

independently associated with platelet engraftment. While in pediatric patients only infused CD34+ cells/kg was significantly associated with platelet engraftment.

Graft-versus-host disease: At days 100, the cumulative incidence was 55.0% for grade II-IV aGVHD, and 23.1% for grade III-IV aGVHD. While cGVHD 44.67%, with 21.3% for limited and 23.3% for extensive. In patients under 14 years old, the cumulative incidence of aGVHD of grade II-IV was 57.2%, and 13.8% for grade III-IV. While cGVHD 56.7% for total and 29.5% for extensive. No associations of HLA disparity with incidence and severity of GVHD were found.

KIR ligand mismatch and a higher dose of CD56bright NK cells ($41.9 \times 106/\text{kg}$) in the allografts are associated with high incidence of aGVHD, while a higher CD56dim/CD56bri NK cell ratio (more than 8.0) in allografts was correlated with a decreased risk of III-IV aGVHD.

Relapse Transplant-related mortality and survival: The 3-year probability of relapse in the standard-risk group was 11.9% and 24.3% for AML and ALL and that in high-risk group was 20.2% and 48.5% for AML and ALL, respectively. The advanced disease status, Higher CD4/CD8 in G-BM and delayed lymphocyte recovery at day 30 post transplantation are correlated with increased relapse rate. While, a higher CD56dim/CD56bri NK cell ratio (more than 8.0) was correlated with a decreased rate of relapse. Modified DLI can be used to treat relapse of patients after the protocol.

The TRM on day 100 in the standard- and high-risk groups was 6.8% and 5.9% for AML and 6.9% and 25.9% for ALL, respectively.

The 3-year probability of LFS for AML was 70.7% and 55.9% and for ALL was 59.7% and 24.8% in the standard-risk and high-risk groups, respectively.

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IMMUNOSUPPRESSIVE CYTOKINE GENE POLYMORPHISMS AND OUTCOMES AFTER RELATED AND UNRELATED HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Transforming growth factor- β (TGF β) and IL10 are pleiotropic regulatory cytokines in the immune system. Clinical data and animal model suggest TGF β and IL10 can suppress aGVHD. The present study was designed to test the influence of gene polymorphisms of TGF β and IL10 on outcomes after related and unrelated HSCT.

Methods: We analysed six single nucleotide polymorphisms (SNPs) in three genes, TGF β 1-509(C > T), +869 (T > C), TGF β 1 receptor II (TGF β 1RII) +1167 (C > T) and IL10 -1082(A > G), -819(T > C), -592(A > C), in a cohort of 138 pairs of recipients and their unrelated donors and a second cohort of 102 pairs of recipients and their HLA-identical sibling donors, who had undergone HSCT from January 2001 to March 2009 at our center.

Results: (1) TGF β 1 -509 T/T genotype in the donors side or T allele-positive in the recipients side showed a significant protective effect on the occurrence of aGVHD and grade II-IV aGVHD in the unrelated transplantation cohort ($P < 0.05$). In the combined cohort, the multivariate analysis confirmed that donors with TGF β 1-509 T/T genotype had a protective effect on the risk of aGVHD. (2) Both in unrelated transplantation cohort and sibling transplantation cohort, We found the IL10-819 C/C and -592 C/C genotype in either recipients side or donors side were significantly associated with a higher incidence of aGVHD ($P < 0.05$). (3) In the combined cohort, the promoter haplotypes of IL10 polymorphic features in positions -1082, -819 and -592 had an influence on the occurrence of aGVHD and death in remission. Recipients without A-T-A haplotype or were transplanted from donors without A-T-A haplotype had a higher incidence of aGVHD and death in remission than with A-T-A homozygous or heterozygous. In multivariate analysis, recipients without A-T-A haplotype was found to be associated with a higher risk of aGVHD (RR = 0.764; $P = 0.096$) and grade II-IV aGVHD (RR = 0.413; $P = 0.009$). (4) No significant association with aGVHD was detected for the TGF β 1 + 869, TGF β 1RII +1167

and IL10-1082 genotypes. No significant association was found between cytokine genes polymorphisms with cGVHD, relapse and overall survival.

Conclusions: This is the first report of the relation of gene polymorphisms of IL10, TGF β 1 and TGF β 1RII to outcomes of allo-HSCT within Chinese population. The results may provide useful information to risk assessment, donor selection, and a guide for appropriate immunosuppressive therapy.

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PTLD IN MINIATURE SWINE FOLLOWING NOVEL LOW INTENSITY CONDITIONING FOR HAPLOIDENTICAL HCT: THE MGH EXPERIENCE

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Haploidentical HCT (haplo-HCT) is a potent and potentially curative therapy for a number of lymphohematopoietic neoplasms. Haplo-HCT has been limited by toxic conditioning regimens and the development of lethal graft-versus-host disease (GVHD). Similar to what has been observed in the clinic, myeloablative HCT outcomes in the pig have a high incidence of GVHD. Less toxic, non-myeloablative haplo-HCTs developed in our laboratory resulted in a greatly reduced incidence and intensity of GVHD. However, post-transplantation lymphoproliferative disease (PTLD) was often observed following these novel reduced intensity conditioning protocols. Haplo-HCT conditioning with 700-1000 cGy thymic irradiation (TI), CD3 immunotoxin and 30-60 days of cyclosporine had a 6% incidence of GVHD (2 of 32) but was complicated by a 33% incidence of PTLD (11 of 32). Of these 11 pigs, 2 resolved their PTLD after cyclosporine was discontinued but then developed GVHD. When thymic irradiation was eliminated from the protocol, no PTLD was observed and GVHD was only observed in 2 of 24 (8.3%) transplanted pigs. Unfortunately this very mild preparatory regimen without TI failed to consistently achieve successful long term engraftment. In an attempt to decrease the incidence of PTLD, avoid GVHD and increase haplo-HCT engraftment outcomes, 100 cGy of total body irradiation (TBI) was introduced to the protocol. Of 46 haplo-HCT recipients, only 4 (<10%) developed PTLD and 2/46 animals developed GVHD, one of which recovered spontaneously. We also attempted to identify serum markers for diagnosing PTLD in our pigs. As it is observed in humans, we identified lactate dehydrogenase (LDH), to be elevated in pigs prior to onset of PTLD. In support of these findings, three porcine PTLD tumor cell lines harvested from animals and passaged in vitro demonstrate higher LDH levels compared to naïve PBMCs. We conclude that: (1) our current haplo-HCT protocol utilizing 100 cGy TBI, porcine CD3 immunotoxin and 45 days of cyclosporine is relatively safe and significantly reduces the incidence of PTLD; (2) stable engraftment and multilineage chimerism can be achieved with minimal GVHD; and (3) LDH is a clinically relevant serum marker for the diagnosis of PTLD in the pig. These findings reinforce the pig model as a valuable tool for HCT translational studies.

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CLOFARABINE \pm FLUDARABINE WITH IV BUSULFAN AND ALLOGENEIC STEM CELL TRANSPLANTATION FOR RELAPSED, REFRACTORY MYELOID LEUKEMIA (ML) AND MDS

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Clofarabine (Clo) is a nucleoside analog (NA) with improved antileukemic efficacy compared with Fludarabine (Flu), previously used with IV Busulfan (Bu) in reduced toxicity conditioning therapy for Allo-SCT. *In vitro* studies of [Clo + Flu + Bu] demonstrated a superior synergistic cytotoxicity compared with either [Clo + Bu] or [Flu + Bu]. We have now investigated [Clo \pm Flu] with IV Bu in pre-transplant conditioning.