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Doxorubicin Delivered Using Nanoparticles Camouflaged with Mesenchymal Stem Cell Membranes to Treat Colon Cancer.

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Author information

Abstract

PURPOSE:

The primary goal of the present study was to design doxorubicin (DOX)-loaded superparamagnetic iron oxide (SPIO) nanoparticles (NPs) coated with mesenchymal stem cell (MSC) membranes and explore their effect on colon cancer in vitro and in vivo.

METHODS:

DOX-SPIO NPs were coated with MSC membranes using an extruder, and the morphological characteristics of MSC membrane-camouflaged nanodrug (DOX-SPIO@MSCs) evaluated by transmission electron microscopy (TEM) and NP-tracking analysis. Drug loading and pH response were assessed by UV spectrophotometry. Intracellular colocalization was analyzed using NP-treated MC38 cells stained with 3,3'-dioctadecyloxacarbocyanine perchlorate and Hoechst 33342. Cellular uptake was analyzed using an inverted fluorescence microscope and flow cytometry and cytotoxicity evaluated by cell counting kit-8 assay. Biological compatibility was assessed by hemolysis analysis, immunoactivation test and leukocyte uptake experiments. Furthermore, intravenous injection of chemotherapy drugs into MC38 tumor-bearing C57BL/6 mice was used to study anti-tumor effects.

RESULTS:

Typical core-shell NP structures were observed by TEM. Particle size remained stable in fetal bovine serum and phosphate-buffered saline (PBS). Compared with DOX-SPIO, DOX-SPIO@MSCs improved cellular uptake efficiency, enhanced anti-tumor effects, and reduced the immune system response. Animal experiments demonstrated that DOX-SPIO@MSCs enhanced tumor treatment efficacy while reducing systemic side effects.

CONCLUSION:

Our experimental results demonstrate that DOX-SPIO@MSCs are a promising targeted nanocarrier for application in treatment of colon cancer.

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Mesenchymal stem cells for the treatment of psoriasis: a comprehensive review.

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Abstract

Mesenchymal stem cells (MSCs) have recently been shown to have not only regenerative capabilities but also immunomodulating properties. For this reason, they are currently under investigation in clinical trials for the treatment of several autoimmune systemic disorders. Psoriasis is a systemic immune-mediated disease for which MSCs could have therapeutic potential. We analysed the existing literature with regard to MSC-based strategies for the treatment of psoriasis. by conduction a review of the existing literature on MSCs as a possible therapy for psoriasis, using the MEDLINE, Embase, Scopus and Cochrane Library electronic databases from inception to the date of study. A number of studies confirm the involvement of MSCs in psoriasis pathogenesis and therefore designate MSCs as an important potential therapeutic tool in this setting. Preclinical data are mostly based on imiquimod-induced (IMQ) murine models of psoriasis, and confirm the anti-inflammatory and immunomodulatory action of MSCs in the setting of psoriasis. Six patients affected by psoriasis were described in four clinical studies. Despite significant differences in terms of therapeutic protocols and clinical outcomes, the MSC-based regimens were efficacious in 100% of the cases. Despite more data still being needed, MSCs could be a promising therapy for psoriasis.

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Comprehensive Molecular Profiles of Functionally Effective MSC-Derived Extracellular Vesicles in Immunomodulation.

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Abstract

Accumulating evidence indicates that mesenchymal stem/stromal cell-derived extracellular vesicles (MSC-EVs) exhibit immunomodulatory effects by delivering therapeutic RNAs and proteins; however, the molecular mechanism underlying the EV-mediated immunomodulation is not fully understood. In this study, we found that EVs from early-passage MSCs had better immunomodulatory potency than did EVs from late-passage MSCs in T cell receptor (TCR)- or Toll-like receptor 4 (TLR4)-stimulated splenocytes and in mice with ocular Sjögren's syndrome. Moreover, MSC-EVs were more effective when produced from 3D culture of the cells than from the conventional 2D culture. Comparative molecular profiling using proteomics and microRNA sequencing revealed the enriched factors in MSC-EVs that were functionally effective in immunomodulation. Among them, manipulation of transforming growth factor β1 (TGF-β1), pentraxin 3 (PTX3), let-7b-5p, or miR-21-5p levels in MSCs significantly

affected the immunosuppressive effects of their EVs. Furthermore, there was a strong correlation between the expression levels of TGF-β1, PTX3, let-7b-5p, or miR-21-5p in MSC-EVs and their suppressive function. Therefore, our comparative strategy identified TGF-β1, PTX3, let-7b-5p, or miR-21-5p as key molecules mediating the therapeutic effects of MSC-EVs in autoimmune disease. These findings would help understand the molecular mechanism underlying EV-mediated immunomodulation and provide functional biomarkers of EVs for the development of robust EV-based therapies.

