別紙 1

学位論文審査結果の要旨

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（学位論文審査結果の要旨）

Eosinophils promote epithelial to mesenchymal transition of bronchial epithelial cells.

【主論文審査結果の要旨】

著者らは本論文において下記の内容を述べている。

Eosinophilic inflammation and remodelling of the airways including subepithelial fibrosis and myofibroblast hyperplasia are characteristic pathological findings of bronchial asthma. Epithelial to mesenchymal transition (EMT) plays a critical role in airway remodelling. In this study, we hypothesized that infiltrating eosinophils promote airway remodelling in bronchial asthma. To demonstrate this hypothesis we evaluated the effect of eosinophils on EMT by in vitro and in vivo studies. EMT was assessed in mice that received intra-tracheal instillation of mouse bone marrow derived eosinophils and in human bronchial epithelial cells co-cultured with eosinophils freshly purified from healthy individuals or with eosinophilic leukemia cell lines. Intra-tracheal instillation of eosinophils was associated with enhanced bronchial inflammation and fibrosis and increased lung concentration of growth factors. Mice instilled with eosinophils pre-treated with transforming growth factor(TGF)-β1 siRNA had decreased bronchial wall fibrosis compared to controls. EMT was induced in bronchial epithelial cells co-cultured with human eosinophils and it was associated with increased expression of TGF-β1 and Smad3 phosphorylation in the bronchial epithelial cells. Treatment with anti-TGF-β1 antibody blocked EMT in bronchial epithelial cells. Eosinophils induced EMT in bronchial epithelial cells, suggesting their contribution to the pathogenesis of airway remodelling.