adult mouse bone marrow, and compared the effects both cell types could exert once grafted inside an injured spinal cord. Cells were injected into the spinal cord of mice that right after thoracic spinal cord contusion. Our results indicate that both MSC and NCSC-injected mice recovered locomotion abilities faster than control mice (as assessed by BMS scoring). Additionally, we observed that after 28d post-injury, the lesion volume tended to decrease in mice that received cell graft compared to control group. Interestingly, it appeared that MSC seemed to be able to modulate inflammation in the lesion, more than NCSC. Indeed, MSC-graft increased early neutrophil and macrophage recruitment in the bloodstream and inside the spinal cord, and increased the number of arginase-1+ cells remaining in the spinal cord after 28d. In parallel, we compared the secretome of both NCSC and MSC: MSC secreted high levels of chemokines reflecting possible immunomodulating properties, by attracting macrophages in a chemotactic manner. Altogether, those results should help to improve and optimize cell-based therapies parameters and/or to define precise and efficient pharmacological treatments for SCI patients.

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HUMAN CORD BLOOD DERIVED CD14 CELL THERAPY PROVIDES NEUROPROTECTION IN AQUIRED BRAIN INJURY

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Our lab is developing cord blood (CB)-derived cell therapies for neuronal damage resulting from hypoxic-ischemic [HI] insult. We are using mouse brain slice cultures subjected to oxygen-glucose deprivation [OGD] to study how CB cells mediate neuroprotection. We previously reported that CD14+ cells account for most of the neuroprotective activity of CB cells in this model. We used immunohistochemistry to further detail the mechanisms of this neuroprotection. Brain slice cultures established from C57BL/6J mice were subjected to 1h OGD on day 9 treated with cell populations or medium immediately after normal conditions were restored. CB CD14+ and CD14+ depleted cells were immunomagnetically prepared from CB mononuclear cells within 48h of collection. Human adult peripheral blood (PB) CD14+ populations were also tested. After 72h, slice cultures were fixed and stained with antibodies to detect astrocytes (GFAP), neurons (NeuN), oligodendrocytes (olig2), and microglia (Iba1). Glial and neuronal cells were enumerated in contiguous images of the periventricular regions using fluorescence confocal microscopy. We also characterized the effects of cell treatment on primary human astrocytes subjected to OGD stress in a microfluidics chamber. In both culture systems treatment with CB-CD14+ cells resulted in an increase in NeuN+ neurons and a decrease in the number of activated GFAP+ astrocytes following OGD shock. Cultures treated with CB-CD14+ had 2-fold more surviving neurons than those not treated. CD14 depleted cells did not protect cultures. We did not detect changes in microglia or oligodendrocytes following cell treatment. We conclude that CB CD14+ cells demonstrate a greater neuroprotective and anti-neuroinflammatory effect than PB CD14+ cells. CB CD14+ cells could mediate neuroprotection either directly on neurons or indirectly through modulation of astrocyte activation. We confirm the therapeutic potential of CB CD14+ cells in the setting of acquired HI.

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ALGEBRAICALLY DESIGNED OF A NOVEL POLY-PEPTIDE TARGETED HIGHLY CONSERVED CHEMO-STRUCTURE ON A REVEALING CORE SIGNALING REGULATORY MECHANISM FOR THE CORD BLOOD STEM CELL SURVIVAL AND SELF-RENEWAL. A VIRTUAL MASS-LOW SCREENING OF CHEMICAL LIBRARIES WITH SUPERAGONIST INSIGHTS INTO THE STEM CELL EXPANSION PATHWAYS

