Microfibrillar-associated protein 4 modulates airway smooth muscle cell phenotype in experimental asthma.

Abstract:
Recently, several proteins of the extracellular matrix have been characterised as active contributors to allergic airway disease. Microfibrillar-associated protein 4 (MFAP4) is an extracellular matrix protein abundant in the lung, whose biological functions remain poorly understood. In the current study we investigated the role of MFAP4 in experimental allergic asthma. MFAP4-deficient mice were subjected to alum/ovalbumin and house dust mite induced models of allergic airway disease. In addition, human healthy and asthmatic primary bronchial smooth muscle cell cultures were used to evaluate MFAP4-dependent airway smooth muscle responses. MFAP4 deficiency attenuated classical hallmarks of asthma, such as eosinophilic inflammation, eotaxin production, airway remodelling and hyperresponsiveness. In wild-type mice, serum MFAP4 was increased after disease development and correlated with local eotaxin levels. MFAP4 was expressed in human bronchial smooth muscle cells and its expression was upregulated in asthmatic cells. Regarding the underlying mechanism, we showed that MFAP4 interacted with integrin \( \alpha_\nu \beta_5 \) and promoted asthmatic bronchial smooth muscle cell...
proliferation and CCL11 release dependent on phosphatidylinositol-3-kinase but not extracellular signal-regulated kinase pathway. MFAP4 promoted the development of asthmatic airway disease in vivo and pro-asthmatic functions of bronchial smooth muscle cells in vitro. Collectively, our results identify MFAP4 as a novel contributor to experimental asthma, acting through modulation of airway smooth muscle cells.

Zeitschriftenzitation / Abkürzung:
Thorax

Jahr:
2015

Band:
70

Heft / Issue:
9

Seiten:
862-72

Sprache:
eng

Pubmed:

Print-ISSN:
0040-6376

TUM Einrichtung:
Institut für Molekulare Allergologie und Umweltforschung

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Molekulare Allergologie > Molekulare Allergologie (Prof. Schmidt-Weber) > 2015

entries: