

BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

AUGUST 2012 NO. 288



Chair's Message

Soon a new academic year begins. This year appears to present great challenges. Our budget for the year is severely restricted, and accomplishing our mission properly with regards to support for seminars, the graduate program and many other support functions will be a challenge. However, in the face of an equally austere research funding atmosphere, I am glad to say that our faculty are doing very well. Everybody is working at 100%, and I am sure we will overcome these difficulties and move on. A sign of our success is that two of our assistant professors, Olivera Nestic-Taylor and Junji Iwahara, were approved for promotion to Associate Professor with Tenure. Our other assistant professors are also doing well considering the situation. In order to improve the odds for success, our faculty now have access to a Grant Development Core that has been established in a collaborative effort with the Sealy Center for Structural Biology and Molecular Biophysics and the Departments of Neuroscience and Cell Biology and Pharmacology and Toxicology, working together with the BMB Internal Study Section being chaired by Jim Lee. For this effort to be truly useful and work in a seamless fashion, you must register months in advance of grant deadlines so that both the Study Section and the Core can best serve you. In addition, you should have a chat with the Core Staff so that they can understand your area of research interest

and be able to suggest non-traditional sources of funding. Believe me, they are very good at this. Their forte is multiinvestigator translational grants, but they will help with individual grants also. Most recently Karon P. Cassidy M. D. and Craig Cassidy, two members of the team, made a very lucid presentation at our last faculty meeting. Be sure to contact them. I should add that David Konkel also remains diligently providing his editing services to our faculty.

One aspect where there are still opportunities for all of us is in the area of teaching in the medical school curriculum. Not all of our faculty are taking advantage of this opportunity.

Another source of good news is that the BSB and MRB renovations are proceeding on schedule, and the impact of these efforts will benefit all of us. Also, recruitment of senior structural biology faculty proceeds on schedule.

I do hope you had a relaxing and pleasant summer, and we are all thankful that to date no major storm has visited our shores.

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Special Items of Interest

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Awards and Announcements



Muralidhar Hegde has been awarded a New Investigator Research Grant in the 2012 International Research Grant Program from the Alzheimer's Association.

He was also *awarded International young scientist travel award (ATW2012)* from American Ataxia society to attend 5th meeting in New Delhi India, Feb 2012 and to present his research on DNA repair deficits in motor neuron diseases.

Jonathan M. Starkey, M.D. in Bruce Luxon's lab has finished all requirements and his thesis has been submitted and accepted for his Ph.D. degree in Health Informatics through the UTMB PMCH/ITS Clinical Science program and he has accepted an appointment as an Assistant Professor for Medical Informatics in the Institute for Translational Science (ITS) with a joint appointment in PMCH.

Christof Straub & Yashoda Hosakote were highlighted in the NHLBI Winter 2012 News Spots Publication.

Levani Zandarashvili, student in Dr. Junji Iwahara's lab received a Protein Science Young Investigator Travel Grant (from Protein Society, May 2012) as well as a Poster Award at the 26th Annual Protein Society Symposium (San Diego, CA; August 2012).

Dr. Michal R. Szymanski, a post-doc in Dr. Bujalowski's laboratory, received a renewal of his Jeane B. Kempner postdoctoral fellowship.

FUNDING BOOT CAMP

GRADUATE SCHOOL OF BIOMEDICAL SCIENCES
POSTDOCTORAL & CAREER DEVELOPMENT AWARDS

Tuesday, September 11
3:00 - 5:00 pm
Levin Hall Rm 3.320

INCLUDES SNACKS & BEVERAGES

This meeting begins to all NIH graduate students and postdoctoral fellows interested in funding

PANEL FEATURES:
Current graduate and postdoctoral fellowship recipients, and presentations on the types of fellowships you can apply for

The Graduate School of Biomedical Sciences will sponsor a Funding Boot Camp geared to graduate students and post-doctoral scientists at UTMB who wish to seek their own funding to jump-start their research careers. Information will be given about NIH, NSF, DOD, NASA, as well as other federal and non-federal fellowships. All graduate students and postdoctoral scientists are encouraged to come to the first session, which will be held Sept 11, 2012 from 3 to 5 pm in Levin Hall 3.320.

