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Enhanced antitumor efficacy of oncolytic adenovirus-loaded menstrual blood-derived mesenchymal stem cells in combination with peripheral blood mononuclear cells.

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Abstract

Several studies have evaluated the efficacy of using human oncolytic adenovirus-loaded mesenchymal stem cells for cancer treatment. For example, we have described the antitumor efficacy of CELYVIR, autologous bone marrow mesenchymal stem cells infected with the oncolytic adenovirus ICOVIR-5, for treatment of neuroblastoma patients. Results from this clinical trial point out the role of the immune system in the clinical outcome. In this context, a better understanding of the immunophenotypic changes of human mesenchymal stem cells upon adenoviral infection and how these changes affect human autologous or allogeneic peripheral blood mononuclear cells (PBMCs) could guide strategies to improve the antitumor efficacy of infected Mesenchymal Stem Cells (MSCs). In this work, we show how infection by an oncolytic adenovirus (OAdv) induces Toll-like receptor 9 overexpression and activation of the NF-κB pathway in menstrual blood-derived mesenchymal stem cells (MenSCs), leading to a specific cytokine secretion profile. Moreover, a pro-inflammatory environment, mainly mediated by monocyte activation that leads to the activation of both T-cells and natural killer cells (NK cells), is generated when OAdv-loaded MenSCs are co-cultured with allogeneic PBMCs. This combination of allogeneic PBMCs and OAdv-loaded MenSCs enhances antitumor efficacy both in vitro and in vivo, an effect partially mediated monocytes and NK cells. Altogether our results demonstrate not only the importance of the immune system for the oncolytic adenovirus-loaded MSCs antitumor efficacy, but in particular the benefits of using allogeneic MSCs for this therapy.

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3D Bone Biomimetic Scaffolds for Basic and Translational Studies with Mesenchymal Stem Cells.

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Abstract

Mesenchymal stem cells (MSCs) are recognized as an attractive tool owing to their self-renewal and differentiation capacity, and their ability to secrete bioactive molecules and to regulate the behavior of neighboring cells within different tissues. Accumulating evidence demonstrates that cells prefer three-dimensional (3D) to 2D culture conditions, at least because the former are closer to their natural environment. Thus, for in vitro studies and in vivo utilization, great effort is being dedicated to the

optimization of MSC 3D culture systems in view of achieving the intended performance. This implies understanding cell⁻biomaterial interactions and manipulating the physicochemical characteristics of biomimetic scaffolds to elicit a specific cell behavior. In the bone field, biomimetic scaffolds can be used as 3D structures, where MSCs can be seeded, expanded, and then implanted in vivo for bone repair or bioactive molecules release. Actually, the union of MSCs and biomaterial has been greatly improving the field of tissue regeneration. Here, we will provide some examples of recent advances in basic as well as translational research about MSC-seeded scaffold systems. Overall, the proliferation of tools for a range of applications witnesses a fruitful collaboration among different branches of the scientific community.

A New Approach for Loading Anticancer Drugs Into Mesenchymal Stem Cell-Derived Exosome Mimetics for Cancer Therapy.

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Abstract

Exosomes derived from mesenchymal stem cells (MSCs) have been evaluated for their potential to be used as drug delivery vehicles. Synthetically personalized exosome mimetics (EMs) could be the alternative vesicles for drug delivery. In this study, we aimed to isolate EMs from human MSCs. Cells were mixed with paclitaxel (PTX) and PTX-loaded EMs (PTX-MSC-EMs) were isolated and evaluated for their anticancer effects against breast cancer. EMs were isolated from human bone marrow-derived MSCs. MSCs (4×10^6 cells/mL) were mixed with or without PTX at different concentrations in phosphate-buffered saline (PBS) and serially extruded through 10-, 5-, and 1-μm polycarbonate membrane filters using a mini-extruder. MSCs were centrifuged to remove debris and the supernatant was filtered through a 0.22-μm filter, followed by ultracentrifugation to isolate EMs and drug-loaded EMs. EMs without encapsulated drug (MSC-EMs) and those with encapsulated PTX (PTX-MSC-EMs) were characterized by western blotting, nanoparticle tracking analysis (NTA), and transmission electron microscopy (TEM). The anticancer effects of MSC-EMs and PTX-MSC-EMs were assessed with breast cancer (MDA-MB-231) cells both *in vitro* and *in vivo* using optical imaging. EMs were isolated by the extrusion method and ultracentrifugation. The isolated vesicles were positive for membrane markers (ALIX and CD63) and negative for golgi (GM130) and endoplasmic (calnexin) marker proteins. NTA revealed the size of MSC-EM to be around 149 nm, while TEM confirmed its morphology. PTX-MSC-EMs significantly ($p < 0.05$) decreased the viability of MDA-MB-231 cells *in vitro* at increasing concentrations of EM. The *in vivo* tumor growth was significantly inhibited by PTX-MSC-EMs as compared to control and/or MSC-EMs. Thus, MSC-EMs were successfully isolated using simple procedures and drug-loaded MSC-EMs were shown to be therapeutically efficient for the treatment of breast cancer both *in vitro* and *in vivo*. MSC-EMs may be used as drug delivery vehicles for breast cancers.

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Fluorescence properties of curcumin-loaded nanoparticles for cell tracking.

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Abstract

BACKGROUND:

Posttransplant cell tracking, via stem cell labeling, is a crucial strategy for monitoring and maximizing benefits of cell-based therapies. The structures and functionalities of polysaccharides, proteins, and lipids allow their utilization in nanotechnology systems.

MATERIALS AND METHODS:

In the present study, we analyzed the potential benefit of curcumin-loaded nanoparticles (NPC) using Vero cells (in vitro) and NPC-labeled adipose-derived mesenchymal stem cells (NPC-ADMSCs) (in vivo) in myocardial infarction and sciatic nerve crush preclinical models. Thereafter, transplantation, histological examination, real time imaging, and assessment of tissue regeneration were done.

RESULTS:

Transplanted NPC-ADMSCs were clearly identified and revealed potential benefit when used in cell tracking.

CONCLUSION:

This approach may have broad applications in modeling labeled transplanted cells and in developing improved stem cell therapeutic strategies.