assessed. VIP-KO mice, WT littermates, and recipients were infected with 5 × 10⁵ PFU murine cytomegalovirus (mCMV) and T cell response to viral antigen was measured by flow cytometry for mCMV peptide-MHC class I-tetramer CD8⁺ T-cells at day 0, 3, 7, 10, and day 15 post infection or 80, 85, 87 and 101 days post-transplant (infection at day 80 post-transplant). Day 15 post mCMV challenge, VIP-KO and WT mice were euthanized. DC and T-cells were purified from BM and SP by FACS and MACS, respectively, 2 × 10⁶/mL DC treated with 1 × 10⁶ PFU mCMV peptide-expressing Listeria-MCMV construct and incubated with 2 × 10⁶/mL T-cells at 37 °C. Cultured 3 days and 7 days, cells were harvested and analyzed with DC and T-cell surface marker, tetramer, and intracellular cytokines by flow cytometry.

**Results:** allogeneic recipients of VIP-KO BM and VIP-KO SP developed more GvHD than recipients of WT grafts using a lower dose of donor SP (1 × 10⁶), while there was no difference in survival. The GvHD scores and the percentage of survival showed no difference among other syngeneic or allogeneic BMT settings. The specific anti-viral immunity was similar among the non-transplanted VIP-KO mice, and allogeneic and syngeneic transplant recipients of VIP-KO donor cells. 3 and 7 days post culture, VIP-KO DC expressed higher-level of CD80, MHC-II and lower-level of PD-L1, VIP-KO T-cells had higher-level of tetramer⁺ CD8⁺ T-cells and intracellular IFN-γ, lower-level of IL-4 and IL-5, PD1, and ICOS.

Taken together, these observations suggest that VIP expressed on immune cells suppresses anti-viral immune responses and Th1 polarization.

**Conclusion:** The anti-viral immune responses of VIP-KO immune cells were independent allogeneic immunity; VIP expressed by neurones cells in WT recipients did not compensate for the lack of VIP in mice transplanted with VIP-KO cells. Modulation of the VIP pathway is a novel method to regulate post-transplant immunity allograft transplant recipients.

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THE LIVER MAINTAINS STRONG POPULATIONS OF INNATE IMMUNE CELLS THAT CONTRIBUTE TO HOST PROTECTION AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

Mueller, A.M.S.1,2, Tran, P.1, Shizuru, J.A.1 1 Stanford School of Medicine, Stanford, CA; 2 University Medical Center, Freiburg i.Br., Germany

The liver is a critical immunocompetent organ armed with lymphocytes, natural killer (NK) cells, and a variety of antigen-presenting cells (APC), including resident macrophages, called Kupffer cells (KC). Exposed to large amounts of both destructive and harmless toxins and antigens, the liver must provide immunogenic and tolerogenic immunity. Here, we studied the role of the liver after hematopoietic cell transplantation (HCT). Lethally irradiated BALB.K mice received MHC-matched, purified hematopoietic stem cells (HSC; cKit⁺ Sca1⁺ Thy1.1LoLin⁻) +/- splenocytes (SP) from AKR/J donors. Ficoll-separated mononuclear cells (MNC) from PBs flushed livers were FACS analyzed post-HCT (pTX). In recipients of HSC + SP the liver was a major target organ of acute graft-vs-host disease (GVHD) with prominent donor T cell (TC) expansion, while NK cell (DX5⁺ CD122⁺) and KC (CD11b⁺ F4⁺/80+) levels were severely decreased. HSC-derived donor cells were rare. In contrast, mice given pure HSC showed no signs of GVHD, and early pTX high proportions of NK cells and KC were present within the livers. NK cells comprised up to ~30% of cells and were mixed donor/host type, while KC were donor derived at 6w pTX. We hypothesized that rapid regeneration of KC may shield against the pathogen and toxin load entering the circulation from irradiation-damaged intestines. In fact, when KC reconstitution was suppressed by silicoadministration mice displayed severe weight loss, hunched posture, ruffled fur, diarrhea, and a >50% mortality. Survivors stabilized ~121, presumably with gut recovery. To test if regeneration APC could protect against GVHD, a lethal dose of SP was given at 0, 4, 7, or 10d pTX, time points at which control livers contained 0, 11, 25, 32% KC, respectively. All mice receiving SP on d0 died, but death occurred in only 50%, 17% and 0% of mice when SP were given on d4, 7, and 10, respectively. Although donor chimerism decreased with delayed SP injection, lymphocyte reconstitution was improved. In conclusion, the role of the liver as an immunologically active organ after conventional HCT is often masked by donor TC expansion and GVHD. Rapid recovery of innate liver immunity may protect the host from endotoxemia and mediate tolerance between donor and host. Elevated proportions of NK cells, which are lacking in GVHD affected mice suggest another beneficial mechanism. Immunohistochemical studies for a better quantitative assessment of resident liver immune cells are underway.