The series will continue every two weeks in small groups focused on hands-on activities until the December 5 deadline for fellowship applications and into January for the career development awards, due February 12. In the small group meetings, assignments from the previous sessions will be reviewed and discussed so participants may benefit from the suggestions provided by facilitating faculty and grant writers/editors.

The series is free, with contributions from the Graduate School, Office of Postdoctoral and Postgraduate Affairs (OPA), Office of Research Services and Sealy Center for Structural Biology and Molecular Biophysics.

Faculty who wish to facilitate the small groups or students and postdocs with questions may contact Jo Bremer, director of the OPA, at 409-772-2684 or jobremer@utmb.edu.

Graduate Program News

Congratulations to:

Tianxin Yu (BMB) for a successful final defense. Dr. Yu will be continuing in Dr. Liu's lab at the University of KY as a postdoc.

Jason Allison (MBET) for a successful final defense. Dr. Allison will be continuing in Dr. Fox's lab at the University of Houston as a postdoc.

Xiaoxi Ju (BMB) for a successful final defense. Dr. Ju will be doing a Research fellow at Hong Kong Food and Drug Administration.

Sai Gandham (MBET) for a successful final defense. Dr. Gandham will be continuing in Dr. Gorenstein's lab at UTHSC as a postdoc.

Keerthi Gottipati (BMB) for a successful final defense. Dr. Gottipati will be continuing in Dr. Choi's lab as a postdoc.

Congratulations to Paige Spencer (BMB) for a successful final defense.

Congratulations to the following students for successfully passing their qualifying exams:

BMB Program - Leon Bae, Juan Conde, Scott McVicar, Paul Nicholls, and Barbara Rolls for passing their qualifying examinations

MBET Track - Pawel Bujalowski

Congratulations to Christof and Marcela Straub on the arrival of their son, Felix!



Welcome

The BMB graduate program extends a warm welcome to our new 2nd year students:

Aaron Brown, Justin Drake, Arijit Dutta, Timi Folorunso, Jim Hsu, and Curtis Nutter

And our new 1st year students:

Kelli Jay, Tom Lucas, and Jordan Speidel



**Hurricane Season
June 1- December 1**



ARE YOU PREPARED? DO YOU HAVE A PLAN?

Publications



Nesbit, J.B., Hurlburt, B.K., Schein, C.H., Cheng, H. and Maleki, S.J. Ara h 1 structure is retained after roasting and is important for enhanced binding to IgE. *Mol. Nutr. Food Res.*, (in press), 2012.

Jeon SH, Lee K, Lee KS, Kunkeaw N, Johnson BH, Holthauzen LMF, Gong B, Leelayuwat C, **Lee YS** (2012) Characterization of the direct physical interaction of nc886, a cellular non-coding RNA, and PKR. *FEBS Letters* (In press)

Kunkeaw N, Jeon SH, Lee K, Johnson BH, Tanasanvimon S, Javle M, Pairojkul C, Chamgramol Y, Wongfieng W, Gong B, Leelayuwat C, **Lee YS** (2012) Cell death/proliferation roles for nc886, a non-coding RNA, in the Protein Kinase R pathway in cholangiocarcinoma. *Oncogene* (In press)

Li L, Willard B, Rachdaoui N, Kirwan JP, **Sadygov RG**, Stanley WC, Previs S, McCullough AJ, Kasumov T. Plasma Proteome Dynamics: Analysis of Lipoproteins and Acute Phase Response Proteins with [²H₂O Metabolic Labeling](#). *Mol Cell Proteomics*. 2012 Jul;11(7):M111.014209.

P. Wu, Y. Zhao, S. J. Haidacher, E. Wang, M. O. Parsley, J. Gao, **R. G. Sadygov**, J. M. Starkey, **B. A. Luxon**, H. Spratt, D. S. DeWitt, D. S. Prough, L. Denner. Detection of Structural and Metabolic Changes in Traumatically Injured Hippocampus by Quantitative Differential Proteomics, *Journal of Neurotrauma*, 2012.

Sadygov RG. High Mass Accuracy Phosphopeptide Identification Using Tandem Mass Spectra. *Int J Proteomics*. 2012;2012:104681.

