ACS chemical biology

Introducing Our Authors

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KAHLIN CHEUNG-ONG

Image courtesy of Kahlin Cheung-Ong.

Current position. Ph.D. candidate in Molecular Genetics at the University of Toronto under the supervision of Dr. Corey Nislow and Dr. Guri Giaever

Education. University of Toronto, Hon. B.Sc. in Human Biology and Physiology, 2007

Nonscientific interests. Traveling, cooking, music, movies

My Ph.D. research focuses on the development and application of high-throughput chemical genomic screens to study drug mechanism of action. I am particularly interested in characterizing current and novel DNA-targeted anticancer compounds by identifying their major cellular targets as well as off-target effects. The study we present here is a collaboration between our group and Uli Bierbach's lab at Wake Forest University. Here, we demonstrate the successful application of chemical genomic screens to understand the biological consequences of structural modifications in a novel class of nonclassical platinum-acridine molecules with high therapeutic potential. (Read Cheung-Ong's article, DOI: 10.1021/cb300320d)

ALLISON COHEN

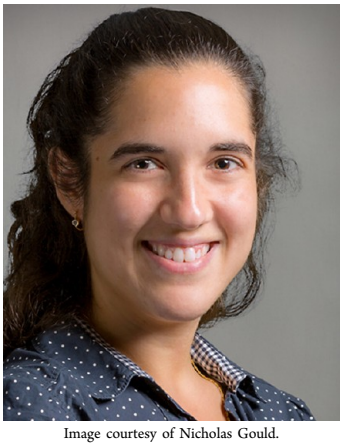

Image courtesy of Nicholas Gould.

Current position. Postdoctoral Research Fellow, H. Lee Moffitt Cancer Center and Research Institute, Department of Cancer Imaging and Metabolism, 2011–Present, Advisors: David L. Morse and Robert J. Gillies

Education. Columbia University, B.A. in Chemistry, 2006, Research Advisor: Laura J. Kaufman; University of California, Berkeley, Ph.D. in Chemistry, 2011, Thesis Advisor: Carolyn R. Bertozzi

Nonscientific interests. Dancing, playing tennis, watching baseball, swimming, traveling

My graduate research focused on the synthesis and development of novel imaging probes and the *in vitro* and *in vivo* evaluation of the probes. The probes were designed to study two important biological processes: glycosylation and fatty acid uptake. In this work, we describe a bioluminescent probe for the imaging of fatty acid utilization. The results demonstrate the potential usefulness of this probe for studying many important physiological processes *in vivo*. This research fostered my interest in using imaging as a tool for understanding diseases. The focus of my postdoctoral research is on targeted molecular imaging of lung cancer. I am especially interested in being able to translate my scientific discoveries into the clinic in order to help patients suffering from life-threatening diseases. (Read Cohen's article, DOI: 10.1021/cb300194b)

AMY HENKIN

Image courtesy of Sasha Henkin.

Current position. Ph.D. student, University of California at Los Angeles, Molecular and Medical Pharmacology Department, Advisor: Steven Bensinger

Education. University of California at Santa Cruz, B.S. in Molecular, Cell, and Development Biology

Nonscientific interests. My cactus and succulent garden, music, making art, spending time with my husband Sasha

Quantifying cellular fatty acid uptake is relevant for understanding a number of physiological and pathological conditions and has further implications in the evaluation of drugs that manipulate metabolic pathways or directly target fatty acids. Thus, we sought to develop the novel fatty acid imaging probe described in this issue. This project resulted from an interdisciplinary collaboration between biologists and chemists at UC Berkeley. After honing my interests in metabolic biology in the laboratory of Andreas Stahl, I went on to pursue a Ph.D. in the laboratory of Steven Bensinger at UCLA. My current research focuses on how the sterol regulatory element binding protein (SREBP) family of transcription factors influences cancer cell biology through modulation of gene

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expression and protein function via acetylation. (Read Henkin's article, DOI: 10.1021/cb300194b)

KRISTOFF HOMAN

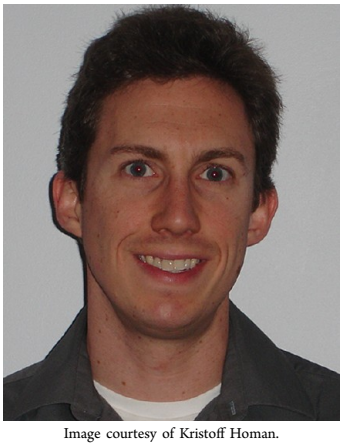

Image courtesy of Kristoff Homan.

