IgE/IgG1 antibody responses to ubiquitin are associated with emergency room attendance due to asthma symptoms

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Background: We had previously identified an IgE-binding low molecular weight component in the house dust mite *Blomia tropicalis*, identified by Edman degradation as ubiquitin. After cloning its sequence from a cDNA library, we found the protein as 100 % identical to the human orthologous.

Objective: Since autoimmune responses has been linked to asthma severity, we aimed to characterize the immunological response to ubiquitin in asthmatic patients and its relationship with symptoms severity.

Methods: The recombinant molecule was produced in *Escherichia coli* and further purified by affinity chromatography and anion exchange FPLC. Specific IgE, IgG1 and IgG4 levels were detected by ELISA in 244 asthmatic patients and 80 healthy controls. Severity of asthma symptoms were assessed by a physician. Lung function was measured by spirometry. Association between clinical indicators of disease severity and antibody responses to ubiquitin was analyzed by multivariate logistic regression. Lymphocyte proliferation assay was performed using CFSE-dilution assay (n = 3).

Results: Frequency of IgE, IgG1, IgG4 to ubiquitin in asthmatic patients were 15.5 %, 16.8 % and 36.1 %, respectively, and in controls 6.25 %, 23.8 % and 26.3 %. Specific-IgE correlated moderately with IgG1 (Spearman-rho = 0.4, p < 0.001) and lightly with IgG4 (Spearman-rho = 0.24, p < 0.001 ) in asthmatic patients, but not in controls (Spearman-rho = 0.056, −0.101; p = 0.62, p = 0.37). A positive IgE or IgG1 test to ubiquitin was associated with emergency room attendance (aOR = 2.28, 95 % CI = 1.14-4.61, p = 0.021) adjusted by age, gender and socioeconomical class. No associations were found with severe dyspnea, hospitalization or lung function outcomes. In the two patients with the highest IgG1 or IgE levels, T cell proliferation (CD4+ or CD8+) was not detected in ubiquitin-stimulated cultures; however, a dose-dependent positive result was observed for B cells. No proliferation was detected in the healthy control.

Conclusions: This work suggests the association of autoantibody response to ubiquitin with an indicator of asthma severity.

Keywords: Asthma; Ubiquitin; Emergency room attendance