Non-IgE aspects of allergic diseases and contributing roles of IgE in autoimmunity

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The important role of immunoglobulin E (IgE) in allergic disorders is well recognized and accepted. On the other hand, the implication of non-IgE components, molecules and mediators in allergic diseases has received relatively less attention despite their role in determining allergy pathogenesis and modulating disease severity and an increasing number of studies now explore the role of these "missing components" as a promising new research avenue to better understand allergy problems.

Several articles in this issue illustrate the crucial role of non-IgE factors in various aspects of allergic diseases ranging from molecular study, animal model, to clinical research. A study from China demonstrated that an increased amount of peripheral blood smooth muscle progenitor cells in a murine model of asthma may be involved in the development of airway remodeling.[1] IL-35 has been identified as a novel immunosuppressive/anti-inflammatory cytokine. Chen Chen, et al. observed decreased levels of plasma IL-35 in patients with asthma and COPD suggesting that IL-35 may have a role in regulating airway inflammatory response.[2] Nitric oxide is released in the airways by nitric oxide synthase from several cell types and fractional exhaled nitric oxide (FeNO) has been introduced as a marker of airway inflammation. The increased FeNO seems to correlate with poor asthma control status according to a study from Siriraj Hospital, Thailand.[3] A 5-year cohort study from Khon Kaen University researchers confirmed an association between lower respiratory infections in early life and subsequent wheezing and asthma as the majority of children who suffered from virus-or atypical bacterial pathogens-induced bronchiolitis in this study, developed recurrent wheezing, although only 16% of them still had wheezing episodes after 5 years.[4] Whether these infections enhance the risk of developing IgE sensitization to aeroallergens or are merely an evidence of impaired immune response to virus is to be determined.[5] Apart from B-cells and T-helper cells, groups of cells once thought to be only associated with innate immunity of mucosal system and autoimmune diseases such as gamma/delta-T-cells and Th17 cells, may in fact be involved in allergic diseases as well. A study from Sun Yat-sen University, China, reported higher percentages of peripheral blood gamma/delta-T-cells and Th17 cells in allergic rhinitis patients compared to the control group suggesting that these cells may contribute to the pathogenesis of allergic rhinitis.[6] Serum levels of thymus and activation-regulated chemokine (TARC), a member of the CC chemokines, was found to be a useful marker of allergic diseases. A Japanese research group reported that serum TARC levels are significantly correlated with peripheral blood eosinophilia and useful for monitoring disease activity and therapeutic response in patients with atopic dermatitis.[7] Together, these findings illustrate the diversity of ways molecular and cellular components other than IgE and mast cells, can contribute to pathogenesis and the modulation of the severity of allergic disorders.

While non-IgE components play a role in allergic diseases, IgE components are known to be involved in non-allergic diseases. For instance, increased total serum IgE levels were observed in patients with systemic lupus erythematosus, even after adjusting for concurrent atopic diseases and there is an evidence that IgE might have a pathogenic role in bullous pemphigoid.[8,9] Recent data revealed that some patients with a history of an immediate reaction to contrast media, previously believed to be non-IgE mediated, can be identified by positive intradermal test and basophil activation test.[10] As the physiological significance of IgE, besides combating parasitic infestations, remains debated and that the allergy patho-mechanism is not as straightforward as it seems, thinking beyond the conventional immunology dogma may be required to demystify

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complex allergic diseases and elucidate the mechanisms underlying them.

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