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Introducing Our Authors

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LESLIE ALEXANDER

Current position: Ph.D. candidate in Chemistry at San Diego State University with Prof. Shelli McAlpine, Department of Chemistry and Biochemistry.

Education: University of California−Santa Barbara, B.S. in Biopsychology, 2006.

Nonscientific interests: Running, backpacking, going to the beach, spending time with my family, friends, and pug.

My graduate research with Prof. Shelli McAlpine focuses on investigating the mechanism of action of potent derivatives of the natural product Sansalvamide A (San A). San A is a cyclic pentapeptide that exhibits low micromolar anticancer activity. We have shown that it acts via inhibition of heat shock protein 90 (Hsp90), a chaperone protein that is up-regulated in many cancers and is associated with numerous oncogenic proteins. San A analogues bind to the interface of the Hsp90s N-M domain and inhibit the binding of Hsp90s C-terminal client proteins and cochaperones, including those that contain tetratricopeptide repeats (TPRs). This mechanism is unique from all Hsp90 inhibitors reported to date and will make this peptide scaffold a valuable tool for investigating Hsp90-associated cell signaling events. (Read Alexander's article, DOI: 10.1021/cb200203m)

VERONICA ARDI

Current position: Core Adjunct Professor at National University, La Jolla, CA.

Education: University of California−Irvine, B.S. in Biological Science and B.S. in Chemistry, 1997; University of California−Irvine, Ph.D. with Dr. Betty H. Olson in Environmental Toxicology, 2005; Postdoctoral Fellow at The Scripps Research Institute with Dr. James P. Quigley, 2005−2009; Postdoctoral Research at San Diego State University with Dr. Shelli R. McAlpine, 2009−2011; Scientific Collaborator at The Scripps Research Institute with Dr. James P. Quigley, 2009−present.

Nonscientific interests: World travel, music, video editing, movies, and Iaido.

I currently teach biology and chemistry at National University in La Jolla, CA. I believe that a well-rounded student should be able to have an understanding of both the practical and theoretical components of science. Through lecture, research, and active learning exercises, I am able to facilitate lively, real world discussions with students about science and the results are rewarding. My previous postdoctoral research at The Scripps Research Institute and SDSU were rich and valuable experiences. The research goals included novel therapeutic discoveries and determining the mechanism of cancer angiogenesis. My areas of interest include Environmental Toxicology and Cancer Biology. (Read Ardi's article, DOI: 10.1021/cb200203m)

JAMES DAY

Current position: Research Associate, Astex Pharmaceutics, Inc.

Education: Kingston University, B.Sc. Medicinal Chemistry; The Institute of Cancer Research, Centre For Cancer Therapeutics, Ph.D. Medicinal Chemistry, Supervisors: Dr. Ted McDonald and Dr. Peter Sheldrake; University of Nottingham, Research Fellow, Department of Chemistry with Prof. Chris Moody.

Nonscientific interests: Golf, martial arts, traveling

The main focus of my research to date has been the development of new cancer therapeutics. A recent cancer drug target that has been identified is the molecular chaperone called heat shock protein 90 (HSP90). Although there are many different types of HSP90 inhibitor, our inspiration came from a natural product called radicicol. This natural product has potent HSP90 inhibition *in vitro* but does not have any *in vivo* efficacy probably due to rapid metabolism. In our paper, we describe the design and synthesis of simplified analogues of radicicol that are potent against HSP90 and metabolically stable. Using co-crystallization with the N-terminal domain ATP site of HSP90, we also showed that one our analogues binds to a hydrophobic

Published: December 16, 2011

   dx.doi.org/10.1021/cb2004719 | *ACS Chem. Biol.* 2011, 6, 1297−1300

pocket previously unobserved in the radicicol class of inhibitors. (Read Day's article, DOI: 10.1021/cb200196e)


IMAGE COURTESY OF ALYSSA NEGRETTE

BYOUNG-CHUL LEE

Current position: Scientist at Genentech, Inc., South San Francisco, California

Education: Lawrence Berkeley National Lab., The Molecular Foundry, Post-Doc in Biological Nanostructures, advisor Dr. Ron Zuckermann, 2010; University of California–San Francisco, Ph.D. in Biophysics, advisors Prof. Ken Dill and Dr. Ron Zuckermann, 2006; Korea Advanced Institute of Science and Technology, Department of Biological Sciences, M.S., advisor Prof. Hyoungman Kim, 1999; Seoul National University, Department of Biology, B.S., 1997

Nonscientific interests: Korean Go Game "Baduk", traveling, reading, movies

This is one of my postdoctoral works. We developed a side chain translocation mutagenesis that the point of attachment of an amino acid is translocated from C α carbon to backbone nitrogen. In this work, semisynthetic approach was taken to conjugate the side-chain translocation mutant peptide segment ("peptoid" mutant) to a recombinant protein using thiazolidine ligation. I believe that the ability to translocate a particular side chain by one atom along the backbone significantly advances a synthetic mutagenesis tool and opens up a new level of protein engineering. (Read Lee's article, DOI: 10.1021/cb200300w)

