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论著

PPAR-α激活对ET-1诱导的心肌肥大和转录因子NFATc4的影响

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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）激活对内皮素-1（ET-1）诱导的心肌肥大和活化T细胞核因子c4(NFATc4)的影响，探讨在心肌肥大发病过程中PPAR-α和NFATc4的相互作用。方法: 培养新生SD大鼠心肌细胞，采用［3H］亮氨酸法和RT-PCR法观察PPAR-α激动剂非诺贝特对ET-1诱导的心肌细胞肥大的影响；应用免疫荧光和免疫共沉淀技术分别检测非诺贝特对ET-1诱导的NFATc4核转位以及PPAR-α和NFATc4相互作用的影响；用Western blotting法检测NFATc4的胞浆和胞核表达。结果: （1）PPAR-α激动剂非诺贝特显著抑制ET-1诱导的肥厚反应。(2)非诺贝特阻止ET-1诱导NFATc4由胞浆到胞核的转位。(3)在心肌细胞中，PPAR-α和NFATc4之间存在相互作用，非诺贝特加强了这种相互作用。结论: PPAR-α激活后可以通过调控转录因子NFATc4来抑制ET-1诱导的心肌肥大反应。

关键词 内皮缩血管肽1； 心肌肥大； 过氧化物酶体增殖物激活受体α； 活化T细胞的核因子

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Effects of PPAR-α activation on ET-1-induced cardiomyocyte hypertrophy and regulation of NFATc4

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Abstract

<FONT face=Verdana>AIM: To investigate the effects of peroxisome proliferator-activated receptor-α (PPAR-α) activation on ET-1-induced cardiomyocyte hypertrophy and the interaction of PPAR-α with nuclear factor of activated T cell (NFAT)c4 in cardiac myocytes. METHODS: Cultured cardiac myocytes of neonatal SD rats were used to establish the experiment models. ［3H］ leucine incorporation assay was performed to examine protein synthesis while reverse transcription-polymerase chain reaction (RT-PCR) was applied to analyze the mRNA level of atrial natriuretic factor (ANF). Immunofluorescence and confocal microscopic assay were used to evaluate the effects of PPAR-α activator fenofibrate on the nuclear translocation of NFATc4. Immunoprecipitation was performed to examine the association of PPAR-α with NFATc4 in cardiomyocytes. Western blotting analysis was performed to investigate the cytoplasmic and nuclear protein levels of NFATc4. RESULTS: (1) ET-1 significantly increased incorporation of ［3H］ leucine (1.73±0.08 fold vs control, P<0.01) and the level of ANF mRNA (1.74±0.25 fold vs control, P<0.01). However, PPAR-α activator fenofibrate (10 μmol/L) significantly inhibited the ET-1-induced protein incorporation in cardiomyocytes (-31% at 5 μmol/L, -49% at 10 μmol/L) and the expression of ANF mRNA in these cells (1.10±0.17 fold of control). (2) ET-1 stimulation markedly changed the translocation of NFATc4 from the cytoplasm to the nucleus while fenofibrate prevented this effect of ET-1. (3) The interactions between PPAR-α and NFATc4 were constitutively detectable while fenofibrate further increased the interaction between NFATc4 and PPAR-α.CONCLUSION: Activation of PPAR-α prevents ET-1-induced cardiac myocyte hypertrophy through negative regulation of NFATc4, possibly via blocking the nuclear translocation of NFATc4 and increasing the interaction of PPAR-α and NFATc4.</FONT>

Key words Endothelin-1 Myocardial hypertrophy Peroxisome-proliferator-activated receptor-α

Nuclear factor of activated T cells

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