BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

DECEMBER 2006 NO. 220

UTMB

BMB Biochemistry & Molecular Biology

Chair's Message

In the early days of January our three new assistant professors (Drs. Kay Choi, Junji Iwahara, and Marc Morais) will be taking up residence in the 6th floor of the Basic Science Building. Do make it point to drop in and visit and get to know our new colleagues. Although I am sure that they will be busy getting their labs going, let's make them feel at home. Another new resident on the 6th floor will be David Konkel, who has moved his quarters up from the first floor.

Sometime in the Spring we will begin our recruitment efforts anew, with emphasis on different areas of research than our most recent search. More on that at a future faculty meeting from the new committee carrying out the recruitment task.

You should all have received a request for opinions on the optimal length of grant proposals from the NIH. Please do take the time to provide input. While shorter applications may sound like a good innovation from the point of view of the reviewer, as Benjamin Franklin once wrote: "I am writing you a long letter, as I do not have time to prepare a short one" – or something to that effect. David Konkel's column this month includes some of his thoughts on the topic; the deadline for responses to the NIH is January 5th.

We congratulate Wlodek Bujalowski who was elected an AAAS Fellow, a prestigious award. He joins other BMB Fellows, Wayne Bolen, Robert Fox, David Gorenstein, James Lee, Sankar Mitra, John Papaconstantinou, Louise Prakash, Satya Prakash, and Brad Thompson. This year's Fellows will be formally announced in the AAAS News & Notes Section in the November 24, 2006 issue of the journal *Science*, and recognized at a ceremony on February 17, 2007 at the Fellows Forum during the annual AAAS meeting in San Francisco. I might add that of the 14 UTMB AAAS Fellows, 10 are members of our Department. We are all proud of the significant accomplishment this represents.

We will be having our annual holiday party on December 8 at the Galveston Yacht Club. There will good food, a band to dance away the night, and good cheer. As in the past we are celebrating together with our Center partners, and it should be a fun event for all.

See you there!

Happy Holidays, and a safe and healthy New Year!

regino

Inside this issue:

Special Items of Interest

- New - Faculty Focus Satish K. Srivastava, Ph.D., page 3
- Dr. Konkel's Research Coordinator's Column Online

Graduate Program News

The BMB Graduate Program proudly announces the dissertation defense of Craig Bush, December 14th at 2pm in the BSB Auditorium. Craig began his education at UTMB in 2001 and joined the laboratories of Drs. Aubrey Thompson and Bruce Luxon. Below is information Craig has provided about his future plans along with certain reflections on his experience at UTMB. We wish him the best of luck in his future endeavors. -Lillian Chan, Ph.D., Director

Starting January of 2007, I'll be working as a post-doctoral fellow under the supervision of Dr. Ching Lau at the Texas Children's Hospital in Houston. Dr. Lau is making a name for himself in the field of oncogenomics and systems biology by focusing on the emerging field of data integration as a means to find biological markers in pediatric brain and bone tumors. In this context, data integration is a statistical problem involving high-throughput biological data sets like functional genomics, proteomics, and metabonomics into a single data set for interpretation. Researchers in any of these three fields can appreciate the size and scope of the problem at hand. Fortunately, both Dr. Lau and I have a substantial collaborative network of researchers in all of these fields, each of whom has spent a great deal of time thinking about these kinds of problems.

Studying bioinformatics and systems biology has given me a great deal of appreciation for collaborative research. The problems, as I've mentioned, are simply too complex for one person to manage. Perhaps most important for this kind of highly collaborative research is fluency in several lexicons, where a researcher acts as a kind of ambassador representing his or her own area of scientific expertise. Studying at UTMB helped me develop this very special skill. I think it was the openness and genuine curiosity amongst the faculty of the new field that allowed me to interact with many disciplines represented on campus. This is one of many pleasant memories I had as a graduate student, and I hope to continue in this spirit as I pursue my career.

- Craig Bush

Awards and Announcements

Dr. Wlodek Bujalowski was elected a fellow of The American Association for the Advancement of Science (AAAS).

Dr. John Papaconstantinou was selected to represent the University of Texas Medical Branch as its candidate for the 2007 Dana Program in Brain and Immuno-imaging. If awarded, this grant will provide funds for a study of up to three years to be conducted on identification of signaling networks in the brain involved in age-associated neurodegenerative diseases such as Alzheimer's.

Faculty Focus: Satish K. Srivastava, Ph.D.

