ACS chemical biology

INTRODUCING OUR AUTHORS

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Guillaume Andre

Image courtesy of Guillaume Andre.

Current position: Université catholique de Louvain (Belgium), Institute of condensed Matter and Nanosciences, postdoctoral researcher with Prof. Yves F. Dufrêne

Education: Université catholique de Louvain, Belgium, B.S. in Bioengineering 2004, M.S. in Chemistry and Bioindustry, 2006; PhD in Bioengineering Sciences with Profs Y.F. Dufrêne and P. Hols, 2010

Nonscientific interests: Gastronomy, travel and trekking, socializing, characterful beers, my cat

At the cross-roads of nanotechnology and life sciences, my research in the Dufrêne lab aims at gaining detailed molecular insight into the nanometer-scale surface architecture and biophysical properties of lactic acid bacteria (*Lactococcus lactis*, *Lactobacillus plantarum*), with emphasis on three major cell wall components, *i.e.*, peptidoglycan, teichoic acids, and cell wall polysaccharides. The nanoscale properties of the bacteria are investigated *in vivo* using advanced atomic force microscopy (AFM) techniques (live-cell imaging, single-molecule force spectroscopy of cell surface polymers). Currently, I am integrating fluorescence and advanced AFM imaging techniques to refine our perception of the Gram-positive cell wall. I am also actively seeking a new postdoc position in the field of live-cell imaging using fluorescence/AFM techniques. (Read Andre's article, DOI: 10.1021/cb1003509)

Bettina Bareth

Image courtesy of Klaus Neifer.

Current position: University of Göttingen, Germany, Department of Biochemistry II, Ph.D. candidate in Biochemistry with Prof. Peter Rehling (since May 2010)

Education: University of Konstanz, Germany, B.Sc. in Life Science, 2006, Bachelor thesis with Prof. Jörg S. Hartig; M.Sc. (with distinction) in Life Science in 2009, Master thesis with Prof. Andreas Marx; University of Guelph, Ontario, Canada, Exchange student (Sept 2007–April 2008)

Nonscientific interests: Music (playing the trumpet), snowboarding, gymnastics

My research interest in chemical biology began during my undergraduate studies in Life Science. As a master student in Prof. Marx's group, I focused on the development of a robot-assisted, high-throughput screening method for inhibitors of human DNA polymerases β and λ. With the help of this method, we screened a 9009-member library of small molecules and identified potential inhibitors. As the two polymerases are very similar in sequence and structure, it was very interesting and surprising that the screening gave specific inhibitors of DNA polymerase λ. This is meaningful as DNA polymerase λ is a DNA repair enzyme and therefore important for genome stability; the identified small molecule inhibitors might serve as therapeutic agents one day in the future. (Read Bareth's article, DOI: 10.1021/cb100382m)

Fabian Buller

Image courtesy of Helmuth Buller.

Current position: Covagen AG, Scientist, Development of Advanced Biopharmaceuticals

Education: Westfälische Wilhelms-Universität Münster, Diploma in Chemistry with Hans-Joachim Galla, 2006; ETH Zurich, Ph.D. in Chemistry and Applied Biosciences with Dario Neri, 2010

Nonscientific interests: Tennis, hiking, sailing, music

My research at the ETH Zurich focused on the development of a novel selection technology for small molecules binding to target proteins of pharmaceutical interest. To overcome limitations in the development of small molecule ligands using conventional screening technologies, we were interested in demonstrating the principle of antibody phage-display, *i.e.*, the linkage of phenotype and genotype could be translated to the world of small molecules. We synthesized a DNA-encoded chemical library of one million small molecules (each molecule is linked to a short DNA barcode), using techniques of organic chemistry and biochemistry, while library decoding was achieved with high-throughput sequencing and bioinformatics. Especially exciting to me was the selection of carbonic anhydrase inhibitors from the presented library which showed preferential tumor targeting in vivo. (Read Buller's article, DOI: 10.1021/cb1003477)

Marie Deghorain

Image courtesy of Marie Deghorain.

