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基础研究

塞来昔布联合5-Fu对人结肠癌裸鼠皮下移植瘤生长的影响

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Effect of p27mt Gene on Growth of Transplanted Human Colorectal Carcinoma in Naked Mice

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- 摘要
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全文: PDF (420 KB) HTML (0 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要 目的 探讨选择性环氧化酶 2（Cyclooxygenase 2，Cox 2）抑制剂 塞来昔布（celecoxib）联合5 氟尿嘧啶（5 fluorouracil，5 Fu）对实验性人结肠癌裸鼠皮下移植瘤生长的影响及作用机制。方法 建立人结肠癌裸鼠皮下移植瘤模型，模型建立后32只实验裸鼠随机分为四组，分别给予塞来昔布及5 Fu药物干预后观察各组皮下移植瘤体积、瘤重和裸鼠实验前后的体重变化，计算抑瘤率。电镜观察细胞凋亡形态,原位凋亡染色检测凋亡指数（AI），免疫组化及Western blot印迹法检测细胞色素C、caspase 3及caspase 9表达。结果 塞来昔布干预组、5 Fu干预组和联合干预组肿瘤生长明显抑制，塞来昔布干预组、5 Fu干预组抑瘤率分别为27.81%和53.02%，联合干预组抑瘤率为78.37%（P<0.01）。干预组较对照组肿瘤细胞凋亡明显增加，干预组各组之间凋亡指数比较差异有统计学意义（P<0.01）。透射电镜下见干预组瘤细胞呈现明显凋亡形态改变，联合干预组凋亡表现尤为典型，对照组无明显凋亡形态改变。免疫组化及Western blot印迹法显示干预组其细胞色素C、caspase 3及caspase 9的表达明显高于对照组，且干预组各组之间比较其表达差异也有统计学意义（P<0.05）。结论 塞来昔布及5 Fu均具有明显的抗肿瘤作用，联合应用时具有协同作用，可显著抑制人结肠癌裸鼠皮下移植瘤的生长，其作用机制可能与上调细胞色素C、caspase 3及caspase 9蛋白表达、激活细胞色素C依赖性凋亡信号通路有关。

关键词： 结肠癌 塞来昔布 细胞色素C 细胞凋亡 信号转导

Abstract: Objective To investigate the anti2tumor effect and explore it s mechanisms of celecoxib (a selec2 tive cox22 inhibitor) combined with 52fluorouracil (52Fu) on the t reatment of human colorectal cancer in BALB/ C nude mice subcutaneous xenograf t model. Methods Effect s of celecoxib combined 52Fu on the proliferatic in xenograf t carcinoma induced by HT229 were investigated. Simultaneously the method of im2 munohistochemist ry and western blot were used to estimate the expression of Cytochrome C、caspase23 and caspase29 ,the apoptosis morphous was detected by elect ron microscope and the apoptosis of tumor cell was detected by TUNEL to determine apoptotic index (A I) . Results The effect of synergistic usage of 52Fu and celecoxib for the t reatment of human colorectal cancer was better than other groups. The re2 spective rates of the tumor inhibition of B group ,C group and D group were 27. 81 %、53. 02 %、78. 37 % , and the differences compared with cont rol group (0) were significant (P < 0. 01) . Compared with cont rol group the apoptosis of tumor cell in t reated groups notably raised and the statistical differences of the ap2 optotic index (A I) among t reated group s were significant (P < 0. 01) . The means of fimmunohistochemis2 t ry and western blot display that the expression of Cytochrome C、caspase23 and caspase29 of t reated groups increased obviously compared with the cont rol group . Meanwhile the statistical differences of the expression of Cytochrome C、caspase23 and caspase29 among the t reated groups were also significant (P < 0. 05) . Conclusion Celecoxib and 52Fu have respective effect to inhibit the growth of tumor. Compared with celecoxib or 52Fu individual drug group , Celecoxib combined with 52Fu significantly inhibited the growth of human colorectal cancer in nude mice subcutaneous xenograf t . The mechanism of antitumor maybe is correlate with inducing apoptosis and activation mitochondrion accommodation pathway by up2 regulating the expression of Cytochrome C、caspase23 and caspase29.

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Key words： Colorectal cancer Celecoxib Cytochrome C Apoptosis Signal transduction

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