phenotype as determined by FACS staining. The cells produced the pro-inflammatory cytokines IL1β, IL6, IL17, IP10, IFNγ and TNFα as determined by Multiplex immuno-assay and the cytotoxins perforin and granzyme B, all necessary for viral elimination.

The generation of HAdV specific T-cells from naive UCB cells in response to 15-mer HAdV peptides seems an essential step in developing a more tailor-made adoptive therapy for HAdV infection for recipients of UCB transplants.

[1] Haveman, LM, Bierings M, Legger E, et al. Novel pan-DR-binding T-cell epitopes of adenovirus induce pro-inflammatory cytokines and chemokines in healthy donors. Int Immunol. 2006;18:1521-9.

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FLAGELLIN-TLR5 IMMUNE RESPONSE: A NOVEL MECHANISM TO REDUCE GVHD IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Immunosuppressive drugs are used to limit GvHD but causes complications. To develop an alternative approach to control GvHD, we tested the immunomodulatory immune properties of flagellin, a bacterial protein that agonistically binds with TLR5.

Methods: We used established B6 to CB6F1 and B10.BR to B6 allogeneic HSCT recipients had both acute and chronic GvHD. 50 μg flagellin administered i.p 3 hours before 11 Gy irradiation. 5 million (M) T-cell depleted bone marrow (TCD BM) and 5 M splenocytes of congeneic donors were transplanted i.v. 24 hours later another dose of flagellin were administered i.p. Control recipients were treated with 0.2 ml PBS i.p. HSCT mice were monitored every day for mortality. Weight of individual mice was measured twice a week until 30 days post transplant and once a week after that to measure GvHD. Immune reconstitution was determined by measuring immune cells/organs and infecting the recipients with 5×10E3 pfu MCMV i.p.

Results: Flagellin treated recipients of in B6 to F1 model survived 100% and gained weight to almost normal level within 66 days post transplant. But the control group survived 80% and had signs of chronic GvHD. Flagellin-treated recipients in B10 to B6 model had 15% weight-loss and 33% transplant-related death by 132 days post transplant versus had severe acute GvHD and 100% early post-transplant mortality among control HSCT recipients. Flagellin-treated recipients in B6 to F1 model showed 100% chimerism with significantly higher number of donor spleen- and BM-derived CD4+ and CD8 + T cells per spleen in untreated recipients compared to control recipients within 66 days post transplant. In the spleen CFSE labeled CD4 + T cells divided faster in flagellin-treated recipients than the control recipients and decreasing the number of CD4 + CD62L+ T cells within 4 days post transplant. B6 to F1 recipients were infected with MCMV on 70+ days post transplant. Control mice died within day 10 post infection whereas flagellin-treated recipients recovered from MCMV infection and had higher number anti-viral+ CD8 + T cells in their blood on day 10 and 35 post infection. Increased numbers of CD25+foxp3 + CD4+ regulatory T cells were also measured from their thymus on day 35 post MCMV infection.

Conclusion: Flagellin treatment successfully controlled GvHD, enhances donor T-cell engraftment, had brisk and persistent cellular immune responses in lymphoid organs to protect recipients from viral infection.

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FACTORS PREDICTING NEW-ONSET DIABETES MELLITUS AND METABOLIC SYNDROME AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: IMPLICATION FOR EARLY PREVENTIVE INTERVENTION

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Background: Incidence and risk factors for post-transplant diabetes mellitus (PTDM) and long-term development of metabolic syndrome (MS) after allogeneic stem cell transplantation (allo-SCT) are not well defined. We conducted a prospective study of 84 patients (pts) undergoing allo-SCT with cyclosporine-based graft-versus-host disease (GVHD) prophylaxis to evaluate risk factors and incidence of PTDM in the first 100 days. Prevalence of MS at long-term followup was assessed.

Methods: Allo-SCT candidates without preexisting DM who met screening criteria were enrolled. Demographic data and baseline laboratory data including fasting blood glucose (FBG), lipids, insulin, c-peptide, and fructosamine were collected. PTDM was defined by FBG > 126 mg/dl or random BG > 200. Peak dose and duration of systemic steroid (SS) treatment for GVHD was collected. MS was defined by NCEP ATPIII criteria based on annual screens.

Results: Median age of pts was 46 years (yrs) (range 21-66). 44 (52%) were male. Median FBG pre-SCT was 97 (range 79-121). 50 of 84 (60%) pts developed DM at median of 23 days (interquartile range 14.2-33.8) post-transplant. 33 pts completed study to day 100 without PTDM and 1 died before day 100 without PTDM. Age was similar regardless of PTDM development. 28 pts (56%) with PTDM and 16 pts (47%) without PTDM were exposed to SS prior to reaching endpoints of PTDM or day 100. Pre-transplant c-peptide levels were higher in pts with PTDM (median 4.45 mg/dL vs 2.55, $p = 0.015$). Among pts receiving SS before day 100, pts with PTDM were more likely to have received > 1 mg/kg/day of SS ($p = 0.002$). Median post-transplant followup was 1.5 yrs (range 18 days-3.6 yrs). 45 pts (54%) were screened for MS at their annual or subsequent visits (17 pts deceased prior to 1 yr post-SCT). Of the pts for whom long-term metabolic data were collected, 17 (38%) met criteria for MS. Compared to pts who did not develop MS, these pts were older (56 vs 41.5 yrs, $p = 0.005$) and had higher pre-transplant fasting triglyceride levels (177 vs 108 mg/dl, $p = 0.005$). Interestingly, GVHD and use of SS were not associated with development of MS.

Conclusions: Our data suggest that pre-SCT c-peptide predicts PTDM, while high triglyceride levels and older age associate with long-term MS. These findings may help with counseling, monitoring, and planning interventions to reduce metabolic sequelae after allo-SCT, which contribute to cardiac complications in young patients after allo-SCT.

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AUGMENTATION OF HEMATOPOIETIC ENGRAFTMENT WITHOUT GRAFT VERSUS HOST DISEASE BY "ADD-BACK" OF PHOTOCHEMICALLY TREATED T LYMPHOCYTES IN MISMATCHED CORD BLOOD TRANSPLANTATION

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Introduction: Unrelated cord blood transplantation (CBT) is associated with a risk of graft rejection due in part to a limiting cellular content of the CB unit. We have investigated the co-infusion of photochemically (psoralen S59) treated mature donor T lymphocytes in a major histocompatibility complex (MHC) [H2-haplotype] mismatched murine transplant model as a new method to facilitate engraftment of donor CB cells.

Methods: We analyzed the rates of donor hematopoietic cell engraftment, graft versus host disease (GVHD), and long-term survival in H2 haplotype disparate [C57BL/6 (H2Kk/Thy1.1) → AKR (H2Kb/Thy1.2)] mice after CBT. Three different experimental groups were transplanted after sublethal radiation. Group 1 received allogeneic full term newborn peripheral blood alone, group 2 was transplanted with the same donor cells and unmanipulated donor T cells, and group 3 was transplanted with the similar donor cells and psoralen (S-59) treated donor T cells.

Results: We observed a low rate of donor engraftment after transplantation with cord blood alone (Group 1). The best results were observed after transplantation with 3 x 10^6 nucleated cord blood cells and 9 x10^6 S-59 treated T cells (Group 3b)($p = 0.007$). The engraftment rate was 75% compared to 12.5% after transplantation with 6 x 10^6 CB cells alone ($p = 0.04$). The long-term survival in group 3 was 100% and the rate and severity of