BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

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UTMB

BMB Biochemistry & Molecular Biology

Chair's Message

Over the next couple of months we will be bringing on campus recruits for faculty positions as planned. We have an excellent roster of applicants, and we should have the new faculty member(s) on campus by September.

This is also the time when the Texas Legislature begins its budgetary planning. News from Austin is very good for UTMB. The mandatory 10% budget cut required of state agencies will not apply to us. Furthermore, the $57 million promised for the matching funds for the Galveston National Laboratory is 99% sure to come through, a savings of close to $5 million to the medical school (construction interest funds). Also, funds for teaching are likely to increase for the first time in years. That budget was kept constant as the number of students increased. Some funds for Rita losses are also finally on the way. In sum, UTMB is likely to get around $25 million more this time around.

In addition, a new research building, to which $30 million is already committed, may benefit from PUF funds to allow construction of a 150,000 sq. ft. building. At a more local level, we are working hard to develop a budget that is realistic to the fulfillment of our educational, research and service mission. Our budget discussion with the Dean will take place during the month of May.

Although rumors galore are afloat, I can honestly say that I have no idea as to the final outcome of the search for a new President, except to say that the finalists will be visiting UTMB during April, and by May I think we will all know who the President is going to be. As I understand it, the candidates will meet with Chairs of Departments and the Research Advisory Task Force. If you have suggestions for questions or information you think the candidates should have, contact Dr. T. Ashizawa (the Chair of the Task Force) or myself (I am also a member) and I will pass it on.

Four of the Basic Science Chairs have met to discuss joint projects. One initial venture may be a Basic Science Seminar Series on a specific topic, with outstanding scientists being invited. This series would replace some of the regular individual departmental seminars. More on this as developments warrant.

Do not forget the Students Research Forum on April 26 and 27 and the coming graduation exercises for the Graduate School and the Medical School during the months to come; please plan to participate in these events.

-regino

Inside this issue:

Special Items of Interest

Graduate Program News—BCSO News

The past couple of months have been very productive for the BCSO. Our students have been organizing the “Pioneering Biological Discovery” seminar series, and this year we have invited two distinguished speakers—Dr. Isaiah Fidler from UT M.D. Anderson in June and Dr. George Somero from Stanford University in November. The BMB student-hosted seminar series have always been very successful in organization and attendance since it was started in 2003, and we plan for this year’s events to be equally impressive. Also, the BCSO has been actively involved in several community-wide events such as the Galveston County Science & Engineering Fair, the Galveston Beach Clean-up, and the Gulf Coast Big Brothers Big Sisters "Bowl for Kids' Sake 2007." To foster friendship and camaraderie among students, we have organized numerous social activities such as trips to an indoor rock climbing gym in League City and a Houston Rockets basketball game. Upon the arrival of Spring and nice weather, we are planning a field trip to see the Cirque du Soleil performance of Corteo in Houston as well as a group event at a nearby winery. If you want to learn more about the BCSO and our activities, you can visit our website http://bmb.utmb.edu/graduate_program/BCSO/ and/or contact any of the BCSO officers.

Corey Theriot, 4th year BMB student .

Awards and Announcements

A new daughter, Lauryn Elizabeth, was born to **Amber and Mike Zwernemann** on March 16. Amber is a Research Associate in the laboratory of Dr. Darrell Carney.

Dr. David Gorenstein and Dr. Darrell Carney were honored during presentation of the Chancellor’s Entrepreneurship and Innovation Awards at the inaugural *Research and Technology Transfer Showcase* sponsored recently by UT System. Dr. Gorenstein was honored for his role in conceiving and launching the Gulf Coast Consortium for Structural Biology. The Consortium was formed to promote and facilitate collaborative research and training in structural biology by the six prominent biomedical research institutions in the Galveston/Houston area. Dr. Carney was recognized for his work on development and commercialization of the thrombin-derived peptide, Chrysalin (TP508), which shows promise for promoting wound healing and fracture repair. A report on the *Showcase* and the presentation of Dr. Carney’s and Dr. Gorenstein’s awards is provided in the March 2007 edition of **Impact,** available at http://www.utmb.edu/impact/stories/07APRIL2/techtransfer.htm

The **Commencement ceremony for the Graduate School of Biomedical Sciences** is scheduled on Saturday, May 5 at 10:00 am in Levin Hall.

