



BIOLOGICAL CHEMISTRY DIVISION AMERICAN CHEMICAL SOCIETY

NEWSLETTER

Secretary: J. P. Richard

<http://www.biochemdivision.org>

August 2007

Message from the Chair Carol Fierke

The Division of Biological Chemistry had a great year in 2007. We are very thankful to Tadgh Begley and the program committee for the enormous effort they put into organizing the wonderful programming at the ACS fall meeting. This year the Biological Chemistry Division hosted exciting award symposia for the Repligen, Pfizer, and Lilly awards as well as the first annual Murray Goodman Memorial Prize. This award was established in memory of Dr. Murray Goodman, founding editor of *Biopolymers*, by John Wiley & Sons and the Editor-in-Chief of *Biopolymers* to recognize outstanding achievement in one or more areas of biochemistry. I would like to congratulate the 2007 and 2008 award winners and to thank the corporate sponsors for their support in recognizing the best of the excellent scientists in the biochemical area.

The Biological Chemistry Division continued two important outreach activities this year. The Division provided funds to subsidize joining the ACS and traveling to the fall ACS meeting for 10 graduate students and postdoctoral fellows so that they could present their work at this meeting. This initiative is important for mentoring and developing the next generation of scientists. Additionally, the Division provides roughly a dozen grants each year to support symposia presented at ACS Regional Meetings and other meetings of interest to the membership of our Division.

I would like to thank the two officers, John Richard, secretary, and Eugene Mueller, treasurer, who are responsible for the hard work of keeping the Division running. In particular, in the past year John Richard and Uli Iserloh of ISERLOH DESIGN launched an updated Website at: <http://www.biochemdivision.org>. This website contains important information about the activities of the Division. Finally, I urge everyone to vote in

the upcoming election for members of key Biological Chemistry Division committees. These elected officials will play an important role in determining the future direction of the Division.

The Division of Biological Chemistry is highly interactive, as evidenced by the many symposia at the 2007 fall ACS meeting that are co-sponsored with other ACS divisions. The DBC welcomes participation by scientists with diverse interests in Biological Chemistry, including those whose interests overlap with analytical, medicinal, inorganic, organic, and carbohydrate chemistry as well as the emerging discipline of chemical biology. To continue this trend, for the first time the Biological Chemistry Division is sponsoring programs at both the Spring (April 5 - 9, 2008 in New Orleans, LA) and the Fall (August 17-21, 2008 in Philadelphia PA) national ACS meetings. In contrast to the fall programming, the spring meeting will consist primarily of short, 20 minute talks selected from the submitted abstracts. The goal of this program is expand the opportunities for the members, especially the younger members, of the Biological Chemistry Division to present their work to the chemical community.

One challenge for all areas of Chemistry is to attract and mentor scientists from diverse backgrounds. The Chemistry community has been actively addressing this challenge by participating in two national workshops developing plans and strategies to increase the representation of women and minorities on the faculty of research universities. These workshops, entitled *Building Strong Academic Programs through Gender Equality* (Jan. 2006) and *Excellence Empowered by a Diverse Academic Workforce: Achieving Racial & Ethnic Equity in Chemistry* (Sept. 2007), are providing information about the barriers to success, developing best practices to encourage participation, and impacting policies in the chemical sciences nationally. The future of Chemistry depends on our ability to attract the best and brightest minds to the chemical disciplines from diverse backgrounds.

DIVISION AWARDS FOR 2008

**Eli Lilly Award in Biological Chemistry:
Professor Paul J. Hergenrother,
Department of Chemistry, University of
Illinois.**

**For outstanding research in biological
chemistry of unusual merit and independence
of thought and originality.**

This award recognizes Professor Hergenrother's application of chemical principals to the study of cellular processes in developing promising new approaches to arresting cancer, and to treating bacterial diseases.

Paul Hergenrother has developed a research program that is grounded in biological chemistry, and combines his expertise in synthetic organic chemistry and molecular biology. He has used this integrated chemical/biochemical approach to identify several new therapeutic strategies for the treatment of cancer and bacterial diseases, and he has validated these strategies by identifying novel cellular targets, and new chemical reagents to affect the cellular activity of these targets.

Plasmids are central to the development of bacterial resistance to a large number of antibiotics. Hergenrother hypothesized that a simple strategy for restoring antibacterial activity in resistant cells would be to induce the elimination of plasmids from the bacteria. He then decided to search for small molecules that interfere with the process that allows a bacterium to decide if a plasmid is native, and trigger the destruction of foreign plasmids. Hergenrother has taken an important step towards this goal by identifying a compound that mimics the properties of an incompatible plasmid. This provides an important validation for a new mechanism-based strategy for the elimination of bacterial plasmids.

