

论著

磷酸二酯酶4B在博来霉素诱导的肺纤维化小鼠肺组织中的表达与作用

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摘要 目的 观察博来霉素诱导的小鼠肺纤维化过程中磷酸二酯酶4B(PDE4B)mRNA和蛋白表达随时间的变化, 初步探究PDE4B在小鼠肺纤维化过程中的作用。方法 采用气道滴入博来霉素 $2.5 \text{ mg} \cdot \text{kg}^{-1}$ 制备肺纤维化模型, 在造模后第3, 7, 14, 21和28天进行支气管肺泡灌洗并取肺组织。应用细胞形态学方法计数支气管肺泡灌洗液(BALF)中白细胞总数和分类; ELISA法测定BALF中巨噬细胞炎症蛋白2(MIP2)、白细胞介素6(IL-6)、IL-1 β 和转化生长因子 β_1 (TGF- β_1)含量; 胶原试剂盒测定法测定肺组织胶原含量; 髓过氧化物酶(MPO)活性测定试剂盒测定组织匀浆液中MPO活性; 实时荧光定量PCR方法检测小鼠肺组织中PDE4B mRNA表达; 免疫组织化学法检测PDE4B的分布。结果 博来霉素气道滴入诱导的肺纤维化随时间持续加重, 第28天最明显, 可见肺组织明显实质化。BALF中白细胞总数、IL-1 β 和IL-6在造模后第3天达峰值, 分别为正常对照组的22.0、2.0和2.8倍; MPO和TGF- β_1 在第7天达峰值, 分别为正常对照组的1.9和5.5倍; 胶原含量、MIP-2和PDE4B mRNA表达从造模后呈持续增长趋势, 分别为正常对照组的1.6、2.7和2.6倍。免疫组织化学法检测结果表明, PDE4B分布于炎症细胞和纤维化的肺组织。结论 PDE4B在肺纤维化中发挥重要作用, 可能是一个特异性的药物作用靶点。

关键词 [磷酸二酯酶4B](#) [肺纤维化](#) [博来霉素](#)

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Expression and action of phosphodiesterase 4B in bleomycin-induced pulmonary fibrosis in mice

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Abstract

OBJECTIVE To observe the preliminary action of phosphodiesterase 4B (PDE4B) in bleomycin-induced pulmonary fibrosis in mice. **METHODS** Pulmonary fibrosis in mice was induced by intratracheal instillation of bleomycin $2.5 \text{ mg} \cdot \text{kg}^{-1}$. On the 3rd, 7th, 14th, 21st and 28th day after instillation, bronchoalveolar lavage and lung tissue specimens were collected. The total number of white blood cells count and differential count in bronchoalveolar lavage fluid (BALF) were recorded. Transforming growth factor- β_1 (TGF- β_1), macrophage inflammatory protein-2 (MIP-2), interleukin-6(IL-6) and IL-1 β levels in BALF were determined by ELISA. Collagen content and myeloperoxidase (MPO) activity were determined by assay kits. PDE4B mRNA expression in mouse lung tissue was detected by quantitative real-time PCR. Immunohistochemistry was used to detect the PDE4B protein expression and distribution in lung tissue. **RESULTS** After airway instillation, the bleomycin-induced pulmonary fibrosis continued to develop, reaching the peak on the 28th day and showing clearly lung fibrosis. After modeling, the total number of leukocytes in BALF, IL-1 β and IL-6 reached the peak on the 3rd day, and the peak value was 22.0, 2.0 and 2.8 fold, respectively, compared with normal control. MPO and TGF- β_1 reached the peak on the 7th day, which was 1.9 and 5.5 fold, respectively, compared with normal control. While the collagen content, MIP-2 and PDE4B mRNA expression from the modeling continued to increase, the peak value was 1.6, 2.7 and 2.6 fold, respectively, compared with normal control. Immunohistochemical results showed that the PDE4B protein was distributed in the inflammatory cells and fibrosis of the lung tissue. **CONCLUSION** PDE4B plays an important role in pulmonary fibrosis, and may be a specific drug target.

Key words [phosphodiesterase 4B](#) [pulmonary fibrosis](#) [bleomycin](#)

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