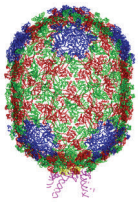
The **117th Commencement of the School of Medicine** will take place on Saturday, June 2 at 10:00 am at Moody Gardens.

Dr. Brad Thompson recently placed 1st in his age group (70-74 men) in the Lonestar Triathlon that was held at Moody Gardens March 31st. He finished ahead of many of the other contestants from other age group as well with a time of 1:39:20.95.

Faculty Focus: Marc Morais, Ph.D., Asst. Professor, BMB

Dr. Marc Morais received his Ph.D. from the department of cellular physiology at the Boston University School of Medicine in 2000. As a graduate student in Dr. Karen Allen's laboratory, Marc used X-ray crystallography, kinetics, molecular biology, and bioinformatics to address questions in mechanistic enzymology. This work explored the ways in which related catalytic chemistry and unique substrate specificity evolve from a common protein scaffold. After graduate school, Marc joined the laboratory of Dr. Micheal Rossmann at Purdue University. The majority of his research has focused on the bacteriophages f29 and fX174. A combination of X-ray crystallography, cryo-electron microscopy, and bioinformatics was used to determine pseudo-atomic structures of different morphological states of the viruses. This work uncovered evolutionary relationships between distantly related viruses, provided insights into the assembly of viral shells, and suggested a mechanism by which a virally encoded molecular motor packages the virus genome within this shell. Dr. Morais was appointed Assistant Professor, Biochemistry and Molecular Biology, in January 2007.

Our laboratory uses a combination of cryo-electron microscopy, x-ray crystallography, and bioinformatics to elucidate the structures of complex macromolecular assemblies and machines. Our work focuses on virus structure and the general principles by which viruses self-assemble. In particular, we are interested in how virus self-assembly strategies can be targeted in the design of anti-viral therapeutics, and how these same strategies might be employed in the construction of nanomachines.



Pseudo-atomic structure of bacteriophage ϕ29 determined using a combination of cryo-EM and X-ray crystallography.

We are also interested in the structures of morphologically heterogeneous viruses with low, partial, or no internal symmetry. Many viruses relevant to human health fit this description, yet their structures remain largely unknown (Ebola, Hantaan, SARS corona, influenza, HIV, and Smallpox are but a few examples). We are developing methods to facilitate structure determination for these types of viruses.

Finally, we are interested in virus evolution and the viruses which infect the archea. Because hyperthermophilic archea possess metabolisms well-suited for the hot anaerobic conditions thought to prevail on an early earth, hyperthermophilic viruses likely played an important role in the early stages of evolution. Studies on genome organization, replication and regulation of gene expression indicate an evolutionary relationship between archeal viruses and viruses of mesophilic bacteria and eukaryotes. Verification of this hypothesis by sequence comparison is difficult because the rapid evolution of viral genes precludes detection of relationships over large evolutionary distances. However, structural similarity often persists during evolution in spite of vanishing sequence homology. Thus, the structures of viruses infecting hyperthermophilic archea should provide insights into virus origin and the evolution of viruses and cells.

Structure of a virus DNA packaging motor determined by cryo-EM. Two protein components of the motor are shown in green and blue, and an RNA component is shown in magenta. The atomic structure of DNA, shown as spheres, was modeled into its corresponding cryo-EM density. The motor tranlocates viral DNA into a preformed virus capsid.

