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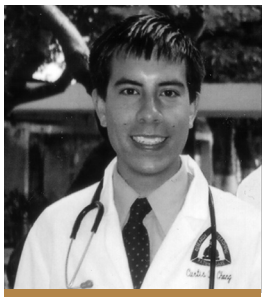
Introducing our AUTHORS



Curtis R. Chong

Current position: The Johns Hopkins University, M.D./Ph.D. candidate with Profs. Jun O. Liu and David Sullivan
Education: Harvard College, A.B. in biochemical sciences, 1998; University of Cambridge, U.K., M.Phil. in chemistry with Sir Alan Fersht, 2000
Nonscientific interests: Participating in medical relief missions overseas, human rights

My scientific interests are applying basic research to solve clinical problems. I first became interested in drug repurposing after caring for patients with HIV, malaria, and cancer in medical school. When I began my Ph.D. in pharmacology, I was shocked to discover that on average it costs $1 billion and takes 15 years to make 1 new drug. Patients with incurable diseases or those who cannot afford existing therapies cannot wait this long, and as a result, we are relentlessly testing existing drugs for new uses. (Read Chong's article on p 263.)

Jing Xu

Current position: The Johns Hopkins School of Medicine, Department of Pharmacology and Molecular Sciences, Ph.D. candidate with Prof. Jun O. Liu
Education: Peking Union Medical College, China, M.D., 2003
Nonscientific interests: I enjoy reading and traveling.

Angiogenesis is essential for the growth and metastasis of solid tumors. Antiangiogenic agents have made their way to the clinic for the treatment of cancer and many other diseases. In our lab, a number of known drugs have been discovered to possess novel antiangiogenic activities. I am most interested in using these newly discovered angiogenesis inhibitors as probes to explore the mechanisms of angiogenesis. We identified itraconazole, a widely used antifungal drug, as a new angiogenesis inhibitor. We found that human 14α-demethylase is required for endothelial cell proliferation and may mediate part of the antiangiogenic effects of itraconazole. Our data also revealed the existence of a potential new target for itraconazole. Thus, further mechanistic investigation of itraconazole and other inhibitors of angiogenesis discovered from the clinical drug library is likely to offer new insights into the regulation of angiogenesis. (Read Xu's article on p 263.)

Stephen J. Mills

Current position: The University of Bath, U.K., Department of Pharmacy and Pharmacology, postdoctoral research officer with Prof. Barry V. L. Potter, 1994–1997 and 2000–present
Education: The University of Bath, U.K., Department of Pharmacy and Pharmacology, Ph.D. in medicinal chemistry with Prof. Barry V. L. Potter, 1994
Nonscientific interests: I enjoy a healthy lifestyle, fitness, and travel. I am also an experienced wine taster and have visited a number of first-class wineries in Bordeaux, Tuscany, and the Mosel.

My interests focus on the synthesis of new tools that modulate the inositol phosphate and phosphoinositide pathways. These tools are compounds that use an aromatic, flat benzene core instead of an inositol ring and are decorated with phosphate and other functional groups. Some of these analogues can interact with proteins in the inositol phosphate and phosphoinositide pathways, such as the pleckstrin homology (PH) domain of protein kinase Bα (PKBα). We found that benzene 1,2,3,4-tetrakisphosphate can cocrystallize with and inhibit the PH domain of PKBα, although it is structurally diverse from the natural lipid headgroup. It is also a good scaffold for molecular modeling studies, and further modifications may uncover druglike compounds with the capacity to modulate PKB. (Read Mills' article on p 242.)

David Komander

Current position: The Institute of Cancer Research (London), Section of Structural Biology, Postdoctoral Fellow, Beit Memorial Fellow for Medical Research with Prof. David Barford
Education: Ruhr-Universität Bochum, Germany, Diploma in biochemistry, 2002; Medical Research Council Protein Phosphorylation Unit, University of Dundee, Scotland, Ph.D. in biochemistry with Profs. Dario Alessi and Daan van Aalten, 2005
Nonscientific interests: Diving, fishing, traveling

I seek to understand cellular signal transduction on a molecular level, and I use X-ray crystallography to obtain atomic resolution models of the involved proteins and complexes. Many signal transduction proteins are dysregulated in disease and, therefore, drug targets. Protein kinase B (PKB) is one of those, as it is aberrantly activated in many cancers. PKB binds to two small molecules: ATP in the active site of the kinase domain, and 3-phosphoinositides in the pleckstrin homology (PH) domain. Although many kinase inhibitors have been developed, targeting PH domains has been difficult. Here we describe a novel compound that binds with nanomolar affinity to the PH domain of PKB and mimics 3-phosphoinositides. Such molecules might serve as a scaffold for future drug-design efforts. (Read Komander's article on p 242.)

