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The senescent status of endothelial cells affects proliferation, inflammatory profile and SOX2 expression in bone marrow-derived mesenchymal stem cells.

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Abstract

Human aging is a physiological process characterized by a chronic low-grade inflammation. Senescence may affect endothelial cells, subsequently involved in the most common age-related diseases (ARDs), as well as mesenchymal stem cells (MSCs) with an impairment of their properties in tissues regeneration. Endothelial cells seem to be able to exert a paracrine effect on BM-MSCs through the secretion of pro-inflammatory factors. This work is aimed to evaluate if the senescent status of human umbilical vein endothelial cells (HUVECs) could affect bone marrow derived MSCs (BM-MSCs) proliferative ability and stemness. HUVECs were cultured until the senescence status. Young (passage 3) and senescent HUVECs (passage 13) were indirectly co-cultured with BM-MSCs for 8 days in order to evaluate the effect of their senescence status on proliferative ability and stemness of MSCs. The co-culture of senescent HUVECs with BM-MSCs was associated with a reduced proliferative ability of BM-MSCs, an enforced pro-inflammatory phenotype of BM-MSCs (increased synthesis of proinflammatory cytokines such as IL-6 and TNF-α) and an increased expression of miR-126a-3p, in association with a significant decrease of SOX2, a stemmness- associated gene, targeted by miR-126a-3p. A more general IPA analysis, revealed as miR-126a-3p also modulates the expression of IRS1, IRS2, IL6ST and PIK3R2, all targets that enforce the hypothesis that senescent endothelial cells may reduce the proliferative ability and the stemness phenotype of bone marrow-derived mesenchymal stem cells.

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Emerging Role of Mesenchymal Stem Cell-derived Exosomes in Regenerative Medicine.

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Abstract

BACKGROUND:

The recent studies have shown the great value of cell therapy over the past few decades. Mesenchymal stem cells (MSCs) have been reported to treat various degenerative diseases not through their differentiation potential but through their paracrine factors of extracellular vesicle (EV) including exosomes. Exosomes are nanosized (70~150 nm) membrane-bound extracellular vesicles, not only involved in cell-to-cell communication but also in the development of tissue injury repair.

OBJECTIVE:

As more and more researches proved the enormous potential of exosomes in the field of repairing damaged tissue currently, it is urgent to explore the concrete mechanism and make exosomes to be a practical treatment tool in clinical medicine. In our study, we analyzed and summarized the work on tissue repair via exosomes in order to give some suggestions about the application of exosomes in clinical reality in the future.

RESULTS:

MSC-derived exosomes (MSC-Ex) contain a wide variety of functional proteins, mRNAs, miRNAs and signaling lipids. Compared with their parent cells, MSC-Ex are more stable and can reduce the inherent safety risks in administering viable cells such as the risk of occlusion in microvasculature. MSC-Ex can be used to develop a cell-free exosome-based therapy for regenerative medicine, and may provide an alternative to MSC-based therapy.

CONCLUSION:

This review summarizes the most recent knowledge of therapeutic potential of MSC-Ex in liver, heart, kidney, bone, brain diseases and cancer, as well as their associated challenges and opportunities.

Materials (Basel). 2019 Feb 27;12(5). pii: E705. doi: 10.3390/ma12050705.

Application of a Bioactive/Bioresorbable Three-Dimensional Porous Uncalcined and Unsintered Hydroxyapatite/Poly-D/L-lactide Composite with Human Mesenchymal Stem Cells for Bone Regeneration in Maxillofacial Surgery: A Pilot Animal Study.

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Abstract

A novel three-dimensional (3D) porous uncalcined and unsintered hydroxyapatite/poly-d/l-lactide (3D-HA/PDLLA) composite demonstrated superior biocompatibility, osteoconductivity, biodegradability, and plasticity, thereby enabling complex maxillofacial defect reconstruction. Mesenchymal stem cells (MSCs)-a type of adult stem cell-have a multipotent ability to differentiate into chondrocytes, adipocytes, and osteocytes. In a previous study, we found that CD90 (Thy-1, cluster of differentiation 90) and CD271 (low-affinity nerve growth factor receptor) double-positive cell populations from human bone marrow had high proliferative ability and differentiation capacity in vitro. In the present study, we investigated the utility of bone regeneration therapy using implantation of 3D-HA/PDLLA loaded with human MSCs (hMSCs) in mandibular critical defect rats. Microcomputed tomography (Micro-CT) indicated that implantation of a 3D-HA/PDLLA-hMSC composite scaffold improved the ability to achieve bone regeneration compared with 3D-HA/PDLLA alone. Compared to the sufficient blood supply in the mandibular defection superior side, a lack of blood supply in the inferior side caused delayed healing. The use of Villanueva Goldner staining (VG staining) revealed the gradual progression of the nucleated

