BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

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UTMB

BMB Biochemistry & Molecular Biology

Chair's Message

The dog days of summer are here, although this year it seems the wet days of summer may be a more appropriate sobriquet and we are facing the possibility of significant storm activity. Please continue to review emergency plans and remain in close communication as we wait to find out what path hurricane Dean will take.

I would like to add that while the storm season will wane in the fall, bringing various aspects of the GNL building online is likely to cause power outages for us, if my memory of the construction of the adjoining
BSL-4 facility serves. Be sure to have flashlights, check which equipment is on red plugs, and make sure that the amperage maximum of each outlet is not exceeded as that would result in a circuit breaker abrogating activation of the red plug.

We have now finished our interviews with candidates for a new tenure-track faculty position. The Recruiting Committee has met and provided me with a prioritized list of the candidates. I am sure that by the time of the next newsletter I will be able to announce our new faculty member. We will be carrying out another recruitment effort in the fall for a position focused on signaling mechanisms and DNA damage and repair. We are also in the midst of a recruitment effort with other partners for a bioinformatics/ biomolecular markers faculty position.

We are still struggling with our budget for next year to make sure that our needs are met and that we meet our SOM target without affecting our ability to carry out our missions. So far, it's okay.

One piece of good news is that we will be replacing one of the autoclaves in the MRB. My plan is to replace one each year. They are all well beyond their expected lifetimes, and we were long overdue in doing this. We will also be able to remodel at least one suite of labs in the BSB next year, so bit by bit we hope to accomplish the goal of refurbishing our research space over the next few years. This is also long overdue.

Congratulations to Junji Iwahara, who has been selected as the UTMB candidate for this year's Searle Award competition. Good luck.

Finally, plans for a review of the Department are underway. As you all know, this is a process that takes place every seven years. We look forward to this process to determine our progress from the last review and make strategic plans for the future.

Hope you get to enjoy your summer vacation, and see you in the fall.

-regino

Inside this issue:

Special Items of Interest

Graduate Program News

The Orientation Committee comprised of Drs. Sarita Sastry and Stan Watowich, student co-chairs Suzanne Tomlinson and Sergio Santa Maria, Rodrigo Diaz-Espinoza, Julie Hou, along with Raghav Kulasegaran, Anu Roychowdhury, Scott Silva, and Brian Tieu have been working hard to organize this fall's new student Orientation event. Please reserve Wednesday, September 26th for our BMB students' and post docs' poster session. Details will be sent from the Program Office. Come support our annual event.

Congratulations to the following students who have successfully completed their qualifying exams and are preparing the paperwork for being admitted into candidacy: BMB: Pavani Gangavarapu, Keerthi Gottipati, Abhisek Mukherjee and David Saenz. BSCB: Rodrigo Diaz-Espinoza, Austin Elam and Travis Schrank.

We welcome our newest BMB MD/PhD students, Sarah Hemauer and David Winters as well as our BSCB Track students, Kurtis Anderson, Jeff Borgeson and Michal Szymañski.

The Curriculum site on our homepage will be undergoing updates to include the syllabi and course times for all our classes, so please check frequently for this new information.

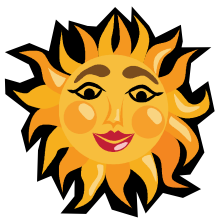
-Deborah Botting, Graduate Program Coordinator

Awards and Announcements

Dr. Brad Thompson took 5th place in his age group in the triathlon at the Sr. Olympic Nationals in Louisville, KY on July 1st.

Dr. Sandhya Das, a post-doc in Dr. Krishna Rajarathnam's lab, has been awarded the McLaughlin post-doctoral fellowship.

Purvi Patel, a SURP (summer undergraduate research program) student in Dr. Kay Choi's lab, received a Sealy Center for Structural Biology and Molecular Biophysics award for excellence on her research. Her poster was titled "Purification, crystallization, and characterization of N-terminal protease from bovine viral dirrhea virus (BVDV)"

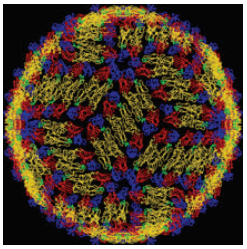


RESEARCH SPOTLIGHT: Software Tools from the Sealy Center for Structural Biology and Molecular Biophysics

Online services are becoming an increasingly important part of biomedical research, and the web as a research bench is moving closer and closer to reality. Need help in your research with computer-related issues? Maybe some of the software tools you need are already available online as downloads or as web servers. In some cases you may not even need to fire up your preferred web search engine to find them. Several research groups of our department (Drs. Braun, Luxon, Gorenstein, Fox, Hilser, Schein, Watowich and White) have developed software packages and web-based services of interest to the research community. Below is a short list of publicly available software tools with links to the web sites where you can find more information on downloading the application packages or the web service. The application areas of these tools range from gene analysis of transcription factors, 3D modeling of proteins, determination and refinement of 3D structures of proteins, and sequence motif and thermodynamic analysis of proteins, to complete online archives of allergenic and viral proteins.

