

Allergy to Mammalian Proteins: At the Borderline between Foreign and Self?

S. Spitzauer

Clinical Institute for Medical and Chemical Laboratory Diagnostics, Vienna General Hospital, University of Vienna, Austria

Key Words

Animal allergy · IgE · Cross-reactivity · Recombinant allergens · Autoallergy

Abstract

Atopic individuals are characterized by their genetically determined tendency to mount IgE antibody responses against otherwise harmless antigens. Many of the environmental allergens (e. g., plant-, insect-, mould-derived allergens) are recognized as foreign intruders by the immune system. However, a substantial proportion of atopic individuals mount IgE responses to allergens of mammalian origin and, as recently reported, certain of them even react with human proteins (i. e., autoallergens). Through the application of molecular biological techniques for allergen characterization, the molecular nature and biological function of an increasing number of mammalian allergens have been revealed. This review provides a summary of well characterized mammalian allergens derived from hair/dander, saliva, serum and urine of animals (cat, dog, rodents, cow, horse) as well as of some recently characterized autoallergens. In addition, mammalian allergens were grouped in protein families with similar sequences and/or biological functions. The importance of cross-reactivities is exemplified for albumins which represent abundant mammalian serum proteins and highly cross-reactive allergens. Finally, possible advantages of using recombinant animal allergens for novel forms of component-resolved diagnosis and treatment of allergies to mammalian proteins are described.

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Introduction

Hypersensitivity to allergens of mammalian origin has long been recognized. Allergic disease is common to pet owners, laboratory animal workers and farmers. Inhalation and skin contact with animal-derived allergens elicit a great variety of symptoms ranging from allergic conjunctivitis, allergic rhinitis, allergic asthma bronchiale, urticaria to atopic eczema in sensitized individuals [1].

IgE antibodies to animal-derived proteins can be found in about 2 % of the general population [2] and in up to 40% of atopic individuals [3, 4]. Therefore, animals are important sources of inhalant allergens at home, in public places and in working environments. Cats and dogs, the most popular pets, with one third to one half of households having mammalian pets [4] are the most common cause of animal allergy [5] followed by rodents, which frequently elicit allergic reactions in laboratory animal workers [6, 7]. Occupational allergy to cow- or horse-derived allergens affects mainly individuals who are in direct contact with these animals and is an important cause of allergic sensitization in farmers [8, 9]. It has recently been reported that almost 50% of the patients suffering from atopic dermatitis bear IgE antibodies to human proteins of different histogenetic origin [10]. The following chapters describe sources for mammalian allergens and provide a summary of those mammalian allergens of which the specific IgE-binding capacity of which has been demonstrated and on which sequence information is available.

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Correspondence to: Dr. Susanne Spitzauer
Clinical Institute of Medicine and Chemical Laboratories Diagnostics, AKH
Währingergürtel 18–20
A–1090 Wien (Austria)
Fax +43 1 40400 5389

Table 1. Allergens of mammalian origin

Species/Allergen	MW, kD	Sources	Function	Reference
Cat				
Fel d 1	35–39	hd, sa	lipocalin?	30
Albumin	65–69	hd, sa, se	serum protein	35
Dog				
Can d 1	19–25	hd, sa	lipocalin	50
Can d 2	25–27	hd, sa	lipocalin	50
Albumin	65–69	hd, sa, se	serum protein	54
Mouse				
Mus m 1	18	u	lipocalin (prealbumin)	55
Albumin	65–69	se, u	serum protein	135
Rat				
Rat 1A	21	u	lipocalin (prealbumin)	72
Rat 1B	17	u	lipocalin (α_{2u} -globulin)	81
Albumin	65–69	hd, se, u	serum protein	135
Cow				
Bos d 2	18–20	hd, sk	lipocalin	93
BDA11	11	sk	calcium-binding protein	98
Albumin	65–69	hd, se	serum protein	135
Horse				
Equ c 1	20	hd, sg	lipocalin	108
Equ c 2	18	hd	lipocalin	9
Albumin	65–69	hd, se	serum protein	135
Man				
Hom s 1	55	nts	tumor specific antigen?	121
Hom s 2	22	nts	transcriptional coactivator/ chaperonin	120
Hom s 3	81	nts	oncogene	120
Hom s 4	>40	nts	calcium-binding protein	120
Hom s 5	40	nts	cytokeratin	120
Profilin	14	nts	cytoskeletal protein	114
Manganese superoxide dismutase	27	nts	enzyme	116
Ribosomal P-2 protein	11	nts	P-2 protein	117

hd = Hair/dander; sa = saliva; se = serum; u = urine; sk = skin; sg = salivary gland; nts = no tissue specificity.

