Conclusions: Kinetics of T-reg and T-cells engraftment were independent, underlying the need for assessing chimerism levels among each T-cells and T-regs in patients given nonmyeloablative conditioning. Our data did not show any significant correlation between T-reg levels and occurrence of chronic GVHD thus far. Data including higher number of patients will be presented.

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PUVA THERAPY FOR ACUTE GRAFT-VERSUS-HOST DISEASE (GVHD) OF THE SKIN

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Glucocorticoids remain the standard for initial treatment of acute GVHD. However, toxicities and immunosuppression are severe and steroid-sparing strategies would be desirable. Between 5/96 and 4/07 we treated 55 patients with isolated skin GVHD with methoxsalen plus ultraviolet-A light therapy (PUVA), with the objective of avoiding systemic immunosuppressive therapy. Patients were treated with PUVA three times/week initially at doses of 0.25 J/m^2, with exposure increased 0.25 J/m^2 per treatment as clinically indicated. The median patient age was 48 (range 4–71) years. Twenty-six received a calcineurin inhibitor plus mycophenolate mofetil for GVHD prophylaxis, 24 received a calcineurin inhibitor plus methotrexate, and 5 received other regimens. Sixteen had related donors (1 HLA-mismatched), and 39 had unrelated donors (15 HLA-mismatched). The median onset of GVHD was 26 days after transplant, and the median start time of PUVA was 43 days. Forty-five patients received PUVA as initial therapy for acute GVHD, and 10 patients received PUVA for recurrent GVHD after discontinuation of prednisone administration. At the start of PUVA therapy, 31 patients (56%) had rash involving $>$ 50% body surface area (BSA), 19 (35%) had rash 26–50% BSA and 5 (9%) had rash $\leq$ 25% BSA. The median number of PUVA treatments was 13 (range 2–26). Sixteen patients (29%) had complete responses after a median of 14 (range 8–26) PUVA treatments and required no subsequent systemic immunosuppressive therapy for treatment of acute GVHD. Twelve patients required systemic therapy after starting PUVA for treatment of isolated gastrointestinal GVHD, although 8 of these patients had cleared or improved skin rash before starting systemic therapy. Twenty-four patients (44%) required systemic immunosuppressive therapy after starting PUVA for treatment of skin GVHD (18) or skin plus gastrointestinal GVHD (6). Three patients had evidence of skin GVHD when PUVA was discontinued early due to readmission to the hospital or discharge home. Only four patients required secondary systemic therapy for treatment of acute GVHD. Thirty-one of 52 patients who could be evaluated developed chronic GVHD. Thirty-seven patients remain alive at a median of 753 days after transplant. Overall, 24 of 55 patients (44%) responded to PUVA with resolution or improvement of rash. These results suggest that PUVA can be effective in treating skin GVHD and in reducing the need for systemic immunosuppressive treatment.

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THE ANALYSIS OF CHRONIC GVHD AFTER CORD BLOOD TRANSPLANTATION IN COMPARISON WITH BONE MARROW TRANSPLANTATION

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Backgrounds: Umbilical cord blood can be an alternative stem cell source for the patients with hematological malignancies requiring allogeneic stem cell transplantation. However, little is known about graft versus leukemia/lymphoma (GVL) effect in cord blood transplantation (CBT). Here, we analyzed chronic GVHD (cGVHD) in CBT compared with that in BMT and evaluated the relevance between cGVHD and GVL. **Patients/Methods:** We retrospectively studied 162 patients who had been free from disease progression for more than 100 days after either unrelated BMT (n = 75) or CBT (n = 87) at Toranomon Hospital from January 2002 to December 2006. Median age of the patients was 52 years old (BMT vs CBT: 49 vs 53). Underlying diseases were acute leukemia (n = 88), myelodysplastic syndrome (n = 17), lymphoma (n = 39) and others (n = 18). Conditioning regimens were mainly composed of Fludarabine 125–180 mg/m^2 with several combinations of Melphalan 80–140 mg/m^2, Busulfan 8–16 mg/kg and/or total body irradiation (4–8 Gy). **Results:** The Median observation period after the transplantation was 612 days (range, 109–1944). The cumulative incidence of cGVHD was 84% in BMT and 62% in CBT (p = 0.09). The severity of cGVHD was analyzed based on its type; limited or extensive. In CBT, the percentage of the former type was 34% (vs 25% in BMT) and the latter was 23% (vs 48% in BMT). High-risk disease (p = 0.03) and preceding acute GVHD(p = 0.03) are related to the occurrence of cGVHD. RICBT tended to increase cGVHD compared to CBT using BU/CY or CY/TBI regimen. Multivariative analysis showed that cGVHD increased overall survival rate ($p < 0.01$) and suppressed recurrence of the disease ($p < 0.01$). During observation period, no patients after CBT were died of cGVHD. **Discussion:** We demonstrated that cGVHD in CBT is tolerable compared with that in BMT and that the occurrence of cGVHD could result in good prognosis. Our analysis also suggested that CBT could have GVL effect as well as BMT.

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PERSISTENT RECIPIENT ANTIGEN-PRESENTING CELLS IN HUMAN HEMATOPOIETIC STEM CELL TRANSPLANTATION: IDENTIFICATION OF A DERMAL SUBSET THAT OUTLIVES EPIDERMAL LANGERHANS CELLS

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Graft versus host disease (GVHD), a lethal complication of hematopoietic stem cell transplantation (HSCT), is initiated by recipient antigen presenting cells (APC) priming donor T cells. The skin, a commonly affected organ, contains diverse APC including heterogeneous dermal dendritic cells (DC) whose contribution to GVHD is not well understood.

We have obtained 22 pairs of skin biopsies pre and post conditioning (high dose BuCy or CyTBI and reduced intensity Flu/Mel) and 85 biopsies at day 40, 100 and 365 post HSCT from patients with sex-mismatched donors. Pre and post conditioning samples were digested and analysed with CD45, HLA-DR, CD14 and CD1a antibodies in a single step Trucount protocol. Chimerism was determined on cytospins of spontaneously migrated dermal APC and collagenase digested dermal cells using sequential four-colour confocal microscopy and X/Y fluorescence in situ hybridization.

We find 3 populations of CD45+ DR+ dermal cells: CD14+ CD1a- fXIIIa-; CD14+ CD1a- fXIIIa+; CD1a+ CD14- fXIIIa-. Characterization of these cells in vitro shows that CD14+ cells are more adherent and phagocytic than CD1a+ cells and that the fXIIIa+ component is in addition, heavily granulated with ingested melanin. CD14+ APC are resistant to depletion by conditioning (210 pre/213 post; cells per mm^2; P 0.86) compared with CD1a+ cells (201 pre/97 post; mean cells per mm^2; P 0.03). Both are reduced in HSCT patients compared with controls (706 CD14+ and 468 CD1a+ cells per mm^2; both P 0.01).

Chimerism analysis at 40, 100 and 365 days post HSCT reveals two strikingly different patterns of engraftment. CD1a+ and CD14+ fXIIIa- cells, obtained either by migration or digestion, engraft rapidly in all patients, ahead of LC, reaching medians of 99% and 100% donor, respectively, at day 40. In contrast, CD14+ fXIIIa+ cells, which are obtained only from digested dermis, are very slow to engraft in the absence of GHVD, reaching only 63% median donor after high dose and 10% median donor chimerism after reduced regimens, at 1 year. Acute GVHD promotes engraftment with 100% donor chimerism seen in nearly all patients at day 100. Cell cycle analysis ndicates that these cells are not actively synthesizing DNA, suggesting a different mode of survival compared with persistent recipient LC.