

W0264

Antibody Complex of a Cockroach Allergen Bla g 2. Alla Gustchina¹, Mi Li^{1,2}, Sabina Wünschmann³, Martin D. Chapman³, Anna Pomés³, Alexander Wlodawer¹, ¹MCL, NCI at Frederick; ²Basic Research Program, SAIC-Frederick, Frederick, MD, USA; ³INDOOR Biotechnologies, Inc., Charlottesville, VA, USA.

Cockroaches excrete a potent allergen, Bla g 2, which elicits IgE responses at exposure levels that are 10-100 fold lower than other common indoor allergens. Exposure and sensitization to cockroach allergens such as Bla g 2 is a major risk factor for asthma mortality and morbidity. IgE-binding inhibition experiments showed that the monoclonal antibody mAb 7C11 inhibits IgE antibody binding up to 25-40%, despite of binding to only a small part of the total Bla g 2 surface. F(ab')₂ fragments of mAb 7C11 were generated by pepsin cleavage and crystal structure of the Bla g 2-Fab complex was solved by molecular replacement. Bla g 2 is present in the complex in a dimeric state, unusual for the aspartic protease family. Two Fab molecules interact with a dimer in such a way that the vast majority of the interactions are formed between one Fab and one of the two Bla g 2 molecules. Interactions with the antibody are dominated by a number of charged residues of the allergen. Determination of the molecular structure of Bla g 2-Fab complexes facilitates epitope mapping and enables a rational approach to the engineering of allergen molecules with reduced IgE antibody binding.