COREX BEST COREX was originally designed to predict hydrogen exchange rates of proteins and was then further developed to simulate thermodynamic fluctuations of proteins under native conditions. In contrast to molecular dynamics simulations, COREX generates a statistical thermodynamic ensemble of protein structures, using a high resolution 3D structure of a protein as input.

FANTOM The main purpose of this empirical energy program is to calculate low-energy conformations of polypeptides and proteins with geometric constraints. The user can run energy minimizations and/or Monte Carlo simulations of an empirical energy function including solvent interactions. The program can also be used to locate low-energy pathway transitions between two conformations.



Flavitrack contains over 475 complete genomic sequences from almost 40 different flaviviruses, as well as related information on known mutations and literature references. In addition, each sequence has been assigned a unique identifier, i.e., a "license plate", which summarizes its date and place of isolation, phenotype, and lethality. This enables us to run very large sequence alignments and interpret the data with regard to vector and symptom specificity within viral subclasses and strain evolution.

GENEREP is an interactive visualization tool to identify relationships in transcription factor (TF) binding sites in gene promoters. It provides a user friendly interface to the Transfac database.

GETAREA GETAREA is a web based server application to calculate the accessible surface areas (SASA) of residues or of individual atoms of a protein structure. The service allows a user to submit a PDB co-ordinate file and calculates the SASA or solvation energies of residues by different models of implicit solvent calculations.

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RESEARCH SPOTLIGHT: Software Tools from the Sealy Center for Structural Biology and Molecular Biophysics (continued)

InterProSurf This web server predicts interacting amino acid residues in proteins that are most likely to interact with other proteins, given the 3D structures of subunits of a protein complex. The prediction method is based on solvent accessible surface area of residues in the isolated subunits, a propensity scale for interface residues and a clustering algorithm to identify surface regions with residues of high interface propensities. Potential application areas of InterProSurf are vaccine development and rational drug design.

MPACK MPACK (Modeling Package) is an integrated protein modeling suite that handles comparative and *ab initio* modeling procedures. The objective of this suite is to facilitate rapid model generation with minimal user effort and to create a biological data-flow pipeline for large scale-scale modeling of protein sequences from genomic projects.

MORASS The MORASS program uses a full hybrid matrix eigenvalue/eigenvector solution to the Bloch equations to derive cross-relaxation rates and interproton distances. MORASS analyzed 2D NMR NOESY data from oligonucleotides and proteins to evaluate cross-relaxation rates from which interproton distances are obtained.

PCPMer This web server detects sequence motifs in a protein family and subsequently identifies related members in protein sequence database. The program calculates conservation of physical-chemical descriptors to define a motif. Applications of PCPMer include identification of functional sites of proteins, to perform large-scale data mining and to annotate translated genomic sequences.

PMB PMB is a wrapper for the CNS program including several user-friendly features for refining 3D structures from X-ray crystallographic data.

PCPMer

SDAP The Structural Data Base of Allergenic Proteins is a web server that integrates a database of allergenic proteins with bioinformatics search tools to investigate cross-reactivity between known allergens, testing the FAO/WHO allergenicity rules for new proteins, and in predicting the IgE-binding potential of genetically modified food proteins. A user can also retrieve information related to an allergen from the most common protein sequence and structural databases (SwissProt, PIR, NCBI, PDB), to find sequence and structural neighbors for an allergen, and to search for the presence of an epitope other the whole collection of allergens.

Publications & Grant Awards

Yajuan Liu, Xuesong Cao, Jin Jiang, and **Jianhang Jia**. Fused-Costal2 protein complex regulates Hedgehog-induced Smo phosphorylation and cell-surface accumulation. Genes and Development 2007, 21(15): 1949-1963.

Fabian, RH , **Perez-Polo, JR**, Kent TA. A decoy oligonucleotide inhibiting NF-kB binding to the IgGkB consensus site reduces cerebral injury and apoptosis in neonatal hypoxic-ischemic encephalopathy. Journal of Neuroscience Res., 85(7):1420-6, 2007.

