ACS chemical biology

Introducing Our Authors

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JENNIFER BRIGHAM

Image courtesy of Sanjay Hari.

Current position: University of Washington, Department of Chemistry, Graduate Student with Prof. Dustin J. Maly

Education: Wittenberg University, B.A. in Chemistry and English, 2006

Nonscientific interests: Hiking in National Parks, fostering rescue dogs, and gardening

My research focuses on developing new tools for studying enzyme families and identifying the cellular targets of small molecules. In this study we develop a new catch-and-release enrichment strategy for proteins. We show that we're able to enrich protein kinases that are both covalently and noncovalently bound to small molecule probes that target the active site of the enzyme. This technology is an exciting alternative to biotin-streptavidin enrichment that minimizes handling steps and uses mild elution conditions that are compatible with mass spectrometry. (Read Brigham's article, DOI: 10.1021/cb300623a)

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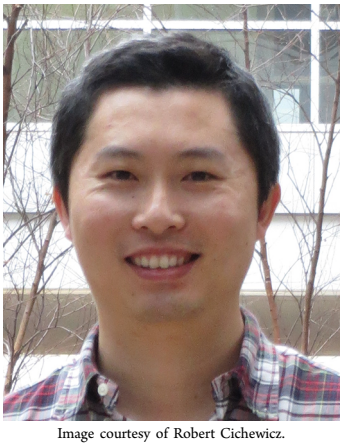

Image courtesy of Robert Cichewicz.

Current position: University of Oklahoma, Department of Chemistry and Biochemistry, Postdoctoral Associate with Dr. Robert Cichewicz

Education: University of Mississippi, School of Pharmacy, Department of Pharmacognosy, Postdoctoral Associate with Dr. Dale Nagle, 2009–2011; Ocean University of China, School of Medicine and Pharmaceutics, Ph.D. in Medicinal Chemistry with Dr. Qianqun Gu, 2004–2009; University of China, School of Medicine and Pharmaceutics, B.S. in Pharmacy, 2000–2004

Nonscientific interests: Soccer, fishing, movies, traveling

My research is focused on the isolation, structure characterization, and pharmacological investigation of natural products from fungi and other microbes. To date, I have isolated over 300 natural products including more than 100 new compounds from diverse natural resources. Most of the new compounds exhibited biofilm inhibition, cancer cell cytotoxicity, and antimicrobial activities. In this study, we established an efficient screening model of fungal natural products that exhibit fungal biofilm disruption activities using a new imaging flow-cytometer technique. A comprehensive chemical investigation of the bioactive extract from a *Penicillium* isolate led to the identification of a new group of shearinine indole-alkaloids that inhibit *Candida* biofilm formation. We also observed that the shearinines showed synergistic activities with amphotericin B against several clinical *Candida* isolates. These data highlight several promising opportunities for developing adjunctive therapies that work in combination with antifungals. (Read Lin's article, DOI: 10.1021/cb400009f)

YAM POUDEL

Image courtesy of Yam Poudel.

Current position: The Scripps Research Institute, Department of Chemistry, California, postdoctoral research associate with Prof. Dale L. Boger

Education: Tribhuvan University, Kathmandu, Nepal, M.S. in Chemistry with Prof. Mohan B. Gewali, 2002; The University of Utah, Ph.D. in Chemistry with Prof. Gary E. Keck, 2010

Nonscientific interests: Traveling, hiking, photography, spending time with family and friends

The central theme of my research is synthesis at the interface of chemistry and biology. My graduate school research focused on the synthesis and biological studies of the bryostatin family of

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natural products, which are highly potent protein kinase C (PKC) ligands. Bryostatin 1 is an anticancer natural product currently being used in 38 phase I and II clinical trials for the treatment of cancer and has also been shown to exhibit promising activity against HIV and Alzheimer's disease. Using the pyran annulation chemistry developed in Professor Keck's laboratories, I have completed the first total synthesis of bryostatin 1 and also prepared bryostatin 7 for biological evaluation. Detailed biological studies on the synthetically more accessible bryostatin 7 revealed that it can serve as an effective functional surrogate for bryostatin 1. (Read Poudel's article, DOI: 10.1021/cb300671s)

ARUMUGAM RAJAVELU

Image courtesy of Arumugam Rajavelu.

Current position: Postdoctoral fellow at Institute of Biochemistry, Stuttgart University, Stuttgart, Germany

Education: Jacobs University Bremen, Germany, Ph.D. under the supervision of Prof. Dr. Albert Jeltsch; Dr. ALM PGIBMS, Taramani campus, University of Madras, Chennai, India, M.Sc.

