

Breakfast Symposium 27: Sister Society Session - Danish Society of Allergology: Basophil Activation as a Measure of Allergic Response

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Type I allergy pathogenesis is tightly linked to pro-inflammatory processes that are triggered or sustained by complex-formation between allergen-specific IgE-antibodies, allergens, and cell-surface bound IgE-receptors, e.g. FcεRI for mast cell- and basophil-activation, and CD23 for facilitated antigen-uptake and -presentation (FAP). The influence of allergen-specific IgE-repertoire complexity on complex formation between IgE, allergen and Fcε receptors has previously been established. However, a detailed description of the contribution of eg IgE repertoire clonality and the affinities, concentrations and relative ratios of individual IgE antibodies in complex human sera have been difficult, primarily due to technical limitations. In order to directly identify the governing factors of basophil degranulation and FAP-mediated T-cell activation we developed a panel of recombinant human or humanized Derp-2 specific IgE antibodies with defined affinities which were combined to yield a number of synthetic human allergic patient's serum analogues (1, 2). Basophil activation/degranulation assays performed with human basophils passively sensitized with various combinations of reIgEs revealed how differently factors such as the overall IgE concentration, the relative ratio between individual allergen-specific IgEs, the clonality of the IgE repertoire, and the affinities of individual IgEs affect basophil degranulation (Figure 1). Similarly, we examined the effect of IgE clonality and individual IgE affinities on CD23-mediated complex formation on the surface of CD23+ B-cells, and monitored the subsequent antigen presentation and T-cell activation (3, Figure 2). Most naturally occurring allergens exist in several different variants (isoallergens) which may be recognized differently by individual IgE antibodies due to distinct variations in the primary amino acid sequences. By combining the different recombinant IgEs mentioned above with a number of different naturally occurring Der p 2 isoforms expressed as defined recombinant proteins in *E.coli* for basophil degranulation assays we could demonstrate that individual IgE antibodies in some instances recognize individual allergen isoforms with different affinities (4). However, when using polyclonal sera from house dust mite

sensitized individuals in the basophil degranulation assays the differences between individual Der p 2 isoforms was lost.

In conclusion, by using defined recombinant allergen-specific IgEs in combination with individual allergen isoforms we have been able to demonstrate how the different parameters of IgE repertoire complexity influence important cellular processes such as effector cell activation/degranulation and FAP-mediated T-cell activation. We have furthermore demonstrated that the extent of the functional IgE repertoire complexity depends on the complexity of isoform variations of the natural allergens.

