Adipose-derived aldehyde-dehydrogenase-expressing cells accelerate re-vascularization of collagen-glycosaminoglycan scaffolds

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INTRODUCTION: Collagen-glycosaminoglycan (CG) scaffolds, also known as dermal regeneration templates, are used for the reconstruction of full-thickness skin defect in patients with extensive resections due to burns, traumatic or inflammatory conditions.[1] The natural process of revascularization typically lasts two to three weeks precluding immediate skin grafting. The usage of stem cells has demonstrated to accelerate wound healing. However, stem cell usage requires several steps of cell culturing that preclude using this method in the acute setting. Aldehyde dehydrogenase (ALDH) is an enzyme that plays an important role in retinoid metabolism and is highly expressed in stem cells.[2] In this study, we isolated ALDH-expressing cells from subcutaneous adipose tissue and tested them for their potential to enhance healing in a full-thickness skin wound in rats by co-implanting them with CG scaffolds.

MATERIALS AND METHODS: Stromal-Vascular-Fraction (SVF) was obtained from subcutaneous adipose tissue of syngeneic rats. $ALDH^{hi}$ cells were isolated using a fluorescence-activated cell sorting technique with ALDEFLUOR assay kit™. Each recipient rat underwent four full-thickness wounds creation on the recipient rat's back, each wound was treated differently. A total of four treatment groups were formed (n=11). Group 1 (control group) consisted of wounds treated with CG and 100 µL normal saline. Group 2 (SVF group) consisted of CG and 1×10^5 cells/cm^2 SVF cells. Group 3 (ALDH group) consisted of CG and 1×10^5 cells/cm^2 $ALDH^{hi}$ cells. Group 4 (ASCs group) consisted of CG and 1×10^5 cells/cm^2 ASCs. Animals were evaluated by histology on day 7 after surgeries.

RESULTS: Scaffolds seeded with $ALDH^{hi}$ cells histologically demonstrated remarkable enhancements in dermal regeneration, vascularization, and collagen growth, if compared to the wound treated with CG alone, CG with SVF, and CG with ASCs groups. Immunofluorescent staining with CD31 emphasized that transplanted $ALDH^{hi}$ cells differentiated into vascular endothelial cells.

CONCLUSIONS: Composite transplantation of CG scaffolds and adipose-derived $ALDH^{hi}$ cells promoted dermal regeneration, not worse than cultured ASC, suggesting that $ALDH^{hi}$ cells could be used in an acute setting as a reliable alternative for cultured ASCs.

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