ACS chemical biology

Introducing Our Authors

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HASSAN AL-ALI

Image courtesy of Robert Camarena.

Current position: Postdoctoral Fellow, Axon Growth and Guidance Lab, Miami Project to Cure Paralysis, University of Miami. Advisors: Dr. John Bixby and Dr. Vance Lemmon.

Education: University of Miami, Ph.D. in Biochemistry and Molecular Biology, Miami-Florida; American University of Beirut, M.S. in Biochemistry, Beirut-Lebanon; Lebanese University, M.S. in Organic Chemistry and B.S. in Chemistry, Hadath-Lebanon.

Nonscientific interests: Painting and art, exercise and outdoor sports, graphic and web design.

I'm curious about what makes life tick and how it operates from the molecular level up. This prompted a keen interest in kinases, as they regulate nearly every cellular function. Currently, I'm developing a novel approach for discovering kinase inhibitors that can overcome challenging selectivity problems and yield good leads for drug development. It combines cell-based screening with kinase activity profiling and machine learning algorithms to construct a predictive computational framework. The strength of this approach is 3-fold: (1) it identifies compounds that can simultaneously inhibit multiple drug targets while avoiding antitargets (favorable polypharmacology), (2) it allows searching for novel hit compounds based on activity patterns rather than chemical structure, and (3) it is readily applicable to other kinase-centric drug discovery campaigns. (Read Al-Ali's article, DOI: 10.1021/cb300584e)

JINHO LEE

Image courtesy of Jinho Lee.

Education: University of Seoul, B.A. in Life Science, 2011; Gwangju Institute of Science & Technology, M.S. in Life Science, 2013, Advisor: Darren R. Williams

Nonscientific interests: Motorsports, traveling, and design

My research is focused on developing a novel way of screening system for the discovery of insulin mimetic compounds using a vertebrate model, the zebrafish. Zebrafish is a notable scientific research model that has numbers of advantages such as low-cost, productivity and highly identical genomic information with human (75%). As described in our manuscript, we showed that glucose uptake can be detected in 3-day-old zebrafish larvae by using fluorescent-tagged glucose probe. Furthermore, we discovered glucose uptake inducing compounds including fraxidin, a methanol fraction of *C. crenata*, from both tests in zebrafish and mammalian adipocytes. Hopefully use of this rapid and inexpensive vertebrate screening model would accelerate the diabetes research development. (Read Lee's article, DOI: 10.1021/cb300687k)

LINGYIN LI

Image courtesy of Lingyin Li.

Current position: Postdoctoral Fellow, Department of Systems Biology, Harvard Medical School, Advisor: Timothy J. Mitchison

Education: University of Science and Technology of China, B.En. Polymer Science and Engineering, 2003; University of Wisconsin-Madison, Ph.D. in Chemistry, 2010, Advisor: Laura L. Kiessling

Nonscientific interests: Running, hiking, movies, and reading.

My current research is focused on chemical genetics of cancer immunology. Exploiting the innate immune response is an exciting new approach in cancer treatment. To help develop immune modulating drugs, we sought to gain insights from drugs that function through unknown mechanisms. The work we reported in this issue is about a drug called DMXAA that shrinks tumors in mice, but not in men. We discovered that DMXAA functions by activating mouse STING but does not interact with the human homologue, which explains DMXAA's lack of activity in human. It is exciting to us that mechanistic studies of existing/successful drugs (successful in mice in this case) can point us to novel targets, such as human STING, and new hypothesis for cancer therapeutics. (Read Li's article, DOI: 10.1021/cb400264n)

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ANDREW NAMANJA

Image courtesy of Andrew Namanja.

Current position: Beckman Research Institute of City of Hope, NIH Career Development Award (K01) Recipient, Mentors: Yuan Chen, David Horne, and Richard Jove

Education: Indiana University South Bend, B.S. in Chemistry, 2002, Advisor: Gretchen Anderson; University of Notre Dame, Ph.D. in Biochemistry, 2009, Advisor: Jeffrey Peng; Beckman Research Institute of City of Hope, Postdoctoral Fellow, 2009–2012, Advisor: Yuan Chen

Nonscientific interests: Soccer, gadgets, entrepreneurship, time with family and friends

My scientific interests include the discovery of small molecule modulators of cellular development and differentiation for the generation of novel therapeutics. I use NMR as the primary biophysical tool for the discovery and characterization of inhibitors of protein–protein interaction interfaces. Of particular interest is the application of fragment-based drug discovery methods on high-molecular-weight systems that have been established as promising therapeutic targets. I also use NMR to characterize the conformational dynamics of both protein and ligand in order to understand how molecular flexibility information can guide inhibitor development. In this article, a multidisciplinary effort resulted in the identification of non-covalent small molecule inhibitors of desumoylation enzymes that bind the 40 kDa SENP/SUMO complex as evidenced by biochemical kinetic assays and NMR binding experiments. (Read Namanja's article, DOI: 10.1021/cb400177q)

MALAY PATRA

Image courtesy of Nils Metzler-Nolte.