Ye, Yuemi, Nishi, SP, Manickavasagam S., Lin Y., Huang Ming-He, **Perez-Polo, JR,** Uretsky BR, **Birnbaum, Y**., Activation of peroxisome proliferator–activated receptor γ (PPAR-γ) by Atorvastatin is Mediated by 15-Deoxy-Delta 12,14-PGJ2. Prostaglandins and other Lipid Mediators 84: 43-43, 2007.

Cittelly DM, **Nesic-Taylor O, Perez-Polo JR,** Phosphorylation of Bcl-xL after spinal cord injury. J. Neuroscience Res., 85(9):1894-1911,2007.

Fernando, H., Nagle, G., and **Rajarathnam, K.** Thermodynamic Basis of Interleukin-8 Monomer Binding to the CXCR1 Receptor N-domain: An Isothermal Titration Calorimetry Study FEBS J 274: 241-251 (2007).

Nasser, M.W., Raghuwanshi, S.K., Malloy, K.M., Gangavarapu, P., Shim, J.Y., **Rajarathnam, K.,** Richardson, R.M. CXCR1 and CXCR2 activation and regulation: Role of aspartate 199 of the second extracellular loop of CXCR2 in CXCL8-mediated rapid receptor internalization. J. Biol. Chem. 282:6906-6915 (2007).

Rajagopalan, L., Chin, C., **Rajarathnam, K.** Role of intramolecular disulfides for stability and structure in a non-covalent homodomer Biophys J. (2007, in press).

Involvement of a Novel Rac/RhoA GTPase-NF-κB Inducing Kinase (NIK) Signaling Pathway Mediating Angiotensin II-Induced RelA Transactivation ,Sanjeev Choudhary, Muping Lu, Ruwen Cui, and **Allan R. Brasier** , Mol. Endocrinol. published June 26, 2007.

Prado, G.N., Suetomi, K., Shumate, D., Maxwell, C., Ravindran, A., **Rajarathnam, K.,** and Navarro, J. Chemokine Signaling Specificity: Essential Role for the N-Terminus Domain of Chemokine Receptors Biochemistry, 46:8961-8968 (2007).

"DNA Repair Volume 6, Issue 8, 1—August 2007, Pages 1064-1070 MGMT: A personal perspective"., Author: **S.Mitra.**

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.

IT Briefs - Lisa Pipper

I read an informative blog article at TechRepublic the other day about some common email habits that waste time and cause problems. I know everyone's mailboxes get extremely difficult to manage at times, so thinking about these things may alleviate some of burden on ourselves and others.

Vague or nonexistent subject line

Make it easy for recipients to know what your message is about. If you're like most people, you have an in-basket that summarizes your incoming messages, probably by date, sender, and subject. Don't you love it when you can get the information you need simply from the subject line? The sender has made it easy for you and has saved you time.

On the other hand, how often have you received an e-mail without a subject or one that's labeled, for example, "Phone number you requested." I would have been better if the sender said, right in the subject line, "The phone number is xxx-xxx-xxxx"?

The incredibly way too long subject line that contains the complete body of the message instead and just goes on and on.

The subject line is just that, a line, brief and meaningful. Many email clients use a preview feature and will never show more than 50 characters of the subject line. Making the subject line the maximum 255 characters is not only obtrusive, but ugly to look at as well.

Changing the topic without changing the subject

For example, you send a note to a co-worker about subject 1. That co-worker later needs to send a note to you on subject 2. However, instead of creating a new note and labeling it "subject 2," he or she simply replies to you, discusses subject 2, but keeps the subject line as "subject 1." Huh? Confusing. When you send e-mail, make sure the subject line matches the actual subject. If you're going to send a note via a reply, change the subject line to match the actual subject; it is very simple and will make the future thread more useful.

Including multiple subjects in one note

Covering multiple topics in one note involves less sending and hence less e-mail traffic and volume. However, this opens the opportunity for the recipient to overlook one or more of those topics. It's better to keep to one topic per message, and keep the topic concise and meaningful.

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Inadvertent replying to all

Before hitting Reply-To-All, make sure you really need to do so. Does everyone really need to see your response? Does your response benefit everyone else, or are you sending merely a private response or addressing a personal issue with the sender? In these situations, it's better just to do a simple Reply to avoid a possibly embarrassing situation. If you need to include another, simply use the cc field.

