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Introducing Our Authors

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PRIYAMVADA ACHARYA

Image courtesy of Palash Gangopadhyay.

Current position: Postdoctoral Researcher, Structural Biology Section, Vaccine Research Center, NIH, USA. Research Advisor: Dr. Peter D. Kwong

Education: Jadavpur University, B.Sc., 1991−1994; Jadavpur University, M.Sc., 1994−1996; Saha Institute of Nuclear Physics, Post-M.Sc., Biology Division, 1996−1997

Nonscientific interests: Traveling, literature, history, early childhood education, and teaching

My research at the Vaccine Research Center at NIH has focused on structural definition of HIV-1 entry. This paper describes the structure-guided discovery of a novel class of HIV-1 entry inhibitors that mimic key residues involved in the interaction of the HIV-1 envelope glycoprotein gp120 with the human cell surface receptor CCR5. Mechanistic analyses reveal that the molecular trickery that HIV-1 uses to evade antibody-mediated neutralization at this highly conserved receptor binding site also diminishes potency of these inhibitors. Yet the broad reactivity of these molecules extending as far as HIV-2 opens up possibilities of further therapeutic development against this target site. I plan to continue research in the fascinating area of HIV-1 entry with the aim of developing an effective vaccine and/or therapeutic. (Read Acharya's article, DOI: 10.1021/cb200068b)

SUPAKARN CHAMNI

Image courtesy of Supakarn Chamni.

Current position: Ph.D. student at Texas A&M University under the supervision of Prof. Daniel Romo; expected graduation in December 2011. Beginning a faculty position at Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Phamaceutical Sciences, Chulalongkorn University, Thailand in January, 2012.

Education: Thammasat University, B.S. in Chemistry, 2005; Texas A&M University, Ph.D. in Chemistry with Prof. Daniel Romo, December 2011

Nonscientific interests: Traveling, camping, snowboarding, and cooking

My research interests are interdisciplinary in nature and include organic synthesis and chemical biology. I am engaged in the total synthesis of natural products and the development of natural product derivatization methodologies for cellular probe synthesis to enable identification of cellular protein targets leading to the discovery of novel drug targets for treatment of human disease. During my Ph.D. career, I synthesized β-lactam derivatives of orlistat employing a SnCl4-promoted tandem Mukaiyama aldol-lactonization (TMAL) reaction as a key step and pursued the synthetic studies toward spongiolactone employing an intramolecular nucleophile-catalyzed aldol-lactonization (NCAL) to construct the fused-tricyclic β-lactone core. In the present work, we have developed second-generation diazo reagents with a smaller steric footprint for simultaneous arming and SAR studies of bioactive natural products via O−H insertion of alcohol-containing natural products. The described α-trifluoroethyl diazo reagents (HTFB) showed clear differences in the IL-2 reporter assay with FK506 derivatives and provided greater retention of biological activity in a hMetAP2 proliferation assay of fumagillol derivatives compared to the first generation p-bromophenyl diazo reagents (HBPA). (Read Chamni's article, DOI: 10.1021/cb2002686)

SHUN-JIA CHEN

Image courtesy of Shun-Jia Chen.

Education: National Chaiyi University, B.S. in Life Science with Prof. Being-Sun Wung, 2005; National Central University, M.S. in Life Science with Prof. Chien-Chia Wang, 2007; National Central University, Ph.D. in Life Science with Prof. Chien-Chia Wang, 2011

Nonscientific interests: Sports, movies, board games, and music

My Ph.D. research focused on translational mechanism in yeast. First, we studied the non-AUG initiation. Our results showed that the translation efficiency of non-AUG initiation is about 30% (or less) relative to AUG initiation. In addition, it appeared that a non-AUG initiator codon is much more sensitive to its sequence context than AUG initiator codon is. Furthermore, AAA (the nucleotides at position-3 to -1 relative to the initiator) is the most favorable sequence context. Second, we focused on glycyl-tRNA synthetase (GlyRS) genes, *GRS1* and *GRS2*. Unlike *GRS1* is a bifunctional gene, *GRS2* is a pseudogene-like gene. We found that activity of GlyRS2 can be rescued by yeast nonspecific tRNA binding domain, Arc1p. These findings highlight not only the structural integrity of the pseudogene-encoded enzyme but the necessity of obtaining an auxiliary tRNA-binding domain as well, in order to maintain the function of yeast tRNA sythetase. (Read Chen's article, DOI: 10.1021/cb200240a)

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YONGJUN DANG

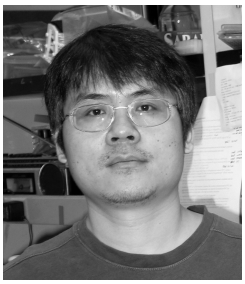

Image courtesy of Yongjun Dang.

