

The Role of Mesenchymal Stem Cells in the Treatment of Hematological Diseases

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The mesenchymal stem cells (MSCs) are a group of cells capable of differentiating into mesenchymal tissues, such as bone, cartilage and fat. Their morphology is fibroblast-like. The surface phenotype of these cells is positive for CD29, CD44, CD73, CD105 and CD166 and negative for CD34, CD45, CD3, CD7, CD14 and CD133. MSCs can be isolated from bone marrow, blood, adipose tissue, placenta, amniotic fluid, Wharton's jelly of the umbilical cord, and cord blood. In spite of the different gene expression profiles seen in MSCs from different origins, a set of core gene expression profiles was preserved in these kinds of MSCs. The similar characteristics of MSCs from different sources support the applicability for cell-based therapies.

MSCs also have the characters of adhesion molecules, cytokine production, interactions with hematopoietic cells, low inherently immunogenic, and immunomodulation. Therefore, MSCs can be applied to regeneration medicine, repair damaged tissue, graft versus host disease (GVHD), immune disorder, rejection of organ allografts, and enhance engraftment of hematopoietic stem cell transplantation (HSCT). At present, MSCs have been used in hematological diseases, cardiovascular diseases, osteogenesis imperfecta, neurological diseases, and some inherited diseases, such as Hurler syndrome and metachromatic leukodystrophy.

Chemotherapy, radiation therapy, or their combination damages the bone marrow microenvironment and may result in diminished or delayed hematopoiesis. MSCs have been suggested to be the precursor cells in the bone marrow stroma that provide a scaffold and promote hematopoiesis. In vivo, in humans, autologous and allogeneic MSCs are safe to infuse with no acute adverse events and no formation of ectopic tissue [1-5].

MSCs have low immunogenicity and immunomodulatory effects. MSCs have been shown to suppress primary and ongoing mixed lymphocyte reactions. The immunomodulatory effects of MSCs make them useful for immunotherapy, although the exact mechanism of action is unknown. The immunomodulatory effect in vivo is evident by reversal of therapy-resistant acute GVHD [4,5]. MSCs are a very promising treatment for severe GVHD.

Many questions regarding MSCs cannot be answered today. When administered in vivo, MSCs have been almost impossible to detect. Clinical effects of MSCs have clearly been observed; however, it is possible that the effect of the MSCs has been due to local production of growth factors rather than to direct participation of MSCs in the healing process. Much more work is required to increase our knowledge about MSCs. However, we need not wait for such additional data, because significant effects have already been noted in the clinic.

Overall, in HSCT, MSCs can enhance engraftment of hematopoietic cells and reduce the risk of graft failure[1-3]. This may be particularly important in cord blood transplantation, in which the limited cell dose delays engraftment and there is an increased risk of graft failure. MSCs can also be used as GVHD treatment in HSCT [4,5].

REFERENCE

1. Lazarus HM, Koc ON, Devine SM, et al. Cotransplantation of HLA-identical sibling culture-expanded mesenchymal stem cells and hematopoietic stem cells in hematologic malignancy patients. *Biol Blood Marrow Transplant*. 2005; 11: 389–398.
2. Le Blanc K, Samuelsson H, Gustafsson B, et al. Transplantation of mesenchymal stem cells to enhance engraftment of hematopoietic stem cells. *Leukemia*. 2007; 21: 1733-1738.
3. Ball LM, Bernardo ME, Roelofs H, et al. Cotransplantation of ex vivo expanded mesenchymal stem cells accelerates lymphocyte recovery and may reduce the risk of graft failure in haploidentical hematopoietic stem-cell transplantation. *Blood*. 2007; 110: 2764-2777.
4. Le Blanc K, Rasmusson I, Sundberg B, et al. Treatment of severe acute graft-versus-host disease with third party haploidentical mesenchymal stem cells. *Lancet*. 2004; 363: 1439–1441.
5. Ringden O, Uzunel M, Rasmusson I, et al. Mesenchymal stem cells for treatment of therapy-resistant graft-versus-host disease. *Transplantation*. 2006; 81: 1390–1397.