**Conclusion:** These demonstrated that safety and feasibility of third party UCB-derived MSCs use and co-infusion of UCB-derived MSCs can overcome graft dysfunction of UCBT.

# HISTOCOMPATIBILITY/ALTERNATIVE STEM CELL SOURCES

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### CORD BLOOD (CB) APGAR SCORE IS PREDICTIVE OF NEUTROPHIL ENGRAFTMENT AND GRAFT FAILURE PROBABILITIES FOR PLASMA DEPLETED/REDUCED CB PRODUCTS

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Nucleated cell (NC), CD34+ cell (CD34), and colony forming unit (CFU) doses have been proposed to measure CB potency - important for engraftment potential prediction and transplantation product selection. Though TNC is widely used for CB selection, its predictive value is not as robust as the progenitor cell measurements. CFU and CD34 suffer from high inter-laboratory coefficient of variance (CV) - decreasing the clinical utility as potency measures. Recently, the Duke Group proposed a CB APGAR scoring system composed of (a) a Pre-Cryopreserved Score (PCS) reflecting pre-freeze CFU, CD34, NC, and CB collected volume, as well as a (b) Composite Score (CS) which combines the PCS score with post-thaw NC, CD34, CFU and mononuclear cell dose. Based on single, myeloablative and first (SMF) transplants of largely pediatric patients performed at Duke and using mostly red cell reduced (RCR) CB, the PCS and CS scores were shown to be predictive of graft failure, neutrophil and platelet engraftment. With CIBMTR-audited outcome data of transplanted CB products from a multi-national CB bank, we sought to validate the CB APGAR system on a patient population with mostly adults, heavy representation of minority and international patients, and on both SMF transplants, and all transplants (All) using plasma depleted/reduced (PDR) CB products. The PCS and CS table below shows the day 42 neutrophil engraftment cumulative incidence (ANC500) and graft failure probability (GF) comparisons of the Duke data with PDR transplants for both SMF and All transplants. For each of the PCS and CS strata compared, ANC500 and GF appeared to be similar among the Duke SMF, StemCyte SMF and All cohorts. We conclude that the CB APGAR score, especially the PCS, is an easy-to-use and reproducible potency measurement for CB selection by transplant centers that is highly predictive of ANC500 engraftment and GF for (1) RCR as well as PDR CB, (2) for mostly pediatric patient population as well as for mixed populations of adults and children, and (3) for minority and international patients. Whether the method can be applied to double, non-myeloablative and repeat CB transplants remains to be seen. Lastly, for the same PCS or CS strata, PDR CB appear to have similar engraftment and GF probabilities as RCR CB; therefore, the Duke CB APGAR is applicable to CB products with or without RBC reduction and reflects potency of CB products processed and stored by various methods at different CB banks.

**Table 1. ANC 500 Engraftment Cumulative Incidence & Graft Failure Probabilities**

| ANC 500 | Duke SMF | PDR SMF | PDR All |
|---|---|---|---|
| PCS≥7.75 | 93% (86-100%) | 100±18% | 83±19% |
| PCS<7.75 | 75% (69-81%) | 78±9% | 76±4% |
| HR | 2.44 (1.78 - 3.59) | 2.43 (0.85 - 6.95) | 1.92 (0.78 - 4.68) |
| CS≥13.5 | 90% (84 - 95%) | 94±14% | 84±11% |
| CS<13.5 | 69% (61 - 78%) | 68±12% | 77±6% |
| HR | 2.31 (1.73 - 3.08) | 1.54 (0.73 - 3.26) | 1.19 (0.78 - 1.82) |
| **Graft Failure Probability** | **Duke SMF** | **PDR SMF** | **PDR All** |
| PCS≥7.75 | 7% (3-17%) | 0±18% | 17±19% |
| PCS≥5.5 & <7.75 | 19% (12-30%) | 15±14% | 18±10% |
| PCS≥4.25 & <5.5 | 26% (16-39%) | 6±13% | 14±9% |
| PCS<4.25 | 32% (22-45%) | 38±12% | 29±5% |

