

# 3<sup>rd</sup> Annual Chemistry-Biology Interface Scientific Picnic

Sponsored by the NIH Chemistry-Biology Interface Fellowship

**WHO:** Penn Chemistry, Biochemistry & Molecular Biophysics, Wistar

**WHAT:** Graduate Student and Post-Doc Presentations and  
Poster Session

**Breakfast, Lunch, Dinner, and Fun included!**

**WHERE:** Swarthmore College

**WHEN:** Friday July 24th, 2009

**\*\*\*Register (for free) by sending an email to Daniela Fera [dfera@sas.upenn.edu](mailto:dfera@sas.upenn.edu)\*\*\***

Interested in presenting a talk or poster??

Speak to your PI or contact: Kate Thorn [kthorn@sas.upenn.edu](mailto:kthorn@sas.upenn.edu)



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# Chemistry-Biology Interface Scientific Picnic

Departments of Chemistry and  
Biochemistry & Biophysics  
University of Pennsylvania  
& The Wistar Institute

Friday, July 24th, 2009  
Swarthmore College  
Swarthmore, PA



## Schedule of Events

- 9:20 – 10:00 Check-in and Breakfast, Science Center 101  
10:00 – 12:00 **Morning Speakers**, Science Center 101  
Julia Richards, Department of Chemistry  
Bryan Gibb, BMB  
Geronda Montalvo, BMB  
Ning Shangquan, Department of Chemistry  
12:00 – 1:00 Picnic Lunch  
Box Lunch pickup at Upper Tarble, Clothier Hall  
1:00 – 2:00 **Poster Session**  
Upper Tarble, Clothier Hall  
2:00 – 4:00 **Afternoon Speakers**, Science Center 101  
Jasna Maksimoska, Department of Chemistry/Wistar  
Brandon Kelley, Department of Chemistry  
Daniel Dowling, Department of Chemistry  
Kathryn Smith, BMB  
4:00 – 5:00 Reception, Outdoor games, Parish Lawn  
5:00 – 6:00 Buffet Dinner, Upper Tarble, Clothier Hall

## The Chemistry-Biology Interface Scientific Picnic Organization Committee:

Julie Aaron, Department of Chemistry (julieaa@sas.upenn.edu)  
Daniela Fera, Department of Chemistry (dfera@sas.upenn.edu)  
Brittani Ruble, Department of Chemistry (burbur@sas.upenn.edu)  
Trey Schroeder, BMB (hws@mail.med.upenn.edu)  
Kate Thorn (kthorn@sas.upenn.edu)

We would like to thank all of the speakers, poster presenters and attendees; this event would not have been possible without your enthusiastic participation.

We would also like to thank the following people for their support and guidance.

Ronen Marmorstein, Faculty Advisor  
Mary Leonard, Webpage Designer  
Ruth Keris, BMB Academic Administrator  
Cheryl McFadden, Wistar Administrative Coordinator  
Rita Manfre, Wistar Associate Director of Grants & Contracts  
Matthew Lane, Executive Director, Department of Chemistry

Finally, we thank the Chemistry-Biology Interface (CBI) training grant from the National Institutes of Health (NIH) and Department of Chemistry for generous funding.

## **Poster Session**

### **Two hydrolase whodunits: on the trail of the yeast histone H4S1 phosphatase and the ant H3 tail clipping protease**

Ed Ballister, Berger Lab, BMB

### **Bio-Inorganic Interface: Ferritin-Nanoparticle Systems**

Jasmina Cheung-Lau, Dmochowski Lab, Department of Chemistry

### **Harnessing Hsp104 to Eliminate A $\beta$ 42 Fibers Implicated in Alzheimer's Disease**

Mimi Cushman, Shorter Lab, Neuroscience Graduate Group

### **Structure Based Drug Design of Human Papillomavirus E7 Inhibitors**

Daniela Fera, Marmorstein Lab, Department of Chemistry/Wistar

### **Photoregulating Gene Expression with Light Activated Oligonucleotides**

Julie Griepenberg, Dmochowski Lab, Department of Chemistry

### **Molecular mechanism and specificity of substrate binding by the E3 Ubiquitin Ligase Pellino**

Yu-San Huoh, Ferguson Lab, BMB

### **A Mechanism of Calcium Binding for the Regulation of Myosin Ib in its Role as a Tension Sensor**

John Lewis, Goldman Lab, CAMB

### **The X-ray Crystal Structure of Acetylpolyamine Amidohydrolase (APAH) from *Mycoplana ramosa***

Pat Lombardi, Christianson Lab, Department of Chemistry

### **Characterization of Novel PtdIns (4,5)P<sub>2</sub> Effector Domains**

Katarina Moravcevic, Lemmon Lab, BMB

### **Motor number controls cargo switching at actin-microtubule intersections in vitro**

Trey Schroeder, Goldman Lab, BMB

### **Dynamics of tRNA motions during protein synthesis: Single molecule studies of ribosomes in the pre- and post-translocation states**

