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Image courtesy of Ophélie Arnaud.

OPHÉLIE ARNAUD

Current position: University of Lyon (France), Centre de Génétique et de Physiologie Moléculaires et cellulaires, post-doctoral researcher with Dr. Olivier Gandrillon since January 2012

Education: University of Lyon, France, Ph.D. in Biochemistry, 2011 with Drs Pierre Falson and Atillio Di Pietro; University of Grenoble, France, PharmD, 2007

Nonscientific interests: Reading, sports

My Ph.D. research was focused on two ABC transporters, ABCB1 and ABCG2, involved in cancer cells chemoresistance. It is therefore critical to elucidate the mechanism by which those ABC transporters export drugs, and then to develop specific and potent inhibitors. My thesis work was divided in two parts. The first one was to study ABCG2 intracellular loops, especially their role in substrate(s) selection. The second one was to develop a new class of inhibitors, focusing on the design of noncompetitive inhibitors based on reversin 121. These compounds are noncytotoxic, able to restore the activity of chemotherapeutic drugs and behave as fully noncompetitive inhibitors toward the ABCB1 and ABCG2 substrates Hoechst 33342, rhodamine 123 and mitoxantrone. The most efficient compound to inhibit ABCG2, CT1364, followed three different mechanisms: transport inhibition, ATP hydrolysis inhibition and fast reduction of ABCG2 expression. Lastly, the first *in vivo* tests appeared to be promising since the association of CT1364 with irinotecan slowed down the growth of mice xenografted human tumors. (Read Arnaud's article DOI: 10.1021/cb200435y).

Image courtesy of Francisco Garcia.

DEVAYANI BHAVE

Current position: The Scripps Research Institute, Florida, Department of Chemistry, Postdoctoral Researcher since Sept 2011, Advisor, Prof. Kate S. Carroll

Education: Fergusson College, University of Pune, India, B.Sc. in Chemistry, 2001; King's College London, University of London, U.K., M.Sc. in Chemical Research, 2002, Advisor, Prof. Michael North; University of Michigan, Ann Arbor, Ph.D. in Chemical Biology, 2011, Advisor Prof. Kate S. Carroll

Nonscientific interests: Tennis, yoga, reading

My graduate research focused on elucidating mechanistic details of enzymes essential for sulfate assimilation in human pathogens such as *Mycobacterium tuberculosis* and *P. aeruginosa*. In this article, by means of metalloprotein engineering, spectroscopic and kinetic analyses, we demonstrate that an iron−sulfur cluster cofactor plays a pivotal role in substrate specificity and catalysis among sulfonucleotide reductases. These findings offer new insights into the evolution of this enzyme family, and extend the known functions of protein-bound iron−sulfur clusters. (Read Bhave's article, DOI: 10.1021/cb200261n)

Image courtesy of Alena Busche.

ALENA BUSCHE

Current position: University of Frankfurt Institute of Biophysical Chemistry, Preparation for PhD in biochemistry, Supervisor: Prof Volker Dötsch

Education: Leibnitz University, Prediploma in chemistry, 2004; Ecole Superieure de Biotechnologie Strasbourg, MS in Biotechnology, 2007

Nonscientific interests: Rock-climbing, volleyball, traveling, diving

During my Ph.D. study, I developed a strong interest in structural biology, enzyme kinetics, and molecular recognition processes. My Ph.D. research focuses on understanding the molecular recognition processes of nonribosomal peptide synthetases (NRPS) and polyketide synthases (PKS) by NMR. Insights into these recognition processes should facilitate re-engineering approaches of these multienzyme machineries. NMR studies of these huge enzyme complexes are challenging

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due to their sizes and the transient nature of interactions. In cooperation with the research group of Hideo Iwai (Helsinki), I developed a protocol to isotopically label the central domain of a multidomain protein. This technique enabled me to study the interaction of a triplet ACP (ACPI−ACPII−ACPIII) with the unique halogenase domain (Hal). In this work we identified the amino acids involved in the very specific and selective interaction of Cur Hal with the triplet ACP. This information will be valuable for future re-engineering approaches. (Read Bushe's article, DOI: 10.1021/cb200352q)

Image courtesy of Charlotte Gauthier.

