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PUMA基因转染胰腺癌AsPC-1细胞增强对5-FU致凋亡的敏感性 [点此下载全文](#)

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摘要:

目的: 探讨 PUMA 基因转染是否增强胰腺癌AsPC 1细胞对5-FU致凋亡的敏感性。方法: 采用脂质体转染法将PUMA pCEP4和空载体pCEP4质粒转染入胰腺癌AsPC 1细胞中, G418筛选阳性细胞。将系列浓度(0.01~100  $\mu\text{mol/L}$ )的5-FU分别作用于AsPC 1、AsPC 1/PUMA和AsPC 1/pCEP4细胞72 h, MTT法测定各组细胞的存活率并计算 $\text{IC}_{50}$ , FCM、断裂DNA琼脂糖凝胶电泳和TUNEL法检测细胞凋亡情况, Western blotting检测各组细胞PUMA蛋白表达的变化。〔HT5〕SS〕 AsPC 1、AsPC 1/PUMA和AsPC 1/pCEP4细胞的5-FU  $\text{IC}_{50}$  分别为(12 $\pm$ 1.9)、(1.6 $\pm$ 0.4)和(10.4 $\pm$ 1.6) $\mu\text{mol/L}$ , AsPC 1/PUMA细胞对5-FU作用的敏感性增加了7.5倍。5-FU以剂量依赖方式诱导AsPC 1细胞凋亡, 但对AsPC 1/PUMA细胞所诱导的凋亡比AsPC 1和AsPC 1/pCEP4 4更明显。低浓度5-FU(0.1  $\mu\text{mol/L}$ )轻微引起AsPC 1/pCEP4〔(1.14 $\pm$ 0.28)%〕和AsPC 1细胞凋亡〔(0.9 $\pm$ 0.23)%〕, 但能诱导AsPC 1/PUMA细胞明显凋亡〔(6.47 $\pm$ 1.42)%〕; 高浓度5-FU(1.0  $\mu\text{mol/L}$ )诱导各组细胞凋亡, 但 AsPC 1/PUMA 细胞凋亡率〔(34.54 $\pm$ 9.36)%〕明显高于AsPC 1〔(12.8 $\pm$ 3.74)%〕和AsPC 1/pCEP4细胞〔(15.8 $\pm$ 5.15)%〕, 差异均有统计学意义( $P < 0.01$ ); FCM、断裂DNA琼脂糖凝胶电泳和TUNEL方法检测显示相同的结果。PUMA蛋白在AsPC 1/PUMA细胞中的表达明显高于AsPC 1和AsPC 1/pCEP4细胞。结论: PUMA 基因转染明显地增强了胰腺癌AsPC 1细胞对5-FU致凋亡作用的敏感性。

关键词: [PUMA 基因](#) [胰腺癌](#) [5-FU 凋亡](#)

PUMA gene transfection increases sensitivity of pancreatic cancer cell line AsPC 1 to 5-FU induced apoptosis [Download Fulltext](#)

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Abstract:

Abstract Objective To investigate whether PUMA gene transfection can increase sensitivity of pancreatic cancer cells (PC) to 5-FU induced apoptosis. Methods: PUMA pCEP4 containing full length PUMA cDNA or pCEP4 was transfected into human pancreatic cancer cell line AsPC 1 by lipofectamine transfection, G418 selection was used to select positive cells. AsPC 1, AsPC 1/PUMA and AsPC 1/pCEP4 cells were separately treated with serial concentrations of 5-FU (0.01-100  $\mu\text{mol/L}$ ). MTT assay was used to determine the cell survival rate in each group and  $\text{IC}_{50}$  of 5-FU was calculated. TUNEL, FCM and DNA ladder observation were employed to study cell apoptosis. Western blotting was performed to detect the expression of PUMA protein. Results: The 5-FU  $\text{IC}_{50}$  values of AsPC 1, AsPC 1/PUMA and AsPC 1/pCEP4 cells were (12 $\pm$ 1.9) $\mu\text{mol/L}$ , (1.6 $\pm$ 0.4)  $\mu\text{mol/L}$  and (10.4 $\pm$ 1.6)  $\mu\text{mol/L}$ , respectively, with the sensitivity of AsPC 1/PUMA cells increased by 7.5 folds. 5-FU induced cell apoptosis of AsPC 1 cells in a dose dependent manner, with the apoptosis of AsPC 1/PUMA cells more prominent than those of AsPC 1 and AsPC 1/pCEP4 cells. Low concentration of 5-FU (0.1  $\mu\text{mol/L}$ ) induced few apoptosis of AsPC 1/pCEP4 cells [(1.14 $\pm$ 0.28)%] and AsPC 1 cells [(0.9 $\pm$ 0.23)%], and induced apoptosis in AsPC 1/PUMA cells [(6.47 $\pm$ 1.42)%]. High concentration of 5-FU (1.0  $\mu\text{mol/L}$ ) induced apoptosis in all groups, with that in AsPC 1/PUMA cells [(34.54 $\pm$ 9.36)%] significantly higher than those in AsPC 1/pCEP4 cells [(15.8 $\pm$ 5.15)%] and AsPC 1 cells [(12.8 $\pm$ 3.74)%], both  $P < 0.01$ . FCM and electrophoresis showed the same results. Expression of PUMA protein in AsPC 1/PUMA cells was significantly higher than those in AsPC 1 and AsPC 1/pCEP4 cells. Conclusion: PUMA gene transfection greatly enhances the sensitivity of AsPC 1 cells to 5-FU induced apoptosis.

Keywords: [p53 up regulated modulator of apoptosis \( PUMA \)](#) [pancreatic neoplasms](#) [5-FU apoptosis](#)

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