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Mesenchymal stem cells in the osteosarcoma microenvironment: their biological properties, influence on tumor growth, and therapeutic implications.

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Author information

Abstract

During tumorigenesis and development, participation of the tumor microenvironment is not negligible. As an important component in the tumor microenvironment, mesenchymal stem cells (MSCs) have been corroborated to mediate proliferation, metastasis, and drug resistance in many cancers, including osteosarcoma. What's more, because of tumor site tropism, MSCs can be engineered to be loaded with therapeutic agents so that drugs can be precisely delivered to tumor lesions. In this review, we mainly discuss recent advances concerning the functions of MSCs in osteosarcoma and their possible clinical applications in the future.

Stem Cells Int. 2017;2017:2156478. doi: 10.1155/2017/2156478. Epub 2017 Dec 14.

Impact of Tissue Harvesting Sites on the Cellular Behaviors of Adipose-Derived Stem Cells: Implication for Bone Tissue Engineering.

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Abstract

The advantages of adipose-derived stem cells (AdSCs) over bone marrow stem cells (BMSCs), such as being available as a medical waste and less discomfort during harvest, have made them a good alternative instead of BMSCs in tissue engineering. AdSCs from buccal fat pad (BFP), as an easily harvestable and accessible source, have gained interest to be used for bone regeneration in the maxillofacial region. Due to scarcity of data regarding comparative analysis of isolated AdSCs from different parts of the body, we aimed to quantitatively compare the proliferation and osteogenic capabilities of AdSCs from different harvesting sites. In this study, AdSCs were isolated from BFP (BFPdSCs), abdomen (abdomen-derived mesenchymal stem cells (AbdSCs)), and hip (hip-derived mesenchymal stem cells (HdSCs)) from one individual and were compared for surface marker expression, morphology, growth rate, and osteogenic differentiation capability. Among them, BFPdSCs demonstrated the highest proliferation rate with the shortest doubling time and also expressed vascular endothelial markers including CD34 and CD146. Moreover, the expression of osteogenic markers were significantly higher in BFPdSCs. The results of this study suggested that BFPdSCs as an encouraging source of mesenchymal stem cells are to be used for bone tissue engineering.

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Bone marrow-derived mesenchymal stromal cells promote colorectal cancer cell death under low-dose irradiation.

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Abstract

BACKGROUND:

Radiotherapy remains one of the cornerstones to improve the outcome of colorectal cancer (CRC) patients. Radiotherapy of the CRC not only help to destroy cancer cells but also remodel the tumour microenvironment by enhancing tumour-specific tropism of bone marrow-derived mesenchymal stromal cell (BM-MSC) from the peripheral circulation. However, the role of local MSCs and recruited BM-MSC under radiation were not well defined. Indeed, the functions of BM-MSC without irradiation intervention remained controversial in tumour progression: BM-MSC was previously shown to modulate the immune function of major immune cells, resulting in an impaired immunological sensitivity and to induce an increased risk of tumour recurrence. In contrast, it could also secrete various cytokines and possess anticancer effect.

METHODS:

Three co-cultivation modules, 3D culture modules, and cancer organoids were established. The induction of cytokines secretion in hBM-MSCs after irradiation was analysed by ELISA array and flow cytometry. AutoMac separator was used to separate hBM-MSC and CRC automatically. Cells from the co-cultured group and the control group were then irradiated by UV-C lamp and X-ray. Proliferation assay and viability assay were performed.

RESULTS:

In this study, we show that BM-MSCs can induce the EMT progression of CRC cells in vitro. When irradiated with low doses of ultraviolet radiation and X-rays, BM-MSCs show an anti-tumour effect by secreting certain cytokine (TNF-α, IFN-γ) that lead to the inhibition of proliferation and induction of apoptosis of CRC cells. This was further verified in a 3D culture model of a CRC cell in vitro. Furthermore, irradiation on the co-culture system induced the cleavage of caspase3, and attenuated the phosphorylation of phosphatidylinositol 3-kinase (PI3K)/AKT and extracellular signal-regulated kinase in cancer cells. The signal pathways above might contribute to the cancer cell death.