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Signature Quality Attributes of CD146^{+} Mesenchymal Stem/Stromal Cells Correlate to High Therapeutic and Secretory Potency.

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Abstract

CD146^{+} bone marrow-derived Mesenchymal Stem/Stromal Cells (BM-MSC) play key roles in the perivascular niche, skeletogenesis, and hematopoietic support, however comprehensive evaluation of therapeutic potency has yet to be determined. In this study, in vitro inflammatory priming to crude human BM-MSC (n = 8) captured a baseline of signature responses including enriched CD146^{+} with co-expression of CD107a^{High} , CXCR4^{High} , and LepR^{High} , transcriptional profile, enhanced secretory capacity, robust immunomodulatory secretome and function, including immunopotency assays with stimulated immune cells. These signatures were significantly more pronounced in CD146^{+} (POS)-sorted subpopulation than in the CD146^{-} (NEG). Mechanistically, POS BM-MSC were showed markedly higher secretory capacity with significantly greater immunomodulatory and anti-inflammatory protein production upon inflammatory priming compared to the NEG BM-MSC. Moreover, immunopotency assays with stimulated peripheral blood mononuclear and T lymphocytes demonstrated robust immunosuppression mediated by POS BM-MSC while inducing significant frequencies of Regulatory T cells. In vivo evidence showed POS BM-MSC treatment promoted pronounced M1-to-M2 macrophage polarization, ameliorating inflammation/fibrosis of knee synovium and fat pad, unlike treatment with NEG BM-MSC. These data correlate the expression of CD146 with innately higher immunomodulatory and secretory capacity, thus therapeutic potency. This high-content, reproducible evidence suggests that the CD146^{+} (POS) MSC subpopulation are the mediators of the beneficial effects achieved using crude BM-MSC leading to translational implications for improving cell therapy and manufacturing. © AlphaMed Press 2020 SIGNIFICANCE STATEMENT: Cell therapies are on the rise for comprehensively treating numerous clinical indications. With advances to manufacturing and commercialization, understanding signature quality attributes correlative to functional potency are necessary indicators of therapeutic efficacy for cell selection optimization. Herein, we demonstrates compelling evidence for a subpopulation of Mesenchymal Stromal/Stem Cells (MSC) that is suggested to be the mediators of the beneficial effects achieved by crude MSC. These results translate to

techniques useful for determining cell qualities and functional capacities, optimizing therapeutic cell selection for efficient manufacturing, and mechanisms of action mediated by cell therapy for the treatment of joint inflammation and fibrosis.

Hum Cell. 2020 May 6. doi: 10.1007/s13577-020-00369-z. [Epub ahead of print]

Interplay between mesenchymal stem cell and tumor and potential application.

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Abstract

Mesenchymal stem cells (MSCs) possess the capabilities of self-renewal and multipotent differentiation. Firstly isolated from bone marrow, MSCs are subsequently identified from various post-natal tissue types. Based the differentiation into tissue-specific cells, MSCs were capable of replacing damaged and diseased tissues. In addition, MSCs have been demonstrated to possess important immunomodulatory properties. Increasing data showed that MSCs exhibited tropism for sites of the tumor microenvironment and interacted with tumor cells closely through paracrine signaling. Therefore, better understanding of crosstalk between MSCs and tumor cells will be able to develop potential strategies in the treatment of tumors in the future. Herein, we summarize the research progress of the influence of MSCs on tumor cells and the prospect of their application in tumor therapy in this review.

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Functional variations between Mesenchymal Stem Cells of different tissue origins: A comparative gene expression profiling.

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Abstract

BACKGROUND:

Mesenchymal Stem Cells (MSCs), regardless of the tissue sources, are considered as excellent candidates for cellular therapy as they are immune-privileged cells containing a multitude of therapeutic functions that aid in tissue regeneration and repair. For the effective application of these cells in cell therapy, it is important to understand and characterize their biological functions.

