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Factors released following stem cell transplantation therapeutically impact serious burns

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Cell transplantation researchers have successfully used bone marrow-derived mesenchymal stromal cells (MSCs) to treat a variety of diseases and conditions. Now, using injections of MSCs, a research team in Brazil has successfully treated laboratory rats modeled with severe burns. They found that the MSCs accelerated healing, enhanced local blood supply, affected the immune system in a positive way, secreted beneficial growth factors with anti-inflammatory properties, and ultimately provided higher survival rates than in control animals not treated with MSCs.

Their study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line as an unedited early e-pub.

"Major skin burns are difficult to treat," said study co-author Dr. Maria Carolina Oliveira Rodrigues of the Department of Internal Medicine at the Ribeiro Preto Medical School in Sao Paulo, Brazil. "Besides complications associated with the wounds, such as infection, there may also be immune system and organ impairment."

The benefit of using MSCs is their ability to self-renew and differentiate into a variety of specialized cell types, such as osteoblasts (cells contributing to bone formation), chondrocytes (cartilage cells), adipocytes (fat cells), myocardiocytes (the muscle cells that make up the cardiac muscle), and neurons (nervous system cells).

MSCs have shown the ability to modulate the immune response and reduce local inflammation. They can be isolated from a variety of sources, such as adipose (fat) tissues, tendons, peripheral blood, umbilical cord blood and bone marrow. MSCs derived from bone marrow have so far been utilized the most and have been successfully transplanted in a number of disease models where they offer therapeutic benefits.

In this study, the researchers used bone marrow-derived MSCs from xenogeneic (other species) sources, in this case MSCs from mouse bone marrow for the treatment of rats, because using xenogeneic sources, said researchers, would allow for faster treatment than using the test animal's own (autologous) MSCs.

"We observed that at 30 days after treatment the MSC-treated animals presented more granulated tissue, which indicates a healing process is underway," said corresponding author Dr. Carolina Caliari-Oliveira. "After 45 days we saw that the MSC-treated group was healing faster than the control group. By 60 days, the MSC-treated group showed a larger portion of healed areas within the burn wounds (90.81 percent) than the control group (76.11 percent). We believe this result may be due to the angiogenic potential of MSCs to enhance local blood supply and thus contribute to tissue regeneration."

The researchers also noted that by day 60 only a few MSCs were detected. "We believe they were likely rejected by the xenogeneic barrier," wrote the researchers. "MSC rejection, however, may indicate that the immune system is able to control the presence of allogeneic (other donated) or xenogeneic cells."

Since their study demonstrated that xenogeneic MSCs were able to decrease mortality, modulate the immune response, and enhance wound healing, the researchers concluded that their study was "an important

step toward future applications of MSCs as a regenerative therapy for patients affected by deep burns."

"Severe thermal burns can result in systemic inflammatory response syndrome (SIRS). Treatment with MSCs seems to quell the immune response to the wounds. In addition, MSCs may also ameliorate the negative effects and expedite healing through secretion of factors that contribute to angiogenesis and lessen skin fibrosis and scar formation. The exact mechanisms behind more rapid and effective healing after MSC treatment needs to be further explored, as does the benefit of using xenogeneic rather than autologous cells." says Dr. Paul Sanberg, Senior Vice President of Research and Innovation at the University of South Florida. "A promising clinical trial is being conducted (ClinicalTrials.gov Identifier NCT02104713) at the University of Miami using allogeneic MSCs to treat 2nd degree burns. Perhaps further studies can help elucidate the effectiveness of such treatment."

More information: Caliari-Oliveira, C.; Yaochite, J. N. U.; Ramalho, L. N. Z.; Palma, P. V. B.; Cunha, F. d.-Q.; De Souza, D. A.; Frade, M. A. C.; Covas, D. T.; Malmegrim, K. C. R.; Rodrigues, M. C. O.; Voltarelli, J. C. Xenogeneic Mesenchymal Stromal Cells Improve Wound Healing and Modulate the Immune Response in an Extensive Burn Model. Cell Transplant. Appeared or available on-line: May 7, 2015. http://ingentaconnect.com/content/cog/ct/pre-prints/content-CT-1389_Caliari-Oliveira_et_al

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