Introducing our AUTHORS

Image courtesy of Clementine Feau.

Clementine Feau

Current position: St. Jude Children's Research Hospital, Department of Chemical Biology and Therapeutics, Postdoctoral Research Associate with Dr. R. Kiplin Guy
Education: Université Louis Pasteur de Strasbourg (France), Ph.D. in Organic Synthesis
Nonscientific interests: Independent movies and music, contemporary arts, playing tennis, hiking, cooking, traveling

My research focuses on the development of small molecule modulators of androgen receptor (AR) transcriptional signaling. In this paper, we describe the study of structural analogs of a hit compound, flufenamic acid, identified during a HTS screening campaign for AR inhibitors. We report the synthesis of derivatives of flufenamic acid and their binding affinities toward AR and other nuclear receptors and confirm their inhibitory activities in cells at the protein and mRNA levels. We were able to fully characterize the mode of action of these small molecules. My research interests are centered on the design and synthesis of small molecules capable of disrupting protein–protein interactions. I am also intrigued by developing molecular probes and tailored bioassays to study the binding events of small molecules. (Read Feau's article, DOI: 10.1021/cb900143a)

Image courtesy of Beverly Lange.

Allison Lamanna

Current position: University of Michigan, Department of Chemistry, Postdoctoral Fellow with Katrin Karbstein
Education: Williams College, B.A. in Chemistry, 1998; University of Wisconsin-Madison, Ph.D. in biochemistry with Laura Kiessling, 2004; University of Michigan, Life Sciences Institute, Postdoctoral Fellow with Rowena Matthews, 2004–2007
Nonscientific interests: Choral performance, traveling, fiber arts, jewelry design, scrapbooking, cats

Throughout my scientific career, my interests have fallen under the broad umbrella of studying conformational changes, while bridging chemical biology, cell biology, and biochemistry. In my graduate work, I studied the conformational changes of chemoreceptors in a number of bacteria. Much of my work focused on how interactions of these receptors result in signaling pathways changes, some of which is demonstrated in the paper presented here. Since then, I have studied conformational changes in protein domains as well as RNA precursors. I am particularly interested in how these molecular changes lead to their intended biological outcomes. (Read Lamanna's article, DOI: 10.1021/cb900132e)

Image courtesy of Jolie Leonard.

Stephen Leonard

Current position: University of Michigan, Chemical Biology Doctoral Program, Ph.D. student with Prof. Kate S. Carroll
Education: Indiana Wesleyan University, B.S. in Chemistry, 2006
Nonscientific interests: Geocaching, hiking, and football

The focus of my research is directed at developing new chemical tools to identify and study posttranslational modification of cysteine to better understand how these modifications are used in cellular processes. This multidisciplinary project has allowed me to use organic chemistry to design small molecule probes which I employ to investigate biological questions. This project has taken me from the hood synthesizing molecules to the bench conducting biochemical experiments. I have been able to see a molecule I developed be successfully put to use in living cells. The combination of selective chemical enrichment and live-cell compatibility makes this probe a powerful new tool with the potential to reveal new regulatory mechanisms in signaling pathways and identify new therapeutic targets. (Read Leonard's article, DOI: 10.1021/cb900105q)

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Image courtesy of Laura Vanderploeg.

Ryan Marcheschi

Current position: University of Wisconsin-Madison, Department of Biochemistry, Ph. D. candidate with Prof. Samuel E. Butcher
Education: Iowa State University, B. S. in genetics, 2004
Nonscientific interests: College sports, gardening, socializing, reading literature, dancing, martial arts

My research is focused on the characterization of translational frameshifting in HIV and SIV. These viruses utilize an RNA stem-loop located at the frameshift site to program a (−1) nucleotide shift in the reading frame during translation. In this paper, I present the results of a high-throughput screen for small molecules that bind the HIV-1 frameshift-site RNA stem-loop. One of these molecules, doxorubicin, was shown to affect both the degree of frameshifting and the stability of the HIV-1 RNA stem-loop. Additionally, molecules showing binding effects were grouped into several structural classes, which may present useful scaffolds for the design of RNA-binding drugs. Since frameshifting is a critical step in the viral infection cycle, further development of these compounds may yield novel treatments for HIV infection. (Read Marcheschi's article, DOI: 10.1021/cb900167m)

Image courtesy of Stephanie Brown.

Timothy C. Meredith

Current position: Merck Frosst Research Laboratories, Antibacterial/Antifungal Biologist
Education: Villanova University, B.Sc. in Chemistry, 2000; University of Michigan, Ph.D. in Medicinal Chemistry, 2005; Harvard Medical School, Postdoctoral research, 2006–2009
Nonscientific interests: Reading and playing with my daughters

Although many putative small molecule antibacterial targets are involved in the assembly of complex cell envelope polymers, the development of inhibitor leads has lagged behind due in part to challenges in working with the molecular machinery. This paper presents a technically straightforward approach to identifying high quality wall teichoic acid inhibitors and in turn suggests broader utility for other targets within similar biochemical pathways. (Read Meredith's article, DOI: 10.1021/cb900151k)

Image courtesy of Trisha Oman.