Allergen Sources, Allergens

Although much work has been done on the biochemical and immunological characterization of allergen extracts prepared from pelt, hair, dander, saliva, serum, urine and feces of different animal sources, such extracts are difficult to standardize [1]. Current extracts prepared from mammalian allergen sources exhibit markedly different contents of major and minor allergens. Therefore several laboratories have started to isolate cDNAs coding for mammalian allergens and to produce recombinant allergens for diagnosis and therapy. The molecular characterization of animal allergens has led to the elucidation of their molecular nature. Table 1 shows an overview of well characterized allergens of mammalian origin.

Cat Allergens

Sensitivity to cat allergens among subjects with asthma ranges from 9 to 41% [4]. Extracts prepared from cat hair and dander, skin, saliva, serum and urine contain allergens [11–24].

More than 80% of the patients allergic to cats display IgE reactivity to the major cat allergen Fel d 1 [13, 17, 20]. Fel d 1 is present in hair, skin and salivary glands of cats [18, 19, 21, 25, 26]. Fel d 1 is a heterodimer with a molecular weight (MW) of 35–39 kD [27–29]. It consists of two chains with an MW of 17–18 kD, as determined by SDS-PAGE [27–29]. Cloning and sequence analysis of Fel d 1 revealed that the mRNAs coding for these two chains are the products of separate genes which are expressed in the salivary glands and the skin of cats [30, 31]. The two

recombinant chains of Fel d 1 have been expressed in *Escherichia coli* and purified [32] and the IgE reactivity of the recombinant protein has been demonstrated [33].

Other cat allergens that have been identified so far are cat immunoglobulins [20, 22] and cat albumin [22, 34]. These allergens are present in cat serum [22] as well as in epithelial extracts [16]. The sequence of cat albumin which represents a cross-reactive allergen for approximately 30% of patients allergic to animals has been determined [35].

Dog Allergens

Up to 40% of asthmatic individuals are sensitized to dog allergens [3].

Extracts prepared from dog hair, dander, saliva, serum and urine contain several allergens [22, 24, 36–49].

The major dog allergens Can d 1 and Can d 2 have been characterized [38, 41, 42, 48, 49]. About 80% of the patients display IgE reactivity to these two allergens with MWs ranging from 19 to 27 kD [38, 41, 42, 48, 49]. Can d 1 and Can d 2 are present in hair, dander and saliva [38, 41–43, 48, 49]. No significant amounts of these allergens were found in dog urine or feces [48]. Sequence analysis of Can d 1 and Can d 2 revealed that these allergens belong to the lipocalin protein family [50]. Both recombinant proteins have been expressed as IgE-reactive proteins in *E. coli* and purified. Their IgE allergenic activity was demonstrated by the histamine release test [50].

Other dog allergens that have been identified so far include dog immunoglobulin [22, 36–38] and dog albumin [22, 36–38, 45, 51], of which the latter represents an important cross-reactive allergen [22, 47]. These allergens are present in dog serum as well as in epithelial extracts [22, 36–38, 42, 45, 51–53]. The sequence of dog albumin has been determined and the recombinant protein was expressed as IgE-reactive protein in *E. coli* [54].

Rodent Allergens

Mice, rats, guinea pigs and rabbits are used worldwide as laboratory animals and, in addition, guinea pigs and rabbits enjoy widespread popularity as pets [6, 7, 55–57]. Laboratory animal allergy (LAA) is an important occupational health problem affecting 10–30% of animal workers [6, 7, 58–64].

The major allergens of mouse, Mus m 1, with a MW of 18 kD and Mus m 2 with an MW of 21 kD, have been described by several investigators [55, 65, 66]. Mus m 1 constitutes more than 90% of mouse urine protein and was identified as urinary prealbumin by Price et al. [55] in 1987. Prealbumin is a member of the lipocalin protein family [67, 68] and the influence of testosterone on urinary protein se-

cretion has been demonstrated [69]. Mus m 2 was detected in dust from mouse facilities and is present in hair follicles [55, 66]. Besides the two major allergens, mouse albumin has been identified as a relevant allergen [70, 71].

