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论著

致密斑细胞COX-2的表达及AP-1、NFκB信号通路

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摘要 摘要：目的 评估低盐(LS)培养对小鼠致密斑（MMDD1）细胞环氧化酶－2（COX-2）表达及核因子-κB(NF-κB）和活化蛋白-1（AP-1）活性的影响。方法 经脂质体转染含NF-κB或AP-1的报告质粒,采用瞬时表达方法检测正常盐(NS)与LS培养对NF-κB和AP-1转录活性的影响。采用RT-PCR检测MMDD1细胞COX-2表达的变化,Western blot方法检测细胞内p-p38 MAPK、p-p44/42、c-Jun、c-Fos 和COX-2蛋白的表达。结果 LS培养促进了MMDD1细胞COX-2 mRNA和蛋白表达(P<0.01)。LS培养后,p38和p44/42的磷酸化程度显著上调(P<0.01),180 min后达到高峰。p38抑制剂SB-203580、p44/42抑制剂PD-98059可降低LS诱导的COX-2表达(P<0.01)。LS培养促进了c-Jun、c-Fos蛋白表达(P<0.01),激活了AP-1和NF-κB的转录活性 (P<0.01)。25 μmol/L NF-κB抑制剂PDTC 和20 μmol/L AP-1抑制剂curcumin下调了LS诱导的NF-κB、AP-1活性(P<0.01)。25 μmol/L PDTC 、20 μmol/L curcumin 降低了LS诱导的COX-2 mRNA和蛋白表达(P<0.01)。结论 LS培养可促进MMDD1细胞COX-2的表达,其作用可能与促进p38MAPK、p44/42激酶的磷酸化,增加NF-κB和AP-1的活性有关。

关键词 环氧化酶－2 核因子-κB 活化蛋白-1 质粒 丝裂素激活蛋白激酶

分类号

Expression of Cyclooxygenase-2 in a Mouse Macula Densa Cell Lines and Signal Transduction of NF-κB and AP-1

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Abstract ABSTRACT:Objective To elvaluate the effect of low salt (LS) on the expression of cyclooxygenase-2 (COX-2) and the activity of nuclear factor kappa B（NF-κB）and activator protein-1（ AP-1） in the mouse macula densa derived (MMDD1) cell line. Methods MMDD1 cells were transfected with luciferase reporter plasmid containing AP-1 or NF-κB. Luciferase reporter assay was used to evaluate the effect of normal salt (NS) and low salt(LS) on the activities of NF-κB and AP-1. The changes of COX-2 expression were examined by RT-PCR. The expression of p-p38 MAPK, p-p44/42, c-Jun, c-Fos, and COX-2 in MMDD1 cells were analyzed by Western blot. Results The expressions of COX-2 mRNA and protein in MMDD1 cells were significantly increased by LS (P<0.01). Phosphorylated p38 and p44/42 MAPkinase were significantly increased by treatment at 180 min (P<0.01). The up-regulated COX-2 protein expression with LS were significantly reduced with SB 203580 (p38 inhibitiors) and PD-98059 (p44/42 inhibitiors) (P <0.01). The expressions of c-Jun and c-Fos were increased by LS. The luciferase activities of AP-1 and NF-κB were stimulated in LS (P<0.01), the up-regulated luciferase activities were attenuated by PDTC at 25 μmol/L (NF-κB inhibitor) and curcumin at 20 μmol/L (AP-1 inhibitor) (P<0.01). LS altered COX-2 mRNA abundance and protein expression were decreased in treatment with PDTC at 25 μmol/L, curcumin at 20 μmol/L (P<0.01). Conclusion LS can induce the expression of COX-2 in MMDD1 cells,which may be involved in the activation of p38 MAPkinase, p44/42 kinase, AP-1, and NF-κB pathways.

Key words cyclooxygenase-2 nuclear factor kappa B activator protein-1 plasmid mitogen-activated protein kinase

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