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Effect of Bone Powder/Mesenchymal Stem Cell/BMP2/Fibrin Glue on Osteogenesis in a Mastoid Obliteration Model.

Jang CH[#1], Cho GW[#2,3], Song AJ[2,3].
Author information

Abstract

BACKGROUND/AIM:

This study aimed to prospectively compare the osteogenesis of bone powder (BP) substances with and without mesenchymal stem cells (MSCs) and evaluate the synergistic effect of topically applied recombinant human bone morphogenic protein-2 (BMP2) on MSC-loaded BP using fibrin glue in a mastoid obliteration model.

MATERIALS AND METHODS:

To determine the expression of osteocyte-specific genes, total RNA was isolated from three MSC groups: Untreated MSCs, MSCs cultured with BP, and MSCs cultured with BP and BMP2. Real-time polymerase chain reaction was carried out with specific primers of osteogenesis-related genes runt-related transcription factor 2, osteocalcin, osteoprotegerin, osterix, alkaline phosphatase, transforming growth factor beta, and type I collagen. Live/dead staining was also performed. To observe the adhesion of MSCs to the BP, MSCs were treated with BP for 2 days and the surface was observed by scanning electron microscopy (SEM). Under general anesthesia, mastoid obliteration was performed in rats using three groups: treated with BP alone, BP/MSCs, and BP/MSC/BMP2. Before decapitation at 8 weeks post operation, in vivo micro computed tomography (micro CT) was performed. The bullae were dissected, fixed, and decalcified. followed by dehydration, paraffin embedding, and staining by hematoxylin and eosin and Masson's trichrome.

RESULTS:

SEM showed the MSCs to be well-attached to the superficial area of the BP. The expression of osteocyte-specific genes was the highest in the MSCs cultured with BP and BMP2, followed by cultured with BP only, and untreated MSCs. The BP/MSC/BMP2 group showed the highest radiodensity of bullae in microCT analysis. The microCT findings revealed that the BP/MSC/BMP2 group showed the most enhanced osteogenesis of the scaffold compared to the other two groups. No significant difference was found in osteoconductive osteogenesis between the control and BP/MSC groups. However, the BP/MSC/BMP2 group showed significantly enhanced osteoconductive osteogenesis and osteoinductive change of the BP as shown by hematoxylin and eosin staining. Histomorphometry of osteogenesis revealed that the difference between the BP/MSC/BMP2 group and the other two groups was statistically significant.

CONCLUSION:

A small amount of BMP2 is necessary during MSC loading to enhance the osteogenesis of BP and avoid complications associated with high doses of BMP2. These results may be applicable to mastoid obliteration in clinical practice.

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Near-infrared control and real-time detection of osteogenic differentiation in mesenchymal stem cells by multifunctional upconversion nanoparticles.

Wang K[1], Wu Q[1], Wang X[1], Liang G[1], Yang A[2], Li J[1].
Author information

Abstract

Finding a method to control and detect the differentiation of stem cells in real time remains a challenge for regenerative medicine. Here we developed the multifunctional upconversion nanoparticle (UCNP) approach for both near-infrared (NIR) control and the real-time detection of osteogenic differentiation in mesenchymal stem cells (MSCs). We first synthesized Tm/Er doped core-shell UCNPs (NaYF4:Yb/Tm/Er@NaYF4), and the core-shell UCNPs were coated with mesoporous silica for drug loading and installing photomechanical azobenzene (azo). Then the Arg-Gly-Asp (RGD) peptide and the matrix metalloproteinase 13 (MMP13) sensitive peptide-black hole quencher-3 group (CGPLGVRGK-BHQ-3) were conjugated on the surface of UCNPs for cell targeting and detection of cell differentiation. The final multifunctional UCNPs are called UCNP@mSiO2-azo-peptide-BHQ-3. The drug icariin (ICA), which can induce the osteogenic differentiation of MSCs, was loaded into UCNP@mSiO2-azo-peptide-BHQ-3 to form the UCNP nanocomplexes. ICA could be released from UCNP nanocomplexes in a NIR-controlled manner that is based on the transformation of the trans-isomer of azo into the cis isomer under the upconverted UV and visible light. Meanwhile, UCNP@mSiO2-azo-peptide-BHQ-3 could also be used as a nanoprobe to detect the activity of the MMP13 enzyme by enzyme digestion and UCNP fluorescence recovery. By detecting MMP13, which is produced by osteogenic differentiation, a real-time detection of cell differentiation in living differentiated MSCs could be achieved using UCNP nanoprobes. Thus, the multifunctional UCNPs combined the control of cell differentiation with the real-time detection of cell differentiation in MSCs, which makes them a powerful tool for regulating and detecting the differentiation of MSCs in regenerative medicine.

