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论著

尿促皮素诱导乳大鼠心肌细胞肥大的作用及信号传导机制

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摘要 目的 探讨尿促皮素(urocortin)诱导大鼠心肌细胞肥大的作用及其信号传导机制。方法 实验分8组，正常对照组、尿促皮素0.1 μmol·L^{-1}组、星形孢菌素（Sta）1 μmol·L^{-1}、H89 0.1 μmol·L^{-1}和维拉帕米（Ver）1 μmol·L^{-1}组及尿促皮素分别加Sta，H89和Ver组。采用体外培养的乳大鼠心肌细胞，应用尿促皮素0.1 μmol·L^{-1}诱导心肌肥大，观察Sta 1 μmol·L^{-1}，H89 0.1 μmol·L^{-1}和Ver 1 μmol·L^{-1}的作用，进一步探讨尿促皮素0.1 μmol·L^{-1}诱导心肌肥厚的作用机制。用消化分离法及计算机图像分析系统检测心肌细胞直径；［^{3}H］亮氨酸掺入法测定心肌细胞蛋白质的合成；用Lowry法检测心肌细胞蛋白质含量；用Western蛋白印迹法测定心房钠尿肽（ANP）表达；采用Till阳离子测定系统，以Fura-2/AM为荧光探针，观察心肌细胞［Ca^{2+}］$_i$瞬间变化。结果 尿促皮素使心肌细胞直径、蛋白质合成、蛋白质含量和ANP表达分别增加30.9%，36.3%，35.5%和34.7%；尿促皮素+Sta组使心肌细胞直径、蛋白质合成、蛋白质含量和ANP表达分别降低了16.5%，22.1%，18.1%和21.3%；尿促皮素+H89组使心肌细胞直径、蛋白质合成、蛋白质含量和ANP表达分别降低了16.6%，21.5%，19.5%和20.6%；尿促皮素+Ver组使心肌细胞直径、蛋白质合成、蛋白质含量和ANP表达分别降低了17.1%，20.9%，17.9%及19.9%；尿促皮素能够使心肌细胞［Ca^{2+}］$_i$瞬间变化水平增高，Sta，H89和Ver能够降低尿促皮素引起的心肌细胞［Ca^{2+}］$_i$瞬间变化升高。结论 尿促皮素可能通过蛋白激酶C和蛋白激酶A信号途径影响L-型Ca^{2+}通道，进而影响细胞［Ca^{2+}］$_i$瞬间变化水平，诱导乳大鼠心肌细胞肥大。

关键词 尿促皮素 肌细胞,心脏 信号传导通路

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Effect and mechanism of signal transduction pathway in urocortin-induced cardiomyocytes hypertrophy in neonatal rat

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Abstract

AIM To investigate the effects and mechanism of cardiomyocyte hypertrophy induced by urocortin. **METHODS** The cardiomyocytes were divided into 8 groups: normal control, urocortin, staurosporine(Sta), verapamil(Ver), H89, urocortin+Sta, urocortin+Ver, and urocortin+H89 groups. The cardiomyocytes diameter was measured by computer photograph analysis system. The protein synthetic rate was obtained through measuring the incorporation of ［^{3}H］-leucine into myocyte protein by liquid scintillation method. The total protein content was assayed by Lowry method. The expression of atrial natriuretic peptide (ANP) was determined by Western blot. ［Ca^{2+}］$_i$ transient was measured by Till image system by cell loading Fura-2/AM. **RESULTS** Urocortin group enhanced cardiomyocyte volume, protein synthesis, total protein content and expression of ANP by 30.9%, 36.3%, 35.5% and 34.7%; urocortin+Sta group decreased cardiomyocyte diameter, protein synthesis, total protein content and expression of ANP by 16.5%, 22.1%, 18.1% and 21.3%; urocortin+H89 group decreased the cardiomyocyte diameter, the protein synthesis,total protein content and expression of ANP by 16.6%, 21.5%, 19.5% and 20.6%; urocortin+Ver decreased the cardiomyocyte diameter, the protein synthesis, total protein content and the expression of ANP by 17.1%, 20.9%, 17.9% and 19.9%; Sta, H89 and Ver could decrease the ［Ca^{2+}］$_i$ transient induced by urocortin. **CONCLUSION** The hypertrophic effect of urocortin in rat neonatal cardiomyocytes is mediated via activation of protein kinase C and protein kinase A pathway and L-type calcium channels.

Key words urocortin myocytes cardiac signal transduction pathway

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