The major allergens of rat, Rat 1A, a prealbumin with an MW of 22 kD, and Rat 1B, an α_{2u} -globulin of 17 kD are both present in rat urine, hair/dander and saliva [72–77]. It has been demonstrated that rat α_{2u} -globulin is expressed in sebaceous [78] and salivary [79] glands. Both proteins were purified by liquid chromatography [80, 81] and characterized by amino acid sequence analysis and mass spectrometric determinations. Both proteins belong to the lipocalin protein family [68, 82, 83]. Besides the two major rat allergens, rat serum albumin has been described as an important cross-reactive allergen by several investigators [58, 70, 84–86], and rat transferrin and immunoglobulin were identified as rat allergens by Gordon et al. [85].

Several allergens were described in guinea pig hair/dander, saliva, serum and urine [56, 70, 87]. By means of crossed radio-immunoelectrophoresis, two major allergens and albumin have been identified [56, 70, 87] but no sequence data are available.

The allergenic activity of rabbit hair/dander, saliva and urine has been investigated by Price and Longbottom [88]. The authors describe a major allergen with an MW of 17 kD, which, in contrast to other rodent major allergens, is present in hair/dander and saliva but can hardly be found in rabbit urine or serum. The most abundant allergenic component in dander and serum was albumin and it was found that particular patients with high RAST values reacted with rabbit albumin [57, 70].

Cow Allergens

Allergy to cow dander is limited to farmers and veterinarians [8] and may thus be regarded as an occupational disease. Three major allergens with MWs of 24, 22 and 20 kD, present in extracts from cow hair/dander have been identified by biochemical techniques [89, 90]. Since 1994, cow dander allergens have been extensively characterized by immunological and molecular biological techniques [91, 92]. cDNA cloning, sequence analysis and expression of recombinant allergens led to the identification of several cow dander allergens. The sequence of the major cow allergen Bos d 2 revealed homology with the lipocalin protein family [93]. The recombinant allergen was expressed in yeast and crystallized [94]. The determination of the three-dimensional structure by x-ray diffraction confirmed the lipocalin structure of Bos d 2, demonstrating the existence of a cavity inside the protein core suitable for ligand binding [95]. By use of PCR techniques and immunohistochemical stain-

ing, the tissue distribution of Bos d 2 was determined. Bos d 2 was detected in the secretory cells of apocrine sweat glands and the basement membranes of the epithelium and hair follicles [96]. In addition, two minor allergens of cow dander were identified by screening a cDNA bovine skin library [97, 98]. One of these minor allergens displayed high sequence homology to the bovine oligomycin sensitivity-conferring protein of the mitochondrial adenosine triphosphatase synthase complex. These proteins play an important role in the energy metabolism of the mammalian cell [97]. The other minor allergen, designated BDA11 [98] represents bovine psoriasin, which displays a sequence homology of 63% with human psoriasin, a calcium-binding protein [99] expressed in human keratinocytes [100].

Bovine serum albumin has been identified as a minor allergen in cow dander and serum but may be important as cross-reactive allergen [101].

Horse Allergens

Several allergens have been described in extracts prepared from horse dander, hair, skin scrapings and serum [102–106]. Three major allergens with MWs of 19, 31 and 51 kD have been described [107]. The major horse allergen Equ c 1, a 20-kD protein, was isolated and purified by Dandeu et al. [108]. The gene encoding the major horse allergen was cloned from a cDNA of horse salivary glands. Amino acid sequence analysis of Equ c 1 indicated that this allergen is a glycoprotein member of the lipocalin protein family. Equ c 1 exhibits 50% sequence homology with urinary proteins from mice and rats and is expressed in liver and salivary glands [109]. Recombinant Equ c 1 was expressed in *E. coli* and crystallized [110]. Two horse dander allergens, termed Equ c 2.0101 and Equ c 2.0102, have recently been identified by Bulone et al. [9]. The sequence analysis of these two allergens revealed that they are also members of the lipocalin protein family.

Horse serum albumin was identified as an allergen present in horse serum and dander by several investigators [102, 105].

