ML 28-20 (21/07/2020)

Cancer Lett

. 2020 Jul 16;S0304-3835(20)30363-3.
doi: 10.1016/j.canlet.2020.07.008. Online ahead of print.

Bone marrow mesenchymal stem cell-derived exosomal miR-206 inhibits osteosarcoma progression by targeting TRA2B

Hongliang Zhang[1], Jun Wang[1], Tingting Ren[1], Yi Huang[1], Xin Liang[1], Yiyang Yu[1], Wei Wang[1], Jianfang Niu[1], Wei Guo[2]
Affiliations expand

- PMID: 32682951

- DOI: 10.1016/j.canlet.2020.07.008

Abstract

Osteosarcoma is the most common primary malignant bone tumor in young people. Recently, extracellular vesicles, especially exosomes, have been reported to play an increasingly important role in the development of many types of tumors. In this research, we found that overexpression of transformer 2β (TRA2B) was associated with tumor progression in osteosarcoma, and TRA2B was the target gene of miR-206, which was downregulated in osteosarcoma tissues. Furthermore, we observed that bone marrow mesenchymal stem cell (BMSC)-derived exosomes could carry and transport miR-206 to osteosarcoma cells. Both in vitro and in vivo results showed that BMSC-derived exosomal miR-206 could inhibit the proliferation, migration and invasion of osteosarcoma cells and induce their apoptosis. Taken together, our study demonstrates that BMSC-derived exosomal miR-206 can be transferred into osteosarcoma cells and inhibit tumor progression by targeting TRA2B, which provides new insight into the molecular mechanism of osteosarcoma and highlights the potential of miR-206 and TRA2B as new therapeutic targets.

Stem Cell Rev Rep

. 2020 Jul 18.
doi: 10.1007/s12015-020-10009-6. Online ahead of print.

Pulsed Electromagnetic Fields Modulate miRNAs During Osteogenic Differentiation of Bone Mesenchymal Stem Cells: a Possible Role in the Osteogenic-angiogenic Coupling

Monica De Mattei[1], Silvia Grassilli[2,3], Agnese Pellati[2], Federica Brugnoli[2], Elena De Marchi[4], Deyanira Contartese[4,5], Valeria Bertagnolo[6]
Affiliations expand

- PMID: 32681233

- DOI: 10.1007/s12015-020-10009-6

Abstract

Despite the high intrinsic ability of bone tissue to regenerate, bone healing fails in some pathological conditions and especially in the presence of large defects. Due to the strong relationship between bone development and vascularization during in vivo bone formation and repair, strategies promoting the osteogenic-angiogenic coupling are crucial for regenerative medicine. Increasing evidence shows that miRNAs play important roles in controlling osteogenesis and bone vascularization and are important tool in medical research although their clinical use still needs to optimize miRNA stability and delivery. Pulsed electromagnetic fields (PEMFs) have been successfully used to enhance bone repair and their clinical activity has been associated to their ability to promote the osteogenic differentiation of human mesenchymal stem cells (hMSCs). In this study we investigated the potential ability of PEMF exposure to modulate selected miRNAs involved in the osteogenic differentiation of human bone mesenchymal stem cells (hBMSCs). We show that, during in vitro hBMSC differentiation, PEMFs up-modulate the expression of miR-26a and miR-29b, which favor osteogenic differentiation, and decrease miR-125b which acts as an inhibitor miRNA. As PEMFs promote the expression and release of miRNAs also involved in angiogenesis, we conclude that PEMFs may represent a noninvasive and safe strategy to modulate miRNAs with relevant roles in bone repair and with the potential to regulate the osteogenic-angiogenic coupling.

Stem Cell Res Ther

. 2020 Jul 17;11(1):293.
doi: 10.1186/s13287-020-01807-3.

Antimicrobial activity of mesenchymal stem cells against Staphylococcus aureus

Haruyo Yagi[1], Antonia F Chen[1,2], David Hirsch[1], Adam C Rothenberg[1,3], Jian Tan[1], Peter G Alexander[1], Rocky S Tuan[4,5]
Affiliations expand

- PMID: 32680544

- DOI: 10.1186/s13287-020-01807-3

Abstract

Introduction: There have been limited advances in the treatment of bone and joint infections, which currently involves a combination of surgery and antibiotic administration. There is a timely need in orthopedics to develop more effective and less invasive forms of antimicrobial prophylaxis and treatment. The antibacterial effect of adult tissue-derived mesenchymal stem cells (MSCs) has recently been investigated against Escherichia coli and Staphylococcus aureus. The main mechanism of action is postulated to be via MSC production of the cationic antimicrobial peptide, LL-37.