Displaying addresses of recipients who are strangers to each other

Were you ever the recipient of an e-mail that had a gazillion other recipients as well? The message header, which had all of those recipient addresses, probably took up half your screen. Besides annoying you, the sender might have compromised your privacy by revealing your e-mail address to all the other recipients. If you're POSITIVE that each of your recipients already knows (or could find out anyway) the address of every other recipient (e.g., they're all at UTMB), and if the number of recipients is fairly small, go ahead and list them. Otherwise, put the recipient addresses in your blind carbon copy (bcc) field. Your recipients will not see who received your note, thus protecting the privacy of each recipient.

Misaddressed recipients

This one is easy to do, especially using the global address book here at UTMB. Since Outlook has a "predictive fill-in" (as you're typing the to: field, the software will complete the entry for you) be sure to pay attention to the resolved name before hitting Send. If it's wrong, and you hit "Send" without noticing, you will have misaddressed your note.

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

Administrator's Notes

BMB Honorees at Employee Service Day

We congratulate the BMB faculty and staff members whose service anniversaries were recognized at the Employee Service Day ceremony on August 16. **Dr. Alex Kurosky** and **Joann Broz**, Financial Analyst, were recognized for their 35 years of service. **Martha Harris**, Laboratory Technician, and **Betty Johnson**, Senior Research Associate in Dr. Thompson's lab, marked their 25th anniversaries at UTMB. **Manjit Saini**, Research Associate in Dr. Awasthi's lab, and **Mala Sinha**, Systems Analyst working with Dr. Luxon and the Bioinformaics Program, received pins for 10 years of service. And 5-year pins were awarded to **Bartosz Szczesny**, Instructor and researcher in Dr. Mitra's lab, and **Jason Vertrees**, Graduate Assistant in Dr. Hilser's lab.

Welcome to Marion Maddox, Coordinator I

The administrative staff welcomes Marion Maddox, who joined BMB a few weeks ago. Marion's previous experience was with companies contracting with NASA, and she acquired extensive expertise in financial analysis and reporting, as well as project management and preparation of technical documentation. She has adapted readily to the academic medical center environment, and we know she will be a very valuable asset, especially as UTMB's administrative systems continue to evolve. Marion is providing administrative assistance for Dr. John Papaconstantinou and will also be managing grant accounts of other faculty members. Please join us in welcoming her to the Department.

What will happen if there is a sudden power failure?

As Dr. Perez-Polo noted in his message, we should be aware that a sudden power failure could occur at any time. While there are generators in place to provide emergency power for MRB and the Basic Science Building, only certain building functions are backed-up. If a power failure is projected to continue for more than a couple of hours, it will generally not be possible to continue regular lab operations, and research groups should focus on managing an orderly shutdown of lab activity. For specific notes on what to expect in the event of a sudden loss of power, please see this document.

Faculty on the Road

Dr. Cheryl Watson attended the Annual Meeting of the Endocrine Society in Toronto, Canada and participated in the Membership Committee meeting for the society on June 1-5, 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.

Featured Abstract by BMB Faculty

Fused Costal2 protein complex regulates Hedgehog-induced Smo phosphorylation and cell-surface accumulation.

Liu Y, Cao X, Jiang J, Jia J.

Sealy Center for Cancer Cell Biology, University of Texas Medical Branch, Galveston, Texas 77555, USA;

The seven-transmembrane protein Smoothened (Smo) acts as a signal transducer in the Hedgehog (Hh) pathway that mediates many key developmental processes. In Drosophila, Hh-induced phosphorylation promotes Smo cell-surface accumulation and signaling activity; however, the mechanisms controlling Smo phosphorylation and cell-surface accumulation are still unknown. The intracellular signaling complex containing Fused (Fu) and Costal2 (Cos2) is thought to transduce the Hh signal downstream from Smo. Here, we identify a novel feedback mechanism that regulates Smo through the Fu-Cos2 complex. We found that Hh-induced Smo accumulation is inhibited in fu mutant clones or by expressing a dominant-negative form of Fu, and such inhibition is alleviated by removal of Cos2. Conversely, overexpressing Cos2 blocks Smo accumulation, which is reversed by coexpressing Fu. Cos2 blocks Smo accumulation through its C-terminal Smo-interacting domain, and Fu antagonizes Cos2 by phosphorylating Cos2 at Ser572. Furthermore, we found that Ser572 phosphorylation attenuates the Cos2-Smo interaction and promotes Cos2 instability. Finally, we provided evidence that Fu and Cos2 control Smo cell-surface accumulation by regulating Smo phosphorylation. Our data suggest that Cos2-Smo interaction blocks Hh-induced Smo phosphorylation, and that Fu promotes Smo phosphorylation by antagonizing Cos2.