Current position: Research Associate at Department of Pharmacology& Molecular Sciences, Johns Hopkins University School of Medicine

Education: Northwest Agriculture University in China, B.S., 1997; Northwest A&F University in China, M.S., 2000; Fudan University in China, Ph.D. with Prof. Long Yu, 2000−2003; Johns Hopkins University School of Medicine, Postdoctoral Fellow with Prof. Jun Liu, 2004−2009

Nonscientific interests: Playing with my daughters, movies, and Ravens football

My research is focused on the elucidation of the mechanisms of action of the bioactive small molecules. So far I have been involved in the mechanistic studies of several natural products, including pateamine A, mycalamide B, cycloheximide, triptolide and lactimidomycin. In collaboration with Dr. Romo's group at Texas A&M University, we have identified eukaryotic translation initiation factor (eIF)-4A as the target of pateamine A using a biotin-pateamine A conjugate. To facilitate the structure−activity relationship studies of complex natural products, we develop the second generation of the method in which *p*-bromophenoyl is replaced with a smaller steric trifluoroethyl group that allows for the direct O−H insertion of a probe or substituent into natural products. Using several natural products, we confirmed the advantages of this improved method. (Read Dang's article, DOI: 10.1021/cb2002686)

JOSEPH DAVIS

Image courtesy of Theresa Wang.

Current position: Ginkgo BioWorks, Inc., Boston, MA, Lead Scientist

Education: Massachusetts Institute of Technology, Ph.D. Department of Biology, 2005−2010, Advisor Robert Sauer, 2010; University of California at Berkeley, B.A. Department of Computer Science, 2000−2003, Advisor Richard Karp, 2003; University of California at Berkeley, B.S. Department of Biological Engineering, 2000−2003, Advisor Michael Marletta, 2003

Nonscientific interests: Climbing, spearfishing, and soccer

My graduate research at MIT focused on the development of molecular tools to manipulate biological systems. Currently, I am interested in applying the tools I have built to both engineer biology and to study natural systems. In the accompanying paper, we describe a novel, small-molecule controlled protein degradation system for use in *E. coli*. The system, based on the ClpXP protease and SspB adaptor, allows researchers to specifically degrade protein targets of interest with great temporal control. Building these tools has helped refine our models of adaptor-mediated proteolysis and has resulted in a system that is highly modular and should be straightforward to port into other bacteria. We hope that these proteolysis-based techniques will prove useful in applications ranging from loss-of-function studies to metabolic engineering. (Read Davis' article, DOI: 10.1021/cb2001389)

ANAT FRYDMAN-MAROM

Image courtesy of Anat Frydman-Marom.

Current position: Tel Aviv University, Department of Molecular Microbiology and Biotechnology, Postdoctoral Researcher under the supervision of Prof. Ehud Gazit.

Education: Tel Aviv University, B.Sc. major in Biology, 2003; Tel Aviv University, M.Sc. in the Department of Molecular Microbiology and Biotechnology under the supervision of Prof. Ehud Gazit, 2005; Tel Aviv University, Ph.D. in the Department of Molecular Microbiology and Biotechnology under the supervision of Prof. Ehud Gazit, 2011.

Nonscientific interests: Traveling, reading, music, and movies.

My research focuses on protein assemblies that appear to play a crucial role in memory impairment in many cases of neurodegenerative diseases. Here, we describe a novel rationally designed inhibitor, based on a natural opioid endomorphin peptide which incorporates aromatic residues and a β-breaker motif. We investigate the Aβ-oligomerization inhibition by the native endomorphins in comparison to the rationally designed analogue, which includes the remarkably efficient β-breaker α-aminoisobutyric acid (Aib). We provide a very comprehensive description of the in vitro Aβ aggregation inhibition process by these compounds, as well as the interaction of Aib-1 with Aβ polypeptide using atomistic molecular dynamic simulations and high-resolution NMR data. Moreover, we showed that Aib-1 can prevent the toxicity of Aβ toward neuronal PC12 cells and can markedly rectify reduced longevity of an Alzheimer's disease fly model. (Read Frydman-Marom's article, DOI: 10.1021/cb200103h).

MARTIN GRÄBER

Image courtesy of Martin Gräber.

