ACS chemical biology

Introducing Our Authors

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ISABELLE BECHER

Image courtesy of Isabelle Becher.

Current position: Ph.D. candidate, Mass Spectrometry department of Cellzome GmbH, a GSK company, Heidelberg; Research advisors: Marcus Bantscheff and Carsten Hopf.

Education: University of Applied Sciences Mannheim, Diploma in Biochemistry, 2010.

Nonscientific interests: Books, baking, spending time with family and friends.

My research interests include the understanding of cellular potency and selectivity of bioactive compounds. Toward my Ph.D., I use chemoproteomics methods such as *in vitro* assays and analysis of post-translational modifications, to study how *in vitro* potencies translate into cellular effects. An important factor for differences between *in vitro* and cellular situations is the presence of cosubstrates, like ATP for kinases. In this work we used our established Kinobeads technology to determine the potencies for the nucleotide cosubstrates ATP, ADP, and GTP and the divalent metal ions Mg^{2+} and Mn^{2+}. The affinity values determined in this system were largely consistent across two cell lines, ranging from low micromolar to millimolar. The results allow a more accurate prediction of cellular effects from inhibitor selectivity profiles. (Read Becher's article, DOI: 10.1021/cb3005879)

AARON M. BENDER

Image courtesy of Blake R. Peterson.

Current position: University of Kansas, Lawrence, Dept. of Medicinal Chemistry, Director, The Center of Molecular Analysis of Disease Pathways (CMADP) Synthetic Molecular Probes Core Facility.

Education: University of Wyoming, B.S. Biology, 1999; University of Wyoming, Ph.D. Molecular Biology, 2006, Advisor: David Fay; Mayo Clinic, Postdoctoral Fellow, 2006–2009, Advisor: Robert Jenkins; University of Kansas, Postdoctoral Fellow, 2009–2012, Advisors: Blake Peterson, Brian Ackley.

Nonscientific interests: Live music, good food, mountain biking, movies, fly fishing.

My research background has transitioned over the years from the fields of developmental and cancer genetics to chemical biology. As a postdoctoral fellow working in the Peterson and Ackley laboratories at the University of Kansas, I used novel pH-sensitive fluorescent probes to study ion trafficking in the nematode worm *Caenorhabditis elegans*. In my current role as Director of the Synthetic Molecular Probes Core Facility at KU, I assist investigators in the use of fluorescent small molecules to probe a wide range of biological processes in model organisms. To this end, we develop fluorescence video microscopy methods to examine the pharmacodynamics and pharmacokinetics of fluorescent compounds in living *C. elegans* and zebrafish (*Danio rerio*). By integrating synthetic chemistry with organismal biology, we create novel molecular probes that allow investigation of how genetic mutations and synthetic small molecules affect biological pathways. (Read Bender's article, DOI: 10.1021/cb300396j)

YIRUI GUO

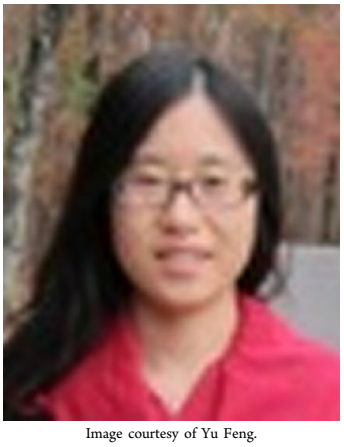

Image courtesy of Yu Feng.

Current position: Ph.D. candidate at UT Southwestern Medical Center, Department of Biophysics; Advisor: Prof. Kevin. H. Gardner.

Education: Sichuan University, B.S. in Chemistry, 2008.

Nonscientific interests: Swimming, traveling, reading, spending time with cats.

My research project focuses on mechanistic studies of a new group of transcriptional coactivators (coiled coil coactivators (CCCs): TACC3, TRIP230, CoCoA), involved in cancer development and progression. Normally, these coactivators

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play an essential role in the HIF hypoxia response, directly interacting with the ARNT subunit of HIF in a novel and promoter-specific way. However, misregulation by overexpression or activating fusions is sufficient for the development of multiple cancers. In the present article, we described two different parallel ways to regulate the ARNT/TACC3 interaction by small molecules via direct or indirect mechanisms. In light of connection between the CCCs in HIF signaling, these artificial ligand tools are promising to examine the linkage between different CCC-containing pathways and may offer a novel route to blocking cancer formation and progression. (Read Guo's article, DOI: 10.1021/cb300604u)

EMILIO LENCE

Image courtesy of Emilio Lence.

Current position: University of Santiago, Santiago de Compostela, Center for Research in Biological Chemistry and Molecular Materials (CIQUS), Postdoctoral student with Prof. Concepción González-Bello, Spain.

Education: University of Santiago de Compostela, Spain, B.S. in Chemistry and Ph.D. in Organic Chemistry with Profs. Concepción González-Bello and Luis Castedo.

