



## DIVISION OF BIOLOGICAL CHEMISTRY AMERICAN CHEMICAL SOCIETY

# NEWSLETTER

<http://www.divbiolchem.org/>

Secretary: T. D. Meek

Fall 2017

### Message from the Chair: Craig Townsend, Ph.D.

First, I hope all attendees to the ACS meeting in Washington DC in August enjoyed the meeting, especially the DBC program. For that, we thank Liz Hedstrom and the Program Committee for the excellent DBC sessions, and we thank Liz again as she passes the mantle to Shana Kelly as head of the Program Committee for 2018. We also acknowledge and thank Vahe Banderian for his service on the Program Committee. Chris Whitman retires as the DBC Treasurer at year's end, and we thank him for his superb job in that role. Others who leave the DBC leadership team with our thanks for an excellent job include: Christine Hrycyna (Nominating Committee), Erin Carlson and Wendy Kelley (Councilors) and Aimin Liu and Karen Buchmueller (Alternate Councilors). Thank you all very much for your service and commitment to the Division.

The DBC leadership team met at the Washington meeting, and here are outcomes of our discussion. The DBC team agreed to, and is pleased to support the following conferences: Oxygen Radicals GRC (Feb 4-8, 2018), GRC Metallocofactors (June 10-15, 2018), Genetic Code Expansion Conference (August 9-11, 2018), GRC/GRS on Bioorganic Chemistry (June 9-15, 2018), GRC Metals in Biology (Jan 21-26, 2018), Metals in Medicine (June 24-29, 2018), R. Bryan Miller

Symposium (March 15-16, 2018), 73rd Annual Southwest Regional Meeting (SWRM) Structural Biology symposium (Oct 29-Nov 1, 2017) and the Texas EMC (January 5-6, 2018).

DBC membership: The DBC leadership team is encouraging all of its members to contact 5 non-members they know and ask them to join the DBC if they have not already done so. The annual dues remain a meager \$15, and the more who join our division, the more influence the DBC will bring to the Society and help our work to sustain the biological chemistry community. So please ask your friends to join. We invite you to gather with us in New Orleans (March 18-22, 2018) for some great science at the spring National meeting in a historic city.

*Biochemistry*. As all of you know, Prof. Alanna Schepartz became Editor of *Biochemistry* last year. She joined us at our business meeting in Washington to inform us about the status of the journal one year into her editorship, including changes and lack of changes. Alanna reported that she (and the ACS) wishes *Biochemistry* to remain the "go-to" journal for biological chemistry, including protein and cellular biochemistry and (mechanistic) enzymology. It also seeks to branch out into other areas including RNA biology and neurosciences. In the past year, the impact factor for the journal rose for the first time in a decade. While manuscript submissions for topics in mechanistic enzymology and structural biology remain

steady in the past year, papers in synthetic and chemical biology are increasing, which could lead to increased total annual pages for the journal. This will necessitate increased rigor in peer review. *Biochemistry* now accepts articles as Communications and Perspectives with emphasis on younger authors. *Biochemistry* is also increasing its profile in social media (Facebook, Twitter), and the journal would be happy to receive videos from DBC members as to why you love *Biochemistry*.

### **Congratulations to 2018 Division of Biological Chemistry Award Winners!**



Professor Mohammad R. Seyedsayamdost is the recipient of the **2018 Pfizer Award in Enzyme Chemistry** in recognition of his contributions to the discovery of new enzymatic transformations in microbial systems. His research blends approaches from microbiology,

bacterial genetics, natural products chemistry, and mechanistic enzymology to characterize the structures, functions, and biosynthesis of bacterial secondary metabolites. These metabolites are of importance to microbial communities, such as the human microbiome, and play decisive roles in human health and disease. One area of focus in the Seyedsayamdost group has been the identification of new metalloenzymes that catalyze unusual transformations during secondary metabolite biosynthesis. Specifically, his group characterized streptide, the founding member of a novel class of peptide natural products produced by the probiotic bacterium *Streptococcus thermophilus*. Structural elucidation of streptide revealed an unprecedented post-translational modification consisting of an intramolecular carbon-carbon crosslink between the side-chains of lysine and tryptophan. Further investigations showed that

a new subfamily of radical SAM metalloenzymes install this unique modification in a single step, the mechanistic basis of which has been delineated in detail. Moreover, his group has examined the biosynthesis of the antibiotic drug-of-last resort, vancomycin, and demonstrated the involvement of cytochrome P450 metalloenzymes in creating some of the aromatic macrocycles, which endow the antibiotic with exquisite biological activity. Together, these studies have expanded our knowledge regarding the capabilities of metalloenzymes in synthesizing complex molecules; they have important implications for the utility of enzymes in the creation of designer natural products with desired biological functions.



