BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

JANUARY 2007 NO. 221

UTMB

BMB Biochemistry & Molecular Biology

Chair's Message

Happy New Year.

Our return to work one day delayed, coupled with all the new grant deadlines and online submission worries, not to mention the state of the NIH budget, reinforces our need to figure out ways in which the Department can enhance our ability to successfully compete for research and graduate training support. For example, providing tuition support for graduate students paid from grants is not possible from certain funding sources, and we need to find alternate sources for some students. It is my plan to focus much of our effort this spring on this venture and enlist partners in other Departments and Centers to help us in this endeavor.

Our staff reorganization is a continuing work in progress; at this point Marianne Miller would welcome feedback and suggestions. We will also be evaluating how this process is coming along, with special reference to the important issues discussed above concerning support of faculty in obtaining research funding.

We also need to continue working with other UTMB units on developing institutional reports that give faculty the ability to keep track of their grants on a month by month basis via a "user friendly" mechanism. I can't make any promises about when this capability might be provided since we have still not seen a satisfactory solution after more than a year of frustrating attempts to get this information in a suitable form. We will continue to push this as actively as possible. In the past, the lack of reliable grant account information had a very negative impact on our departmental budget. Now we simply cannot afford to go forward blind, as it were.

As mentioned previously, we plan to showcase our faculty and students more frequently in our Newsletter and, apart from the merit of the thing in itself, another good reason is to facilitate collaborative opportunities for our faculty with the rest of the University.

In summary, my goals for the Department for this year will be to 1) Provide more opportunities for our faculty, staff and students to succeed; 2) Work with our staff to develop the management tools to make certain processes more manageable; and 3) to provide a level of financial stability amidst changes external to the department so that we can continue to focus on the academic nature of our missions.

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Inside this issue:

Special Items of Interest

- New - Faculty Focus Wlodek Bujalowski, Ph.D., page 3
- Research Spotlight—Molecular Genetics Core, page 5
- Dr. Konkel's Research Coordinator's Columns Online (no new column this month)

Graduate Program News—BCSO News

Once again, the BCSO topped off the year with a successful Christmas Toy Drive. This is an annual event whereby the BCSO raises funds to buy presents for kids under the care of the Children's Protective Services of Galveston County. This year, we sponsored two girls—Lindsey and Minnie—and received over $370 in donations. The BCSO would like to thank the faculty members, post-docs, staff members, and students for their generous contributions. We would also like to thank Dr. Stan Watowich, the current BCSO faculty advisor, for helping to broadcast our fundraising efforts. As the BCSO has grown over the years, we are extremely happy to give back to the community and bring some joy to those in need.

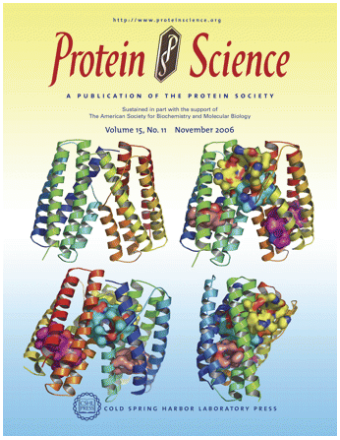
We would also like to extend an invitation to all our faculty members, postdocs and fellow students to attend our student seminars starting January 19 (Fridays at noon - Basic Science Auditorium). This is a wonderful opportunity to get to know our students and their research accomplishments.

The first presenters will be: Ragav Kulasegaran Shylini (Dr. Gorenstein) and Suzanne Tomlinson (Dr. Watowich) on January 19 and Jennifer Rodriguez Rivera (Dr. Dineley) on January 26th.

Awards and Announcements

Dr. Robert Fox's group published a paper that was featured on the cover of Protein Science, viewed here: http://www.proteinscience.org/content/vol15/issue11/cover.shtml

Hindupur A, Liu D, Zhao Y, Bellamy HD, White MA, Fox RO. The crystal structure of the E. coli stress protein YciF. Protein Sci. 2006 Nov;15 (11):2605-11. Epub 2006 Sep 25.



Faculty Focus: Wlodek Bujalowski, Ph.D.