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Decellularized human bone as a 3D model to study skeletal progenitor cells in a natural environment.

Pereira AR[1], Rudert M[2], Herrmann M[3].
Author information

Abstract

There has been an increasing interest in exploring naturally derived extracellular matrices as an material mimicking the complexity of the cell microenvironment in vivo. Bone tissue-derived decellularized constructs are able to preserve native structural, biochemical, and biomechanical cues of

the tissue, therefore providing a suitable environment to study skeletal progenitor cells. Particularly for bone decellularization, different methods have been reported in the literature. However, the used methods critically affect the final ultrastructure and surface chemistry as well as the decellularization efficiency, consequently causing complications to draw conclusions and compare results in between studies. In this chapter, an optimized protocol for the preparation of human bone derived scaffolds is described, including processing techniques and further characterization methods, which allow the final construct to be recognized as a major platform for bone therapeutic and/or diagnostic applications.

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Suicide Gene Therapy Mediated with Exosomes Produced by Mesenchymal Stem/Stromal Cells Stably Transduced with HSV Thymidine Kinase.

Pastorakova A[1], Jakubechova J[2], Altanerova U[2], Altaner C[2,3].
Author information

Abstract

Mesenchymal stem/stromal cells (MSCs) prepared from various human tissues were stably transduced with the suicide gene herpes simplex virus thymidine kinase (*HSVTK)* by means of retrovirus infection. *HSVTK*-transduced MSCs express the suicide gene and in prodrug ganciclovir (GCV) presence induced cell death by intracellular conversion of GCV to GCV-triphosphate. The homogenous population of *HSVTK*-MSCs were found to release exosomes having mRNA of the suicide gene in their cargo. The exosomes were easily internalized by the tumor cells and the presence of ganciclovir caused their death in a dose-dependent manner. Efficient tumor cell killing of glioma cell lines and primary human glioblastoma cells mediated by *HSVTK*-MSC exosomes is reported. Exosomes produced by suicide gene transduced MSCs represent a new class of highly selective tumor cell targeted drug acting intracellular with curative potential.

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Role of cancer stem cells in the development of giant cell tumor of bone.

War AR[#1,2,3], Dang K[#1,2,3], Jiang S[1,2,3], Xiao Z[4], Miao Z[1,2,3], Yang T[5], Li Y[1,2,3], Qian A[1,2,3].
Author information

Abstract

The primary bone tumor is usually observed in adolescence age group which has been shown to be part of nearly 20% of the sarcomas known today. Giant cell tumor of bone (GCTB) can be benign as well as malignant tumor which exhibits localized dynamism and is usually associated with the end point of a long bone. Giant cell tumor (GCT) involves mononuclear stromal cells which proliferate at a high rate, multinucleated giant cells and stromal cells are equally present in this type of tumor. Cancer stem cells (CSCs) have been confirmed to play a potential role in the development of GCT. Cancer stem cell-based microRNAs have been shown to contribute to a greater extent in giant cell tumor of bone. CSCs and microRNAs present in the tumors specifically are a great concern today which need in-depth

knowledge as well as advanced techniques to treat the bone cancer effectively. In this review, we attempted to summarize the role played by cancer stem cells involving certain important molecules/factors such as; Mesenchymal Stem Cells (MSCs), miRNAs and signaling mechanism such as; mTOR/PI3K-AKT, towards the formation of giant cell tumor of bone, in order to get an insight regarding various effective strategies and research advancements to obtain adequate knowledge related to CSCs which may help to focus on highly effective treatment procedures for bone tumors.