeh
Heterogeneity of HLA-B27 is represented by a family of 24 closely related alleles/subtypes. Frequency and disease association of these alleles with spondyloarthropathies differ among ethnic groups. Accurate investigation of frequencies of alleles is often hindered by the size and demographic region of sample tested. With an ever-increasing number of B27 alleles being discovered, it is becoming imperative to establish disease association of each individual allele and its biological importance. In a large number of normal healthy Taiwanese Chinese individuals (75,777) tested nationally, over a period of five years, in a single immunogenetics centre, we found additional B27 subtypes not revealed in a previous Taiwanese Chinese population study. The subtypes found in Taiwanese Chinese and the frequencies of each of the subtypes are reported.