

BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY



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Chair's Message

There has been a recent plethora of announcements with regards to analyses being carried out with internal and external components of the academic and administrative structures in the School of Medicine. Not surprisingly, these have led to rumors and some anxiety. This is normal; any change in the day-to-day topic of emails from the administration, together with the appointment of a new provost, is bound to exacerbate the already high level of anxiety that surrounds everybody in these times.

In my interactions with some of the consultant participants and both the old and new leadership, I saw a focus on the ever-present need to develop visions for the future. I emphasized the need for long-term planning and the understanding that evolution rather than abrupt change is more likely to lead to the desired goals of our institution.

Our department in particular performs at

a high level, and working with colleagues in other departments and the centers with whom we have strong ties, I am sure we will continue on that path even as there remain obstacles, in particular in the arena of funds for our scientific mission.

I do believe that especially during the last year we have developed a strategy for aid to faculty in grant development that will benefit all of us.

I guess what I am trying to say is that while things are uncertain and not encouraging, there do remain opportunities, and "the sky is not falling down".

I look forward to continuing to serve the department, and encourage any queries from our department members.

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Special Items of Interest

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Awards and Announcements

Dr. Olivera. Nestic was awarded a grant from the TIRR foundation: Novel Treatment for Spinal Cord Injury Pain.

Drs. John Wiktorowicz, Biochemistry & Molecular Biology, and Massoud Motamedi (Center for Biomedical Engineering) received notice of funding as Co-PIs for their DoD USAF contract for biomarker discovery of ocular laser injury using proteomics discovery approaches.

Dr. Muraldihar Hegde was awarded a pilot project grant from NIEHS Center in Environmental Toxicology at UTMB to study Genotoxicity of amyloid proteins. This grant includes Dr. Hegde as PI and **Dr. Tapas K. Hazra** as co-PI.

Dr. Yong Sun Lee was awarded an International Joint Research Projects: KRCF (Korea Research Council of Fundamental Science and Technology) in South Korea, "A novel type of noncoding RNA, nc886 – its role and diagnostic utility in gastric cancer".



Graduate Program News

Congratulations to:

Alexandre Esadze and **Paige Spencer** for selection as recipients of Barbara Bowman awards (to be awarded at the annual GSBS awards luncheon);

Levani Zandarashvili for selection as recipient of the Irma Mendoza award (to be awarded at the annual GSBS awards luncheon);

Kimberlee Burckart and **Abhijnan Chattopadhyay** for selection as recipients of the BCSO student award (to be awarded at the annual GSBS awards luncheon)

Wenzhe Lu was awarded a joint pre-doctoral fellowship of the Institute for Human Infections & Immunity and the Sealy Center for Structural Biology & Molecular Biophysics for the project "Computational Design of Vaccines against Multiple Strains of Encephalitic Alphaviruses".

Publications



Larry A Denner, Jennifer Rodriguez-Rivera, Jordan B Jahrling, **J Russ Carmical**, Sigmund J Haidacher, **Rovshan Sadygov**, Jonathan M. Starkey, Heidi Spratt, **Bruce A Luxon**, **Thomas G Wood**, Kelly T Dineley, "Cognitive Enhancement with Rosiglitazone Links the Hippocampal PPAR γ and ERK MAPK Signaling Pathways", in press *JNeurosci* July 2012

Gelman BB, Chen T, Lisinicchia JG, Soukup VM, Carmical JR, Starkey JM, Masliah E, Commins DL, Brandt D, Grant I, Singer EJ, Levine AJ, Miller J, Winkler JM, Fox HS, **Luxon BA**; Susan Morgello for the National NeuroAIDS Tissue Consortium, "The National NeuroAIDS Tissue Consortium Brain Gene Array: Two Types of HIV-Associated Neurocognitive Impairment.", *PLoS One*. 2012;7(9):e46178. doi: 10.1371/journal.pone.0046178. Epub 2012 Sep 26, PMID: PMC3458860

Lau D, Lemon S, **Luxon BA**, Sinha M, Gale M, "Innate Immune Tolerance and the Role of Kupffer Cells in the Differential Response to Interferon Therapy in HCV Genotype 1 Patients.", in press *Gastroenterology* Oct 2012.

Meiling Lu, Yan Huang, **Mark A. White**, Xuri Wu, Nan Liu, Xiaodong Cheng and Yijun Chen, "Dual catalysis mode for the dicarbonyl reduction catalyzed by diketoreductase", *Chem. Commun.*, 2012, 48, 11352–11354.

Zhao W, Saha M, Ke A, **Morais MC**, Jardine PJ, Grimes S (2012) "A Three-Helix Junction Is the Interface between Two Functional Domains of Prohead RNA in ϕ 29 DNA Packaging" *J. Virol.* 86(21):11625-32 PMID: 22896620

Harjes E, Kitamura A, Zhao W, **Morais MC**, Jardine PJ, Grimes S, Matsuo H. (2012) "Structure of the RNA claw of the DNA packaging motor of bacteriophage ϕ 29" *Nucleic Acids Res.* PMID: 22879380, PMID: PMC3479190

Mandal SM, **Hegde ML** Chatterjee A, Hegde PM, **Szczesny B**, Banerjee D, Boldogh I, Gao R, Falkenberg M, Gustafsson CM, Sarkar PS, **Hazra TK**. Role of human DNA glycosylase Nei-like 2 (NEIL2) and single strand break repair protein polynucleotide kinase 3'-phosphatase in maintenance of mitochondrial genome. *J Biol Chem.* 2012: 287:2819-29.