CHARLOTTE GAUTHIER

Current position: Institute of Protein Biology and Chemistry, BMSSI (UMR5086) CNRS-University of Lyon, Drug Resistance Mechanism and Modulation team, Ph.D. Student in Biochemistry, advisor Dr. Attilio Di Pietro

Education: Preparatory class to access an Engineering school, Rouen, France, 2004−2006; Ecole Supérieure de Physique Chimie et Electronique de Lyon, (ESCPE Lyon), France, engineering degree in chemistry, 2006−2010

Nonscientific interests: Playing handball or judo and watching sport, reading, movies, music

My Ph.D. research focuses on the development of specific modulators of ABCG2, an ABC transporter involved in the MDR (MultiDrug Resistance) phenotype of cancer cells. Actually, some resistant cancer cells overexpress ABCG2, which transports chemotherapeutic drugs outside, preventing their cytotoxic activity. Our aim is, on the one hand, to identify molecules able to selectively kill ABCG2-overexpressing resistant cancer cells, by targeting their Achille's heel. On the other hand, we would like to better understand the mechanism of the transporter in order to facilitate the design and optimization of modulators. To reach these objectives, I am focusing on molecules already known to interact with the protein such as the present inhibitors characterized in our paper. Then, by comparing the different activities induced upon molecule interaction with the protein, we hope to get a better view of the different mechanisms of ABCG2 activity. (Read Gauthier's article DOI: 10.1021/cb200435y).

Image courtesy of Jiyoung Hong.

JIYOUNG A. HONG

Education: Undergraduate, University of Louisville; Graduate, University of Michigan (Advisor: Kate S. Carroll)

Nonscientific interests: Traveling, reading, music

My graduate research focused on inhibitor design and mechanistic studies of adenosine-5′-phosphosulfate reductase (APR). APR is an iron−sulfur protein that catalyzes the first committed step in the *de novo* biosynthesis of cysteine in mycobacteria and a validated target for the development of new anti-TB agents, particularly for the treatment of latent infection. We have combined virtual ligand screening (VLS), rational structure-based design, and enzyme mechanism analysis. In this work, we provide kinetic evidence that the Fe−S cluster cofactor plays an essential role in substrate specificity of sulfonucleotide reductases. These data further our understanding of the APR reaction mechanism and pave the way for development of new inhibitors to target this therapeutically important class of enzymes. (Read Hong's article, DOI: 10.1021/cb200261n)

Image courtesy of Benjamin Josey.

BENJAMIN JOSEY

Current position: Graduate student pursuing Ph.D. at the Medical University of South Carolina under the supervision of Dr. C. James Chou and Dr. Xuejun Wen in the Department of Pharmaceutical and Biomedical Sciences

Education: University of South Carolina in Aiken, South Carolina, B.S. in Psychology, Chemistry, 2008

Nonscientific interests: Spending time with friends, reading, movies, live music, cooking, gardening, fishing, playing guitar, surfing, kiteboarding

My current research primarily focuses on developing therapeutics designed to be both neuroprotective as well as to help regenerate the brain and spinal cord. Because many fundamental mechanisms are common to several neurodegenerative diseases, stroke, brain trauma, and seizures, by studying and targeting these mechanisms, we hope to develop a better understanding of how the brain responds to stress with a specific focus on therapeutic development. At present, I am involved in two projects working toward these goals, as well as helping with a project developing novel histone deacetylase inhibitors for the treatment of leukemia. My main work involves exploring the chemical space around potentially neuroprotective natural products by synthesizing and testing derivatives in both *in vitro* and *in vivo* model systems and using this knowledge to create chemical probes to aid in novel target identification. In collaboration with Xiaowei Lei of the Clemson-MUSC Bioengineering Department, I have also been working to develop biomaterials and drug delivery systems that promote neural stem cell proliferation, migration, and differentiation by synthesizing novel ligands that interact

with receptors critical to these processes and conjugating them to biodegradable hydrogels and nanoparticles. (Read Josey's article, DOI: 10.1021/cb200134p)

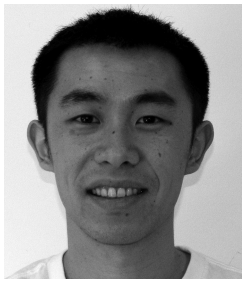

Image courtesy of Matt Berta.