Ben Stevens, Goldman Lab, BMB

### **Conformational changes of Hsp104 seen by Small Angle X-ray Scattering (SAXS)**

Elizabeth Sweeny, Shorter Lab, BMB

## **The Crystal Structure of the Rtt109-Vps75 HAT-Histone Chaperone Complex**

Yong Tang & Katie Meeth, Marmorstein Lab, Wistar

## **Development of Novel Methods for the Synthesis and Control of Protein Structure.**

Mark Fagley & Anne Wagner, Petersson Lab, Department of Chemistry

## **Validation of 1-aminoanthracene as a fluorescent general anesthetic**

Zhengzheng (Katie) Liao, Dmochowski Lab, Department of Chemistry

## **Presentation Abstracts**

### **Photoregulation of the 10-23 DNAzyme**

**Julia Richards**, Dmochowski Lab

The timing and location of gene expression within the cell is important for differentiation and development. In recent years, caged oligonucleotides, whose function is blocked by a photoactive moiety and restored after irradiation, have been investigated for their ability to control gene expression with high spatial and temporal control. One method of inhibiting gene expression involves the use of catalytic DNAs known as DNAzymes with the ability to cleave RNA. We have designed DNAzymes that either activate or inactivate upon irradiation, depending on the placement of a light-induced strand break. Three positions within the DNAzyme were investigated: a) the catalytic core, b) the binding arms, and c) joining the 5' and 3' ends. By placing a photocleavable spacer at specific positions, we found we could make enzymes that turned off or on upon irradiation.

### **Breaking down the active site of Cre recombinase: understanding the mechanism of cleavage and ligation**

**Bryan Gibb**, Van Duyne Lab,

Cre recombinase is part of the large family of tyrosine recombinases which itself is a member of the larger superfamily of type Ib topoisomerases. This superfamily shares a conserved phosphoryl transfer mechanism in the cleavage and ligation of DNA. Despite this, the recombinases and topoisomerases have vastly different functions. The enzymes have no significant sequence identity and the reaction rates for topoisomerases are several orders of magnitude faster than the tyrosine recombinases. In an attempt to understand the evolutionary relationship between these enzymes and also learn about the catalytic mechanism the crystal structures of transition state intermediates of cre

recombinase and variola topoisomerase Ib were solved. Surprisingly, they have nearly super imposable active sites with one glaring exception. A conserved histidine in the tyrosine recombinases is not found in the topoisomerases. What is the function of this histidine? Why is this histidine conserved? How important are the other conserved residues in the active site? The use of biochemical assays has been used in an attempt to address these questions and help test the tolerance for change in the active site of Cre.

## **Infrared Spectroscopy and Folding Kinetics of a $\beta$ -Peptide Helix**

**Geronda Montalvo**, DeGrado Lab

Protein folding is a critical problem in chemistry, biochemistry, biophysics, and molecular biology. By elucidating the mechanisms of protein folding, unfolding, and stabilization, we gain significant insight into the links between folding dynamics and disease, and lay the groundwork for the design of new materials. As our understanding of protein folding has expanded, scientists have designed synthetic “foldamers”, including  $\beta$ -peptides, which are non-biological sequence-specific oligomers of  $\beta$ -amino acids that can fold into a diverse variety of secondary and tertiary structures.  $\beta$ -Peptides form stably folded helices similar to those formed by  $\alpha$ -peptides, but the folding kinetics of this new class of peptides is not nearly as well understood. In this study we used Circular Dichroism (CD) Spectrometry, Infrared (IR) Spectroscopy, and Laser Induced Temperature Jump (T-jump) to characterize the thermodynamic stability and folding kinetics of a  $\beta$ -peptide. Results show that the  $\beta$ -peptide studied has medium-stability and demonstrates slow relaxation kinetics, on the order of a few hundred nanoseconds.

## **Roquefortine C and Related Biological Activities**

**Ning Shangguan**, Joullie Lab

Roquefortine C is a natural product whose structure exhibits a rare E-dehydrohistidine moiety. Isoroquefortine C is the Z-isomer of roquefortine C that was prepared from roquefortine C by UV light treatment but never found in nature. While roquefortine C shows potent biological activities and strongly binds to heme, isoroquefortine C does not show any significant biological activity and only binds to metal weakly. The E and Z configurations of dehydrohistidine moiety determine the accessibility of the imidazole nitrogen lone pairs, and are responsible for the difference in biological activities of the respective compounds. The synthetic methodology needed to prepare roquefortine C and isoroquefortine C will also be discussed.

