

BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

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BMB
Biochemistry & Molecular Biology

Chair's Message

It seems these are really the "dog days of summer," with folks taking last minute vacations, preparing kids for return to school, and wrapping up their UTMB compliance requirements (HINT). We have now received the reviews of the Department and the Graduate Program and BSCB Track; in the fall we will begin our development of a strategic plan for the future of the Department. I'd think the best way to proceed would be to have a small task force plan a one-day retreat where we can all discuss the way to go forward.

Speaking of going forward, we have to congratulate Lillian Chan for receiving the go-ahead from UT System to prepare a full-fledged application entitled "*The BioNext Initiative: Enhancement of UTMB's Graduate Program in Biochemistry and Molecular Biology*". This is a wonderful

opportunity, and Lillian and her team deserve credit for preparing the initial submission.

Another important item re the graduate school -- at the students' request, an "Academic Skills" course is being planned that will take advantage of the excellent course put together by Pomila Singh for the Cell Biology Program. Kathleen O'Connor and her curriculum committee should be making an announcement soon. Because of the importance of such a course, if you volunteer to teach it, you will fulfill your obligation to teach in the medical school.

Although proceeding at a snail's pace, plans for renovation of BSB continue, including the elevators! You will also soon be contacted by our Orientation Committee to provide information for the coming Orientation presentation to the new cadre of graduate students. This would be a good

opportunity to update your BMB website information.

At the last faculty meeting there were a number of interesting presentations. Since not all could attend, we are including in the news letter some of the IS presentation, all good news. There was also some discussion as to the offsite capabilities for storage of important frozen samples. Check with Bob Fox if you want more information.

We have a new faculty member in our midst, Dr. Rovshan Sadygov: Please see the [short profile of his work](#) in this newsletter.

Enjoy the last of summer, and see you in the fall!

-regino

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Graduate Program News

New Students

We are very excited to welcome into the BMB Program the following 2nd year students:

Abhijnan Chattopadhyay, of the Hilser laboratory

Marlene Starr, of the Saito laboratory

Christof Straub, of the Kurosky laboratory

David Winters, of the Mitra laboratory

Tianxin Yu, of the Liu laboratory

Joining our BSCB Track, we have the following first year students: Andrea Garces, Wenzhe Lu and Jing Li.

BBSC Orientation

This fall's new student orientation will be a completely new venue. We will join all the graduate programs within the GSBS on Tuesday, September 23rd in Levin Hall to showcase our program to the incoming first year BBSC class. Each graduate program will have its own booth in the Levin Hall Dining Room, and posters will be displayed in the Levin Hall Foyer. The BMB Orientation Committee has been working hard to create an outstanding and unique booth. More details to follow.

We are asking for faculty support and have sent a few emails calling for abstracts. If you are interested in showcasing the top research in your lab, please send your abstract to either **Raghav Kulasegaran** (rakulase@utmb.edu) or **Hung Doan** (hqdoan@utmb.edu) by **August 29, 2008**.

Student Accomplishments

Congratulations to Travis Schrank, of the Bolen/Hilser laboratory, for contributing a winning poster at the recent Protein Society National Meeting.

Also deserving of great recognition is Debashish Sahu, of the Iwahara laboratory for his recent publications:

Direct Evidence for Deprotonation of a Lysine Side Chain Buried in the Hydrophobic Core of a Protein, Takayama, Yuki, Castañeda, Carlos A., Chimentí, Michael, García-Moreno, Bertrand, and Iwahara, Junji *J. Am. Chem. Soc.*, 130, 21, 6714 - 6715, 2008.

Observing in-phase single-quantum ¹⁵N Multiplets for NH₂/NH₃⁺ Groups with Two-dimensional heteronuclear correlation spectroscopy, Takayama, Yuki, Sahu, Debashish, and Iwahara, Junji *J. Magn. Res.*, In Press, Accepted Manuscript, Available online 23 July 2008.

Grant Proposal for BioNext

For several months, the BMB Program has been working on a project called BioNext. We have been invited by the UT System Graduate Programs Initiative to submit a full proposal entitled "*The BioNext Initiative: Enhancement of UTMB's Graduate Program in Biochemistry and Molecular Biology*".