Nonscientific interests: Science fiction, 007, cycling.

As a Ph.D. candidate I worked on solid phase synthesis, and after my Ph.D. I started working on computational chemistry. As a part of Prof. Concepción González-Bello's group, my work focuses on the study of the interactions between small molecules and enzymes. Our group is very much interested in the development of inhibitors of the shikimic acid pathway for the discovery of new drugs for the treatment of bacterial infections, such as tuberculosis and gastric and duodenal ulcers caused by *Helicobacter pylori*, etc. In our article (DOI: 10.1021/cb300493s), we studied the loop differences of the type II Dehydroquinase from *M. tuberculosis* and from *H. pylori* by molecular dynamics simulations in an effort to understand the significant inhibition potency differences observed between some of the competitive reversible inhibitors and also to obtain more information about the possible movements of the loop. (Read Lence's earlier article, DOI: 10.1021/jm030987q)

LECH-GUSTAV MILROY

Photo courtesy of Katja Petkau-Milroy.

Current position: Assistant Professor, Chemical Biology, Technical University Eindhoven, The Netherlands.

Education: University of Edinburgh, Scotland, MChem, Research Advisor: Prof. Dr. Michael Greaney, 2004; University of Cambridge, England, Ph.D. Synthetic Organic Chemistry, 2008, Research Advisor: Prof. Dr. Steve V. Ley, CBE FRS; Max-Planck-Institute for Molecular Physiology, Dortmund, Germany, Alexander von Humboldt Fellowship, Chemical Biology, Research Advisors: Prof. Dr. Herbert Waldmann and Prof. Dr. Hans-Dieter Arndt, 2008−2010; Technical University Eindhoven, The Netherlands, Postdoc, Chemical Biology, Research Advisor: Prof. Dr. Luc Brunsveld, 2010−2012.

Nonscientific interests: Guitar, traveling, cycling.

The ubiquitous eukaryotic adapter protein 14−3−3 is an exciting target for chemical biologists as there are currently very few small molecule modulators − inhibitors or stabilizers − of this physiologically significant target, and thus plenty of room for innovation. The fungal secondary metabolite fusicoccin (FC) is a unique example of a 14−3−3 modulator, which stabilizes the 14−3−3 protein−protein interaction (PPI) with the proton pump PMA2. This serves as a model system to devise small molecule stabilizers of other pathophysiologically relevant 14−3−3 PPIs, e.g., with FOXO or CFTR. In this regard, the total synthesis, semisynthesis, or biosynthesis of fusicoccin-derivatives or high throughput screening are expected to deliver a toolbox of small molecules with the capacity to program 14−3−3 ternary complex formation to match the intended therapeutic target. (Read Milroy's article, DOI: 10.1021/cb300599t)

JOSÉ OTERO

Image courtesy of José Otero.

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Current position: Postdoctoral researcher at University of Santiago de Compostela, Department of Biochemistry and Molecular Biology, Spain.

Education: University of Santiago de Compostela, Spain, B.S. in Chemistry, 2001 and Ph.D. in Chemistry, 2007; Institute of Biologie Structurale, France, Postdoctoral Research Fellow, 2010; Leiden Institute of Chemistry, The Netherlands, Postdoctoral Research Fellow, 2011.

Nonscientific interests: Traveling, spend time with family and go to basketball and motorsport events.

Formed in Organic Synthesis during my Ph.D., my postdoctoral work is focused in the Structural Biology field, more specifically in protein and peptide crystallography and their structural determination by X-ray diffraction. Protein crystallography is a wonderful and challenging technique. We have to go in opposite direction to the entropy and artificially create ordered systems from chaotic mixtures of molecules in solution. Then we employ spectacular facilities such as the Synchrotrons for measuring the X-ray diffraction that our crystals are able to produce and use sophisticated software to decipher the structural information codified in these tangle of points accurately arranged in the diffraction images. (Read Otero's article, DOI: 10.1021/cb300493s)

ANTONIO PEÓN

Image courtesy of Antonio Peón.

Current position: Ph.D. student at University of Santiago de Compostela, Center for Research in Biological Chemistry and Molecular Materials (CIQUS), Spain.

Education: University of Santiago de Compostela, Spain, B.S. in Chemistry, 2008 and Ph. D. Candidate in Organic Chemistry; short stays as FPU fellow in the University of Zürich (Switzerland) and in the University of Alcalá de Henares (Spain).

Research advisors: Profs. Concepción González-Bello and Luis Castedo.

Nonscientific interests: Sports, gardening, photography, hiking, trekking, traveling, cooking and tropical fish.

