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Mesenchymal stem cell-mediated transfer of mitochondria: mechanisms and functional impact

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Abstract

There is a steadily growing interest in the use of mitochondria as therapeutic agents. The use of mitochondria derived from mesenchymal stem/stromal cells (MSCs) for therapeutic purposes represents an innovative approach to treat many diseases (immune deregulation, inflammation-related disorders, wound healing, ischemic events, and aging) with an increasing amount of promising evidence, ranging from preclinical to clinical research. Furthermore, the eventual reversal, induced by the intercellular mitochondrial transfer, of the metabolic and pro-inflammatory profile, opens new avenues to the understanding of diseases' etiology, their relation to both systemic and local risk factors, and also leads to new therapeutic tools for the control of inflammatory and degenerative diseases. To this end, we illustrate in this review, the triggers and mechanisms behind the transfer of mitochondria employed by MSCs and the underlying benefits as well as the possible adverse effects of MSCs mitochondrial exchange. We relay the rationale and opportunities for the use of these organelles in the clinic as cell-based product.

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Therapeutic effects of mesenchymal stem cells loaded with oncolytic adenovirus carrying decorin on a breast cancer lung metastatic mouse model

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Abstract

Oncolytic adenoviruses (OAds) are alternative immune therapeutic strategies for tumors. However, liver uptake and antibody neutralization are two major barriers for systemic delivery during the treatment of tumor metastasis. Mesenchymal stem cells (MSCs) have emerged as potential vehicles to improve delivery. In this study, we loaded umbilical-cord-derived MSCs (UC-MSCs) with OAds expressing decorin (rAd.DCN) or without foreign genes (rAd.Null) to treat breast cancer lung metastasis. *In vivo*, rAd.Null, MSCs.Null, and rAd.DCN exhibited antitumor effects compared with other groups in a mouse model. Unexpectedly, MSCs.Null showed much greater antitumor responses than MSCs.DCN, including improved survival and reduced tumor burden. Compared with rAd.Null, both MSCs.Null and MSCs.DCN could improve the viral spread and distribution in metastatic tumor lesions in the lung. MSCs.DCN produced much more decorin in lungs than rAd.DCN; however, rAd.DCN reduced the downstream target genes of decorin much more strongly than MSCs.DCN, which was consistent with *in vitro* findings. In addition, rAd.DCN, MSCs.Null, and MSCs.DCN could reduce The cytokine levels in the lung. In conclusion, MSCs improved oncolytic adenoviral delivery and spread in tumor tissues and enhanced therapeutic effects. However, MSCs.DCN reduced OAd-evoked antitumor responses, possibly via a contact-dependent mechanism.

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Paper based microfluidic platform for single-step detection of mesenchymal stromal cells secreted VEGF

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Abstract

Low cost and user-friendly paper microfluidic devices, combined with DNA-based biosensors with binding capacities for specific molecules, have been proposed for the developing of novel platforms that ease and speed-up the process of cell secretion monitoring. In this work, we present the first cellulose microfluidic paper-based analytical device for the single-step detection of cell secreted Vascular Endothelial Growth Factor through a self-reporting Structure Switching Signaling Aptamer. A three-part Structure Switching Signaling Aptamer was designed with an aptameric sequence specific for VEGF, which provides a quantifiable fluorescent signal through the displacement of a quencher upon VEGF recognition. The VEGF biosensor was integrated in cellulose paper, enabling the homogenous distribution of the sensor in the paper substrate and the detection of as low as 0.34 ng of VEGF in 30 min through fluorescence intensity analysis. As a proof-of-concept, the biosensor was incorporated in a microfluidic paper-based analytical device format containing a VEGF detection zone and a control zone, which was applied for the detection of cell secreted VEGF in the supernatant of mesenchymal stem cells culture plates, demonstrating its potential use in cell biology research.