

Study of inhibit the proliferation and induce apoptosis of human colon adenocarcinoma cell line HCT¹¹⁶

Gui-Ying Zhang, Wei-Jian Yuan, Chun-Mei He

Gui-Ying Zhang, Wei-Jian Yuan, Department of Alimentary Disease, Affiliated Xiangya Hospital of Hunan Medical University, Changsha 410008, Hunan Province, China

Chun-Mei He, Institute of Cancer Research of Hunan Medical University, Changsha 410078, Hunan Province, China

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Correspondence to: Dr. Gui-Ying Zhang, Department of Alimentary Disease of Internal Medicine Affiliated Xiang-ya Hospital, Hunan Medical University, 141 Xiangya road, Changsha 410008, Hunan Province, China

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Abstract

AIM: To explore the anti tumor effect of indomethacin (IN) on human colon adenocarcinoma cells and determine the influence of indomethacin on cancer cell proliferation and apoptosis and elucidate the anti-tumor mechanism of Indomethacin.

METHODS: Human colon adenocarcinoma HCT116 cell line were cultured separately *in vitro*. Indomethacin (final concentration 100-800 μm) was administered alone or altogether with 5-Fu (50 μm). Agarose gel electrophoresis, MTT, and Flow cytometry were used to study cell proliferation and apoptosis in human colon carcinoma cell RT-PCR, western blot were used to detect the

expression level of *Bcl-2*, *bax* gene and cdk4 protein expression in HCT116 cell lines after treated with IN for 24 h.

RESULTS: Indomethacin can inhibit significantly the proliferation of HCT116 cell, change the morphology, and cause the cells to accumulate in the G0/G1 phase of the cell cycle, and induce apoptosis. The apoptosis of tumor cells was confirmed by DNA ladder formation on gel electrophoresis and sub-G1 peak on flow cytometry. These responses were time-and concentration dependent. A synergic effect of inhibiting cancer cell proliferation was observed when combined with Indomethacin and 5-Fu. RT-PCR results showed that IN down-regulated *Bcl-2* mRNA expression, and did not change *Bax* mRNA expression. Western blot results confirmed that IN inhibited *Bcl-2* protein expression. No influence was found in the translation of *Bax* protein. IN inhibited cdk4 protein expression.

CONCLUSION: Our study results indicate that IN induce apoptosis of HCT116 cell by down-regulating *Bcl-2* expression and inhibiting cdk4 protein expression partially. This explains the mechanisms of antitumor activity of the Indomethacin.

Key words: Colonic neoplasms; Indomethacin; Apoptosis; Flow cytometry; Polgmerase chain reaction

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