Current position: Postdoctoral researcher in the lab of Pr. L. Van Melderen in Gosselies, Belgium (Laboratoire de Génétique et Physiologie Bactérienne (LGPB), Institut de biologie et de médicine moléculaire (IBMM), Faculté des Sciences, Université Libre de Bruxelles (ULB), Gosselies, Belgium

Education: Undergraduate: Faculty of agronomy, Université catholique de Louvain (UCL), Louvain-La-Neuve, Belgium, Bioengineer; Graduate: Biochemistry and molecular genetics of bacteria (BMGB), Institute of Life Sciences, Université catholique de Louvain (UCL), Louvain-La-Neuve, Belgium. (Supervisors: Pr. J. Delcour, Pr. B. Hallet, Pr. P. Hols); Postdoctoral training in the laboratory of Dr. F. Cornet, LMGM, CNRS/Université Paul Sabatier, Toulouse, France

Nonscientific interests: Dancing, sailing, trekking, photography, knitting

Bacteria must sustain growth and division to maintain cell integrity and to ensure proper propagation of genetic material to the progeny. Investigating the subtle mechanisms that control the cell cycle progression is a fascinating topic. One of my scientific interests focuses on the control of cell wall synthesis during the morphogenesis process. Cell wall is constituted of multiple components that form an intricate and dynamic network surrounding the cell. The work presented here aims at better understanding the organization of bacterial cell wall polymers with respect to their physiological function. We used a multidisciplinary approach combining genetics, fluorescence microscopy and AFM, a high-resolution imaging method. The result is an example of fruitful collaboration between specialized research teams where high technologies serve fundamental biological issues. (Read Deghorain's article, DOI: 10.1021/cb1003509)

Sheng Ding

Image courtesy of Chang Zhong.

Current position: Stanford University, Department of Bioengineering, Ph.D. candidate with Prof. Annelise Barron

Education: Tsinghua University, Beijing, China, B.S. in Biosciences and Biotechnologies, 2005; Northwestern University, M.S. in Interdepartmental Biological Sciences, 2007

Nonscientific interests: Traveling, hiking, ping-pong, music

My work as a graduate student is focused on the design, development and study of novel types of recombinant proteins for tissue engineering. I am deeply interested in biomimicry of collagens, centrally important human proteins that are abundant and elaborate in their diversity of structures and functions yet based on relatively simple amino acid sequence motifs. Many intriguing proteins, which are not part of extracellular matrix (C1q, surfactant proteins A & D) have collagenous stalk domains that endow them with exotic nanostructures. Full investigations of such molecules are hampered by the lack of a prokaryotic expression system that includes the post-translational modification machinery needed for the biosynthesis of stably assembled, triple-helical collagen. We have "built in" the capability of post-translational modification of collagenous protein motifs into bacteria, and reconstituted a simple collagen folding pathway in a simple prokaryotic system. Our work, reported in this issue, has resulted in the creation of a novel platform for the study of collagenous protein assemblies as well as post-translational enzyme mechanisms. (Read Ding's article, DOI: 10.1021/cb100298r)

Agnes Hajduczki

Image courtesy of Charles A. Phoenix.

Current position: University of California, Irvine, Department of Molecular Biology and Biochemistry, Ph.D. candidate with Prof. Gregory A. Weiss

Education: University of California, Los Angeles, B.S. in Microbiology, Immunology and Molecular Chemistry, 2003

Nonscientific interests: Playing with my daughter, going to the beach, writing, music

My graduate research focuses on the challenging area of membrane protein engineering. Membrane proteins serve many important functions on the cell; however, due to their hydrophobic nature they are notoriously difficult to work with *in vitro*. Solubilization of membrane proteins opens the door to structural studies, which could allow elucidation of the functions of these proteins and provide insight into their associated diseases. Through generating a library of mutations using phage display, I was able to produce a soluble variant of the human membrane protein, caveolin-1, which has been previously inaccessible to biophysical characterization. In the future I would like to pursue protein engineering and structural biology, but applied in the field of virology in the development of vaccines and therapeutics. (Read Hajduczki's article, DOI: 10.1021/cb1001729)

Olivier A. Pierrat

Image courtesy of Olivier A. Pierrat.

Current position: Medical Research Council, Laboratory of Molecular Biology, Cambridge, U.K., in the group of Dr. Matthew Freeman, Head of Cell Biology Department

Education: Paris-XI, Orsay, France and University of Sussex, Brighton, U.K., ERASMUS exchange student, B.S. in Molecular Biology and Genetics, 1991; University of Technology of

Compiègne, France, M.S., 1992, and Ph.D. in Enzyme Engineering, Bioconversion, Microbiology, 1997.

Nonscientific interests: Rock 'n roll and cycling; I like reading about history and visiting museum on paintings and antiques.