Fu, C.Y., Morais, M.C., Battisti, T.J., Rossmann, M.G., & Prevelige, PE Jr (2007) "Molecular dissection of f29 scaffolding protein function in an in vitro assembly system", *J. Mol. Biol.* Mar 2;336(4):1161-73

Morais, M.C., Choi, K.H., Koti, J., Chipman, P.R., Anderson, D.L. & Rossmann, M.G. (2005). "Conservation of the capsid structure in tailed dsDNA bacteriophages: the pseudo-atomic structure of f29", *Mol. Cell,* **18(2)** 149-159

Morais, M.C., Fisher, M., Kanamaru, S., Przybyla, L., Burgner, J., Fane, B.A., & Rossmann, M.G. (2004). "Conformational switching by the scaffolding protein D directs assembly of bacteriophage fX174", *Mol. Cell.* **15(6)** 991-997.

Morais, M.C., Zhang, G., Zhang, W., Olsen, D.B., Dunaway-Mariano, D., & Allen, K.N. (2004). "X-ray crystallographic and site-directed mutagenesis analysis of the mechanism of Schiff-base formation in phosphonoacetaldehyde hydrolase catalysis", *J. Biol Chem.* **279(10)** 9353-9361.

Morais, M.C., Kanamaru, S., Badasso, M.O., Koti, J., Owen, B.A.L, McMurray, C.T., Anderson, D.L., and Rossmann, M.G. (2003). "Bacteriophage f29 scaffolding protein gp7 before and after prohead assembly", *Nat Struct Biol*. **7(10)** 572-576.

Morais, M.C., Tao, Y., Olson, N.H., Grimes, S., Jardine, P.J., Anderson, D.L., Baker, T.S., & Rossmann, M.G. (2001). "Cryo-electron microscopy image reconstruction of symmetry mismatches in bacteriophage f29", *J. Struct. Biol.* **135** 38-46.

Simpson, A., Tao, Y., Leiman, P., He, Y., Badasso, M.O., Olson, N., Jardine, P., *Morais, M.C., Anderson, D., Baker, T.S., & Rossmann, M.G., (2000). "The structure of the bacteriophage f29 DNA packaging motor at near atomic resolution", *Nature* **408** 745-750.

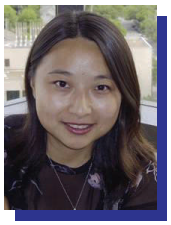
SPOTLIGHT: BMB Students Set to Receive Ph.D. in May

Three BMB students have completed all requirements for awarding of the PhD and will be receiving their doctor's hoods from their mentors at the May 5 Commencement of the Graduate School of Biomedical Sciences.

Craig Bush

Working with his mentors, Dr. Bruce Luxon and Dr. Aubrey Thompson, Mayo Comprehensive Cancer Center in Florida, Craig completed his degree requirements in December 2006. Craig's abstract of his dissertation research: "We have used a novel bioinformatics approach to analyze the genomic consequences of the activation of the transcription factor Peroxisome Proliferator-Activated Receptor Gamma (PPARy) in human colorectal cancer cells. From this approach, we revealed a yet unappreciated link between PPARy and a caclcium-mediating signaling in the proliferation and invasion in colorectal cancer". Craig has started his post doctoral employment with Ching Lau, MD, Ph.D at Texas Children's Hospital Cancer Genomics Research Laboratory.

Song Liu



Song's mentor is Dr. David McAdoo and she completed her degree requirements in November 2006. The research reported in her dissertation "I have been working on the mechanism of secondary injury in spinal cord injury, especially the effect of glutamate. I found that interleukin-1 beta is involved in glutamate-induced spinal cord injury and MAPKs are also involved. The administration of IL-1ra, an interleukin-1 receptor antagonist helps rat locomotor function recovery from glutamate-induced spinal cord injury." Song and her husband are expecting their first child.

Rodrigo Maillard

Rodrigo is the first graduate of the BSCB Program. He completed his degree requirements in March 2007 under the guidance of Dr. James Lee. Rodrigo has begun working with Dr. Carlos Bustamante at University of California at Berkeley, in the Physical Biosciences Division of the Lawrence Berkeley National Laboratory. His dissertation research involved the study of The Molecular Basis for Evasion of Antibody-mediated Neutralization in Flaviviruses. Rodrigo received numerous awards during his education at UTMB. Among them were the Barbara Bowman award, the first Biological Chemistry Student Organization (BCSO) $1,000 award, and Who's Who Among Students in American Universities & Colleges.

