Study on the molecular mechanisms of denbinobin-induced anti-tumorigenesis effect in colon cancer cells

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摘要

Abstract

AIM: To explore both the in vitro and in vivo effects of denbinobin against colon cancer cells and clarify its underlying signal pathways.METHODS: We used COLO 205 cancer cell lines and nude mice xenograft model to study the in vitro and in vivo anti-cancer effects of denbinobin. RESULTS: Denbinobin at concentration of 10-20 μmol/Ldose-dependently suppressed COLO 205 cell proliferation by NTT test. Flow cytometry analysis and DNA fragmentation assay revealed that 10-20 μmol/L denbinobin treatment induced COLO 205 cells apoptosis. Western blot analysis showed that caspases 3, 8, 9 and Bid protein were activated by denbinobin treatment to COLO 205 cells accompanied with cytochrome c and apoptosis-inducing factor (AIF) translocation. Pretreatment of MEK 1 inhibitor (U10126), but not p38 inhibitor (SB203580) and JNK inhibitor (SP600125), reversed denbinobin-induced caspase 8, 9 and Bid activation in COLO 205 cells suggesting that extracellular signal-regulated kinase were involved in the denbinobin-induced apoptosis in COLO 205 cells. Significant regression of tumor up to 68% was further demonstrated in vivo by treating nude mice bearing COLO 205 tumor xenografts with denbinobin 50 mg/kg intraperitoneally. CONCLUSION: Our findings suggest that denbinobin couldinhibit colon cancer growth both in vitro and in vivo. Activation of extrinsic and intrinsic apoptotic pathways and AIF were involved in the denbinobin-induced COLO205 cell apoptosis.