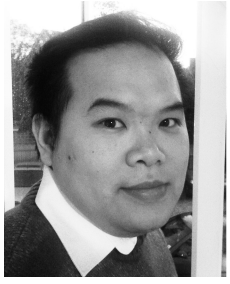
IMAGE COURTESY OF LOK HANG MAK

LOK HANG MAK

Current position: Imperial College London, Department of Chemistry, Postdoctoral researcher with Dr. Rudiger Woscholski

Education: University of Muenster, Germany, Diploma in Chemistry, 2002; Institute of Physical Chemistry and Center for Nanotechnology, Muenster, Germany, Ph.D. in Chemistry with Prof. Meinhard Knoll, 2006

Nonscientific interests: Badminton, martial arts, cooking

My Ph.D. research has focused on developing an electrochemical biosensor for the sensitive detection of protein–protein interactions. After my Ph.D., I moved to work with Prof. Gianfranco Gilardi at Imperial College London, where I was engaged in the development of a microfluidic chip-based platform for Cytochrome P450s drug metabolism profiling. Currently, as a postdoctoral researcher in Dr. Rudiger Woscholski's laboratory, my research focuses on elucidating the phosphoinositides signaling pathway with high emphasis on employing chemical tools to unravel the signal transduction mechanism. In the present paper my co-author and I demonstrated the successful development of a chemical receptor able to bind stereospecifically $PI(4,5)P_2$ and modulate $PI(4,5)P_2$-dependent signaling events. (Read Mak's article, DOI: 10.1021/cb2003187)


IMAGE COURTESY OF JOEL MELBY

JOEL MELBY

Current position: University of Illinois at Urbana–Champaign, Ph.D. student with Prof. Douglas A. Mitchell

Education: University of Evansville, B.S. in Professional Chemistry, 2009

Nonscientific interests: Running, biking, and hiking

My research is focused on the biosynthesis and structural elucidation of an uncharacterized thiazole/oxazole-modified microcin. The enzymes involved in thiazole and (methyl)oxazole synthesis are found in two domains of life, and the products characterized to date display a wide range of functions. Notable examples include microcin B17, a DNA gyrase inhibitor and streptolysin S, a cytolytic virulence factor. The explosion of genomic data enables a reverse genetics approach to discovering novel natural products in this family, some of which exhibit unique bioactivity. (Read Melby's article, DOI: 10.1021/cb200339d)


IMAGE COURTESY OF COURTNEY L. COX

KATIE MOLOHON

Current position: University of Illinois at Urbana–Champaign, Department of Microbiology, Graduate Student with Prof. Douglas A. Mitchell

Education: Illinois State University, B.S. in Biological Sciences, 2009; Undergraduate Researcher for Prof. Kevin A. Edwards

Nonscientific interests: Board games, sports, geocaching, musical theater, animals.

My research focuses on identifying a new class of bacterial natural products. I am particularly interested in this branch of science because we have the potential to discover new antibiotics and biomedically relevant compounds. Antibiotic

resistance is a constant pressure that today's scientists must overcome, and I strive to be a part of the team of researchers that helps to eliminate this problem. This paper describes the unique chemical structure and discriminating antibiotic activity of a newly discovered natural product. This metabolite is a target of future research in our laboratory, for it may play a role in the never-ending fight against bacterial infections. (Read Molohon's article, DOI: 10.1021/cb200339d)


IMAGE COURTESY OF ANDREW PALMER

■ ANDREW PALMER

Current position: Research Associate with Professor Helen Blackwell, University of Wisconsin−Madison, Department of Chemistry

Education: Department of Chemistr, Florida State University, B.S. in Biochemistry fwith Professor Timothy Logan, 2001; Emory University, Department of Chemistry, Ph.D. with Professor David G. Lynn, 2008

Nonscientific interests: Cooking, hiking, music, playing with my son, and comics.

I am fascinated with how organisms regulate behaviors through small molecule signals and developing strategies and chemical probes aimed at "translating" and "speaking" these chemical dialogues has been a major goal of my research career. As a postdoctoral fellow, I have focused on the small-molecule regulated phenomenon known as quorum sensing (QS) in which bacteria regulate the transition between specific phenotypes based on their population density. Specifically, I have been developing a toolbox of small molecule probes for agonizing or antagonizing QS-dependent behaviors of bacteria in the presence of prospective host eukaryotes. Toward this goal, we have been studying the QS-dependent release of virulence factors by the plant pathogens *Pectobacterium carotovora* and *Pseudomonas syringae* during infection assays of host plants. (Read Palmer's article, DOI: 10.1021/cb200298g)


IMAGE COURTESY OF LAUREN PURINGTON

■ LAUREN PURINGTON

Current position: Assistant Professor of Pharmaceutical Sciences, Albany College of Pharmacy and Health Sciences, Albany NY

Education: Clarkson University, Potsdam, NY, B.S. in Biomolecular Science and Chemistry; University of Michigan, Ann Arbor MI, Ph.D. in Pharmacology, Advisors: John R. Traynor, Ph.D. and Henry I. Mosberg, Ph.D.