-Dr. Lillian Chan, Program Director; Dr. D. Wayne Bolen, Director; BSCB Educational Track, Deborah Botting

12th Annual Structural Biology Symposium

The Sealy Center for Structural Biology and Molecular Biophysics (SCSB) again is hosting its annual Symposium, which will be held on **May 18-19, 2007** in Levin Hall. Drs. Braun and Epstein have put together an outstanding slate of speakers for the program, including James A. Spudich, Ph.D., from Stanford, as the Keynote speaker, who will be speaking on the "Regulation of the Cell's Dynamic City Plan and the Myosin Family of Molecular Motors." All details about the program, including the on-line Registration form, can be accessed at: **www.scsb.utmb.edu/symposium**

The Program Chairs are extending the Abstract Deadline through April 20th, or the date when 100 abstracts have been submitted. As of yesterday, there were 91 abstracts accepted, so if you are interested in submitting a poster for this meeting, please do not delay. 2007 marks the twelfth year of SCSB sponsoring the Annual Symposium, with support from the Department of Biochemistry and Molecular Biology and the Keck Center for Interdisciplinary Bioscience Training of the Gulf Coast Consortia. Please direct any questions to Angelina Johnson at: **ajohnson@utmb.edu** **or 409-772-8083**.

Administrator's Notes

Level of Effort Reporting by Researchers

We appreciate the cooperation of research faculty, students, and staff who have completed the online "Level of Effort" report for the period of September 2006 through February 2007. Researchers who have not yet completed the report are asked to make certain to **enter their estimates of effort on specific projects by April 16**. To check the reconciliation of reported effort with recorded salary allocations, Departmental Financial Group staff members, Ernest Leal and Brenda Romero, will be sampling certain reports and may be contacting individual researchers if any problems are noted. For questions about Level of Effort reporting requirements or for assistance with entry of the effort report, Department members should e-mail Ernest (eleal@utmb.edu) or Brenda (bgromero@utmb.edu).

Special Cleaning Efforts in the Basic Science Building

Staff members and managers of Environmental Services have been making a concerted effort to restore corridors, labs, and other spaces in the Basic Science Building to an appropriately clean state and to maintain those conditions once the restoration of specific areas is completed. An additional staff member has been assigned to the custodial team for the building: **Michael Fontenot has joined the dedicated Associates, Jessica Scott, Elizabeth Arrequin, and Alberto Lujan**. Kaye Mears, Operations Manager for Environmental Services, and Alton Caldwell, Operations Supervisor, have been coordinating the effort to achieve a cleaner, brighter environment in this aging and challenging building. BSB occupants appreciate all these individuals' hard work.

Administrative Staff Members Achieving Important Results

Working with Dr. Allan Brasier and Margie Wronski, **Shirley Broz** has provided expert coordination for the visits by five candidates for two new faculty positions in the Sealy Center for Molecular Medicine – one position to be focused on Bioinformatics and one on Biomarker Discovery. The candidates came from areas as close as Dallas and as far away as Dublin.

The BMB and BSCB Graduate Programs are wrapping up a busy recruitment and admissions season. Working with the Graduate Program Admissions Committees chaired by Dr. Jose Barral (BMB) and Dr. Andres Oberhauser (BSCB), **Debora Botting** has kept all the administrative and organizational processes running well and has worked hard to assure that the large quantity of information relating to individual student applications was appropriately collected, summarized, and presented to support the committee's decision-making. Debora also provided critical liaison with the Graduate School Admissions Office throughout the process, making sure that GSBS requirements were met as well as assuring that the Department's concerns were appropriately addressed.

The **48th National Student Research Forum** will be held on April 26th and 27th on the UTMB campus. BMB's **Dr. Jeffrey Rabek and Dr. E. Brad Thompson are Faculty Advisors** for the event, which will feature Paula Tallal, Ph.D. as the 2007 Abreu Memorial Keynote Speaker. Dr. Tallal currently serves as the Board of Governors Professor of Neuroscience and is also a Co-Director for the Center for Molecular & Behavioral Neuroscience at Rutgers University. More information is available at the NSRF website.