Current position: University of Leipzig, Germany, Department of Organic Chemistry, Postdoctoral Researcher with Thorsten Berg

Education: University of Regensburg, Germany, Prediploma in Biology, 2003; Ecole Superieure de Biotechnologie, Strasbourg, France, Diploma in Biotechnology, 2006; Max Planck Institute of Biochemistry, Martinsried, Germany, and University of Leipzig, Germany, Ph.D. in Chemical Biology with Thorsten Berg, 2011.

Nonscientific interests: Music, playing the guitar, and mountain biking

Research in my Ph.D. studies has focused on the modulation of protein−protein interactions with small molecules. The inhibition of protein−protein interactions is an exciting new approach by which to target protein functions involved in healthy and diseased states. However, owing to the general lack of suitable starting points, rational inhibitor design for this

target class is difficult. Since nature has provided a large number of good lead structures for drug discovery for more traditional targets, we wondered whether nature's prominent role would also hold true for phosphorylation-dependent protein−protein interactions. By screening of chemical libraries containing a large proportion of natural products or derivatives thereof I identified two phosphate prodrugs with documented prior clinical use as selective inhibitors of two unrelated antitumor targets. Based on our results, we propose the phosphorylation of appropriately chosen natural products as an initial step for the identification of ligands of phosphorylation-dependent protein−protein interactions. (Read Gräber's article, DOI: 10.1021/cb2001796)

ANDREW KALE

Image courtesy of Stephanie Farkas.

Current position: University of California at San Diego, Scripps Institution of Oceanography, Ph.D. candidate with Prof. Bradley Moore

Education: University of Minnesota, B.S. in Biology, 2005

Nonscientific interests: Traveling, reading, hiking, and water sports

My graduate research focuses on understanding the enzymatic processes of secondary metabolism in marine actinobacteria. Natural product biosynthesis presents opportunities to uncover unique enzymology. By understanding the biosynthetic pathways of these compounds, we may exploit the enzymes for use as *in vitro* biocatalysts or manipulate the genetic instructions *in vivo* to develop structural analogs. Outside of these biosynthetic pathways, additional biochemical modifications may also be needed at the organismal level to cope with such specialized metabolism. The study published here examines how a potent proteasome inhibitor can be produced by an actinobacteria which utilizes the target protein in primary metabolism. This discovery may correlate to clinical drug resistance in humans where proteasome inhibitors are used in the treatment of multiple myeloma and also facilitate the discovery of new natural proteasome inhibitors. (Read Kale's article, DOI: 10.1021/cb2002544)

CASE MCNAMARA

Image courtesy of Stacey Winters.

Current position: 2007-present, Postdoctoral Fellow, Department of Infectious Disease, Genomics Institute of the Novartis Research Foundation (GNF), Advisor: Elizabeth A. Winzeler

Education: University of California, San Diego, Ph.D. in Chemistry & Biochemistry, 2006; California State University, San Marcos, B.S. in Chemistry, 2000

Nonscientific interests: Everything football, running, movies, and reading

Due to my strong interest in infectious disease and drug discovery, I joined Elizabeth Winzeler's lab as a postdoctoral fellow to study *Plasmodium falciparum*, the causative agent of human malaria. To assist in target identification of uncharacterized antimalarial compounds, I use a chemical genetics approach. Small-molecule inhibitors of interest are used to evolve drug-resistant parasites. A subsequent comparative, whole-genome analysis between the drug-resistant and drug-sensitive parasite lines are performed with a custom DNA microarray to reveal acquired genomic differences. Frequently, resistance-conferring mutations are acquired in the molecular target of the antimalarial compound, thus providing a "genetic foothold" for follow-up experiments. Here, in collaboration with Drs. Peter Schultz and Tae-gyu Nam, we describe the successful application of this approach to identify cytochrome *b* as the target of decoquinate. Read McNamara's article, DOI: 10.1021/cb200105d)

JOSHUA PRICE

Image courtesy of Levi Price.

Current position: Assistant Professor in the Department of Chemistry and Biochemistry at Brigham Young University

Education: Brigham Young University, B.S. in Biochemistry, 2003; University of Wisconsin-Madison, Ph.D. in Chemistry with Prof. Samuel H. Gellman, 2008; The Scripps Research Institute, NIH postdoctoral fellow with Prof. Jeffery W. Kelly, 2008−2011

Nonscientific interests: Playing with my four sons, swimming, landscaping, reading, playing the organ and piano

In Sam Gellman's group at Wisconsin, I developed a strategy for generating unnatural tertiary and quaternary structures by replacing natural amino acid residues in helix-bundle assemblies with homologous β-amino acids. In Jeff Kelly's group at Scripps, I discovered and characterized a new protein side-chain/carbohydrate interaction motif called the enhanced aromatic sequon, which makes asparagine glycosylation of certain reverse turns thermodynamically stabilizing to beta-sheet proteins. In this paper, we show that PEGylation of a reverse turn can also stabilize proteins, most likely via an excluded volume effect, whereas N-glycosylation of the enhanced aromatic sequon stabilizes proteins via native-state protein-glycan interactions. We ultimately hope to develop engineering guidelines for stabilizing proteins by PEGylation in both research and pharmaceutical settings. (Read Price's article, DOI: 10.1021/cb200277u)

CHRIS RATH

Image courtesy of Ryan Andresen.