More recently, Hergenrother has validated a new concept in anti-cancer drug discovery: the *direct* activation of procaspase-3, the precursor of the antiapoptotic protein caspase-3. Most cancer cells have mutations at some point in their apoptotic pathways that disable this important process for effecting cell death, Hergenrother therefore hypothesized that by directly activating a protein at a very "low" point in the apoptotic cascade one could bypass the defective portion of the cascade and reestablish apoptosis.

Hergenrother has identified a small molecule (called PAC-1) that activates procaspase-3 to its active form *in vitro* and *in vivo*. He has shown that this compound is effective in killing a range of cancer cell lines. This demonstration that small molecules can activate this class of proenzymes opens up totally new avenues and targets in medicinal chemistry.

In summary, Hergenrother has demonstrated a unique capacity to discover compounds with fascinating biological activity. His rapid progress at a young age reflects a capacity to combine a deep understanding of chemical principals with an appreciation, at the molecular level, of the cellular process that cause the disease state.

**Pfizer Award in Enzyme Chemistry:
Professor Carsten Krebs, Department of
Chemistry, The Pennsylvania State
University.**

**For outstanding work in enzyme chemistry
where the presence of enzyme action is
unequivocally demonstrated.**

This award recognizes Professor Krebs's stellar contributions to our understanding of oxygen and C-H activation by metalloenzymes. He and his many collaborators have explored a vast body of new territory in applying Mössbauer spectroscopy to the study of enzyme mechanisms, and have made discoveries that are destined to be included in textbooks.

Krebs was trained in Mössbauer spectroscopy as a postdoctoral fellow with B. H. Huynh in the Physics Department at Emory University. He moved to Penn State in 2002, where he has worked with an outstanding group of young investigators on difficult and important problems in metallo-biochemistry. Krebs first major contribution as an individual investigator was in a collaborative study with Martin Bollinger on the non-heme iron dependent α -ketoglutarate dioxygenases. This family of proteins is involved in DNA repair, sensing of oxygen levels, hydroxylation of asparagines involved in blood clotting etc. The Krebs/Bollinger team has provided the first example of a kinetically competent iron (IV) oxo species long sought by the bioinorganic community. They have provided evidence for the formation of similar iron (IV) oxo species in two different hydroxylase systems: taurine dioxygenase and prolyl hydroxylase.

Krebs and Bollinger have identified a fourth class of ribonucleotide reductase in the intracellular human parasite *Chlamydia*. Their characterization of the active site of this enzyme settles a long-standing debate by demonstrating the presence of a manganese-dependent ribonucleotide reductase. These novel and unexpected results have demonstrated the presence of a new Mn^{4+}/Fe^{3+} cluster and shown that this cluster supports kinetically competent enzyme-catalyzed reduction of ribonucleotides. Finally, in a collaborative study with Chris Walsh, on a chlorination reaction catalyzed by another α -ketoglutarate dependent protein, Krebs and Bollinger have observed two ferryl species as reaction intermediates. These results are exciting, novel and provide a starting point for determining how these proteins prevent hydroxylation and effect chlorination.

In summary, Krebs many investigations are highlighted by several major advances in bioinorganic chemistry. This work has earned the respect of the community of mechanistic enzymologists for its creativity and depth.

Repligen Award in Chemistry of Biological Processes: Professor Hung-Wen (Ben) Liu, Department of Medicinal Chemistry, University of Texas.

For outstanding contributions to the understanding of the chemistry of biological processes with particular emphasis on structure, function and mechanism.

This award recognizes Professor Liu's studies to elucidate and exploit Nature's strategies to synthesize unusual sugars and secondary metabolites. His discoveries in this area have changed the way chemists and biologists think about the biosynthetic pathways for unusual sugars. Most notably, Liu has been a pioneer in the field of combinatorial biosynthesis that leads to the diversification of sugars found in macrolide antibiotics.

Professor Liu's research focuses on the elucidation of the chemistry of mechanistically novel biological reactions that are of unusual physiological importance. The Repligen award recognizes his research accomplishments in three areas at the interface of chemistry and biology.

Many of the most intriguing and complex enzymatic transformations proceed through radical intermediates that are transient in nature and exceedingly difficult to detect and characterize. Professor Liu has made many seminal contributions to the characterization of radical intermediates. Two prominent examples are medium-chain acyl-CoA dehydrogenase, which Liu showed proceeds by two successive single electron transfers from the reduced flavin to the α,β -unsaturated CoA ester; and, ascarylose biosynthesis where Liu established a new role for coenzyme B₆. These studies were driven by the development of several useful radical probes and have greatly increased our understanding of radical-based enzymatic transformations.

