Editorial
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Highly Cytokinergic IgE Antibodies and Autoimmune Mechanisms

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Immediate type hypersensitivity reactions can occur after allergen exposure followed by allergen-specific IgE-FcεRI interactions on mast cells/basophils in sensitized subjects.[1] In comparison, chronic allergic inflammation induced by Th1 responses can occur without exposure to environmental allergens; instead, an IgE-mediated response to autoallergens can activate Th1 cells, causing them to release pro-inflammatory cytokines.[2,3] Kitaura et al.[4] demonstrated that mast cells with sensitized IgE antibodies on their surface can display a wide spectrum of heterogeneity in their ability to induce cytokine production and secretion. The spectrum of IgE antibodies has two extremes: highly cytokinergic IgE antibodies that induce potent survival promotion, degranulation, cytokine production, and migration, and poorly cytokinergic IgE antibodies that release minimal amounts of cytokines.[4]

An article published in this issue demonstrated that human IgE antibodies as well as mouse IgE antibodies show heterogeneity.[5] This is clinically relevant for two reasons. First, human IgE antibodies showed heterogeneity in cytokine production and second, highly cytokinergic IgE antibodies showed polyreactivity to autoantigens. This concept was tested in serum from atopic dermatitis patients, since some of these patients have high levels of ssDNA- (or dsDNA-) or β-galactosidase-reactive IgE antibodies with high levels of histamine releasing factor-reactive IgE antibodies. Most atopic dermatitis patients had very high total IgE levels in their serum, and polyclonal IgE antibodies detected in serum from these patients enhanced the survival of and cytokine production by mast cells.[6] These findings suggest that an autoimmune mechanism is a part of chronic inflammation in a subset of atopic dermatitis patients, although they did not screen serum specific IgE to potential auto-antigens related with skin inflammation. Further studies investigating the mechanisms how polycytokinergic IgE antibodies reacting various kinds of autoantigens can activate other inflammatory cells and mast cells in various phenotypes of atopic dermatitis are essential. Furthermore, the IgE antibodies exhibited polyreactivity to the autoantigens tested in this study.[5] Some autoantigens are multivalent, and potentially capable of activating highly cytokinergic IgE antibodies bound to the surface of mast cells and basophils. An autoimmune component might be a part of the pathogenesis of chronic skin allergic inflammation. High serum specific IgE to Staphylococcal superantigens were noted in atopic dermatitis[7] and chronic urticaria.[8] This hypothesis might be extended to Staphylococcal superantigens, which play a role in the activation of mast cells in patients with atopic dermatitis and chronic urticaria.

Several studies have suggested that autoimmune mechanisms play an important part in the development and progression of chronic allergic inflammation in subsets of asthma,[9,10] chronic urticaria,[11] and atopic dermatitis patients.[12] Moreover, the chronic urticaria patients with high specific IgE to thyroid peroxidase showed a favorable response to anti-IgE therapy.[13] In addition, various autoantigens were suggested. Several environmental allergens sharing structural similarities with human proteins can be autoantigens.[14-16] Some tissue antigens were thought to be derived from thyroid proteins and epithelial cells interacting with environmental factors.[9,10,17] This study[5] also confirmed the presence of human IgE antibodies reacting to thyroglobulin, which is closely associated with the autoimmunity of chronic urticaria.[11] In addition, these IgE antibodies reacted with histamine releasing factor and induced mast cell degranulation. Additional studies are essential to understand the exact mechanisms by which these IgE antibodies activate skin mast cells, as this will be useful for classifying various phenotypes of chronic urticaria and atopic dermatitis, and developing new therapeutic strategies based on the heterogeneity of these phenotypes.

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