Introducing our AUTHORS

Image courtesy of Oya Bermek.

Aitziber L. Cortajarena

Current position: Yale University, Department of Molecular Biophysics and Biochemistry, Research Affiliate with Prof. Lynne Regan; IMDEA Nanociencia, Spain, Junior Group Leader

Education: Universidad del País Vasco/Euskal Herriko Unibertsitatea, Bilbao, Spain, M.S. in Biochemistry, 1997 and Ph.D. in Biochemistry, 2002; Yale University, Department of Molecular Biophysics and Biochemistry, Postdoctoral Researcher with Prof. Lynne Regan 2003–2009

Nonscientific interests: Traveling, reading, cooking

My research focuses on understanding the fundamental principles of protein structure, stability and function, and extract guidelines for protein design. In these works we present first a general method to create new proteins that recognize a desired target, using combinatorial libraries and a screen based on the split-GFP reassembly assay. In the second manuscript, we present an exciting example of novel protein modules that bind tightly and specifically to Dss1, a small human protein that interacts with the tumor suppressor protein BRCA2. We show that these modules are active in binding and in inhibition of Dss1 activity *in vivo* and used them to specifically alter cellular networks. This work thus represents an important step toward the realization of the control required to reprogram cellular function. (Read Cortajarena's articles, DOI: 10.1021/cb900272j and 10.1021/cb9002464)

Image courtesy of Lydia Finney.

Lydia Finney

Education: State University of New York at Albany, 1998, B.S. in chemistry (summa cum laude), 1998; Northwestern University, Ph.D. in Inorganic Chemistry, 2005, advisor: Dr. Tom O'Halloran; Postdoc, Biosciences Division of Argonne National Laboratory, advisor: Dr. David Glesne

Nonscientific interests: I enjoy playing piano, gardening, and jogging

Our paper on imaging metals in proteins highlights new methods we've been developing in collaborative work between the Biosciences Division and the X-ray science Division of the Advanced Photon Source (APS) of Argonne National Laboratory, along with the School of Chemistry at the University of Sydney. In this work, we use new methods and instrumentation to demonstrate, in a very vivid way, the interactions between chromium and blood serum proteins. As exciting as it is to me personally to use the world-class X-ray fluorescence microprobes at APS to learn more about the roles of metals in biology, as in our work on angiogenesis, it is equally if not more satisfying to help make new things possible, as we have done here. (Read Finney's article, DOI: 10.1021/cb1000263)

Image courtesy of Meredith Jackrel.

Meredith Jackrel

Current position: Yale University, Department of Chemistry, Ph.D. candidate with Prof. Lynne Regan

Education: The College of New Jersey, B.S. in chemistry, 2004

Nonscientific interests: Tennis, travel, cooking

My research focuses on understanding the principles of protein–ligand interactions and applying these principles to the design of small repeat proteins with desired binding specificities. In order to successfully identify interacting partners in protein libraries, higher throughput screening techniques allow for the screening of large libraries. Here we present the development of a split-GFP reassembly assay for the screening of libraries in order to identify proteins with novel binding properties. We have demonstrated the utility of this method by using it to develop small proteins that bind the c-Myc epitope tag and the Dss1 protein. (Read Jackrel's articles, DOI: 10.1021/cb900272j and 10.1021/cb9002464)

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Image courtesy of Tina Liu.

Tina Liu

Current position: Harvard Medical School, Department of Cell Biology, Ph.D. student with graduate research advisor Prof. Tom Rapoport
Education: Yale University, B.S. in Molecular Biophysics & Biochemistry, 2008 with undergraduate research advisor Prof. Lynne Regan
Nonscientific interests: Chamber music, drawing, cooking, photography

As an undergraduate in Lynne Regan's laboratory, I sought to use the architecture of tetratricopeptide repeat (TPR) domains as a basis for engineering novel ligand-binding partners. Specifically, I was interested in designing a binding partner for Dss1, a small protein associated with BRCA2. By creating a combinatorial library and screening it using the split-GFP reassembly assay, we generated a novel TPR protein that can specifically bind Dss1 and block its function *in vivo*. This project was exciting to me because it gets at what governs the specificity of protein−protein interactions and demonstrates how we can use that knowledge to make tools to study biological systems. Since then, I have moved on to become a Ph.D. student in Tom Rapoport's laboratory. Currently, my project focuses on how atlastin, a dynamin-like GTPase, remodels membranes in the endoplasmic reticulum. (Read Liu's articles, DOI: 10.1021/cb900272j and 10.1021/cb9002464)

Image courtesy of Kimberly Mendes.

