

BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY



Chair's Message

The withdrawal of winter weather, in a somewhat recalcitrant mode this year, coincides with two joyful harbingers of Spring: the annual Structural Biology Symposium and commencement ceremonies. The Symposium is a celebration of outstanding scientific accomplishment and camaraderie that not only is enjoyed by our local "structural biologists" but is shared with an ever-growing number of local and mainland scientists. (Here "mainland" is meant in the broader sense of the word as referring to the world beyond the Causeway). It does not happen by accident, and we have to thank the dedication of our staff and faculty for its perennial success. Commencements celebrate the success of our educational mission in the context of both the medical school and the graduate school, again involving our students and faculty. These two celebratory events speak to our success in the three arenas of our mission: education, research and service. If you missed attending these in 2010, make an effort to join your colleagues next year, though there's still time to sign up for regalia and attend this year's commencement if you act by Monday the 29th.

Over the next few months I am assured that much restoration, mediation and plain "fixing and expansion of our infrastructure" will finally go beyond the

MARCH 2010 NO. 253



paperwork stage to the reality of physical improvements. While these much-welcomed efforts are underway, there will most likely be some nuisance due to the interruption of some services as various systems are tested and replaced. Again let us be patient, given that we all need the improvements.

If all goes as planned with our budget requests, we will continue to replace autoclaves and add another backup -80 freezer. One consequence of Ike may be an abbreviated lifespan for some of our individual -80 freezers. Our plan is to add one more "backup" departmental freezer to the two already on board for emergency failures of the many -80 freezers individual investigators rely upon.

The coming academic year should bring with it the first of the Presidential graduate students on campus. These will have been selected on a stiff competitive basis cutting across disciplines. Now that the program is in full swing, proper advertising of this opportunity to potential students should result in an influx of very high-caliber students. If you wish to help in the recruitment effort, please contact Dr. Sarita Sastry for details.

As we have discussed, we are embarking on a significant faculty recruitment effort in the area of structural biology. Dr.

Wayne Bolen is now the Director ad interim of the SCSB, and he has appointed three committees to aid in this effort. I personally want to thank Wayne for his dedication to the task at hand. All of BMB owes him a debt of gratitude for his efforts. If you feel that you know of appropriate candidates or if you want to be included in the recruitment effort in some capacity, please contact Wayne. As Chair, I am giving this our highest departmental priority for the next two years. Both Wayne and I will be meeting on a weekly basis; Wayne is now our newly appointed Vice-Chair, working together with Darrel Carney and me. We all wish the recruitment process to be transparent and inclusive, reflecting the standards of the Department. This is also a good opportunity to thank Vince Hilser for his service to the SCSB, the graduate program and BMB over the last 15 years. I specifically want to thank him for helping us make the transition to new leadership. We wish him and his family well at Johns Hopkins. Be sure to come to the farewell party in his honor on April 26.

All in all, this Spring is likely to be a busy time. Enjoy.

regino

Inside this issue:

MGC	3
Awards and Announcements	2
Faculty Travels	3
Publications	3

Special Items of Interest

- ✦ [Molecular Genomics Core Launches new website and LIMS](#)

Awards and Announcements

Abhisek Mukherjee received a Alzheimer's Drug Discovery Foundation 2010 ADDF Young Investigator Scholarship Award in February. These highly prestigious Awards and Scholarships recognize the early achievements of talented young investigators and seek to encourage the career development of the next generation of research scientists in the field of neurodegenerative diseases. Abhisek is a graduate assistant in Dr. Claudio Soto's lab.



Ali Sabahi joined Choi laboratory as a post-doctoral fellow in February. He received his Ph.D on hepatitis C virus entry from Tulane university.

Grants

Dr. Catherine H. Schein received a grant from the Institute for Translational Sciences entitled "Testing PCP-consensus proteins for multivalent Dengue vaccine design".

Dr. Yumei Ye received a grant from Novartis Pharmaceuticals Corporation entitled: Aliskiren (Tekturna) versus Valsartan (Diovan) and Myocardial protection Against Ischemia-Reperfusion Injury in Diabetic Hearts. Potential Synergistic Effects and Mechanisms of Action.

