Allergen cleavage by effector cell-derived proteases regulates allergic inflammation.

Abstract:

The key event of allergic inflammation, allergen-induced crosslinking of mast cell-bound IgE antibodies, is accompanied by release of inflammatory mediators, cytokines, and proteases, in particular beta-tryptase. We provide evidence that protease-mediated cleavage of allergens represents a mechanism that regulates allergen-induced mast cell activation. When used in molar ratios as they occur in vivo, purified beta-tryptase cleaved major grass and birch pollen allergens, resulting in defined peptide fragments as mapped by mass spectrometry. Tryptase-cleaved allergens showed reduced IgE reactivity and allergenic activity. The biological relevance is demonstrated by the fact that lysates from activated human mast cells containing tryptase levels as they occur in vivo cleaved allergens. Additionally, protamine, an inhibitor of heparin-dependent effector cell proteases, augmented allergen-induced release of mediators from effector cells. Protease-mediated allergen cleavage may represent an important mechanism for terminating allergen-induced effector cell activation.