Kimberly R. Mendes

Current position: Boston College, Department of Chemistry, Ph.D. candidate in chemistry with Prof. Evan Kantrowitz
Education: Boston College, B.S. in chemistry and economics, 2005
Nonscientific interests: Traveling, aquariums, exercising, and the Boston Red Sox

My research focuses on a molecular-level understanding of the allosteric enzyme *E. coli* aspartate transcarbamoylase (ATCase), the enzyme responsible for the regulation of pyrimidine nucleotide biosynthesis. The understanding of how cells regulate and control all aspects of their function is vital for our ability to intervene when these control mechanisms break down. Almost all modes of cellular regulation can be related in some manner to protein conformational changes such as the quaternary conformational changes of allosteric enzymes that alter enzyme activity. In this work we make use of the method that Dr. Peter Schultz and coworkers at Scripps have developed to introduce unnatural amino acids into proteins. In particular we incorporated a fluorescent amino acid into the allosteric binding site of the ATCase. Although Schultz's lab has developed methods to insert many unnatural amino acids, reports of the utility of unnatural amino acids in experimental systems has not kept pace with their development. In this work, the fluorescent amino acid we introduced is exquisitely sensitive to the binding of the allosteric effectors, and this new tool has allowed us to dissect allosteric regulation in a fashion that has not yet been possible using other common techniques. We are excited by our results and hope to see this technology applied to other complex biological systems soon. (Read Mendes' article, DOI: 10.1021/cb9003207)

Introducing our AUTHORS

Image courtesy of Dominic Sloane.

Dominic Sloane

Current position: University of Sheffield, YCR Institute for Cancer Studies, Postdoctoral Research Associate with Dr. Patrick Eyers, 2009–present
Education: University of Sheffield, Department of Molecular Biology & Biotechnology, Ph.D. student with Prof. Jon Waltho, 2008; University of Manchester Institute of Science and Technology (UMIST), B.Sc. (Hons) in biochemistry with applied molecular biology, 2001
Nonscientific interests: Cross-country running, badminton, cooking, eating

My research interests are focused on understanding the mechanism of action of protein kinase inhibitors and employing chemical biology techniques to determine the critical factors affecting inhibitor specificity and activity. The potential of chemical genetic techniques to simultaneously dissect signaling pathways and identify the specific target of clinical kinase inhibitors is demonstrated in our paper. An *in vitro* mutagenic analysis of Aurora A kinase identified amino acid requirements for the efficacy of the inhibitors MLN8054 and MLN8237. A human cell line model was then used to demonstrate that drug resistant mutants of Aurora A survive in the presence of these inhibitors, validating Aurora A as the central target of these compounds. In the future I am keen to investigate the cofactors and activating proteins that influence drug resistance, while expanding my research to include other proteins of clinical interest. (Read Sloane's article, DOI: 10.1021/cb100053q)

Image courtesy of A. Platts.

Michael Zivojin Trikic

Current position: Yorkshire Cancer Research (YCR) Institute for Cancer Studies, University of Sheffield, U.K., Postdoctoral Research Associate 2009–present
Education: University of Sheffield, Department of Molecular Biology and Biotechnology, Ph.D. with Dr. Lynda Partridge; University of Reading, B.Sc. (Hons) in biological sciences
Nonscientific interests: Rock climbing, mountain biking, growing plants

I love science, and the reasons for this are encapsulated in our paper. Based on the X-ray structure of Aurora A bound to the nonspecific kinase inhibitor MLN8054, we employed a rational molecular biochemistry approach to dissect binding and identify mutations that conferred resistance to this compound series. This data was then applied to a beautifully simple cell culture system to determine which mutations mimicked "bench top" inhibitor resistance in the complex environment of the cell. In doing this, we validated the target of this class of compounds, as well as identifying mutations that might allow additional customization of clinical cytotoxic therapies. For me, this represents the beauty of our field; using basic science to test a hypothesis with potential benefit to clinical science. (Read Trikic's article, DOI: 10.1021/cb100053q)