## **Structure based design of organometallic PAK1 inhibitors**

**Jasna Maksimoska** .Marmorstein Lab

p21 activated kinase 1 (PAK1), a member of a p21 activated kinase family, is a kinase that plays an important role in a variety of cellular processes such as cytoskeletal remodeling, cell motility and gene expression. In addition, recent studies show altered PAK1 expression in various human cancers including breast cancer, neurofibromatosis, colon, ovarian and bladder cancer making it an important therapeutic target. However, there are no selective inhibitors available for PAK1 with IC<sub>50</sub> values in the nanomolar range. There is therefore a growing need for potent and selective PAK1 inhibitors as probes to further elucidate the molecular mechanism of PAK1 signaling in cancer and to serve as a lead compounds for development of therapeutic agents. Here, we report on the development of organoruthenium PAK1 inhibitors with IC<sub>50</sub> values in the nanomolar range. Using the crystal structure of PAK1 in complex with a lead organoruthenium compound and through structure-activity studies, we developed two octahedral ruthenium complexes  $\Lambda$ -**FL172** and  $\Lambda$ -**FL411** that exhibit mid-low nanomolar inhibition of PAK1 *in vitro*. Testing **FL172** against a panel of 264 kinases demonstrated that the majority of kinases cannot accommodate these relatively bulky octahedral complexes as well as PAK1 since only 15 kinases were inhibited up to 80% when using 3  $\mu$ M of compound. Finally, the octahedral ruthenium complexes were shown to be cell permeable and able to evoke cellular responses associated with PAK1 inhibition in mammalian cells. Thus, the bulky organoruthenium compounds  $\Lambda$ -**FL172** and  $\Lambda$ -**FL411** are promising starting points for the generation of improved and highly selective PAK1 inhibitors.

### **Nucleophilic Ring-Opening of Trisubstituted Aziridines**

**Brandon Kelley**, Joullie Lab

Aziridines are synthetically useful intermediates in organic chemistry due to a highly strained ring system that allows for a wide range of reactivity via ring-opening reactions. However, di- and trisubstituted aziridines often show diminished regioselectivity. Nonetheless, in the syntheses of ustiloxin and phomopsin an ethynyl, trisubstituted aziridine was employed to construct a tertiary alkyl-aryl ether linkage and the ring-opening reaction occurred with complete regio- and stereoselectivity. To investigate the regioselectivity, functional group homologated and alkyl aziridines were synthesized to change the electronics of the aziridine ring to determine if a mixture of regioisomers would be obtained. Regardless, both were regioselective with attack occurring exclusively at the more substituted carbon. In each case a phenol nucleophile was used, however the use of the nucleophiles and the construction of a new carbon-carbon bond would be of high synthetic interest. Using the ethynyl, trisubstituted aziridine we set out to build the new carbon-carbon bond through the use of a Nicholas reaction

## **An unexpected protein superfamily: Arginase, Histone Deacetylase, and Acetylpolyamine Amidohydrolase**

**Daniel P. Dowling**, Christianson Lab

Despite sharing less than 15% sequence homology, histone deacetylase (HDAC) enzymes adopt the fold first discovered for rat arginase in 1996 by Kanyo *et al.* Additionally, the enzyme acetylpolyamine amidohydrolase (APAH), which similarly catalyzes a deacetylation reaction, shares moderate sequence identity with the HDAC enzymes, and recent work in our lab indicates that APAH adopts the arginase fold. These enzymes are metallohydrolases and require one or two divalent metal cation cofactors in catalysis. Structural comparisons reveal key features of the core fold that contribute to the divergent metal ion specificity and stoichiometry required for the chemical and biological functions of these enzymes.

## **Probing the Mechanism of Action of Antimicrobial Peptides through Lipid Diffusion**

**Kathryn B. Smith**, Gai Lab

Antimicrobial peptides (AMPs) are an essential component of the innate immune response and are known to selectively interact with target bacterial membranes. The mechanisms of these AMPs have been the focus of many recent studies; however, the antimicrobial mechanisms of these peptides are complex and hence are still not well understood. Here, we present a new method, which is based on monitoring the diffusion behaviors of the lipid molecules in membranes that are invaded by an AMP, for probing how AMPs function. Our preliminary results obtained with two well-studied AMPs, magainin2 and mastoparan X, indicate that this method is capable of revealing structural information that is otherwise difficult to attain using other methods. Thus, it is useful in providing new insights into the mechanism of action of AMPs from the perspective of lipid diffusion. In this talk, the details of the method will be discussed.