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### CD300A AND CD300C ON PLASMACYTOID DENDRITIC CELLS ARE DOWN-REGULATED BY TLR7 AND TLR9 LIGAND INDUCED TYPE I INTERFERON

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Plasmacytoid dendritic cells (pDC) constitute a distinct population of DC in the peripheral and secondary lymphoid organs. After activation with the ligands for Toll-like receptors (TLRs), particularly TLR7 and TLR9, pDC secrete large amounts of type I interferons and differentiate into mature DC, expressing co-stimulatory molecules and other cytokines. New immunoregulatory molecules on human pDC were sought and their regulation by TLR ligands assessed by pDC gene expression profiling. We established that both the CD300a and CD300c cell surface molecules are expressed by pDC. Because CD300 molecules play important roles in regulating immune responses, we investigated their contribution to pDC function in more detail. First, their down-regulation by CpG-ODN was confirmed by real time PCR and RT-PCR for CD300a and CD300c. Using the monoclonal antibody CMRF-35, to detect both CD300a and CD300c, we demonstrated that both TLR7 and TLR9 ligands down-regulated cell surface CD300a and CD300c. We showed that exogenous IFN-$\alpha$ down-regulated CD300a/c expression in pDC suggesting that the TLR ligands induced down-regulation of CD300a/c might be an indirect effect. In subsequent experiments, we added neutralizing antibody to IFN-$\alpha$ and found that it abolished the CpG-ODN induced CD300a/c down-regulation.

The effect of CD300a and CD300c activation on the function of pDC was investigated by cross-linking CMRF-35 on pDC. This had no effect on CD80, CD83 and CD86 expression, but decreased MHC-II expression. Significant reductions in pDC TNF-$\alpha$ and IL-6 production occurred after CMRF-35 cross-linking, however, in marked contrast, CpG-ODN induced IFN was increased in these experiments. Thus the immune regulators CD300a and CD300c regulate the cytokine production in pDC, whilst the pDC released cytokines regulated the CD300a/c expression. This suggests that CD300 molecules may play a pivotal role in fine tuning pDC driven immune responses and may contribute to the pDC biology of allogeneic bone marrow transplantation.

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### RECENT TRENDS IN UNRELATED DONOR STEM CELL TRANSPLANTATION: A REPORT FROM THE ABMTRR

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**Aim:** To investigate and highlight recent trends among patients undergoing allogeneic haematopoietic stem cell transplant (HSCT) with unrelated donors (URD) in Australia and New Zealand. **Methods:** Patients were selected from the database of the Australasian Bone Marrow Transplant Recipient Registry (ABMTRR). Patients selected for this study had undergone HSCT with URD between the years of 2001 and 2006. **Results:** A total of 891 allogeneic HSCT with URD were performed in the years 2001 to 2006. The annual numbers have increased steadily, from 101 in 2001 to 172 in 2005 and 146 in 2006. A total of 257 HSCT (29%) involved patients aged up to 15 years, and 634 (71%) involved patients aged 16 or over. Among paediatric transplants, 128 (50%) utilised cord blood (including double cord), 96 (37%) utilised bone marrow and 33 (13%), peripheral blood. The major indication for transplant in paediatric HSCT was ALL (79, 31% of paediatric HSCT). Among adult transplants, the stem cell source was peripheral blood in 407 (64%), marrow in 188 (30%) and cord blood in 39 (6%). The major indication for adult transplant was AML (228, 36% of adult HSCT). The number of adult HSCT for patients aged 50 years or over increased from 20 in 2001 to 39 in 2006. The number of adult HSCT involving reduced intensity conditioning also increased, from 11 in 2001 to 48 in 2005 and 30 in 2006. **Conclusions:** The annual numbers of URD HSCT in Australasia have increased steadily in recent years. Recent trends in practice include increases in numbers of older patients and HSCT using reduced intensity conditioning. The ABMTRR is a valuable national resource which provides accurate and timely information on HSCT activity and outcome in these two countries.

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### EFFICACY AND TOXICITY OF A CONDITIONING REGIMEN WITH 8-GY TOTAL BODY IRRADIATION, FLUDARABINE AND CYCLOPHOSPHAMIDE FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC HEMATOLOGIC MALIGNANCIES

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We examined the efficacy and toxicity of a conditioning regimen with fractionated 8-Gy total body irradiation, fludarabine, and cyclophosphamide in allogeneic hematopoietic stem cell transplantation (HSCT) for pediatric hematologic malignancies. Among a total of 22 children who received related or unrelated HSCT, nine were transplanted with refractory disease and/or from HLA 2 or more-loci mismatched family donors. The Seattle grading system revealed that 18 patients had no regimen-related toxicity, whereas the remaining patients had grade I gastrointestinal toxicity alone. According to the National Cancer Institute Common Toxicity Criteria, Grade II or higher toxicity in the liver, mucosa, and gastrointestinal tract among eight organs was documented in approximately 10–35% of patients, and was attributed to engraftment syndrome and/or acute graft-versus-host disease. None of the patients developed graft failure. The estimated overall survival and leukemia-free survival (LFS) at 2 years were 56.3% and 46.7%, respectively, in 10 patients with acute lymphoblastic leukemia; 91.7% and 81.5%, respectively, in 12 patients with myeloid leukemia. The incidence of treatment-related mortality was 5.3% at 2 years. It is possible that our preparative regimen confers successful engraftment combined with minimized regimen-related toxicity, and a favorable LFS rate for children with hematologic malignancies, especially for those with myeloid leukemia.

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### ROLE OF RITUXIMAB FOR PROPHYLACTIC OR PREEMPTIVE THERAPY OF EBV-DNA-emia AND THERAPY OF EBV-PTLD IN HSCT RECIPIENTS: A SYSTEMATIC REVIEW

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**Objective:** To evaluate the role of rituximab for prevention and treatment of posttransplant lymphoproliferative disorder (EBV-PTLD) in HSCT recipients. DATA SOURCES: A PubMed search (1966-September 2007) was conducted using the key words: EBV, posttransplant lymphoproliferative disorder, stem cell transplantation, rituximab. References of relevant articles and abstracts from recent hematology and stem cell transplantation scientific meetings (2003–2007) were also reviewed. STUDY SELECTION AND DATA EXTRACTION: Prospective and retrospective studies identified from the data sources were evaluated, and all data deemed relevant were included in this analysis. DEFINITIONS: Prophylaxis of EBV-DNA-emia (EBV reactivation) – rituximab given to seropositive, EBV-DNA-negative patient (or when donor was seropositive) to prevent EBV reactivation. Preemptive therapy – rituximab given to an asymptomatic patient with EBV detected by a screening assay. Treatment of PTLD – rituximab applied to a patient with an overt EBV-PTLD. **Results:** High risk HSCT for PTLD development were allogeneic HSCT with following risk factors: unrelated/mismatch HSCT; T-cell depletion or ATG/OKT3 use; EBV serology mismatch; primary EBV infection; splenectomy. The risk increased with the number of risk factors. In addition to quantification of EBV DNA load, analysis of the level of EBV-specific T cell reconstitution during EBV reactivation might be an