

BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

SEPTEMBER 2010 NO. 256



Chair's Message

The new academic year is well on its way, and although we have had some summer storms and a number of named storms, none of these have posed a threat to the Upper Texas Coast or Galveston. So far, so good!

This will be a busy and challenging year for us. While we expand our teaching efforts to accommodate planned increases in all Schools over the next several years, Texas is facing financial shortfalls that although modest by comparison to other states, will nevertheless have some impact. At the same time, NIH has been communicating that the next couple of years will be difficult for investigators seeking NIH grants. At the departmental level, we are committed to keep a close watch on grant expenditures to help our faculty make the best use of their funds. To that end we are developing tools that will allow all PIs to keep close watch over their budgets. We have also asked faculty to submit names of likely speakers for seminar programs in our SOM who because of their participation in Study Sections should be made aware of our recovery and expansion plans.

We are in the midst of a strong faculty recruitment program in various areas. On November 1, Dr. Muge N. Kuyunku-Martinez, Ph. D. from Baylor College of Medicine, will join our Department as an Assistant Professor. Dr. Kuyunku-

Martinez has a research interest in degenerative mechanisms of myotonic dystrophies. She will also have an appointment to the Neuroscience and Cell Biology Department and be a member of the Mitchell Center for Neurodegenerative Diseases. We welcome her on board. Our recruitment for three senior faculty with expertise in biophysics and structural biology is ongoing, as is our recruitment for another senior position with expertise in mass spectroscopy, in collaboration with the Sealy Centers for Molecular Medicine and Cancer Cell Biology.

Now that we are returning to a post-Ike normalcy as our infrastructure recovers, it will be a good time to have a one-day faculty retreat in early 2011. As always, suggestions for topics are welcome. As in the past the event will take place at the Galveston Convention Center on the Seawall. Details will follow once a date and topic has been worked out.

As part of the strategic planning process, the Provost will be carrying out a School-wide audit of research space to better plan the ongoing expansion of research programs. We plan to carry out a departmental research space audit this fall to better prepare us for our ongoing recruitments, as well as document our space needs. In consultation with the Office of Sponsored Programs, a metric of \$350/sq.ft. in total external support



(direct + indirect costs) for research space has been assigned as desirable for the SOM. It is acknowledged that certain kinds of research have special requirements – for example, NMR – and that newly recruited faculty cannot be expected to meet such criteria. Swing space for renovations or being reserved for recruitments are also special cases. We will keep everybody informed as we learn more.

In the tradition of summer books to read, I read two books that I would recommend to any student wanting to look at the research and education enterprise from a different perspective: ["Three Cups of Tea: One Man's Mission to Promote Peace... One School at a Time"](#) by Greg Mortenson and David Oliver Relin and ["The Immortal Life of Henrietta Lacks"](#) by Rebecca Skloot.

Both in their own way lead to thoughtful appraisals of the importance of ethical considerations in medical research and the importance of education, as well as the impact a single individual can make. Both look at real people. I would suggest that all of our students read these. You will not regret the time invested.

Although still early, we do have a date and venue for our Christmas/Holiday Party: December 10th at Fisherman's Wharf. Keep the date open.

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Special Items of Interest

- ✦ Awards and Announcements
- ✦ Featured Abstract

Awards and Announcements

Wei Han, first year Medical Student, received first place poster award in the NIAID Infectious Diseases & Inflammatory Disorders program of the 2010 Medical Student Summer Research Program for his summer research project "Large-scale 3D modeling of allergens" in the laboratory of Dr. W. Braun.

Dr. Werner Braun received a grant from the United States Environmental Protection Agency entitled: "Prediction of Allergenicity by Epitopes".

Dr. Catherine Schein received a grant ITS Pilot Protocol #809, entitled "Testing PCP-Consensus Proteins for multivalent Dengue Vaccine Design: Stage 2".



Graduate Program News

We are extremely pleased to announce this year's winners for the BMB Graduate Program Awards. The competition this year was terrific and we are very lucky to have such wonderful students in our Program.