Current position. University of Michigan, Ann Arbor, MI, in the lab of John Tesmer in the Life Sciences Institute (John also has joint appointments in Pharmacology and Biological Chemistry)

Education. University of Illinois at Urbana−Champaign, B.S. in Physics, 2003, B.S. in Mathematics, 2003; Purdue University, Ph.D. in Structural Biology, 2010, in the lab of Cynthia Stauffacher in the department of Biological Sciences

Nonscientific interests. Cooking, running, college sports

I'm interested in the structural characterization of cellular signaling systems, particularly phosphorylation. Along these lines, in my graduate research I performed several screens for inhibitors of a phosphatase; however, I have identified only weak inhibitors that have not progressed very far. Thus, I'm very excited to have been part of the team that identified paroxetine as a selective inhibitor of G protein-coupled receptor (GPCR) kinase 2(GRK2) that retains its activity *in vivo*. I'm optimistic that we will be able to continue to develop paroxetine into a tool that can be used to elucidate the underlying structural and functional roles of ligand interactions with GRK2 as well as related kinases. Hopefully this will ultimately lead to deeper insights into GPCR signaling and future treatments for heart failure. (Read Homan's article, DOI: 10.1021/cb3003013)

TAMER KAOUD

Image courtesy of Tamer Kaoud.

Current position. The University of Texas at Austin, College of Pharmacy, Postdoctoral Fellow with Professor Kevin N. Dalby

Education. Tanta University (Egypt), B.S. in Pharmaceutical Sciences (BPharm), 1999; Minia University (Egypt), M.S. in Pharmaceutical Sciences, Medicinal Chemistry (MPharm), 2002; The University of Texas at Austin, Ph.D. in Pharmacy (Medicinal Chemistry), 2012

Nonscientific interests. Traveling, biking, running, and watching movies with my wife

Currently I am studying mechanisms of regulation of protein kinases by employing both chemical and biology approaches. By investigating these processes I hope to identify novel targets to treat cancer. During graduate school I focused on drug discovery. The training by Prof. Kevin Dalby provided me with a variety of skills in medicinal chemistry, enzymology, physical biochemistry, and molecular and cell biology. Herein we are introducing a new selective inhibitor of the JNKs (c-Jun N-terminal kinases). JNKs are attractive targets for the treatment of a variety of diseases, including cancer. However, no inhibitors of JNK have been approved for use in humans. Recently, in a virtual screening strategy to identify new compounds targeting the D-recruitment site (DRS) of the c-Jun *N*-terminal kinases (JNKs) we identified the natural product (−)-zuonin A. We show here that (−)-zuonin A is a selective inhibitor of the JNKs and identify two mechanisms as likely contributors to its ability to inhibit JNK signaling in cells: (i) (−)-zuonin A inhibits JNK activation by MKK4 and MKK7, and (ii) it inhibits substrate phosphorylation. The activity of (−)-zuonin toward JNK is the basis for its ability to inhibit Akt signaling and breast cancer cell migration. (Read Kaoud's article, DOI: 10.1021/cb300261e)

THOMAS KEATING

Image courtesy of Thomas Keating.

Current position. Principal Scientist, AstraZeneca Infection Innovative Medicines, Waltham, MA

Education. Harvard University, A.B. in Chemistry, 1993 with Gregory Verdine; University of California, Los Angeles, Ph.D. in Organic Chemistry, 1998 with Robert Armstrong; Harvard Medical School, Postdoctoral Fellow in Enzymology, 1998−2001 with Christopher Walsh

Nonscientific interests. Coaching and playing sports, traveling, and growing orchids

Discovering and developing new antibacterials to treat drug-resistant infections is the goal of our group. One of the more difficult yet rewarding paths we pursue is pioneering novel targets for therapeutic intervention. This begins with establishing target essentiality and then proceeds through assay development, screening for lead biochemical inhibitors, development of whole-cell activity, and then optimizing for *in vivo* exposure, efficacy, and safety. Along the way we employ the tools of molecular biology,

biochemistry, medicinal chemistry, microbiology, and pharmacology. Thymidylate kinase (TMK), the focus of our recent work, is one of the more promising new targets we have encountered. (Read Keating's article, DOI: 10.1021/cb300316n)

WENZONG LI

Image courtesy of Leqian Liu.

