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论著

普罗布考抑制bFGF和H_2O_2引起的大鼠主动脉平滑肌细胞增殖

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摘要 目的： 研究普罗布考抑制碱性成纤维细胞生长因子（bFGF）和H 2O 2促大鼠主动脉平滑肌细胞（RASMCs）增殖的机制。方法: 采用MTT、［^{3}H］-TdR掺入法、流式细胞术和RT-PCR观察普罗布考对bFGF和H_2O_2刺激条件下细胞周期、细胞增殖和凋亡的影响。结果: ①普罗布考抑制bFGF和H_2O_2刺激RASMCs增殖。细胞计数、A值和［^{3}H］-TdR掺入量分别下降了40.0%、39.1%、45.5%和46.9%、45.0%、39.5%（P<0.05，P<0.01）。②普罗布考使RASMCs生长停滞在G_0/G_1期，抑制bFGF刺激的细胞增殖，通过诱导细胞凋亡和抑制细胞生长2种方式抑制H_2O_2刺激的细胞增殖。③bFGF和H_2O_2分别使ERK1mRNA表达量增加近4倍和6倍，MKP-1mRNA表达量下降了62.4%和82.2%。普罗布考抑制ERK1mRNA表达，使H_2O_2诱导的MKP-1表达下降上调，而对bFGF诱导MKP-1表达下降无明显影响。结论: 普罗布考通过降低ERK1mRNA表达抑制细胞周期运转和诱导RASMCs凋亡，从而抑制bFGF和H_2O_2刺激引起的细胞增殖。

关键词 普罗布考； 成纤维细胞生长因子 2； 过氧化氢； 主动脉平滑肌细胞
分类号 R921

Antiproliferative mechanisms of probucol in H_2O_2/bFGF-stimulated rat aortic smooth muscle cells

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Abstract

<FONT face=Verdana>AIM: To investigate the antiproliferative mechanisms of probucol in rat aortic smooth muscle cells (RASMCs) stimulated by basic fibroblast growth factor (bFGF) and hydrogen peroxide (H₂O₂). METHODS: Effects of probucol on cell cycle, DNA synthesis, proliferation and apoptosis in the presence of bFGF and H₂O₂ were observed by means of MTT test, cell number counting, ［3H］-TdR incorporation, FCM and RT-PCR. RESULTS: ① Probucol significantly inhibited proliferation and DNA synthesis in RASMCs stimulated by bFGF and H₂O₂, with a dose-dependent manner. Cell numbers, A value and ［3H］-TdR incorporation in probucol+bFGF group and probucol+H₂O₂ group were reduced by 40.0%, 39.1%, 45.5% and 46.9%, 45.0%, 39.5%, respectively, compared with bFGF group and H₂O₂ group (P<0.05, P<0.01, respectively). ② Probucol protected against bFGF-induced VSMCs proliferation through inducing cell growth arrested at G₀/G₁ phase and H₂O₂-induced RASMCs proliferation through inducing cell apoptosis as well as cell growth arrested at G₀/G₁ phase. ③ bFGF and H₂O₂ increased ERK1 mRNA expression by 4 and 6 times and decreased MKP-1 mRNA expression to 62.4% and 82.2%, respectively, compared with controls. Probucol attenuated the increases in bFGF- and H₂O₂-stimulated ERK1 mRNA level and up-regulated H₂O₂-decreased MKP-1 mRNA level, however, no effect on MKP-1 mRNA expression down-regulated by bFGF was observed. CONCLUSION: Probucol dramatically suppresses bFGF-and H₂O₂-stimulated RASMCs proliferation by inhibiting cell

cycle progression via down-regulating ERK1 mRNA transcriptional level, as well as inducing cell apoptosis.</FONT>

Key words Probucol Fibroblast growth factor 2 Hydrogen peroxide Aortic smwth muscle cells

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