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Title: The serotoninergic receptor subtype 5-HTR1B contributes to the pathogenesis of allergic airway inflammation

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Body: In addition to its well described role in the nervous and cardiovascular system 5-hydroxytryptamine (5-HT, serotonin), has also potent immuno-regulatory properties. Furthermore, elevated levels of free serotonin have been detected in the serum of symptomatic asthmatics. However, the exact serotoninergic receptor subtypes involved have not been elucidated, yet. In this study we questioned whether the subtype 5-HTR1B is involved in the pathogenesis of experimental asthma. Expression of 5-HTR1B receptors in lung tissue was analyzed by immunohistochemistry. Allergic airway inflammation was studied in the classical OVA-alum model and in a model of house dust mite (HDM) induced airway inflammation. The experimental induction of allergic airway inflammation led to an increased 5-HTR1B expression in the lungs of animals sensitized to OVA and challenged with OVA-aerosols. 5-HTR1B expression was even higher in animals with chronic asthma. To confirm the in-vivo relevance of this finding, animals sensitized to OVA were treated intratracheally with the selective 5-HTR1B antagonist NAS 181 prior to challenge with OVA aerosols resulting in decreased allergic airway inflammation as depicted by reduced broncho alveolar lavage eosinophils and lymphocytes, by reduced perivascular and peribronchial inflammation, as well as by reduced production of Th2 cytokines by re-stimulated mediastinal lymph node cells. The intratracheal application of NAS 181 had also protective effects in HDM-induced asthma. Here we provide evidence that 5-HTR1B receptors modulates asthmatic airway inflammation. Therefore, 5-HTR1B receptors might be promising targets for the development of new anti-asthmatic drugs.