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.