Autoallergens

It was before the discovery of IgE antibodies that several investigators reported that extracts prepared from human dander can elicit immediate type skin reactions in certain patients suffering from severe and chronic forms of atopy (e. g., atopic dermatitis) [111, 112]. The classical book on *The Chemistry of Atopic Allergens* published by Berrens [113] in 1971 contains a section on ‘The Human Dandruff Allergen’ within its chapter on ‘Allergens from Epithelial Tissue’, which summarizes experimental support for the ex-

istence of autoallergens. Since then, the concept of autoallergy fell into oblivion until the molecular characterization of environmental allergens, in the early 90s, revealed striking similarities between exogenous allergens and human proteins [114]. Using serum IgE from a patient allergic to birch pollen, a cDNA coding for birch pollen profilin, a highly conserved component of the eukaryotic cytoskeleton, was isolated. The finding of immunological and structural similarities between birch and human profilin gave rise to the idea that IgE autoreactivity based on the cross-reactivity between environmental and human proteins might be a pathogenetic factor in severe forms of atopy [114, 115]. It was later demonstrated that *Aspergillus fumigatus* allergens cross-reacted with human proteins and that the human counterparts induced T cell proliferation and skin reactions in patients sensitized to the mould [116, 117]. Several other environmental allergens with similarities to human proteins were reported. They included dog as well as cat albumin [47], calcium-binding allergens from plants and fish [118] and cytochrome plant allergens [118]. The finding that some patients suffering from atopic dermatitis displayed IgE reactivity to a great variety of nitrocellulose-blotted human cellular proteins [10] led to attempts at isolating cDNAs coding for autoallergens by IgE immunoscreening of human expression cDNA libraries [120, 121]. When serum IgE from atopic dermatitis patients was used to screen a cDNA library prepared from human epithelial cells, several cDNAs coding for autoallergens could be isolated [120, 121]. It was suggested to name the autoallergens according to the International Allergen Nomenclature. The cloned autoallergens comprise: (1) Hom s 1, a protein which has also been described as an epithelial antigen recognized by cytotoxic T cells of a patient suffering from squamous esophageal cancer [121]; (2) Hom s 2, the α -chain of the human nascent polypeptide-associated complex (α -NAC) [120]; (3) Hom s 3, BCL7B, a putative oncogene [120]; Hom s 4, a protein containing a typical calcium-binding motif [120] and (5) Hom s 5, human cytokeratin II [120].

IgE-Cross-Reactivities with Animal Allergens: The Nature of Cross-Reactive Animal Allergens

Several publications report that certain atopic individuals show co-/ cross-sensitization to several mammalian allergen sources [14, 22, 122, 123]. Hollander et al. [123] demonstrated that pet allergy represents a risk factor for the development of occupational allergy in laboratory animal workers. They found that persons who either had a positive

skin prick test to pets, elevated total IgE levels or a history of symptoms upon contact with pets, had an elevated risk to develop allergy to rats and mice.

Therefore, studies were carried out to investigate the presence of cross-reactive antigens/allergens in dog and cat extracts in order to explain the clinical observation that dog allergy is frequently associated with cat allergy [14, 22, 40, 53]. Brandt et al. [124] described the presence of IgE antibodies to cat allergens present in 70% of dog allergic patients. The IgE response of fur farmers and fur garment workers to dander and urine extracts prepared from mink, blue fox, silver fox, racoon dog and fitchew was investigated by Savolainen et al. [125]. The allergens defined by immunoblotting were very similar to those present in dog dander extracts. IgE reactivities to allergens with MWs of 18–19, 23–25 and 62–67 kD were observed. RAST inhibition experiments indicated the presence of common allergens in extracts from all five species investigated. In addition, the authors observed IgE binding to fur extracts from these species using sera from patients allergic to cats and dogs in RAST and immunoblotting experiments, suggesting that these species share common allergens with cats and dogs. In a study performed by Wüthrich et al. [52] in 1985 cross-reactive components were described in dog and cat allergen extracts and it was shown that cat hair/dander inhibited antibody binding to dog hair/dander and vice versa. By means of RAST inhibition experiments, Viander et al. [126] were able to demonstrate cross-reactivity between cat hair/dander and dog hair/dander extracts, whereas IgE reactivity to cat and dog saliva and urine extracts were shown to be more species specific.

Sequence analysis of animal allergens identified related allergens from various species that can be grouped into protein families according to their biological function.

Albumins represent the most conserved family of cross-reactive mammalian allergens [22, 40, 47, 53]. Other serum proteins (e.g. immunoglobulins, transferrins) may represent cross-reactive allergens too, but are recognized at low frequency. The major allergens from dog, mouse, rat, cow and horse seem to be members of the lipocalin protein family but there is controversy whether they represent cross-reactive allergens. It is also not clear whether the major cat allergen Fel d 1 belongs to the lipocalin protein family [68, 127].