Two students were awarded the Barbara Bowman Award, Hung Doan of Dr. Ken Fujise's laboratory and Christof Straub of Dr. Alex Kurosky's laboratory. The Irma Mendoza Award went to Michal Szymanski of Dr. Wlodek Bujalowski's laboratory and Michal also won the Biological Chemistry Student Organization (BCSO) Award.

The BMB Program would like to welcome our newest student Huzhang Mao who joined Dr. Marc Morais' laboratory. MBET welcomes two new students, Pawel Bujalowski who is doing a rotation in Dr. Kay Choi's laboratory and Rahul Pal who is doing a rotation in Dr. Junji Iwahara's laboratory.

We had a very busy summer with 4 BMB and 3 MBET students passing their qualifying exams. Congratulations and we look forward to seeing great research projects from them.

BMB & MBET also have several students who have successfully defended and are looking forward to their new futures at Post Docs; Dr. Aishu Ravindran of Dr. Krishna Rajarathnam's laboratory and Drs. Suzanne Tomlinson and Kristen Lamb of Dr. Stan Watowich's laboratory.

Earlier in the summer, we had two MD/PhD students defend and they have since returned to the final stages of their medical school training; Dr. Sarah Hemauer of Dr. Mahmoud Ahmed's laboratory and Dr. Travis Schrank of Drs. Vince Hilser and Wayne Bolen laboratories.

Some exciting news, one of our MD/PhD alumni, Dr. Lee Wiederhold, of Dr. Sankar Mitra's laboratory is returning to campus to collaborate with Dr. Vicente Resto and Dr. Susan McCammon in the Department of Otolaryngology/Head and Neck Surgery.

Graduate Program News (cont)

Please make a note on your calendar for the annual BBSC Program Fair to be held Thursday, October 7th from 2-5pm in the Levin Hall Dining room. If you would like to display the research of your laboratory, please contact Debora Botting, dmbottin@utmb.edu for a poster slot.

Many of our students attend conferences throughout the year and recently, Christof Straub of Dr. Kurosky's laborator, attended the 4th HMGB1 Symposium in Helsinki, Finland. The meeting started with a keynote address by Kevin Tracey and included discussions on HMGB1, HMGB1 receptors and S100 proteins in the context of different inflammatory conditions. Much emphasis was on post-translational modifications of the protein and their implications on its proinflammatory potential. The atmosphere at the meeting was very collegial and dinners included much of the local Finish cold-fish specialties. The meeting happened to be during summer solstice and Christof managed to capture the sunset at 12:30 AM.



For an enjoyable read, we thank Dr. James Lee for bringing to our attention an interesting article for graduate students.

-Debora Botting

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BCSO News

The BCSO held their 2010 elections during our August meeting and are pleased to announce their new officers:

Chair - Hung Doan (Fujise Laboratory)

Vice Chair - Abhijnan Chattopadhyay (Fujise Laboratory)

Treasurer - Michal Szymanski (Bujalowski Laboratory)

Secretary – Kimberlee Burckart (Carney and Sastry Laboratories)

We invite and encourage all students within the department to actively participate in the upcoming year. The BCSO would like to thank the BMB graduate program and BMB/MBET faculty for their support over the past year and is looking forward to another great year. Special thanks go to our faculty advisor of the past year, Dr. Kay Choi, as well as to Dr. Sarita Sastry and Debora Botting for their continuous support over the years.

-Christof Straub, 2009-10 BCSO Chairman

Publications



Bruce, N.J., Chen, D., Dastidar, S.G., Marks, G.E., **Schein, C.H.** and Bryce, R.A. (2010) [Molecular Dynamics Simulations of A \$\beta\$ Fibril Interactions with \$\beta\$ -sheet Breaker Peptides.](#)

O. Nestic, L. M. Sundberg, J. J. Herrera, V. U.L. Mokkapati, J. Lee, and P. A. Narayana: Vascular Endothelial Growth Factor and Spinal Cord Injury Pain. J. Neurotrauma. In press.

