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Introducing Our Authors

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Image courtesy of Alessandro Angelini.

ALESSANDRO ANGELINI

Current position: Massachusetts Institute of Technology, Cambridge, MA, Postdoctoral Fellow in the laboratory of Professor K. D. Wittrup at the Koch Institute for Integrative Cancer Research

Education: University of Padua, Italy, M.S. in Biotechnology, 2004; Department of Biological Chemistry, University of Padua, Italy, Ph.D. in Biochemistry in the group of Professor G. Zanotti, 2005−2008; Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne, Switzerland, Postdoctoral Associate in the group of Professor C. Heinis, 2008−2011.

Nonscientific interests: Soccer, good restaurants, wine tasting, traveling, "il bocia", skiing, cinema, and reading.

My research interests are interdisciplinary in nature and include protein engineering, structural and chemical biology. As graduate student in the Prof. G. Zanotti's laboratory, I applied biochemical tools and X-ray crystallography to determine the tridimensional structure of some proteins forming the macromolecular type IV secretion system of the human pathogen *H. pylori*. After a short research training with Dr. D. Hart at EMBL, Grenoble, I joined Prof. C Heinis' laboratory as a postdoctoral associate to develop innovative peptide macrocycle inhibitors using a combinatorial approach based on phage display. In the present work, we describe the generation of a potent and selective bicyclic peptide ligand inhibiting the therapeutic target urokinase-type plasminogen activator (uPA), a serine protease implicated in tumor growth and metastasis. In order to investigate the binding mode of the bicyclic peptide to its target, we determined the crystal structure of uPA in complex with the bicyclic peptide. The tridimensional structure revealed that small highly constrained bicyclic peptide (<2 kDa) appears to have properties typical of proteins, with a large interface of interaction with target, and multiple directional hydrogen and electrostatic bonds from both loops of the peptide, explaining the high binding affinity and exquisite specificity of the inhibitor. Such small protein mimics may thereby possess features of both small molecule and protein therapeutics. I recently joined Prof. K.D. Wittrup's laboratory and I am currently developing multispecific protein based binders capable to interrupt the pro-tumorigenic communication between cancer and stromal cells within the tumor microenvironment. (Read Angelini's article, DOI: 10.1021/cb200478t)

Image courtesy of Hadas Ganin.

HADAS GANIN

Current position: Graduate student pursuing Ph.D. at the Department of Chemistry, Ben-Gurion University of the Negev, Israel, under the supervision of Prof. Michael M. Meijler

Education: Ben-Gurion University of the Negev, Israel, B.Sc. in Chemistry, 2006; M.Sc. in Chemistry, 2008

Nonscientific interests: Aerobics, kick boxing, step-dance, baking, and music

During my M.Sc. studies I got acquainted with chemical communication between bacteria, in a field termed "Quorum Sensing" (QS). QS allows bacteria to regulate gene expression in response to changes in cell population density so it can compete with multicellular organisms and survive adverse conditions. My Ph.D. research focuses on the synthesis of small bacterial signaling molecules (AI-2, CAI-1) and bioactive analogues, followed by their use as highly specific biological tools to probe QS controlled phenotypes such as biofilm formation, virulence factor expression and bioluminescence induction. In addition, I have tried to further our understanding of interspecies effects of common QS molecules, especially in the human pathogens *Vibrio cholerae* and *Pseudomonas aeruginosa*. Some of the interesting findings during my studies were that small structural changes in the AI-2 signal yields potent attenuators of QS in several bacteria, and we recently discovered an additional role for CAI-1 (the primary QS molecule of *Vibrio cholerae*) as an anti-QS and antimicrobial molecule against *P. aeruginosa.* (Read Ganin's article, DOI: 10.1021/cb2004675)

Image courtesy of Ahmet Karabulut.

AHMET KARABULUT

Current position: Research Technician II at Dr. Gerald Smith's laboratory. Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle WA.

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Education: Istanbul Technical University, B.S. in Molecular Biology and Genetics, 2004; University of Cincinnati, M.S in Molecular Genetics, 2008.

Nonscientific interests: Playing guitar, hiking and mushroom hunting.

My research project in Dr. Gerald Smith's laboratory focuses on the discovery and development of small-molecule inhibitors of bacterial RecBCD and AddAB helicase-nucleases. These helicases are thought to be important for mutagenicity and evolution of antibiotic resistance in bacteria. We found several classes of inhibitors through our collaboration with Scripps Research Institute Florida Molecular Screening Center. This study provides such helicase inhibitors that can be further developed as useful antibiotics to combat antibiotic resistance. Biochemical assays with purified enzymes indicated that each inhibitor class seems to have a unique mechanism of action that correlates with the sophisticated activity of these helicase-nuclease complexes. Besides their potential for the development of useful antibiotics, these small-molecules will also be valuable tools to understand how bacterial helicases function and to elucidate the molecular mechanism of hotspots of recombination. (Read Karabulut's article, DOI: 10.1021/cb300018x)

Image courtesy of NCI-Frederick.

