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论著

PPAR-α参与高糖高胰岛素诱导的心肌细胞肥大

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摘要 目的： 研究过氧化物酶体增殖物激活受体-α(PPAR-α）在高糖高胰岛素(HGI)诱导心肌肥大中的作用。方法: 利用乳鼠心肌细胞培养，以细胞表面积、蛋白含量和心房利钠因子（ANF)mRNA表达为心肌肥大反应指标，观察PPAR-α激动剂非诺贝特（FF）对HGI致肥大作用的影响。利用RT-PCR和Western blotting方法检测mRNA及蛋白水平的表达。结果: HGI诱导细胞表面积、总蛋白含量和ANF mRNA表达增加（P<0.01）；但PPAR-α mRNA和蛋白的表达明显降低（P<0.05）；而其下游因子环氧酶-2（COX-2）的表达则增加（P<0.05）。FF浓度依赖性地抑制HGI诱导的心肌细胞肥大（P<0.01），并上调PPAR-α的表达，同时阻遏COX-2的表达（P<0.05）。PPAR-α阻断剂MK 886可完全取消FF的上述作用（P<0.05），使COX-2表达增加至HGI模型组水平。结论: PPAR-α可能参与了HGI诱导的心肌肥大，同时COX-2可能是其重要下游因子。

关键词 过氧化物酶体增殖物激活受体-α 环氧化酶-2 心肌肥大 高糖高胰岛素

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PPAR-α involves in cardiomyocyte hypertrophy induced by high glucose and insulin

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Abstract

<FONT face=Verdana>AIM: To study the role of peroxisome proliferator-activated receptor-α (PPAR-α) signal transduction pathway in cardiac hypertrophy induced by high glucose and insulin (HGI). METHODS: The cultured neonatal rat cardiomyocytes were used to observe the effect of fenofibrate (FF), a selective PPAR-α agonist, on cardiomyocyte hypertrophy induced by HGI (glucose at concentration of 25.5 mmol/L and insulin at 0.1 μmol/L). The cardiomyocyte hypertrophic responses were assayed by measuring the cell surface area, protein content, and mRNA expression of atrial natriuretic factor (ANF). The expressions of mRNA and protein were assayed by real -time PCR and Western blotting. RESULTS: In cultured cardiomyocytes, HGI induced profound change of hypertrophic morphology, the significant increase in cell surface area, protein content and ANF mRNA expression compared to those in vehicle control (P<0.01), but the expressions of PPAR-α mRNA and protein decreased significantly (P<0.05). At the same time, the expression of cyclooxygenase 2 (COX-2), one of the PPAR-α downstream effectors was obviously elevated (P<0.05). However, FF (0.1, 0.3 and 1 μmol/L) inhibited the cardiomyocyte hypertrophy induced by HGI in a concentration-dependent manner (P<0.01). FF at concentration of 0.3 μmol/L increased the expressions of PPAR-α in both mRNA and protein levels (P<0.05) and inhibited the expressions of COX-2 (P<0.05), which were abolished by MK 886 (0.3 μmol/L), a selective PPAR-α antagonist (P<0.05). CONCLUSION: PPAR-α signal transduction pathway and its downstream effector COX-2 might involve in the cardiomyocyte hypertrophy induced by HGI.</FONT>

Key words Peroxisome proliferator-activated receptor-α Cyclooxygenase-2 Myocardial hypertrophy High glucose and high insulin

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