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论文

ERK1/2通路参与大鼠肠系膜动脉平滑肌细胞ET_B受体上调表达

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摘要：

目的探讨细胞外信号调节激酶1/2(ERK1/2)信号转导通路在血管平滑肌细胞内皮素-1 B型受体(ET_B)上调中的作用。方法用大鼠肠系膜上动脉离体培养模型，以敏感的离体小血管张力描记技术记录血管张力变化，实时PCR定量ET_B受体mRNA，PhosphoELISA法测定细胞内磷酸化的ERK1/2蛋白水平。结果大鼠肠系膜上动脉培养3 h，细胞内ERK1/2蛋白磷酸化水平明显增高，培养24 h ET_B受体mRNA表达水平显著上调，选择性ET_B受体激动剂蛇毒类似物(sarafotoxin 6c，S6c)引起的收缩增强；与特异性ERK1/2通路阻滞剂SB386023共同孵育24 h，S6c引起的最大收缩E_{max}明显下降，ET_B受体mRNA水平也显著降低。结论ERK1/2信号转导通路参与大鼠肠系膜上动脉离体平滑肌细胞ET_B受体上调过程。

关键词： 信号转导 细胞外信号调节激酶1/2 ET_B受体 血管平滑肌 蛋白磷酸化

ERK1/2 pathway involved in the expression of ET_B receptors of the culturing smooth muscle cells of rat mesenteric artery

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Abstract:

AimTo determine the involvement of extracellular signal-regulated kinase 1/2 (ERK1/2) pathway in the expression of endothelin receptor type B (ET_B) during culture. MethodsSB386023, a specific inhibitor for ERK1/2 pathway, was used to define the intracellular signaling pathway for the up-regulation of ET_B receptors and sarafotoxin 6c (S6c), a selective agonist for ET_B receptors，induced contraction in isolated rat superior mesenteric arteries. The contraction was recorded by a sensitive *in vitro* myograph and the receptor mRNA was quantified by a real-time PCR. The phosphorylated ERK1/2 proteins were analyzed by phosphoELISA assay. ResultsS6c induced strong contractile responses of the artery after culture for 24 h, while there was no response to S6c in fresh vessel segments. The enhanced contractile response to S6c paralleled with an increase of mRNA for ET_B receptors. The phosphorylated ERK1/2 proteins significantly increased after culture for 3 h. After co-culture with SB386023 for 24 h, S6c-induced contractions significantly decreased with reduction of *E*max from (217±14)% to (127±23)% ($P<0.01$). This response paralleled with a decreased level of ET_B receptor mRNA. Conclusion ERK1/2 pathway was involved in the up-regulation of ET_B receptors on smooth muscle cells isolated from rat mesenteric arteries during culture.

Keywords: ERK1/2 ET_B receptor vascular smooth muscle protein phosphorylation signal transduction

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