Current position: University of California at San Diego, Skaggs School of Pharmacy and Pharmaceutical Sciences, Post-Doctoral Researcher with Prof. Pieter Dorrestein

Education: University of Michigan, Ph.D. in Chemical Biology, 2011; University of California at Santa Cruz, B.S. in Biochemistry and Molecular Biology, 2003.

Nonscientific interests: Photography, snowboarding, cycling, live/electronic music, and technology-based art

My research is centered on exploring the chemistry of host−symbiont interactions with mass spectrometry. As an undergraduate

in Prof. Phil Crews' laboratory, I applied mass spectrometry and NMR to elucidate novel natural products from sponge-derived fungi. After a stint in industry at PDL BioPharma, I continued my training under the mentorship of Prof. David Sherman and Prof. Kristina Håkansson, where I investigated natural product biosynthesis with FTICR mass spectrometry. My recent paper illustrates how this toolkit can be applied to characterize biosynthesis in a challenging host-symbiont system. Currently, I am developing mass spectrometry for chemical imaging of host-symbiont metabolic exchange in the Dorrestein laboratory. My long-term goal is to establish an independent research program to characterize medicinally relevant host-symbiont systems. (Read Rath's article, DOI: 10.1021/cb200244t)

SANDER VAN KASTEREN

Image courtesy of Sander van Kasteren.

Current position: Netherlands Cancer Institute, Amsterdam, The Netherlands. Veni Research Fellow with Huib Ovaa

Education: University of Edinburgh, U.K., MChem in Organic and Medicinal Chemistry; University of Oxford, DPhil in Carbohydrate Chemistry; University of Dundee, Henry Wellcome Postdoctoral Fellowship in cell biology and immunology

Nonscientific interests: Music, rock climbing, kick-boxing, and reading

The research conducted during my Henry Wellcome postdoctoral fellowship focused on the creation of an inhibitor of all three families of endosomal proteases in an attempt to overcome the functional redundancy that is found when specific endosomal proteases are knocked out. Our single inhibitor could reduce endosomal protease activity nearly completely. By targeting all proteases simultaneously we found a striking stabilizing effect of the EGF-receptor after EGF-stimulation, leading to EGFR still being present and signaling up to 2 h after stimulation. We also looked at the effect of our endosomal protease inhibition on the processing of antigens and found that proteolytically destabilized antigens, which are presented poorly to the immune system, could be protected to the level of their native, well-presented, analogs. (Read van Kasteren's article, DOI: DOI: 10.1021/cb200292c)

ANNELISE E. VON BERGEN GRANELL

Image courtesy of Annelise E. von Bergen Granell.

Current position: Second year Master's student (Part time) at New York University (NYU). Full time Researcher at New York University Langone Medical Center (NYULMC), Department of Anesthesiology, with Dr. Esperanza Recio-Pinto.

Education: Universidad Central de Venezuela at Caracas-Venezuela, B.Sc. Biology, Specialty in Cell Biology, 2008; New York University, M.Sc. Candidate in Biology, Research Advisor: Dr. Esperanza Recio-Pinto.

Nonscientific interests: Spending time with my family and friends, photography, bike riding, and traveling.

My research focus consists of studying how sialilation contributes to changes in neuronal excitability and animal behavior in *Drosophila melanogaster* (*Dm*). Our collaborators developed a mutant that lacks sialic acid synthetase (*Dm*SAS). This mutant displays abnormal phenotypes, suggesting that sialilation modulates behavior and lifespan. By labeling newly synthesized sialo-glycoconjugates with covalently attached fluorophores we showed that indeed sialic acid (SA) incorporation was eliminated in the *Dm*SAS mutant and no redundant SA biosynthetic activity exists in *Dm*. In mammals abnormalities in sialilation can lead to disease. Complete knockout of SA in mammals is fatal; hence the role of sialilation has been mostly limited to cells in culture. Our results indicate that *Dm* is a valid whole animal model to study sialilation including behavior and neuronal excitability in native neurons. (Read von Bergen Granells' article, DOI: 10.1021/cb200238k)