Sci Rep. 2018 Sep 6;8(1):13325. doi: 10.1038/s41598-018-31707-9.

Pro inflammatory stimuli enhance the immunosuppressive functions of adipose mesenchymal stem cells-derived exosomes.

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Author information

Abstract

The predominant mechanism by which adipose mesenchymal stem cells (AMSCs) participate to tissue repair is through a paracrine activity and their communication with the inflammatory microenvironment is essential part of this process. This hypothesis has been strengthened by the recent discovery that stem cells release not only soluble factors but also extracellular vesicles, which elicit similar biological activity to the stem cells themselves. We demonstrated that the treatment with inflammatory cytokines increases the immunosuppressive and anti-inflammatory potential of AMSCs-derived exosomes, which acquire the ability to shift macrophages from M1 to M2 phenotype by shuttling miRNA regulating macrophages polarization. This suggests that the immunomodulatory properties of AMSCs-derived exosomes may be not constitutive, but are instead induced by the inflammatory microenvironment.

Eur J Histochem. 2018 Sep 3;62(3). doi: 10.4081/ejh.2018.2969.

Low ozone concentrations promote adipogenesis in human adipose-derived adult stem cells.

Costanzo M[1], Boschi F, Carton F, Conti G, Covi V, Tabaracci G, Sbarbati A, Malatesta M.
Author information

Abstract

Ozone is a strong oxidant, highly unstable atmospheric gas. Its medical use at low concentrations has been progressively increasing as an alternative/adjuvant treatment for several diseases. In this study, we investigated the effects of mild ozonisation on human adipose-derived adult stem (hADAS) cells i.e., mesenchymal stem cells occurring in the stromal-vascular fraction of the fat tissue and involved in the tissue regeneration processes. hADAS cells were induced to differentiate into the adipoblastic lineage, and the effect of low ozone concentrations on the adipogenic process was studied by combining histochemical, morphometric and ultrastructural analyses. Our results demonstrate that ozone treatment promotes lipid accumulation in hADAS without inducing deleterious effects, thus paving the way to future studies aimed at elucidating the effect of mild ozonisation on adipose tissue for tissue regeneration and engineering.

Clin Orthop Surg. 2018 Sep;10(3):271-278. doi: 10.4055/cios.2018.10.3.271. Epub 2018 Aug 22.

Mesenchymal Stem Cell Therapy for Bone Regeneration.

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Author information

Abstract

Mesenchymal stem cells (MSCs) have been used in clinic for approximately 20 years. During this period, various new populations of MSCs have been found or manipulated. However, their characters and relative strength for bone regeneration have not been well known. For a comprehensive understanding of MSCs, we reviewed the literature on the multipotent cells ranging from the definition to the current research progress for bone regeneration. Based on our literature review, bone marrow MSCs have been most widely studied and utilized in clinical settings. Among other populations of MSCs, adipose-derived MSCs and perivascular MSCs might be potential candidates for bone regeneration, whose efficacy and safety still require further investigation.

Int J Radiat Oncol Biol Phys. 2018 Oct 1;102(2):407-416. doi: 10.1016/j.ijrobp.2018.05.068. Epub 2018 Jun 6.

Therapeutic Effects of Human Umbilical Cord-Derived Mesenchymal Stem Cells on Canine Radiation-Induced Lung Injury.

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Abstract

PURPOSE:

To investigate the effect of human umbilical cord-derived mesenchymal stem cell (MSC) transplantation on canine radiation-induced lung injury.

METHODS AND MATERIALS:

Beagle dogs received localized 15-Gy x-ray radiation to the right lower lung to establish the model of radiation-induced lung injury. After 180 days, dogs were divided into 2 groups (4 per group). The MSC group received intratracheal MSC transplantation, and the saline group received the same volume of normal saline by lavage. The effect of MSC transplantation on lung injury was then evaluated 180 days after transplantation.

RESULTS:

At 180 days after 15-Gy radiation, canine arterial blood oxygen partial pressure was significantly decreased, and the levels of hydroxyproline and transforming growth factor (TGF)-β in peripheral blood were significantly increased, whereas that of TGF-α was significantly decreased. Computed tomography evaluation revealed visible honeycomb shadows in the right middle and lower pulmonary pleurae. Blood oxygen partial pressure of the MSC group gradually increased over time, whereas the levels of hydroxyproline and TGF-β in the peripheral blood showed a decreasing trend; TGF-α levels gradually increased, which differed significantly from the results observed in the saline group. In addition, computed tomography and pathologic examination showed that the degree of lung injury in the

MSC group was milder. The MSC group also showed significantly increased pulmonary superoxide dismutase levels and significantly decreased tumor necrosis factor-α, Interleukein-1, and hyaluronic acid levels. Further study confirmed that MSC transplantation inhibited the activation of TGF-β-Smad2/3 in lung tissues, and in vitro experiments showed that medium conditioned with MSCs effectively inhibited the increase in Smad2 and 3 levels induced by TGF-β1.

CONCLUSION:

Canine radiation-induced lung injury could be observed at 180 days after radiation at 15 Gy. MSC transplantation can reduce oxidative stress, inflammatory reactions, and TGF-β-Smad2/3 pathway activation, thereby reducing lung injury.

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Effect of microfragmented adipose tissue on osteoarthritic synovial macrophage factors.