Trent Oman

Current position: University of Illinois at Urbana–Champaign, Department of Chemistry, Ph.D. candidate with Professor Wilfred A. van der Donk
Education: Indiana University, B.S. in Biochemistry, 2006
Nonscientific interests: Spending time with family, soccer, hiking

My graduate research has been focused on the mode of action and biosynthesis of lantibiotics. These post-translationally modified peptides show promising antibiotic activity against a range of pathogenic bacteria. The biosynthesis of this lantibiotic was recently reconstituted *in vitro* and prompted further investigation of its mode of action. The mode of action of haloduracin is of particular interest because it is a member of the growing class of two-peptide lantibiotics. Interestingly, haloduracin exerts its antimicrobial activity in a manner similar to that of lacticin 3147 despite considerable structural differences between the two lantibiotic systems. The high potency of haloduracin against pathogenic bacteria and stability of the peptides at physiological pH make haloduracin a great example for future efforts in antibiotic development and design. (Read Oman's article, DOI: 10.1021/cb900194x)

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Image courtesy of Stephen Leonard.

Khalilah G. Reddie

Current position: University of Michigan, Life Science Institute, Postdoctoral Research Fellow with Prof. Kate S. Carroll
Education: University of the West Indies, Jamaica, B.S in Chemistry 1998; University of Georgia, Ph.D. in Chemistry with Prof. Timothy M. Dore, 2007

Scientific endeavors at the interface of chemistry and biology has been an exciting phase of my research career. The application of organic chemistry to answer fundamental questions about biological systems formed the basis of both my graduate and postdoctoral work. Oftentimes, key pieces of a biological puzzle come together or new insight is obtained through the direct application of small molecules to interrogate such systems. The challenge we often encounter is finding the most compatible chemical system for the application. One of my primary goals is to contribute innovations that help to remove these obstacles to exciting scientific discoveries. Toward this end, my most recent efforts have been aimed at the utilization of a powerful chemical tool for investigating cysteine thiol oxidative modifications in living systems. (Read Reddie's article, DOI: 10.1021/cb900105q)

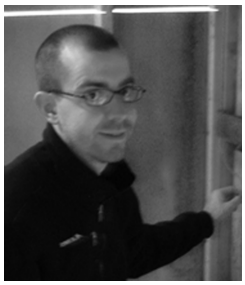

Image courtesy of Amy Malhowski.

Jonathan G. Swoboda

Current position: Harvard Medical School, Department of Microbiology and Molecular Genetics, Postdoctoral researcher with Suzanne Walker
Education: Brown University, B.Sc. in Biochemistry, 2003; Harvard University, M.A. in Chemical Biology, 2004; Harvard University, Ph.D. in Chemical Biology, 2009; Postdoctoral researcher with Suzanne Walker, 2009–present
Nonscientific interests: Swimming, biking, running, kayaking, traveling, watching cinematic adventures

I am interested in the discovery of small molecules with potential therapeutic value. The WTA pathway has long been speculated to be an antibiotic target, but no one has developed a strategy to discover inhibitors for it. We report a novel, general assay to discover WTA inhibitors that is applicable to many important bacterial pathways. We found the first WTA-specific antibiotic, and it is active against *S. aureus*, including methicillin-resistant strains. The WTA pathway represents a new paradigm for antibiotics since resistant mutants arise by deletion of the pathway, making the organisms incapable of surviving in a host. I think of the small molecule as both an antibiotic that inhibits growth *and* as a selection pressure to channel the evolution of pathogenic bacteria toward avirulence. (Read Swoboda's article, DOI: 10.1021/cb900151k)

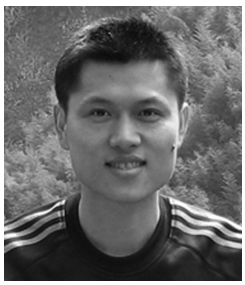

Image courtesy of Yi Yu.

Yi Yu

Current position: Chinese Academy of Sciences, Shanghai Institute of Organic Chemistry, State Key Laboratory of Bioorganic and Natural Products Chemistry, Postdoctoral Researcher with Prof. Wen Liu
Education: Huazhong Agricultural University, B.S. and M.S. in Biochemistry & Molecular Biology, 2002; Chinese Academy of Sciences, Institute of Microbiology, Ph.D. in Genetics, 2007
Nonscientific interests: Basketball, traveling, racing

My research interest focuses on the biosynthesis of microbial natural products for answering the following questions: what are the enzymatic mechanisms of novel reactions, and how are these reactions sequentially collaborated to constitute certain biosynthetic pathways for affording unusual structures? As shown in this paper, we cloned, sequenced, and characterized the biosynthetic gene cluster of nosiheptide, providing new insights into thiopeptide biosynthesis for structural diversity. Thiopeptides are a class of highly modified heterocyclic peptides with potent activity against various bacterial pathogens. This study confirmed the generality of the thiopeptide specific framework formation that features a ribosomally synthesized precursor peptide and conserved posttranslational modifications. However, nosiheptide biosynthesis is unique, apparently proceeding via a different route for tailoring the framework by installing an unusual indole side ring system and two regiospecific hydroxyl groups, characteristics of *e* series thiopeptides. (Read Yu's article, DOI: 10.1021/cb900133x)