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Anal Chem

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Single-Cell Infrared Microspectroscopy Quantifies Dynamic Heterogeneity of Mesenchymal Stem Cells during Adipogenic Differentiation

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Abstract

The central relevance of cellular heterogeneity to biological phenomena raises the rational needs for analytical techniques with single-cell resolution. Here, we developed a single-cell FTIR microspectroscopy-based method for the quantitative evaluation of cellular heterogeneity by calculating the cell-to-cell similarity distance of the infrared spectral data. Based on this method, we revealed the infrared phenotypes might reflect the dynamic heterogeneity changes in the cell population during the adipogenic differentiation of the human mesenchymal stem cells. These findings provide an alternative label-free optical approach for quantifying the cellular heterogeneity, and the combination with other single-cell analysis tools will be very helpful for understanding the genotype-to-phenotype relationship in cellular populations.

Stem Cells Transl Med

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Comparison of concentrated fresh mononuclear cells and cultured mesenchymal stem cells from bone marrow for bone regeneration

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Free article

Abstract

Autologous bone marrow mononuclear cell (BMMNC) transplantation has been widely studied in recent years. The fresh cell cocktail in BMMNCs, without going through the in vitro culture process, helps to establish a stable microenvironment for osteogenesis, and each cell type may play a unique role in bone regeneration. Our study compared the efficacy of concentrated fresh BMMNCs and cultured bone marrow-derived mesenchymal stem cells (BMSCs) in Beagle dogs for the first time. Fifteen-millimeter segmental bone defects were created in the animals' tibia bones. In BMMNCs group, the defects were repaired with concentrated fresh BMMNCs combined with β-TCP (n = 5); in cultured BMSC group, with in vitro cultured and osteo-induced BMSCs combined with β-TCP (n = 5); in scaffold-only group, with a β-TCP graft alone (n = 5); and in blank group, nothing was grafted (n = 3). The healing process was monitored by X-rays and single photon emission computed tomography. The animals were sacrificed 12 months after surgery and their tibias were harvested and analyzed by microcomputed tomography and hard tissue histology. Moreover, the microstructure, chemical components, and microbiomechanical properties of the regenerated bone tissue were explored by multiphoton microscopy, Raman spectroscopy and nanoindentation. The results showed that BMMNCs group promoted much more bone regeneration than cultured BMSC group. The grafts in BMMNCs group were better mineralized, and they had collagen arrangement and microbiomechanical properties similar to the contralateral native tibia bone. These results

indicate that concentrated fresh bone marrow mononuclear cells may be superior to in vitro expanded stem cells in segmental bone defect repair.

Front Cell Dev Biol

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Tumor Microenvironment Uses a Reversible Reprogramming of Mesenchymal Stromal Cells to Mediate Pro-tumorigenic Effects

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Affiliations expand

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Free PMC article

Abstract

The role of mesenchymal stromal cells (MSCs) in the tumor microenvironment is well described. Available data support that MSCs display anticancer activities, and that their reprogramming by cancer cells in the tumor microenvironment induces their switch toward pro-tumorigenic activities. Here we discuss the recent evidence of pro-tumorigenic effects of stromal cells, in particular (i) MSC support to cancer cells through the metabolic reprogramming necessary to maintain their malignant behavior and stemness, and (ii) MSC role in cancer cell immunosenescence and in the establishment and maintenance of immunosuppression in the tumor microenvironment. We also discuss the mechanisms of tumor microenvironment mediated reprogramming of MSCs, including the effects of hypoxia, tumor stiffness, cancer-promoting cells, and tumor extracellular matrix. Finally, we

summarize the emerging strategies for reprogramming tumor MSCs to reactivate anticancer functions of these stromal cells.

Front Cell Dev Biol

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The Bone-Forming Properties of Periosteum-Derived Cells Differ Between Harvest Sites