Dr. Wlodek M. Bujalowski received his Ph.D. in 1982 from Poznan University, Poland in Physical Biochemistry of nucleic acid structure and protein - nucleic acid interactions. After a year as a visiting scientist at the Department of Chemistry at the University of Stony Brook, New York, in the laboratory of Dr. Benjamin Chu, he undertook postdoctoral studies in the laboratory of Nobel laureate Dr. Manfred Eigen and Dr. Ditmar Pörschke at the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, where he was involved in chemical relaxation studies of the dynamics of tRNA structure and Codon - Anticodon recognition processes. In 1986, he joined the group of Dr. Timothy M. Lohman at Texas A&M University in College Station, where his work concentrated on statistical mechanical analyses of single-strand-binding protein interactions with DNA and development of general quantitative methods to examine multiple ligand - macromolecule binding processes, using optical spectroscopic methods.

In 1990, Dr. Bujalowski joined the Faculty of the University of Texas Medical Branch at Galveston, where he currently is a professor at the Department of Biochemistry and Molecular Biology and the Department of Obstetrics and Gynecology. He is also a Senior Scientist in both the Sealy Center for Structural Biology, and the Sealy Center for Cancer Cell Biology.

The research of my group concentrates on the quantitative understanding of the structure-function relationships in protein-nucleic acid interactions in solution and the mechanism of free energy transduction in these complexes. Particular attention is directed toward elucidation of the molecular mechanism of substrate recognition and catalysis by the motor proteins of DNA metabolism, DNA helicases and polymerases. We are among the few that have initiated such studies and are currently among the leading groups worldwide in quantitative studies of the mechanism of hexameric helicases in solution. This is an essential class of enzymes involved in all aspects of nucleic acid metabolism.

DNA replication and repair are fundamental processes for the transmission of genetic information from one cell generation to another. At the heart of these processes is the synthesis of DNA, catalyzed by DNA polymerases. DNA repair polymerases are at the front of the organism's defense against damage to its DNA. Activities of these enzymes have been implicated in several human cancers and genetic diseases, as well as in the development of viral infections. Therefore, it is of fundamental importance to understand the molecular mechanism by which DNA repair polymerases function.

Part of our work is devoted to development of quantitative methods to study the thermodynamics, kinetics, and structure of macromolecular complexes in solution, using spectroscopic and hydrodynamic techniques. The methods include relaxation kinetics, time-dependent fluorescence spectroscopic methods, static and dynamic fluorescence energy transfer approaches, applications of analytical ultracentrifugation, and dynamic light scattering.

In general, we have a long-term interest in understanding structure-function relationships in macromolecular interactions in solution and protein-nucleic acid interactions in particular. The famous Sherlock Holmes statement expresses the underlying "philosophy" of our approach: "*It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories instead of theories to suit facts*". Such understanding can be achieved through quantitative thermodynamic, kinetic, and structural (spectroscopic and hydrodynamic) studies of relevant complexes. Only then can biomedical design and application analyses be performed in the most rational and efficient manner.

Publications & Grant Awards

Ferreon AC, Ferreon JC, **Bolen DW, Rösgen J.** Protein Phase Diagrams II: Nonideal Behavior of Biochemical Reactions in the Presence of Osmolytes. *Biophys J.* 2007 Jan 1;92(1):245-56.

Hindupur A, Liu D, Zhao Y, Bellamy HD, **White MA**, **Fox RO**. The crystal structure of the *E. coli* stress protein YciF. *Protein Sci.* 2006 Nov;15(11):2605-11. Epub 2006 Sep 25.

Mukherjee M, Dutta K, **White MA**, Cowburn D, **Fox RO**. NMR solution structure and backbone dynamics of domain III of the E protein of tick-borne Langat flavivirus suggests a potential site for molecular recognition. *Protein Sci.* 2006 Jun;15(6):1342-55.

Das A, Wiederhold L, Leppard JB, Kedar P, Prasad R, Wang H, Boldogh I, Karimi-Busheri F, Weinfeld M, Tomkinson AE, Wilson SH, **Mitra S**, **Hazra TK**. 2006 NEIL2-initiated, APE-independent repair of oxidized bases in DNA: Evidence for repair complex in human cell. *DNA Repair:* **5**: 1439-48

J. Regino Perez-Polo Introduction: Discovery of NGF. In: Handbook of Neurochemistry and Molecular Neurobiology, 3rd Edition Neuroactive Proteins and Peptides, Abel Lajtha and Ramon Lim, Springer, Germany, 2006.