Prof. Brad Pentelute is the winner of the **2018 Eli Lilly Award in Biological Chemistry**. Throughout evolution, Nature has developed molecular machines to rapidly manufacture, tailor, and deliver large functional biopolymers such as proteins into

specific cells. Inspired by these mechanisms of nature, the Pentelute Lab has aimed to invent new chemistry for the efficient and selective modification of proteins, to 'hijack' these biological machines for efficient drug delivery into cells and to create new machines to rapidly and efficiently manufacture peptides and proteins. The invention of new chemistry is sought to modify Nature's proteins to enhance their therapeutic properties for human medicine. This goal has posed immense challenges because proteins contain 20 amino acids that present different reactive functional groups and have a 3D shape that is moderately stable. In light of these obstacles, the newly developed chemistry needs to be protein compatible, site-selective, quantitative, and carried out in water at reasonable

temperatures to maintain protein integrity and function. The Pentelute Lab has met these challenges and has developed a series of highly efficient and selective chemistries that can modify the amino acid cysteine and lysine within peptides and proteins. These newly developed chemistries can be catalyzed by enzymes or even promoted by a motif discovered by Pentelute's group, which is coined a 'pi-clamp'. This extensive protein modification toolkit has enabled the production of some powerful molecules including peptide macrocycles that cross cell membranes to disrupt cancer or antibody drug conjugates to kill breast cancer cells.

The Pentelute group is also focused on the delivery of large biomolecules into the cell cytosol. The group has developed a chemical approach for the systematic investigation of a nontoxic form of anthrax toxin, which transports enzymes into cells via a protective antigen-protein pump. The Pentelute Lab has recently discovered that the protein pump can deliver a wide range of cargo molecules into cells including antibody mimics, mirror-image proteins, small molecules, and enzymes. Once in the cytosol, the cargo activates biologically and in certain cases perturbs protein-protein interactions that drive cancer. The Pentelute group made a noteworthy cell biology discovery with this biomolecular delivery platform: the act of simply installing a single D-amino acid on an otherwise large L-protein turns off a key mechanism for cytosolic protein degradation. This discovery will aid in the development of durable cell-based protein therapeutics.

The Pentelute group has also invented a fully automated fast-flow machine to accelerate the chemical manufacture of polypeptides. It has built the world's fastest and most efficient machine that can produce thousands of amide-bonds orders of magnitude faster than commercially available instruments. The machine is inspired by Nature's ribosome that can incorporate 9 amino acids into a polypeptide chain per second. While the Pentelute group's fast-flow technology is not

as fast as the ribosome, it can form one amide bond in 7 seconds. This technology not only facilitates rapid polypeptide generation but also has enabled the group to carry out an entire D-scan of proteins to investigate protein folding and functions. This technology may solve the manufacturing problem for personalized peptide cancer vaccines.

Prof. Michael Gelb is the winner of the **2018 Repligen Corporation Award in the Chemistry of Biological Processes** in



recognition of his research contributions in the area of enzymology applied to medicine. Major accomplishments have been made in 4 areas. The first is two decades or work with the late Mahendra Jain (Univ. of Delaware) and Otto Berg (Univ. of Uppsala) on developing the fundamental paradigm for studying the action of enzymes at the membrane-water interface (interfacial enzymology). This work has led to methods for the proper evaluation of enzyme inhibitors and substrate specificity of interfacial enzymes, most notably phospholipases. More recent work in this area have helped to understand the role of phospholipases A<sub>2</sub> in pro-inflammatory eicosanoid cascades relevant to asthma and arthritis.

