ACS chemical biology

Introducing Our Authors

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Image courtesy of Simon Becker.

SIMON BECKER

Current position: Graduate student pursuing a M.S. in Physics at the University of Bremen, writing the thesis in the Ultrafast-Nanooptics group of Prof. Dr. Lienau, University of Oldenburg

Education: University of Bremen, Germany, B.S. in Physics, 2009

Nonscientific interests: Bird watching, running, traveling, photography

My research interest in the Ultrafast-Nanooptics group at the University of Oldenburg is focused on photophysical investigations of biophysical specimens. In this context I am currently building a microscope for single molecule spectroscopy. In our paper, we carried out systematic time-resolved fluorescence studies to investigate conformational changes in the neuronal Ca^{2+} sensor protein GCAP2. It plays an important role in signal transduction in vertebrate photoreceptor cells. By means of fluorescence lifetime and rotational anisotropy measurements on the dye-labeled protein we show clear correlations between Ca^{2+} concentration and the dynamics of the protein−dye complex. (Read Becker's article, DOI: 10.1021/cb3000748)

Image courtesy of Aya Klein-Borgert.

ANDREW BORGERT

Current position: Independent Scientific Consultant

Education: University of Minnesota, B.S. Physics, B.S. Astrophysics, 2003; University of Minnesota, Ph.D. Medical Physics, 2008, Advisor: David Live, Ph.D.; Department of Psychiatry and the Center for Magnetic Resonance Research, University of Minnesota, Postdoc, 2008−2011, Mentor: Kelvin Lim, M.D.

Nonscientific interests: Spending time with my wife and children, hiking, astronomy, reading

My scientific interests span the entire range of natural scale, from astrophysics to molecular structure and molecular recognition events. I am particularly interested in projects that take a wide view of a subject and meld multiple lines of inquiry into a coherent picture. My work with Dr. David Live is an excellent example of this type of scientific endeavor, bringing together structural data derived from high resolution NMR experiments with carbohydrate microarray data to form a better understanding of the relationship between glycoprotein structure and recognition events. My recent postdoctoral work with Dr. Kelvin Lim continued this theme, combining data on brain metabolite concentrations from *in vivo* MR spectroscopic data with clinical and behavioral data to investigate the relationship between neurochemistry, drug addiction, and depression. (Read Borgerts' article, DOI: 10.1021/cb300076s)

Image courtesy of Lubos Stepanek.

AMY GRUNBECK

Current position: Ph.D. student, Rockefeller University, Tri-Institutional Training Program in Chemical Biology, Advisor: Thomas P. Sakmar

Education: Dickinson College, B.S. Chemistry, 2007

Nonscientific interests: Distance running, traveling with a focus on outdoor activities

G protein-coupled receptors (GPCRs) represent the most common class of therapeutic drug targets, but precisely how GPCR ligands modulate cellular signaling pathways are not well understood. My Ph.D. project has been to develop a targeted photo-cross-linking strategy to study the chemical determinants of binding interactions in GPCR-ligand complexes. I have employed an amber stop codon suppression strategy to introduce genetically a photo-cross-linker moiety at a specific location in an expressed GPCR. I focused on the chemokine receptors CXCR4 and CCR5, which are HIV-1 coreceptors. Earlier I identified sites in CXCR4 that were in close proximity to the binding site of a peptide called T140. Most recently I applied targeted photo-cross-linking to identify the binding site of an FDA-approved small molecule HIV-1 entry inhibitor, maraviroc, on CCR5. (Read Grunbeck's article, DOI: 10.1021/cb300059z)

MIN GUO

Current position: Ph.D. candidate at Department of Chemistry and Biochemistry, University of Maryland, College Park with Prof. Herman O. Sintim.

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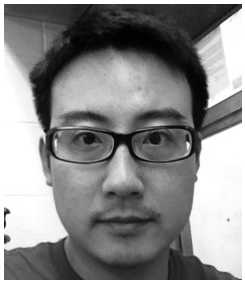
Image courtesy of Min Guo.

Education: Nanjing University, M.S. in Organic Chemistry, advisor Prof. Gui Yin, 2009; Nanjing University, B.S. in Chemistry, 2006.

Nonscientific interests: Weightlifting, bodybuilding, boxing and MMA

My research in Prof. Sintim's group is multidisciplinary. I started with developing methodology in C−H insertion reactions to obtain tertiary and quaternary stereocenters, which are still challenging in organic synthesis. Now, I am more interested in the interface of chemistry and biology, using tools of organic chemistry to synthesize biological active molecules, such as analogues of novel antibiotic platensimycin and agonists/antagonists of AI-2 signaling molecules. It is promising to develop selective quorum sensing quenchers as the trend of next generation antibiotics. (Read Guo's article, DOI: 10.1021/cb200524y)


Image courtesy of Eric Horowitz.

■ ERIC D. HOROWITZ

Current position: University of North Carolina at Chapel Hill, Gene Therapy Center, Postdoctoral researcher since May 2009, Advisor Prof. Aravind Asokan.

