12 month median 2729 vs. 12062.5 unique TCR sequences, $P = .22$). Median lymphocyte counts did not increase between 3 and 12 months in the PD group as in the U+UD group, but the proportion of $CD3^+$ cells within lymphocytes increased in both groups. PD T cell repertoires were less clonal than U+UD samples at 3 months (1-normalized entropy: 0.14 vs. 0.25, $P = .09$) and 12 months (1-normalized entropy: 0.11 vs. 0.23, $P = .95$), with more even frequency distribution of TCRs. PD T cell repertoire was more dynamic than the U+UD controls with a significantly decreased T cell clonal persistence between 3 and 12 months (TCR sequence overlap: 8.73% vs. 38.84%, $P = .027$).

Conclusions: *Ex vivo* $dmPGE_2$ modulation with $dmPGE_2$ dominance results in delayed T cell and lymphocyte recovery, but less clonality despite a T cell repertoire restricted by low $CD3^+$ counts. The reduced oligoclonality and rapid T cell turnover may indicate enhanced thymopoiesis. Correlation with TRECs and clinical infectious outcomes is ongoing.

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Monitoring CMV-Specific CD8+ T-Cell Responses After Allogeneic Stem Cell Transplantation: A New Way of Guiding Anti-Viral Therapy

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CMV reactivation after allo-SCT is usually monitored by CMV-PCR. We present the results of a pilot study looking at the additional use of Multimers for monitoring CMV-specific CD8+ T-cells at different intervals after allo-SCT.

10 patients (4 males) that underwent allo-SCT from HLA-identical siblings (n=4) or HLA-matched unrelated (n=6) donors between May 2010 and May 2012 were enrolled. The diagnosis was acute leukemia (n=6), lymphoproliferative disorders (n=2) and myelodysplastic syndromes (n=2). All patients and 8 donors were CMV seropositive. All patients were positive for the HLA-A*0201 allele. Pentamers (Proimmune, UK) and Streptamers (Gottingen GmbH, Germany) were directed against the epitope NLVPMVATV of the $pp65_{495\text{-}503}$ protein of CMV in the context of HLA-A*0201. Samples were obtained from engraftment at 30-day intervals until day +180 and 2-monthly thereafter.

The median follow-up was 12.6 (4-21) months after SCT. Engraftment occurred in all patients at a median of 21.2 (15-27) days. Acute GVHD was diagnosed in 4 patients at a median of 63.3 (25-92) days. One patient developed acute GVHD following infusion of donor lymphocytes for the treatment of mixed chimerism on day +323.

Three patterns were observed. In 2 patients no CMV-specific CD8+ T-cells could be detected after SCT despite several episodes of CMV-PCR reactivation requiring prolonged antiviral treatment. In 5 patients CMV-PCR reactivation triggered a rapid increase of CMV-specific CD8+ T-cells (median 112.2 x 10^5/L, range 1.3-279.7 x 10^5/L). However, the CMV-PCR became immediately negative and antiviral treatment was stopped in all reactivations within 2 weeks. Subsequent CMV-PCR reactivations also lasted under 2 weeks in this group. Finally, 3 patients showed an early immune reconstitution with CMV-specific CD8+ T-cells detected (median 1.3 x 10^5/L, range 0.3-2.3 x 10^5/L) at a median of 21 (17-33) days post-SCT. No CMV-PCR reactivation was observed in this group.

We conclude that monitoring CMV-specific T-cell immunity after allo-SCT in combination with CMV-PCR may be able to distinguish patients at higher risk of CMV reactivation and in need of prolonged antiviral therapy. Patients with CMV-specific CD8+ T-cells detectable at the time of CMV-PCR reactivation may only need a short course of antiviral therapy, while those with early and persistent CMV-specific CD8+ T-cells may be at a very low risk of developing CMV disease in the long-term.

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Elevated Gamma Delta T Cell Recovery Following Hematopoietic Stem Cell Transplantation Associated with Improved Long Term Overall Survival in Pediatric Patients with Acute Leukemia

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Recent studies show that accelerated γδ T cell reconstitution after hematopoietic stem cell transplantation (HSCT) is associated with improved overall survival (OS) though the mechanisms have not been elucidated. We evaluated 102 consecutive pediatric patients with acute leukemia undergoing HSCT at St. Jude Children's Research Hospital from 1996-2011. The median age of the patients was 10.5 ± 5.9 yrs. (range, 0.6-25.2) and median follow up was 2.7±1.8 yrs. (range 0.2-6.0). There were 57% males, 43% females and 59% with ALL and 41% with AML. There were 14 patients with elevated γδ T cells ($\geq 1.75x10^5$ cells/ml) and 88 with low/normal γδ T cells ($<1.75x10^5$ cells/ml). There were no significant differences between the two groups with respect to age, sex, disease or donor source, p=0.7, 0.5, 1 and 0.07 respectively. Fours years after HSCT, Overall Survival (OS) was significantly higher for patients in the elevated group compared to the patients in the low/normal group, 93% and 60%, respectively, p=0.0173. Survival without relapse or graft failure, Event Free Survival (EFS), was significantly higher in the elevated group compared to the low/normal group, 85.7% and 58.0%, respectively. Since T cell reconstitution following HSCT is age dependent, we determined if γδ T cell recovery correlated with age and/or $CD3^+$ cells. Multivariate analysis showed no correlation between the number of $CD3^+$ and γδ T cells. In fact, 13 of 14 patients that recovered with increased number of γδ T cells had normal or low numbers of $CD3^+$ cells. Thus, γδ T cell recovery is not a simple correlate of T cell reconstitution. Because γδ T cells play a central role in maintaining intestinal epithelium integrity, we evaluated the incidence of gut GVHD. We found a significant lower rate of gut GVHD in the elevated group compared to the low/normal group, 0% and 17% respectively. Furthermore, the number of γδ T cells in patients with cGVHD (2.3 $x10^5$ cells/ml) was significantly lower compared to patients without cGVHD (6.2 $x10^5$ cells/ml), p=0.01. This suggests that γδ T cell may protect against gut and cGVHD. Since accumulating evidence suggests that γδ T cells contribute to both innate and adaptive immune responses during infections, we evaluated the rate and types of infection between the two groups. We found a significant lower incidence of infections reported in the elevated group compared to the low/normal group, 21% and 54% respectively p=0.02. Furthermore, the elevated group had only viral infections while the low/normal group had viral, bacterial and fungal infections. In summary, this is the first reported study of γδ T cell recovery after HSCT in pediatric patients and adds new insights into the role γδ T