Plasma proteome changes linked to late phase response after inhaled allergen challenge in asthmatics

Maria Weitoft[1], Måns Kadefors[1], Henning Stenberg[2], Ellen Tufvesson[2], Zuzana Diamant[2], Sara Rolandsson Enes[1], Leif Bjermer[2], Oskar Rosmark[1], and Gunilla Westergren-Thorsson[1]

[1]Department of Experimental Medical Science Division of Lung Biology Lund University Lund Sweden
[2]Lunds Universitet Lungmedicin och Allergologi

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Abstract

Background. A subset of individuals with allergic asthma develops a late phase response (LPR) to inhaled allergens, which is characterized by a prolonged airway obstruction, airway inflammation and airway hyperresponsiveness. The aim of this study was to identify changes in the plasma proteome and circulating hematopoietic progenitor cells associated with the LPR following an inhaled allergen challenge. **Methods.** Serial plasma samples from asthmatics undergoing inhaled allergen challenge were analyzed by mass spectrometry and immunosorbent assays. Peripheral blood mononuclear cells were analyzed by flow cytometry. Mass spectrometry data was analyzed using a linear regression to model the relationship between airway obstruction during the LPR and plasma proteome changes. Data from immunosorbent assays was analyzed using linear mixed models. **Results.** Out of 396 proteins quantified in plasma, 150 showed a statistically significant change 23 h post allergen challenge. Among the most upregulated were three protease inhibitors: alpha-1-antitrypsin, alpha-1-antichymotrypsin and plasma serine protease inhibitor. Altered levels of 13 proteins were associated with the LPR, including increased factor XIII A and a decreased von Willebrand factor. No relationship was found between the LPR and changes in the proportions of classical, intermediate, and non-classical monocytes. **Conclusions.** Allergic reactions to inhaled allergens in asthmatic subjects was associated with changes in a large proportion of the measured plasma proteome, whereof protease inhibitors showed the largest changes, likely to influence the inflammatory response. Many of the proteins altered in relation to the LPR are associated with coagulation, highlighting potential mechanistic targets for future treatments of type-2 asthma.

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