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Mesenchymal stem cells as a double-edged sword in tumor growth: focusing on MSC-derived cytokines

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Abstract

Mesenchymal stem cells (MSCs) show homing capacity towards tumor sites. Numerous reports indicate that they are involved in multiple tumor-promoting processes through several mechanisms, including immunosuppression; stimulation of angiogenesis; transition to cancer-associated fibroblasts; inhibition of cancer cell apoptosis; induction of epithelial-mesenchymal transition (EMT); and increase metastasis and chemoresistance. However, other studies have shown that MSCs suppress tumor growth by suppressing angiogenesis, incrementing inflammatory infiltration, apoptosis and cell cycle arrest, and inhibiting the AKT and Wnt signaling pathways. In this review, we discuss the supportive and suppressive impacts of MSCs on tumor progression and metastasis. We also discuss MSC-based therapeutic strategies for cancer based on their potential for homing to tumor sites.

Clin Transl Med

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Reiterative infusions of MSCs improve pediatric osteogenesis imperfecta eliciting a pro-osteogenic paracrine response: TERCELOI clinical trial

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Abstract

Background: Osteogenesis imperfecta (OI) is a rare genetic disease characterized by bone fragility, with a wide range in the severity of clinical manifestations. The majority of cases are due to mutations in the COL1A1 or COL1A2 genes, which encode type I collagen. Mesenchymal stem cells (MSCs), as the progenitors of the osteoblasts, the main type I collagen secreting cell type in the bone, have been proposed and tested as an innovative therapy for OI with promising but transient outcomes.

Methods: To overcome the short-term effect of MSCs therapy, we performed a phase I clinical trial based on reiterative infusions of histocompatible MSCs, administered in a 2.5-year period, in two pediatric patients affected by severe and moderate OI. The aim of this study was to assess the safety and effectiveness of this cell therapy in nonimmunosuppressed OI patients. The host response to MSCs was studied by analyzing the sera from OI patients, collected before, during, and after the cell therapy.

Results: We first demonstrated that the sequential administration of MSCs was safe and improved the bone parameters and quality of life of OI patients along the cell treatment

plus 2-year follow-up period. Moreover, the study of the mechanism of action indicated that MSCs therapy elicited a pro-osteogenic paracrine response in patients, especially noticeable in the patient affected by severe OI.

Conclusions: Our results demonstrate the feasibility and potential of reiterative MSCs infusion for two pediatric OI and highlight the paracrine response shown by patients as a consequence of MSCs treatment.

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Delivery of mesenchymal stem cells for tackling systemic disorders

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Abstract

Development of methods of manipulating and culturing stem cells has enabled the emergence of stem cell therapy as a promising approach in diverse applications, ranging from tissue repair to treatment of intractable diseases such as diabetes, cardiovascular diseases and neurological disorders. Along with technological advances in systemic stem cell delivery, treating multiple injured or pathological sites simultaneously has been made possible. Despite this, most of the works on systemic stem cell transplantation at the moment have focused on the efficiency of tackling local disorders. The prospect of the therapy for enhancing systemic tissue repair, as well as for tackling systemic degenerative disorders, has rarely been seriously considered. The objective of this article is to fill this gap by reviewing the current status of research on systemic stem cell delivery, and by presenting the opportunities and challenges for translating systemic stem cell delivery from the laboratory to the clinic.

Adv Med Sci
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A brief very-low oxygen tension regimen is sufficient for the early chondrogenic commitment of human adipose-derived mesenchymal stem cells

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Abstract

Purpose: The aim of this study was to evaluate the effects exerted over chondrogenic commitment of human adipose-derived mesenchymal stem cells (ADSCs) by a very low oxygen tension (<1% pO_2).

Materials/methods: Cell morphology, mRNA levels of chondrocyte-specific marker genes and the involvement of p38 MAPK signalling were monitored in human ADSCs under a very low oxygen tension.

Results: Cell morphology was significantly changed after two days of hypoxic preconditioning when they featured as elongated spindle-shaped cells. SRY-box containing gene 9, aggrecan and collagen type II mRNA levels were enhanced under severe hypoxic culture conditions. Moreover, the inhibition of p38 MAPK resulted in a substantial reduction in transcription of the above-mentioned specific genes, proving the pivotal role of this pathway in the transcriptional regulation of chondrogenesis.

Conclusions: Here, we propose a protocol showing the early commitment of stem cells towards the chondrogenic phenotype in only 2 days of culture via a very low hypoxic environment, in the absence of growth factors added in the culture medium.