The Graduate Programs Initiative was designed to stimulate creative and innovative approaches to nonprofessional graduate education in the UT System. In response to the request for proposals in March 2008, 37 pre-proposals from 13 UT institutions were received. A maximum of two grants will be funded per institution. Grants up to a total amount of \$500,000 for new initiatives in graduate education will be funded, with funding scheduled to begin between January 1 and September 30, 2009. If awarded, Dean Garland Anderson has agreed to match this funding to make a total of \$1 million for 5 years.

We are very excited about being selected for submitting a full proposal. Wish us luck!

-Debora Botting

Awards and Announcements

Dr. Kay Choi has received a USDA National Research Initiative grant (for 3 years). The title of the proposal is "Structural and biochemical characterization of Npro form bovine viral diarrhea virus and classical swine fever virus".

Dr. Krishna Rajarathnam's Summer Undergraduate Research Program student, Rachita Navara, recently won the Robert A. Welch Foundation Award in Chemistry for Outstanding Biochemical Research for her poster titled "EXPLORING THE ROLE OF N-LOOP LYS-15 FOR INTERLEUKIN-8 STRUCTURE AND IN VIVO FUNCTION". Rachita is a student at Franklin W. Olin College of Engineering in Needham, MA.

BMB UTMB Service Pin Recipients

<i>30 Years of Service</i>	<i>15 Years of Service</i>
Darrell Carney Lillian Chan	Satya Prakash Louise Prakash Deqian Liu
<i>25 Years of Service</i>	<i>10 Years of Service</i>
Brenda Romero	Kevin Rosenblatt Xin Li
<i>20 Years of Service</i>	<i>5 Years of Service</i>
Harriett Rea	Narottam Acharya Venkateswarlu Gangavarapu Chunming Liu RavinderTammali Vincent Dimayuga DianaFerrari TzintzuniGarcia AdityaJoshi Kristen Lamb Robert Malmstrom JenniferRodriguez-Rivera SergioSanta Maria Guerra Corey Theriot

Faculty Focus

Rovshan Sadygov, Ph.D., Assistant Professor, Biochemistry & Molecular Biology



Dr. Rovshan Sadygov received his Ph.D. in Biophysics from M. V. Lomonosov Moscow State University (Moscow, Russia) in 1992. In his graduate work he studied the mechanisms of photo-induced electron transfer processes in biological systems. He also holds a Ph.D. (1995) in Computational Quantum Chemistry from The University of Akron (Akron, OH). After post-doctoral work at The Johns Hopkins University (1995-98) and UCLA (1998-2000) he joined the group of John R. Yates, III at the Scripps Research Institute (La Jolla, CA), where he worked on several large-scale proteomics projects and developed computational algorithms for protein identification, validation and quantification using mass spectral data from proteomics experiments. His algorithms are used for studies of potential biomarker discovery, protein-protein interactions and post-translational modifications and are currently being distributed by ThermoFisher Scientific (San Jose, CA).

Our research interests are in the use of computational analysis of mass spectral data from proteomics experiments to infer biological information. For these purposes we adopt methods of probability/statistics, signal processing and pattern recognition to analyze mass spectral data and uses this biological knowledge base for interpretation. Proteomics research plays an important role in the studies of primary structure of proteins, protein interaction networks, biomarker discovery, post-translational modifications and signaling pathways.

Proteomics experiments generate large amounts of data relevant to the protein content and complexity of a sample. The interpretation of these data requires efficient bioinformatics tools to process, store, visualize and disseminate the data. We develop algorithms for error tolerant database search, protein grouping, spectral quality assessment, in silico sequence hybridization (to reduce sequence redundancy), spectral library search, elemental composition determination and for processing chromatographic surfaces for alignments in time and mass-to-charge ratio domains and normalization in abundance domain, peak detection, background subtraction and peak area integration. These algorithms will serve as a base for inferring primary protein content information of a biological sample. We will then use this information to generate probabilistic models for protein interaction networks, signaling pathways and statistical models for potential biomarker discovery and validation and for absolute and relative protein quantification.