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A TREND FOR BETTER IMMUNE RECONSTITUTION AND LOWER INCIDENCE OF INFECTIONS AFTER UNRELATED CORD BLOOD TRANSPLANTATION IN CHILDREN COMPARED TO ADULTS

Legendre, F.1, Vincent, E.2, Laroué, F.1, Gremonet, E.1, Caquette, A.1, Maison, E.1, Ledu, K.1, Saus, P.1,2, Deconinck, E.1, Rohrlich, P.S.2,4, Hôpital Jean Minjoz, Besançon, France, Metropolitan; 2 Hôpital Saint Jacques, Besançon, France, Metropolitan; 3 Hôpital Jean Minjoz, Besançon, France, Metropolitan; 4 Hôpital Saint Jacques, Besançon, France, Metropolitan; 5 EFS, Besançon, France, Metropolitan; 6 EFS, Besançon, France, Metropolitan

In umbilical cord blood transplantation (UCBT), the lower infused cell dose might lead to an increased infectious risk. To get further insights on this issue, we retrospectively analyzed infectious events and immune restoration in 35 consecutive patients (pts) treated by UCBT from Jan 2005 to Dec 2008 in the University Hospital of Besançon.

There were 7 children and 28 adults aged 6 to 62 y (median 35y). All pts suffered from malignant diseases. Nine pts were in CR1, 10 in CR2 and 16 in ≥CR3 or in PR. Nine pts were CMV⁺ and 29 EBV⁺. A myeloablative conditioning regimen with 12 GY TBI (16pts) or Busulfan (2 pts) + 120 mg/kg cyclophosphamide + 75 mg/m² fludarabine was given to 18 pts, one child received ALG instead of fludarabine. A fludarabine based reduced intensity conditioning (RIC) was given to 17 pts. There were 29 double and 6 single unit transplants. The median follow-up is 638 days (259-1499).

All pts engrafted except 3 after RIC. Fifteen pts died (43%), 10 of relapse, 4 of infection (1 ARDS, 1 zygomycosis, 1 fusariosis and 1 HHV6 encephalitis) and 1 died of post-conditioning toxicity. There were 8 infectious events in 7 children, (mean 1.14/patient) with 1 death in the pt who received ALG and 86 infectious events in 28 adults (mean 3.07/patient) causing 5 deaths.

Viral infections occurred in 27 pts (77%) in majority before D100 (73%). BKV⁺ hemorrhagic cystitis (HC) occurred in 15 pts, VZV (6), CMV (5), HHV6 (1), HSV (1), and RSV (1). We recorded 22 documented bacterial infections caused by 13 Gram negative and 9 Gram positive agents. Invasive fungal infections were diagnosed in 9 pts (26%) with 6 proven or probable aspergillosis, 2 fungal septicaemias and 1 zygomycosis. Fungal infections seemed more frequent in pts experiencing chronic GVHD (35% versus 21.4%, hazard ratio = 1.6, p = 0.91).

The immune reconstitution appeared quicker in children, the median CD4⁺ T-cell count at 3-6-12 months post UCBT was 224-1008-1335/mm³ in children and 119-216-364 in adults. Median B cell count at 6 mo post UCBT was 868 in children versus 106 in adults. Among the 20 survivors at 1 year post transplant, the vaccine response was complete in 15 pts, incomplete in 2, non available in 3.

The lower incidence of infectious events in children might be due to a better immune reconstitution. The overall infectious mortality rate is relatively low (11%). The high prevalence of HC advocates for a prospective follow-up of BK virus and the high rate of Zoster warrants preventive strategies.

**LATE EFFECTS/QUALITY OF LIFE**

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A PROSPECTIVE STUDY OF IRON OVERLOAD (IO) MANAGEMENT IN ALLOGENEIC HEMATOPOIETIC-CELL TRANSPLANT (ALLO HCT) SURVIVORS

Majhail, N.S.1, Lazarus, H.M.2, Burns, L.J.1 1 University of Minnesota, Minneapolis, MN; 2 Case Western Reserve University, Cleveland, OH

While transfusional IO occurs in 30-60% of allo HCT survivors, the treatment of post-HCT IO is not well described. We