

Cord Blood Hematopoietic Stem Cell Expansion Ability of Mesenchymal Stem Cells Isolated From Different Sources

Authors : Ana M. Lara, Manuela Llano, Felipe Gaitán, Rosa H. Bustos, Ana Maria Perdomo-Arciniegas, Ximena Bonilla

Abstract : Umbilical cord blood is used as a source of progenitor and stem cells for the regeneration of the hematopoietic and immune system to treat patients with different hematological or non-hematological diseases. This stem cell source represents an advantage over the use of bone marrow or mobilized peripheral blood because it has a lower incidence rate of graft-versus-host disease, probably due to fewer immunological compatibility restrictions. However, its low cellular dose limits its use in pediatric patients. This work proposes the standardization of a cell expansion technique to compensate for the dose of infused cells through the ex-vivo manipulation of hematopoietic progenitor cells from umbilical cord blood before transplantation. The expansion model is carried out through co-cultures with mesenchymal stem cells (MSC) from bone marrow (BM) and less explored fetal tissues such as Wharton's jelly (WJ) and umbilical cord blood (UCB). Initially, a master cell bank of primary mesenchymal stem cells isolated from different sources was established and characterized following International Society of Cell Therapies (ISCT) indications. Additionally, we assessed the effect of a short 25 Gy cycle of gamma irradiation on cell cycle arrest of mesenchymal cells over the support capacity for the expansion of hematopoietic stem cells from umbilical cord blood was evaluated. The results show that co-cultures with MSC from WJ and UCB allow the cellular dose of HSPC to be maximized between 5 and 16 times having a similar support capacity as BM. In addition, was evaluated the hematopoietic stem progenitor cell's HSPC functionality through the evaluation of migration capacity, their differentiation capacity during culture time by flow cytometry to evaluate the expression of membrane markers associated with lineage-committed progenitors, their clonogenic potential, and the evaluation of secretome profile in the expansion process was evaluated. So far, the treatment with gamma irradiation maintains the hematopoietic support capacity of mesenchymal stem cells from the three sources studied compared to treatments without irradiation, favoring the use of fetal tissues that are generally waste to obtain mesenchymal cell lines for ex-vivo expansion systems. With the results obtained, a standardized protocol that will contribute to the development of ex-vivo expansion with MSC on a larger scale will be achieved, enabling its clinical use and expanding its application in adults.

Keywords : ex-vivo expansion, hematopoietic stem cells, hematopoietic stem cell transplantation, mesenchymal stem cells, umbilical cord blood

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