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Abstract

Cell-based therapies using adipose-derived mesenchymal stromal cells (ADMSCs) have shown promising results for the treatment of osteoarthritis (OA). In fact, ADMSCs are now indicated as one of the most powerful cell sources through their immunomodulatory and anti-inflammatory activities. Recently, an innovative one-step closed device was developed to obtain microfragmented adipose tissue (MF) to avoid the need for good manufacturing practices for ADMSCs expansion while maintaining their regenerative potential. The aim of this study was to assess the mechanisms of action of MF and ADMSCs from MF (MF-ADMSCs) on an inflammatory cell model of OA synoviocytes. We found that MF produced low levels of inflammatory factors such as interleukin 6 (IL-6), CC-chemokine ligand 5/receptor-activated normal T-cell expressed and secreted (CCL5/RANTES), CC-chemokine ligand 2/monocyte chemoattractant protein-1 (CCL2/MCP-1), and CC-chemokine ligand 3/macrophage inflammatory protein-1α (CCL3/MIP-1α), and a higher level only of CXC-chemokine ligand 8/interleukin 8 compared with MF-ADMSCs. Matrix metalloproteinase 9 (MMP-9) degradative factor but released a lower level of its inhibitor tissue inhibitor of the metalloproteinase (TIMP-1). MF in coculture with synoviocytes significantly induced both the metabolic activity and the release of IL-6. In contrast, MF, not MF-ADMSCs, partially decreased CCL5/RANTES. Moreover, MF reduced the release of both macrophage-specific chemokines (CCL2/MCP-1 and CCL3/MIP-1α) and degradative marker MMP-9. Interestingly, MF increased TIMP-1 (the MMP-9 inhibitor) and down-modulated toll-like receptor (TLR4) receptor and key molecules of NFκB pathways. These data evidenced different effects of MF versus MF-ADMSCs on inflamed synoviocytes. MF reduced typical macrophages markers and its potentiality by switching off macrophages activity was strictly dependent on TLR4 and NFκB signaling

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Aerosolised Mesenchymal Stem Cells Expressing Angiopoietin-1 Enhances Airway Repair.

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Author information

Abstract

BACKGROUND:

The aim of this study was to investigate the effects of MSCs and MSC-expressing ANGPT1 (MSC-pANGPT1) treatment via aerosolisation in alleviating the asthma-related airway inflammation in the rabbit model.

METHODS:

Rabbits were sensitised and challenged with both intraperitoneal injection and inhalation of ovalbumin (Ova). MSCs and MSC-pANGPT1 cells were aerosolised into rabbit lungs using the MicroSprayer® Aerosolizer Model IA-1B 48 h after injury. The post mortem was performed 3 days following cell delivery. Histopathological assessments of the lung tissues and inflammatory response were quantitatively scored following treatments.

RESULT(S):

Administration of aerosolised MSCs and MSC-pANGPT1 were significantly reduced inflammation of the airways ($p < 0.001$), as reflected by improved of structural changes such as thickness of the basement membrane, epithelium, mucosa and sub-mucosa regions. The airway inflammation score of both treatment groups revealed a significant reduction of inflammation and granulocyte infiltration at the peribronchiale and perivascular regions ($p < 0.05$). Administration of aerosolised MSCs alone was resulted in significant reduction in the levels of pro-inflammatory genes (IL-4 and TGF-β) while treatment with aerosolised MSC-pANGPT1 led to further reduction of various pro-inflammatory genes to the base-line values (IL4, TNF, MMP9 and TGF-β). Treatment with both aerosolised MSCs and MSC-pANGPT1 cells was also alleviated the number of airway inflammatory cells in the bronchoalveolar lavage (BAL) fluid and goblet cell hyperplasia.

CONCLUSION(S):

Our findings suggest that treatment with MSCs alone attenuated airway inflammation and structural changes of the airway. Treatment with MSC-pANGPT1 provided an additional effect in reducing the expression levels of various pro-inflammatory genes. Both of these treatment enhancing airway repair and therefore may provide a basis for the development of an innovative approach for the treatment and prevention of airway inflammatory diseases.

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Influence of hydrodynamic pressure on chondrogenic differentiation of human bone marrow mesenchymal stem cells cultured in perfusion system.

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Author information

Abstract

The natural conditions of chondrocytes in native cartilage including mechanical forces and surface topology could be simulated to enhance chondrogenesis. A perfusion system recapitulating the hydrodynamic pressure of cartilage tissue is designed. Mesenchymal stem cells (MSCs) are isolated and seeded on aligned nanofibrous PCL/PLGA scaffolds that mimic the structure of superficial zone of articular cartilage. The cell-seeded scaffolds are placed into the perfusion bioreactor and exposed to chondrogenic differentiating medium. The chondrogenesis is then investigated by histological analysis and real time PCR for cartilage-specific genes. The highest expression levels of aggrecan and type II collagen are observed in the cells cultured in the presence of differentiating medium and mechanical stimulation. The expression level of type II collagen is higher than aggrecan in presence of differentiating medium and absence of mechanical stimulation. On the contrary, the expression ratio of aggrecan is higher than type II collagen in presence of mechanical stimulation and absence of differentiating medium. These results show the dominant role of mechanical stimulation and differentiating medium on upregulated expression of aggrecan and type II collagen, respectively. The application of mechanical stimulation upon cells-seeded scaffolds could mimic superficial zone of articular cartilage tissue and increase derivation of chondrocytes from MSCs.