

# Understanding Donor-Patient HLA-DPB1 Mismatches Improves HCT Risk Stratification

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Hematopoietic cell transplant (HCT) has been successfully used to treat a large number of patients with a variety of hematological disorders. Use of unrelated donor cells has greatly expanded the number of patients treated by HCT, however these patients are at a higher risk for post-transplant complications resulting from genetic disparities between donor and patient. To minimize the risk of acute graft-versus-host disease (aGVHD) and mortality following HCT, unrelated patients and donors are matched for ten alleles of HLA-A, C, B, DRB1 and DQB1, genes of the human leukocyte antigen (HLA) system. Mismatches at an additional HLA allele, HLA-DPB1, increase the risk of aGVHD, however HLA-DPB1 matched donors are very difficult to find and hence, this gene is not routinely considered for donor selection. Furthermore, HLA-DPB1 mismatches associate with a lower risk of relapse. To better understand how HLA-DPB1 mismatches influence patient outcome, Dr. Effie Petersdorf and colleagues in the Clinical Research Division and the International Histocompatibility Working Group (IHWG)\*, used a novel concept of mapping T-cell epitopes to classify HLA-DPB1 mismatches associated with increased risk (“non-permissive”) and mismatches that did not negatively impact clinical outcome (“permissive”).

As Project Leader of the Transplantation Working Group and host to the IHWG, Dr. Petersdorf *et al.* were able to examine the effect of HLA-DPB1 T-cell epitope mismatches on aGVHD in more than 8500 unrelated donor transplants, of which 5428 were matched for all ten HLA alleles and 3111 were matched for 9 of 10 HLA alleles. Of the group overall, 20% were HLA-DPB1 matched, 49% were permissive HLA-DPB1 mismatches, and 31% were non-permissive HLA-DPB1 mismatches. Outcomes for patients transplanted from donors with HLA-DPB1 permissive mismatches were similar to those of patients transplanted from HLA-DPB1 matched donors. In contrast, in both the 9/10 and 10/10 HLA-allele matched populations, HLA-DPB1 non-permissive mismatches were associated with a significantly increased risk of severe aGVHD, overall mortality, and non-relapse mortality.

In conclusion, these data provide a better understanding of HLA-DPB1 mismatches on patient outcome and will aid in more precise risk stratification for the individual patient. It is predicted that 50% of all patients in search of a donor will have donors with permissible HLA-DPB1 mismatches.

Avoidance of an unrelated donor with a non-permissive mismatch at HLA-DPB1 might provide a practical clinical strategy for lowering the risks of mortality after unrelated-donor hematopoietic-cell transplantation.

*\*FHCRC and Dr. Petersdorf's laboratory manages the IHWG, maintaining a database that encompasses clinical information, high-resolution HLA allele typing, and non-HLA genetic polymorphisms for over 20,000 unrelated donor transplants performed worldwide since 1996. Collectively, the IHWG represents 240 transplant centers, 21 donor and transplant registries, and 37 laboratories, which work towards understanding barriers posed by genetic variance in transplantation.*

[Fleischhauer K](#), [Shaw BE](#), [Gooley T](#), [Malkki M](#), [Bardy P](#), [Bignon JD](#), [Dubois V](#), [Horowitz MM](#), [Madrigal JA](#), [Morishima Y](#), [Oudshoorn M](#), [Ringden O](#), [Spellman S](#), [Velardi A](#), [Zino E](#), [Petersdorf EW](#); on behalf of the [International Histocompatibility Working Group in Hematopoietic Cell Transplantation](#). 2012. Effect of T-cell-epitope matching at HLA-DPB1 in recipients of unrelated-donor haemopoietic-cell transplantation: a retrospective study. *Lancet Oncol*. DOI:10.1016/S1470-2045(12)70004-9.

