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Connexin expression decreases during adipogenic differentiation of human adipose-derived mesenchymal stem cells

Giuliana Mannino[1], Nunzio Vicario[1], Rosalba Parenti[1], Rosario Giuffrida[2], Debora Lo Furno[1]

Affiliations expand

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Abstract

Adipose-derived stem cells (ASCs) represent a valuable tool for regenerative medicine being able to differentiate toward several cell lines, such as adipocytes, chondrocytes and osteocytes. During ASC adipogenic differentiation, changes in connexin (Cx) expression were evaluated in the present study. Three different Cxs were investigated: Cx43, Cx32 and Cx31.9. Cx43 is the most abundant in human tissues, Cx32 is prevalently found in nervous tissue and Cx31.9 is found at the myocardial level. Human ASCs undergoing adipogenic differentiation were isolated from raw lipoaspirate and characterized as mesenchymal stem cells. After multiple days of culture (1, 7, 14, 21 and 28 days), adipogenic differentiation was assessed by Oil Red O staining and Acetyl-CoA carboxylase (ACC) levels by western blotting. Cx expression was evaluated by western blotting at the same time points. In treated ASCs, lipidic vacuoles were detected from day 7 of treatment. Their number and size progressively increased over the entire period of observation. A parallel increase of ACC expression was also found. Lower levels of Cx expression were detected during adipogenic differentiation. Such decreases were particularly evident for Cx32, already after the first day of treatment. Cx31.9 and Cx43 also decreased, but starting from day 7. Our results suggest that ASCs may initially be equipped with a variety of Cxs, which is not

surprising assuming their multipotential differentiation ability. Although some Cxs may be selectively enhanced depending on specific induction strategies toward different tissues, they seem markedly downregulated during adipogenic differentiation.

Biology (Basel)

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Concentrated Growth Factors (CGF) Induce Osteogenic Differentiation in Human Bone Marrow Stem Cells

Alessio Rochira[1], Luisa Siculella[1], Fabrizio Damiano[1], Andrea Palermo[2], Franco Ferrante[3], Maria Annunziata Carluccio[4], Nadia Calabriso[1,4], Laura Giannotti[1], Eleonora Stanca[1]

Affiliations expand

- PMID: 33143015

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Free article

Abstract

Bone regeneration is a complex process regulated by several factors that control overlapping biological processes, coordinating interactions among distinct cell populations. There is a great interest in identifying new strategies for inducing osteogenesis in a safe and efficient manner. Concentrated Growth Factor (CGF) is an autologous blood derived product obtained by centrifugation of venous blood following the procedure set on the Silfradent device. In this study the effects of CGF on osteogenic differentiation of human Bone Marrow Stem Cells (hBMSC) in vitro have been investigated; hBMSC were cultured with CGF or osteogenic medium, for 21 days. The osteogenic differentiation was evaluated measuring alkaline phosphatase (ALP) enzyme activity, matrix mineralization by alizarin red staining and through mRNA and protein quantification of osteogenic differentiation markers by Real-time PCR and Western blotting, respectively. The treatment with CGF stimulated ALP activity and promoted matrix mineralization compared to control and seems to be more effective than osteogenic medium. Also, hBMSC lost mesenchymal markers and showed other osteogenic features. Our study

showed for the first time that CGF alone is able to induce osteogenic differentiation in hBMSC. The application of CGF on hBMSC osteoinduction might offer new clinical and biotechnological strategies in the tissue regeneration field.

Cancer Manag Res

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Antitumor Activity of Cabazitaxel and MSC-TRAIL Derived Extracellular Vesicles in Drug-Resistant Oral Squamous Cell Carcinoma

Yongle Qiu[1], Jieming Sun[2], Junping Qiu[2], Guoling Chen[2], Xiao Wang[2], Yaxu Mu[2], Kunshan Li[1], Wenjing Wang[1]

Affiliations expand

- PMID: 33149686

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Free PMC article

Abstract

Introduction: TRAIL (tumor necrosis factor-related apoptosis-inducing ligand) can induce apoptosis in a variety of cancer cells. However, drug resistance of tumor and short half-life seriously affects its clinical targeted therapy. Cabazitaxel (CTX) is a taxane drug, which can induce apoptosis or autophagy by inhibiting the phosphorylation of PI3K/Akt/mTOR and sensitive to some drug-resistant tumors. Therefore, we explored the possibility of developing a mesenchymal stem cell-derived exosomes (MSC-EXO) vector for oral squamous cell carcinoma (OSCC) to deliver CTX/TRAIL combinations.