CONCLUSIONS:

Taken together, we show that BM-MSC can potentially promote the effect of radiotherapy in CRC.

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Effective treatment of steroid and therapy-refractory acute graft-versus-host disease with a novel mesenchymal stromal cell product (MSC-FFM).

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Abstract

The inability to generate mesenchymal stromal cells (MSCs) of consistent potency likely is responsible for inconsistent clinical outcomes of patients with aGvHD receiving MSC products. We developed a novel MSC manufacturing protocol characterized by high in vitro potency and near-identity of individual doses, referred to as "MSC-Frankfurt am Main (MSC-FFM)". Herein, we report outcomes of the 69 patients who have received MSC-FFM. These were 51 children and 18 adults with refractory aGvHD grade II (4%), III (36%) or IV (59%). Patients were refractory either to frontline therapy (steroids) (29%) or to steroids and 1-5 additional lines of immunosuppressants (71%) were given infusions in four weekly intervals. The day 28 overall response rate was 83%; at the last follow-up, 61% and 25% of patients were in complete or partial remission. The median follow-up was 8.1 months. Six-month estimate for cumulative incidence of non-relapse mortality was 27% (range, 16-38); leukemia relapse mortality was 2% (range, 0-5). This was associated with a superior six-month overall survival (OS) probability rate of 71% (range, 61-83), compared to the outcome of patients not treated with MSC-FFM. This novel product was effective in children and adults, suggesting that MSC-FFM represents a promising therapy for steroid refractory aGvHD.

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The extracellular vesicles-derived from mesenchymal stromal cells: A new therapeutic option in regenerative medicine.

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Abstract

Mesenchymal stem cells (MSCs) are adult multipotent cells that due to their ability to homing to damaged tissues and differentiate into specialized cells, are remarkable cells in the field of regenerative medicine. It's suggested that the predominant mechanism of MSCs in tissue repair might be related to their paracrine activity. The utilization of MSCs for tissue repair is initially based on the differentiation ability of these cells; however now it has been revealed that only a small fraction of the transplanted MSCs actually fuse and survive in host tissues. Indeed, MSCs supply the microenvironment with the secretion of soluble trophic factors, survival signals and the release of extracellular vesicles (EVs) such as exosome. Also, the paracrine activity of EVs could mediate the cellular communication to induce

cell-differentiation/self-renewal. Recent findings suggest that EVs released by MSCs may also be critical in the physiological function of these cells. This review provides an overview of MSC-derived extracellular vesicles as a hopeful opportunity to advance novel cell-free therapy strategies that might prevail over the obstacles and risks associated with the use of native or engineered stem cells. EVs are very stable; they can pass the biological barriers without rejection and can shuttle bioactive molecules from one cell to another, causing the exchange of genetic information and reprogramming of the recipient cells. Moreover, extracellular vesicles may provide therapeutic cargo for a wide range of diseases and cancer therapy

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The Exosomes Released from Different Cell types and Their Effects in Wound Healing.

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Abstract

Despite important advances in regenerative medicine and tissue engineering, still, wound healing remains a challenging clinical problem. Cell therapy has opened a new viewpoint in medicine as well as wound management, Although it has some limitations. on the other hand, there are some hopes for the eliminated of cellular therapies limitations by "exosomes". the term "exosome" has been frequently used to describe all vesicles released by different cells into the extracellular environment and can influence tissue responses to injury, infection, immune system, and healing. Exosomes contain cytokines and growth factors, signalling lipids, mRNAs, and regulatory miRNAs that have been found in some body fluids and can be transferred between cells to mediating cell-to-cell communication and interactions. Recently, several studies have demonstrated that exosomes are one of the key secretory products of various cell type especially mesenchymal stem cells (MSCs) to regulate many biological processes such wound healing. Hence, understanding these exosomes effects may help to improve wound management and highlight a new therapeutic model for cell-free therapies with decreased side effects for the wound repair