ACS chemical biology

INTRODUCING OUR AUTHORS

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Li Cai

Image courtesy of Li Cai.

Current position: The Ohio State University, Department of Chemistry and Biochemistry, Ph.D. candidate with Prof. Peng George Wang

Education: Peking University, Beijing, China, B.S. in Pharmaceutical Science, 2005, M.S. in Medicinal Chemistry with Prof. Zhenjun Yang, 2007

Nonscientific interests: Basketball, electronics, movies

My graduate research has centered on the following three areas at the interface of chemistry and biology: (1) chemoenzymatic synthesis of unnatural sugar nucleotides and their applications, (2) synthesis of rare sugars with aldolases *in vitro* and *in vivo*, and (3) chemoenzymatic synthesis of building blocks involved in bacterial polysaccharide biosynthesis. The enzymatic approach is known for high efficiency and region/stereoselectivity. A combination of enzymatic routes with classic organic synthesis could thus generate diverse molecules of biological interests and applications. For example, we have successfully assembled a library of sugar nucleotides from our chemically synthesized unnatural sugars using enzymes kinase (NahK) and pyrophosphorylase (GlmU or AGX1). (Read Cai's article, DOI: 10.1021/cb100318z)

Wenlan Chen

Image courtesy of Jinjin Zhang.

Current position: NewLink Genetics, Postdoctoral Researcher

Education: Shandong University, B.S. in Chemistry, 2000; Shandong University, M.S. in Material Science, 2003; The Ohio State University, Ph. D. in Organic Chemistry with Prof. Peng G. Wang, 2010

Nonscientific interests: Traveling, fishing, movies, sports

My graduate research has focused on the design and synthesis of immunogenically active molecules, *e.g.*, glycolipid and glycoprotein antigens, for cancer immunotherapies. In addition to traditional chemical synthesis, I exploit and develop efficient conjugation strategy to link carbohydrate antigens to varied molecules, such as ceramide lipids and proteins. These approaches enable us to evaluate the crucial roles of carbohydrates in immune systems and facilitate the development of carbohydrate-based vaccines for cancer immunotherapies. Recent identification of ubiquitous anti-rhamnose antibody in human serum initiated our research on L-rhamnose for potential therapeutic applications. As demonstrated in this paper, we efficiently synthesize L-rhamnose immunogens and successfully induce significant titers of anti-rhamnose antibodies in wildtype mice. This study suggests L-rhamnose is a promising alternative to α-Gal for antigen/antibody-mediated vaccine development by employing wildtype mice. We believe that this work would accelerate the development of potential carbohydrate-based vaccine in the future. (Read Chen's article, DOI: 10.1021/cb100318z)

Li Gu

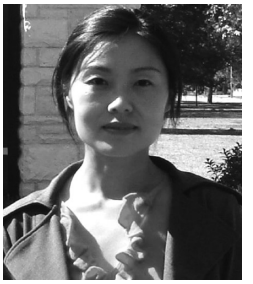

Image courtesy of Li Gu.

Current position: Shandong University, The State Key Laboratory of Microbial Technology and National Glycoengineering Research Center, Associate Professor in Glycobiology, 2007—present

Education: Yan'an Medical college, B.S. in Clinical Medicine, 1997; Xi'an Jiaotong University, M.S. in Pathology, 2000; Peking University, Ph.D. in Biophysics, 2003; Departments of Biochemistry and Chemistry, The Ohio State University, Postdoctoral researcher with Prof. Peng George Wang, 2009—2010

Nonscientific interests: Reading, music, playing with my kid

I am so interested in high titers of natural anti-carbohydrate antibodies in normal human serum, in which the antibody against α-Gal epitope has been investigated for a long time. Targeting autologous vaccines to antigen-presenting cells through the *in vivo* α-Gal/anti-Gal presents a promising cancer immunotherapy with enhanced immunogenicity. My research here is aimed at verification of other natural anti-carbohydrate antibodies in high titers (such as L-rhamnose) in human serum and the development of a mouse model with anti-rhamnose antibody, which reached levels similar to those observed in humans. Our studies suggest that the monosaccharide L-rhamnose could become a promising alternative to α-Gal epitope in the modification of carbohydrate cancer vaccines and that

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wildtype mice could be directly used for preclinical evaluations. (Read Gu's article, DOI: 10.1021/cb100318z)

William Hallows


Image courtesy of William Hallows.