In the late 1980s, the Gelb lab in collaboration with the late John Glomset (Univ. of Washington) discovered a post-translational protein modification in eukaryotic cells called protein prenylation. The discovery that Ras proteins are farnesylated led to a massive campaign in pharma to develop novel anticancer drugs. Gelb and Glomset also

discovered that most G-proteins are bound to membranes via 15-carbon farnesyl or 20-carbon geranylgeranyl groups.

The third area of research in the Gelb lab is aimed at discovery of new drugs for treating neglected diseases caused by parasites (malaria, African sleeping sickness, Chagas, and Leishmaniasis). Some of the top ranking pre-clinical drug candidates in this area have been put forward by the Gelb lab in collaboration with parasitologists Fred Buckner and Wes Van Voorhis (Univ. of Washington).

The final area, and the one that is prominent in Gelb's lab now, is the use of mass spectrometry for quantitative proteomics and clinical chemistry. The Gelb lab developed Isotope-Coded Affinity Tag reagents (ICAT) in collaboration with Frank Turecek and Ruedi Aebersold (Univ. of Washington). As a team, Gelb, Turecek and C. Ronald Scott (Univ. of Washington) have advanced the use of tandem mass spectrometry for screening of newborns to detect inborn errors of metabolism, most notably lysosomal storage diseases. This work has led to the first worldwide effort to screen for these disorders and is rapidly becoming part of the newborn screening panels in each state's newborn screening laboratory in the USA. With newborn screening in place, treatments for these diseases can be initiated before the onset of irreversible symptoms and lead on to a greatly improved quality of life for infants and children.

**DBC Elections.** November was elections month not only nationally but for the DBC! The following have been elected to officer roles on the DBC, beginning in the new year, and we congratulate them, as well as look forward to working with them!

Treasurer: Christine Chow

Program Committee: Mark Distefano

Nominating Committee: Sarah Michel

Councilors: Barb Golden and Lana Saleh

Alternate Councilors: Tonya Zeczycki and Andy Fisher

Best wishes, and I hope to see you in New Orleans,

Craig Townsend

Chairman  
Division of Biological Chemistry

### **255th ACS National Meeting, March 18-22, 2018, New Orleans, LA**

The ACS Division of Biological Chemistry will organize a program of talks and posters for the ACS Spring National Meeting in New Orleans, LA. The program will consist mainly of oral sessions composed of short 20 minute talks and poster sessions. Program Chair: [Shana Kelley](#), University of Toronto.

**Travel Awards:** The Division offers travel awards for graduate students and postdoctoral fellows to attend the National Meetings. The level of support is \$750, which can be used to offset travel costs and registration fees. Detailed information about these awards can be found on the [Travel Awards](#) page.

**Spring 2018 Program Preview (to be published in C&E News Jan 22, 2018.**

### **Travel Awards**

The division offers travel awards for graduate students and postdoctoral fellows to attend the 255<sup>th</sup> ACS National Meeting in 2018. **The deadline for submission is January 15, 2018, and submission details may be found here**(<http://www.divbiolchem.org/awards/travel-awards>) The level of support is \$500, which can be used to offset travel costs and registration fees. Detailed information about these awards

is provided later in this Newsletter and on the division website.

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### **Future National Meetings**

**255<sup>th</sup> ACS National Meeting, March 18-22, 2018, New Orleans, LA.** Program Chair: Shana Kelly ([shana.kelley@utoronto.ca](mailto:shana.kelley@utoronto.ca))

**256<sup>th</sup> ACS National Meeting, August 19-23, 2018, Boston, MA.** Program Chair: Shana Kelly ([shana.kelley@utoronto.ca](mailto:shana.kelley@utoronto.ca))

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### **Regional ACS Meetings**

#### **9<sup>th</sup> Southeast Enzyme Meeting**

**April 7, 2018 – Atlanta, GA.** The Southeast Enzyme Conference (SEC), a one-day annual event, will take place Saturday, April 8, at Georgia State University in Atlanta, Georgia. The conference will feature eight talks by faculty, post-doctoral scholars, and graduate and undergraduate students selected from submitted abstracts. The conference will include two poster sessions to facilitate discussion and collaborative interactions between scientists from all career stages. The meeting strongly encourages the participation of students and postdoctoral associates and provides opportunities for discussions and networking. A keynote presentation by Professor Tadhg Begley of Texas A&M, College Station, will conclude the event.

