Title	Helper T-lymphocyte precursor frequency (HTLPf) predicts the occurrence of graft-versus-host disease (GVHD) and disease relapse after allogeneic bone marrow transplantation
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S-HM-7

Helper T-Lymphocyte Precursor Frequency ($HTLP_f$) Predicts the Occurrence of Graft-Versus-Host Disease (GVHD) and Disease Relapse after Allogeneic Bone Marrow Transplantation

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Introduction: Graft-versus-host disease (GVHD) after bone marrow transplantation (BMT) is attributed to the recognition of histocompatibility antigens on recipient cells by donor T-lymphocytes. Donor helper cells play a pivotal role in amplifying the alloimmune response that initiates GVHD and may also contribute to the graft-versus-leukaemia effect that is commonly observed in allogeneic BMT recipients. We have developed a functional assay that may be used to predict the occurrence of GVHD and disease relapse after BMT.

Patients and Methods: Forty-three adult BMT patients and their donors (HLA-identical siblings 39, Matched-unrelated donors 4) were recruited. Before BMT, $HTLP_f$ was measured as a function of IL-2 secretion by alloreactive donor T-cells using a limiting dilution assay in which irradiated mononucleated cells (MNC) from the recipients (stimulators) were cultured with serial dilutions of MNC from the donors (responders). IL-2 contents in the culture was assayed by measuring its effects on the proliferation of the IL-2 dependent CTLL-2 cells. The patients were followed prospectively after BMT to assess the severity of GVHD and the relapse of diseases.

Results: The median age of the patients were 36 (Range: 17-57) and median duration of follow up was 15 months (Range: 1-31). Ten patients developed severe GVHD (>Grade 2) and nine patients developed disease relapses within the follow-up period. Patients with high $HTLP_f$ ($>10^{-5}$) before BMT were at higher risk of developing severe GVHD ($p=0.02$) and lower risk of disease relapse after transplantation ($p=0.1$). The development of GVHD and disease relapse were not associated with the underlying diseases, the sourse of stem cells and the conditioning regimens.

Conclusion: $HTLP_f$ might be useful in predicting the severity of GVHD and the likelihood of disease relapse after BMT.

S-HM-8

Polyoma BK Viruria in Bone Marrow Transplantation Patients - An Update after One-Year

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Background: Polyoma BK virus is frequently identified in the urine of bone marrow transplantation (BMT) patients with hemorrhagic cystitis (HC). However, viruria is common even in asymptomatic patients, so that a direct causative role of BKV is difficult to establish. We tested the hypothesis that although qualitative testing of BK viruria is non-discriminating, quantification of BK viruria might be useful in predicting HC in BMT patients.

Patients and Methods: Prospective serial quantification of BK viruria in 24-hour urine and viremia was performed in fifty patients at a median of seven time points during BMT. A total of more than 800 patients samples were quantified for BKV *VP-1* gene sequence with a real-time quantitative Polymerase chain reaction (Q-PCR).

Results: Twenty patients (40%) developed HC, of whom six had overt cystitis with gross hematuria (HC=grade 2), and 14 had microscopic hematuria (HC grade 1). Patients with HC, when compared with asymptomatic patients, had significantly higher peak BK viruria (6×10^{12} vs 5.7×10^{7} genome copies/day, $p<0.001$) and larger total amount of BKV excreted during BMT (4.9×10^{13} vs 7.7×10^{8} genome copies, $p<0.001$). HC of severity = grade 2 occurred after engraftment, and was significantly later than HC of grade 1 that usually occurred before engraftment (day 37 vs day 4, $p<0.01$). Multivariate analysis showed that HC was not related to age, conditioning regimens (cyclophosphamide and total body irradiation), type of BMT (allogeneic/autologous) and graft versus host disease. BK viruria, both peak value and total BKV excretion, was the only risk factor that predicted the occurrence of HC.

Conclusion: Quantification of BKV excreted in the urine of BMT patients predicted the occurrence of HC.