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论文

特异性p38 MAPK抑制剂SB203580对乳鼠小脑颗粒神经元的保护作用

黎明涛;王文雅;林穗珍;颜光美

中山医科大学药理教研室， 广东 广州 510089;*中国人民解放军第一军大学分校（原广州医学高等专科学校）药理教研室，广州510315

摘要：

目的 研究p38丝裂原激活蛋白激酶（MAPK）选择性抑制剂SB203580对乳鼠小脑颗粒神经元凋亡的保护作用。方法 SD乳鼠小脑颗粒神经元培养，琼脂糖凝胶电泳，SAPK/JNK分析试剂盒作激酶分析。结果 PI-3-K的特异性抑制剂LY294002诱导小脑颗粒神经元凋亡，但SB203580通过抑制细胞凋亡而促进小脑颗粒神经元的存活，且有浓度依赖性。LY294002诱导凋亡的颗粒神经元中c-Jun的表达量和磷酸化水平均升高，JNK被激活。但是，当小脑颗粒神经元生长在含SB203580的高钾培养基中，c-Jun的表达量、磷酸化水平和JNK的活性都明显的降低。结论 SB203580通过抑制JNK的活性，降低c-Jun的表达和磷酸化水平，对小脑颗粒神经元产生保护作用。

关键词： 特异性p38 MAPK抑制剂SB203580 凋亡 小脑颗粒神经元 蛋白激酶 磷脂酰肌醇-3-激酶

PROTECTIVE ACTION OF THE SPECIFIC P38 MAPK INHIBITOR SB203580 IN CEREBELLAR GRANULE NEURONS OF RAT PUPS

LI Ming-Tao; WANG Wen-Ya; LIN Sui-Zhen; YAN Guang-Mei

Abstract:

AIM To study the effect of the specific p38 MAPK inhibitor SB203580 on apoptosis induced by PI-3-K inhibitor LY294002 and its mechanisms in cerebellar granule neurons.METHODS Cerebellar granule neurons culture, agar gel eletrophoresis, and SAPK/JNK assay kit were used to measure SAPK/JNK activity. RESULTS Cultured cerebellar granule neurons died by apoptosis in a concentration-dependent manner when treated with LY294002, a specific inhibitor of PI-3-K. But the specific p38 MAPK inhibitor SB203580 promoted the survival of cerebellar granule neurons by blocking apoptosis. This protective action was shown to be in a concentration-dependent manner. The expression and phosphorylation of c-Jun increased, and the activity of c-Jun N-terminal protein kinase (JNK) was elevated when cerebellar granule neurons were cultured with LY294002 50 μmmol.L^{-1} in cHK medium. But when the cerebellar granule neurons treated with LY294002 50 μmmol.L_{-1} were exposed to SB203580 25 μmmol.L^{-1}, the expression and phosphorylation of c-Jun， and the activity of JNK all decreased evidently. CONCLUSION SB203580 inhibited the activation of JNK and decreased the expression and phosphorylation of c-Jun to protect granule neurons from apoptosis induced by LY294002.

Keywords: apoptosis cultured cells protein kinase PI-3-K specific p38 MAPK inhibitor SB203580

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通讯作者: 王文雅

作者简介:

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