Alam TM, Neerathilingam M., Alam MK, Volk DE, Ansari GAS, Sarkar S, and **Luxon BA**, "1H Nuclear Magnetic Resonance (NMR) Metabolomic Study of Chronic Organophosphate Exposure in Rats.", *Metabolites* 2012 July 24, 2, 479-495; doi:10.3390/metabo2030479

Finnerty CC, Ju H, Spratt H, Victor S, Jeschke MG, Hegde S, Bhavnani SK, **Luxon BA**, Brasier AR, Herndon DN, "Proteomics improves the prediction of burns mortality: results from regression spline modeling.", *Clin Transl Sci*. 2012 Jun 5(3):243-9; PMID: 22686201

Wu P, Zhao Y, Haidacher SJ, Wang E, Parsley M, Gao J, **Sadygov RG**, Starkey JM, **Luxon BA**, Spratt H, DeWitt DS, Prough DS, Denner L. "Detection of Structural and Metabolic Changes in Traumatically Injured Hippocampus by Quantitative Differential Proteomics.", *J Neurotrauma* 2012 Jul 3, PMID: 22757692

Zandarashvili, L, Vuzman, D, Esadze, A, Takayama, Y, Sahu, D, Levy, Y, **Iwahara, J** (2012) Asymmetrical roles of zinc fingers in dynamic DNA-scanning process by the inducible transcription factor Egr-1. *Proc Natl Acad Sci U S A* 109, E1724-32.

Schein, C.H., Bowen, D.M., Lewis, J.A., **Choi, K.**, Paul, A., van der Heden van Noort, G.J., Lu, W. and Filippov, D.V. (2012) Physicochemical property consensus sequences for functional analysis, design of multivalent antigens and targeted antivirals. *BMC Bioinformatics*, (in press).

Bowen, D.M., Lewis, J.A., Lu, W. and **Schein, C.H.** (2012) Simplifying complex sequence information: a PCP-consensus protein binds antibodies against all four Dengue serotypes. *Vaccine*, (in press).

Publications (cont.)

Hegde ML, Banerjee S, Hegde PM, Bellot LA, **Hazra TK**, Boldogh I and **Mitra S**. Enhancement of NEIL1-Initiated Oxidized DNA Base Excision Repair by Heterogeneous Nuclear Ribonucleoprotein U (hnRNP-U) via Direct Interaction. *J Biol Chem, In Press*.

Hegde ML, Izumi T and **Mitra S**. Oxidized Base Damage and Single-Strand Break Repair in Mammalian Genomes: Role of Disordered Regions and Posttranslational Modifications in Early Enzymes. *Progress in Molecular Biology and Translational Science*. 110:123-53.

Boldogh I, Hajas G, Aguilera-Aguirre L, **Hegde ML**, Radak Z, Bacsı A, Sur S, **Hazra T**, **Mitra S**. Activation of Ras Signaling by the DNA Repair Enzyme OGG1 Bound to Its Excision Product 8-Oxoguanine. *J Biol Chem*, 287: 20769-20773.

Mandal SM*, **Hegde ML*** (* equal contribution), Hegde PM, Banerjee D, Boldogh I, Gustafsson MK, Gustafsson C, Sarkar PS and **Hazra TK**. The role of DNA glycosylase NEIL2 and single-strand break repair protein Polynucleotide kinase 3' phosphatase in mitochondrial genome maintenance: New insights into single-strand break repair. *J Biol Chem*. 287:2819-29.

Hegde ML, Mantha AK, **Hazra TK**, **Bhakat KK**, **Mitra S** and **Szczesney B**. Oxidative genome damage and its repair: implications to aging and neurodegenerative diseases. *Mech Aging Develop*. 133:157-68.

Bujalowski, W.M and Jezewska, M.J. Using structure-function constraints in FRET studies of large macromolecular complexes. *Methods Mol Biol*. 2012;875:135-64.

Bujalowski, W.M and Jezewska, M.J. Fluorescence intensity, anisotropy, and transient dynamic quenching stopped-flow kinetics. *Methods Mol Biol*. 2012;875:105-33.

Bussetta C, **Choi KH**. Dengue Virus Nonstructural Protein 5 Adopts Multiple Conformations in Solution. *Biochemistry*. 2012 Jul 16.

Apte-Sengupta, S., Negi, S.S., Leonard, V.H.J., Oezguen, N., Navaratnarajah, C.K., W. **Braun, W.** and Cattaneo, R. Base of the measles virus fusion trimer head receives the signal that triggers membrane fusion. *J. Biol. Chem.*, (in press), 2012.