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High Throughput nano-druggable-based screening approaches of existed chemical libraries have been carried out to identify small binding pocket domains for the interaction docking molecule analysis of the self-renewal of human cord blood cell related regulatory peptide transcripts. Stem cell factor (SCF) is a cytokine that mediates its diverse cellular responses by binding to and activating the receptor tyrosine kinase (RTK) KIT (also known as SCF receptor). KIT was initially discovered as an oncogene in a feline retrovirus that captured an activated and truncated form of the surface receptor (Besmer et al., 1986). Here, for the first time we used a multi-algorithm faced approach consisted of the following four principle steps: recore fragment-ligand based extraction out of commercially available chemical compounds, selection of high enthalpically energy candidate core fragments, docking of recored fragments, and fragment linkage expansion. Using our automated docking and linking high-throughput chemical screening, we identified twenty small molecules with high free energy docking energy against human cord stem cells (SCF) KIT. By characterizing their mechanisms of action, we discovered an essential newly intelligent computer-aided designed poly-pharmacophore and its signaling activities for the mechanistic stimulation of the KIT-SCF cytokine mediated complex for with Super-Agonist Insights into the Stem Cell Expansion Pathways.

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G-CSF PRIMED DONOR HAEMATOPOIETIC STEM CELL COLLECTIONS ARE ASSOCIATED WITH REDUCED VIABLE T CELL YIELD FOR DONOR LYMPHOCYTE INFUSION

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Donor Lymphocyte Infusions (DLI) are frequently used to enhance donor engraftment or treat relapse following allogeneic stem cell transplant. We aim to determine the factors that influence post-thaw viable $CD3^+$ recovery of cryopreserved DLI's. Unprimed DLI($CD3^+$) at some time after transplant (n=38) and G-CSF primed DLI cryopreserved from the stem cell product after minimum infusion of $5.0x10^6$/kg viable $CD34^+$ cells for transplant (n=35) were analysed. Factors analysed included viable $CD45^+$,$CD3^+$ and total nucleated cell (TNC), pre- and post-thaw recovery, donor sex/age, neutrophil and platelet content, cryopreserved nucleated cell concentration and the time interval between collection and freezing. Statistical analysis included parametric and non-parametric tests and two way analysis of variance.

DLI harvests were obtained from 42 related donors and 31 unrelated donors. G-CSF primed collections contained a higher percentage of granulocytes, a lower number of platelets and were cryopreserved at a higher cell concentration. Although recovery of TNC was improved after thawing of G-CSF primed products, recovery of viable $CD3^+$ cells was reduced (62% for unprimed collections v 49% for G-CSF primed). Multivariate analysis showed the factors significantly affecting viable $CD3^+$ recovery were: 1) harvest type: G-CSF primed compared to unprimed: $P<0.001$; 2) Time to cryopreservation $P=0.002$ for <10 hours compared to 10-24 hours and >24 hours.

Achieving adequate viable T cell doses for DLI infusions requires cryopreservation of over 10^8/kg $CD3^+$ cells. Our lab makes allowance for thawing losses of around 30% to 50% when freezing DLIs. Using G-CSF primed stem cell products and/or delaying time to cryopreservation can reduce viable T cell numbers upon thawing and may limit DLI doses available for infusion, particularly unrelated collections from overseas. BMT Hospitals planning to administer multiple DLIs post-transplant may need to take these factors into consideration.

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SAFETY PROFILE OF TRANSPLANTS WITH HPC, APHERESIS PRODUCTS POST THAW DILUTED 1:2 WITH 10% DEXTRAN40 COMPARED TO POST THAW UNMANIPULATED HPC, APHERESIS TRANSPLANTS IN ADULT PATIENTS

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Reducing post-thaw osmotic shock will maintain viability of all cellular fractions, including highly fragile granulocytes, will reduce cytokines release and dead cell clumping. The rate of severe adverse reactions has been shown to be associated with a high TNC / granulocyte counts.

Methods: We validated a post thaw dilution procedure for HPC, Apheresis products using only 10%Dextran vs. washing or dilution with 5% Dextran40 /2.5% Human Serum Albumin (Dex/HSA).There is no significant difference in CD34+ cell viability among those dilution and wash methods; however,