Albumins

Albumins represent the major component (about 40 mg/ml) in the circulatory system of mammals. They are nonglycosylated transport proteins with MWs ranging from 65 to 69 kD. The sequences and three dimensional struc-

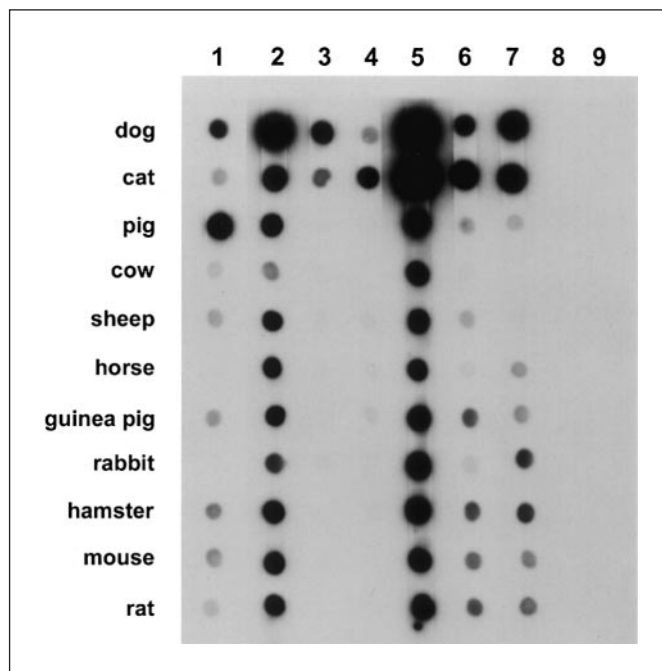
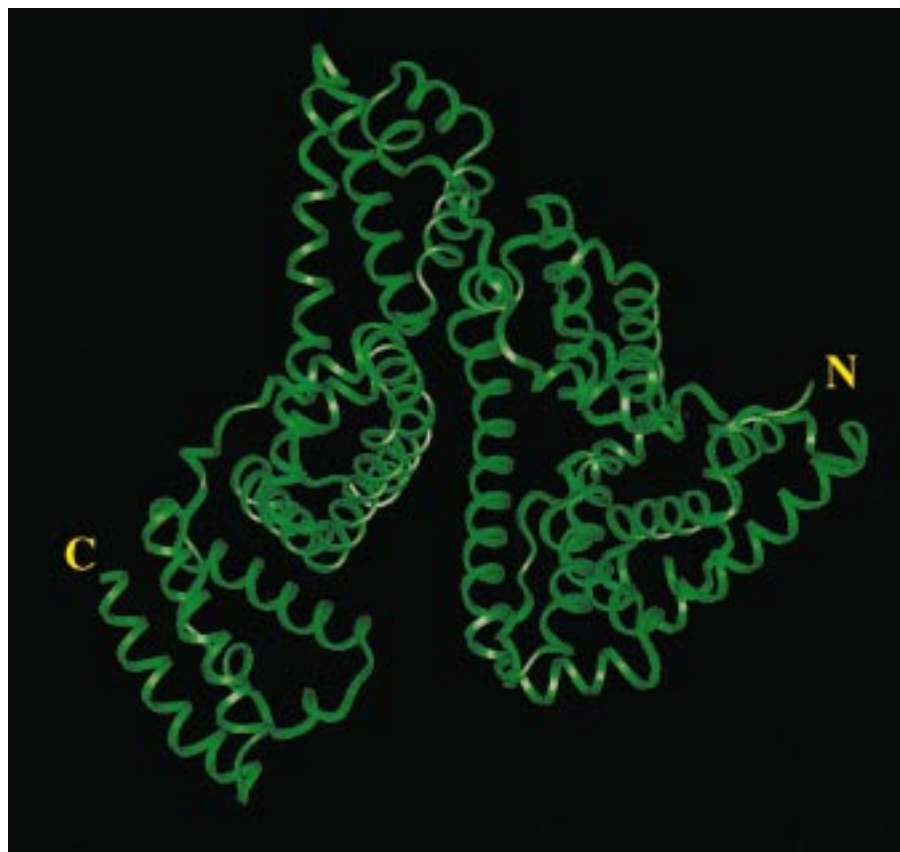