My research interests have been focused on the function of enzymes and their regulation by small natural or synthetic molecules. Academic drug discovery can provide a new paradigm to prime the early drug discovery pipeline. The project at the Laboratory of Molecular Biology, Cambridge, U. K. is a good example, as it combines an academic expertise on a potential drug target (Freeman's laboratory working on rhomboid intramembrane protease) with that of the Medical Research Council-Technology on assay development and early drug discovery. A lot of biological functions are emerging regularly for rhomboids. Small molecules inhibitors or activators will be valuable tools to probe the enzyme mechanism, unravel new biological functions, and validate rhomboids as new drug target. (Read Pierrat's article, DOI: 10.1021/cb100314y)

Melanie Priestman

Image courtesy of Melanie Priestman.

Current position: University of North Carolina at Chapel Hill, School of Pharmacy, Postdoc with Dr. David S. Lawrence, 2007−pesent

Education: Northern Arizona University, B.S. in Chemistry, 1998; University of Kansas, Department of Medicinal Chemistry, Ph.D. with Prof Ernst Schoenbrunn, 2005

Nonscientific interests: Hiking, traveling, cooking, reading, sports

My research focuses on the development and utilization of spatiotemporal reagents related to the cAMP and cGMP dependent protein kinase signaling pathways. These two pathways are both believed to be involved in similar physiological phenomena such as cardioprotection and yet are reported in other areas to have opposing biological outcomes. To begin to understand how the activation of one or both of these signaling nodes relates to such phenomena requires the ability to activate each pathway independently of the other with precise spatial and temporal control. In this paper we describe the first dual wavelength photoactivatable system for these pathways and utilize them to characterize VASP phosphorylation patterns in smooth muscle cells. (Read Priestman's article, DOI: 10.1021/cb100398e)

Robin Sibert

Image courtesy of Jessica Machata.

Current position: Georgia Institute of Technology, Post-Doctoral Researcher with Professor Bridgette A. Barry

Education: Mercer University, B.S., 2003; Georgia Institute of Technology, Ph.D. in Chemistry with Professor Bridgette A. Barry, 2009

Nonscientific interests: Church ministry, bible studies, socializing with friends and meeting new people, learning new cultures

My research uses novel β hairpin peptides to explore protein structure/function relationships. Redox-active tyrosines conduct electrons over long distances in proteins. I have used beta hairpins as tractable systems to investigate how noncovalent interactions with other amino acids influence the redox properties of tyrosine. One fascinating aspect of my research is that it can be applied in several ways. Because redox active tyrosine residues are found in a number of enzymes, including photosystem II, prostaglandin synthase, and ribonucleotide reductase, results from my work can potentially be used to control enzymatic function. They may also be used in drug design. In this paper, the effects of proton coupled electron transfer, hydrogen bonding, and π-cation interactions on the redox potential of tyrosine are examined using spectroscopic techniques and electrochemistry. I find this work fulfilling because design and exploitation of beta hairpins combines the art of creation with the technical and analytical skills of science. (Read Sibert's article, DOI: 10.1021/cb100138m)

Kvido Strisovsky

Image courtesy of Kvido Strisovsky.

Current position: Postdoctoral fellow with Dr. Matthew Freeman, Medical Research Council Laboratory of Molecular Biology, Cambridge, UK

Education: M.Sc. in Biochemistry, Institute of Chemical Technology, Prague, Czech Republic, 1997; Ph.D. in Molecular Biology, Charles University in Prague, Czech Republic, 2003

Nonscientific interests: Hiking, orienteering, skiing, swimming, badminton

I have been interested in how intramembrane proteases regulate cellular processes. Although several of these widespread and diverse enzymes are already known to control biologically important processes, relatively little is known about their mechanism, specificity, structure, and regulation. During my postdoc I have been studying substrate specificity and mechanism of the rhomboid family of intramembrane proteases and developing methods of substrate identification.

Along the way we have developed a high-throughput activity assay that we have used in the present paper to discover a new class of mechanism-based rhomboid inhibitors, thus providing a platform to generate research tools for rhomboids that have been lacking. Now that I am establishing my independent career, I aim to exploit my earlier work to elucidate the biological functions of rhomboids in selected medically significant contexts ranging from bacterial pathogens to mammalian cells. (Read Strisovsky's article, DOI: 10.1021/cb100314y)

Tobias Strittmatter

Image courtesy of Tobias Strittmatter.