Current position. Ph.D. candidate with Dr. Yan Jessie Zhang at The University of Texas at Austin, Department of Chemistry and Biochemistry

Education. Shandong Normal University, B.S. Biotechnology, 2005−2007; East Tennessee State University, B.S. Biochemistry, 2007−2009

Nonscientific interests. Traveling with friends, swimming, dog shelter volunteer, reading

My research in Zhang lab is focused on the study of the first plant-type asparaginase found in human (hASRGL1). Human-ASRGL1 is an N-terminal nucleophile hydrolase protein. This protein has autoprocessing property to expose the active site for its hydrolytic activity. Using a *de novo* protein engineering method, we designed a circularly permutated hASRGL1to resolve the complication posed by partial activation and to provide an understanding of its autoprocessing mechanism. We observed a dramatic structural change in a glycine-rich loop located near the active site. The kinetics of the genetic variants of this loop was characterized demonstrating a potent effect on both hASRGL1 autoprocessing and substrate hydrolysis. In addition, we demonstrated that the methyl group introduced a restrained energy for autoprocessing initiation using differential scanning fluorometry and structure modeling. This is the first explanation of threonine as the unique nucleophile active site for hASRGL1. (Read Li's article, DOI: 10.1021/cb300232n)

DAVID M. THAL

Image courtesy of David M. Thal.

Current position. Monash University, Monash Institute of Pharmaceutical Sciences, Postdoctoral Fellow with Prof. Arthur Christopoulos

Education. University of Texas, B.S. in Biochemistry with Prof. Kenneth A. Johnson, 2005; University of Michigan, Ph.D. in Chemical Biology with Prof. John J. G. Tesmer, 2010.

Nonscientific interests. Soccer, college football, rock climbing, fishing, and homebrewing.

My graduate research focused on the identification and characterization of small molecule inhibitors for G protein-coupled receptor kinase 2 (GRK2), which is a therapeutic target for the treatment of heart failure. My initial interest in GRK2 involved characterizing a class of GRK2 inhibitors that are extremely potent and selective for the GRK2 subfamily. We found that these inhibitors likely achieve their selectivity by stabilizing a unique inactive conformation of GRK2. We were also interested in discovering new inhibitors against GRK2, and in this work we developed a high-throughput screen targeting the inactive conformation of GRK2. We identified the selective serotonin reuptake inhibitor (SSRI) paroxetine as a selective inhibitor of GRK2 activity both *in vitro* and in living cells. We also show that paroxetine binds in the active site of GRK2 stabilizing a novel conformation. Overall, this study provides a new starting point for the development of GRK2 inhibitors. (Read Thal's article, DOI: 10.1021/cb3003013)

MICHAEL D. URBANIAK

Image courtesy of Dr. Allyson Clelland.

Current position. Senior Research Associate in the laboratory of Prof. Mike Ferguson in the Division of Biological Chemistry and Drug Discovery, University of Dundee, U.K.

Education. BSc. in Chemistry at the University of York, UK in 1998; Ph.D. in Chemistry with Prof. Stephen Caddick and Prof. Dek Woolfson at the University of Sussex, UK, in 2002; Postdoctoral research with Prof. Stephen Caddick and Prof. Dek Woolfson at the University of Sussex 2002−3; Postdoctoral researcher with Prof. Mike Ferguson in the Division of Biological Chemistry and Drug Discovery, University of Dundee, UK, 2003 to present.

Nonscientific interests. Archery, baking and cycling.

I use a combination of chemical and biological techniques to probe biological systems at the molecular level and translate my basic research into early stage drug discovery. My current research is focused on the characterization of dynamic protein phosphorylation in the parasite *Trypanosoma brucei* using genetic, proteomic, and chemical biology techniques. *T. brucei* protein kinases are potential antiparasitic drug targets, but it is unclear if protein sequence similarity will translate into inhibition

by typical mammalian kinase inhibitor scaffolds. My article examines the similarity of the chemical space that parasite and mammalian protein kinase inhibitors occupy using chemical proteomic profiling, and provides the first molecular evidence that trypanosome protein kinases can be inhibited by typical ATP-competitive inhibitors with nanomolar potency. (Read Urbaniak's article, DOI: 10.1021/cb300326z)