She also received a grant from BYS-MD-36 Forest Research Institute entitled: Does Nebivolol Induce Different Profile of MicroRNA's and Can it Explain Some of the Favorable Effects of Nebivolol.

Dr. Olivera Nestic-Taylor received an ITS-TRC Pilot grant award for the grant application: "Novel therapeutic treatment of neuropathic pain after spinal cord injury".

Faculty on the Road

Dr. Wlodek Bujalowski attended the Biophysical Society 54th Annual Meeting February 20-24, 2010 in San Francisco, California. He presented a poster on Dynamics of the recognition by the RepA Hexameric helicase of plasmid RSF1010. Analyses using fluorescence stopped-flow intensity and anisotropy methods.



Maria J. Jezewska, attended the Biophysical Society 54th Annual Meeting February 20-24, 2010 in San Francisco, California. She presented a poster on Mechanism of Nucleotide Cofactor Interactions with the RepA Protein of Plasmid RDF1010.

Michal R. Szymanski attended the Biophysical Society 54th Annual Meeting February 20-24, 2010 in San Francisco, California where he presented a poster on Energetics of the E. Coli PrA Helicase Interactions with the Double Stranded DNA. Biophysical Journal, 98(3) 1 January 2010.

He also attended the 15th Annual Structural Biology Symposium. March 19, 2010. Galveston, Texas.

Faculty on the Road (cont)

He presented a poster on Interactions of the *E. coli* Primosomal PriB Protein with the Single-stranded DNA. Solution vs. Crystallographic Studies.

Dr. Catherine H. Schein attended American Academy of Allergy Asthma & Immunology 2010 Annual Meeting in New Orleans, La. Feb. 25 – March 2, 2010 where she presented her abstract entitled Identifying Similar IgE-epitopes in Peanut and Walnut Allergens.

Drs. John Wiktorowicz, Alexander Kurosky and Kizhake Soman attended the 6th Annual Conference of the U.S. Human Proteome Organization, Denver, CO, March 7-10, 2010.

Dr. Bo Xu and Steve Smith attended the Association of Biomolecular Resource Facilities in Sacramento, CA, March 20-23, 2010.

Drs. Konrad Pazdrak, Alexander Kurosky and Mr. Christof Straub attended the AAI in New Orleans, LA

Kizhake Soman, Anjana Kalita, Sanjiv Sur, Susan Stafford, Xuemei Luo, John Wiktorowicz, and Alexander Kurosky, A Phosphoproteomic Study Of Pollen-Induced Signaling In Murine Dendritic Cells; Proteomics – from Bench to Clinic: The 6th Annual Conference of the U.S. Human Proteome Organization, Denver, CO, March 7-10, 2010.

Publications



Michal R. Szymanski, Maria J. Jezewska and Wlodzimierz Bujalowski. Interactions of the Escherichia coli Primosomal PriB Protein with the Single-stranded DNA. Stoichiometries, Intrinsic Affinities, Cooperativities, and Base Specificities. *J Mol Biol.* 2010 Feb 12. [Epub ahead of print]

Alexander G. Kozlov, Maria J. Jezewska, Wlodzimierz Bujalowski and Timothy M. Lohman. Binding Specificity of E. coli SSB protein for the chi subunit of DNA pol III Holoenzyme and PriA helicase. *Biochemistry.* 2010 Mar 23. [Epub ahead of print]

G.C. Bowick*, K.V. Soman*, H. Wang*, J.F. Aronson, B.A. Luxon, L.O. Lomas, D.G. Gorenstein, and N.K. Herzog., Proteomic Analysis of Pichinde virus Infection Identifies Differential Expression of Prothymosin- α , *Journal of Biomedicine & Biotechnology* (in press, 2010) [*these authors contributed equally].

