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3D Printing PLA/Gingival Stem Cells/ EVs Upregulate miR-2861 and -210 during Osteoangiogenesis Commitment.

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Abstract

Bone tissue regeneration strategies require approaches that provide an osteogenic and angiogenic microenvironment able to drive the bone growth. Recently, the development of 3D printing biomaterials, including poly(lactide) (3D-PLA), enriched with mesenchymal stem cells (MSCs) and/or their derivatives, such as extracellular vesicles (EVs) has been achieving promising results. In this study, in vitro results showed an increased expression of osteogenic and angiogenic markers, as RUNX2, VEGFA, OPN and COL1A1 in the living construct 3D-PLA/human Gingival MSCs (hGMSCs)/EVs. Considering that EVs carry and transfer proteins, mRNA and microRNA into target cells, we evaluated miR-2861 and miR-210 expression related to osteoangiogenesis commitment. Histological examination of rats implanted with 3D-PLA/hGMSCs/EVs evidenced the activation of bone regeneration and of the vascularization process, confirmed also by MicroCT. In synthesis, an upregulation of miR-2861 and -210 other than RUNX2, VEGFA, OPN and COL1A1 was evident in cells cultured in the presence of the biomaterial and EVs. Then, these results evidenced that EVs may enhance bone regeneration in calvaria defects, in association with an enhanced vascularization offering a novel regulatory system in the osteoangiogenesis evolution. The application of new strategies to improve biomaterial engraftment is of great interest in the regenerative medicine and can represent a way to promote bone regeneration.

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Alteration of the extracellular matrix and alpha-gal antigens in the rat lung scaffold reseeded using human vascular and adipogenic stromal cells.

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Abstract

Regenerated organs are expected to solve the problem of donor-organ shortage in transplantation medicine. One approach to lung regeneration is to decellularize the organ and reseed it with selected cells. Advantage of the procedure includes reduced immunogenicity, since all cells can be theoretically replaced by autologous cells. However, little is known regarding the extracellular matrix (ECM) damage during decellularization and ECM reconstruction process in the organ regeneration. We aimed to evaluate ECM damage and reconstruction of the decellularized- recellularized rat lung, including the removal of alpha-gal xenoantigens. Rat lungs were perfused with sodium dodecyl sulfate and Triton X-100 via the pulmonary artery, after which the decellularized scaffold was reseeded with rat or human

endothelial cells and adipose mesenchymal stem cells (ASCs). The ECM and alpha-gal antigen were evaluated using immunohistochemistry, western blotting, and a glycosaminoglycan assay. Alcian blue staining revealed increased production of proteoglycan following the addition of ASCs to the rat lung recellularized with rat lung microvascular endothelial cells. Glycosaminoglycan levels decreased in the decellularized lung and increased in the recellularized lung, especially in the ASC-treated group. Immunohistochemical expression of the alpha-gal protein was decreased to undetectable level in the decellularized lung tissue, and disappeared after recellularization with human cells. In western blot analysis, the bands of alpha-gal protein almost disappeared after recellularization with human cells. In conclusion, characteristics of the regenerated ECM might depend on the species and type of cells used for recellularization. Therefore, alpha-gal antigen might be eliminated after a prolonged culture, when using human cells.

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Adipose-Derived Stem Cells in Cancer Progression: New Perspectives and Opportunities.

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Abstract

Growing importance has been attributed to interactions between tumors, the stromal microenvironment and adult mesenchymal stem cells. Adipose-derived stem cells (ASCs) are routinely employed in regenerative medicine and in autologous fat transfer procedures. To date, clinical trials have failed to demonstrate the potential pro-oncogenic role of ASC enrichment. Nevertheless, some pre-clinical studies from in vitro and in vivo models have suggested that ASCs act as a potential tumor promoter for different cancer cell types, and support tumor progression and invasiveness through the activation of several intracellular signals. Interaction with the tumor microenvironment and extracellular matrix remodeling, the exosomal release of pro-oncogenic factors as well as the induction of epithelial-mesenchymal transitions are the most investigated mechanisms. Moreover, ASCs have also demonstrated an elective tumor homing capacity and this tumor-targeting capacity makes them a suitable carrier for anti-cancer drug delivery. New genetic and applied nanotechnologies may help to design promising anti-cancer cell-based approaches through the release of loaded intracellular nanoparticles. These new anti-cancer therapies can more effectively target tumor cells, reaching higher local concentrations even in pharmacological sanctuaries, and thus minimizing systemic adverse drug effects. The potential interplay between ASCs and tumors and potential ASCs-based therapeutic approaches are discussed.