lymphoma. Within the 11-mere, the peptide with the highest affinity to an MCH allele was a 9-mere and tetramers with the MCH allele A2402 and the 9-mere positively stained expanded T-cells. The tetramer positive T-cells were found to be CD107a-positive after stimulation with dendritic cells pulsed with the peptide. T-cells specific for that HY minor were found after expansion in two of four A2402 positive patient/donor pairs with female donor and male patient.

Conclusion: A new HY minor has been identified using a high-throughput method for identifying more HY minors and possibly also auto- and cross-reactivity antigens.

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IS LIVER BIOPSY NECESSARY IN THE MANAGEMENT OF ALLOGENIC STEM CELL TRANSPLANT RECIPIENTS WITH GRAFT-VERSUS-HOST DISEASE?
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Background: Liver function abnormalities are common after hematopoietic stem cell transplantation (HSCT) and liver biopsy is often used to directly treat. We reviewed 117 consecutive liver biopsies during the last 8 years at our institution.

Materials and Methods: From 2003 to 2010, 117 liver biopsies were performed on patients who had undergone HSCT for hematological malignancies and presented with liver dysfunction. All slides were evaluated for features of GVHD by cholestasis, fibrosis, lobular inflammation, iron deposition and were graded from 0 to 3 (0 = none, 1 = mild, 2 = moderate and 3 = severe).

Results: The median age of the patients was 49 (range 14-66). Fifty seven (49%) patients underwent related donor (RD) and 60 (51%) unrelated donor (URD) transplantations. Preparative regimens were applied based on their disease; GVHD prophylaxis was tacrolimus and mycophenolic acid in 105 (88%) patients; tacrolimus, sirolimus and thymoglobulin in 6 (5%), and other regiments in 6 (5%). Fifty nine patients were alive with a median follow up for the survivors of 4.2 years (range 0.9-9.3 years). Kaplan-Meier estimate of overall survival at 6 years was 43% +/- 5%. Liver biopsies were preformed at a median of 173 days post-transplant (range 22-1366 days). At the time of the liver biopsy, the median AST was 168 IU/L (range 18-1425 IU/L), ALT 250 IU/L (range 38-1495 IU/L), total bilirubin 1.1 mg/dL (range 0.1-26.8 mg/dL) and alkaline phosphatase 278 IU/L (range 69-1547 IU/L). On biopsy there were 107 (91%) patients with histological features of GVHD: mild 29 (27%), moderate 56 (52%) or severe 22 (21%). Iron deposition studies showed 5 (4%) patients without iron deposition, 23 (20%) patients grade 1, 38 (32%) patients grade 2, and 51 (44%) patients grade 3. In multivariate analysis of relevant prognostic factors including age, donor, total bilirubin, ALT and histological grade of cholestasis, only total bilirubin of < 1.5 IU/L predicted favorable survival (hazard ratio = 0.34, 95% CI 0.19 - 0.63, p = 0.001).

Conclusion: Liver biopsy confirmed the presence of GVHD in most patients. The histological features of GVHD and iron deposition did not adversely influence the survival. The most significant predictor of survival was the presence of cholestasis on biopsy and the elevation of total bilirubin of > 1.5 mg/dL. Our data indicated limited value of liver biopsy in management of patients with liver dysfunction after allogeneic stem cell transplantation.

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GENETIC VARIATIONS IN THE ACTIVATION AND EFFECTOR PATHWAYS OF CYTOTOXIC T LYMPHOCYTES MODULATE ALLOIMMUNE REACTIVITIES AND HAVE PROGNOSTIC SIGNIFICANCE FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION
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Objectives: Donor T lymphocytes play a critical role in alloimmune reactivities after allogeneic hematopoietic stem cell transplantation (allo-HSCT). CD28, inducible co-stimulator (ICOS) and cytotoxic T-lymphocyte antigen 4 (CTLA-4) belong to the same family of T-cell costimulatory molecules. After activation, three effector pathways have been described for T-cell cytotoxicity: granzyme B/perforin, Fas/Fas ligand (FasL) and secreted molecules such as TNF-alpha. Near recently, several important polymorphisms have been identified in those genes and reported to be associated with the risk of autoimmune diseases, malignancies and allograft rejection in solid organ transplantation patients. However, such information is less available in allo-HSCT. In the present study, we first investigated the influence of the genetic polymorphic features on the abilities of T-cell alloimmune responses in allo-HSCT setting.

Methods: We analyzed 10 single nucleotide polymorphisms (SNPs) in the CD28, ICOS, CTLA-4, Granzyme B, Fas and FasL genes in 138 pairs of recipients and their unrelated donors (URDs) and 102 pairs of recipients and their HLA-identical sibling donors.

Results: (1) We found two SNPs in donors influenced the risk of aGVHD. The association was particularly strong in the URD transplant cohort. Unrelated donor with Granzyme B +55 mutated genotype (AA) was an independent risk factor for grades II-IV aGVHD (P = 0.024, RR = 1.811, 95%CI, 1.080-3.038). While unrelated donor with CTLA-4 CT60 mutated genotype (AA) was protective (P = 0.025, RR = 3.806, 95%CI, 1.187-12.204). (2) However, donor with CTLA-4 CT60 AA genotype was a risk of early CMV infection (P < 0.0001, RR = 0.383, 95%CI, 0.243-0.695) and relapse after allo-HSCT in AML patients (P = 0.047, RR = 2.792 95%CI, 1.013-7.596). Furthermore, AML patients with Fas -670 homogeneous mutated allele (TT genotype) also had a higher risk of relapse (P = 0.003, RR = 5.823 95%CI, 1.566-9.337). (3) The presence of those susceptible alleles in donor and/or recipient (patients receiving CTLA-4 CT60 AA donor, patients receiving Granzymeb +55 AA donor, AML patients with Fas -670 TT genotype or with all) resulted in a reduced overall survival compared with those with wild-type genotypes (54.9% vs 69.5%, P = 0.029).

Conclusions: The results of this study highlight the important effect of genetic variations in T-cell activation and effector pathways from the donors and recipients on the outcomes of allo-HSCT.

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SEVERE CHRONIC GRAFT-VERSUS-HOST DISEASE IS ASSOCIATED WITH IMPAIRED THYMOPOIESIS AND PERIPHERAL LYMPHOCYTE EXPANSION
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Allogeneic hematopoietic stem cell transplantation (AHSC) is a curative therapy for hematologic malignancies. Chronic GVHD (cGVHD) is a significant barrier to successful AHSC. Although T cells have been implicated in cGVHD pathobiology, the role of the thymus in this process has yet to be clearly defined. We characterized thymus and spleen T cell subsets in a murine model of cGVHD (B10.D2→BALB/c) to investigate the role of the thymus in this process. Once cGVHD was well-established, 4-6 weeks post AHSC, total thymocyte numbers in mice with cGVHD were more than 20-fold depleted compared to syngeneic controls. Furthermore, the double positive thymocyte cell population (CD4+ CD8+) was most markedly reduced, with a 90-fold reduction in numbers compared to syngeneic controls. Despite evidence of thymic atrophy and diminished thymopoiesis, thymic CD4+ single positive cells were decreased less proportionally (13-fold). Congenic AHSC demonstrated that this CD4+ population was comprised of donor peripherally derived TCRD44α memory T cells, representing an allogeneic infiltrate. Further evidence of diminished thymic output was found in the periphery. Live splenocytes were 3-fold depleted in...