Selected publications (5 out 25)

1. **R.G. Sadygov**, Z. Hao, A. FR. Huhmer. Charger: a combination of signal processing and statistical learning algorithms for charge state determination from MS/MS. *Anal. Chem.*, 2008;80:376-386.
2. **R.G. Sadygov**, F. M. Maroto, A. Huhmer ChromAlign: A Two-Step Algorithmic Procedure for Time Alignment of Three Dimensional LC-MS Chromatographic Surfaces. *Anal. Chem.* 2006;78:8207-8217.
3. **R.G. Sadygov**, D. Cociorva, J.R. Yates III, Large-scale Database Searching using Tandem Mass Spectra: Looking up the answer in the Back of the Book, *Nature Methods* 2004;1:195-202.
4. **R.G. Sadygov**, H. Liu, and J.R. Yates III, Statistical Models for Protein Validation using Tandem Mass Spectral Data and Protein Amino Acid Sequence Databases, *Analytical Chemistry*, 2004;76:1664-1671.
5. **R.G. Sadygov**, and J. R. Yates III, A Hypergeometric Probability Model for Protein Identification and Validation using Tandem Mass Spectral Data and Protein Sequence Databases, *Analytical Chemistry* 2003;75:3792-3798.

FY 2009 Holiday Schedule

Date	Event	Weekday	Schools & Institutional Support
9/1/2008	Labor Day	Monday	Holiday
11/11/2008	Veteran's Day	Tuesday	Holiday
11/27/2008	Thanksgiving Day	Thursday	Holiday
11/28/2008	Thanksgiving Holiday	Friday	Holiday
12/22/2008	Winter Holiday	Monday	Holiday
12/23/2008	Winter Holiday	Tuesday	Holiday
12/24/2008	Christmas Eve Day	Wednesday	Holiday
12/25/2008	Christmas Day	Thursday	Holiday
12/26/2008	Day after Christmas	Friday	Holiday
12/31/2008	Winter Holiday	Wednesday	Holiday
1/1/2009	New Year's Day	Thursday	Holiday
1/19/2009	Martin Luther King Day	Monday	Holiday
2/16/2009	President's Day	Monday	Holiday
5/25/2009	Memorial Day	Monday	Holiday
6/19/2009	Emancipation Day	Friday	Holiday

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



IT Briefs - Lisa Pippet

Todd Leach from Information Services made brief presentation at the August Faculty meeting updating the department on some IT projects. Below are a few of the topics he highlighted.

10 Gbps Connectivity to the campus core network

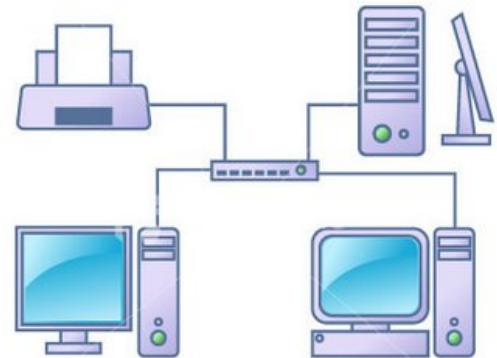
- ✦ Building router and switches upgraded
- ✦ MRB completed May 5, 2008, BSB completed May 20, 2008

Exchange E-mail Upgrade

- ✦ Converted 16,000 mailboxes in a six week period. Completed July 3, 2008.
- ✦ Faculty mailboxes increased from 150 MB to 200 MB
- ✦ Student mailboxes from 75 MB to 200 MB
- ✦ Staff mailboxes from 50 MB to 200 MB

Office 2007 conversion support

- ✦ To assist users during the transition to Office 2007, Information Services will be partnering with PC Helps--a phone-based support service--beginning July 21. Accessed through the existing help desk, PC Helps will answer common "how to...?" questions and provide related support. Call extension 25200 and select option 5 to get your Office 2007 questions answered 24 hours a day, 7 days a week.



New campus telephone switch project

- ✦ Voice mail to e-mail
- ✦ Caller ID
- ✦ Reduced phone costs

Wireless expansion

- ✦ 522 new access points, 250 access points in inventory
- ✦ 465 active now in student & patient care areas

**3rd US-EU Conference on Endogenous Genome
Damage**

Moody Gardens Hotel and Conference Center

November 5-9, 2008

Abstract Submission Deadline October 3, 2008

Administrator's Notes

The Department's newest faculty member, **Dr. Rovshan Sadygov**, is working in 6.630 Basic Science Building. (This was formerly the office of Dr. Ed Czerwinski.) He will use this office temporarily until reconstruction of the SE quadrant of the 5th floor of BSB is completed in Fall 2009. His phone number is 772-3287 and e-mail address is rgsadygo@utmb.edu.