Methods: After ultracentrifugation and dialysis, CTX/TRAIL loaded exosomes transfected MSC (MSCT)-derived exosome (EXO) (MSCT-EXO/CTX) were isolated and purified. The expression of CD63, CD9 and TRAIL was detected by BCA to confirm the origin of EXO. High-performance liquid chromatography (HPLC) was used to determine the drug loading of VPF and draw the in vitro release profile. MTT assay, flow cytometry and Western blot were used to detect the antitumor effect of MSCT-EXO/CTX in vitro. Subsequently, the antitumor effect of MSCT-EXO/CTX in vivo was verified by mouse model.

Results: The diameter of the membrane particles was about 60-150 nm. We have proved that the incorporation and release of CTX in MSCT-EXO can inhibit the activation of PI3K, Akt and mTOR, which is a possible synergistic mechanism of CTX. MSCT-EXO and CTX can induce the apoptosis of SCC25 tumor cells in a dose-dependent manner and exert a good synergistic effect in the proportion range of 10:1-5:1. The inherent activity of MSCT-EXO and the direct effect of MSCT-EXO/CTX on OSCC confirm that MSCT-EXO/CTX makes MSCT-EXO and CTX have an efficient synergistic effect and a highly effective pharmacological inhibition on cancer cells, as verified by the subsequent mouse model. MSCT-EXO/CTX showed the lowest relative tumor volume and the highest tumor inhibition rate ($P<0.05$) in vivo.

Cancer Biomark

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Bone mesenchymal stem cells derived extracellular vesicles promotes TRAIL-related apoptosis of hepatocellular carcinoma cells via the delivery of microRNA-20a-3p

Lu Deng[1], Chang Wang[2], Chao He[3], Li Chen[4]

Affiliations expand

- PMID: 33136092

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Abstract

Objective: Bone mesenchymal stem cells (BMSCs) have been widely researched in cancer treatment, including hepatocellular carcinoma (HCC). This study intended to discuss the mechanism of miR-20a-3p in BMSCs-extracellular vesicles (EVs) in HCC apoptosis.

Methods: BMSCs were isolated and identified. EVs derived from BMSCs were extracted and identified. After overexpressing or inhibiting miR-20a-3p expression in BMSCs, EVs were extracted and acted on HCC cells and transplanted tumors. HCC cell apoptosis in the treatment of BMSCs-conditioned medium, BMSCs-EVs and/or miR-20a-3p mimic/inhibitor were evaluated, with the detection of levels of TRAIL and TRAIL-related proteins. A functional rescue experiment about c-FLIP was carried out in HCC cells. The target binding relationship between miR-20a-3p and c-FLIP was detected. The subcutaneous tumorigenesis model of mice was established and injected with BMSCs-EVs to estimate the effect of BMSCs-EVs-miR-20a-3p on HCC growth.

Results: EVs isolated from BMSCs conditioned medium promoted the apoptosis of HCC cells. After BMSCs-EVs treatment, TRAIL levels, downstream proteins and miR-20a-3p were increased significantly, but the expression of c-FLIP was decreased. miR-20a-3p could target c-FLIP. BMSCs-EVs inhibited the growth of HCC cells, decreased c-FLIP expression, increased TRAIL levels, and promote the of HCC cell apoptosis. BMSCs-EVs with overexpressing miR-20a-3p further enhanced the apoptotic effect of HCC cells in vitro and in vivo.

Conclusion: BMSCs-EVs-carried miR-20a-3p targets c-FLIP and increases TRAIL levels in HCC cells, thus promoting TRAIL-related apoptosis.

PLoS One

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Mesenchymal stem cells promote metastasis through activation of an ABL-MMP9 signaling axis in lung cancer cells

Jing Jin Gu[1], Jacob Hoj[1], Clay Rouse[2], Ann Marie Pendergast[1]
Affiliations expand

- PMID: 33119681

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Free article

Abstract

Mesenchymal stem cells (MSCs) are recruited and activated by solid tumors and play a role in tumor progression and metastasis. Here we show that MSCs promote metastasis in a panel of non-small cell lung cancer (NSCLC) cells. MSCs elicit transcriptional alterations in lung cancer cells leading to increased expression of factors implicated in the epithelial-to-mesenchymal transition (EMT) and secreted proteins including matrix metalloproteinase-9 (MMP9). MSCs enhance secretion of enzymatically active MMP9 in a panel of lung adenocarcinoma cells. High expression of MMP9 is linked to low survival rates in lung adenocarcinoma patients. Notably, we found that ABL tyrosine kinases are activated in MSC-primed lung cancer cells and functional ABL kinases are required for MSC-induced MMP9 expression, secretion and proteolytic activity. Importantly, ABL kinases are required for MSC-induced NSCLC metastasis. These data reveal an actionable target for inhibiting MSC-induced metastatic activity of lung adenocarcinoma cells through disruption of an ABL kinase-MMP9 signaling axis activated in MSC-primed lung cancer cells.