Introducing our AUTHORS

Image courtesy of Christopher Liu.

Sara Buhrlage

Current position: Organic Synthesis Fellow at The Broad Institute
Education: University of Michigan, Ph.D. in chemistry with Professor Anna Mapp, 2008; Miami University, B.S. in biochemistry, 2002
Nonscientific interests: Soccer, running, cooking

The ability to mimic protein−protein interactions with small molecules remains a challenging problem in molecular recognition and a primary research interest of mine. My graduate work focused on synthesizing and characterizing small molecules designed to mimic peptide- and protein-based transcriptional activation domains. Transcriptional activation domains (TADs), one module of transcriptional activator proteins, interact with transcriptional coactivator proteins to upregulate gene expression. We have previously reported small molecule isoxazolidines that replicate the function of transcriptional activation domains. Here we show that these molecules also mimic the binding profile of their endogenous counterparts. This new piece of data in the development of this first class of small molecule transcriptional activation domains suggests the molecules function by a similar mechanism as natural TADs. (Read Buhrlage's article, DOI 10.1021/cb900028j.)

Image courtesy of Pat Knerr.

Leigh Anne Furgerson Ihnken

Current position: University of Illinois at Urbana−Champaign, Department of Chemistry, Ph.D. candidate with Professor Wilfred A. van der Donk
Education: Lake Forest College, B.A. in chemistry and biology, 2004
Nonscientific interests: Spending time with family, sports, music

My graduate research has been focused on the biosynthesis of lantibiotics, cyclic antimicrobial peptides that are ribosomally synthesized and posttranslationally modified. One such posttranslational modification is the formation of unsaturated amino acids from enzyme-catalyzed dehydration of serine and threonine residues. These reactions occur by initial phosphorylation of the hydroxyl group in the side chains of serines and threonines, followed by elimination to give the unsaturated residues dehydroalanine and dehydrobutyrine, respectively. In a previous study, a protein that normally catalyzes this transformation, lacticin 481 synthetase (LctM), was mutated such that it could no longer perform the elimination part of the reaction, in effect creating an engineered kinase. In this work, the mutant LctM is utilized as a general kinase to phosphorylate serine and threonine residues of a random peptide library. The technique is complementary and potentially advantageous to the current synthetic methodologies of producing phosphopeptides. (Read Furgerson's article, DOI 10.1021/cb800309v.)

Published online May 15, 2009 • 10.1021/cb900100h CCC: $40.75

Introducing our AUTHORS

Image courtesy of Brahma Ghosh.

Brahma Ghosh

Current position: Massachusetts General Hospital, Department of Radiology, Research Chemist with Dr. Anna V. Moore

Education: Indian Institute of Technology, Ph.D. in chemistry, 2004; Louisiana State University, Postdoctoral Researcher with Prof. Kevin M. Smith, 2004–2005; University of Minnesota, Research Associate with Prof. Carston R. Wagner, 2005–2009

Nonscientific interests: Music, movies, crossword, useless trivia, spectator sports

My work in the Wagner laboratory involved applying the areas of synthetic and medicinal chemistry to the design of agents capable of selectively regulating biological processes and to the development of new approaches for targeted drug delivery. The published article highlights both these facets, and presents a useful chemical biological methodology for pro-drug construction as an approach toward the development of compounds designed to normalize capdependent translation as novel chemo-preventive agents and therapeutics for cancer and fibrosis. My current research focuses on the development of Zn^{2+}-sensitive molecular probes for human pancreatic β-cell imaging and *in vivo* noninvasive monitoring of β-cell function, with the long-term goal of applications in diabetes treatment and diagnosis. (Read Ghosh's article, DOI 10.1021/cb9000475.)

Image courtesy of Amy Olson.

Yan Jia

Current position: University of Minnesota, Department of Chemistry, Ph.D. Candidate with Prof. Carston R. Wagner

Education: Peking University, Beijing, China, B.S. in chemistry, 2004

Nonscientific interests: TV series, ice skating, snowboarding

My research focuses on the development of small molecule antagonists of eukaryotic initiation factor (eIF) 4E, which is a validated anticancer target. Using *in silico* modeling, we have further elucidated key interactions involved in cap binding and developed three-dimensional quantitative structure activity relationship (3D-QSAR) models that should facility the design of new and more potent inhibitors. In addition, my work includes metabolic studies of eIF4E antagonists and the development of cell-based delivering of eIF4E inhibitors. (Read Jia's article, DOI 10.1021/cb9000475.)

Image courtesy of Lucas P. Labuda.

Melissa Lee

Current position: The State University of New York at Buffalo, Department of Chemistry, Ph.D. candidate with Prof. Matthew D. Disney

Education: The State University of New York at Buffalo, B.S. in chemistry and medicinal chemistry, 2006

Nonscientific interests: Playing the piano and scrapbooking

Traditionally, RNA is viewed as a static intermediary between DNA and protein. The diverse roles played by coding and noncoding RNAs in protein synthesis, gene regulation, and other functions, however, have brought this macromolecule to the forefront as a therapeutic target. RNA's ability to form diverse secondary structures through arrangements of its 4-nucleotide code prompted the Disney laboratory to develop a database of preferred RNA motif-ligand interactions as a basis for drug design. My research focuses on establishing methods to rationally target RNA through the application of this database. Specifically, I utilized rational design to target the repeating units of the RNA implicated in myotonic dystrophy 2. These studies highlight the potential of employing rational drug design as a general approach to target RNA. (Read Lee's article, DOI 10.1021/cb900025w.)

Introducing our AUTHORS

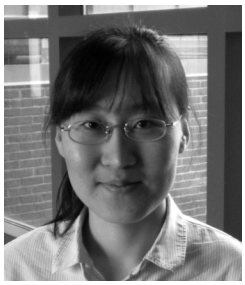

Image courtesy of Chiara Valenzano.

Young-Ok You

Current position: Brown University, Postdoctoral Researcher with David Cane
Education: Seoul National University, B.S. in pharmacy, 1999; University of Illinois at Urbana−Champaign, Ph D. in biochemistry with Wilfred van der Donk, 2008
Nonscientific interests: Raising my 7-month old son

Based upon the understanding of its mechanism, a lantibiotic synthetase turns into a Ser/Thr kinase that phosphorylates target residues of various peptide sequences. For me, the most interesting point in this study was that the sequence and the length of modified region of the different peptides tested were totally different from the original peptide substrate. The leader peptide region was identical to that of wild-type since that is important for recognition by the enzyme. In previous studies, peptide substrates were designed to mimic the original sequence as much as possible. However, the enzyme turns out to be much more progressive in accepting alien sequences than we thought. I try not to let my previous experiences or knowledge limit the observations that I make during my study. (Read You's article, DOI 10.1021/cb800309v.)