Education: Midnapore College (under Vidyasagar University), West Bengal, India, B.Sc. in Chemistry 2005; IIT Mumbai, India, M.Sc. in Chemistry 2007; Ruhr-University of Bochum, Germany, Ph.D. in Chemistry, 2011, Advisor: Nils Metzler-Nolte; University of Zurich, Switzerland, Postdoc 2011–13, Advisor: Gilles Gasser.

Nonscientific interests: Sports (in particular cricket), music, Bollywood movies

Toward my Ph.D. work in Germany, I was involved in the development of novel organometallic-based antibacterial agents. The structures of my compounds were inspired by a rather complicated natural product called platensimycin. The synthesis of these compounds, which included a range of different metals and the development of synthetic strategies toward enantiomerically pure organometallic complexes, was very challenging, and I was thrilled to see decent activity at least in the most promising candidates. The excitement of antimicrobial research continued during my postdoc in Switzerland, where I am currently working on the development of novel organometallic-based drug candidates against the parasitic disease schistosomiasis. Given the lack of affordable medicines against many microbes and the rapid development of resistance in many bacteria and parasites, there is an urgent need for novel medicines, and I believe that metal-based drugs in particular hold great promise. (Read Patra's article, DOI: 10.1021/cb4000844)

THAO NGUYEN

Image courtesy of Thao Nguyen.

Current position: Researcher, Institute of Microbiology and Biotechnology, Vietnam National University, Hanoi, Vietnam

Education: Hanoi University of Science, Vietnam, B.S. Biology, 2005; University of Utah, USA, Ph.D. Bioengineering, 2012, Advisor: Dr. Kuberan Balagurunathan

Nonscientific interests: Traveling, reading

My Ph.D. thesis research aims at investigating the structural requirements of glycosaminoglycan (GAG) chains in their interactions with fibroblast growth factors (FGFs). In this manuscript, we examined the importance of GAG multivalency in regulating FGF signaling *in vivo* by using a library of synthesized small molecules, named xylosides. We have shown that upon injection of xylosides into zebrafish embryos, only cluster-xylosides, which stimulate the production of multimeric GAG chains, caused an elongation phenotype, representing the hyperactivation of FGF signaling. Therefore, this chemical tool has demonstrated the essential role of GAG multivalency in FGF signaling. Our work hopefully could facilitate the establishment of GAG structure–function relationships in a comprehensive manner. (Read Nguyen's article, DOI: 10.1021/cb400132r)

VY TRAN

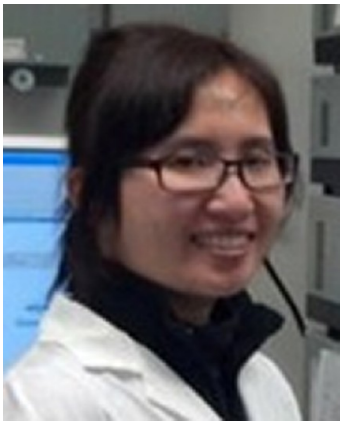

Image courtesy of Vy Tran.

Current position: Postdoctoral Fellow, at Department of Chemistry, University of Utah, 2012– Present, Advisors: Professor Kuberan Balagurunathan

Education: University of Utah B.Sc. in Chemistry, 2006, University of Utah, Ph.D. in Bioengineering, 2006–2012, Thesis Advisor: Professor Kuberan Balagurunathan

Nonscientific interests: Cooking, hiking, and traveling

My graduate research in Professor Balagurunathan's lab is focused on the design, synthesis and development of a library of xylosides via click-chemistry that can prime or inhibit specific proteoglycan biosynthesis. Proteoglycan chains play important roles in wound healing, cell signaling, cell proliferation, cell migration, cell differentiation, tumor metastasis, blood clotting, various infections, and numerous other biological processes. I specifically designed and synthesized cluster-xylosides (including bis-xylosides and tris-xylosides) in order to prime multiple glycosaminoglycan chains per scaffold and mimic naturally occurring proteoglycans. I also studied the inhibition of endogenous GAG production using 4-fluoro-xylosides in collaboration with Professor Koketsu at Gifu University. Furthermore, I synthesized linear and cyclic RGD-xylosides that selectively target activated endothelial and cancer cells. In my lab, these xylosides were also found to regulate many important biological processes such as the elongation of zebrafish embryos, angiogenesis and invasion. Therefore, these synthetic molecules are very useful in studying the structure–function relationship of proteoglycan chains *in vitro* and *in vivo*. (Read Tran's article, DOI: 10.1021/cb300665u)

