EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
M. WECKMANN ET AL.

# COL4A3 is degraded in allergic asthma and degradation predicts response to anti-IgE therapy

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**A novel, serological biomarker predicts the anti-IgE therapy response in asthmatics. The neo-epitope biomarker C4Ma3 measures the increase of lung collagen 4 degradation in severe exacerbating type 2 asthma and depends on mast cell chymase activity.** https://bit.ly/3ejFp7i

**Cite this article as:** Weckmann M, Bahmer T, Sand JM, *et al*. COL4A3 is degraded in allergic asthma and degradation predicts response to anti-IgE therapy. *Eur Respir J* 2021; 58: 2003969 [DOI: 10.1183/13993003.03969-2020].



## Abstract

***Background*** Asthma is a heterogeneous syndrome substantiating the urgent requirement for endotype-specific biomarkers. Dysbalance of fibrosis and fibrolysis in asthmatic lung tissue leads to reduced levels of the inflammation-protective collagen 4 (COL4A3).

***Objective*** To delineate the degradation of COL4A3 in allergic airway inflammation and evaluate the resultant product as a biomarker for anti-IgE therapy response.

***Methods*** The serological COL4A3 degradation marker C4Ma3 (Nordic Bioscience, Denmark) and serum cytokines were measured in the ALLIANCE cohort (paediatric cases/controls: n=134/n=35; adult cases/

Received: 20 April 2020
Accepted: 28 April 2021

controls: n=149/n=31). Exacerbation of allergic airway disease in mice was induced by sensitising to ovalbumin (OVA), challenge with OVA aerosol and instillation of poly(cytidylic-inosinic). Fulacimstat (chymase inhibitor; Bayer) was used to determine the role of mast cell chymase in COL4A3 degradation. Patients with cystic fibrosis (n=14) and cystic fibrosis with allergic bronchopulmonary aspergillosis (ABPA; n=9) as well as patients with severe allergic uncontrolled asthma (n=19) were tested for COL4A3 degradation. Omalizumab (anti-IgE) treatment was assessed using the Asthma Control Test.

***Results*** Serum levels of C4Ma3 were increased in asthma in adults and children alike and linked to a more severe, exacerbating allergic asthma phenotype. In an experimental asthma mouse model, C4Ma3 was dependent on mast cell chymase. Serum C4Ma3 was significantly elevated in cystic fibrosis plus ABPA and at baseline predicted the success of the anti-IgE therapy in allergic, uncontrolled asthmatics (diagnostic OR 31.5).

***Conclusion*** C4Ma3 levels depend on lung mast cell chymase and are increased in a severe, exacerbating allergic asthma phenotype. C4Ma3 may serve as a novel biomarker to predict anti-IgE therapy response.