GRANTS

"Anti-Apoptosis Treatment for Hypoxia/Resuscitation" Principal Investigator: J.Regino Perez-Polo, PhD Agency: 8540 The Shriners Hospital for Children, Period: January 1, 2007 through December 31, 2007.

To have your publication or award included in the monthly newsletter, please send the information directly to Lisa Pipper (lpipper@utmb.edu) by the 1st of each month.

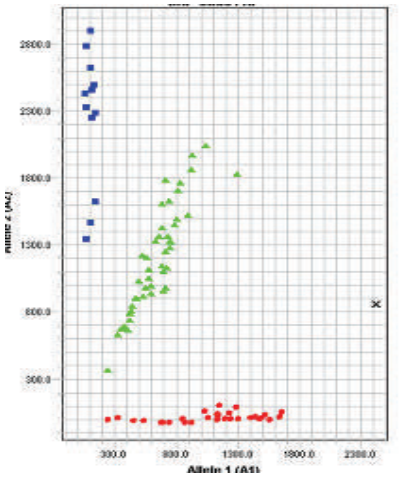
Administrator's Notes

The Spring Term course "Molecular Basis of Disease: Cell Volume Regulation in Health and Disease", coordinated by Drs. Papaconstantinou, Bolen, and Nesic, will feature invited lectures by five noted scientists. Presentation of these lectures is being supported by the Mary Huling Edens Lectureship, an endowment established in 1975 by Lee Edwards Edens, M.D., UTMB Class of 1921, in memory of his wife. The first lecture will be presented on February 1 by Dr. Martha O'Donnell. The complete schedule for the 2007 Edens Lectures will be distributed shortly, along with more information about Dr. and Mrs. Edens and Dr. Edens' vision for the memorial lectureship.

The Department sends its best wishes to Diane Strain, the Coordinator assisting Drs. Papaconstantinou and Carney, as she recovers from injuries she sustained in an accident. We hope Diane will be back in three or four weeks.

Marianne

Spotlight:
Molecular Genetics Core



Dr. Tom Wood is director of the Molecular Genomics Core (MGC) which offers services for analysis of both gene expression and genetic variance. The core offers high throughput analysis of single nucleotide polymorphisms (SNPs) for those investigators searching for SNPs associated with a clinical outcome (Affymetrix SNP Chip) and low throughput for those with a known association (Allelic Specific PCR).

Single nucleotide polymorphisms or SNPs (pronounced "snips") are DNA sequence variations that occur when a single nucleotide (A,T,C,or G) in the genome sequence is altered. For example a SNP might change the DNA sequence A**A**GGCTAA to A**T**GGCTAA. For a variation to be considered a SNP, it must occur in at least one percent of the population. SNPs, which make up about nine percent of all human genetic variation, occur every 100 to 300 bases along the 3-billion-base human genome. Many SNPs have no effect on cell function, but researchers believe others could predispose people to disease or influence their response to a drug.

Although more than 99 percent of human DNA sequences are the same across the population, variations in DNA sequence can have a major impact on how humans respond to disease; to environmental insults such as bacteria, viruses, toxins, and chemicals; and to drugs and other therapies. This makes SNPs of great value for biomedical research and for developing pharmaceutical products or medical diagnostics. SNPs are also evolutionarily stable –exhibiting little change from generation to generation --making them easier to follow in population studies.

Researchers believe SNP maps will help them identify the multiple genes associated with such complex diseases as cancer, diabetes, vascular disease, and some forms of mental illness. These associations are difficult and cost prohibitive to establish with conventional “gene-hunting” methods.

Finding SNPs in genes that cause or contribute to a disease is one of the most challenging tasks for a researcher, because the SNP could be anywhere in the 3.1 billion A, C, T and G molecules that make up our genome. It's like looking for a needle in a haystack, and researchers often don't even know where to begin. SNP analysis tells them what section of the genetic haystack to start looking in, and Affymetrix GeneChips allows them to find the disease-causing gene much more quickly.