My Ph.D. is focused on the design and synthesis of new inhibitors of the third enzyme of the shikimic acid pathway for the discovery of new antibiotics by using diverse computational tools. The type II Dehydroquinase is an essential enzyme in important pathogenic bacteria such as *Mycobacterium tuberculosis* and *Helicobacter pylori*. I have carried out computational studies to understand the role of the essential residues involved in the enzymatic mechanism and the dynamic behavior of the enzyme in the presence of competitive reversible inhibitors. (Read Peon's article, DOI: 10.1021/cb300493s)

KENNY BRAVO-RODRIGUEZ

Image courtesy of Kenny Bravo-Rodriguez.

Current position: Max-Planck-Institut für Kohlenforschung (Theory Department), Mülheim an der Ruhr, Germany: Ph.D. Student in the group of Elsa Sanchez-Garcia since October 2011, fellowship awarded by the Fonds der Chemischen Industrie.

Education: Silver medalist at the 35th International Chemistry Olympiads, Greece, 2003. Universidad de La Habana, Cuba, Summa Cum Laude Diploma in Chemistry, 2009.

Nonscientific interests: Chess, music, traveling, hiking, winter sports.

My Ph.D. research focuses on the theoretical investigation of molecular interactions in biologically relevant systems. One of these systems is the sixth acyltransferase domain of the enzyme 6-deoxyerythronolide B Synthase, currently used to produce the antibiotic erythromycin. Extensive experimental genetic manipulation of the enzyme expressed in its natural producer bacteria *Saccharopolyspora erythraea* combined with our computational models of wild type and mutants with the natural substrate (2*S*)-methylmalonyl-CoA provided a better understanding of the key interactions controlling the action of the sixth acyltransferase domain. Furthermore, our theoretical models allowed us to successfully predict which single point mutations of the whole multienzyme complex would result in the incorporation of a non-natural substrate. (Read Bravo-Rodriguez's article, DOI: 10.1021/cb300505w)

USCHI SUNDERMANN

Image courtesy of Susanna Kushnir.

Current position: Technical University of Dortmund, Germany: postdoctoral researcher in the group of Frank Schulz since October 2012.

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Education: Athlone Institute of Technology, Ireland, B.Sc. in Toxicology; University of Applied Science Emden, Germany, Dipl.-Ing. (FH) in Biotechnology/Chemical Engineering; doctoral studies at the Technical University of Dortmund and Max Planck Institute of Molecular Physiology, Germany, research advisor Frank Schulz, Predoctoral fellowship of the foundation of the German chemical industry, Fellow of the International Max Planck Research School in Chemical Biology.

Nonscientific interests: Horseback riding, reading, traveling.

My graduate studies in the laboratory of Frank Schulz focus on the exploration and manipulation of the substrate specificity of type I polyketide synthases, the central enzymes in polyketide biosynthesis. The goal is to explore knowledge-driven strategies toward the biosynthetic derivatization of these natural products based on site-directed mutagenesis of the giant polyketide synthase enzymes. For example we engineered these enzymes toward natural products with altered redox patterns and thus different bioactivities. Here we develop a model for substrate recognition and turnover by an acyltransferase domain and devise a mutagenesis scheme to change its substrate specificity. We construct an acyltransferase variant which catalyzes the incorporation of a fully synthetic and not biosynthetically known building block analog into the antibiotic erythromycin. This building block carries an orthogonal functional group, opening the way toward straightforward semisynthetic elaboration of polyketides in a chemo-microbial synthesis toward novel drug candidates. (Read Sundermanns article, DOI: 10.1021/cb300505w)

BYUNG-KUK YOO

Image courtesy of Byung-Kuk Yoo.

Current position: California Institute of Technology, Physical Biology Center for Ultrafast Science and Technology, Post-doctoral scholar in Dr. Ahmed Zewail's group since 2012.

Education: Korea University, B.S. in Chemistry, 2004; Seoul National University, M.S. in Physical Chemistry, 2006; Ecole Polytechnique, Ph.D. in Biophysics, 2010, Advisor: Dr Michel Negrerie.

Nonscientific interests: Hiking, music and movies.

My research interests are focused on structural dynamics and time-resolved spectroscopy of proteins. My Ph.D. research was focused on the study of various allosteric heme proteins using transient absorption and Raman spectroscopy toward the understanding of fundamental biological mechanisms. The main protein was the endogenous NO-receptor (soluble guanylate cyclase, sGC), and I investigated its activation and deactivation mechanisms. I also studied the synergistic action of carbon monoxide (CO) on sGC with the allosteric activator BAY 41-2272 . In the present article, we tried to capture a proof of allosteric changes in sGC and NO-sensors. We recorded in the very broad time range from 1 ps to 1 s the dynamics of the interaction of CO binding to full length sGC, to its isolated heme domain β1(200) and to the homologous bacterial NO-sensor from *Clostridium botulinum*. Observing the changes in kinetics induced by BAY 41-2272 in both proteins validated the method and confirmed our hypothesis. I am currently working on time-resolved electron diffraction. (Read Yoo's article, DOI: 10.1021/cb3003539)