Nonscientific interests: Reading, cooking, spending time with family

My graduate work focused on interactions between the mu and delta opioid receptors in the development of analgesic tolerance and dependence. Clinically used opioid analgesics promote their effect by activating the mu opioid receptor and tolerance develops rapidly to this effect. Several studies postulate that activation of the mu opioid receptor with concurrent delta opioid receptor antagonism could provide analgesia with decreased propensity for analgesic tolerance. The studies performed for this work examined the synthesis and characterization of novel cyclic opioid peptides that were designed to have both mu opioid agonist and delta opioid antagonist properties and bind equally well to both receptors. Development of these peptide ligands represents a step forward in the development of novel pain therapeutics with decreased tolerance liability. (Read Purington's article DOI: 10.1021/cb200263q)


IMAGE COURTESY OF TIANYIN ZHOU

■ REMO ROHS

Current position: Assistant Professor of Biological Sciences and Chemistry, Molecular and Computational Biology Program, University of Southern California, Los Angeles, United States.

Education: Humboldt University Berlin, Germany, M.Sc. in Physics; Free University Berlin, Germany, Ph.D. in Biochemistry; Weizmann Institute of Science, Rehovot, Israel, Postdoctoral training in Structural Biology; Howard Hughes Medical Institute and Columbia University, New York, Postdoctoral training in Computational Biology and Bioinformatics.

Nonscientific interests: Spending time with my family, outdoor activities, traveling.

The goal of my laboratory is to integrate two areas of research that have developed along parallel lines, largely disconnected from each other: sequence and structure. Sequence research concentrates on high-throughput analysis of one-dimensional data and is closely connected to advancements in sequencing technologies. Structure research describes a nucleotide not as a letter but as an ensemble of atoms with different chemical identities at different locations in space. As a consequence, three-dimensional or sometimes four-dimensional structure research is a low-throughput approach, compared to sequence analysis. My postdoctoral research provided me with an extensive training in DNA and protein−DNA structure analysis and prediction. In my own laboratory, we are currently developing a new methodology for the high-throughput prediction of DNA shape. The ability to predict

DNA structure on a genomic scale will change how sequence data is analyzed, and hydroxyl cleavage intensity measurements will provide an important comparison of our predictions with experimental data. (Read Rohs' article, DOI: 10.1021/cb200155t)


IMAGE COURTESY OF BRYAN SEVERYN

BRYAN SEVERYN

Current position: Genomics Group Member, Screening and Protein Sciences, Merck & Co., Inc.

Education: The Pennsylvania State University, B.S. in Microbiology, 1991; The Pennsylvania State University, M.S. in Entomology, 1999.

Nonscientific interests: Guitar, skiing, tennis, mountain biking, bugs, home repair, and spending time with my family.

My initial scientific career was in the field of agriculture either studying biological pesticides or the genome of oak and chestnut trees. I then switched to the medicinal sciences where I am at present a biologist in the central high-throughput screening laboratory for Merck & Co, Inc. Recently our laboratory has become interested in developing new screening paradigms that enable us to easily identify synergistic drug pairs, as therapies using these combinations may lend themselves to decreased drug dosing and subsequent negative side effects. In the study described here, we tested pools of compounds from a small self-deconvoluting compound library in an anti-inflammatory HTS assay using the THP-1 monocyte derived cell line and were able identify drug pairs that synergistically inhibit IL-6 secretion, our readout for the immune system's acute phase response. This work thus provides a very manageable approach for testing much larger libraries for synergistic combinations that are applicable for other therapeutic areas. (Read Severyn's article, DOI: 10.1021/cb2003225)


IMAGE COURTESY OF GENHUA ZHENG

GENHUA ZHENG

Current position: Instructor at University of Texas Southwestern Medical Center, Department of Cell Biology and of Biochemistry

Education: University of Science and Technology of China, B.S. in Polymer Chemistry and B.S. in Computer Science, 2000; University of Science and Technology of China, Ph.D. in Chemistry with Prof. Caiyuan Pan, 2005; University of Texas Southwestern Medical Center, Postdoctoral fellow with Wenhong Li, 2006–2010.

Nonscientific interests: Reading, traveling, photography

My research focuses on developing new reagents or assays to study biology using chemistry as a tool. I have been developing both optical and magnetic probes for tracking cells and monitoring their functions. Most recently I have been developing novel methods to study and control small RNAs based on antisense technique and organic synthetic chemistry. As a long-term goal, I am also interested in polymeric gene delivery vesicles. In this work, we developed a photoactivatable microRNA inhibitor by conjugating two oligonucleotides with a novel bifunctional caged linker. The resultant caged antimirs (cantimirs) provide high spatial and temporal resolution for the regulation of microRNAs *in vivo*. (Read Zheng's article, DOI: 10.1021/cb200290e)