Current position: University of Konstanz (Germany), Department of Chemistry and Konstanz Research School Chemical Biology, Ph.D. student in the group of Prof. Andreas Marx

Education: Institut Dr. Flad, Stuttgart (Germany), apprenticeship as chemical-technical assistant, 2004; University of Konstanz (Germany), Department of Chemistry, studies of chemistry, diploma thesis in organic and cellular chemistry (Dipl. Chem.) in the group of Prof. Andreas Marx, 2009

Nonscientific interests: Traveling, socializing with friends, music, movies, sports

My interest in chemical biology began during my undergraduate research in Prof. Marx's laboratory. As a graduate student, I continue my studies in his interdisciplinary group. The aim of my research is to discover and design chemical probes to gain insights into the mechanistic principles of complex chemical and biological systems. To reach this goal, I combine the principles and potentials of organic chemistry and processes of molecular biology to develop molecules with novel biological functions. In particular, the Marx group is interested in DNA polymerases and nucleic acid chemistry. In this paper, we present a new generally applicable high-throughput screening for small molecule inhibitors of DNA polymerases. Applying this method we identified novel small molecule inhibitors of human DNA polymerase λ. The identified small molecules are useful chemical probes to study DNA polymerase λ in more complex systems and could even serve as leads for new therapies. (Read Strittmatter's article, DOI: 10.1021/cb100382m)

Liang Sun

Image courtesy of Liang Sun.

Current position: The University of North Carolina at Chapel Hill, School of Pharmacy, Postdoctoral Fellow with Prof. David S. Lawrence

Education: Nankai University, B.S. in Chemistry, 2002; Stony Brook University, Ph.D. in Organic Chemistry with Prof. Iwao Ojima, 2008

Nonscientific interests: Classic music, photography, video games

My current research has been focused on synthesis of caged cAMP/cGMP derivatives and their application in chemical biology. (Read Sun's article, DOI: 10.1021/cb100398e)

Yunzhou Wei

Image courtesy of Mable Fok.

Current position: Princeton University, Department of Molecular Biology, Ph.D. candidate with Prof. Bonnie Bassler

Education: Tsinghua University, B. S. in Biological Sciences, 2006

Nonscientific interests: Movies, basketball (and other sports), traveling, karaoke

The Bassler laboratory studies a bacterial cell−cell communication process called quorum sensing. Quorum sensing involves the production and detection of signaling molecules called autoinducers. This process enables bacteria to monitor the cell-density of the community and carry out tasks as a collective. I study quorum sensing in the *Vibrio cholerae*. Among other traits, quorum sensing controls biofilm formation and virulence factor production in this globally important pathogen. My research focuses on the biosynthesis of the major *V. cholerae* autoinducer (called CAI-1) and its interactions with its cognate membrane-bound receptor. In this manuscript, we define the biosynthetic pathway for CAI-1, show that the synthase, CqsA, works by a novel two-step mechanism and demonstrate that the substrate for the reaction is (*S*)-adenosylmethionine (SAM). At least two other major types of autoinducers are also made from SAM suggesting bacteria have evolved a strategy to leverage an abundant substrate to produce a variety of these ancient communication signals. (Read Wei's article, DOI: 10.1021/cb1003652)

Peng Zou

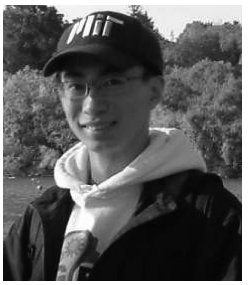

Image courtesy of Peng Zou.

Current position: Massachusetts Institute of Technology, Department of Chemistry, Ph.D. candidate in Biological Chemistry with Prof. Alice Y. Ting

Education: Peking University, Beijing, China, B.S. in Chemistry and Physics, 2007

Nonscientific interests: Volleyball, history, Go

Nearly all cells communicate with their environment via receptors on the plasma membrane, whose functions are often regulated by their trafficking behavior and oligomerization state. Currently, few methods are available for investigating receptor interactions during endocytic trafficking in the context of living cells, and my study aims at expanding this toolbox. By applying site-specific protein labeling and fluorescence imaging techniques to single living cells, I developed a "co-internalization assay" for determining the receptor oligomerization state. The basic idea behind this assay is the causality between receptor association and linked trafficking behavior of two receptor isoforms. In other words, receptors that bind together travel together. (Read Zou's article, DOI: 10.1021/cb100361k)