cells and new bone from the scaffold border into the central pores, indicating that 3D-HA/PDLLA loaded with hMSCs had good osteoconductivity and an adequate blood supply. These results further demonstrated that the 3D-HA/PDLLA-hMSC composite scaffold was an effective bone regenerative method for maxillofacial boney defect reconstruction.

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Stem Cells for Bone Regeneration: Current State and Future Directions.

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Abstract

Mesenchymal stem cells (MSCs) are capable of differentiating into osteoblasts, chondrocytes, and adipocytes, each of which is important for musculoskeletal tissue regeneration and repair. Reconstruction and healing of bony defects remains a major clinical challenge. Even as surgical practices advance, some severe cases of bone loss do not yield optimal recovery results. New techniques involving implantation of stem cells and tissue-engineered scaffolds are being developed to help improve bone and cartilage repair. The invasiveness and low yield of harvesting MSCs from the bone marrow (BMSCs) has led to the investigation of alternatives, including adipose-derived mesenchymal stem cells (ASCs). A review of the literature yielded several studies concerning the use of BMSCs and ASCs for the treatment of bone defects in both in vitro and in vivo models. Although both ASCs and BMSCs have demonstrated bone regenerative capabilities, BMSCs have outperformed ASCs in vitro. Despite these in vitro study findings, in vivo study results remain variable. Analysis of the literature seems to conclude there is no significant difference between bone regeneration using ASCs or BMSCs in vivo. Improved study design and standardization may enhance the application of these studies to patient care in the clinical setting.

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Optimising proliferation and migration of mesenchymal stem cells using platelet products: A rational approach to bone regeneration.

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Abstract

This study investigates how mesenchymal stem cell's (MSCs) proliferation and migration abilities are influenced by various platelet products (PP). Donor-matched, clinical- and control laboratory-standard PPs were generated and assessed based on their platelet and leukocyte concentrations. Bone marrow derived MSCs were exposed to these PP to quantify their effect on in vitro MSC proliferation and migration. An adapted colony forming unit fibroblast (CFU-F) assay was carried out on bone marrow aspirate using clinical-standard PP-loaded electrospun poly(ϵ-caprolactone) (PCL) membrane to mimic future clinical applications to contain bone defects. Clinical-standard PP had lower platelet (2.5 fold,

P < 0.0001) and higher leukocyte (14.1 fold, P < 0.0001) concentrations compared to laboratory-standard PP. It induced suboptimal MSC proliferation compared to laboratory-standard PP and fetal calf serum (FCS). All PP induced significantly more MSC migration than FCS up to 24 hours. The removal of leukocytes from PP had no effect on MSC proliferation or migration. The PP-loaded membranes successfully supported MSC colony formation. This study indicates that platelet concentrations in PP impact MSC proliferation more than the presence of leukocytes, whilst MSC migration in response to PP is not influenced by platelet or leukocyte numbers. Clinical-standard PP could be applied alongside manufactured membranes in the future treatment of bone reconstruction.

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Adipose-derived mesenchymal stem cells exhibit tumor tropism and promote tumorsphere formation of breast cancer cells.

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Abstract

Mesenchymal stem cells reportedly have a marked effect on tumor growth or suppression. However, it remains uncertain whether adipose-derived mesenchymal stem cells (ADSCs) from grafted fat can contribute to breast cancer growth and recurrence. In the present study, interactions between ADSCs and MCF-7 breast cancer cells were evaluated in a Matrigel co-culture system and in an in vivo nude mouse model. Results suggested that MCF-7 cells exerted tumor tropism effects on ADSCs and this may be regulated by chemokines, such as the macrophage inflammatory protein (MIP)-1δ and MIP-3α. Additionally, ADSCs significantly induced tumorsphere formation in vitro and promoted tumorigenicity in vivo. RT-qPCR analysis indicated that tumorsphere formation by MCF-7 cells was associated with the induction of stem-like properties, which was mediated by epithelial--mesenchymal transition. Together, the present findings indicated that ADSCs exhibit tropism and induce tumorsphere formation of MCF-7 cells.