



ALLOGENEIC MESENCHYMAL STEM CELLS IMPROVE THE WOUND HEALING PROCESS OF SHEEP SKIN

Gomiero Chiara (1), Martinello Tiziana (1), Perazzi Anna (2), Gemignani Francesco (2), DeBenedictis Giulia Maria, Ferro Silvia (1), Zuin Matteo (3), Martines Emilio (3), Brun Paola (4), Maccatrozzo Lisa (1), Melotti Luca (1), Broeckx Sarah (5), Spaas Jan (5), Chiers Koen (6), Iacopetti Ilaria (2), Patruno Marco (1)

(1) University of Padua, Department of Comparative Biomedicine and Food Science. (2) University of Padua, Department of Animal Medicine, Production and Health. (3) Consorzio RFX, Padua. (4) University of Padua, Department of Molecular Medicine. (5) Global Stem Cell Technology-ANACURA group, Evergem, Belgium. (6) Department of Pathology, Bacteriology and Poultry Diseases, University of Gent, Belgium.

Skin wound healing includes a system of biological processes, collectively restoring the integrity of the skin after injury. Healing by second intention refers to repair of large and deep wounds where the tissue edges cannot be approximated and substantial scarring is often observed [1]. The objective of this study was to evaluate the therapeutic effects of allogeneic mesenchymal stem cells (MSCs) in second intention healing using a surgical wound model performed on the back of six Bergamasca sheep. MSCs are known to contribute to the inflammatory, proliferative, and remodeling phases of the skin regeneration process in rodent models, but data are lacking for large animal models [2]. This study used three different approaches (clinical, histopathological, and molecular analysis) to assess the putative action of allogeneic MSCs at 15 and 42 days after lesion creation. At 15 days post-lesion, the wounds treated with MSCs showed a higher degree of wound closure, a higher percentage of re-epithelialization, and increased contraction in comparison to a control group. At 42 days, the wounds treated with MSCs had more mature and denser cutaneous adnexa compared to the control group. The MSCs-treated group showed a complete absence of inflammation and expression of CD3+ and CD20+. Moreover, the mRNA expression of hair-keratine (hKER) was observed in the MSCs-treated group 15 days after wound creation and had increased significantly by 42 days post-wound creation. Collagen1 gene (Col1 α 1) expression was also greater in the MSCs-treated group compared to the control group at both days 15 and 42. Peripheral blood-derived MSCs may improve the quality of wound healing not only for superficial injuries, but also for deep lesions. MSCs did not induce an inflammatory response and sped up the appearance of granulation tissue, neovascularization, structural proteins, and skin adnexa.

[1] You HJ, Han SK. Cell therapy for wound healing. *Journal of Korean Medical Science* 2014;29:311-319. [2] Music E et al. Sheep as a model for evaluating mesenchymal stem/stromal cell (MSC)-based chondral defect repair. *Osteoarthritis Cartilage*. 2018 Mar 23.