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Free PMC article

Abstract

The development of alternatives for autologous bone grafts is a major focus of bone tissue engineering. To produce living bone-forming implants, skeletal stem and progenitor cells (SSPCs) are envisioned as key ingredients. SSPCs can be obtained from different tissues including bone marrow, adipose tissue, dental pulp, and periosteum. Human periosteum-derived cells (hPDCs) exhibit progenitor cell characteristics and have well-documented *in vivo* bone formation potency. Here, we have characterized and compared hPDCs derived from tibia with craniofacial hPDCs, from maxilla and mandible, respectively, each representing a potential source for cell-based tissue engineered implants for craniofacial applications. Maxilla and mandible-derived hPDCs display similar growth curves as tibial hPDCs, with equal trilineage differentiation potential toward chondrogenic, osteogenic, and adipogenic cells. These craniofacial hPDCs are positive for SSPC-markers CD73, CD164,

and Podoplanin (PDPN), and negative for CD146, hematopoietic and endothelial lineage markers. Bulk RNA-sequencing identified genes that are differentially expressed between the three sources of hPDC. In particular, differential expression was found for genes of the HOX and DLX family, for *SOX9* and genes involved in skeletal system development. The *in vivo* bone formation, 8 weeks after ectopic implantation in nude mice, was observed in constructs seeded with tibial and mandibular hPDCs. Taken together, we provide evidence that hPDCs show different profiles and properties according to their anatomical origin, and that craniofacial hPDCs are potential sources for cell-based bone tissue engineering strategies. The mandible-derived hPDCs display - both *in vitro* and *in vivo* - chondrogenic and osteogenic differentiation potential, which supports their future testing for use in craniofacial bone regeneration applications.

Mater Sci Eng C Mater Biol Appl

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Demineralized bone matrix scaffold modified with mRNA derived from osteogenically pre-differentiated MSCs improves bone repair

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Abstract

Gene therapy based on mRNA provides a promising approach for bone regeneration. Quick mRNA translation and controlled protein production could be earned by implantation of mRNA-activated scaffold in bone remodeling region. Furthermore, the expression levels of osteogenic-related mRNA in the cytoplasm of osteogenically pre-differentiated mesenchymal stem cells (MSCs) were high and the expression levels were different at different stages of osteogenically differentiated MSCs. This study intended to investigate the effect of osteoinductive-mRNAs (Oi-mRNAs), derived from osteogenically

pre-differentiated MSCs at various stages (Day 1 (Oi1-mRNA), Day 3 (Oi3-mRNA), Day 7 (Oi7-mRNA), Day 14 (Oi14-mRNA) and Day 21 (Oi21-mRNA), respectively), on the osteogenic differentiation of MSCs. Further, the Oi-mRNAs combined with cationic polymer polyethylenimine (PEI) were loaded onto demineralized bone matrix (DBM) scaffold (Oi-mRNA/DBM). The results revealed that the Oi1-mRNA, Oi3-mRNA and Oi21-mRNA had no obvious effect on the osteogenic differentiation of MSCs, while the Oi7-mRNA increased the expression of alkaline phosphatase (ALP) and the Oi14-mRNA significantly promoted the expression of osteocalcin (OC) and osteopontin (OPN), and calcium deposition. In addition, the Oi14-mRNA/DBM scaffold could significantly enhance extracellular matrix (ECM) secretion and new collagen formation of MSCs. After being implanted into rat critical-sized cranium defect model, the Oi14-mRNA/DBM scaffold could promote the infiltration of cells and repair of bone defect in vivo. The DBM scaffold loaded with mRNA encoding osteoinductive protein may provide a powerful tool for bone defect repair.

Neoplasia

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Bone marrow mesenchymal stem cells interact with head and neck squamous cell carcinoma cells to promote cancer progression and drug resistance

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Free article

Abstract

Head and neck cancers are often diagnosed at later stages with poor outcomes. Mesenchymal stem cells (MSC) are recruited to primary tumor sites where they can have pro- and antitumorigenic influence. In trying to better understand the dynamics between MSC and cancer cells, we found that head and neck cancer-MSC exposure resulted in mesenchymal features, elevated proliferation rate, and were more motile, like the same cells that fused with MSC. We orthotopically grafted the parental head and neck cancer cells, those fused with MSC, or those exposed to MSC into the tongues of mice. The cancer cells originally incubated with MSC developed larger more aggressive tumors compared to the parental cell line. RNA sequencing analysis revealed the expression of genes associated with drug resistance in the cancer cells exposed to MSC compared to parental cancer cells. Strikingly, MSC exposed cancer cell lines developed paclitaxel resistance that could be maintained up to 30 d after the initial co-incubation period. The secretory profile of the MSC suggested IL-6 to be a potential mediator of epigenetic imprinting on the head and neck cancer cells. When the MSC-imprinted cancer cells were exposed to the demethylation agent, 5-aza-2'deoxycytidine, it restored the expression of the drug resistance genes to that of parental cells. This study demonstrated that the recognized recruitment of MSC to tumors could impart multiple protumorigenic properties including chemotherapy resistance like that observed in the relatively rare event of cancer/MSC cell fusion.