CHRIS VICKERS

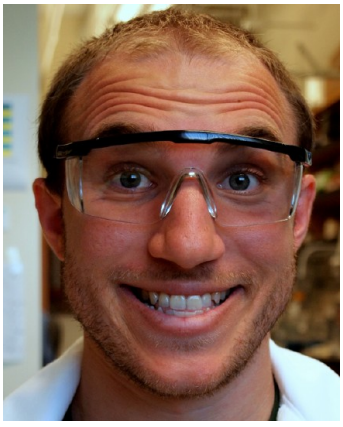

Image courtesy of Ana Wang.

Current position: Ph.D. student at The Scripps Research Institute; Advisor: Prof. Dennis W. Wolan

Education: Florida State University, B.S. Biochemistry, 2009; Advisor: Prof. Marie E. Krafft

Nonscientific interests: Eating, soccer, movies, and spending time with my grandma

My current research revolves around the identification and characterization of activity-based probes (ABPs) for cysteine proteases with a primary focus on compounds that selectively recognize specific caspase isoforms. Caspases are widely known for their role in apoptosis; however, they are also critical in other processes, including differentiation, inflammation, and cell survival. A major problem in caspase biology is the inability to determine the individual contributions of each caspase isoform toward these important biological phenomena. In the present article, we have created a new fluorescent and biotinylated probe that is 40-fold more selective for caspase-3 than caspase-7. I am excited to utilize this new tool in a biological setting to elucidate the role of caspase-3 in specific cellular processes. (Read Vickers' articled, DOI: 10.1021/cb400209w)

MICHAELA WENZEL

Image courtesy of Hanno Boeddinghaus.

Current position: Ruhr University Bochum, Germany, Biology of Microorganisms, Ph.D. candidate with Julia E. Bandow

Education: Ruhr University Bochum, Germany, B.Sc. in Biology, 2009, Advisor: Julia E. Bandow

Nonscientific interests: Horseback riding, running, swimming, music, literature, and visual arts

My Ph.D. project focuses on the antibacterial mechanisms of action of novel antibiotic compounds and their impact on cellular physiology. In the face of increasing microbial antibiotic resistance, structurally novel antibacterial compounds targeting cellular structures, which have not been exploited so far, are highly desirable. Organometallic complexes are promising building blocks as they might offer metal-specific modulation of a compounds' mode of action. In the present study, we report on the novel heterotri-organometallic compound FcPNA, which contains ferrocene, cymantrene, and a (dipicolyl)$Re(CO)_3$ moiety and inhibits growth of resistant bacteria at low micromolar concentrations. Its mechanism of action is characterized by perturbation of the bacterial cytoplasmic membrane and formation of reactive oxygen species, the latter of which was shown to depend on the ferrocene moiety. (Read Wenzel's article, DOI: 10.1021/cb4000844)

DING XU

Image courtesy of Ding Xu.

Current position: University of California, San Diego, Dept. of Cellular and Molecular Medicine, Assistant Project Scientist, in Dr. Jeffrey Esko's lab.

Education: Central China Normal University, B.S. in Biochemistry, 1999; University of North Carolina at Chapel Hill, Ph.D. in Pharmaceutical Sciences with Jian Liu, 2006; University of California, San Diego, American Heart Association Postdoctoral Fellow with Dr. Jeffrey Esko

Nonscientific interests: Gardening, hiking, classical music, and reading.

My research focuses on understanding how heparan sulfate regulates the structure and function of heparan sulfate-binding proteins. All mammalian cells express heparan sulfate, an unbranched sulfated polysaccharide. As a major component of the landscape at the cell surface, heparan sulfate plays essential roles in cell signaling and cell−cell interactions by interacting with hundreds of secreted and membrane-attached proteins. Binding to heparan sulfate often improves the functionality of heparan sulfate-binding proteins by mechanisms of oligomerization, scaffolding, allosteric regulation or simply tethering. As described in our manuscript, we have characterized the structural details of heparan sulfate-dependent oligomerization of the receptor RAGE, which facilitated development of a monoclonal antibody that specifically disrupting RAGE oligomerization, and consequently, signal transduction. This study might serve a paradigm for blocking other heparan sulfate-binding proteins of therapeutic interest. (Read Xu's article, DOI: 10.1021/cb4001553)