Introducing our AUTHORS

Image courtesy of Matthew Mattozzi.

Jeffrey A. Dietrich

Current position: University of California–Berkeley and University of California–San Francisco, Joint Graduate Group in Bioengineering, Ph.D. candidate with Prof. Jay D. Keasling
Education: Rice University, B.S. in bioengineering, 2001
Nonscientific interests: Soccer, running, traveling

I am interested in developing new tools to improve our ability to engineer microbes for the production of fine chemicals. A dearth of information at almost every level (sequence, protein, regulation) currently inhibits us from reconstructing metabolic pathways for many natural compounds. In this article, we describe a novel method to produce the anti-malarial compound artemisinin. We combine *in silico* protein design, metabolic engineering, and synthetic chemistry to achieve high-level production of a key intermediate along this route. A takeaway point for me from this work is the need for better screening methods that enable metabolic engineers to create broader changes to a system and decipher the impact each has on the final measured output. (Read Dietrich's article, DOI 10.1021/cb900006h.)

Image courtesy of Anita Engh.

Daniel A. Kraut

Current position: Northwestern University, Department of Biochemistry, Molecular Biology and Cell Biology, Postdoctoral Fellow with Prof. Andreas Matouschek
Education: Swarthmore College, B.A. in biochemistry, 2000; Stanford University, Ph.D. in biochemistry, 2006, with Prof. Daniel Herschlag
Nonscientific interests: Cooking, gardening, playing with my 10-month-old son

The focus of my graduate work was on better understanding physical mechanisms underlying how enzymes are able to efficiently and specifically catalyze chemical reactions. Most of my work focused on hydrogen bonding in enzyme active sites. Recently, it has been suggested that halogen bonds can substitute for and complement hydrogen bonds in supramolecular chemistry and, potentially, drug design. We set out to determine whether halogen bonds could substitute for hydrogen bonds in a very sensitive position, the oxyanion hole of an enzyme. We used peptides containing unnatural amino acids, which were attached to an expressed protein fragment using native chemical ligation to create semisynthetic enzyme containing potential halogen bond donors. Although wild-type protein synthesized in this manner was fully active, none of the halogen-containing mutants were rescued, suggesting that halogen bonds cannot substitute for hydrogen bonds in this active site. (Read Kraut's article, DOI 10.1021/cb900016q.)

Image courtesy of Melissa M. Lee.

Lucas Labuda

Current position: The State University of New York at Buffalo, Ph.D. candidate with Prof. Matthew Disney
Education: Rutgers, the State University of New Jersey at Newark, B.A. in chemistry, 2007
Nonscientific interests: Baseball, weightlifting, reading

My research is focused on the subjection of biologically relevant RNA systems to high-throughput screening *via* chemical microarrays. Libraries, which are constructed to encompass a diverse yet RNA-focused portion of chemical space, were synthesized and spotted onto microarrays. These arrays were subsequently hybridized with radiolabeled RNA. Binding of RNA to these spots has been shown to correlate with the affinities of the compounds to RNA. Using statistical analysis, this data can be used to construct new and more potent molecules. These experiments are supported by PAGE analysis to determine the efficacy of the ligand in inhibiting normal Group I intron RNA function in *Candida albicans*. (Read Labuda's article, DOI 10.1021/cb800313m.)

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Image courtesy of J. Christopher Love.

Kerry Love

Current position: Massachusetts Institute of Technology, Department of Chemical Engineering, Postdoctoral Associate with Prof. Danny Wang
Education: University of Virginia, B.S. in chemistry, 1999; Massachusetts Institute of Technology, Ph.D. in organic chemistry with Prof. Peter Seeberger, 2004; Department of Microbiology and Molecular Genetics, Harvard Medical School, Postdoctoral Fellow with Prof. Suzanne Walker, 2004–2006; Whitehead Institute for Biomedical Research, Postdoctoral Fellow with Prof. Hidde Ploegh, 2006–2008
Nonscientific interests: Going to the playground with my son, watching the Red Sox, cooking, hiking

My research interests have been focused on understanding the post-translational modification of proteins using a variety of tools, including synthetic chemistry, protein biochemistry, molecular biology, and enzyme engineering. Specifically, I am interested in the enzymes that participate in the modification of other proteins and how someone unskilled in chemical synthesis might use these enzymes as tools for the synthesis of complex biomolecules useful for biological studies or for therapeutics. In this paper, we discuss the development of ubiquitin-based electrophiles to identify enzymes involved in the process of ubiquitin conjugation to target proteins. We anticipate these chemical tools will facilitate the identification and mechanistic understanding of further members of this enzyme class. Currently, I am developing a general method for the *ex vivo* screening of enzyme libraries with the aim of creating useful catalysts for glycosylation *via* directed evolution. (Read Love's article, DOI 10.1021/cb9000348.)

Image courtesy of Stefan H. Millson.

Stefan H. Millson

Current position: University of Sheffield, Department of Molecular Biology and Biotechnology with Prof. Peter W. Piper, Postdoctoral researcher
Education: Liverpool John Moores University, B.Sc. in biochemistry, 1994; University of Grenwich, Ph.D. in biochemistry with Dr. Ivor Evans and Prof. Ian Bruce, 2001
Nonscientific interests: Snowboarding, trekking, playing fetch with my dog

I am interested in the study of protein–protein interactions of molecular chaperones, mainly focusing on the heat shock protein 90 (Hsp90). Hsp90 is an essential molecular chaperone in eukaryotic cells, known to catalyze the final activation step of many key signaling/regulatory proteins, and is a promising cancer drug target. Selective Hsp90 inhibitors, including the natural antibiotic radicicol (produced by the fungus *Humicola fuscoatra*), occupy the ATP binding site on Hsp90 so as to block the essential ATP-binding step of the chaperone cycle. We analyzed the *H. fuscoatra* Hsp90 and identified a conservative amino acid substitution in the ATP-binding pocket that, when introduced into the Hsp90 of yeast, selectively compromises radicicol binding and generates *in vivo* radicicol resistance. This is the first demonstration of Hsp90 inhibitor resistance being generated by subtle alteration to the structure of Hsp90 itself. (Read Millson's article, DOI 10.1021/cb9000316 and Point of View, DOI 10.1021/cb9000712.)

Image courtesy of Ankur Pandya.

Renuka Pandya

Current position: Massachusetts Institute of Technology, Department of Biology, graduate student with Prof. Hidde Ploegh
Education: Cornell University, B.A. in biology, 2004
Nonscientific interests: Distance running, cooking

Ubiquitin (Ub) conjugation to target proteins regulates many cellular processes, including protein stability, progression through the cell cycle, DNA repair, transcription, signal transduction, and protein trafficking. The covalent modification of substrates with ubiquitin is balanced by the action of enzymes responsible for ubiquitin deconjugation. The focus of my Ph.D. work has been to use molecular biology, biochemical, and structural approaches to further understand the mechanism by which these enzymes function. Here we discuss the development of chemical tools for identification and mechanistic study of Ub conjugation machinery. My current work focuses on biochemical and structural studies of one particular ligase we identified, ARF-BP1, to identify structural elements critical to maintaining its catalytic activity. (Read Pandya's article, DOI 10.1021/cb9000348.)