Rovshan G. Sadygov*, Yingxin Zhao, Sigmund J. Haidacher, Jonathan M. Starkey, Ronald G. Tilton and Larry Denner. Using Power Spectrum Analysis to Evaluate 18O-Water Labeling Data Acquired from Low Resolution Mass Spectrometers pp 4306-4312 Publication Date (Web): Jun 23, 2010 <http://pubs.acs.org/doi/abs/10.1021/pr100642q>

Mohammad Jamaluddin, John E. Wiktorowicz, Kizhake V. Soman, Istvan Boldogh, Jeffrey D. Forbus, Heidi Spratt, Roberto P. Garofalo and Allan R. Brasier, *Role of Peroxiredoxin-1 and -4 in Protection of RSV-induced Cysteinyl-oxidation of Nuclear Cytoskeletal Proteins*, Journal of Virology, 84:9533-9545 (2010).

S Sengupta, A K Mantha, S Mitra and K K Bhakat ,Human AP endonuclease (APE1/Ref-1) and its acetylation regulate YB-1-p300 recruitment and RNA polymerase II loading in the drug-induced activation of multidrug resistance gene MDR1.Oncogene advance online publication, September 20, 2010

Russo AT, Malmstrom RD, White MA, Watowich SJ. Structural basis for substrate specificity of alphavirus nsP2 proteases. J Mol Graph Model. 2010 Aug 24;29(1):46-53. Epub 2010 Apr 24.PMID: 20483643

Tsalkova T, Blumenthal DK, Mei FC, White MA, Cheng X. Mechanism of Epac activation: structural and functional analyses of Epac2 hinge mutants with constitutive and reduced activities. J Biol Chem. 2009 Aug 28;284(35):23644-51. Epub 2009 Jun 24.PMID: 19553663

Faculty on the Road

Dr. Sankar Mitra traveled to Copenhagen, Denmark to give a talk at the Workshop on "Genome Integrity and Consequences" at the Niels Bohr Institute on September 1-2, 2010.



Dr. Mark White visited the Stanford Synchrotron Radiation Laboratory (SSRL) on June 1-3 in Menlo Park, CA to perform crystallographic experiments.

-He also was in Madison Wisconsin on July 7-8 to collect crystallographic data at the headquarters of Bruker-AXS.

- and on July 18-23, he attended the Gordon Research Conference on Diffraction Methods, at Bates College, Lewiston, Maine.

Featured Abstract by BMB Faculty

Specific Inhibition of NEIL-initiated Repair of Oxidized Base Damage in Human Genome by Copper and Iron

POTENTIAL ETIOLOGICAL LINKAGE TO NEURODEGENERATIVE DISEASES

Muralidhar L. Hegde[‡], Pavana M. Hegde[‡], Luis M. F. Holthausen[‡], Tapas K. Hazra^{‡§}, K. S. Jagannatha Rao[¶], and Sankar Mitra^{‡†}

Dyshomeostasis of transition metals iron and copper as well as accumulation of oxidative DNA damage have been implicated in multitude of human neurodegenerative diseases, including Alzheimer disease and Parkinson disease. These metals oxidize DNA bases by generating reactive oxygen species. Most oxidized bases in mammalian genomes are repaired via the base excision repair pathway, initiated with one of four major DNA glycosylases: NTH1 or OGG1 (of the Nth family) or NEIL1 or NEIL2 (of the Nei family). Here we show that Fe(II/III) and Cu (II) at physiological levels bind to NEIL1 and NEIL2 to alter their secondary structure and strongly inhibit repair of mutagenic 5-hydroxyuracil, a common cytosine oxidation product, both *in vitro* and in neuroblastoma (SH-SY5Y) cell extract by affecting the base excision and AP lyase activities of NEILs. The specificity of iron/copper inhibition of NEILs is indicated by a lack of similar inhibition of OGG1, which also indicated that the inhibition is due to metal binding to the enzymes and not DNA. Fluorescence and surface plasmon resonance studies show submicromolar binding of copper/iron to NEILs but not OGG1. Furthermore, Fe(II) inhibits the interaction of NEIL1 with downstream base excision repair proteins DNA polymerase and flap endonuclease-1 by 4–6-fold. These results indicate that iron/copper overload in the neurodegenerative diseases could act as a double-edged sword by both increasing oxidative genome damage and preventing their repair. Interestingly, specific chelators, including the natural chemopreventive compound curcumin, reverse the inhibition of NEILs both *in vitro* and in cells, suggesting their therapeutic potential.