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论著

p38 MAPK- Pim-3通路可能介导预处理对抗心肌细胞缺氧/复氧损伤

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摘要 目的： 研究MAPK通路在原癌基因Pim-3抗心肌急性缺氧复氧损伤中的作用。方法：采用原代培养新生大鼠的心肌细胞，随机分为4组：正常对照组（control）、缺氧复氧组(A/R)、缺氧预适应组(APC+A/R)、阻断剂组。在缺氧预处理前分别用终浓度为10 μmol/L SB203850(p38 MAPK阻断剂)、U0126（ERK1/2阻断剂）、SP600125（SAPK/JNK阻断剂）与细胞孵育30 min。实验结束后测定MAPKs通路中ERK1/2、JNK、p38 MAPK 磷酸化蛋白表达水平及Pim-3蛋白的表达水平，同时检测培养液中乳酸脱氢酶(LDH) 活性、四唑盐（MTT）比色试验测定细胞存活率、TUNEL法检测细胞凋亡。结果： SB203850、U0126、SP600125能分别取消由APC或A/R所诱导ERK1/2、JNK、p38 MAPK的磷酸化水平的升高；由APC所诱导的Pim-3表达的升高在p38 MAPK通路被阻断后明显下调(P<0.01)，并且心肌细胞LDH值升高，细胞存活率则下降，心肌细胞的凋亡指数升高。结论： p38 MAPK的激活可上调原癌基因Pim-3的表达，从而可能对心肌细胞起到保护作用。

关键词 基因,Pim-3； MAPK通路； 心肌细胞； 预处理

分类号 R363

p38 MAPK-Pim-3 signal pathway may be involved in cardiomyocyte anoxia preconditioning against anoxia/reoxygenation injury

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Abstract

<FONT face=Verdana>AIM: To investigate the role of mitogen-activated protein kinases (MAPKs) pathways and the molecular mechanism by which the proto-oncogene Pim-3 protects cardiomyocyte against anoxia/reoxygenation (A/R) injury. METHODS: The primarily cultured neonatal rat ventricular cardiomyocytes were randomly divided into 4 groups: control group; A/R group; APC+A/R group; SB203850, U0126 or SP600125+APC+A/R group. The cells were pre-incubated with U0126 (ERK1/2 inhibitor), SP600125 (SAPK/JNK inhibitor), or SB203850 (p38 MAPK inhibitor) at concentration of 10 μmol/L for 30 min before the APC. The activities of p38 MAPK, JNK and ERK1/2 were detected by Western blotting. The viability of cardiomyocytes was assayed by MTT and the apoptosis of cardiomyocyte was detected by TUNEL. RESULTS: U0126, SB203850, and SP600125 abolished the increased expression of ERK1/2, p38-MAPK, and JNK proteins induced by APC+A/R or A/R, respectively. The expression level of Pim-3 protein significantly decreased when the p38 MAPK signal pathway was inhibited. Meanwhile, the activity of LDH and the apoptosis index increased, and the viability of cardiomyocytes decreased. CONCLUSION: Pim-3 expression through a p38 MAPK signaling pathway may protect cardiomyocytes from A/R injury.</FONT>

Key words Genes Pim-3 MAPK pathway Cardiomyocytes Preconditioning

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