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Introduction

X-ray structure analysis of food allergens

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1. Introduction

The following research articles by Huntington and Stein, Sharma et al. and Rouvinen et al. summarize structural features of food allergens as ovalbumin, α-lactalbumin, β-lactoglobumin, casein and lipocalins. These articles demonstrate how complicated the problem is, due to the limited number of allergen structures available today, to decode the main unifying structural features and to specify the structure–function relationships in view of allergy. The structural mystery of allergy has dogged medical sciences since Pharaoh Menes of Egypt died of a wasp sting in 2641 B.C. Allergies are caused by the immune reaction in response to a molecule, which is not usually found in the body. The physiological as well as structural mechanism of allergy is deeply complex and the individual steps of molecular recognition are only very primarily understood [1,2]. The basic understanding of allergies has taken a long time and only now the modern molecular biology enables us to postulate cellular and molecular mechanism providing an elementary knowledge of allergic diseases [3]. Presently allergens leading to sensitization and production of IgE antibodies in susceptible individuals are grouped according to their source and the order in which they were discovered and are termed as major allergens if at least 50% of sensitized patients react to them. During the last few years the primary structures of about 300 different allergens have been evaluated (for reference see Rouvinen et al. [1]). However, only for a few allergens the three-dimensional structure has been analyzed by NMR techniques and X-ray crystallography.

Up to now the three-dimensional structures of about 12 different specific allergenic proteins have been published. Two structures were assigned by model building studies, two other by NMR spectroscopy, seven were solved by X-ray crystallography and one was determined by NMR investigations and X-ray crystallography [4–16]. According to their classification, they all belong to different structural families such as globular β-sheet-, α/β-structures and four-helix-bundle proteins [17]. Unfortunately, none of these three-dimensional structures can explain the allergenic activity of the proteins. However, some intriguing evidences are coming up which might help to understand the mechanism of allergy on a three-dimensional structural basis. The allergen structures reported so far have approximately the same size and show up as compact spherical and relative flat molecules [1]. More pleasantly puzzling is the fact that the struc-

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tures display some level of internal symmetry and are even reported as homo-dimeric structures [17]. The potential functional symmetry might indicate that allergens are accessible to other molecules, such as antibodies and IgE molecules, from altered directions in a most effective way. Whether this structural property can be directly correlated to allergenicity remains to be further clarified by analyses of more allergens to high resolution.

It is also necessary to have in mind that particular allergens are associated with different types of allergic illnesses and these differences should be correlated with the physical properties and surface characteristics of these molecules. Further on, in spite of investigating biochemically the complicated, predominantly on molecular recognition based, allergic track of the individual components of the immune system, we have to consider the principle pathways of the allergens before triggering the allergic reaction by binding to IgE molecules on mast cells. Proteins, known as allergens, can enter the human body by inhalation, with food, or by injection as may occur with an insect sting. Inhaled allergens, as pollen and grains, turned out to be very stable in the presence of nasal secretion, as shown for the functional fragment of the major grass pollen allergen Phl p5. This effect verifies the observation that the muscosa does not contain proteases which are able to destruct the allergen completely. On the other hand this category of allergens can be very effectively hydrolyzed by gastric secretions [18]. This means also that it is certainly more difficult to trace and to characterize food allergens or the final functional domain responsible for allergic response, considering the gastric secretion and diversified digestive environment the allergen will be initially in contact. Our present knowledge on the mechanism of allergic reactions makes difficult to answer the question how food or respiratory allergens induce the respective diseases. However, it is known that food allergies can be very severe and can lead, for example, to anaphylaxis. Anaphylaxis occurs because some allergens, as found for example in peanuts and shellfish, act very specific and cause the mast cells to open very rapidly which is known to cause an over-response leading to complete closure of the air passage [19]. Subsequently, we can expect also that food allergens are stable as the structural integrity is an overall important and functional prerequisite for binding IgE and the induction of the allergic response.

Taking into account the overall complex molecular situation, described very briefly before, all authors postulate the urgent need to assess more allergen structures at high resolution to understand the molecular basis for allergenicity in combination with the structural information on IgE binding as well as epitopes from B- and T-cells. This knowledge will be mandatory for the design of hypoallergenic and specific derivatives of allergenic proteins or protein domains without IgE-binding capacity which can be applied for specific immunotherapy of allergic diseases.

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