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Erik B. Puffer

Current position: University of Wisconsin–Madison, Paul P. Carbone Comprehensive Cancer Center, Associate Instrumentation Specialist for the Flow Cytometry Core Facility
Education: University of Massachusetts at Dartmouth, research project with Prof. Bal-Ram Singh, B.S. in chemistry, 1999; University of Wisconsin–Madison, Ph.D. in biochemistry with Prof. Laura L. Kiessling, 2007
Nonscientific interests: Cooking, running, spending time with friends and family, fantasy literature, re-upholstering furniture

My graduate research focused on examining the role of antigen valency and coreceptor engagement in B cell signaling. The majority of work performed in the field to investigate the importance of antigen structure in initiation of B cell functions has been done with antibodies or hapten-conjugated protein scaffolds. To systematically explore the issues of antigen valency in B cell signaling, we used ring-opening metathesis polymerization (ROMP) to generate a series of multivalent ligands of defined valencies. I found that the extent of signaling, degree of B cell receptor clustering, and antibody production are all influenced by antigen valency. These findings underscore the utility of polymers generated by ROMP for investigating cell signaling both *in vitro* and *in vivo*. I believe these experiments set the stage for future studies that will use multivalent ligands to illuminate the mechanisms by which B cells respond to antigens, with outcomes ranging from immunity to tolerance, and may guide the development of new therapies to treat altered immune responses. (Read Puffer's article on p 252.)

Huricha Baigude

Current position: University of Massachusetts Medical School, Worcester, Department of Biochemistry and Molecular Pharmacology, Postdoctoral Research Associate in Prof. Tariq M. Rana's group
Education: Inner Mongolia University, China, M.S. in biochemistry, 1999; Teikyo University of Science and Technology, Japan, Ph.D. in chemistry with Prof. Toshiyuki Uryu, 2004
Postdoctoral work: Kitami Institute of Technology, Japan, Department of Chemistry with Prof. Takashi Yoshida, 2004–2005
Nonscientific interests: Outdoor fitness, movies

I have been working on the synthesis of polymeric delivery agents for small molecules, peptides, and nucleic acids. My special interest is the design and synthesis of biocompatible nanomaterials for the delivery of short interfering RNA (siRNA) *in vivo*. siRNAs are triggers of RNA interference (RNAi), which holds a great promise in developing new therapeutic agents; however, efficient delivery of siRNA doses that will be clinically feasible in humans remains a big challenge. As described in our paper, a well-defined functionalized lipid nanoparticle is created to bind chemically modified siRNA, which can effectively protect it from hydrolysis by the serum enzymes and then release it in the cells. Consequently, the target gene is efficiently silenced in animals producing a desired phenotype, lowering plasma cholesterol in our studies. In addition, these nanoparticles can be further modified by peptides or other molecules to give a tissue-specific RNAi delivery agent. (Read Baigude's article on p 237.)

Rebecca A. Scheck

Current position: University of California, Berkeley, Department of Chemistry, Ph.D. candidate with Prof. Matthew B. Francis
Education: Columbia University, B.A. in chemistry, 2004
Nonscientific interests: Spending time with family, cooking, watching movies, exploring the San Francisco Bay Area

Since I began graduate school, my research has focused on the development of a site-specific protein bioconjugation strategy mediated by pyridoxal 5′-phosphate (PLP). This reaction is selective for protein N-termini and occurs under very mild conditions, so it is perfectly suited for the generation of well-defined functional protein conjugates for use in a variety of applications. In addition, this method requires no mutagenesis and can be used in conjunction with other existing techniques. It is also ideal for the modification of proteins that are otherwise difficult to modify selectively. I am very pleased that, in this paper, we have been able to demonstrate the utility of this strategy for antibody substrates. I anticipate that these advances will allow for an expansion of current methodologies, both in terms of reaction development and the accessibility of novel applications. (Read Scheck's article on p 247.)