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Structure and Epitopes of Chi t 1.01

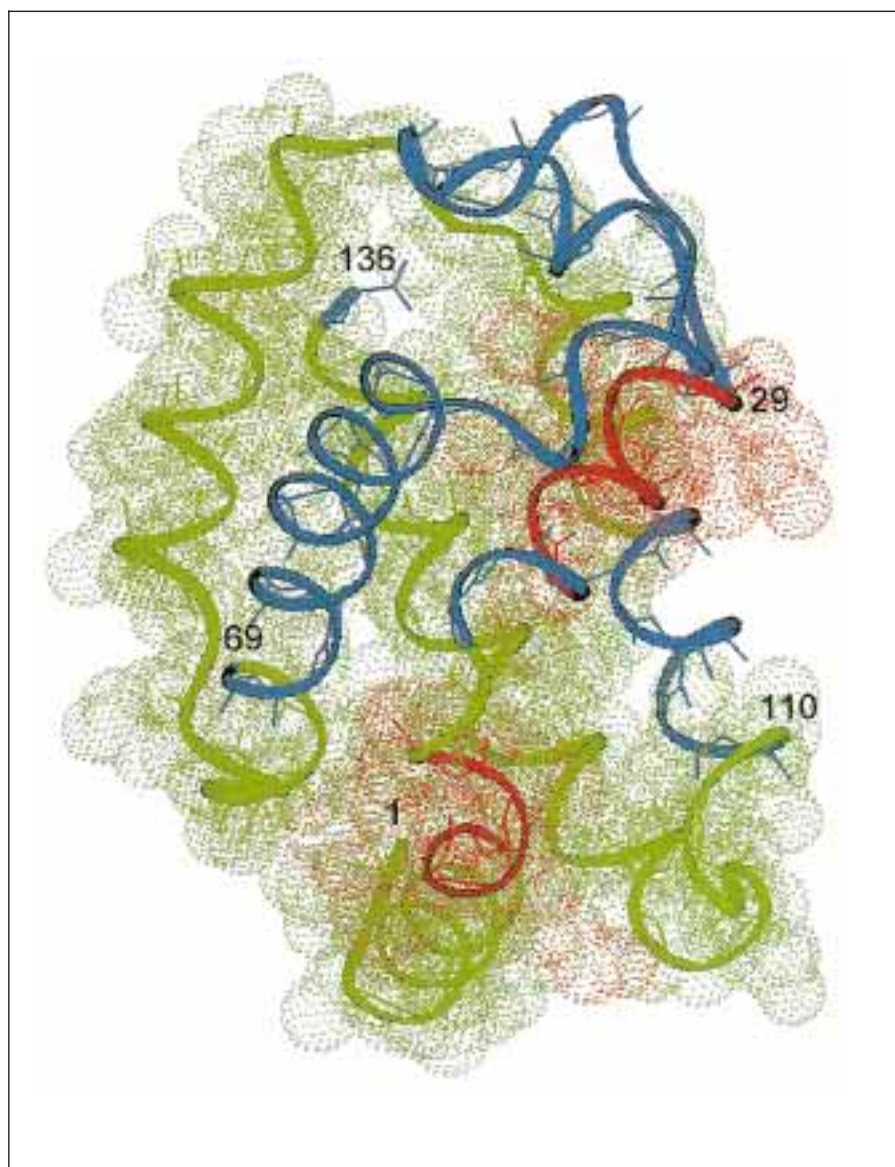


Fig. 1. Computer model (ribbon) of Chi t 1.01 according to X-ray data [6]. The 136 amino acids form eight α -helices. The carbon backbone is schematically represented in ribbon structure. Sequences 1–19, 69–101 and 110–135 including T cell as well as B cell (IgE) epitopes are shown in green with van der Waals dot representation (computer program Insight II). Regions 13–17 and 23–29 recognized by a monoclonal antibody are indicated in red.

One possibility to perform immunotherapy of allergic diseases is the design of peptides which bind to the T cell and do not cross-link IgE molecules. The characterization of B and T cell epitopes is therefore of great importance. A general relationship between antigenicity at the B cell level and various parameters like hydrophilicity, flexibility, surface accessibility and structural motifs is assumed. In contrast to this, structural motifs for T cell recognition are thought to be less important since T cells recognize the allergen after fragmentation into peptides. Various algorithms of epitope prediction exist but they are mostly not better than random. However, the N terminus of the insect allergen Chi t 1.01 (hemoglobin component of *Chironomus thummi* [1]) was predicted to contain B and T cell epitopes [2, 3]. These predictions could be confirmed experimentally. Using a proliferation assay with synthetic peptides and peripheral blood lymphocytes of 14 patients sensitized to the allergen it could be shown that T cell epitopes exist along the whole sequence [3]. However, differences in the percentage of responding patients and the intensity of reactions were found. The N- and the C-terminal sequences of Chi t 1.01 (1–19 and 110–135) as well as the central part of the molecule, i.e. residues 69–100 containing the hem-binding region, were immunodominant with regard to T cell epitopes.

B cell epitope mapping revealed antibody binding sites for monoclonal antibodies at residues 13–17 and 23–29 [4] and for human IgE at residues 1–17, 91–101 and 110–135 [5]. Therefore, B and T cell epitopes are mainly located in the same regions for Chi t 1.01 covering several sites of the molecules (fig. 1). The determination of B and T cell epitopes has been performed with peptides of Chi t 1.01. This raised the question of whether allergen fragments are similar in structure to the respective sequences in the whole molecule.

The structure of the whole molecule was identified by X ray in 1979 [6] as eight α -helical regions (fig. 1). Recent NMR studies of synthetic peptides [7] revealed that conformational preferences in peptides with a length of 20 amino acids still exist. The most stable α -helix was found in the N terminus (1–19) which contains B and T cell epitopes as mentioned before. NMR measurements showed that the peptides used for epitope mapping in vitro correspond to the native antigen in terms of their structural features.

With regard to T cell recognition, the expression of T cell receptors must also be considered. In response to *Chironomus* allergen, a significant increase in V β 8 was determined [8]. Further analysis will show whether structural elements of the allergen molecules are important for the identification of the T cell receptor increase.

References

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