Adenosine A_{2A} receptor ($A_{2A}R$) have been reported to promote T cell tolerance in several in vivo models, particularly in the GVHD setting; however it's role in engraftment is unclear. In this study, we examined the ability of an $A_{2A}R$ agonist to promote engraftment in a murine allogeneic bone marrow transplantation model. B6D2F1/J recipients were conditioned with 300 cGy and transplanted 24 hours later via lateral tail vein infusion with 2×10^6 T-cell depleted bone marrow cells from C57BL/6J (B6) donor cells ($H2^{kb}$ into $H2^{kb/d}$). Recipients received an $A_{2A}R$ agonist orally in a chow formulation (1000 mg/kg/day) beginning 2weeks before cell infusion and continuing for 9 weeks post transplantation. A second cohort also received the $A_{2A}R$ agonist using osmotic pumps (100 ng/kg/min) placed subcutaneously 48 hours prior to cell infusion, for 28days post transplantation as well as orally via the chow for the same time as the first group. A non-treatment transplant group was used as a control.

There was no apparent toxicity from the radiation or the drug, and all animals maintained normal blood counts throughout. Engraftment was observed in only the $A_{2A}R$ agonist treated groups and a 13 fold higher level of engraftment in the mice treated both subcutaneously and orally was observed. This engraftment appeared to be long term as the mice were followed out 5 months post transplant with all mice surviving.

As a possible mechanism of this effect, we measured the level of CXCR4 expression on the donor bone marrow cells (Lin^-) *in vitro* and observed that $A_{2A}R$ agonist (10 μM) treatment increased CXCR4 expression 1.6 fold compared to non-treatment on donor cells *in vitro*. To further investigate the effect of the $A_{2A}R$ agonist on engraftment, we are now repeating the same type of transplant using an $A_{2A}R$ Knock out mouse strain as the donor. We are also assessing the levels of SDF-1 in the serum of the recipients.

These preliminary results demonstrate that $A_{2A}R$ agonists may improve engraftment by increasing homing of the donor cells without increasing the risk of graft versus host disease and may be a significant addition to transplant regimens.

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Young Male Donors Provide the Best Chance of Meeting Requested Cell Dose for PBSC and Bone Marrow Transplantation

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Background: Be The Match Registry® facilitated over 3,300 peripheral blood stem cell (PBSC) transplants and over 1,000 bone marrow (BM) transplants in 2011. The dose of CD34+ cells for PBSC and total nucleated cell (TNC) count for BM impact engraftment after unrelated allogeneic transplant. This study was performed to evaluate the frequency of unrelated donor PBSC and BM collections that meet the transplant physician's requested dose and the role of the potential donor factors including age and gender.

Methods: A cohort of 1,020 BM and 3,469 PBSC collections from June 2011 through September 2012 were analyzed to compare whether the collected cell dose achieved the requested dose. Male and female donors were stratified in age groups according to their age at the time of collection (18-30, 31-40, 41-50, 51+) and assessed for the frequency their donated product met the requested cell dose and the number of cells collected per kg of donor weight.

Results: Of 1,020 BM collections analyzed, a median cell dose of 5.0 x 10-8 TNC/kg was requested with a median cell dose of 4.2 x 10^{-8} TNC/kg collected, resulting in 403 (39.5%) meeting the requested TNC dose. Of 3,469 PBSC collections, a median cell dose of 5.0 x 10^{-6} CD34+/kg was requested with a median cell dose of 8.1 x 10^{-6} CD34+/kg collected, resulting in 2,740 (79.0%) meeting the requested CD34+ dose. Increasing donor age resulted in a reduction of the donor's ability to supply the requested dose for both PBSC and BM collections. A statistically significant reduction in the number of cells collected per kg of donor weight was observed for PBSC collections, but not BM collections (Table 1). In addition, male donors met the requested cell dose more frequently than female donors for both BM (42% vs 35%) and PBSC (85% vs 65%) collections, as well as providing a significantly larger CD34+ cells/kg donor weight for PBSC (8.54 vs 7.59).

Conclusions: This study shows that younger donor age results in an increased likelihood of meeting the transplant physician's requested TNC or CD34+ dose. Lower donor age also increases the CD34+ cells/kg that are obtained from PBSC collections but not the TNC/kg obtained from marrow collections. In addition, male donors provided increased CD34+ cells/kg donor weight than female donors. Transplant center practice is often to select young male donors for patients, and this data provides evidence to support that such practice may increase the likelihood of a providing a product meeting a center's request.

Table 1

Donor Age (Gender)	Bone Marrow			PBSC		
	Requested Cell Dose Met	TNC X 10-8/kg Donor Weight	p Value	Requested Cell Dose Met	CD34+ X 10-6/kg Donor Weight	p Value
18-30	43%	2.95		80%	8.54	
31-40	39%	2.88	0.188	80%	8.15	0.002
41-50	32%	2.83	0.052	75%	7.66	< 0.0001
51-60	25%	2.96	0.906	72%	6.78	< 0.0001
18-60 (M)	42%	2.84		85%	8.54	
18-60 (F)	35%	3.05	0.004	65%	7.59	< 0.0001

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Novel Reduced Toxicity Conditioning Regimen for Older Severe Thalassemia Patients: Sequential Immunoablative Concept

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CIBMTR reported that severe thalassemia patients older than 7 years with hepatomegaly (> 2 cm below costal margin) achieved poor outcome after transplant; DFS = 55% since they had high rejection and mortality rates (Blood, 2011). We therefore developed the novel reduced toxicity conditioning (RTC) regimen to overcome these problems. Fifteen severe thalassemia patients, median age 17 years;