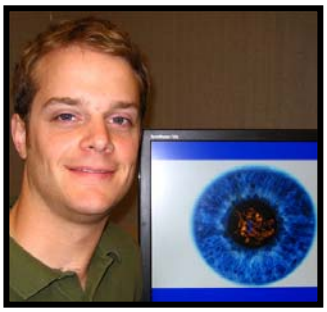
Clemens C. Heikaus



Current Position: Graduate student in the laboratory of Dr. Rachel Klevit in the Department of Biochemistry at the University of Washington in Seattle, WA

Education: Undergraduate Studies in Biochemistry at the University of Tübingen in Germany

Non-scientific Interests: Triathlon, backpacking, and world travel

I came to the University of Washington as a fellow of the German-American Fulbright Commission in 2004. During my exchange year, I became interested in protein structure and function and joined Dr. Rachel Klevit's laboratory for my thesis research. In collaboration with Dr. Joseph Beavo's laboratory, I have been investigating the structure and dynamics of GAF domains from cyclic nucleotide phosphodiesterases. In the present study, I teamed up with Dr. Sergio Martinez, a crystallographer in the Beavo lab to describe the atomic structure of the GAF A domain from phosphodiesterase 6C. Using NMR, we were able to visualize the large cGMP-dependent conformational change within the GAF domain and present functional implications from the gained structural insights. The presented structure is the first atomic-resolution view at phosphodiesterase 6, a central regulator in the visual signal transduction and responsible for control of the cellular concentrations of the second messenger cGMP. I am currently supported by a Boehringer Ingelheim Fonds Ph.D. Scholarship and anticipate defending my Ph.D. thesis in March 2009.

Sergio E. Martinez

Current Position: Research Associate in the laboratory of Dr. Eddy Arnold in the Department of Chemistry and Chemical Biology at Rutgers, the State University of New Jersey in Piscataway, NJ

Education: Ph.D in Structural Biology from Purdue; B.A. from Cornell University

Non-scientific Interests: Hiking, nature

In second or third grade, I grew crystals of alum for show-and-tell. Little did I know that many years later I would actually become a crystallographer growing crystals of proteins. I began work on cyclic nucleotide phosphodiesterases (PDEs) during my postdoctoral studies at the University of Washington. In the labs of Professors Joe Beavo and Wim Hol, we determined the first x-ray structure of a cGMP-bound, regulatory GAF domain from a PDE, enzymes that are essential parts of many cGMP and cAMP signaling pathways in mammalian cells. In humans, GAF domains are rare and present almost entirely in 5 of the 11 PDE family members, but they are widespread in plants and bacteria, specialized to bind many different ligands. Our paper focuses on the regulation of the photoreceptor phosphodiesterase PDE6, a central enzyme in visual transduction in rod and cone cells in the retina. In this enzyme, the role of cGMP in regulating this enzyme is not well understood. Our x-ray structure of the cGMP-bound regulatory GAF A domain, and other closed GAF structures from previous work, revealed the binding site and dimerization states but do not suggest a regulatory mechanism. An NMR study by co-authors Clemens Heikaus and Professor Rachel Klevit of the open apo-GAF A shows a large conformational change. We hope that this and future studies will elucidate the regulatory mechanism of this important group of enzymes.

Read Clemens Heikaus and Dr. Sergio Martinez's article entitled: The Structure of the GAF A domain from Phosphodiesterase 6C Reveals Determinants of cGMP Binding, a Conserved Binding Surface, and a Large cGMP-dependent Conformational Change … http://www.jbc.org/cgi/content/full/283/38/25913