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Knockdown of TGF-β1 expression in human umbilical cord mesenchymal stem cells reverts their exosome-mediated EMT promoting effect on lung cancer cells

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Abstract

The effect of mesenchymal stem cells (MSCs) on lung cancer cells is controversial, and the underlying mechanisms remain unclear, which harms the utilization of MSCs in tumor therapy. In this study, we found that human umbilical cord MSC-conditioned medium (MSC-CM) promotes EMT, invasion, and migration, yet inhibits proliferation and promotes apoptosis of lung cancer cells. The EMT-promoting effect of MSCs was mediated by exosomes derived from MSCs (MSC-exo) and eliminated by inhibiting exosome release. Moreover, silencing TGF-β1 expression in MSCs can revert the EMT-promoting effect and enhance the anti-proliferative and pro-apoptotic effect of MSCs on lung cancer cells via MSC-exo. Further investigation found that Smad2/3, Akt/GSK-3β/β-catenin, NF-κB, ERK, JNK, and p38 MAPK in TGF-β1 signaling pathways could be activated by MSC-exo in lung cancer cells, while silencing TGF-β1 expression in MSCs may deactivate these pathways. These findings suggest a method by which MSCs may be safely employed in lung cancer therapy.