Nonscientific interests: Playing cricket, volley ball, traveling and music

My research interest will focus on study the regulation of DNA methyltransferases particularly Dnmt3a. I work primarily on the structure and regulation of Dnmt3a enzyme, and my Ph.D. work mostly covered a project where we identified that the Dnmt3a forms higher order oligomers, such structural properties being altered by interaction by its regulatory protein called Dnmt3L. I also worked on the regulation of the Dnmt3a enzyme activity mediated by its interaction with chromatin through its N-terminal domains. We have reported that Dnmt3a ADD domain and Dnmt3a PWWP domain interact with H3K4 unmethylated tails and H3K36me3 modification, respectively. The site-specific hypermethylation in cells leads to carcinogenesis by silencing of tumor suppressor genes. Hypermethylation could be caused by aberrant expression of DNA methyltransferase or abnormal activity of DNA methyltransferases. To revert the hypermethylation at gene promoters or to suppress the hyperactivity of DNA methyltransferases, specific inhibitors are required, which could be further used in epigenetic therapy. Using a newly developed high-throughput assay developed by our collaborator, we have identified novel inhibitor molecules to Dnmt3a from chemical libraries, which could be further used in epigenetic therapy. (Read Rajavelu's article, DOI: 10.1021/cb300565z)

MIN SHAN

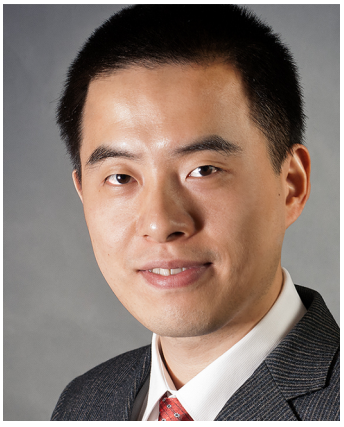

Image courtesy of Min Shan.

Current position: Postdoctoral fellow at Freie Universität Berlin, Institute of Chemistry and Biochemistry, Berlin, Germany

Education: Suzhou Railway Teacher's College, China, B.S. in Chemistry Teaching, 2001; Freie Universität Berlin, Germany, M.S. in Chemistry, 2006, Mentor: Jürgen-H Fuhrhop; Freie Universität Berlin, Germany, Ph.D. in Chemistry, 2011, Advisor: Rainer Haag; Freie Universität Berlin, Germany, Postdoctoral Fellow, Chemical Biology, 2012, Advisor: Rainer Haag

Nonscientific interests: Detective novels reading, aviation technology, and swimming

My research interests lie in addressing questions arising from biological discipline by utilizing chemical knowledge. My core work in past years includes design, synthesis, and evaluation of novel biological active molecules such as gabapentin-lactam, estrogen ligand, and sialic acid in order to better understand the molecular mechanisms in the living organisms. Nowadays, one of the major challenges in the diagnosis and chemotherapy of virus infection and cancer is to selectively targeting the virus and tumor cells. Multicomponent bioconjugate molecules have become more and more attractive during the past decade. Unlike small biological active molecules, many factors such as scaffold and spacer need to be considered in the application of such bioconjugate molecules. Additionally, in order to better apply these multivalent interactions, we should understand and reveal the nature of protein/cell−ligand interactions at a thermodynamic and kinetic level as well. (Read Shan's article, DOI: 10.1021/cb3006243)

JIANLAN YOU

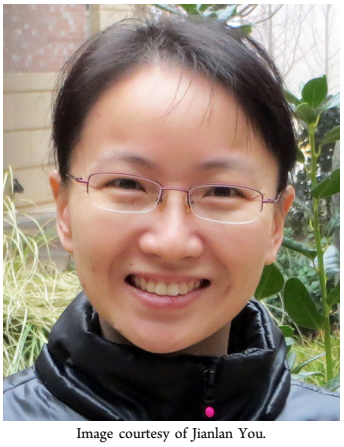

Image courtesy of Jianlan You.

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Current position: University of Oklahoma, Dept. of Chemistry and Biochemistry, postdoctoral research associate in Dr. Cichewicz Lab since January 2011

Education: Sun-Yat-Sen University, China, B.S. in Microbiology; Sun-Yat-Sen University, China, Ph.D. in Microbiology with Prof. Shining Zhou; Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Research Associate, with Prof. Lixin Zhang and Xiaoping Chen

Nonscientific interests: Drawing, stamp collection

My current research focuses on the characterization of natural products that inhibit biofilm formation processes of *Candida* spp. Unlike bacteria, pathogenic fungi such as *Candida* spp. readily undergo morphological transitions among several forms including yeast, pseudohyphal, and hyphal. These forms play critical roles in biofilm development, which contribute to the maintenance of infections. The unique chemical diversity of natural products makes these compounds a very inviting resource for identifying bioactive substances that inhibit biofilms and alter *Candida* morphology. In my current work, I have developed a new imaging flow-cytometry technique, which can provide a quantitative assessment tools for analyzing the full range of cell types contained within *Candida* biofilms. Using this method, two small-molecule suppressors of *Candida* biofilm formation were identified, and both of these compounds also synergistically enhanced the antifungal activity of amphotericin B. It is anticipated that this method will enable our lab and others the opportunity to discover additional new biofilm inhibitors, as well as probe their unique inhibitory mechanisms. (Read You's article, DOI: 10.1021/cb400009f)