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论文

AP-1在锌离子诱导BEAS-2B细胞COX-2基因转录中作用

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摘要：

目的 探讨外源性锌离子对人支气管上皮细胞环氧化酶2(COX-2)基因诱导表达及转录因子激活蛋白-1(AP-1)的转录活性调节作用。方法 以人支气管上皮细胞株BEAS-2B作为体外模型,Real-time PCR方法检测锌离子对BEAS-2B细胞COX-2基因表达影响;染色质免疫沉淀(ChIP) 实验检测50.0 μmol/L锌离子温育8 h后c-Jun(AP-1亚单位)和COX-2启动子的结合;用野生型和AP-1结合位点突变的COX-2启动子报告质粒转染BEAS-2B细胞,50.0 μmol/L锌离子温育8 h,采用荧光素酶报告基因检测COX-2基因启动子转录活性。结果 50.0 μmol/L Zn^{2+}组BEAS-2B细胞中COX-2的mRNA相对表达量为(1.23±0.16),是对照组表达量(0.16±0.02)的7.68倍,表达明显升高(P<0.5);AP-1可与COX-2的基因启动子结合,COX-2基因启动子区AP-1结合位点突变可使锌离子所致的COX-2高转录活性降低82%。结论 转录因子AP-1可调节外源性锌离子所致人支气管上皮细胞COX-2基因的转录表达。

关键词： 锌离子 激活蛋白-1(AP-1) 环氧化酶(2COX-2)基因 BEAS-2B细胞

Regulational role of AP-1 to COX-2 transcriptional activity induced by exogenous zinc in bronchial epithelial cells

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Abstract:

Objective To examine cycloxygenase 2(COX-2) transcriptional activity induced by exogenous zinc in bronchial epithelial cells and the regulatory role of activator protein-1(AP-1).Methods Human bronchial epithelial cells (BEAS-2B) were employed as the *in vitro* model.Expression of COX-2 mRNA was determined by real-time reverse transcription PCR (RT-PCR).Chromatin immunoprecipitation assay (ChIP) was used to investigate whether AP-1(c-Jun) could bind to the COX-2 gene promoter in BEAS-2B cells incubated with 50.0 μmol/L Zn^{2+} for 8 hours.Transcriptional activity of COX-2 promoter in Zn^{2+}-treated BEAS-2B cells was measured using transient gene transfection luciferase reporter construct which was wild type or mutated at AP-1 binding site in the COX-2 promoter.Results Exposure of BEAS-2B cells to 50.0 μmol/L Zn^{2+} induced significantly high expression of COX-2 mRNA which was 7.68 folds over the control group of 0 μmol/L Zn^{2+}. Zn^{2+} stimulation resulted in a marked increase in the binding of AP-1(c-Jun) to the COX-2 gene promoter.Mutation of the AP-1 site significantly reduced Zn^{2+}-induced COX-2 promoter activity.Conclusion AP-1 regulates COX-2 expression in BEAS-2B cells exposed to exogenous Zn^{2+}.

Keywords: Zn^{2+} AP-1 COX-2 BEAS-2B cell

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