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Comparative study between two *ex vivo* cell expansion models of CD34+ cells from cryopreserved umbilical cord blood co-cultured with encapsulated mesenchymal stem cells

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The expansion of primitive hematopoietic stem cells (HSCs) with long-term restocking capacity is a technological development necessary to increase the use of umbilical cord blood units in HSC transplantation. At present, CD34+ and CD133+ HSC expansions are reported with adequate expansion factors, however a model is required in which maturation is not induced to compromise lineage progenitors. This work compares the expansion factor (EF) of HSC CD34+/CD90+/CD49f+ using two models of expansion (static and perfusion), the model incorporates mesenchymal cells of Wharton gelatin of CD146+ umbilical cord encapsulated in calcium alginate 2%, and recombinant human cytokines involved in self-renewal (SCF, TOP, FL, IL3, IL6), and the activation of the NOTCH pathway using the DLK-1 agonist in a 12-day culture. NOTCH uses the DLK-1 agonist in a 12-day culture. The perfusion culture vs the static yielded higher EFs for both CD34/45- (8.46 vs. 3.99) and CD49+/CXCR4+HSC (12.97 vs. 2.95) cells. When comparing the two models, it is evident that the perfusion model is statistically significant until day 8 with respect to the static one $p<0.005$. These results are superior to any study published to date. Comparing the expansion factor in the two culture models, this study suggests the importance of MSC CD146+ in co-cultures with HSC, by sustaining the selective expansion of cd34+/CD90+CD49f+ without favoring the expansion of other subpopulations of Progenitors taken from unknown lineages. These findings need to be replicated in larger sample sizes in *in vivo* models and clinical trials of HSC transplantation in humans to demonstrate their importance in important clinical outcomes.

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