OBJECTIVES:

The present study attempts to characterize the variations in multipotent function such as cell surface antigen levels, proliferation, differentiation and stemness (pluripotency) potential of MSCs isolated from foetal [wharton's jelly (WJ), foetal and maternal side of placenta (PF and PM)] and adult tissue sources [bone marrow (BM) and adipose tissue (AT)] using gene expression by real time PCR (qRT-PCR).

RESULTS:

Amongst the different tissue sources, PM, PF and AT-MSCs exhibited significant increase ($p < 0.001$, $p < 0.001$ and $p < 0.01$ respectively) in CD 73 expression and therefore could have a role in immunomodulation. WJ-MSCs exhibited superior proliferation potential based on growth curve, PCNA and Wnt gene expression. BM-MSCs were superior in exhibiting trilineage differentiation. Enhanced stemness potential (Oct 4 and Nanog) was observed for both BM and WJ-MSCs. In addition, BM and WJ-MSCs expressed high levels of CD 90 making them suitable in bone repair and regeneration.

CONCLUSION:

Thus to conclude, out of the five different sources tested, BM an adult source and WJ-MSCs a foetal source were superior in exhibiting most of the biological functions indicating that these sources may be suitable candidates for cell repair and regeneration studies.

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Bone Marrow Aspirate Concentrate: Its Uses in Osteoarthritis.

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Author information

Abstract

Human bone marrow (BM) is a kind of source of mesenchymal stem cells (MSCs) as well as growth factors and cytokines that may aid anti-inflammation and regeneration for various tissues, including cartilage and bone. However, since MSCs in BM usually occupy only a small fraction (0.001%) of nucleated cells, bone marrow aspirate concentrate (BMAC) for cartilage pathologies, such as cartilage degeneration, defect, and osteoarthritis, have gained considerable recognition in the last few years due to its potential benefits including disease modifying and regenerative capacity. Although further research with well-designed, randomized, controlled clinical trials is needed to elucidate the exact mechanism of BMAC, this may have the most noteworthy effect in patients with osteoarthritis. The purpose of this article is to review the general characteristics of BMAC, including its constituent, action mechanisms, and related issues. Moreover, this article aims to summarize the clinical outcomes of BMAC reported to date.

Virol J. 2020 May 5;17(1):64. doi: 10.1186/s12985-020-01326-w.

Oncolytic Newcastle disease virus delivered by Mesenchymal stem cells-engineered system enhances the therapeutic effects altering tumor microenvironment.

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Abstract

BACKGROUND:

Human papillomavirus (HPV)-associated malignancy remain a main cause of cancer in men and women. Cancer immunotherapy has represented great potential as a new promising cancer therapeutic approach. Here, we report Mesenchymal stem cells (MSCs) as a carrier for the delivery of oncolytic Newcastle disease virus (NDV) for the treatment of HPV-associated tumor.

METHODS:

For this purpose, MSCs obtained from the bone marrow of C57BL mice, then cultured and characterized subsequently by the flow cytometry analysis for the presence of cell surface markers. In this study, we sought out to determine the impacts of MSCs loaded with oncolytic NDV on splenic T cell and cytokine immune responses, caspase-3 and -9 expression, and myeloid and myeloid-derived suppressor cells (MDSCs) by histological and immunohistochemical studies in the tumor microenvironment (TME).

RESULTS:

Our findings proved that MSCs possess both migratory capacity and tumor tropism toward transplanted tumor tissue after peritumoral administration. Tumor therapy experiments indicated that oncolytic NDV delivered by MSCs-engineered system significantly reduces tumor growth, which is associated with the enhancement of E7-specific lymphocyte proliferation, CD8+ T cell cytolysis responses, and splenic IFN-γ, IL-4 and IL-12 responses compared with control groups. Moreover, the treatment upregulated the concentration of apoptotic proteins (caspase 9) and increased infiltration of tumor microenvironment with CD11b + myeloid and Gr1 + MDSCs cells.

CONCLUSIONS:

Our data suggest MSCs carrying oncolytic NDV as a potentially effective strategy for cancer immunotherapy through inducing splenic Th1 immune responses and apoptosis in the tumor microenvironment.