Haplo-Matched versus Haplo-Identical

- Russ Martin[1], Zahra Kashi[1], Cierra Wikman[1], Alex Hafner[1], Farzan Modaresi[1], Fatoumata Jallow[1]
- [1] Kashi Clinical Laboratories, Portland, Oregon, United States

Background

In Hematopoietic stem cell transplantation (HSCT), HLA identical siblings are preferred as donors because differences between polymorphic HLA antigens of donor-recipient pair stimulate alloimmune reactions causing graft-versus-host disease (GVHD) or graft rejection. HSCT from a haploidentical donor, however, is increasingly becoming a standard donor option for patients without a matched sibling or unrelated donor. Haplotypes are a combination of alleles at different loci along the same chromosome that are inherited as a unit.

Methods

Parental chromosomes may by chance carry the same HLA alleles. This increases the chance for selecting only HLA haplo-matched but not HLA haplotype identical donors since similar haplotypes with the same HLA alleles in different combinations segregate in a family. This was the case for our patient whose sibling was HLA haplo-matched at classical HLA-A,B,C,DRB1,DQB1,DPB1. However, due to the fact that the parents share HLA haplotype, this donor was therefore classified merely as HLA haploidentical-by-state, rather than "haplotype" identical-by-descent (Figure 1). If this haploidentcial-by-state sibling was selected as donor, it would expose the recipient to higher risk of GVHD due to non-HLA antigens present on the opposing chromosome

Results

	HLA-A		HLA-B		HLA-C		HLA-DRB1		HLA-DQB1		HLA-DPB1	
Recipient	01:01	68:01	08:01	51:01	07:01	15:02	03:01	15:01	02:01	06:02	04:02	04:01
Sibling 1	01:01	01:01	08:01	08:01	07:01	07:01	03:01	03:01	02:01	02:01	04:02	01:01
Sibling 2	02:01	01:01	44:02	08:01	05:01	07:01	01:03	03:01	05:01	02:01	04:01	01:01
Sibling 3	02:01	01:01	44:02	08:01	05:01	07:01	01:03	03:01	05:01	02:01	04:01	01:01
Sibling 4	02:01	68:01	44:02	51:01	05:01	15:02	01:03	15:01	05:01	06:02	04:01	04:01
Sibling 5	01:01	68:01	08:01	51:01	07:01	15:02	03:01	15:01	02:01	06:02	04:02	04:01
Sibling-X	02:01	01:01	44:02	08:01	05:01	07:01	01:03	03:01	05:01	02:01	04:01	01:01

Figure 1

Conclusion

The MHC harbors more than 400 genes, but the total number of transplantation antigens that contribute to GVHD risk after haplotype-mismatched transplantation is unknown. There is emerging evidence that non-HLA variations within the MHC may be associated with GvHD risk. GVHD remains a significant complication after haploidentical HCT, hence every effort to identify haplotype-matched donors-by-descent would provide a level of protection against GVHD, in particular in a subpopulation of patients who are more prone to severe GVHD. When possible, HLA laboratories are encouraged to pay particular attention to haplotype assignment when performing family studies.

KASHI CLINICAL LABORATORIES

Kashi Clinical Laboratories
10101 SW Barbur Blvd
Portland, Oregon 97219
www.kashilab.com