To prevent life-threatening encephalitis associated with HHV-6 reactivation following SCT, we weekly examined plasma HHV-6 DNA loads using real-time quantitative-polymerase chain reaction methods until five weeks post-SCT in 11 unrelated umbilical cord blood transplantation (CBT) and 42 unmanipulated HLA-mismatched/haploidentical related SCT (haplo-SCT).

CBT recipients were conditioned with cytarabine 12 g/m^2, cyclophosphamide 120 mg/kg, and total body irradiation (TBI) 12 Gy as a myeloablative regimen and fludarabine 200 mg/m^2, cyclophosphamide 50 mg/kg, and TBI 3 Gy for a reduced-intensity regimen. Prophylaxis for graft-versus-host disease (GVHD) consisted of cyclosporine A, with mycophenolate mofetil (MMF) or a short course of methotrexate (sMTX).

Haplo-SCT recipients were conditioned with fludarabine 120 mg/m^2, cytarabine 8 g/m^2, cyclophosphamide 120 mg/kg, and TBI 8–12 Gy for a myeloablative regimen and fludarabine 180 mg/m^2, rabbit ATG 8 mg/kg (Fresenius, Munich, Germany) or 4 mg/kg (Genzyme, Tokyo, Japan), and busulfan 8 mg/kg or melphalan for a reduced-intensity regimen. Bone marrow and peripheral blood stem cells were infused freshly without T-cell depletion. GVHD prophylaxis against myeloablative and reduced-intensity haplo-SCT was performed with tacrolimus, sMTX, MMF, and methylprednisolone 2 mg/kg, and tacrolimus and methylprednisolone 1 mg/kg, respectively.

Compared to all of 11 CBT recipients (100%), plasma HHV-6 DNA was detected in 3 of 42 haplo-SCT recipients (7.1%) despite methylprednisolone use for graft-versus-host disease prophylaxis. As preemptive therapy, 8 CBT and 3 haplo-SCT recipients were administered foscarnet or ganciclovir at a median of four days (range, 0 to 9) after detection of HHV-6 DNA, followed by its rapid resolution except for one CBT recipient who had repeatedly positive results. The remaining 3 CBT recipients were administered foscarnet before detection of plasma HHV-6 DNA. Despite HHV-6 reactivation, no patients developed HHV-6-associated encephalitis.

In the present observations both HLA disparity, and the use of methylprednisolone and antithymocyte globulin was not necessarily a risk factor for development of HHV-6 reactivation in our haplo-SCT fashion. Furthermore, preemptive or prophylactic administration of antivirals potentially prevents HHV-6-associated encephalitis by suppression of HHV-6 reactivation at an early stage of SCT.

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Selection of DPB1 T-Cell Epitope Permissive Matching Likely for Patients with 10/10 Unrelated Donors

Kevin Tram [1], Gretta Stritesky [2], Kimberly Wadsworth [2], Deidre M. Kiefer [3], Jennifer Ng [4], Claudio Anasetti [5], Jason Dehn [1]. *[1] National Marrow Donor Program, Minneapolis, MN; [2] Immunogenetic Operations and Research, National Marrow Donor Program, Minneapolis, MN; [3] Center for International Blood and Marrow Transplant Research, National Marrow Donor Program, Minneapolis, MN; [4] C.W. Bill Young/Department of Defense Marrow Donor Center, Georgetown University, Rockville, MD; [5] Blood and Marrow Transplantation, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Recent research suggests that beyond 8/8 allele level matching at HLA-A, B, C, DRB1, matching at HLA-DPB1 should be considered to improve patient survival rates in allogeneic stem cell transplantation. DPB1 alleles have been separated into three T-cell epitope (TCE) groups based on reactivity in functional assays for matching: 1) high 2) intermediate 3) low immunogenic potential. Non-permissive TCE mismatches at DPB1 are associated with a higher incidence of transplant related mortality in patients that have a 10/10 matched donor.

Table 1
Combined TCE Group of Patients and Likelihood of Identifying a DPB1 allele/permissive mismatched donor.

Patient TCE Group	Pre-Typing TCE Match (%)	Post-Typing TCE Match (%)	Total
Group 1	2 (18%)	6 (55%)	11
Group 2	12 (34%)	25 (71%)	35
Group 3	74 (63%)	114 (97%)	117
Total	**88 (54%)**	**145 (89%)**	**163**

We performed a study to identify the likelihood of having a DPB1 permissive TCE matched donor for patients with 10/10 high resolution matched donor options (HapLogic® prediction of ≥75%) in the Be The Match Registry®. 163 patient searches from US transplant centers that submitted a preliminary search request with DPB1 typing were evaluated for DPB1 TCE permissive mismatched donors, either identified through existing registry typing or by prospectively typing up to 10 donors per patient.

88 of 163 patient searches had a DPB1 TCE permissive mismatch present on the initial search results, 11 patient searches did not have a potential DPB1 matched donor, and the remaining 64 patient searches had up to 10 donors per patient selected for DPB1 typing, prioritizing young male donors. 57 out of 64 patients were able to find a DPB1 TCE permissive match via donor typing resulting in an overall TCE permissive match rate of 89%. Table 1 shows the condensed TCE groups of the patients assessed in the study, with patients being classified by their highest immunogenic TCE reactivity (*i.e.* 1>2>3). On initial donor search results, patients carrying any DPB1 TCE group 1 allele found a match 18% of the time, 34% for group 2 and 63% for group 3. Typing donors significantly improved the identification of a DPB1 permissive mismatched donor for all 3 groups to 55% for TCE group 1, 71% group 2 and 97% for group 3.

This study selection process focused on patients with more productive searches and shows that identifying a DPB1 TCE permissive matched donor in these cases is likely for the majority of patients. HLA typing donors who are predicted to be 10/10 matches for HLA-DPB1 may provide a feasible strategy for optimizing donor selection regardless of patient TCE group.

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Complete Loss of HLA Class I Heterozygosity in a Patient with Acute Myeloid Leukemia

Christine Zollikofer [1], Mark Ringhoffer [2], Lukas Kündgen [2], Daniel Fürst [1], Hubert Schrezenmeier [1], Joannis Mytilineos [1]. *[1] Transplantation Immunology, Institute for Clinical Transfusion Medicine and Immunogenetics Ulm gGmbH (IKT), Ulm, Germany; [2] 3rd Department of Medicine, Municipal Hospital, Karlsruhe, Karlsruhe, Germany*

Loss of heterozygosity (LOH) for certain HLA class I alleles provides tumor cells with an efficient mechanism to escape the T cell immune response. Here we report a case of complete class I LOH in a patient suffering from acute myeloid leukemia, which was associated with an intriguing HLA-typing procedure. The patient was diagnosed with AML FAB M1 and further analysis revealed a nucleophosmin1 (NPM1) mutation and normal male karyotype 46XY.

In February 2013 two independently collected EDTA blood samples (S1 + S2) arrived at our lab for HLA testing. Primary HLA class I and II typing was done for S1 with Sanger