Targeting HIF-1α by the Curcumin and its Novel Analogs EF-31 and UBS-109 Reduces Growth and Angiogenesis of Colorectal Cancer

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ABSTRACT

Hypoxia-inducible factors (HIFs) play essential roles in cancer cell growth and metastasis by stimulating angiogenesis. Curcumin inhibits the activity of several oncogenic transcriptional factors including HIF-1α, thus we investigated whether curcumin and its analogs EF-31 and UBS-109, could disrupt angiogenesis using colorectal cancer cells (CRC). HCT-116 and HT-29 cells were used in these experiments. HUVEC tube formation assay, Matrigel plug assay, Western blotting, and VEGF activity assay were carried out to determine the curcumin, EF-31 and UBS-109 role in angiogenesis. Conditioned medium from HCT116 or HT29 cells exposed to curcumin, EF-31 and UBS-109 *in vitro* significantly blocked HUVEC tube assembly in comparison to control. The overexpression of HIF-1 resulted in increased tube formation and these effects were inhibited by curcumin, EF-31 and UBS-109. *In vivo*, EF-31 and UBS-109 blocked the vascularization of subcutaneous matrigel plugs and the growth of CRC xenografts. We observed significant inhibition of VEGF synthesis and secretion in both colon cell lines treated with curcumin, EF-31 and UBS-109 in concert with the loss of HIF-1α expression, of which transcriptionally regulate VEGF. These results suggesting that curcumin, EF-31 and UBS-109 inhibits VEGF production in part through the degradation of HIF-1α. Taken together, destabilization of HIF-1α may be important contributing factors to the antiangiogenic action of curcumin, EF-31 and UBS-109 in CRC.