论著

p38阻断剂对鼠关节炎软骨细胞金属蛋白酶表达的作用

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摘要 摘要:目的 观察p38信号转导途径阻断剂SB203580经关节腔注射对实验性鼠膝骨关节炎基质金属蛋白酶 (MMP)-3、MMP-13表达的影响,探讨MMP-3、MMP-13表达与创伤性软骨退变之间的关系。方法 40 只SD大鼠随机分为A~D组,每组10只。各组均行单侧膝关节前交叉韧带切除术。A、

B组分别于术后立即行关节腔内注射0.1ml高、低浓度的p38阻断剂SB203580(100、10μmol/L), 每周1次, 连续6 周。C组注射等量生理盐水, D组不做任何处理。术后7

周处死动物。于解剖显微镜下行股骨关节面软骨退变大体观察,免疫组织化学的方法检测MMP-3、MMP-13 在软骨中的表达及分布,Western blot方法检测软骨中MMP-3、MMP-13 蛋白表达水平。结果 大体观察显示高、低浓度组软骨退变显著轻于生理盐水组和关节炎组 (P< 0.05);免疫组织化学显示高、低浓度组软骨MMP-3、MMP-13表达降低 (P< 0.05);Western blot显示注射抑制剂后MMP-3、MMP-13的蛋白表达降低(P<0.01)。结论p38阻断剂SB203580能抑制MMP-3、MMP-13的表达,对软骨有一定的保护作用。

关键词 <u>骨关节炎</u> <u>基质金属蛋白酶</u> <u>信号转导</u> <u>阻断剂</u> 分类号

Effects of Intra-articular Injection of p38 Mitogen-activated Protein Kinase Inhibitor on Matrix Metalloproteinase in Articular Cartilage of a Rat Model of Osteoarthritis

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Abstract ABSTRACT:Objective To observe the effect of intra-articular injection of SB203580, a selective p38 mitogen-activated protein kinase inhibitor, on the expression of matrix metalloproteinase (MMP) -3, MMP-13 in a rat model of osteoarthritis(OA) and to explore the relationship between the MMP-3/MMP-13 expressions and the severity of OA. Methods Fourty SD rats underwent unilateral anterior cruciate ligament transection (ACLT) and then randomly divided into four groups, with 10 rats in each group. Group A received 0.1 ml intra-articular injection of SB203580 at a high concentration of 100µmol/L (once a week) immediately after surgery, and group B were treated under the same condition using SB203580 with a low concentration of 10µmol/L. Group C received 0.1ml intra-articular normal saline, and group D were not injected as controls after ACLT. All rats were sacrificed seven weeks after the surgery. Macroscopic and immunohistochemical studies were performed on the cartilage. Protein expressions of MMP-3 and MMP-13 were determined by Western blot. Results Cartilage degradation was significantly milder in group A and group B than in the control groups, as shown by morphological studies (P< 0.05) and immunohistochemical studies (P< 0.05). The protein expressions of MMP-3 and MMP-13 in cartilage were significantly lower in groups A and B than in groups C and D (P<0.01). Conclusion SB203580 can inhibit the expressions of MMP-3 and MMP-13 and thus protect the cartilage.

Key words osteoarthritis matrix metalloproteinase signal transduction inhibitor

DOI:

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