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论著

Caspase-9途径在丁酸钠诱导结肠癌细胞株HT-29凋亡中的作用

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摘要 目的： 探讨caspase-9途径在丁酸钠(NaBt)诱导人结肠癌细胞株HT-29凋亡中的作用。方法： HT-29细胞体外培养至对数生长期，分别及联合给予5.0 mmol/L丁酸钠、20 μmol/L z-VAD-fmk、z-DEVD-fmk、z-IETD-fmk、z-LEHD-fmk处理24 h，并设空白对照。以Annexin V-FITC法联合PI染色，流式细胞术检测细胞凋亡，JC-1染色检测线粒体膜电位变化，caspase活性检测试剂盒检测caspase-3、caspase-8、caspase-9的活性。结果： (1)丁酸钠诱导的HT-29细胞凋亡［（35.40±0.70）%］可被z-VAD-fmk抑制［（1.33±0.59）%］，亦可被z-DEVD-fmk抑制［（1.40±0.52）%］，并可被z-LEHD-fmk抑制［（1.27±0.91）%］，均P<0.01；但是z-IETD-fmk不能够抑制该作用［（32.10±2.33）%］，P>0.05；(2)丁酸钠干预HT-29细胞后，线粒体膜电位降低(5.53±0.91)，z-VAD-fmk、z-DEVD-fmk、及z-LEHD-fmk 能够阻断这种作用(9.80±1.15, 10.23±0.50, 10.33±1.02), P<0.05；而z-IETD-fmk未显示对该作用的改变（5.93±1.31）, P>0.05；(3)丁酸钠干预HT-29细胞后，caspase-3、caspase-9的活性增高2-3倍，caspase-8的活性无显著变化，P>0.05。结论： 丁酸钠主要是通过线粒体途径，激活caspase-9，启动细胞凋亡环节，从而激发下游的效应caspases，诱导HT-29细胞凋亡。

关键词 结直肠肿瘤； 细胞凋亡； 线粒体； 半胱氨酸天冬氨酸蛋白酶类； 丁酸盐类

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Role of caspase activation in butyrate-induced apoptosis of HT-29 colon carcinoma cells

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Abstract

<FONT face=Verdana>AIM: Sodium butyrate has antitumor effects on colon cancer cells such as inhibiting cell growth and promoting differentiation and apoptosis. The aim of this study is to investigate whether sodium butyrate induces apoptosis in human colon cancer cell line HT-29 and to examine the intracellular mechanisms involved, especially the role of caspase activation in the process. METHODS: HT-29 cells were cultured to logarithmic phase before treatment with sodium butyrate at concentration of 5.0 mmol/L and caspase inhibitors at the concentration of 20 μmol/L. The latter were added in the medium ahead of sodium butyrate for 1 h. Then, the staining of Annexin V-FITC and PI were used to analyze HT-29 apoptosis and the dye JC-1 was applied to detect mitochondrial membrane potential by flow cytometry. Caspase activity within the cells was measured respectively using a specific caspase activity assay kit and a microplate reader. RESULTS: Preincubation of HT-29 cells with sodium butyrate significantly increased apoptosis ［(35.40±0.70)%］ and decreased mitochondrial membrane potential (5.53±0.91). This effect was blocked when pretreatments were enforced with z-VAD-fmk, z-DEVD-fmk and z-LEHD-fmk. The apoptosis percentages were (1.33±0.59)%, (1.40±0.53)% and (1.27±0.91)%， respectively and mitochondrial membrane potentials were 9.80±1.15, 10.23±0.50 and 10.33±1.02, respectively. However, the role of reduction by z-IETD-fmk, which presented the apoptosis percentage of (32.10±2.33)% and mitochondrial membrane potential of 5.93±1.31, was not observed. An enhancement of caspase-3 and -9 activities (2-3-fold) but no change of caspase-8 activity was confirmed. CONCLUSION: Apoptosis of HT-29 colon carcinoma cells induced by sodium butyrate is tightly linked to caspase activation via mitochondrial pathway other than tumor necrosis factor-alpha and has the potential to inhibit proliferation and thereby may contribute to the progression of colon cancer.</FONT>

Key words Colorectal neoplasms Apoptosis Mitochondria Caspases Butyrates

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