Mast cell-derived proteases control allergic inflammation through cleavage of IgE.

BACKGROUND: Cross-linking of mast cell-bound IgE releases proinflammatory mediators, cytokines, and proteolytic enzymes and is a key event in allergic inflammation.

OBJECTIVE: We sought to study the effect of proteases released on effector cell activation on receptor-bound IgE and their possible role in the regulation of allergic inflammation. METHODS: Using molar ratios of purified recombinant tryptase and human IgE, we studied whether tryptase can cleave IgE. Similar experiments were performed with mast cell lysates in the presence or absence of protease inhibitors. IgE cleavage products were detected in supernatants of allergen cross-linked, cultivated mast cells and in tissue fluids collected from patients' skin after IgE-mediated degranulation. The effects of protamine, an inhibitor of heparin-dependent proteases on IgE-mediated allergic in vivo skin inflammation in human subjects were studied. RESULTS: We show that beta-tryptase, a major protease released during mast cell activation, cleaves IgE. IgE degradation products were detected in tryptase-containing tissue fluids collected from sites of allergic inflammation. The biologic significance of this mechanism is demonstrated by in vivo experiments showing that protease inhibition enhances allergic skin inflammation.
CONCLUSION: We suggest that IgE cleavage by effector cell proteases is a natural mechanism for controlling allergic inflammation.