

论著

降钙素基因相关肽对异丙肾上腺素诱导心肌成纤维细胞增殖和胶原表达的影响

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摘要: 目的: 探讨降钙素基因相关肽(CGRP)对异丙肾上腺素诱导心肌成纤维细胞增殖和胶原表达的抑制作用及其潜在的机制。方法: 异丙肾上腺素(10^{-5} mol/L)孵育48 h以诱导体外培养的心肌成纤维细胞增殖和胶原表达,不同浓度的CGRP(10^{-8} 或 10^{-7} mol/L)在异丙肾上腺素孵育前1 h给药。药物处理结束后,用MTT法检测细胞活性,RT-PCR检测I和III型胶原和结缔组织生长因子(CTGF)mRNA的表达,DCFH-DA荧光法检测细胞内ROS的水平。结果: 异丙肾上腺素能明显促进成纤维细胞的增殖,上调I和III型胶原以及CTGF mRNA表达,同时伴随着ROS产生的增加。预先给予CGRP可显著抑制异丙肾上腺素的上述效应,但CGRP的有益效应可被选择性CGRP受体拮抗剂CGRP₈₋₃₇所取消。结论: CGRP可抑制异丙肾上腺素诱导的心肌成纤维细胞增殖和胶原表达,其机制与抑制ROS的产生进而下调CTGF的表达有关。

关键词: 降钙素基因相关肽 异丙肾上腺素 心肌成纤维细胞 胶原 结缔组织生长因子 活性氧

Effect of calcitonin gene-related peptide on isoprenaline-induced cardiac fibroblast proliferation and collagen expression

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Abstract: Objective: To explore the inhibitory effect of calcitonin gene-related peptide (CGRP) on cardiac fibroblast proliferation and collagen synthesis induced by isoprenaline and the underlying mechanism.

Methods: The primary cultured cardiac fibroblasts were incubated with isoprenaline (10^{-5} mol/L) for 48 h after pretreatment with CGRP (10^{-8} or 10^{-7} mol/L) for 1 h. Cell activity was detected by MTT. The mRNA expression of collagen (types I and III) and connective tissue growth factor (CTGF) was determined by RT-PCR, and the levels of intracellular ROS were determined by DCFH-DA fluorescent probe.

Results: Isoprenaline significantly promoted fibroblast proliferation and up-regulated collagen (types I and III) and CTGF mRNA expression concomitantly with an increase in ROS production, which were attenuated by CGRP. The effect of CGRP on cardiac fibroblasts was inhibited by CGRP₈₋₃₇, a selective antagonist of CGRP receptor.

Conclusion: CGRP is able to protect cardiac fibroblasts against isoprenaline-induced proliferation and collagen expression, which might be related to the down-regulation of CTGF expression through inhibition of ROS production.

Keywords: calcitonin gene-related peptide isoprenaline cardiac fibroblast collagen connective tissue growth factor reactive oxygen species

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