POSTER SESSION 2: HISTOCOMPATIBILITY/ALTERNATIVE STEM CELL SOURCES

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A Novel State Funded Program to Increase Cord Blood Collections for Public Banking

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The Umbilical Cord Blood Collection Program (UCBCP), administered by UC Davis Health System, is a new statewide public program designed to capture the genetic diversity of Californians through collection of cord blood units (CBUs) for unrelated transplantation. This program is funded with revenue from California state birth certificate fees. The vision for the implementation of the mission by UCBCP is to expand access to cord blood stem cells by targeting current inventory deficiencies to provide greater probabilities that people of any race or ethnicity will find an appropriately matched CBU in the National Cord Blood Inventory (NCBI). In support of these goals, the UCBCP plans to promote targeted education programs for health professionals and to utilize best practices for cord blood collections. Through this process UCBCP will facilitate the provision of high quality CBUs for transplantation, as well as promote research and development of effective treatments utilizing cord blood stem cells by making the CBUs collected that do not meet the criteria for banking available to researchers.

Much progress has been made toward developing a sustainable cord blood collection program for the state over the first year. The UCBCP leadership team has been developed and we have identified cord blood banks through an RFP bidding process that will be partnered with hospitals in various parts of the state. The UCBCP is in varying stages of contract negotiations with three of the public banks who responded to the RFP. To date negotiations are in place for California collections in Southern California to occur at five Scripps hospitals, funded in part by the UCBCP; and by collections set to begin at 13 Kaiser Hospitals, also with support from the UCBCP. In the Central Valley, a collection site is being developed in Fresno, at the Community Regional Medical Center. In the Bay area the UCBCP is in negotiations with several hospitals, including California Pacific Medical Center and Alta Bates. In the Sacramento area, the UCBCP has commitments from 2 hospitals and are seeking the same from two additional birthing centers. At UCDHS, we have received IRB approval for the program, and have now initiated cord blood collections for purposes of collector training and process validation.

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Immunophenotypic, Proteomic and Genomic Characterization of Human Cord Blood (CB) vs Peripheral Blood (PB) CD56^{+dim} NK Cells: A More Pro NK Phenotype in CB

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CB is a viable alternative source of allogeneic HSC for the treatment of malignant and non-malignant disease (Cairo et al *BBMT* 2008, Szabolcs/Cairo et al *Sem in Hem* 2010). NK cells play a role in innate and adaptive immunity and are characterized as CD56^{+} cell population. Cytotoxic CD56^{+dim} cells make up 90% of PB NK populations (Shereck/Cairo *PBC* 2007). We previously ex-vivo expanded CB MNC into various phenotypes of CD56$^{+dim\ and\ +bright}$ NK cells (Ayello/Cairo *BBMT* 2006; *Exp. Hematology* 2009). NK cell anti-leukemic and anti-rejection activities may be essential to the interplay between GVT effects and GVHD after haploidentical HSCT (Dunbar et al, *Haematologica*, 2008).

Objective: To determine differential expression, immunophenotype and genomic and proteomic signatures in CB vs PB CD56^{+dim}NK cells.

Methods: CB NK CD56 cells (94% enrichment) isolated using a standard kit (Miltenyi Biotec) and sorted into CD3^{-}/CD56^{bright} and CD3^{-}/CD56^{dim} subsets. NKR expression was measured by flow-cytometry. Isolated RNA from CB and PB CD56^{+dim}cells underwent microarray studies (Affymetrix, U133A_2). (Agilent GeneSpring and Ingenuity pathway analyses, IPA). Proteomic performed by LC MS/MS with iTRAQ labeling and analyzed with SEQUEST, ProteinProphet, and INTERACT.

Results: There was no difference in NKR expression of CD16, KIR2DL1, KIR2DS1, KIR2DL2, CD161, NKG2C, NKp44, and NKp46 in CB vs. PB CD56^{dim}. There was a significant difference in CB vs PB CD56^{+dim} NK cells in gene expression including: pro-apoptotic genes: CASP10 (3.1F), TNFSF11 (4.7F), CDC2 (3.0F), BCL2L1 (4.3F), NOTCH2 (1.5F); and cell development: PBX1 (7.6F), IL1RN (5.1F), CD24 (5.3F), CD34 (3.5F), CD55 (2.1F), CCL13 (2.2F). Further, there was a significant change in protein expression, CB vs PB CD56^{+dim}cells over 35 proteins, including CELSR1 (25.0F), BLM (25.0F), BDNF (20.0F), PKD1 (16.7F), NOTCH2 (16.7F), BIRC2 (12.5F), AIFM1 (12.5F), EP400 (5.3F), PBX1 (3.9F), SIRT2 (2.9F), LETM1 (2.9F), and ESR2 (2.4F). qRT-PCR and Western blot analysis validated the genomic and proteomic results, respectively.

Conclusion: These results suggest that CB vs PB CD56^{+dim} NK cells are more prone to undergo programmed cell death (apoptosis), over expression of numerous pro-apoptotic genes, and may be earlier in development (pro-NK) with significant over expression of CD34.

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Double-Unit Cord Blood Transplantation (DCBT) for Acute Leukemia: High Disease-Free Survival in Adults and Children with Comparable Survival in European and Minority Patients

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