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Although immediate-Type I skin reactions to human dander have been described six decades ago, only the recent application of molecular biology to allergology research allowed fast and detailed characterization of IgE-binding autoantigens. These can be functionally subdivided into three classes: (1) self-antigens with sequence homology to environmental allergens belonging to the class of phylogenetically conserved proteins, (2) self-antigens without sequence homology to known environmental allergens, and (3) chemically modified self-antigens deriving from workplace exposure. As environmental allergens, also IgE-binding autoantigens belong to different protein families without common structural features that would explain their IgE-binding capability. Many of the self-antigens showing sequence homology to environmental allergens, are phylogenetically conserved proteins like manganese dependent superoxide dismutase, thioredoxin or cyclopilin. Their IgE-binding capability can be explained by molecular mimicry resulting from shared B-cell epitopes. A common factor of IgE-binding self-antigens without sequence homology to known environmental allergens is that they elicit IgE responses only in individuals suffering from long-lasting atopic diseases. In contrast, IgE-mediated reactions to modified self-antigens might be explained with the generation of novel B-cell epitopes. Chemically modified self-antigens are likely to be recognized as non-self by the immune system. The clinical relevance of IgE responses to self-antigens remains largely unclear. Well documented is their ability to induce immediate Type I skin reactions *in vivo*, and to induce mediator release from effector cells of sensitized individuals *in vitro*. Based on these observations it is reasonable to assume that IgE-mediated cross-linking of FcRIε receptors on effector cells can elicit the same symptoms as those induced by environmental allergens, and this could explain exacerbations of chronic allergic diseases in the absence of external exposure. However, because most of the described IgE-binding self-antigens are intracellular proteins normally not accessible for antigen–antibody interactions, local release of the antigens is required to explain the induction of symptoms.