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专栏

细胞外信号调节激酶磷酸化对十字孢碱诱导肝星形细胞凋亡的调控

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摘要:

目的:肝星形细胞(hepatic stellate cells, HSCs) 是参与肝纤维化和肝硬化发展过程的主要细胞。在肝纤维化过程中, 肝星形细胞增殖并发生表型转化, 从静止状态向肌纤维母细胞样转化。后者的归宿可为凋亡, 也可重归静止状态。目前转化肌纤维母细胞样细胞的凋亡机制尚未明确。本文研究细胞外信号调节激酶(extracellular signal-regulated kinases, ERKs)磷酸化状态对十字孢碱诱导HSCs凋亡的影响。**方法**:采用Western 印迹和流式细胞术检测4种肝星形细胞株(CFSC-8B, -2G, -3H and-5H) 的ERKs表达水平和细胞凋亡状态。**结果**:4种肝星形细胞株各具有形态特异性, 并与其内α-SMA表达水平相符, 其中 CFSC-8B 细胞株 α-SMA表达水平为最高。虽然 ERK1/2 总蛋白表达水平在4种细胞株相似, 但磷酸化 ERK1/2在 CFSC-8B 和 CFSC-2G 2个细胞株中表达明显高于 CFSC-3H 和 CFSC-5H细胞株。进一步采用CFSC-8B 细胞(ERK1/2 高磷酸化水平)和 CFSC-5H 细胞(ERK1/2 低磷酸化水平), 通过staurosporine 诱导细胞凋亡。结果显示 CFSC-8B 细胞对staurosporine诱导的细胞凋亡敏感性明显增加。同时, staurosporine还可进一步增加这2株细胞内ERK1/2的磷酸化程度。**结论**:HSCs中ERK1/2 的磷酸化程度决定细胞对 staurosporine 所致细胞凋亡的敏感性。

关键词: 细胞外信号调节激酶 肝星形细胞 staurosporine 凋亡 流式细胞术

Extent of extracellular signal-regulated kinases phosphorylation determines the sensitivity of hepatic stellate cells to staurosporine-induced apoptosis

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Abstract:

Objective: Hepatic stellate cells (HSCs) are the principal cells responsible for the development of hepatic fibrosis and cirrhosis. During the fibrotic process, HSCs undergo proliferation and transdifferentiation from a quiescent to myofibroblast-like phenotype. The fate of myofibroblast-like HSCs includes apoptosis or reversion back to a quiescent phenotype. The mechanisms involved in the apoptotic process of HSCs have yet to be determined. The purpose of the present study is to determine the effects of extracellular signal-regulated kinases (ERKs) phosphorylation on the apoptosis of HSCs induced by staurosporine. Methods: We used Western blot and flow cytometry to detect the expression level of ERK and cell apoptosis status in four rat hepatic stellate cell lines (CFSC-8B, -2G, -3H and-5H). Results: Each hepatic stellate cell line had a distinct morphology consistent with their expression level of α-SMA and that CFSC-8B cells had the highest α-SMA expression. Although all four cell types expressed similar levels of ERK1/2, phosphorylation levels were significantly higher in CFSC-8B and CFSC-2G than in CFSC-3H and CFSC-5H cells. When CFSC-8B cells (high ERK1/2 phosphorylation) and CFSC-5H cells (low ERK1/2 phosphorylation) were employed to examine staurosporine-induced apoptosis, CFSC-8B cells were significantly more sensitive. Staurosporine further increased ERK1/2 phosphorylation in both cell lines. Conclusion: ERK1/2 phosphorylation in HSCs determines the sensitivity of HSCs to staurosporine-induced apoptosis.

Keywords: ERKs hepatic stellate cells staurosporine apoptosis flow cytometry

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