Fig. 1. IgE reactivity of albumin-allergic patients (1–7), of a non-atopic individual (8) and buffer without addition of serum (9) to dot-blotted albumins from different species (dog, cat, pig, cow, sheep, horse, guinea pig, rabbit, hamster, mouse, rat).

tures of albumins are highly conserved throughout evolution [128]. Structural analyses of albumins demonstrate that these proteins have a high alpha-helical content and a large number of disulfide bonds, the latter being a feature which is thought to contribute to the stability of plasma proteins in the circulation [129–131]. The albumin molecule is organized into three domains consisting of three loops each [130, 132]. Figure 1 shows a model of the three-dimensional structure of dog albumin, which due to the high sequence similarity between dog and human albumin, could be modelled according to the three-dimensional structure of human albumin [131].

Boutin et al. [40] performed RAST inhibition experiments and immunoblot studies to investigate IgE cross-reactivities with dander extracts from cat and dog. They observed different IgE binding patterns to cat allergens in patients allergic to cat only (strong reactivity to a 18-kD protein) and patients with allergy to cats and dogs (strong reactivity to a 69-kD protein accompanied by a weak binding to the 18-kD protein) and identified albumins from cat and dog as cross-reactive components present in epithelial allergen extracts. In 1989 they demonstrated the existence of common epitopes on cat and dog albumin using mouse monoclonal antibodies [133]. By RAST inhibition experi-

Fig. 2. Ribbon representation of the structure of dog albumin as modelled by homology from the structure of the human protein. The two proteins share 79.4% identity and 88% similarity without gaps or insertions. The N and C termini of the protein are indicated.



ments, it was further demonstrated that certain monoclonal antibodies were able to inhibit binding of human IgE to cat and dog extracts [133]. Goubran Boutros et al. used three short peptides, containing loops 1 and 2 of the first domain (peptide 1), loop 4 of the second domain (peptide 2), loop 9 of the third domain (peptide 3) to investigate the cross-antigenicity of horse serum albumin with albumins from dog and cat [134]. They were able to demonstrate that all three peptides contained epitopes shared by horse, cat and dog albumin [134]. The allergenic activity of rat serum albumin was studied using two proteolytic fragments of rat albumin in histamine release tests with basophils from patients allergic to rat albumin. Wahn et al. [86] demonstrated the existence of at least two epitopes on each of the fragments. However, a loss of allergenic activity of the proteolytic fragments compared to the activity of the whole protein was observed. These authors suggested that this loss was due to cleavage of rat albumin in the middle of the protein where they expected a third epitope domain. In addition, it was shown that basophils from all patients reactive to rat albumin responded to mouse albumin and 2 patients displayed IgE reactivity with bovine serum albumin,

demonstrating the cross-reactive potential of albumins from rodents [86].

Later dog albumin was identified as an important cross-reactive allergen, which was detected by 35% of patients allergic to dogs and bound a high percentage (70–90%) of dog-specific IgE antibodies [47]. Dog albumin was shown to contain most of the IgE epitopes present on albumins from other species and was able to induce a dose-dependent histamine release from basophils of a patient allergic to dogs [47]. In another study, the degree of IgE reactivity and cross-reactivity of albumins from dogs, cats, pigs, cows, sheep, horses, guinea pigs, rabbits, hamsters, mice and rats was investigated. It was shown that albumin from dogs, cats and horses represent the most important crossreactive allergens in patients allergic to animals [135]. Despite the high degree of sequence homologies among albumins from different species, a remarkable variability of IgE cross-reactivities was observed, indicating that some patients were sensitized preferentially to certain albumins [135]. The varying IgE cross-reactivity of patients allergic to albumin is exemplified in figure 1.

The clinical importance of IgE antibodies cross-reactive with albumins has been pointed out by Hilger et al. [136]. The authors report a case where a patient allergic to cats experienced an anaphylactic reaction after consumption of ham. They further report that the frequency of sensitization to cat albumin in patients allergic to cats ranged from 14 to 23% and sensitization to porcine albumins was found in 3–10% of the patients. Since one third of the patients with IgE antibodies to cat albumin are at risk of exhibiting allergic reactions upon pork consumption, they recommend screening for sensitization to cat albumins. A severe anaphylactic reaction due to IgE antibodies to – in that case – bovine serum albumin occurred at the first attempt at artificial insemination as reported by Wüthrich et al. [137].