Current position: Department of Neurology, University of California at San Francisco, Postdoctoral Fellow in the lab of Ying-Hui Fu and Louis Ptacek

Education: University of Oregon, B. S. in Biochemisrty 2001; University of Wisconsin, Ph.D. in Biomolecular Chemistry 2010

Industrial work: Zymogenetics 2001−2004 Microbial Development protein expression and purification

Nonscientific Interests: Rock climbing, bicycling, music

My graduate work focused on the regulation of metabolic enzymes and pathways by reversible acetylation. We characterized a number of metabolic enzymes that are regulated by sirtuin-mediated reversible acetylation. In our current study, we developed a peptide array to identify new substrates of Sirt3, a potentially important regulator of mitochondrial metabolism and function. Currently, I am studying human familial mutations in transcriptional and posttranslational regulatory mechanisms of the circadian cycle. I am working to better understand circadian regulatory pathways through the development of novel biochemical approaches and techniques. (Read Hallows' article, DOI: 10.1021/cb100218d)

Rahul Palchaudhuri


Image courtesy of Kathy Partlow.

Current position: University of Illinois at Urbana−Champaign, Department of Chemistry, Ph.D. candidate in Organic Chemistry with Prof. Paul J. Hergenrother

Education: Grinnell College, Grinnell, Iowa, B.A. in Chemistry, 2005

Nonscientific interests: Golf, soccer, motorcycles, world traveling

My research involves the development of novel small molecules with anticancer activity and the identification of their mechanisms of action. I have investigated the role of the triphenylmethyl motif in anticancer agents, identified novel inhibitors of tubulin polymerization, and discovered quinones that elicit anticancer activity through an oxidative stress mechanism. The review I authored focuses on systems biology approaches to identify small molecule mechanisms and therapeutic potential which are significant challenges in the field of drug discovery. For my postdoctoral research I will be working with Prof. David T. Scadden at the Harvard Stem Cell Institute/Massachusetts General Hospital Center for Regenerative Medicine where I will work toward the development of novel hematopoietic stem cell-based therapies for the treatment of hematological diseases. (Read Palchaudhuri's review, DOI: 10.1021/cb100310h)

James Patterson


Image courtesy of James Patterson.

Current position: Indiana University, Department of Chemistry, Ph. D. candidate with Prof. Richard DiMarchi

Education: Indiana University, B.S. in Biochemistry w/Honors, with Prof. Donald Burke, 2005

Nonscientific interests: Religion, art and music, fitness, traveling

My graduate research at Indiana University has focused on determining the underlying structural principles of peptide-ligand GPCR agonism and antagonism. A specific target of my work has been the GLP-1 receptor and the discovery of improved therapy for treatment of metabolic diseases. As reported herein, the determinants for GLP-1 receptor antagonism have been identified through the synthesis and *in vitro* characterization of a family of GLP-1 and structurally related exendin-4 peptide analogues. The best performing antagonist was highly effective when tested after acute *in vivo* challenge with glucose. Site-specific fatty-acylation with palmitic acid yielded a functional GLP-1 receptor antagonist of sustained duration suitable for once a day administration. This antagonist of sustained pharmacology is currently being studied in larger animals with the prospect of clinical investigation given its increased homology to the native hormone sequence. The structural basis for antagonism is also being extended to related peptide hormones. I remain focused on questions where chemical biology can facilitate translational research. (Read Patterson's article, DOI: 10.1021/cb1002015)

Burr Settles


Image courtesy of Natalie Settles.

Current position: Carnegie Mellon University, Machine Learning Department, Postdoctoral Fellow with Prof. Tom Mitchell

Education: DePauw University, B. A. in Computer Science, 2000; University of Wisconsin-Madison, Ph. D. in Computer Sciences with Prof. Mark Craven, 2008

Nonscientific interests: Music composition and performance, running, cooking, and wordplay

My research focuses on machine learning and its ability to help people solve interesting problems. In a biological context, such as the study published in this issue, this can mean developing computer systems that assist scientists in predicting and explaining experimental observations (especially data gathered using modern high-throughput techniques such as SPOT arrays). I believe that the future of scientific discovery is a collaboration between computers and human experts, where

learning machines participates in designing experiments and proposing hypotheses. My primary current project is NELL (Never-Ending Language Learner), an interactive computer that is learning to read English and summarize information from the Internet. You can follow NELL on Twitter: @cmunell. (Read Settles' article, DOI: 10.1021/cb100218d)

Brian Smith

Image courtesy of Sarah Wynia Smith.