Della-Maria J, **Hegde ML**, McNeill DR, Matsumoto Y, Tsai MS, Ellenberger T, Wilson DM, **Mitra S**, Tomkinson AE. The interaction between Polynucleotide Kinase Phosphatase and the DNA Repair Protein XRCC1 is Critical for Repair of DNA Alkylation Damage and Stable Association at DNA Damage Sites. *J Biol Chem In Press.* 2012, Sep 19. [Epub ahead of print].

Wang Q, Lee I, Ren J, Ajay SS, **Lee YS*** and Bao X* (2012) Identification and functional characterization of tRNA-derived RNA fragments (tRFs) in respiratory syncytial virus infection. *Molecular Therapy*, in press (* co-corresponding authors)

Jeon SH, Johnson BH, **Lee YS** (2012) A tumor surveillance model: a non-coding RNA senses neoplastic cells and its protein partner signals cell death. *Int J Mol Sci* 13(10): 13134-13139

Faculty on the Road

Dr. Catherine Schein gave a seminar entitled From Interferons to Allergens: Computational Analysis for Novel Therapies at the NIGMS in Bethesda, MD, September 24, 2012.

She also gave a seminar "Targeting toxins, the lethal drones of bacteria" at Texas Womens University in Denton, TX September 14, 2012.



Dr. Alex Kurosky attended the NHLBI PI Advisory Board Meeting Attendees, Bethesda, MD - August 1-2, 2012.

Dr. Bruce Luxon attended the UT System UT Research Cyberinfrastructure Executive Committee meeting in Austin August 30th

He also was at the UT System UT IT Roadmap Steering Committee meeting in Austin August 31th

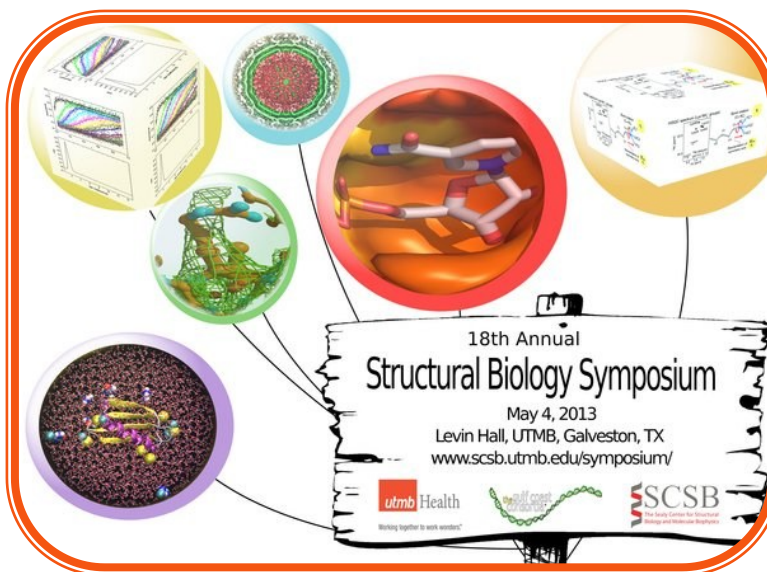
On September 10-11 he attended the NSF Review Panel for Drug Discovery Platforms in Arlington, VA.

Dr. Sankar Mitra participated in the review of intramural program at the National Institute on Aging in Baltimore MD on October 22, 2012.

He also traveled to Bellevue, WA to give a talk at the annual meeting of Environmental Mutagenesis Society on September 9-12.

Dr. Kay Choi attended *Emerging Viruses: Disease Models and Strategies for Vaccine Development* A Symposium in Honor of CJ Peters, October 23-24, Galveston, and presented a poster titled Subversion

Save the Date Structural Biology Symposium



Featured Abstract by BMB Faculty

A Three-Helix Junction Is the Interface between Two Functional Domains of Prohead RNA in 29 DNA Packaging.

J Virol. 2012 Nov;86(21):11625-32. doi: 10.1128/JVI.01370-12. Epub 2012 Aug 15.

Zhao W, Saha M, Ke A, Morais MC, Jardine PJ, Grimes S.

The double-stranded-DNA bacteriophages employ powerful molecular motors to translocate genomic DNA into preformed capsids during the packaging step in phage assembly. *Bacillus subtilis* bacteriophage 29 has an oligomeric prohead RNA (pRNA) that is an essential component of its packaging motor. The crystal structure of the pRNA-prohead binding domain suggested that a three-helix junction constitutes both a flexible region and part of a rigid RNA superhelix. Here we define the functional role of the three-helix junction in motor assembly and DNA packaging. Deletion mutagenesis showed that a U-rich region comprising two sides of the junction plays a role in the stable assembly of pRNA to the prohead. The retention of at least two bulged residues in this region was essential for pRNA binding and thereby subsequent DNA packaging. Additional deletions resulted in the loss of the ability of pRNA to multimerize in solution, consistent with the hypothesis that this region provides the flexibility required for pRNA oligomerization and prohead binding. The third side of the junction is part of a large RNA superhelix that spans the motor. The insertion of bases into this feature resulted in a loss of DNA packaging and an impairment of initiation complex assembly. Additionally, cryo-electron microscopy (cryoEM) analysis of third-side insertion mutants showed an increased flexibility of the helix that binds the ATPase, suggesting that the rigidity of the RNA superhelix is necessary for efficient motor assembly and function. These results highlight the critical role of the three-way junction in bridging the prohead binding and ATPase assembly functions of pRNA.