Methods: This study examines the antimicrobial activity of adipose-derived human MSCs (ASCs) on S. aureus, specifically examining the role of LL-37 and regulation of its expression. Bacteria colony-forming unit (CFU) assay was used to assess antimicrobial activity.

Results: Our results showed that the ASC-conditioned medium significantly inhibited the growth of S. aureus under standard culture conditions with or without the continued presence of ASCs. Also, the treatment of ASCs with 1,25-dihydroxy vitamin D_3 elevated LL-37 expression and enhanced their antimicrobial activity. In support, treatment with the vitamin D receptor inhibitor, GW0742, blocked the antimicrobial activity of ASCs.

Conclusion: Our findings clearly demonstrate the antimicrobial activity of adult ASCs against S. aureus and implicate a key regulatory role for vitamin D. Further testing in in vivo models is being pursued to assess the potential application of ASCs as a biocompatible, adjunct treatment for musculoskeletal infections.

Tissue Eng Part A

. 2020 Jul 17.
doi: 10.1089/ten.TEA.2020.0092. Online ahead of print.

The survey on cellular and tissue-engineered therapies in Europe in 2016 and 2017

Max Hans-Peter Gay[1], Helen Baldomero[2], Dominique Farge-Bancel[3], Pamela Gehron Robey[4], Scott Rodeo[5], Jakob Passweg[6], Magdalena Müller-Gerbl[7], Ivan Martin[8]
Affiliations expand

- PMID: 32680446

- DOI: 10.1089/ten.TEA.2020.0092

Abstract

This report describes activity in Europe for the years 2016 and 2017 in the area of cellular and tissue-engineered therapies, excluding hematopoietic stem cell treatments for the reconstitution of hematopoiesis. It is the eighth of its kind and is supported by five established scientific organizations. In 2016 and 2017, a combined 234 teams from 29 countries responded to the cellular and engineered tissue therapy survey; 227 teams reported treating 8236 patients in these two years. Indications were categorized in hematology/oncology (40%; predominantly prevention or treatment of graft versus host disease and hematopoietic graft enhancement), musculoskeletal/rheumatological disorders (29%), cardiovascular disorders (6%), neurological disorders (4%), gastrointestinal disorders (<1%), as well as miscellaneous disorders (20%), which were not assigned to the previous indications. The predominantly used cells were autologous (61%). The majority of autologous cells were used to treat musculoskeletal/rheumatological (44%) disorders, whereas allogeneic cells were mainly used for hematology/oncology (78%). The reported cell types were mesenchymal stem/stromal cells (MSCs) (56%), hematopoietic cells (21%), keratinocytes (7%), chondrocytes (6%) dermal fibroblasts (4%), dendritic cells (2%), and other cell types (4%). Cells were expanded in vitro in 62% of the treatments, sorted in 11% of the cases, and rarely transduced (2%). The processing of cells was out-sourced to external facilities in 30% of the cases. Cells were delivered predominantly intravenously or intra-arterially [47%], as suspension [36%], or using a membrane/scaffold (16%). The data are compared with those from previous years to identify trends in a rapidly evolving field. In this edition, the report includes a critical discussion of data collected in the space of orthopedics and the use of MSCs.

Stem Cell Res Ther

. 2020 Jul 16;11(1):287.
doi: 10.1186/s13287-020-01810-8.

10-year follow-up results of the prospective, double-blinded, randomized, controlled study on autologous bone marrow buffy coat grafting combined with core decompression in patients with avascular necrosis of the femoral head

Mengyuan Li[1], Yuanchen Ma[1], Guangtao Fu[1], Ruiying Zhang[1], Qingtian Li[1], Zhantao Deng[1], Minghao Zheng[2], Qiujian Zheng[3]
Affiliations expand

- PMID: 32678055

- DOI: 10.1186/s13287-020-01810-8

Free article

Abstract

Background: Avascular necrosis of the femoral head (ANFH) is a severely disabling disease of the hip. Several clinical trials have shown promising outcomes on the use of mesenchymal stem cells for the treatment of ANFH, but long-term clinical assessments are lacking. Previously, we reported the 2-year follow-up results of a prospective, double-blinded, randomized, controlled study on autologous bone marrow buffy coat grafting combined with core decompression in patients with ANFH. Here, we report the 10-year follow-up results of this study.