For those Researchers who know the SNPs they wish to survey, Allelic discrimination assays offer an inexpensive means to evaluate a large number of samples. Through TaqMan® based chemistry, these assays provide SNP detection capabilities with high-confidence results. Custom TaqMan® SNP Genotyping Assays can be used for almost any possible SNP with both accurate and reproducible results.

The MGC is located in the Medical Research Building, Rm. 6.156 and more information can be found online at www.scmm.utmb.edu/genomics/.

Featured Abstract by BMB Faculty

The crystal structure of the *E. coli* stress protein YciF

Aditya Hindupur[1,4], Deqian Liu[1,4], Yonghong Zhao[1,3], Henry D. Bellamy[2], Mark A. White[1], and Robert O. Fox[1]

[1] Department of Biochemistry and Molecular Biology and The Sealy Center for Structural Biology & Molecular Biophysics, The University of Texas Medical Branch, Galveston, Texas 77555-0647, USA
[2] Center for Advanced Microstructures and Devices, Louisiana State University, Baton Rouge, Louisiana 70806, USA

(RECEIVED April 27, 2006; FINAL REVISION July 19, 2006; ACCEPTED July 20, 2006)

YciF is a protein that is up-regulated when bacteria experience stress conditions, and is highly conserved in a range of bacterial species. YciF has no known structure or biochemical function. To learn more about its potential molecular function and its role in the bacterial stress response, we solved the crystal structure of YciF at 2.0 Å resolution by the multiple wavelength anomalous diffraction (MAD) technique. YciF is a dimer in solution, and forms a homodimer in the crystal asymmetric unit. The two monomers form a dimer with a molecular twofold axis, with a significant burial of solvent-accessible surface area. The protein is an all-alpha protein composed of five helices: a four-helix bundle, and a short additional helix at the dimer interface. The protein is structurally similar to portions of the diiron-containing proteins, rubrerythrin and the *Bacillus anthracis* Dlp-2.

New Employees

Junji Iwahara, Ph.D., Assistant Professor in BMB, 6.614 Basic Science Bldg.
(Dr. Iwahara will be featured in the "Faculty Focus" section of the February edition of this newsletter)

Shubhra Dastidar,Ph.D., Postdoctoral Fellow working in Dr. Catherine Schein's lab.

Mikhail Kochukor, Ph.D., Senior Res. Assoc. working in Dr. Cheryl Watson's lab.

Christian Wilson, Student Research Assistant working in Dr. James Lee's lab.

Faculty on the Road

Dr. Stanley J. Watowich was an invited speaker at the M.D. Anderson Cancer Systems Biology Symposium in Houston, TX on Thursday, December 14th. The title of his talk was "Top-down and Bottom-up Approaches to Understanding Complex Systems."

Dr. Darrell Carney, John Bergmann and Dr. Barbara Olszewska-Pazdrak attended the American Society for Cell Biology annual meeting in San Diego, California from 12/9/2006 - 12/14/2006. John Bergmann and Dr. Pazdrak presented posters.

Dr. Ching-chyuan (Winston) Hsieh from Dr. Papaconstantinou's laboratory also presented a poster while attending the American Society of Cell Biology annual meeting in San Diego, California from 12/9/2006 - 12/14/2006.

Dr. Cheryl Watson traveled to Chapel Hill, NC to attend the NIEHS Expert panel whitepaper workshop on the actions of bisphenol A.

Dr. Watson was also invited to M.D. Anderson, the Department of Genitourinary Medical Oncology, to present a seminar entitled "Membrane steroid receptors and their role in cancer cell responses" on Dec. 12, 2006.

To have your travels included in the monthly newsletter, please send the information directly to Lisa Pipper (lpipper@utmb.edu) by the 1st of each month.

New - ONLINE Version
Research Coordinator's Corner
www.bmb.utmb.edu/department/RCC/

Dr. Konkel's Column will not be published this month.

JANUARY 2007 NO. 221

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Our Department is home to a broad spectrum of research activities and expertise. Our most singular quality is a culture of interdisciplinary research and collaboration. We believe that teaching and research are interdependent activities, and so give high priority to the education of our graduate students and postdoctoral fellows.

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