ML 39-20 (08/11/2020)

Front Physiol
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. 2020 Sep 16;11:553198.
doi: 10.3389/fphys.2020.553198. eCollection 2020.

Skeletal Muscle-Derived Human Mesenchymal Stem Cells: Influence of Different Culture Conditions on Proliferative and Myogenic Capabilities

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- PMID: 33041857

- PMCID: PMC7526461

- DOI: 10.3389/fphys.2020.553198

Free PMC article

Abstract

Skeletal muscle tissue is characterized by restrained self-regenerative capabilities, being ineffective in relation to trauma extension both in time span (e.g., chronic diseases) and in size (e.g., large trauma). For these reasons, tissue engineering and/or cellular therapies represent a valuable solution in the cases where the physiological healing process failed. Satellite cells, the putative skeletal muscle stem cells, have been the first solution explored to remedy the insufficient self-regeneration capacity. Nevertheless, some limitation related to donor age, muscle condition, expansion hitch, and myogenic potentiality maintenance have limited their use as therapeutic tool. To overcome this hindrance, different stem cells population with myogenic capabilities have been investigated to evaluate their real potentiality for therapeutic approaches, but, as of today, the perfect cell candidate has not

been identified yet. In this work, we analyze the characteristics of skeletal muscle-derived human Mesenchymal Stem Cells (hMSCs), showing the maintenance/increment of myogenic activity upon differential culture conditions. In particular, we investigate the influence of a commercial enriched growth medium (Cyto-Grow), and of a medium enriched with either human-derived serum (H.S.) or human Platelet-rich Plasma (PrP), in order to set up a culture protocol useful for employing this cell population in clinical therapeutic strategies. The presented results reveal that both the enriched medium (Cyto-Grow) and the human-derived supplements (H.S. and PrP) have remarkable effects on hMSCs proliferation and myogenic differentiation compared to standard condition, uncovering the real possibility to exploit these human derivatives to ameliorate stem cells yield and efficacy.

Stem Cells Int

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. 2020 Oct 5;2020:8883616.

doi: 10.1155/2020/8883616. eCollection 2020.

Effect of Mesenchymal Stem Cell-Derived Exosomes on Retinal Injury: A Review of Current Findings

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- PMID: 33082789

- PMCID: PMC7556062

- DOI: 10.1155/2020/8883616

Free PMC article

Abstract

In recent years, various studies have followed in the literature on the therapeutic effects of mesenchymal stem cells (MSC) on damage in retinal cells. The evidence that MSCs exert their regenerative and damage reduction effect in a paracrine way, through the release of

soluble factors and exosomes, is now consolidated. Exosomes are microvesicles formed by a double layer of phospholipid membrane and carry proteins and RNA, through which they play a therapeutic role on target cells. Scientific research has recently focused on the use of exosomes derived from MSC in various models of retinal damage in vitro and in vivo as they, compared to MSCs, have similar functions and at the same time have different advantages such as greater stability and handling, a lower chance of immunological rejection and no risk of malignant transformation. The purpose of this review is to summarize current knowledge on the therapeutic use of exosomes derived from MSCs in retinal damage and to stimulate new clinical perspectives regarding their use.

J Transl Med

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. 2020 Oct 20;18(1):399.

doi: 10.1186/s12967-020-02565-9.

Mesenchymal stromal cells for osteonecrosis

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- PMID: 33081809

- PMCID: PMC7576732

- DOI: 10.1186/s12967-020-02565-9

Free PMC article

Abstract

Osteonecrosis (ON) is an acquired debilitating skeletal disorder, which is caused by a multitude of traumatic and non-traumatic etiological factors. Vascular damage, mechanical stress and increased intraosseous pressure have been discussed as contributors to ON. The optimal treatment of ON remains to be determined, since the current gold standard, core decompression, is insufficiently effective. Specific properties of mesenchymal stromal cells (MSCs) provide the rationale for their assessment in advanced stages of ON: Osteoinductive potential has been demonstrated and MSC preparations of suitable quality

for use as medicinal products have been developed. Here we review the scant information on the use of allogeneic or autologous MSCs in advanced ON as well as potentially supportive data from pre-clinical studies with autologous bone marrow mononuclear cells (auto BM-MNCs), which have been studied quite extensively and the presumed therapeutic effect of which was attributed to the rare MSCs contained in these cell products. Outcomes in clinical trials with MSCs and auto-BM-MNCs remain preliminary and non-definitive, at best promising, with respect to their pharmacological effect. Clearly, though, the application of any of these cell therapies was technically feasible and safe in that it was associated with low complication rates. The heterogeneity of cell type and source, study protocols, cell manufacturing, cell properties, cell doses and surgical techniques might contribute to inconsistent results.

Mol Ther

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. 2020 Oct 14;S1525-0016(20)30543-8.

doi: 10.1016/j.ymthe.2020.10.009. Online ahead of print.