Ben Liu has a well-developed program in the design, synthesis and use of novel mechanism-based inhibitors of enzymatic reactions. These inhibitors have potential applications as drugs that target enzymes in pathogenic bacteria. Most notably, Liu has designed and synthesized several fluorinated substrate analogue inhibitors. The design and study of these compounds is characterized by an elegant fusion of synthetic organic chemistry and mechanistic enzymology.

Finally, Professor Liu has recognized that the biological activities of macrolide antibiotics are often controlled by the type, position and number of unusual sugars contained in the macrolide. Liu has concentrated on the portions of antibiotic biosynthetic pathway responsible for biosynthesis and attachment of unusual sugars. He has cloned the genes responsible for the biosynthesis of several unusual sugars, and expressed these genes in engineered *Streptomyces* species capable of producing antibiotics. This has led to the construction of new bacteria that produce hybrid antibiotics. This work opens the door for even more extensive engineering of these biosynthetic pathways.

Liu is thickly involved in the scientific enterprise. Under his wing as the George H. Hitchings Regents Chair in Drug Design are some two-dozen graduate students and postdoctoral fellows. He is a member of many scientific societies, an organizer of conferences, a grant reviewer, and an editor or adviser for a range of scientific journals. When asked what accomplishment makes him most proud, Liu says "the best things have yet to come."

In summary, Ben Liu is an outstanding representative of a new generation of bioorganic

chemists. His laboratory is a training ground for future scientists, to whom he transfers his passion and enthusiasm for chemistry and biology.

FUTURE NATIONAL MEETINGS

235th National Meeting, April 5 - 9, 2008 - 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, April 6 - 10, 2008. The goal of the Division's officers is to expand the opportunities for our members to present their work to the chemical community. The officers strongly encourage members to submit abstracts for this meeting, and to support one another by attending these the oral and poster sessions.

The program for the spring meeting is being organized by the program chair Tadhg Begley, Department of Chemistry, Cornell University (tpb2@cornell.edu). The program will run for two days [April 8 and 9] and include four sessions:

Frontiers in Chemical Biology Biological Macromolecules New Techniques in Chemical Biology Enzymes and Pathways

Each session will consist primarily of short 20 minute talks selected from the submitted abstracts. In addition there will be a poster session held on April 7.

236th National Meeting, August 17-21, 2008 - Philadelphia PA. James Stivers at the Department of Pharmacology and Molecular Sciences, Johns Hopkins School of Medicine will serve as the Chair of the Program Committee for this meeting (jstivers@jhmi.edu).

237th National Meeting, March 22-26, 2009 - Salt Lake City, UT.

238th National Meeting, August 16-20, 2009 - Washington DC. Suzanne Walker, Department of Microbiology and Molecular Genetics, Harvard University will serve as the Chair of the Program Committee for this meeting (suzanne_walker@hms.harvard.edu).

Updated Website for the Division of Biological Chemistry

The Division has launched an updated Website at:

<http://www.biochemdivision.org>

The website was designed by Uli Iserloh of ISERLOH DESIGN with the assistance of the Division's secretary. The website will allow our members quick access to the following information.

- (1) The Division's newsletter.
- (2) Information about the ACS National and Regional meetings and Gordon Conferences relevant to Biological Chemistry.
- (3) Information about other Conferences of interest to our members
- (4) Information about the Divisions awards and the Award recipients.
- (5) Information about career opportunities in Biological Chemistry, including job openings and information about people who are seeking positions.

Members interested in posting information of any type on this web site should contact the Division's secretary at: (biochdiv@chem.buffalo.edu)

Regional Meetings.

The Division of Biological Chemistry provides grants to its members of up to \$1500 to support the expenses of a one day symposium at any ACS Regional meeting. Members interested in organizing a symposium at a regional meeting in 2007 should provide an outline for the proposed program to:

Suzanne Walker
**Department of Microbiology and
Molecular Genetics**
Harvard Medical School
200 Longwood Ave.
Boston, MA 02115
suzanne_walker@hms.harvard.edu

These proposals will be reviewed twice a year at the Division's Officer meetings, which are generally held during the Spring and Fall ACS meetings.

Division Election. The election this year will fill the following offices.

Program Committee Member (4 year term).
Nominating Committee Member (3 year term).
Executive Committee (Two for 3 year terms).
Councilors (Two for 3 year terms)

The division is grateful for the hard work of the nominating committee, Phillip A. Cole, Eric Brown and Anna Mapp in identifying this slate of exceptional candidates. The strength of our Division depends upon the willingness of its members to offer their time to serve as officers. The Division is indebted to the following members who have agreed to stand for office this year.

The election ballot, biographies of the candidates, and an envelope addressed to the Division's secretary were sent to our members by regular mail. Please return this ballot, using the enclosed envelope, by October 15, 2007.