FA LIU

Current position: Research Scientist in the Peptide Lead Optimization Group within the Bio-Therapeutic Discovery and Research Division, Lilly Research Laboratories.

Education: Nankai University, B.S. in Chemistry, 1999; Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Ph.D. in Synthetic Organic Chemistry, with Prof. Zhu-Jun Yao, 2004; National Cancer Institute at Frederick, Laboratory of Medicinal Chemistry, Postdoctoral Fellow with Dr. Terrence Burke, Jr., 2004–2007.

Nonscientific interests: Hiking, traveling, fishing.

My research focuses on the discovery of peptides that disrupt protein–protein interactions (PPIs). While at the National Cancer Institute, I developed postsolid phase approaches to peptide library diversification. These combine fragment screening together with consensus sequences, in ways that have proven to be highly useful in identifying new binding interactions. Typically, a consensus sequence is fixed as one fragment, and a chemical handle (hydrazine, aminooxy, phosphate, *etc.*) is installed to allow facile postsolid phase conjugation with secondary fragments. We have used this approach to successfully block PPIs between human Tsg101 and HIV-Gag, and the polo like kinase 1 and its substrate proteins. I recommend these approaches as being widely applicable to targeting PPIs, particularly the use of oxime-based peptide library diversification. (Read Liu's article, DOI: 10.1021/cb200469a)

Image courtesy of Ryan Phelan.

RYAN PHELAN

Current position: Postdoctoral Research with Prof. Jay D. Keasling, University of California, Berkeley/Joint BioEnergy Institute, Emeryville, California.

Education: Michigan State University, East Lansing, Michigan, B.S. in Chemistry; Undergraduate research with Prof. John W. Frost and Prof. Joan B. Broderick; Johns Hopkins University, Baltimore, Maryland, Ph.D. in Chemistry, Thesis supervisor Prof. Craig A. Townsend.

My thesis focused on developing a chemoenzymatic synthesis of substituted carbapenem β-lactam antibiotics as well as defining the biosynthetic path to an important naturally occurring member of the family, thienamycin. Effort toward these two goals was highly interdisciplinary and is well represented in recent publications from the Townsend Lab. To facilitate generation of new biocatalysts to aid in the production of thienamycin-like compounds we developed a high-throughput screen that couples a fluorescence response to the *in vivo* production of β-lactam antibiotics. This assay was used to demonstrate the necessity of a specific tyrosine that had previously been implicated as a catalytic radical shuttle in carbapenem synthase (CarC), the terminal enzyme in the biosynthetic path to the basic carbapenem. Results have defined one essential parameter for future engineering of CarC. Additional studies on CarC using this assay will facilitate protein redesign efforts to provide a chemoenzymatic route to thienamycin-like compounds. I am currently a postdoctoral researcher in Prof. Jay D. Keasling's lab at UC, Berkeley continuing my studies of natural product biosynthesis. Work here focuses on the polyketide biosynthesis, in particular, how we can modify polyketide synthases to produce new compounds to serve as advanced pharmaceuticals and next-generation biofuels. (Read Phelan's article, DOI: 10.1021/cb200504g)

Image courtesy of Christoph Rademacher.

CHRISTOPH RADEMACHER

Current position: Group leader at the Max Planck Institute of Colloids and Interfaces, Department of Biomolecular Systems (Prof. Peter H. Seeberger).

Education: Luebeck University, Germany, B.S. in Molecular Biotechnology, 2004; M.S. in Molecular Life Science, 2006; Ph.D. with Prof. Dr. Thomas Peters, 2009; The Scripps Research Institute, EMBO postdoctoral fellow with Prof. Dr. James C. Paulson, 2009–2011.

Nonscientific interests: Traveling, movies, reading.

My research focuses on carbohydrate-mediated interaction processes and their analysis from a structural as well as a functional perspective in biology. The involvement of glycans in a wide variety of biological processes such as development, cancer progression and immunology as signaling and organizing elements, together with their dynamic behavior on a molecular level renders these biopolymers complex and challenging to explore. My lab seeks to find common principles of these processes and develop tools to explore glycobiology using biophysical methods such as nuclear magnetic resonance combined with computational techniques. One aspect of the latter is to develop a formal approach to deal with glycan structures and their complexity in order to describe their function. In particular, we are interested in immune regulatory roles of carbohydrates. (Read Rademacher's article, DOI: 10.1021/cb300003z)

Image courtesy of Yogo Sakakibara.

YOGO SAKAKIBARA

Current position: Ph.D. candidate under the supervision of Prof. Christine S. Chow at Wayne State University, Department of Chemistry, Detroit, Michigan.

Education: Waseda University, Tokyo, Japan, B.S. in Applied Chemistry, 2004; Kyoto University, Kyoto, Japan, M.S. in Chemistry, 2006

Nonscientific interests: Swimming, reading, watching soccer games, traveling by train

My research is focused on understanding the molecular basis of bacterial ribosome helix 69 (H69) RNA conformational changes and the role of a common modified nucleoside, pseudouridine, which occurs in H69. H69 is a conformationally dynamic small domain of the ribosome, which has been proposed to play important roles in translation. I have employed chemical probing methodologies to elucidate different conformational states of H69 in 50S and 70S ribosomes. I have also studied the influence of pseudouridine modifications on H69 conformational states, as well as the interactions of small molecules with this RNA domain. (Read Sakakibara's article, DOI: 10.1021/cb200497q)

Image courtesy of Yukiko Sasazawa.