Current position: University of California-Berkeley, California Institute for Quantitative Biosciences, Postdoctoral Fellow with Prof. Michael Marletta, 2009-present

Education: University of Illinois at Urbana−Champaign, B.S. in Chemistry with Prof. Scott Silverman, 2003; University of Wisconsin-Madison, Ph.D. in Chemistry with Prof. John Denu, 2008

Industrial research: Research Assistant, Genentech, Department of Medicinal Chemistry, 2005

Nonscientific interests: Listening to, playing, and writing music; playing and watching golf and other sports; hiking and letterboxing with my wife

I am interested in the chemistry and biology of post-translational modifications. My graduate research focused on the enzymology of sirtuin deacetylases. My interest in post-translational modifications continues into my postdoctoral work on S-nitrosation. During my thesis work, I discovered several acetyl-lysine analogues that bind tightly to sirtuins. Here, we employed a novel acetyl-lysine analogue and peptide libraries to examine the substrate specificity of SIRT3, a mitochondrial sirtuin that may control major metabolic pathways through enzyme deacetylation. I turned to Burr Settles, a computer scientist and fellow musician with whom I have collaborated on several music projects, for machine learning analysis of the library data. These analyses suggested several SIRT3 substrates in metabolic pathways such as the urea cycle, ATP synthesis, and fatty acid oxidation. (Read Smith's article, DOI: 10.1021/cb100218d)

Thomas Styslinger

Image courtesy of Thomas Styslinger.

Current position: The Ohio State University, Department of Chemistry

Education: North Carolina State University, B.S. in Chemistry and B.S. in Biology, 2007

Nonscientific interests: Sailing, running, and reading

My research has been focused on the design and synthesis of immunogenically active molecules, *e.g.*, glycoprotein antigens, for cancer immunotherapies. In addition to traditional chemical synthesis, I have been developing new methods for glycoprotein synthesis and exploring potential applications. The potential applications currently being explored range from the glycosylation of hemoglobin, as a potential oxygen therapeutic (or "blood substitute"), to the glycosylation of organphosphorous hydrolases as catalytic bioscavengers. Similar to PEGylation, glycosylation aims at increasing the hydrodynamic radius of biopharmaceuticals shielding their surface and thus leading to a prolonged half-life, reduced side effects, and increased treatment efficiency. (Read Styslinger's article, DOI: 10.1021/cb100318z)

Fan Wang

Image courtesy of Fan Wang.

Current position: Rice University, Department of Chemical and Biomolecular Engineering, Ph.D student with Dr. Laura Segatori

Education: Tianjin University, China, B.S. in Chemical Engineering, 2007

Nonscientific interests: Music, traveling, skiing

My research interest is in cellular protein folding, particularly in association with disease development. My research project focuses on the development of therapeutic strategies for Gaucher's Disease (GD). GD is characterized by deficient lysosomal glucocerebrosidase activity and cellular accumulation of its substrate, glucosylceramide. I am specifically interested at glucocerebrosidase variants with unstable structure that are typically degraded before they can reach native folding and exhibit biologic function. I am investigating approaches to modulate the folding quality control of the cell and enhance the chaperone capacity to restore folding and activity of unstable glucocerebrosidase variants. In this paper we demonstrated that restoring Ca^{2+} homeostasis, which is impaired by substrate build-up in GD cells, facilitates the folding of a severely destabilized GC variant. Particularly, we reported that $[Ca^{2+}]$ modulation recreates a "wild type-like" folding environment in GD cells, more amenable to glucocerebrosidase mutant folding rescue through proteostasis regulation. (Read Wang's article, DOI: 10.1021/cb100321m)

Wenpeng Zhang

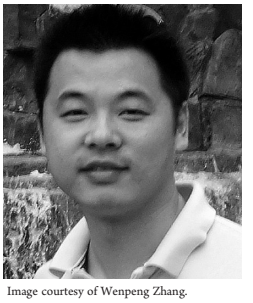

Image courtesy of Wenpeng Zhang.

Current position: The Ohio State University, Department of Biochemistry, Postdoctoral Researcher with Prof. Peng G Wang

Education: Peking University, China, B.S. in Biological Sciences, 2003; The Ohio State University, Ph.D. in Biochemistry with Prof. Peng G. Wang, 2009

Nonscientific interests: Traveling, movies, tennis, Ohio State football

My graduate research focused on studying the biological function of glycosylceramides on Natural Killer T (NKT) cell activity. By combining immunology, cell biology and

biochemistry methodologies, I conducted a structure−activity relationship (SAR) study on the sugar moiety of the glycosylceramides to understand how the varied modifications on the glycosylceramide hydroxyl groups would affect the NKT cell immune function, which also helped to design novel NKT ligands. Currently, I am more interested in clinical applications of glycosylceramides and other potential therapeutic reagents. I have developed a liposome formulation for the glycosylceramide and studied its therapeutic effects. Also, I am trying to illustrate the pharmaceutical properties of glycosylceramide and other potential therapeutic reagents by studying their *in vivo* stability, metabolism pathway and other related characteristics. (Read Zhang's article, DOI: 10.1021/cb100318z)