WALLACE LIU

Current position: University of Colorado Denver, Department of Pharmacology, Ph.D. candidate with Dr. Mair Churchill

Education: University of California San Diego, B.S. in Biochemistry and Cell Biology

Nonscientific interests: Table tennis, trail running

My research at the Sanford-Burnham Institute under Dr. Lutz Tautz involved characterizing small molecules that target protein tyrosine phosphatases in T lymphocytes. In this paper, we describe an inhibitor of HePTP that prolongs the kinetics of MAPK signaling, a novel strategy to probing this pathway. Importantly, we accomplished this *via* a varied approach, which started with *in silico* drug screening and eventually progressed to *ex vivo* and *in vivo* discoveries. This demonstrates the interdisciplinary potential behind the field of chemical biology. Currently, I am a third year Ph.D. student in Dr. Mair Churchill's laboratory at UC Denver, where I am using biophysical and pharmacological approaches to study the histone chaperone activities of Asf1 and CAF-1, proteins which are intimately linked to chromatin assembly, epigenetics, and cancer. (Read Liu's article, DOI: 10.1021/cb2004274)

Image courtesy of Michael Madonna.

MICHAEL MADONNA

Current position: Ph.D. Candidate in Chemistry, University of California at Santa Cruz, Advisor: Glenn Millhauser

Education: California Polytechnic State University at San Luis Obispo, B.S. in Chemistry & Biochemistry, 2004

Nonscientific interests: Music, cooking, swimming, biking, running

My graduate research in the Millhauser Research Group focuses on the Melanocortin System, a family of ligands and receptors involved in many important physiological processes, including feeding behavior and energy homeostasis. Specifically, my research emphasizes the study of structural determinants for activity of the Agouti-Related protein (AgRP), an endogenous antagonist of the melanocortin 3 and 4 receptors. In the current study, I investigate the effects of novel mutations on appetite stimulation in rats. Mutations that increased the net positive charge resulted in a significant appetite increase. These studies have the potential to lead valuable therapies for people who suffer from cachexia, a debilitating metabolic disorder causing loss of appetite and severe weight loss, that is associated with chronic diseases like cancer, AIDS, and heart disease. (Read Madonna's article, DOI: 10.1021/cb2003412)

Image courtesy of Maria Serena Vinci.

ALESSANDRO PINTO

Current position: Ph.D. candidate at Universitat Rovira i Virgili, Tarragona, Spain, department of chemical engineer, under the supervision of Prof. Ciara K. O'Sullivan

Education: Universitá degli Studi di Milano-Bicocca-Milan, Italy, B.S. in Biotechnology and M.S. in Industrial Biotechnology; Universitat Rovira i Virgili, Tarragona, Spain, M.S. in Nanoscience and Nanotechnology

Nonscientific interests: Reading, soccer, movies, traveling

During my Ph.D. study, I have been working with nucleic acid aptamers and their uses in biological sample analysis. Nucleic acid aptamers are artificial receptors, characterized by high affinity and specificity for their cognate target. Among the other natural and chemical receptors, aptamers have the advantages of well-known chemistry and a remarkable stability; moreover aptamers can be selected virtually against any target, in any condition as no animal host is required. Moreover, all these proprieties come together with the high flexibility and adaptability intrinsic to the nucleic acids nature. Exploiting the features of aptamers, I focused on the development of a novel assay referred as aptaPCR that combines the target recognition mediated by specific aptamers with the sensitivity of the PCR amplification, achieving ultralow detection of analytes. (Read Pinto's article, DOI: 10.1021/cb2003835)

Image courtesy of Luciana Pereira Rangel.

LUCIANA PEREIRA RANGEL

Current position: Universidade Federal do Rio de Janeiro, Instituto de Bioquímica Médica, Brazil, Postdoctoral Researcher with Professor Jerson L. Silva

Education: Universidade Federal do Rio de Janeiro, Brazil, B.S. in Pharmacy, 2003; M.Sc. in Microbiology and Immunology, 2005; Ph.D. in Microbiology and Immunology, 2009 with Prof. Antonio Ferreira-Pereira

Nonscientific interests: Literature, music, arts, traveling, cats

My Ph.D. research with Prof. Antonio Ferreira-Pereira was focused on the discovery of new inhibitors for ABC transporters, such as *S. cerevisiae* Pdr5p. During this period, with a Sandwich-Ph.D. fellowship, I had the chance to work with Dr. Attilio Di Pietro, in Lyon, France, on new ABCG2 inhibitors. In this work, we have performed flow cytometry measurements of the inhibition of ABCG2-mediated drug efflux by low-cytotoxicity stilbene derivatives. At the present, on my postdoctoral research with Prof. Jerson L. Silva, I have been studying the interaction of the prion protein and p53 with nucleic acids and their aggregation, aiming to develop new therapeutical aptamer-based strategies for amyloidoses and cancer. (Read Pereira Rangel's article DOI: 10.1021/cb200435y).

Image courtesy of Raghuvir Sengupta.

