No. 10609. CCL3 promotes tumor angiogenesis by dysregulation of miR-374b/VEGF axis in human osteosarcoma

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Abstract

Background: Osteosarcoma is the most common primary malignant bone tumor and is characterized by a high metastatic potential. Chemokine (C-C motif) ligand 3 (CCL3) has been reported to facilitate tumor progression and metastasis. Vascular endothelial growth factor (VEGF), a highly specific mitogen for endothelial cells, is an interesting inducer of angiogenesis. However, the crosstalk between CCL3 and VEGF has not been well explored in human osteosarcoma.

Questions/Purposes: To clarify the crosstalk between CCL3 and VEGF in human osteosarcoma. It probably provides a new therapeutic target for osteosarcoma patients.

Patients and Methods: The human osteosarcoma cell lines (U-2 OS and MG-63) were purchased from the American Type Cell Culture Collection and maintained. The protein and mRNA expression of CCL3 and VEGF were detected by western blot, ELISA, and quantitative real-time PCR. The expression of miR-374b was detected by quantitative real-time PCR. The angiogenesis was detected by migration ability and tube formation of endothelial progenitor cells (EPCs) *in vitro*, and chick chorioallantoic membrane assay as well as Matrigel plug assay *in vivo*.

Results: CCL3 increased VEGF expression and angiogenesis through CCR5 receptor. Co-transfection with miR-374b mimic reversed CCL3-mediated VEGF expression and angiogenesis. JNK, p38, and ERK inhibitors reduced the CCL3-increased VEGF expression and miR-374b suppression.

Conclusions: CCL3 promotes osteosarcoma angiogenesis and VEGF expression through activation of the JNK, p38, and ERK signaling pathways and down-regulation of miR-374b expression. CCL3 may represent a potential therapeutic target against human osteosarcoma.