

The cancer-related transcription factor RUNX2 modulates expression and secretion of the matricellular protein osteopontin in osteosarcoma cells to promote adhesion to endothelial pulmonary cells and lung metastasis

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© 2019 Wiley Periodicals, Inc. Osteosarcomas are bone tumors that frequently metastasize to the lung. Aberrant expression of the transcription factor, runt-related transcription factor 2 (RUNX2), is a key pathological feature in osteosarcoma and associated with loss of p53 and miR-34 expression. Elevated RUNX2 may transcriptionally activate genes mediating tumor progression and metastasis, including the RUNX2 target gene osteopontin (OPN/SPP1). This gene encodes a secreted matricellular protein produced by osteoblasts to regulate bone matrix remodeling and tissue calcification. Here we investigated whether and how the RUNX2/OPN axis regulates lung metastasis

of osteosarcoma. Importantly, RUNX2 depletion attenuates lung metastasis of osteosarcoma cells in vivo. Using next-generation RNA-sequencing, protein-based assays, as well as the loss- and gain-of-function approaches in selected osteosarcoma cell lines, we show that osteopontin messenger RNA levels closely correlate with RUNX2 expr