event free survival was 54%. In conclusion, UCBT is an alternative source of hematopoietic stem cells for the treatment of children with malignant and non-malignant diseases who lack a suitable related donor.

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A-LOCUS MISMATCH DOES NOT ADVERSELY INFLUENCE OUTCOME FOLLOWING RELATED-DONOR STEM CELL TRANSPLANTATION (SCT)

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For pts with hematologic diseases requiring SCT who lack a histocompatible sibling, alternative related-donors (ARD) may be considered. Recent evidence suggests that outcome may also depend upon the parental source of the mismatched (M/M) haplotype. We reviewed data on 42 pts that underwent ARD-SCT at VGH between 01/83 and 05/02: 24 males and 18 females with a median age of 36 years. Diagnoses included AML (13 pts), CML (11 pts), ALL (8 pts) and other (10 pts). Fourteen pts had good risk disease. HLA testing was serologic until DNA techniques were instituted for class I (02/01) and class II (03/93) typing. Donor/recipient were phenotypic matches (PM)(3 pts), one-antigen M/M (36 pts; A-locus 19 pts, B-locus 6 pts, DR-locus 11 pts) or two-antigen M/M. Donors included a sibling (31 pts), a parent (8 pts), a child (1 pt) or a first cousin (2 pts). Stem cell source was bone marrow in 38 pts, blood in 3 pts or both in 1 pt. Forty pts initially engrafted; the remaining 2 pts were rescued with autologous (1 pt) or allogeneic (1 pt) blood cells. One pt experienced late graft failure requiring a second SCT from the original donor. Nine pts died of acute/chronic GVHD, 2 pts from infection and 5 from other causes. Seven pts died of recurrent disease. Nineteen pts (45%) remain alive (17 pts in CR, 2 pts in relapse) with a median followup of 8.8 (0.3-13.1) years. Pts having had a BMT from a one-antigen A-M/M or PM donor (Group 1, n=22) have a 5 year overall survival (OAS) of 63%, treatment related mortality (TRM) of 25% and relapse rate (RR) of 16%. For all other pts (Group 2) OAS is 19% (p=0.01), TRM is 71% (p=0.01) and RR is 45% (p=0.05). Incidence of acute GVHD for Group 1 and Group 2 pts was similar[73% and 65%, respectively (p=0.4)]. There were more good-risk pts in Group 1 than in Group 2 (48% vs 20%, p=0.10). Five pts received SCT from sibling donors mismatched for noninherited maternal antigens (NIMA), 2 of whom are alive at 9.8 and 8 years respectively. Two pts received SCT from a sibling donor mismatched for noninherited paternal antigens (NIPA), both of whom have died. ARD-SCT pts that are PM or one-antigen A-locu M/M with their donor appear to have outcomes similar to that reported for histocompatible siblings. Due to low pt numbers, the influence of parental donation and the use of a sibling with NIMA (rather than NIPA) couldl not be determined.

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THE ABSENCE OF MHC CLASS I ON NEURAL STEM CELLS DOES NOT PERMIT NK KILLING AND PREVENTS RECOGNITION BY ALLOREACTIVE CTL

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Potential applications of neural stem cells (NSC) in syngeneic and allogeneic progenitor cell transplantation models requires understanding of expression of MHC molecules and the ability of T cells and NK cells to recognize this progenitor population. Cells from the cortices of day 13 embryonic (E13) B6 (H-2^b) mice were explanted and cultured in serum free N2 media with basic fibroblast growth factor to select for NSC. Flow cytometric analysis of cells from P2 through P17 cultures using anti-MHC class I and II mAb showed marginal levels of MHC H-2K and H-2D class I and H-2IA class II expression. However, titration of mrIFNγ in NSC cultures demonstrated that MHC molecules could be strongly upregulated following addition of 3 ng/ml mrIFNγ for 60 hours. To assess the susceptibility of NSC with marginal versus high levels of MHC expression to lysis by CTL and NK populations, 4 hour ^{51}Cr release assays employing untreated and mrIFNγ treated NSC target cells were performed. Results showed that untreated NSC were not recognized by BALB/c (H-2^d) allospecific anti-H-2^b CTL, consistent with the anti-MHC class I mAb findings. However, upregulation of class I and II products on both early and later passaged NSC resulted in their efficient lysis by CTL. NK cells were prepared from syngeneic B6 or allogeneic BALB/c mice. Although NK cells effectively killed control YAC-1 target cells, they did not kill MHC deficient (or expressing) NSC targets. IL-2 augmented NK effector cells also failed to lyse NSC target cells. The findings suggest that following transplant of NSC into syngeneic recipients, these progenitor cells may not be susceptible to clearance by host NK cells. Their lack of MHC expression may also help to shield such cells from immediate host allogeneic T cell recognition.

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HAPLOIDENTICAL CD34 POSITIVE CELL TRANSPLANTATION IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Much more stem cell sources for allogeneic hematopoietic stem cell transplantation (HST) have been available in this decade such as unrelated donors from marrow bank and cord blood bank in addition to HLA identical siblings. However, in cases of the urgent settings, transplant from haplo-identical related donors is the only choice for HST. A multi-center retrospective study is conducted to evaluate the feasibility of haplo-identical CD34 positive cell transplant from related donors with more than 2 HLA loci mismatch. Between 1996 and 2001, a total of 25 patients with a variety of hematological malignancy received HST from haploidentical related donors after CD34 positive cell selection. Patient mean age was 29 years old ranging from 17 to 69. Two patients with ALL/CR1 and 1 MDS (RA) patient were classified as a low risk group and 22 as a high risk group with advanced stage which is above CR1 including 9 cases of second transplantation. All patients received positively selected CD34 peripheral blood stem cells isolated by CliniMACS (n=15) or Isolex 50 (n=10) system. Nineteen patients were conditioned with a conventional TBI containing regimen and 6 with a reduced-intensity regimen (RIST). GVHD prophylaxis were as follows; cyclosporine-based in 18, tacrolimus-based in 7 and MMF was added in 3 cases. Primary engraftment failure was observed in 6 out of 25 patients. Out of 6 cases in RIST group, 3 patients were rejected. Later rejection after engraftment in day 28 was seen in 1 out of 19 patients evaluable. Sepsis with bacterial infection was seen in 9 patients, 2 of whom died. Fungal infections occurred in 9 patients, 2 of whom died. Regimen-related toxicity (RRT) was also highly observed, 3 patients died of RRT. Three cases died of lethal GVHD and 5 cases of tumor progression. Eight of 9 second transplant cases died within 120 days. The estimated probability of relapse free survival (RFS) at 1 year was 23.3 % in all patients, 33.3 % (n=3) in the low-risk group and 21.6% in the high risk group (n=22). Engraftment failure, infectious disease, RRT and tumor progression were the major cause of death. These data indicate that the more immunosuppressive regimen for engraftment, infection and tumor control at transplant are important to obtain better results.

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ALTERNATIVE DONOR HEMATOPOETIC STEM CELL TRANSPLANTATION (HSCT) FOR ACUTE AND CHRONIC LYMPHOID MALIGNANCIES: 20 YEAR EXPERIENCE OF THE LEUKEMIA/BMT PROGRAM OF BRITISH COLUMBIA

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The role of alternative, unrelated (UD) or HLA mismatched related (mmrd) HSC donors for acute and chronic lymphoid