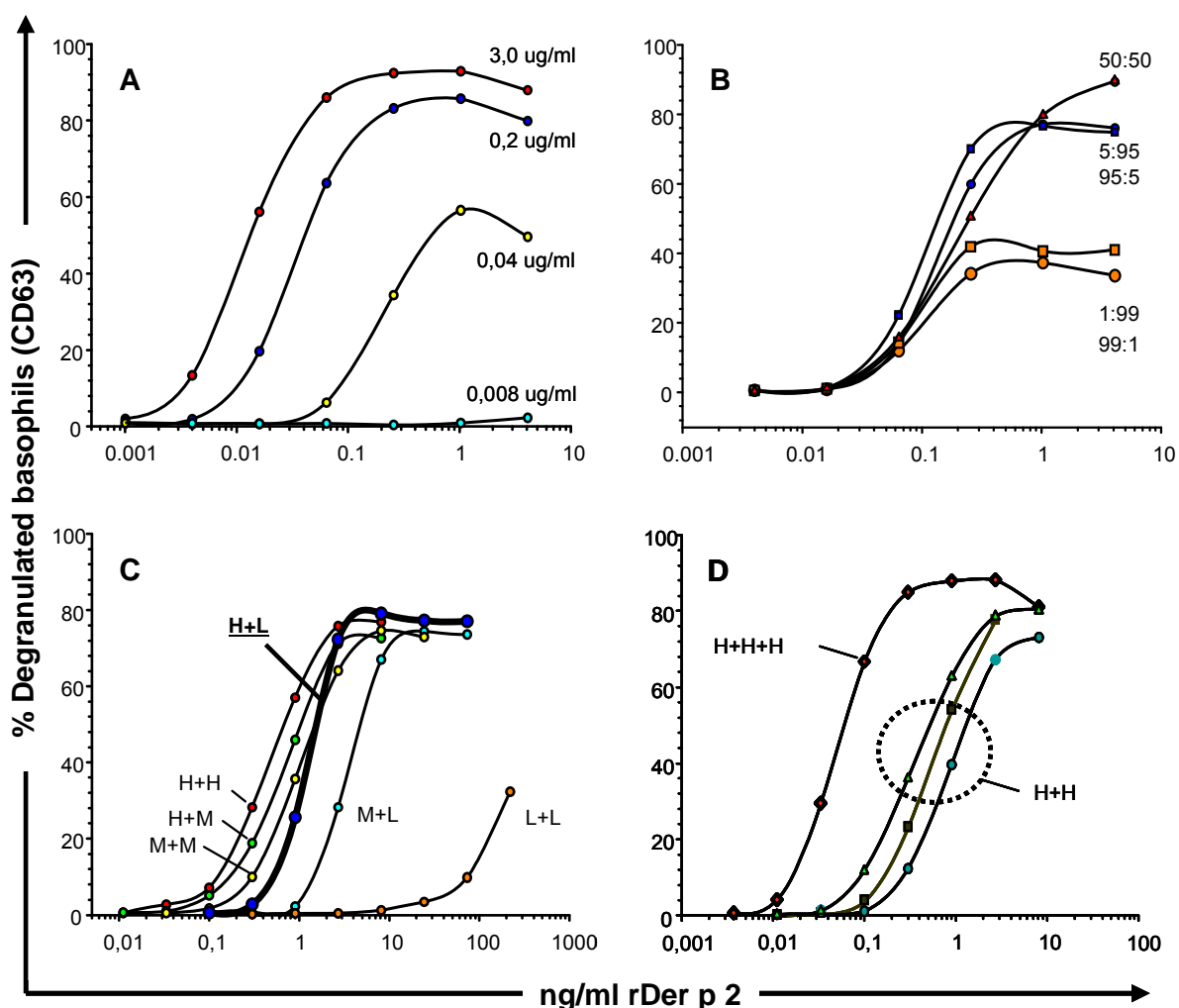


Figure 1 – Effects of IgE repertoire complexity on basophil activation. A) effect of allergen-specific IgE concentration B) Effect of different relative ratios of individual IgEs C) effect of individual IgE affinities (D) effect of IgE clonality. H= high affinity, M=medium affinity, L=low affinity recombinant IgEs. Figure adapted from (2).

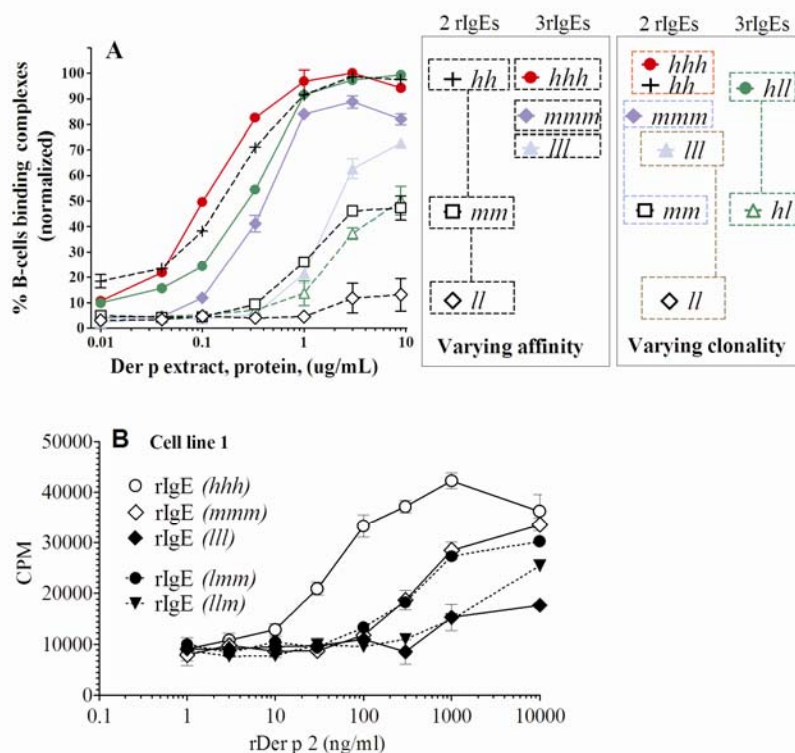


Figure 2 – Effects of IgE repertoire clonality and individual IgE antibody affinities on A) complex formation between IgE, allergen and CD23 on the surface of CD23+ B-cells, and B) subsequent T-cell activation. Figure adapted from (3)

References

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