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### IN-VIVO EXPANSION OF T REGULATORY CELLS BY RAPAMYCIN IN A CALCINEURIN-INHIBITOR FREE GVHD PROPHYLAXIS IN UNMANIPULATED HAPLOIDENTICAL STEM CELL TRANSPLANTATION (SCT)

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**Background:** Tregs are attractive candidates for clinical modulation of excessive immune responses. In SCT mouse models, the adoptive transfer of purified natural Tregs has been shown to prevent GvHD, while sparing a significant GvL effect. Tregs' suppressor function has been demonstrated to be critically dependent on IL-2, therefore cyA significantly reduces the function of allostimulated Tregs.

**Aim:** To address the role of Tregs in human SCT, we focused on a calcineurin inhibitor-free GvHD prophylaxis. We tested this hypothesis in haploidentical peripheral blood stem cells SCT without any *in-vitro* manipulation.

**Patients and Methods:** Since 2007, 68 pts underwent allo-SCT for AML (43), ALL (9), MDS (3), MPD (4), NHL (4) or HD (5). Median age was 48 years (range 14-69). At SCT all but 8 pts were in advanced phase. Conditioning included Treosulfan (14 g/m$^2$ for 3), Fludara (30 mg/m$^2$ for 5) and an *in-vivo* T and B-cell depletion, by ATG-Fresenius (10 mg/kg for 3) and Mabthera (a single 500 mg dose). All pts received allogeneic PBSC from an HLA-haploidentical related donor without any *in-vitro* positive selection. GvHD prophylaxis consisted of Rapamycin (target level 8-15 ng/ml, till day +60) and MMF (15 mg/kg tid till day +30).

**Results:** All pts but 3 had neutrophil engraftment. CI of grade 2-4, grade 3-4 aGvHD and cGvHD were 22%, 11% and 26%. 100 days TRM and relapse incidence at 1 year were 17% and 44%. Projected OS at 1 year is 39%. Immunoreconstitution was fast and sustained with a median 220 circulating CD3+cells/µL on day +30. We detected high levels of CD4+CD25+CD127- FOXP3+ Tregs (up to 30% of circulating CD4+ T lymphocytes) on day +30. These cells were able to suppress in vitro proliferation of autologous effector cells. This observation was further reinforced at a molecular level. We applied a quantitative RT-PCR based methylation assay that enables a specific and sensitive determination of T regs numbers by measuring demethylated FOXP3 at T reg specific demethyleted region (TSDR). An expansion of cells carrying FOXP3 demethylation was evident in our pts, but not in a control group of pts receiving mismatched SCT and cyclosporine.

**Conclusions:** Rapamycin-Mycophenolate-ATG are effective as GvHD prophylaxis in unmanipulated haploidentical peripheral SCT and are associated with an early T-cell immunoreconstitution characterized by the *in-vivo* expansion of Tregs. Further studies are warranted to gain insight correlations between Tregs expansion and SCT outcome.

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### 8/8 HIGH-RESOLUTION HLA MATCH RATE: THE IMPACT OF RACE

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**Aim:** Calculation of the 8/8 (HLA-A, B, C, DRB1) high-resolution (HR) match rate using real patient unrelated donor (URD) searches presents a biased sample for reasons including access to treatment, financial barriers and incomplete donor testing. A study was designed to estimate the true match rate for Caucasian (CAU), Hispanic (HIS), Asian/Pacific Islander (API), and African American (AFA) groups, representing the four largest race groups in the US population.

**Methods:** 1344 URD searches were performed for pseudopatients (PP) who were randomly selected, previously HR tested donors in the NMDP's Be The Match Registry (BTMR). Searches were based on a fixed BTMR file as of January 2009. Search results from CAU, HIS, API, and AFA PP were classified as follows: