A cockroach derived serine protease allergen activates airway epithelial cells via PAR2 receptors

Sagar L Kale\textsuperscript{1,2}, Naveen Arora\textsuperscript{1}

\textsuperscript{1}Allergy and Immunology Section, CSIR-Institute of Genomics and Integrative Biology, Delhi University Campus, Mall road, Delhi- 110007, India.
\textsuperscript{2}Department of Biotechnology, University of Pune, Ganeshkhind, Pune-411007, India

Correspondence: Naveen Arora
E-mail: naveen@igib.res.in and navdelhi@hotmail.com
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Both endogenous and exogenous proteases have been implicated in allergic airway diseases. Though recent studies have demonstrated the role of airway epithelial cells in pathophysiology of allergic diseases, the mechanisms of epithelial activation remain largely unknown. Recently published study (Kale and Arora, 2014) focused on elucidating the role of proteolytic activity of Per a 10 on airway epithelial activation and to gain an insight into possible mechanism. We found that airway epithelial activation by Per a 10 is dependent on its serine protease activity. Further we showed that this activation is PAR2 dependent and leads to Ca\textsuperscript{2+} mobilisation. This Research Highlight discusses the findings of our recent study and active research endeavors.


Prevalence of allergic diseases is increasing drastically all over the world with 30–40 \% of the population suffering from one or the other allergic disease \cite{1}. Allergic responses occur as a result of a complex interplay between allergens and immune system. In the past few decades, several allergens from different sources like fungi, pollens, house dust mite, cockroaches etc. have been identified, isolated, purified and characterized. The properties or characteristics that allow allergens to elicit allergic response are not well understood in susceptible individuals. Evidence suggests that intrinsic biochemical activity of allergens plays a role in sensitization. Certain potent allergens from cockroaches, HDM, fungi and pollens have been shown to possess proteolytic activity \cite{2-4}. Protease allergens enhance IgE responses and play a part in allergen presentation. Cockroach extracts are rich in proteases \cite{5} and are an important source of aeroallergens.

Per a 10, a serine protease allergen was isolated from \textit{Periplaneta americana}, characterized and shown to be a major allergen \cite{4}. Per a 10 induces allergic airway inflammation in mice and provides an adjuvant effect towards self and other allergens in the same microenvironment \cite{6}. Moreover, by virtue of its serine protease activity, Per a 10 modulates dendritic cells by increased CD86 expression, higher IL-6 and lower IL-12 secretion, towards Th2 polarisation. Inactive Per a 10 did not upregulate CD86 expression on DCs but significantly induced IL-12 secretion \cite{7}. Immunotherapy with inactive Per a 10 in Per a 10 or cockroach extract sensitized mice was more effective than with active Per a 10 \cite{8}. These studies indicate a potential role for proteolytic activity of Per a 10 in allergenicity.

Airway epithelial cells are the first line of defense that separates the inhaled environment from the immune cells \cite{9}. Airway epithelium senses the changes in its environment through expression of various receptors. There is a mounting evidence suggesting a possible role of epithelial dysfunction
in pathogenesis of allergic diseases like asthma, rhinitis and dermatitis. In our recent research titled “Per a 10 activates human derived epithelial cell line in a protease dependent manner via PAR-2” we exposed airway epithelial cell line A549 with Per a 10 (active and inactive) in order to investigate the role of its proteolytic activity on airway epithelial cells [10]. Active Per a 10 lead to the secretion of proinflammatory cytokines from A549 cells in a dose and time dependent manner. Furthermore, inhibiting protease activity of Per a 10 by heat treatment or using a proteolytically inactive recombinant Per a 10 [11] failed to activate airway epithelial cells. To ascertain the role of protease activated receptors on secretion of proinflammatory cytokines, the epithelial cells were incubated with receptor cleavage blocking antibodies. SAM-11 a PAR-2 blocking antibody and not ATAP-2 (PAR-1 blocking antibody) significantly reduced proinflammatory cytokine expression. Per a 10 also cleaved a PAR-2 receptor derived peptide to unmask the PAR-2 ligand. Our results are in accordance with previous studies where proteases from house dust mite, have shown to induce proinflammatory cytokine secretion from airway epithelial cells [12]. Cells treated with Per a 10 showed Ca2+ mobilization. In conclusion, Per a 10 activates airway epithelial cells via PAR-2 receptors. Proteolytic activity of Per a 10 contributes to its allergenicity and proteolytically inactive recombinant Per a 10 has a potential for immunotherapy.

Conflict of interest

The author(s) declare that they have no conflicting interests.

References