B17

Antrodia cinnamomea fruiting bodies extract suppresses the invasive potential of human liver cancer cell line PLC/PRF/5 through inhibition of nuclear factor κB pathway

樟芝子實體萃取透物過抑制 NF-κB 路徑降低人類肝癌細胞株 PLC/PRF/5 腫瘤入侵作用

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Abstract

Background and Purpose: Tumor invasiveness and metastasis are characteristics of highly malignant cancers with poor clinical outcome. Tumor invasion is a perplexing cascade process involving a finely tuned interaction between cancer cells and various regulated factors. In this study, we first report the anti-invasive effect of ethylacetate extract from *Antrodia cinnamomea* (EAC) fruiting bodies in the human liver cancer cell line PLC/PRF/5.
Methods: Cell invasion assay. Electrophoretic mobility shift assay (EMSA). NF-κB reporter assay. MMP-2, MMP-9, and VEGF assay. Gelatin zymography. Western blot analysis. Matrigel plug angiogenesis assay. *In vivo* tumor model.
Results: Treatment with EAC decreased the cancer invasion of PLC/PRF/5 cells in a dose-dependent manner. This effect was strongly associated with a concomitant decrease in either the level or activity of VEGF, MMP-2, MMP-9 and MT1-MMP, and an increase in the expression of TIMP-1 and TIMP-2. EAC inhibited constitutively activated and inducible NF-κB in both its DNA-binding activity and transcriptional activity. Furthermore, EAC also inhibited the TNF-α-activated NF-κB-dependent reporter gene expression of MMP-9 and VEGF, and the invasion of cancer cells. EAC also exhibited an inhibitory effect on angiogenesis in a Matrigel Plug Angiogenesis Assay. Further investigation revealed that EAC's inhibition of cancer cell growth and invasion was also evident in a nude mice model. Our results indicate that EAC inhibits the activation of NF-κB, and may provide a molecular basis for drug development using EAC as an anti-invasive agent in the prevention and treatment of cancer.
Conclusions: We have provided evidence demonstrating that EAC inhibits invasion and both MMPs and VEGF protein expression and enzyme activity. EAC suppresses invasion of PLC/PRF/5 cells by inhibition of NF-κB activity and sequentially reducing the expression and activity of MMP-9 in the cells. Therefore, we suggest that EAC could be potentially explored as a useful antiinvasive agent in the treatment of human liver carcinoma.