### **Support for Meetings**

The Division of Biological Chemistry provides grants to support symposia at ACS Regional meetings and for conferences in research areas of interest to the division membership. Members interested in applying for support from the Division for a symposium or conference during 2018-2019 should submit

an outline for the event as an e-mail attachment to the Treasurer Chris Whitman ([whitman@austin.utexas.edu](mailto:whitman@austin.utexas.edu)). These proposals will be reviewed twice a year at the Division's business meetings, which are held during the Spring and Fall ACS national meetings. The deadlines for receipt of applications are **March 1** and **August 1** for review at the Spring and Fall meetings, respectively. Unfortunately, due to increased numbers of funding requests, proposals received after a given deadline will only be considered at the business meeting held after the next deadline. These awards are intended to provide Division members with new forums in which to present their work as well as to support focused conferences in biochemistry and chemical biology. Proposals that are judged not to meet these objectives, such as requests for blanket support of regional ACS meetings, are unlikely to be funded. Currently for 2016, the Division will provide support for the following symposia and meetings held this year:

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### **Murray Goodman Memorial Prize**

Dr. Hilary Crichton is the new Editor-in-Chief of the journal *Biopolymers*, and this journal that sponsors the Murray Goodman Memorial Prize in Biopolymers. This award recognizes outstanding accomplishments in one or more of the areas of biochemistry, biophysical chemistry, biophysics and/or chemical biology. The award was established in honor of the late Dr Murray Goodman, a world-renowned bio-organic chemist, and the Founding Editor of *Biopolymers*.

Nominations for the Murray Goodman Prize should contain a statement of 1,000 words or fewer, detailing the research accomplishments of the nominee, as well as the nominee's current CV and two letters in support of the nomination. Nominations should be sent via e-mail attachment to:

Dr. Hilary J. Crichton  
Editor, *Biopolymers*  
[biopolymers@wiley.com](mailto:biopolymers@wiley.com)

### **Travel Awards to Attend the 253<sup>st</sup> ACS National Meeting**

The division offers travel awards on a competitive basis for graduate students and postdoctoral fellows to attend the meeting and present a poster on their research in the DBC. The selected awardees will be reimbursed up to \$500 for travel and registration expenses. Receipts must be submitted along with a request for reimbursement after the meeting. No more than two awards will be made to one laboratory for any single ACS meeting. In addition, **please note that no individual can win more than one division travel award in his/her lifetime.**

#### **How to apply for a Travel Award**

- (1) Fill in the Travel Award Application (next page).
- (2) Attach a printed copy of your abstract.
- (3) Attach a one page CV.
- (4) Attach a signed letter of recommendation from your faculty advisor.
- (5) Send **ONE COMPLETE PDF FILE** of this material as *single* EMAIL attachment to the Program Chair, Shana Kelly ([shana.kelley@utoronto.ca](mailto:shana.kelley@utoronto.ca)). Be sure to use a subject line of "**ACS Travel Awards**" in your electronic application.

**The deadline for submission of an application for a travel award to the 253<sup>st</sup> ACS National Meeting (New Orleans, LA) is **January 15, 2018.****

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**Application for a Travel Award for Graduate Students  
and Postdoctoral Fellows**

**Deadline: January 15, 2018 (New Orleans, LA)**

Name: \_\_\_\_\_ Advisor: \_\_\_\_\_

Department \_\_\_\_\_ Graduate Student: \_\_\_\_\_  
Postdoctoral Fellow: \_\_\_\_\_

Institution: \_\_\_\_\_ Street: \_\_\_\_\_

City, State, Zip: \_\_\_\_\_

Tel: \_\_\_\_\_ E-mail: \_\_\_\_\_

Is an Abstract attached? \_\_\_\_\_ Is a CV attached? \_\_\_\_\_

Is the advisor's recommendation letter (one page) attached? \_\_\_\_\_