

# Rationale for ethnic-based haematopoietic stem cell transplantation cooperative groups

## Introduction

The Chinese Society of Blood and Marrow Transplantation (CSBMT) is a unique ethnic-based haematopoietic stem cell transplantation (HSCT) group involving units from China, Hong Kong, and Taiwan. Haematopoietic stem cell transplantation is a unique clinical procedure, transfusing fresh or cryopreserved blood cells from human leukocyte antigen (HLA)-compatible donors to replace the haematopoietic and immunological system of the host. It ventures into true international medicine, since donors and recipients may be far separated in space (or even in time). On the other hand, the requirement for HLA matching limits the possibility of donation. In the absence of matched siblings, voluntary matched unrelated donors, cryopreserved umbilical cord blood, or haploidentical family donors are some alternatives.

## Human leukocyte antigen composition of ethnic Chinese

The chance of finding a compatible stem cell unit depends on the particular haplotype of HLA genes at the A, B, Cw, DR, and DQ loci. Voluntary donor and cord blood registries are available worldwide. The chance of matching increases with registry size. The limited size of the Hong Kong Bone Marrow Donor Registry (67 000 strong) and cord blood bank (3000 units) under Hong Kong Red Cross Blood Transfusion Service means that some HSC donations come

from the Taiwan Tzu Chi (0.3 million) and China Red Cross registries (0.95 million). Since many alleles and haplotypes showed strong ethnic links, most unrelated donors come from the same ethnic group. With the global presence of Chinese, donations had also gone international. This is helped by the Han Chinese's relative HLA homogeneity, as seen from the local HLA makeup (Table). The possibility of homozygous HLA alleles also helps haploidentical family donation. The CSBMT provides a platform for harmonising these shared Chinese resources of stem cells and experience in sibling, unrelated, cord and haploidentical donor HSCT.

## Disease entities endemic to ethnic Chinese

Various malignant and non-malignant haematological diseases requiring HSCT have unique ethnic distributions. In Southern China, the prevalence of thalassaemia carriage reaches up to 10%, and thalassaemia major patients face lifelong transfusion. Our paediatric transplanters have made huge progress in curative HSCT for this problem, especially with cord blood and unrelated HSCT. Disseminated nasal NK/T cell lymphoma and acute myeloid leukaemia t(7;11)(p15;p15) are two Oriental diseases incurable without allogeneic HSCT. The incidence of low-grade lymphoma, myeloma, myelodysplasia and aplastic anaemia are different in Chinese compared with Caucasians. Hence, there is a need to tailor HSCT to our demand. A large extent of this variability is determined

TABLE. Incidences of the most frequent HLA-A, HLA-B, DRB1 alleles and haplotypes in Hong Kong (data courtesy of Dr Janette Kwok, Queen Mary Hospital, Hong Kong)

A*	%	B*	%	DRB1*	%	A-B-DRB1 Haplotype	%
11XX	33.80%	4001	15.45%	0901	16.15%	A*0201-B*4601-DRB1*0901	4.84%
0201g <sup>†</sup>	19.18%	4601	14.85%	1202	13.47%	A*3303-B*5801-DRB1*0301	4.64%
2402	14.09%	1502	9.23%	1501	8.72%	A*11XX-B*1502-DRB1*1202	3.53%
3303	10.35%	5801	8.67%	0301	6.62%	A*11XX-B*4601-DRB1*0901	1.66%
0203	8.08%	1301	6.66%	0405	5.76%	A*11XX-B*1301-DRB1*1501	1.42%
0206	4.21%	3802	4.77%	0803	5.07%	A*3303-B*5801-DRB1*1302	1.25%
2601	1.98%	5101	3.51%	1602	4.89%	A*11XX-B*1502-DRB1*1501	1.17%
3001	1.60%	5502	2.86%	1101	4.63%	A*0203-B*3802-DRB1*1602	1.16%
2901	1.13%	5401	2.66%	0701	4.02%	A*11XX-B*4001-DRB1*0901	1.05%
0301	0.97%	1501	2.27%	1401	3.45%	A*11XX-B*4001-DRB1*0405	0.86%
Other	4.60%	Others	30%	Others	27%	Others	78.40%

\* HLA-A\*11XX typing does not identify the specific allele(s)

<sup>†</sup> A\*0201g# includes allele \*0207 which is frequently seen in Asian populations

by genetics, and regional wide collaboration is needed to unravel the issue.

### Complications unique to ethnic Chinese

Screening tests are in place before HSCT to protect the interests of both donors and recipients. The spectrum of red cell antibody in Chinese is different from Caucasians.<sup>1</sup> Donors with thalassaemia carriage and glucose 6-phosphate-dehydrogenase deficiency pass on these characteristics after HSCT. A high incidence of thyroid complications results from HLA A2B46DR9 haplotype.<sup>2</sup> The incidence of human immunodeficiency virus and hepatitis C virus are low in Chinese donors and recipients. However, hepatitis B virus (HBV) carriage is common, and carries risk for hepatic failure and liver cancer. Antiviral purine analogues may be useful in Chinese donors and recipients,<sup>3</sup> and HSCT may provide immunologically HBV clearance. Tuberculosis is common and HTLV-1 is endemic in Fujian and Taiwan. In humid Southern China, aspergillus outranks candida species for fungal complications. Seropositivities are high for Epstein-Barr virus and cytomegalovirus exposure due to our living habits. Drug toxicity and graft-versus-host disease (GVHD) are also important post-HSCT hazards. Single nucleotide polymorphisms associated with GVHD in Caucasians (eg NOD2/CARD15) may not exist in Chinese.<sup>4</sup> Similarly, aspects of pharmacogenetics and immunogenetics in Chinese are likely to be unique.<sup>5</sup>

### Social and public health issues in Chinese

Due to our global presence, different HSCT centres serving Chinese patients face different challenges. The health care and insurance systems of Hong Kong, China, and Taiwan differ significantly. Family size, domestic income, urbanisation and vaccination schedules, and the accessibility to medications, blood products, treatment facilities and expertise may also vary. It is not uncommon for patients with dual (or more) residences in the region to be treated by several centres. Apart from genetics and environs, ethnic

beliefs, food and language further define our Chinese population. Validated information sheets, consent forms and score questionnaires in Chinese will be useful to a population that makes up 25% of the world total. Complications from HSCT such as nausea, pain, infertility, disfiguring and death may take on different psychological, religious, and social meanings. Herbal and traditional Chinese medicine supplements are widely used,<sup>6</sup> and unexpected toxicity may result from food and fruits. The CSBMT network may serve to explore and tackle these issues.

### Conclusions

An ethnic-based clinical cooperative group is complementary to international and national registries. Various ethnic- and language-based cooperative groups in other haematological diseases have been successfully established beyond international borders. It would be logical for this trend to be extended to HSCT studies, since transplants represent true international medicine. Similar cooperative groups will emerge in other ethnic groups, driven by the need for stem cell sources.<sup>7</sup>

### Declaration

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WY Au 區永仁\*

E-mail: auwing@hotmail.com

Albert KW Lie 李國維\*

Raymond Liang 梁憲孫\*

Department of Medicine

Queen Mary Hospital

Pokfulam Road

Hong Kong

China

\* Guest Editors

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