RAGHUVIR SENGUPTA

Current position: Graduate student pursuing a Ph.D. in Biochemistry at Stanford University under the supervision of Daniel Herschlag

Education: University of Chicago, B.A. in Biology, 2007 (advisor Joseph Piccirilli). University of Chicago, Research technician, 2007–2009 (supervisor Joseph Piccirilli)

Nonscientific interests: Exercising, music, documentary films, looking for the best burritos around the Bay Area

Hydrogen bonding and metal ion coordination are important strategies used by enzymes to facilitate catalysis. My research in the Piccirilli lab at the University of Chicago focused on identifying important hydrogen bond interactions in the Tetrahymena ribozyme reaction. Using a series of chemically modified nucleosides, we were able to infer whether important 2′-hydroxyl groups on the substrates contribute to catalysis through a functionally significant hydrogen bond interaction. This work also led to a fruitful collaboration with the Herschlag lab at Stanford University where we used chemically modified nucleosides to reconcile conflicting structural models of a catalytic interaction mediated by a conserved residue on the Tetrahymena ribozyme. Currently, as a graduate student in the Herschlag lab, my research is directed toward identifying and characterizing catalytic metal ion interactions in the Tetrahymena ribozyme reaction. (Read Sengupta's article, DOI: 10.1021/cb200202q)

Image courtesy of Grace Tan.

GRACE TAN

Current position: Research Associate with Dr. Marianthi Kiriakidou at University of Pennsylvania School of Medicine, Rheumatology Division since January 2010

Education: Bethany College (WV), B.S. in Biology, 1999; Drexel University College of Medicine, Ph.D. in Molecular and Cell Biology, 2006, Advisor: Dr. Katrina Cooper; Postdoctoral Associate, University of Medicine and Dentistry of New Jersey (UMDNJ- Stratford), 2005–2006, Advisor: Dr. Randy Strich; Postdoctoral Fellow, University of Pennsylvania School of Medicine, 2006–2009, Advisor: Dr. Marianthi Kiriakidou

Nonscientific interests: Music, traveling, international cuisines

My graduate work centered on the regulatory mechanism of Ama1-directed protein degradation during meiosis in *S. cerevisiae*. Currently, my research focuses on the function of Ago2 as the effector protein of the microRNP/RISC in the microRNA (miRNA) pathway. In this study, we developed an *in vitro* assay for high-throughput screen of RISC modulators, based on the changes in fluorescence polarization of TAMRA-labeled miRNAs when loaded onto purified Ago2. With this assay, we identified three small molecule inhibitors of RISC loading *in vitro* and *de novo* assembly of RISC *in vivo*. Our assay provides a novel large-scale molecular platform to explore the function of individual miRNAs, Ago proteins, and other key RNA-binding proteins in the miRNA pathway. (Read Tan's article, DOI: 10.1021/cb200253h)

Image courtesy of Glaucio Valdameri.

GLAUCIO VALDAMERI

Current position: Ph.D. student at Federal University of Paranà (UFPR), Department of Biochemistry and Molecular Biology, Curitiba, Brazil with Prof. Dr. Maria E. M. Rocha,, and a research scholar period at Institute of Biology and Chemistry of Proteins (IBCP), BMSSI, Drug Resistance Mechanism and Modulation laboratory, Lyon, France, under supervision of Dr. Attilio Di Pietro

Education: Unochapecó, B.S. in Pharmacy, 2006; Federal University of Paranà, M.Sc. in Biochemistry, 2008

Nonscientific interests: Music, archery, soccer, traveling

My master's degree in Biochemistry was focused on mitochondrial bioenergetics. We studied the importance of the core structure of flavones in promoting inhibition of the mitochondrial respiratory chain coupled to membrane modifications. My Ph.D. research was divided in two parts. The first one was performed at Federal University of Paranà assessing the flavones effects in human hepatoma cells and the involvement of ROS in the mechanism of cell death. The second one involved the identification and characterization of new classes of breast cancer resistance protein (BCRP/ABCG2) inhibitors and was carried out at IBCP with Dr. Attilio Di Pietro. Moreover, we are also exploring the transport and inhibition mechanisms of ABCG2. In this paper, we have replaced the hydroxyl groups of resveratrol (transported by ABCG2) by methoxy groups. We identified methoxy derivatives of stilbene as a new class of potent, specific, untransported and noncytotoxic inhibitors of breast cancer resistance protein. These new inhibitors are promising candidates for future *in vivo* experiments. (Read Valdameri's article DOI: 10.1021/cb200435y).

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