YUKIKO SASAZAWA

Current position: Keio University, Yokohama, Japan, Ph.D. candidate in Faculty of Science and Technology under the supervision of Professor Msaya Imoto.

Education: Keio University, Yokohama, Japan, B.S. in Faculty of Science and Technology, 2007; Keio University, Yokohama, Japan, M.S. in Faculty of Science and Technology, 2008

Nonscientific interests: Tennis, walking, and Japanese calligraphy

My research at Keio University focus on major cellular evens: apoptosis and autophagy, which are essential for maintenance of homeostasis, from a viewpoint of chemical biological approach. In this paper, we have carried out the screening for autophagy modulating compounds and identification of target protein of this compound. Studying autophagy through chemical genetics could be an ideal approach to gaining a better understanding of autophagy signaling pathways. (Read Sasazawa's article, DOI: 10.1021/cb200492h)

Image courtesy of Hideo Takakura.

HIDEO TAKAKURA

Current position: Department of Chemistry, School of Science, The University of Tokyo, Postdoctoral Researcher with Prof. Takeaki Ozawa.

Education: The University of Tokyo, B.S. in Pharmaceutical Sciences, 2004; The University of Tokyo, Ph.D. in Pharmaceutical Sciences with Prof. Tetsuo Nagano, 2010.

Nonscientific interests: Playing and watching sports, outdoor activity, playing board game.

My research interest has been focused on analyzing and visualizing of biological molecules or events for elucidating biological phenomena and discovery of drugs using luminescence or fluorescence probes. Specifically, I developed bioluminescence probes based on firefly luciferin−luciferase reaction. In this paper, using split luciferase complementation, we demonstrated quantitative analysis of the protein−protein interaction between β2-adrenergic receptor and β-arrestin2 in a 96-well plate assay, living single cells and animal models. In particular, using the hydrodynamic tail vein method, we successfully obtained the luminescence signal from the liver upon stimulation of an agonist in the intact systems of mice. We believe that this *in vivo* system can contribute to effective evaluation and expedite the development of new drugs. (Read Takakura's article, DOI: 10.10121/cb200360z).

JUSTYNA WOJNO

Current position: University of Strathclyde, Department of Pure and Applied Chemistry, Postdoctoral Research Associate with Prof. Nicholas Tomkinson.

Education: Warsaw University of Technology, The Faculty of Chemistry, M.Sc. in Chemical Technology, 2007; University of Birmingham, School of Chemistry, Ph.D. in Organic Chemistry, 2011.

Nonscientific interests: Hiking in the Tatra Mountains, road-trips with my family and friends, sports, and music.

My scientific interests are focused on chemical biology, drug discovery and the design of chemical tools to tackle complex

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Image courtesy of Justyna Wojno.

biological questions. During my postgraduate research under the supervision of Dr Liam Cox and Prof. Del Besra I had great opportunity to work at the interface of synthetic organic chemistry and immunology. I worked on the synthesis of analogues and derivatives of α-galactosyl ceramide, α-GalCer, a synthetic glycolipid, which is the prototypical agonist of the CD1d protein, and one of the strongest activators of invariant Natural Killer T Cells (*i*NKT Cells). Our close collaboration with Prof. Vincenzo Cerrundolo's group at the Weatherall Institute of Molecular Medicine in Oxford introduced me to various methods of determining structure–bioactivity relationships, protein crystallography, *in vitro* and *in vivo* immunological assays. In 2011, I moved to University of Strathclyde as a postdoctoral research associate joining a medicinal chemistry project focusing on the orphan nuclear receptors REV-ERBα and RORα as novel targets for respiratory diseases. (Read Wojno's article, DOI: 10.1021/cb2005017)


Image courtesy of Sharla Wood.

SHARLA WOOD

Current position: Graduate student at Wayne State University, Department of Chemistry with Prof. David Rueda

Education: Lake Superior State University, B.S. in Chemistry, 2006

Nonscientific interests: Camping, hiking, gardening and baking

My research at Wayne State University is focused on using fluorescence and single molecule fluorescence to elucidate how RNA binds a target, from a small molecule to a complementary oligonucleotide. Exploring how RNA recognizes and binds targets offers insight into how RNA performs a variety of functions in the cell as well as how RNA can be exploited as an analytical tool. I utilized single molecule FRET to reveal the conformational dynamics of the c-di-GMP riboswitch that preorganize the RNA via tertiary interactions distant from the ligand-binding site. This preorganization would allow the riboswitch to rapidly fold and recognize its ligand and effectively respond to varying intracellular levels of c-di-GMP. (Read Wood's article, DOI: 10.1021/cb300014u)

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