

THE ROLE OF TRANSFORMING GROWTH FACTOR- β 1 IN AIRWAY INFLAMMATION OF CHILDHOOD ASTHMA

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TGF- β -targeting structural and inflammatory cells has been implicated in the mechanisms leading to the inflammatory and restructuring processes in asthma, suggesting an impact of TGF- β 1 signaling on the development and persistency of this disease. We investigated the potential early involvement of TGF- β 1 activity in the immunological and molecular mechanisms underlying progression of inflammation in childhood asthma. We evaluated the levels of TGF- β 1 in induced sputum supernatants (ISSs) and the expression of small mother cell against decapentaplegic (Smad) 2 and Smad7 proteins in induced sputum cells (ISCs) from children with intermittent asthma (IA), moderate asthma (MA) and control subjects (C). Furthermore, we investigated the regulatory role of TGF- β 1 activity on eosinophil and neutrophil adhesion to epithelial cells using adhesion assay, and on the granulocyte expression of adhesion molecule CD11b/CD18 Macrophage-1 antigen (MAC-1), by flow cytometry. We found that the levels of TGF- β 1 are increased in ISSs of IA and MA in comparison to C, concomitantly to the activation of intracellular signaling TGF β /Smads pathway in ISCs. In MA, TGF- β 1 levels correlated with the number of sputum eosinophils and neutrophils. Furthermore, we showed the ability of sputum TGF- β 1 to promote eosinophil and neutrophil adhesion to epithelial cells, and to increase the expression of MAC-1 on the granulocyte surface. This study shows the activation of TGF β /Smad signaling pathway in the airways of children with IA and, despite the regular ICS treatment, in children with MA, and provides evidence for the contribution of TGF- β 1 in the regulation of granulocyte activation and trafficking.

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