Education: The Pennsylvania State University in State College, PA, B.S. in Chemistry, 2003; Georgia Institute of Technology in Atlanta, GA, Ph.D. in Analytical Chemistry with Prof. Nicholas V. Hud, 2009

Nonscientific interests: Rock climbing, hiking, reading science fiction, playing board games, and watching movies

My graduate work was primarily focused on how the interactions between small molecules and nucleic acids affect nucleic acid assembly, structure, and dynamics. Findings were used to build an understanding of the origin of genetic material and transfer of genetic information on the primitive earth. From there I chose to focus on studying structure/function relationships in viral capsids. Specifically, my postdoctoral work at the UNC Gene Therapy Center has focused on how I can modulate adeno-associated viral infection by chemical modification of the capsid protein surface. In this article we have used site-specific tyrosine cross-linking to understand a critical step in the AAV infection pathway. Cross-linking effectively stitches the capsid, which prevents the exposure of a phospholipase domain required for endosomal escape and nuclear trafficking. (Read Horowitz's article, DOI: 10.1021/cb3000265)


Image courtesy of Heiko Kollmann.

■ HEIKO KOLLMANN

Current position: Graduate student pursuing Ph.D. at the University of Oldenburg in the Ultrafast-Nanooptics group of the Physics Department under supervision of Prof. Dr. Lienau.

Education: University of Oldenburg, Germany, B.S. in Physics, 2008;University of Oldenburg, Germany, M.S. in Physics, 2011

Nonscientific interests: Music, sports, movies

My main research interest lies in the field of single molecule spectroscopy and single nanoparticle spectroscopy. In my Ph.D. work, I want to study the dipole−dipole coupling dynamics and the interaction between excitons and plasmons in hybrid particles comprised of metal and semiconductor nanostructures. In my more recent work in collaboration with Prof. K.-W. Koch, I investigated the conformational change of the protein GCAP2 by site specific labeling with a fluorescent dye Alexa647 and by monitoring its fluorescence dynamics. GCAP2 is a Ca^{2+}-sensing protein which regulates the membrane bound guanylate cyclase in the vertebrate retina. The activity of GCAP2 is triggered by the change of Ca^{2+} concentration in its environment and goes along with a conformational change of the protein. Our investigation of the fluorescence and anisotropy decay dynamics of Alexa647 showed some first evidence for a piston-like movement model for the conformational change of GCAP2. (Read Kollmann's article, DOI: 10.1021/cb3000748)


Image courtesy of Jaime Noguez.

■ JAIME NOGUEZ

Education: Postdoctoral Fellow University of Florida, Advisor: Professor Rebecca Butcher; University of South Florida, Ph.D. Organic Chemistry, Advisor: Professor Bill Baker, May 2010; Sweet Briar College, B.S. Chemistry, Virginia, May 2004

Nonscientific interests: Music, traveling, reading, spending time with my family

My Ph.D. work in natural products chemistry allowed me to easily transition into my postdoctoral research at the University

of Florida involving the bioassay-guided fractionation of crude extracts from entomopathogenic nematodes. This type of fractionation allows for the isolation and structure elucidation of small-molecule chemical cues relevant in signaling. One facet of this research is the development of biological assays that provide information about the chemical nature of these cues as well as a better understanding of the interactions within the bacterium-nematode-insect tripartite system. This paper is the first report of ascaroside pheromones as important regulators of development in a parasitic nematode species and these studies may facilitate the development of chemical agents that can be used to control them. (Read Noguez's article, DOI: 10.1021/cb300056q)

Image courtesy of Yu Wang.

YU WANG

Current position: Research Associate with Dr. James A. Thomson at the Morgridge Institute for Research.

Education: University of Science and Technology of China, B.S. in Biology, 2004; Harvard University, Ph.D. in Chemistry and Chemical Biology, 2010; Harvard University, postdoctoral fellow in Stem Cell and Regenerative Biology, 2010−2011.