Methods: We recruited 43 (53 hips) patients from 2009 to 2010. The hips were randomly allocated to code decompression (CD) with or without bone marrow buffy coat (BBC) grafting. Participants underwent follow-up at 24, 60, and 120 months postoperatively. The visual analogue scale (VAS), Lequesne algofunctional index, and Western Ontario and McMaster Universities Arthritis Index (WOMAC) osteoarthritis scores were recorded.

Survival rate analysis and prognostic factor analysis were performed. The endpoint was defined as progression to Ficat stage IV or conversion to hip arthroplasty.

Results: A total of 31 patients (41 hips) were included in the final analysis. The CD + BBC group had better subjective assessment scores than the CD group. The average survival times were 102.3 months and 78.1 months in the CD + BBC group and CD group, respectively (log-rank test, P = 0.029). In the univariate Cox proportional hazards regression model, age [hazard ratio (HR) = 1.079, P = 0.047] and preoperative Ficat stage (HR = 3.283, P = 0.028) indicated a high risk for progression, while the use of BBC (HR = 0.332, P = 0.042) indicated a low risk. Preoperative Ficat stage III was isolated as an independent risk factor for clinical failure in the multivariate model (HR = 3.743, P = 0.018).

Conclusion: The 10-year follow-up results of this prospective, double-blinded, randomized, controlled study showed that the use of autologous BBC in combination with core decompression was more effective than the use of core decompression alone.

Trial registration: ClinicalTrials.gov, NCT01613612 . Registered on 13 December 2011-retrospectively registered.

Stem Cell Res Ther

. 2020 Jul 16;11(1):283.
doi: 10.1186/s13287-020-01789-2.

A glance on the role of actin in osteogenic and adipogenic differentiation of mesenchymal stem cells

Asmat Ullah Khan[1], Rongmei Qu[1], Tingyu Fan[1], Jun Ouyang[2], Jingxing Dai[3]
Affiliations expand

- PMID: 32678016

- DOI: 10.1186/s13287-020-01789-2

Free article

Abstract

Mesenchymal stem cells (MSCs) have the capacity to differentiate into multiple lineages including osteogenic and adipogenic lineages. An increasing number of studies have indicated that lineage commitment by MSCs is influenced by actin remodeling. Moreover, actin has roles in determining cell shape, nuclear shape, cell spreading, and cell stiffness, which eventually affect cell differentiation. Osteogenic differentiation is promoted in MSCs that exhibit a large spreading area, increased matrix stiffness, higher levels of actin polymerization, and higher density of stress fibers, whereas adipogenic differentiation is prevalent in MSCs with disrupted actin networks. In addition, the mechanical properties of F-actin empower cells to sense and transduce mechanical stimuli, which are also reported to influence differentiation. Various biomaterials, mechanical, and chemical interventions along with pathogen-induced actin alteration in the form of polymerization and depolymerization in MSC differentiation were studied recently. This review will cover the role of actin and its modifications through the use of different methods in inducing osteogenic and adipogenic differentiation.

Stem Cells Int

. 2020 Jun 30;2020:5690252.
doi: 10.1155/2020/5690252. eCollection 2020.

Clinical Application Status of Articular Cartilage Regeneration Techniques: Tissue-Engineered Cartilage Brings New Hope

Shuangpeng Jiang[1,2], Weimin Guo[2], Guangzhao Tian[2], Xujiang Luo[2], Liqing Peng[2], Shuyun Liu[2], Xiang Sui[2], Quanyi Guo[2], Xu Li[1]
Affiliations expand

- PMID: 32676118
- PMCID: PMC7345961
- DOI: 10.1155/2020/5690252

Free PMC article

Abstract

Hyaline articular cartilage lacks blood vessels, lymphatics, and nerves and is characterised by limited self-repair ability following injury. Traditional techniques of articular cartilage repair and regeneration all have certain limitations. The development of tissue engineering technology has brought hope to the regeneration of articular cartilage. The strategies of tissue-engineered articular cartilage can be divided into three types: "cell-scaffold construct," cell-free, and scaffold-free. In "cell-scaffold construct" strategies, seed cells can be autologous chondrocytes or stem. Among them, some commercial products with autologous chondrocytes as seed cells, such as BioSeed®-C and CaReS®, have been put on the market and some products are undergoing clinical trials, such as NOVOCART® 3D. The stem cells are mainly pluripotent stem cells and mesenchymal stem cells from different sources. Cell-free strategies that indirectly utilize the repair and regeneration potential of stem cells have also been used in clinical settings, such as TruFit and MaioRegen. Finally, the scaffold-free strategy is also a new development direction, and the short-term repair results of related products, such as NOVOCART® 3D, are encouraging. In this paper, the commonly used techniques of articular cartilage regeneration in surgery are reviewed. By studying different strategies and different seed cells, the clinical application status of tissue-engineered articular cartilage is described in detail.