We also want to welcome **Alisha Goldberg**, who has just joined UTMB as **Science Writer/Editor**. Alisha is camping with BMB until the new "Research Grant Proposal Group" has taken shape. Along with Dr. David Konkel, Alisha is currently working with Dr. Allan Brasier on a new application to the NIH for an Institutional Clinical Translational Science Award (ICTSA). After the proposal has been submitted in late October, Alisha will be available to assist faculty members with preparation of proposals and manuscripts. Alisha holds a Master's Degree in Marine Biology and has extensive experience writing grant proposals and supporting complex research programs. Alisha's temporary location is on the 2nd floor of BSB. She can be reached at 772-2224 and her e-mail address is argoldbe@utmb.edu.

Bill New, Associate Dean for Research Services, informed department administrators that UT System has initiated a program for **capturing the combined purchasing power of UT investigators to negotiate preferred pricing contracts for supplies, services and equipment**. Mr. New relates, "This effort so far has saved an estimated \$2.5 Million for PIs. Since the federal sponsors have relatively level budget these days, the PI's purchasing power is declining. It is estimated that the NIH investigator has lost over 7% of his/her purchasing power over the last three years while the companies supplying biomedical researchers have had healthy profit growth." Mr. New is forming a UTMB group that will gather information and give input to this system-wide purchasing negotiation initiative. It's essential for researchers to participate directly in this effort. Please contact me if you would like more information about this group or would like to be a member.

- Marianne

Faculty on the Road

Dr. Cheryl Watson was a scientific session chair at the FASEB Summer Conference on the Integration of Membrane and Nuclear Effects of Steroids, in Carefree AZ, July 27-Aug 1

She was also an invited speaker at the Gordon Conference on Environmental Endocrine Disruptors, June 8-13, 2008. The meeting was held in Waterville Valley, NH.



Dr. Kay Choi attended the FASEB virus assembly conference June 22-27 in Saxtons River, Vermont and presented a poster titled "The structure of bacteriophage N4: insight into protein transport"

Dr. Stan Watowich traveled to the International Conference for High Performance Computing, USA & CeNAT as an invited speaker. The conference was held at EARTH University in Guacimo, Costa Rica. He was invited to lecture/teach at a workshop entitled "Nanotechnologies and High Performance Computing in Education and Research" from June 29 - Jul 5, 2008.

Dr. Robert Fox attended the Futures Conference: Pathways to Personalized Medicine, on June 13-14 in Houston, Texas.

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

BMB Faculty Publications

Ivanciuc, O., Garcia, T.I., Torres, M., **Schein, C.H.** and **Braun, W.** Characteristic Motifs for Families of Allergenic Proteins. *Mol. Immunol.*, (in press), 2008.

Chen, D., Misra, M., Sower, L., Peterson, J.W., Kellogg, G.E. and **Schein, C.H.** Novel inhibitors of Anthrax edema factor. *Bioorg. Med. Chem.*, Jun 28. [Epub ahead of print], 2008.

Oezguen, N., Zhou, B., Negi, S.S., Ivanciuc, O., **Schein, C.H.**, Labesse, G. and **Braun, W.** Comprehensive 3D-modeling of allergenic proteins and amino acid composition of potential conformational IgE epitopes. *Mol. Immunol.*, Jul 11. [Epub ahead of print], 2008.

Natalia Mast, **Mark Andrew White**, Ingemar Bjorkhem, Eric F. Johnson, C. David Stout, and Irina A. Pikuleva. Crystal structures of substrate-bound and substrate-free cytochrome P450 46A1, the principal cholesterol hydroxylase in the brain published 9 July 2008, 10.1073/pnas.0803717105

Leonard, H.J.V., Sinn, P.L., Hodge, G., Miest, T., Devaux, P., Oezguen, N., **Braun, W.**, McCray, P.B. Jr., McChesney, M.B. and Cattaneo, R. Measles virus blind to its epithelial cell receptor remains virulent in rhesus monkeys but cannot cross the airway epithelium and is not shed. *J. Clin. Invest.*, 118(7), 2448-2458, 2008.

Ye, Yumei, **Martinez JD**, **Perez-Polo JR**, Lin Y, Uretsky BF, **Birnbaum, Y.** The role of eNos, iNos and NFkB in upregulation and activation of cyclooxygenase-2 and infarct size reduction by atorvastatin. *AJP: Heart & Circulatory Physiology* 295:343-351 -2008. doi:10.1152/ajpheart.01350.2007

Jung Hun Oh, Young Bun Kim, Prem Gurnani, **Kevin Rosenblatt**, and Jean X. Gao. Biomarker selection and sample prediction for multi-category disease on MALDI-TOF data. *Bioinformatics*. 2008 Aug 15;24(16):1812-8. Epub 2008 Jun 18.