Regional hyperthermia enhances mesenchymal stem cell recruitment to tumor stroma: Implications for mesenchymal stem cell-based tumor therapy

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- PMID: 33068779

- DOI: 10.1016/j.ymthe.2020.10.009

Abstract

The tropism of mesenchymal stem cells (MSCs) for tumors forms the basis for their use as delivery vehicles for the tumor-specific transport of therapeutic genes, such as the theranostic sodium iodide symporter (NIS). Hyperthermia is used as an adjuvant for various

tumor therapies and has been proposed to enhance leukocyte recruitment. Here, we describe the enhanced recruitment of adoptively applied NIS-expressing MSCs to tumors in response to regional hyperthermia. Hyperthermia (41 °C, 1h) of human hepatocellular carcinoma cells (HuH7) led to transient increased production of immunomodulatory factors. MSCs showed enhanced chemotaxis to supernatants derived from heat-treated cells in a 3D live cell tracking assay and was validated in vivo in subcutaneous HuH7 mouse xenografts. CMV-NIS-MSCs were applied 6-48h after or 24-48h before hyperthermia treatment. Using ^{123}I-scintigraphy, thermo-stimulation (41 °C, 1h) 24h after CMV-NIS-MSC injection resulted in a significantly increased uptake of ^{123}I in heat-treated tumors compared to controls. Immunohistochemical staining and RT-PCR confirmed tumor-selective, temperature-dependent MSC migration. Therapeutic efficacy was significantly enhanced by combining CMV-NIS-MSC-mediated ^{131}I therapy with regional hyperthermia. We demonstrate here for the first time that hyperthermia can significantly boost tumoral MSC recruitment thereby significantly enhancing therapeutic efficacy of MSC-mediated NIS gene therapy.

Acta Biomater

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. 2020 Oct 14;S1742-7061(20)30611-5.

doi: 10.1016/j.actbio.2020.10.022. Online ahead of print.

Extracellular matrix derived from allogenic decellularized bone marrow mesenchymal stem cell sheets for the reconstruction of osteochondral defects in rabbits

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- PMID: 33068746

- DOI: 10.1016/j.actbio.2020.10.022

Abstract

Bioactive scaffolds from synthetical polymers or decellularized cartilage matrices have been widely used in osteochondral regeneration. However, the risks of potential immunological reactions and the inevitable donor morbidity of these scaffolds have limited their practical applications. To address these issues, a biological extracellular matrix (ECM) scaffold derived from allogenic decellularized bone marrow mesenchymal stem cell (BMSC) sheets was established for osteochondral reconstruction. BMSCs were induced to form cell sheets. Three different concentrations of sodium dodecyl sulfate (SDS), namely, 0.5%, 1%, and 3%, were used to decellularize these BMSC sheets to prepare the ECM. Histological and microstructural observations were performed in vitro and then the ECM scaffolds were implanted into osteochondral defects in rabbits to evaluate the repair effect in vivo. Treatment with 0.5% SDS not only efficiently removed BMSCs but also successfully preserved the original structure and bioactive components of the ECM When compared with the 1% and 3% SDS groups, histological observations substantiated the superior repair effect of osteochondral defects, including the simultaneous regeneration of well-vascularized subchondral bone and avascular articular cartilage integrated with native tissues in the 0.5% SDS group. Moreover, RT-PCR indicated that ECM scaffolds could promote the osteogenic differentiation potential of BMSCs under osteogenic conditions while increasing the chondrogenic differentiation potential of BMSCs under chondrogenic conditions. Allogenic BMSC sheets decellularized with 0.5% SDS treatment increased the recruitment of BMSCs and significantly improved the regeneration of osteochondral defects in rabbits, thus providing a prospective approach for both articular cartilage and subchondral bone reconstruction with cell-free transplantation.

FEBS J

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. 2020 Jul 13.

doi: 10.1111/febs.15483. Online ahead of print.

Roles of cell fusion between mesenchymal stromal/stem cells and malignant cells in tumor growth and metastasis

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- PMID: 33070450

- DOI: 10.1111/febs.15483

Abstract

Invasion and metastasis are the basic characteristics and important markers of malignant tumors, which are also the main cause of death in cancer patients. Epithelial-mesenchymal transition (EMT) is recognized as the first step of tumor invasion and metastasis. Many studies have demonstrated that cell fusion is a common phenomenon and plays a critical role in cancer development and progression. At present, cancer stem cell fusion has been considered as a new mechanism of cancer metastasis. Mesenchymal stromal/stem cell (MSC) is a kind of adult stem cells with high self-renewal ability and multi-differentiation potential, which is used as a very promising fusogenic candidate in the tumor microenvironment and has a crucial role in cancer progression. Many research results have shown that MSCs are involved in the regulation of tumor growth and metastasis through cell fusion. However, the role of cell fusion between MSCs and malignant cells in tumor growth and metastasis are still controversial. Several studies have demonstrated that MSCs can enhance malignant characteristics, promoting tumor growth and metastasis by fusing with malignant cells, while other conflicting reports believe that MSCs can reduce tumorigenicity upon fusion with malignant cells. In this review, we summarize the recent research on cell fusion events between MSCs and malignant cells in tumor growth and metastasis. The elucidation of the molecular mechanisms between MSCs fusion and tumor metastasis may provide an effective strategy for tumor biotherapy.