Effective August 31, 2012, all UTMB owned laptops are required to be fully encrypted. Please be advised that best practices dictate that personal computers should not be used to conduct UTMB business.

What is required to be encrypted?

- ⇒ All UTMB laptops
- ⇒ Personally-owned laptops and desktops **that are used to directly access confidential information, and/or store any type of UTMB data that is not considered public information.**



What doesn't need to be encrypted?

- ⇒ Personally-owned laptops and desktops that are used only to access email and other ancillary systems, such as Kronos, employee self-service, etc., which don't involve downloading UTMB data to the device.
- ⇒ Personally-owned laptops and desktops that connect to UTMB using a CITRIX or VPN to establish a remote desktop connection to their office or virtual computer.

Faculty on the Road



Dr. Sarita Sastry presented a talk entitled "PTP-PEST targets a novel tyrosine site in the p120ctn N-domain to control epithelial motility and Rho GTPase activity" at the 2012 Gordon Research Conference "Signaling by Adhesion Receptors" at Colby College, Maine, June 24-29.

Dr. Catherine Schein was an invited speaker at the Collaborative Research Alliances for the Cure of Lung Diseases at Baylor College of Medicine, June 21, 2012

Dr. Muge Kuyumcu-Martinez attended Gordon Conference titled "The Biology of Post-transcriptional Gene Regulation" from July 15-20 and presented a poster "Alternative Splicing Regulation During Cardiac Differentiation".

Dr. Kizhake Soman Attended the "Lung Research Day" meeting of the Gulf Coast Consortia; Houston, TX, June 21, 2012

Dr. Bruce Luxon and **Dr. Alex Kurosky** attended the NIH NHLBI Proteomics Centers Fourth PI/Advisory Panel Meeting in Bethesda, MD August 1st & 2nd.

Dr. Luxon also attended the University of Texas Research Cyberinfrastructure (UTRC) Executive Committee meeting with the Vice Chancellor for Media Affairs in Austin July 26 as well as the Texas Regional CTSA Consortium meeting at Moody Gardens July 23 & 24

Dr. Kay Choi attended the annual American Society of Virology meeting and presented a poster on "Structure and activity of the endonuclease domain of the Pichinde virus L protein".

Featured Abstract by BMB Faculty

Enhancement of NEIL1-initiated oxidized DNA base excision repair by heterogeneous nuclear Ribonucleoprotein U (hnRNP-U) via direct interaction.

[Hegde ML, Banerjee S, Hegde PM, Bellot LA, Hazra TK, Boldogh I, Mitra S.J Biol Chem. 2012 Aug 17. \[Epub ahead of print\]](#)

Repair of oxidized base lesions in the human genome, initiated by DNA glycosylases, occur via the base excision repair (BER) pathway using conserved repair and some non-repair proteins. However, the functions of the latter non-canonical proteins in BER are unclear. Here we elucidated the role of heterogeneous nuclear ribonucleoprotein-U (hnRNP-U), identified in the immunoprecipitate of human NEIL1, a major DNA glycosylase responsible for oxidized base repair. hnRNP-U directly interacts with NEIL1 in vitro via NEIL1's common interacting C-terminal domain which is dispensable for its enzymatic activity. Their in-cell association increases after oxidative stress. hnRNP-U stimulates NEIL1's in vitro base excision activity for 5-hydroxyuracil (5-OHU) in duplex, bubble, forked or single-stranded DNA substrate, primarily by enhancing product release. Using eluates from FLAG-NEIL1 immunoprecipitates from human cells, we observed 3-fold enhancement in complete repair activity after oxidant treatment. The lack of such enhancement in hnRNP-U-depleted cells suggests its involvement in repairing enhanced base damage after oxidative stress. NEIL1's disordered C-terminal region binds to hnRNP-U at equimolar ratio with high affinity ($K_d \sim 54\text{nM}$). The interacting regions in hnRNP-U, mapped to both termini, suggest their proximity in the native protein; these are also disordered, based on PONDR prediction and circular dichroism spectra. Finally, depletion of hnRNP-U and NEIL1 epistatically sensitized human cells at low oxidative genome damage, suggesting that hnRNP-U's protection of cells after oxidative stress is largely due to enhancement of NEIL1-mediated repair.