Cha, S.-K., Ortega, B., Kurosu, H., **Rosenblatt, K.P.**, Kuro-o, M., and Huang, C.-L. (2008) Removal of sialic acid involving Klotho causes cell-surface retention of TRPV5 channel via a binding to galectin-1. *Proceedings of the National Academy of Sciences (USA)*, in press.

Exploring the Impact of Polyproline II (P_{II}) Conformational Bias on the Binding of Peptides to the SEM-5 SH3 domain. Steven Whitten, Huan-Wang Yang, **Robert O. Fox**, **Vincent J Hilser** *Protein Science* (2008) 17:1200-1211.

Choksi KB, Jackson Roberts L, **DeFord JH**, **Rabek JP**, and **Papaconstantinou J.** Lower levels of F²-isoprostanes in serum and livers of long-lived Ames Dwarf Mice : A possible mechanism of resistance to oxidative stress and longevity. *Biochem. Biophys. Res. Commun* 364, 761-764 ; 2007. PMID : 17964285 PMC2238179.

Nuss, JE, Choksi KB, **DeFord JH**, and **Papaconstantinou J.** Decreased enzyme activities of chaperones PDI and BiP in aged mouse livers. *Biochem. Biophys. Res. Commun.* 365 (2), 355-361; 2008. PMID : 17996725 PMC2238339.

Choksi KB, and **Papaconstantinou J.** Age-related alterations in oxidatively damaged proteins of mouse heart mitochondrial electron transport chain complexes. *Free Rad. Biol. & Med.* 44 : 1795-805; 2008. PMID : 18331850 PMC2423468

Takayama Y, Castaneda CA, Chimenti M, Garcia-Moreno B, **Iwahara J** (2008) Direct evidence for deprotonation of a lysine side-chain buried in the hydrophobic core of a protein. *J Am Chem Soc* 130, 6714-6715.

Anzor G. Gvritshvili, **Alexey V. Gribenko**, and George I. Makhatadze. Cooperativity of complex salt bridges. *Protein Science* 17:1285-1290

*To have your publications included in the monthly newsletter, please send the information directly to Lisa Pipper
(lpipper@utmb.edu)*

Featured Abstract by BMB Faculty

Removal of sialic acid involving Klotho causes cell-surface retention of TRPV5 channel via binding to galectin-1.

Cha, S.-K., Ortega, B., Kurosu, H., **Rosenblatt, K.P.**, Kuro-o, M., and Huang, C.-L.

[Proceedings of the National Academy of Sciences \(USA\), 2008 Jul 15;105\(28\):9805-10. Epub 2008 Jul 7.](#)

Departments of Medicine and Pathology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.

Klotho is a mammalian senescence-suppression protein that has homology with glycosidases. The extracellular domain of Klotho is secreted into urine and blood and may function as a humoral factor. Klotho-deficient mice have accelerated aging and imbalance of ion homeostasis. Klotho treatment increases cell-surface abundance of the renal epithelial Ca(2+) channel TRPV5 by modifying its N-linked glycans. However, the precise sugar substrate and mechanism for regulation by Klotho is not known. Here, we report that the extracellular domain of Klotho activates plasma-membrane resident TRPV5 through removing terminal sialic acids from their glycan chains. Removal of sialic acids exposes underlying disaccharide galactose-N-acetylglucosamine, a ligand for a ubiquitous galactoside-binding lectin galectin-1. Binding to galectin-1 lattice at the extracellular surface leads to accumulation of functional TRPV5 on the plasma membrane. Knockdown of beta-galactoside alpha2,6-sialyltransferase (ST6Gal-1) by RNA interference, but not other sialyltransferases, in a human cell line prevents the regulation by Klotho. Moreover, the regulation by Klotho is absent in a hamster cell line that lacks endogenous ST6Gal-1, but is restored by forced expression of recombinant ST6Gal-1. Thus, Klotho participates in specific removal of alpha2,6-linked sialic acids and regulates cell surface retention of TRPV5 through this activity. This action of Klotho represents a novel mechanism for regulation of the activity of cell-surface glycoproteins and likely contributes to maintenance of calcium balance by Klotho.