Publications & Grant Awards

Kang, J, Lee MS, **Gorenstein DG**. Characterization of heparin-living bacteria interactions by chemiluminescence electrophoretic mobility shift assay. **Anal Biochem.** 2007 Apr 15;363(2):312-4. Epub 2007 Feb 2.

Liu T, Whitten ST, **Hilser VJ**. Functional residues serve a dominant role in mediating the cooperativity of the protein ensemble. **Proc Natl Acad Sci U S A.** 2007 Mar 13;104(11):4347-52. Epub 2007Mar 5.

Fennewald SM, Scott EP, Zhang L, Yang X, Aronson JF, **Gorenstein DG**, **Luxon BA**, Shope RE, Beasley DW, Barrett AD, Herzog NK. Thioaptamer decoy targeting of AP-1 proteins influences cytokine expression and the outcome of arenavirus infections. **J Gen Virol.** 2007 Mar;88(Pt 3):981-90.

Guan X, Bai H, Shi G, Theriot CA, **Hazra TK**, **Mitra S**, Lu AL. The human checkpoint sensor Rad9-Rad1-Hus1 interacts with and stimulates NEIL1 glycosylase. Nucleic Acids Res. 2007 Mar 29; [Epub ahead of print]

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.

Featured Abstract by BMB Faculty

Functional residues serve a dominant role in mediating the cooperativity of the protein ensemble.

Liu, T., Whitten, S.T., Hilser, V.J. **Proc Natl Acad Sci U S A.** 2007 Mar 13;104(11):4347-52. Epub 2007 Full Text Link

Department of Biochemistry and Molecular Biology, and Sealy Center for Structural Biology and Molecular Biophysics, University of Texas Medical Branch, Galveston, TX 77555-1068.

Conformational fluctuations in proteins have emerged as a potentially important aspect of biological function, although the precise relationship and the implications have yet to be fully explored. Numerous studies have reported that the binding of ligand can influence fluctuations. However, the role of the binding site in mediating these fluctuations is not known. Of particular interest is whether in addition to serving as structural scaffolds for recognition and catalysis, active-site residues may also play a role in modulating the cooperative network. To address this question, we employ an experimentally validated ensemble-based description of proteins to elucidate the extent to which perturbations at different sites can influence the cooperative network in the protein. Applying this method to a database of test proteins, it is found statistically that binding sites are located in regions most able to affect the cooperative network, even for cooperative interactions between residues distant to the binding sites. This indicates that the conformational manifold under native conditions is determined by the network of cooperative interactions within the protein and suggests that proteins have evolved to use these conformational fluctuations in carrying out their functions. Furthermore, because the energetic coupling pattern calculated for each protein is robust and relatively insensitive to sequence, these studies further suggest that binding sites evolved in regions of the protein that are inherently poised to take advantage of the fluctuations in the native structure.

Faculty on the Road

Dr. Lillian Chan traveled to Taiwan March 12-16, as an invited speaker at the National Health Research Institute, Chunan, Taiwan. The title of her talk was “Permissive Infection by SARS Coronavirus of Cells from Transgenic Mice Expressing Human Angiotensin-converting Enzyme 2”.

Dr. Satish Srivastava traveled to Kona, Hawaii on March 22-28, 2007 to attend the International Conference: "Diabetic Complications 2007: The Role of Aldose Reductase and Related Pathways" and presented an abstract entitled, "Aldose Reductase in Inflammatory Disorders"

Dr. G.A. Shakeel Ansari attended and presented his research entitled, "Longitudinal Toxicogenomic Analysis of Trichlorethene Exposure in Liver of MRL+/+ Mice" on March 25-28, 2007.

Dr. Ansari also attended an NIEHS Study Section Meeting and reviewed U54/U01 grant applications on March 29-31, 2007.

Dr. Cheryl Watson was a member of the NIH Study section for Women’s Health SCOR Center Grants on March 21-23, 2007.

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 Employees

Kim Taylor, Ph.D., Postdoctoral Fellow with Dr. Gorenstein’s lab.