Stem Cells Int

. 2020 Jun 27;2020:5684250.
doi: 10.1155/2020/5684250. eCollection 2020.

Screening and Functional Pathway Analysis of Pulmonary Genes Associated with Suppression of Allergic Airway Inflammation by Adipose Stem Cell-Derived Extracellular Vesicles

Sung-Dong Kim[1], Shin Ae Kang[2], Yong-Wan Kim[3], Hak Sun Yu[2], Kyu-Sup Cho[1], Hwan-Jung Roh[4]
Affiliations expand

- PMID: 32676117

- PMCID: PMC7336241

- DOI: 10.1155/2020/5684250

Free PMC article

Abstract

Background: Although mesenchymal stem cell- (MSC-) derived extracellular vesicles (EVs) are as effective as MSCs in the suppression of allergic airway inflammation, few studies have explored the molecular mechanisms of MSC-derived EVs in allergic airway diseases. The objective of this study was to evaluate differentially expressed genes (DEGs) in the lung associated with the suppression of allergic airway inflammation using adipose stem cell- (ASC-) derived EVs.

Methods: C57BL/6 mice were sensitized to ovalbumin (OVA) by intraperitoneal injection and challenged intranasally with OVA. To evaluate the effect of ASC-derived EVs on allergic airway inflammation, 10 μg/50 μL of EVs were administered intranasally prior to OVA challenge. Lung tissues were removed and DEGs were compared pairwise among the three groups. DEG profiles and hierarchical clustering of the identified genes were analyzed to evaluate changes in gene expression. Real-time PCR was performed to determine the expression levels of genes upregulated after treatment with ASC-derived EVs. Enrichment analysis based on the Gene Ontology (GO) database and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis were also performed to further identify the function of DEGs.

Results: Expression of paraoxonase 1 (PON1), brain-expressed X-linked 2 (Bex2), insulin-like growth factor binding protein 6 (Igfbp6), formyl peptide receptor 1 (Fpr1), and secretoglobin family 1C member 1 (Scgb1c1) was significantly increased in asthmatic mice following treatment with ASC-derived EVs. GO enrichment and KEGG pathway analysis showed that these genes were strongly associated with immune system processes and their regulation, cellular processes, single-organism processes, and biological regulation.

Conclusion: These results suggest that the DEGs identified in this study (PON1, Bex2, Igfbp6, Fpr1, and Scgb1c1) may be involved in the amelioration of allergic airway inflammation by ASC-derived EVs

Viruses

. 2020 Jul 12;12(7):E750.
doi: 10.3390/v12070750.

Canine Adipose-Derived Mesenchymal Stem Cells (cAdMSCs) as a "Trojan

Horse" in Vaccinia Virus Mediated Oncolytic Therapy against Canine Soft Tissue Sarcomas

Ivan Petrov[1], Ivaylo Gentschev[1], Anna Vyalkova[1], Mohamed I Elashry[2], Michele C Klymiuk[2], Stefan Arnhold[2], Aladar A Szalay[1,3]
Affiliations expand

- PMID: 32664672

- DOI: 10.3390/v12070750

Free article

Abstract

Several oncolytic viruses (OVs) including various human and canine adenoviruses, canine distemper virus, herpes-simplex virus, reovirus, and members of the poxvirus family, such as vaccinia virus and myxoma virus, have been successfully tested for canine cancer therapy in preclinical and clinical settings. The success of the cancer virotherapy is dependent on the ability of oncolytic viruses to overcome the attacks of the host immune system, to preferentially infect and lyse cancer cells, and to initiate tumor-specific immunity. To date, several different strategies have been developed to overcome the antiviral host defense barriers. In our study, we used canine adipose-derived mesenchymal stem cells (cAdMSCs) as a "Trojan horse" for the delivery of oncolytic vaccinia virus Copenhagen strain to achieve maximum oncolysis against canine soft tissue sarcoma (CSTS) tumors. A single systemic administration of vaccinia virus-loaded cAdMSCs was found to be safe and led to the significant reduction and substantial inhibition of tumor growth in a CSTS xenograft mouse model. This is the first example that vaccinia virus-loaded cAdMSCs could serve as a therapeutic agent against CSTS tumors.