Solving the Mystery of IgE

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Immunoglobulin E (IgE) is the main actor in the drama of allergy. The biological role of IgE in the immune response of an organism and the lack of control leading to allergy is the research topic of Gernot Achatz, Molekular Biology, University of Salzburg. At the 2nd European Congress of Immunology ECI 2009 held in Berlin the scientist presents new data revealing the evolution of IgE.

Allergic diseases have risen dramatically during the last decades. They represent a major health problem, which affects up to one third of the whole population. A prerequisite for the development of effective therapeutic strategies is the detailed analysis of the biological role of IgE and its control mechanisms.

IgE is an evolutionary conserved member of the immunoglobulin (Ig) family. Immunoglobulins are antibodies, which play a key function in immune response. Compared to all other immunoglobulin classes, which are present in concentrations of micrograms to milligrams per ml serum, the titre of IgE is very low (nano- to micrograms per ml range) in plasma of normal healthy individuals and of normal laboratory mouse strains. IgE is most prominent in epitheliae and mucosae where it is bound to specific receptors on highly potent effector cells like eosinophilic granulocytes and mast cells. Bound to these cells IgE has a long half-life (weeks to months), while free in plasma the half-life is very short (~ 6 hours). “This suggests that IgE plays a role in local immune defence mechanisms”, says Achatz.

However, the core function for IgE is still unknown. From an

evolutionary point of view, IgE is conserved and can be found in all mammalia. It therefore originated at least 160 million years ago, possibly even more than 300 million years ago, from a gene duplication of IgY, in which the anaphylactic and opsonic activities of IgY were separated, giving rise to IgE and IgG, respectively. IgG now represented the opsonic activities, which are needed to label antigens with antibodies and complement factors to enable scavenger cells to recognizes and destroy the enemy. IgE was responsible for anaphylactic activities, which represent another way of immune defense, which may involve the whole body. Apparently, in an evolutionary sense, anaphylactic defence mechanisms are needed, but at a potentially high price to the organism. “The division of anaphylactic and opsonic activities in separate genes allowed principally a tighter and more specific control of both immune mechanisms”, stresses Achatz.

In these days IgE is best known for its strong, unwanted effector functions, in the form of allergic reactions. These can range from annoying, local symptoms, like hay fever, to life-threatening, systemic reactions like anaphylactic shock. This underlines the potential hazard of high systemic IgE titres. Remarkably, over the last four decades the incidence of allergic disease has risen. This represents an intriguing problem from a medical, epidemiological, immunological, genetic and evolutionary view. Unfortunately, it is also a major socio-economic problem. Achatz’ interpretation of these data is that control mechanisms, that were adequate in the past and honed in evolution, are failing. In the recent past he and others have described several B cell specific control mechanisms that indicate a tight control of the IgE response. The understanding of these mechanisms, combined with the analysis of the biological function of the IgE molecule during an immune response are the prerequisite for the establishment of new systemic IgE targeted therapeutic strategies in the future.

Source: German Society for Immunology