Lipocalins

The lipocalin protein family is a large group of small extracellular proteins that bind small hydrophobic ligands, such as pheromones, retinoids, steroids and arachidonic acids [138]. Lipocalins are present in vertebrates [138], arthropods [139–141] and bacteria [142, 143], suggesting that they belong to an ancient and widespread protein family. Lipocalins display low levels of overall sequence conservation (often below 20%) but contain short characteristic conserved sequence motifs that have been used to define family members [144]. The lipocalin protein family consists of two subgroups: the kernel lipocalins, possessing three of the conserved motifs and the outlier lipocalins possessing only one or two of the motifs [138].

Despite the heterology of sequences among lipocalins, the analysis of their crystal structures [83, 145, 146] reveals that the overall folding pattern of lipocalins is highly conserved [138]. It comprises a single eight-stranded continuously hydrogen-bonded antiparallel β -barrel which encloses an internal ligand binding site.

The major dog allergen Can d 1 displayed 54% sequence homology with the rat von Ebner's gland proteins (VEG P1 and VEG P 2), which are outlier lipocalins [50]. Can d 2 shows 30% similarity to mouse urinary protein (MUP) [147] and rat α_{2u} -globulin [148], both proteins representing kernel lipocalins. Prealbumins and α_{2u} -globulins from mice and rats belong to the kernel lipocalins [68]. In 1998 it was demonstrated that the major cow allergen Bos d 2 [93] and two horse allergens, termed Equ c 2.0101, Equ c 2.0102 [9], are members of the lipocalin protein family as well.

The question whether Fel d 1 is a lipocalin protein is a controversial issue. Virtanen et al. [127] claim that Fel d 1 is the only major mammalian allergen cloned and sequenced so far that does not belong to the lipocalin protein family; on the other hand chain 1 of Fel d 1 displays sequence ho-

mology with rabbit uteroglobulin and a mouse salivary protein as well as with a lipocalin protein cloned from Syrian hamster [30, 149]. Moreover, studies investigating the influence of hormones (testosterone) on the production of Fel d 1 indicate that Fel d 1 synthesis is controlled by male hormones [150, 151], a phenomenon that has been described for other lipocalins such as MUP and α_{2u} -globulin, the major rat allergen [69, 152].

Deer allergens with MWs of 22 and 25 kD, which are probably lipocalins, and a 60-kD allergen, which was identified as albumin, were described in deer extracts [153]. Immunoblot inhibition studies revealed that IgE binding to these deer allergens could be inhibited by preincubation of patients' sera with cow dander extract.

A study on the cross-reactivity of animal allergic patients demonstrated that 68 of 109 of these patients displayed IgE reactivity to cat and dog allergens. Immunoblot inhibition experiments revealed the presence of common epitopes of the major cat and dog allergens [154]. Whether cat and dog lipocalins contain cross-reactive IgE epitopes remains to be answered.

Transferrins and Immunoglobulins

Transferrins are circulating plasma proteins with an MW of 75–79 kD; they are members of a family of iron-binding glycoproteins. The major function of transferrins is the transport of iron [155]. They consist of a single polypeptide chain organized as two domains of equal size, each containing one high-affinity metal-binding site which binds Fe^{3+} reversibly. The sequence and three-dimensional structure of transferrin and other iron-binding glycoproteins are highly conserved. The molecules are bilobal, each lobe consists of one domain and is further organized into two subdomains separated by a cleft which contains the metal-binding site [156, 157].

Rat transferrin has been identified as an allergen by Gordon et al. [85] in 1997. Immunoglobulins from cats, dogs and rats have been identified as minor allergens [20, 36, 85].

Conclusion and Future Perspectives

The application of molecular biological techniques to the characterization of mammalian allergens has revealed the nature of many important animal-derived proteins and thus has implications for basic research as well as for diagnosis and therapy. According to similarities in sequence, structure and biological function, mammalian allergens can be grouped into allergen families of which certain (e. g., albumins) are highly cross-reactive. Striking similarities of

many mammalian allergens with human proteins indicate that allergy to mammalian proteins may be at a borderline between discrimination of foreign and self. An increasing number of recombinant mammalian allergens is currently being produced by recombinant DNA technology and it is expected that these molecules will represent well-defined tools for diagnostic and therapeutic purposes.

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