Aalberse, R. C., Crameri, R. (2011). IgE-binding epitopes: a reappraisal. *Allergy,* 66: 1261-1274

Here, we discuss various questions related to IgE epitopes: What are the technical possibilities and pitfalls, what is currently known, how can we put this information into hypothetical frameworks and the unavoidable question: how useful is this information for patient care or allergenicity prediction? We discuss the information obtained by (i) 3D structures of allergen–antibody complexes; (ii) analysis of allergen analogues; (iii) mimics without obvious structural similarity; (iv) mAbs competing with IgE; (v) repertoire analysis of cloned IgEs, and other developments. Based on limited data, four suggestions are presented in the literature: (i) IgE might be more cross-reactive than IgG; (ii) IgE might be more often directed to immunologically 'uninviting' surfaces; (iii) IgE epitopes may tend to cluster and (iv) IgE paratopes might have a higher intrinsic flexibility. While these are not proven facts, they still can generate hypotheses for future research. The hypothesis is put forward that the IgE repertoire of switched B-cells is less influenced by positive selection, because positive selection might not be able to rescue IgE-switched B cells. While this might be of interest for the discussion about mechanisms leading to allergen-sensitization, we need to be modest in answering the 'clinical relevance' question. Current evidence indicates the IgE-epitope repertoire is too big to make specific IgE epitopes a realistic target for diagnosis, treatment or allergenicity prediction. In-depth analysis of a few selected IgE epitope-peptides or mimitopes derived from allergen-sequences and from random peptide libraries, respectively, might well prove rewarding in relation to diagnosis and prognosis of allergy, particularly food allergy.