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Significance of leukotriene blockade in an allergic model of asthma

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Keywords

Airway inflammation, allergen challenge, asthma, FLAP, leukotrienes, 5-LO, Zileuton

Context

As a result of their ability to regulate leukocyte influx and trafficking, vasopermeability and bronchial smooth muscle contraction, metabolic products of 5-lipoxygenase (5-LO) such as leukotriene (LT) B_4, LT C_4 and LT D_4 are involved in promoting airway inflammation in asthma. In this study, the authors further investigated the role of 5-LO in asthma by studying the cellular distribution of 5-LO and 5-LO activating protein (FLAP), the cofactor required for LT synthesis, in lung tissues of mice after allergen challenge. The authors also examined the effects of 5-LO inhibition on the cellular distribution of 5-LO and FLAP in a model of allergen-induced airway inflammation.

Significant findings

Using polymerase chain reaction (PCR), *in situ* PCR based on a digoxigenin detection system, and immunocytochemistry of mouse lung tissue, the authors show that, following allergen challenge, levels of 5-LO and FLAP are significantly increased in alveolar macrophages, eosinophils and pulmonary endothelial cells. In addition, the 5-LO inhibitor Zileuton significantly reduced allergen-induced increases in 5-LO and FLAP expression. Together, these data showed the potential importance of leukotriene blockade in allergen-induced airway inflammation in an animal model of asthma.

Comments

Growing evidence now shows that inhibiting leukotriene synthesis or action is effective in the treatment of asthma. By preventing allergen-induced 5-LO and FLAP expression in the lungs of a murine model of asthma, the authors have demonstrated a potential mechanism by which leukotriene modifier agents may exert their protective effects in allergic asthma. Further studies will also be necessary (1) to understand the mechanisms that regulate the expression of 5-LO and FLAP in this model and (2) to show similar 5-LO-dependent variations of 5-LO and FLAP expression in asthmatic patients.

Methods

In situ PCR, immunocytochemistry, Southern blot, morphometry, mice sensitization

Additional information

References

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