The domestic cat (*Felis domesticus*) is a common household pet and a significant source of indoor allergens. IgE mediated sensitization to allergens from *F. domesticus* affects approximately 10% of the western world. Symptoms range from mild rhinitis and conjunctivitis to life-threatening asthmatic responses. Fel d 1 is the most potent allergen in cat dander (1;2), eliciting IgE responses in 95% of patients with allergy to cat. (1;3) The most important sources of the allergen are the sebaceous, salivary and perianal glands, while the skin and the fur represent the principal reservoirs. (4) Fel d 1 is a thermostable 35kDa tetrameric glycoprotein formed by two non-covalently linked heterodimers (Fig.1). (5-7) The heterodimers are composed of a 70 residue light chain and a glycosylated heavy chain of 92 amino acids, referred to as chain 1 and chain 2, respectively. Within each heterodimer, chains are linked through disulfide bridges. (8) It has been reported that natural epithelia extracts and house dust extracts can contain complete tetramers (35kDa), separate heterodimers (17kDa), and separate chains 1 and 2. (9) Expression of recombinant Fel d 1 in *Pichia pastoris* results in hyperglycosylated and non-glycosylated heterodimers and tetramers, while dis-
ruption of the N-glycosylation motif (N103) in rFel d 1 removes the hyperglycosylated forms (Fig.1, inset). This improved rFel d 1 behaves as the structural and antigenic equivalent of natural Fel d 1. The recent resolution of the crystal structure of Fel d 1 suggests that Ca\textsuperscript{2+} plays a key role in the formation of the tetramer. While the physiological role of Fel d 1 remains unclear, the structure is strikingly similar to uteroglobin, a steroid-inducible molecule with potent anti-inflammatory and immunomodulatory properties. A unique feature of Fel d 1 is its ability to induce a form of tolerance described as a modified T\textsubscript{H}	extsubscript{2} response. This immune response, characterized by high titer Fel d 1-specific serum IgG and IgG4 in the absence of IgE (IgG\textsuperscript{+}IgE\textsuperscript{neg}) is not associated with allergic symptoms or asthma. Fel d 1 T-cell epitopes have been identified on both chains (Fig.2) and IL-10-producing CD4+ T cells were recognized as key elements of the modified T\textsubscript{H}	extsubscript{2} response. In a recent study of Hulse et al induction of this specific T-cell subset was approached by targeting Fel d 1 to the high–affinity IgG receptor (Fc\textgamma RI) on antigen-presenting cells. Fc\textgamma RI-targeted Fel d 1 induced T-cell subsets characteristic of a protective T-cell reponse, including T\textsubscript{H}0, regulatory T\textsubscript{H}1 and regulatory T\textsubscript{H}2, in subjects with allergy. This approach may be useful to improve T-cell based therapies for cat allergy.

*Fig.2: T cell epitopes in Chain 2 (white) (P2:1 in yellow, P2:2 in turquoise blue and overlapping residues in green) and in Chain 1 (grey) of Fel d 1 (IPC-1 in red and IPC-2 in blue).
References


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