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MSC-Derived Exosomes Suppress Colorectal Cancer Cell Proliferation and Metastasis via miR-100/mTOR/miR-143 Pathway

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Abstract

Exosomes derived from mesenchymal stem cells (MSCs) are mostly responsible for the therapeutic effects of MSCs. To show the therapeutic effects of the human bone marrow MSC-derived exosomes (MSC-Exos) on colorectal cancer and explore the molecular cross-talks between them, CRC cells were treated with the MSC-Exos. We found that MSC-Exos were enriched with miR-100 and miR-143, which effectively downregulated mTOR, Cyclin D1, K-RAS, HK2 while upregulated p-27 expression. All these effects were reversed by concurrent treatment with MSC-Exos and antagomiR-100, confirming that they were caused by exosomal transfer of miR-100 into recipient CRC cells. Moreover, exosomal miR-100 promoted endogenous miR-143 expression. The flow cytometry, MTT and trypan blue assays revealed that MSC-Exos could efficiently suppress proliferation and induce apoptosis of the CRC cells. Furthermore, wound healing, transwell migration and invasion assays confirmed their inhibitory effects on the migration and invasiveness of SW480 cells. We further confirmed these effects by analyzing the expression levels of epithelial to mesenchymal transition (EMT) factors and metastasis-related genes. Results showed that MSC-Exos significantly suppressed the expression of MMP2 and MMP9 (metastasis-related genes), SNAIL and TWIST (EMT-inducing transcription factors), Vimentin and N-cadherin (mesenchymal cell markers), whereas E-cadherin (epithelial cell marker) was remarkably up-regulated. Collectively, our data indicated that MSC-Exos could suppress proliferation,

migration, invasion and metastasis while inducing the apoptosis of the CRC cells via miR-100/mTOR/miR-143 axis. Our findings highlight that MSC-Exo treatment as well as miR-100 restoration might be considered as potential therapeutic strategies for CRC.

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Simultaneous Labeling of Adipogenic and Osteogenic Differentiating Stem Cells for Live Confocal Analysis

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Abstract

Adipocytes and osteoblasts derive from a common mesenchymal progenitor present in a range of connective tissues. Differentiation of the progenitors toward the two cell lineages can be induced in vitro through well-established protocols, and leads to the appearance of lipid-laden adipocytes and osteoblasts embedded in a mineralized matrix. The formation of these two lineages in cell cultures can be monitored using lipophilic dyes such as Oil Red O and substances binding to mineral deposits such as Alizarin Red S, respectively. However, these common staining techniques require cell fixation and are thus incompatible with live analyses. Recently, alternative approaches using vital stains have allowed the dual visualization and fluorescence imaging of adipogenic and osteogenic lineages in live cultures. Here we present the concomitant analysis of cultures containing adipogenic and osteogenic cell types using live staining, combining LipidTox Red and tetracycline with NucRed nuclear counterstain for confocal imaging. This approach can be applied to visualize the kinetics and 3D structure of differentiating mesenchymal cultures over time and highlights the interaction of adipose and mineralized compartments associated with bone marrow stroma.