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# The role of the IgE repertoire in allergic disease

**Background**
The discovery and characterisation of the IgE antibody back in the late 60's arguably represent one of the most crucial advancements in our understanding of the immunological basis of allergic disease. Thus, although present in minute amounts in the blood, this class of antibodies is effectively responsible for mediating allergen exposure into immunocellular responses, i.e. enhanced T-cell activation through facilitated antigen presentation (FAP) and degranulation of effector cells (see figure), affecting both immediate and late phase allergic symptoms but also amplifies and maintains an already ongoing allergic inflammatory response.

Despite its low blood concentration, the IgE repertoire is generally fairly complex in composition and an essential aspect of the evolving IgE response is the accumulating evidence that both class-switch recombination and somatic hypermutation followed by clonal expansion and IgE production occur in local airway mucosa under the influence of the inflamed tissue. Hence, each allergic individual possesses his/her own unique IgE repertoire which can be dissected into distinct properties such as clonality, concentration and affinity: The *clonality* covers the sensitisation pattern and includes the number of allergen sources (house dust mite, grass pollens, cat, etc.), the number of individual allergens from each source (Der p 1, Der p 2, Der p 3 etc.), the number of isoallergens of each particular allergen (Der p 1.0101, Der p 1.0102, Der p 1.0103 etc.) and even the number of epitopes on each single allergenic molecule to which IgE antibodies have developed and are able to differentiate between. The *concentration* of each individual IgE antibody is unlikely the same for all IgE clones and hence, the ratio between individual allergen specific IgE (as well as non-allergen specific IgE) may span over a considerably dynamic concentration range. The final aspect is the binding strength or the *affinity* of each IgE antibody for a particular allergen.

**Application of recombinant IgE antibodies**
The importance of IgE repertoire diversity for cellular mechanisms of allergy has been investigated by a number of laboratories over the years by the use of polyclonal human sera. However, the contribution of individual serum IgEs to the overall complexity of a polyclonal serum is challenging, if not impossible, to determine due to the inability to isolate individual IgE antibodies from allergic patients' sera.

In order to directly assess and identify the governing factors of basophil degranulation and FAP mediated T-cell activation, we recently developed a panel of highly characterised and well defined recombinant IgE antibodies. By use of these recombinant antibodies, we were able to design cellular experiments with control of absolute IgE concentration as well as ratio between each single IgE antibody, their epitope specificity and even their affinity for the allergen.

**Summary and conclusion**

In summary, the IgE repertoire is complex and varies greatly among allergic individuals. To dissect and investigate how distinct properties of the IgE repertoire affect central mechanisms of allergic disease, i.e. effector cell degranulation and enhanced T-cell activation through facilitated allergen presentation, we have made a panel of highly well characterised recombinant IgE antibodies. We identified the following factors as being of great importance:

- The concentration of allergen specific IgE antibodies
- The ratio between allergen specific IgE antibodies
- The ratio between allergen specific and non-binding IgE antibodies (only effector cells)
- The clonality of allergen specific IgE antibodies
- The affinity of individual allergen specific IgE antibodies and evidence that low affinity IgE antibodies may play a role in allergic reactions

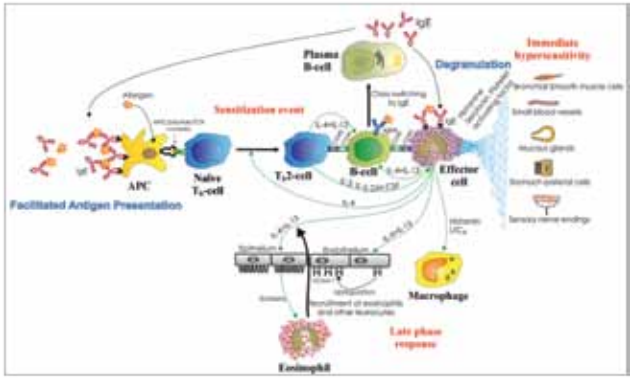


Figure illustrating central roles of IgE antibodies in effector cell degranulation and enhanced T-cell activation through facilitated antigen presentation

In conclusion, these results tremendously expand our knowledge about central mechanisms of allergy and may eventually contribute to the improvement of future diagnostic tests based on individual IgE repertoire compositions.

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