Sarah J Hemauer, Svetlana L Patrikeeva, Tatiana N Nanovskaya, Gary DV Hankins, Mahmoud S Ahmed. Role of human placental apical membrane transporters in the efflux of glyburide, rosiglitazone, and metformin. *American Journal of Obstetrics and Gynecology.*

Moen, S.T., Slater, T.M., Patel, S.D., Tutt, C.B., Estrella-Jimenez, M.E., Pawlick, J., Sower, L., Popov, V.L., Schein, C.H., Gilbertson, S.R., Peterson, J.W. and Torres, A.G. Testing efficacy and toxicity of adenyl cyclase inhibitors against enteric pathogens during in vitro and in vivo models of infection. *Infect. Immun.*, (in press), 2010.

Yadav UC, Sriavstava SK and Ramana KV. Inhibition of Aldose Reductase Attenuates Endotoxin Signals in Human Non-pigmented Ciliary Epithelial Cells. *Exp. Eye Res.* 2010 (in press)

Ramana KV and Srivastava SK. Aldose reductase inhibition for the treatment of asthma. *Expert. Rev. Clin. Immunol.* 2010. 6: 1-4.

Reddy AB, Ramana KV. Aldose Reductase Inhibition: Emerging Drug Target for the Treatment of Cardiovascular Complications. *Recent Pat Cardiovasc Drug Discov.* 2010 (in press).

Yadav UC, Srivastava SK and Ramana KV. Understanding the role of aldose reductase in ocular inflammation. *Cur. Mol. Med.* 2010 (in press).

Ramana KV, Tammali R and Srivastava SK. Inhibition of Aldose Reductase Prevents Growth Factor - Induced G1/S Phase Transition via AKT/PI3K/E2F-1 Pathway in Human Colon Cancer Cells. *Mol. Cancer. Ther.* 2010 (in press).

Zhang, S., Bovshik, E., Maillard, R., Gromowski, G., Volk, D.E., Schein, C.H., Huang, C., Gorenstein, D.G., Lee, J., Barrett, A. and Beasley, D.W.C. Role of BC loop residues in structure, function and antigenicity of the West Nile virus envelope protein receptor binding domain III. *Virology*, (in press) 2010.

Featured Abstract by BMB Faculty

Interactions of the Escherichia coli Primosomal PriB Protein with the Single-stranded DNA. Stoichiometries, Intrinsic Affinities, Cooperativities, and Base Specificities

[J Mol Biol. 2010 Feb 12.](#)

Szymanski MR, Jezewska MJ, Bujalowski W

Department of Biochemistry and Molecular Biology, Department of Obstetrics and Gynecology, Sealy Center for Structural Biology, Sealy Center for Cancer Cell Biology, University of Texas Medical Branch at Galveston, 301 University Boulevard, Galveston, TX 77555-1053, USA.

Quantitative analysis of the interactions of the Escherichia coli primosomal PriB protein with a single-stranded DNA was done using quantitative fluorescence titration, photocrosslinking, and analytical ultracentrifugation techniques. Stoichiometry studies were done with a series of etheno-derivatives of single-stranded (ss) DNA oligomers. Interactions with the unmodified nucleic acids were studied, using the macromolecular competition titration (MCT) method. The total site-size of the PriB dimer-ssDNA complex, i.e. the maximum number of nucleotides occluded by the PriB dimer in the complex, is $12+/-1$ nt. The protein has a single DNA-binding site, which is located centrally within the dimer and has a functionally homogeneous structure. The stoichiometry and photocrosslinking data show that only a single monomer of the PriB dimer engages in interactions with the nucleic acid. The analysis of the PriB binding to long oligomers was done using a statistical thermodynamic model that takes into account the overlap of potential binding sites and cooperative interactions. The PriB dimer binds the ssDNA with strong positive cooperativity. Both the intrinsic affinity and cooperative interactions are accompanied by a net ion release, with anions participating in the ion exchange process. The intrinsic binding process is an entropy-driven reaction, suggesting strongly that the DNA association induced a large conformational change in the protein. The PriB protein shows a dramatically strong preference for the homo-pyrimidine oligomers with an intrinsic affinity higher by about three orders of magnitude, as compared to the homo-purine oligomers. The significance of these results for PriB protein activity is discussed. Copyright © 2010. Published by Elsevier Ltd.