# Phenotype and severity of asthma determines bronchial epithelial immune responses to a TLR3 agonist

Celeste Porsbjerg[1], Juan Nieto-Fontarigo[2], Samuel Cerps[2], Sangeetha Ramu[2], Mandy Menzel[1], Morten Hvidtfeldt[1], Silberbrandt A[1], Froessing L[1], Ditte Klein[1], Asger Sverrild[1], and Lena Uller[2]

[1]Bispebjerg Hospital
[2]Skanes universitetssjukhus Lund

April 05, 2024

## Abstract

**Background** Asthma is characterized by an aggravated immune response to respiratory viral infections: This phenomenon is a clinically well-recognized driver of acute exacerbations, but how different phenotypes of asthma respond immunologically to virus is unclear. **Objectives** To describe the association between different phenotypes and severity of asthma and bronchial epithelial immune responses to viral stimulation. **Methods** In the Immunoreact study, healthy subjects (n=10) and 50 patients with asthma were included; 30 (60%) were atopic, and 34 (68%) were eosinophilic; 15 (25%) had severe asthma. All participants underwent bronchoscopy with collection of bronchial brushings. Bronchial epithelial cells (BECs) were expanded and stimulated with the viral replication mimic poly (I:C) (TLR3 agonist) *in vitro*. The expression of TLR3-induced pro-inflammatory and anti-viral responses of BECs were analyzed using RT-qPCR and multiplex ELISA and compared across asthma phenotypes and severity of disease. **Results** Patients with atopic asthma had increased production of IL-4, IFN-β, IL-6, TNF-α, and IL-1β after poly (I:C) stimulation compared to non-atopic patients, whereas patients with eosinophilic asthma and non-eosinophilic asthma did not differ in the response to poly (I:C). Patients with severe asthma displayed a decreased antiviral IFN-β, and increased expression of IL-8, most pronounced in atopic and eosinophilic asthmatics. Interestingly, release of IL-33 and TSLP in response to poly (I:C) was increased in severe eosinophilic asthma, but not in severe atopic asthma. **Conclusions** The bronchial epithelial immune response to a viral mimic stimulation differs between asthma phenotypes and severities, which may be important to consider when targeting novel asthma treatments.

## Hosted file

`Manuscript_Immunoreactivity relates to asthma phenotype and severity.docx` available at https://authorea.com/users/514446/articles/711533-phenotype-and-severity-of-asthma-determines-bronchial-epithelial-immune-responses-to-a-tlr3-agonist