[文章编号] 1007-3949(2011)19-03-0265-02

细胞外信号调节激酶1/2在血管内皮细胞凋亡中的表达变化及作用

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[关键词] 细胞外信号调节激酶；内皮细胞；动脉硬化；细胞凋亡

目的 观察细胞外信号调节激酶1/2（ERK1/2）在血管紧张素Ⅱ诱导的内皮细胞中不同时点的表达变化，为阐明血管内皮细胞凋亡对动脉粥样硬化的诊治具有重要意义。**方法** 制备血管紧张素Ⅱ RPMI1640培养液（10^{-6}mol/L）培养人脐静脉内皮细胞，采用四甲基偶氮唑蓝比色法测定内皮细胞存活率，通过AnnexinV-FITC/PI双染流式细胞仪检测细胞凋亡率、Hochest33258荧光染色观察凋亡细胞形态学的变化，利用RT-PCR法分析凋亡调控基因Bcl-2、Bax mRNA表达变化，Western-Blot测定磷酸化ERK1/2水平。**结果** 血管紧张素Ⅱ诱导内皮细胞的凋亡率明显高于对照组（$P<0.01$），与对照组相比，Bcl-2 mRNA表达

呈持续性降低;Bcl-2/Bax 比值下降,ERK1/2 磷酸化水平于 12 h 明显增加,18 h 达到高峰($P<0.01$),24 h 下降至稳定,总 ERK1/2 蛋白水平无明显变化。**结论** ERK1/2 信号转导途径参与血管紧张素Ⅱ诱导内皮细胞的凋亡发生、发展过程,并可能通过调控内皮细胞 Bcl-2/Bax 比值来实现。

Effect of ERK1/2 Signal Transduction Pathway in Vascular Endothelial Cell Apoptosis

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[**KEY WORDS**] Extracellar Signal-regulated Protein Kinase; Endothelial Cell; Atherosclerosis; Cell Apoptosis

[**ABSTRACT**] **Aim** To explore the changes in extracellar signal-regulated protein kinase (ERK1/2) in endothelial cell induced by Angiotensin Ⅱ at the different time courses, and its possible molecular mechanism. **Methods** Human umbilical vein endothelial cell (HUVEC) were cultured in vitro and intervened by Ang Ⅱ. HUVEC were divided into 2 groups, the control group, Ang Ⅱ group (stimulated by Ang Ⅱ 10^{-6} mol/L for 24h). Flow cytometery with Annexin V-FITC/PI double staining and Hoechst33258 fluorescence staining were used to detect apoptosis of HUVEC. The expressions of apoptosis-association genes Bcl-2, Bax were detected by RT-PCR and ERK1/2 levels were detected by Western-blotting at different time points. **Results** 10^{-6} mol/L Angiotensin Ⅱ stimulation stimulated cell apoptosis. Bcl-2mRNA levels were time-dependently decreased, the radio of Bcl-2/Bax was decreased markedly ($P<0.05$). Phosphorylation of ERK1/2 began to increase and reach the peak at 18 h ($P<0.01$). **Conclusions** Cell apoptosis is possibly important factor for atherosclerosis. One of its molecular mechanisms might be associated with decreasing the expression level of Bcl-2 and the radio of Bcl-2/Bax. There is a probability that activated ERK1/2 signal pathway is involved in the process of pathologic and physiologic reaction in the apoptosis of endothelial cell induced by Angiotensin Ⅱ.

[**基金项目**] "973"国家重点基础研究发展基金(2007CB507405);辽宁省科学技术厅课题(2007225004)

(此文编辑 曾学清)