Curcumin regulates miR-21 expression and inhibits invasion and metastasis in colorectal cancer.


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Abstract

Curcumin has promising potential in cancer prevention and therapy by interacting with proteins and modifying their expression and activity, which includes transcription factors, inflammatory cytokines, and factors of cell survival, proliferation, and angiogenesis. miR-21 is overexpressed in many tumors, promoting progression and metastasis. In the present study, we examined the potential of curcumin to regulate miR-21, tumor growth, invasion, and in vivo metastasis in colorectal cancer. In Rko and HCT116 cells, we identified two new transcriptional start sites of the miR-21 gene and delineated its promoter region. PMA stimulation induced miR-21 expression via motifs bound with AP-1 transcription factors. Curcumin treatment reduced miR-21 promoter activity and expression in a dose-dependent manner by inhibiting AP-1 binding to the promoter, and induced expression of tumor suppressor Pdcd4, which is a target of miR-21. Curcumin treated Rko and HCT116 cells were arrested in the G2/M phase with increasing concentrations. Furthermore, curcumin inhibited tumor growth, invasion and in vivo metastasis in the chicken-embryo-metastasis assay (CAM). Additionally, curcumin significantly inhibited miR-21 expression in primary tumors generated in vivo in the CAM assay by Rko and HCT116 cells (p<0.00006; p<0.035 respectively). Taken together, this is the first report to show that curcumin inhibits the transcriptional regulation of miR-21 via AP-1, suppresses cell proliferation, tumor growth, invasion, and in vivo metastasis, and stabilizes expression of tumor suppressor Pdcd4 in colorectal cancer.

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