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论著

T-bet基因转染对哮喘小鼠气道炎症的影响

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摘要 目的： 观察气道内T-bet基因转染对哮喘小鼠气道炎症的影响。方法: C57BL/6小鼠40只，随机分为4组，每组10只，分别为正常对照组（A组）、哮喘模型组（B组）、空质粒干预组(C组) 和T-bet质粒干预组(D组)。卵白蛋白(OVA) 抗原溶液腹腔注射致敏，滴鼻造模。正常对照组用生理盐水代替OVA，空质粒干预组和T-bet质粒干预组OVA激发48 h前，分别经鼻滴入50 μg空质粒和重组T-bet质粒。观察各组实验小鼠的肺组织炎症以及BALF中各类炎症细胞以及IL-4、IFN-γ水平的变化。 结果: Western blotting检测发现，小鼠气道转染pcDNA3-T-bet质粒48 h后肺组织T-bet蛋白表达显著增加。pcDNA3-T-bet质粒转染能较好抑制给药后48 h OVA激发的哮喘小鼠气道炎症（包括炎症细胞浸润，上皮细胞损伤、黏液分泌、血管壁水肿及管腔缩窄）；下调小鼠BALF中Th2因子IL-4并上调Th1因子IFN-γ水平。 结论: 气道内转染T-bet质粒能有效改善哮喘小鼠的气道炎症。

关键词 基因,T-bet 基因疗法 哮喘

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Inhibitory effect of T-bet gene transfer on airway inflammation in a established murine allergic asthmatic model

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Abstract

<FONT face=Verdana>AIM: To investigate the effect of T-bet plasmid gene transfer to airway on allergen induced airway inflammation in a murine asthmatic model. METHODS: A mouse asthma model was established by sensitization with ovalbumin (OVA). Forty C57BL/6 mice were divided into 4 groups (10 mice in each group): the normal control group (group A), the asthmatic model group (group B), the pcDNA3 plasmid group (group C), and the pcDNA3-T-bet group (group D). The animals in group B, C and D were sensitized and challenged with OVA. The animals in group A were applied with normal saline. pcDNA3 plasmid at dose of 50 μg was intranasally administered at 24 h before intranasal challenges to the mice in group C, and the 50 μg pcDNA3-T-bet plasmid for the mice in group D. Bronchial alveolar lavage fluid (BALF) was collected and lung tissues were resected at 48 h after OVA challenge for later assay. RESULTS: After administration with pcDNA3-T-bet plasmid, high level of T-bet expression at 48 h was detected in the lung tissue by Western blotting. In pcDNA3-T-bet treated asthmatic models, histological evaluation revealed the significant suppression of eosinophil peribronchial and perivascular infiltration, and reduction of epithelial damage. The numbers of eosinophils, neutrophils and lymphocytes in BALF from pcDNA3-T-bet treated mice were significantly reduced compared to those in asthmatic control group (P<0.05). The level of IL-4 in BALF was significantly decreased in pcDNA3-T-bet group compared to that in asthmatic control group (P<0.05), while the level of IFN-γ in BALF was significantly increased in pcDNA3-T-bet group. No significant change of inflammation cells and cytokines in pcDNA3 plasmid group and asthmatic control group was observed (P>0.05). CONCLUSION: Intranasal pcDNA3-T-bet plasmid transfer inhibits asthmatic airway inflammation in the murine asthmatic model, suggesting a new therapeutic strategy for allergic asthma.</FONT>

Key words Genes T-bet Gene therapy Asthma

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