Nonscientific interests: Traveling, reading, and movies

My graduate and postdoctoral research with Dr. Andrew P. McMahon and Dr. Lee L. Rubin at Harvard University focused on pharmacological modulation of the Hedgehog pathway at its central stage, the primary cilium. We primarily pursued a better understanding of the mechanism of action of Smoothened, the principle therapeutic target of Hedgehog signaling, accumulation of which in the primary cilium is a critical regulatory event in the pathway. In collaboration with the lab of Dr. Christopher T. Walsh, we first applied a novel post-translational labeling technique, phosphopantetheinyl transferase labeling, and demonstrated that ciliary Smoothened mainly originates from an intracellular source. Meanwhile, we observed a surprising divergence of Smoothened ciliary translocation and its activation by characterizing modulation of Smoothened by various small molecule agonists and antagonists. As an antagonist, cyclopamine induces a ciliary accumulation of Smoothened similar to that induced by Hedgehog ligand and several Hedgehog agonists, whereas other antagonists abrogate Smoothened ciliary accumulation. The action of promoting Smoothened ciliary accumulation correlates with prolonged hypersensitivity to pathway stimulation after drug removal, raising potential concerns in using antagonists that harbor this property in cancer therapy. Given the importance of understanding Smoothened ciliary accumulation, we established a novel high content screening platform that directly monitors the process and selectively screened compounds for inhibition of Sonic hedgehog-driven Smoothened ciliary accumulation. New inhibitors with both conventional mechanisms of action and novel mechanisms were discovered. Noticeably, one we named "SMANT" displayed similar effectiveness in inhibiting activity of wildtype Smoothened and that of SmoM2, a dominant active form that causes human cancer and is refractory to current therapeutic options. As a result, the expanded resource of Hedgehog pathway inhibitors offers new opportunities for drug development in treating a range of Hedgehog-dependent cancers. On the other hand, as findings which will be published elsewhere, a counterpart screen identified a number of FDA approved drugs that promote Smoothened ciliary translocation and induce hypersensitive cellular response to Hedgehog stimuli as well as impairment of Hedgehog pathway inhibition by Vismodegib upon coadministration, thus implicating potential concerns of using these drugs. (Read Wang's article, DOI: 10.1021/cb300028a)

Image courtesy of Isaac Yonemoto.

ISAAC YONEMOTO

Current position: Postdoctoral Researcher, J. Craig Venter Institute, Synthetic Biology and Bioenergy Laboratories with Phillip Weyman and Hamilton Smith.

Education: University of Chicago, B.A. Mathematics, 2003; The Scripps Research Institute, Ph.D. Chemistry, 2009 with William Balch and Jeffery Kelly

Nonscientific interests: Lindy hop

Overall, I am interested in problems in synthetic biology, from low level engineering of enzymes to large scale editing of operons and genomes. My postdoctoral work at the University of Maryland with Barbara Gerratana focused on the scale-up, characterization, and testing of the 9-deoxy congener of the orphaned anticancer target sibiromycin. My efforts focused on refactoring the isolation conditions, analyzing the NMR spectra, conducting in vitro bioassays on antibiotic potency, and measuring DNA binding strength of both the parent compound and the engineered compound. In 2010, I began work at the Craig Venter Institute on chromosome assembly and improving microbial hydrogenase enzymes *in silico*, *in vitro*, and *in vivo*. (Read Yonemoto's article, DOI: 10.1021/cb300056q)

Image courtesy of Hideaki Yoshimura.

HIDEAKI YOSHIMURA

Current position: The University of Tokyo, Department of Chemistry, Tokyo, Japan, Research. Associate with Prof. Takeaki Ozawa.

Education: Kyoto University, Japan, B.S. in Chemistry, 2001; Kyoto University, Japan, M.S. in Molecular Engineering, 2003;

The Graduate University for Advanced Studies, Japan, Ph.D. in Chemistry, 2007; Kyoto University, Japan, Postdoctoral Fellow with Prof. Dr. Akihiro Kusumi, 2009.

Nonscientific interests: Skiing (free style), music (jazz, Didgeridoo), playing with my son

My research interests include single molecule physiology. All organisms and cells are sophisticated assemblies of molecules. To observe and analyze a dynamics of each molecule in living cells is an excellent way to understand the functional mechanism of living things. In the recent decade, single molecule imaging of proteins in living cells have been developed due to improvement of fluorescent molecules and microscopic technologies. However, there are no reports to observe mRNA in living cells on a single molecule level by using single fluorescent probes. The present work involves a novel fluorescent probe with which a target mRNA in living cells is visualized on a single molecule level. This probe would be a promising tool for single mRNA observation in living cells. (Read Yosimura's article, DOI: 10.1021/cb200474a)

Image courtesy of Yi-Fan Zhang.

YI-FAN ZHANG

Current position: Postdoctoral visiting fellow with Dr. Mitchell Ho in Antibody Therapy Section, National Cancer Institute, U.S. National Institute of Health.

Education: Fudan University, China, Bachelor of Medicine, 2006; Hong Kong University of Science and Technology, Hong Kong SAR, China, Ph.D. in Biology, 2011; Postdoctoral Fellow with Prof. Pei-Yuan Qian, 2011.

Nonscientific interests: Music, movies, cooking, hanging out with friends and family

My research interest focuses on the development and evaluation of useful pharmaceutical or chemical products. When I was working with my Ph.D. mentor Prof. Pei-Yuan Qian at HKUST, I studied the pharmacology and toxicology of two potential anti-marine-fouling compounds (butenolide and isocyanide), as we believe environmental responsibility requires a better understanding of their pharmacology and toxicology before their commercialization. I am now working with Dr. Mitchell Ho at NIH to develop effective antibody therapies against hepatocellular carcinoma, a common and dangerous tumor that currently lacks an effective therapy. (Read Zhang's article, DOI: 10.1021/cb200545s)