Dr. Satish K. Srivastava was appointed Professor of Human Genetics in the Department of Human Biological Chemistry and Genetics (HBC&G) in 1974 and soon had a joint appointment as Professor of Ophthalmology. He received his Ph.D. in Biochemistry from Lucknow University, India and did his Post-Doc in the same university. After teaching at a Post-Graduate Institute in Chandigarh, India for two years, he joined the City of Hope Medical Center at Duarte, California in 1966 as a Senior Research Scientist with a joint appointment as Assistant Professor of Pharmacology at USC Medical School, Los Angeles. In 1973 he co-chaired a session on Inborn Errors of Metabolism with the late Dr. Barbara Bowman, then Chairperson of HBC&G and was soon recruited and joined UTMB. Dr. Srivastava brought with him three persons who worked with him at City of Hope. One was Dr. Yogesh Awasthi, who later became a faculty member and is currently a Professor in BMB. Dr. John Wiktorowicz received his Ph.D. with Dr. Srivastava and after working at various places he is back as Associate Professor and Director of the Proteomics section of the Biomolecular Resource Facility at UTMB. Dr. Steve Miller, the third person, is now CEO of a Pharmaceutical Company in San Diego. Dr. Naseem H. Ansari joined Dr. Srivastava's group in 1976, received her Ph.D. and is now a Professor in BMB. There have been sixteen graduate students who have been taught under Dr. Srivastava, and at least 40 post-doctorate fellows that have been trained under his guidance. Most of his students and fellows have done exceedingly well in their careers.

Dr. Srivastava's collaborators include his long-time associates, Drs. Yogesh Awasthi; Naseem Ansari; Aruni Bhatnagar (who worked with him from 1986 to 1998 and is now Professor of Cardiology at Louisville); Sanjay Srivastava, Associate Professor at Louisville; Mark Petrash, a student who received his Ph.D. in 1981 and is now Professor at Washington University; Deepak Srivastava, Dr. Srivastava's son who is a Professor at UCSF; Sanjay Awasthi, Professor at U.T. Arlington; Juretta Horton, Professor at UT Southwestern; and several other faculty at UTMB including Drs. Kota Venkat Ramana, Stan Watowich and Mark White.

In the sixties, Dr. Srivastava started working on oxidative stress-mediated cellular toxicity that leads to various diseases including cataractogenesis, hemolytic anemia, and diabetes. Lipid peroxidation and glutathione metabolism were the main approaches. He was the first to show that an organic molecule such as oxidized glutathione (GSSG) could be actively transported out in a biological system such as the red blood cell and ocular lens. Another project that Dr. Srivastava has been working on for the past 37 years is to investigate and understand the mechanisms of diabetic and senile cataractogenesis. The main approach has been to investigate sorbitol formation by an enzyme aldose reductase, glutathione metabolism and oxidative stress. Dr. Srivastava is still working on related aspects of that project. In the early nineties, he found that aldose reductase, besides reducing glucose to sorbitol, efficiently reduces lipid peroxidation products such as 4-hydroxynonenal and their glutathione conjugates. In the late nineties and early 2000 this opened up new avenues for understanding the role of aldose reductase in various diseases. The demonstration by Dr. Srivastava and his collaborators, Drs. Naseem Ansari, Aruni Bhatnagar, Kota Ramana and Mark Petrash and a number of others from UTMB and outside, helped Dr. Srivastava to demonstrate that aldose reductase-catalyzed product such as GS-DHN is the major mediator of high glucose-, endotoxins-, cytokines-, chemokines- and growth factors-signals that activate NF-kB and AP1 and cause cellular toxicity. These results have opened up new opportunities to investigate the pathophysiology of various diseases in which oxidative stress is a major contributor, such as aetherosclerosis, restenosis after balloon injury of carotid arteries, sepsis subsequent to bacterial infections, colorectal and lung cancers. Dr. Srivastava plans to continue collaboration with clinical faculty Drs. Mark Evers, Charles Lui, and Edward Sherwood.

Dr. Venkat Ramana is currently one of the main contributors to Dr. Srivastava's research efforts. Post-docs in Dr. Srivastava's laboratory, Drs. Ravi Tammali, Umesh Yadav and Reddy Aramati (Bindu) heavily contribute to Dr. Srivastava's research. Now his major goals are to identify the exact mechanism of aldose reductase's mediation in Reactive Oxygen Species, identify effective inhibitors and develop siRNA-based techniques to down-regulate AR and eventually transfer the technology to clinical trials for the treatment of sepsis and colon cancer. Dr. Srivastava received his first NIH R01 grant in 1968 and he still has that project funded. He has always been well funded by NIH and is a merit award holder on the role of aldose reductase in diabetic complications.

Besides mentoring post-doctoral fellows and junior faculty, Dr. Srivastava participates in Medical School teaching in the Problem-based Learning component. He also participates in ICEE exams for medical students. In the Graduate School , Dr. Srivastava offers a special topic course in Inborn Errors of Metabolism.

Dr. Srivastava usually recruits post-docs from their applications and recommendations by his friends in the USA and outside. His advice for success is "always remain in the company of brilliant young scientists and listen to their suggestions even though most of them may not be good. With seniority, try to refrain from working at the bench as much as possible".

Publications & Grant Awards

Publications:

Chen, D, Menche, G, Power, T.D., Peterson, J.W. and **Schein, C.H.** Accounting for Ligand-bound Metal Ions in Docking Small Molecules on Adenylyl CyclaseToxins. Proteins (in press), 2006.

Schein, C.H., Volk DE, Oezguen N, Paul A. Novel, structure-based mechanism for uridylylation of the genome-linked peptide (VPg) of picornaviruses. Proteins 63(4):719-726, 2006.

Cummins, S.F., Nichols, A.E., **Schein, C.H.** and Nagle, G.T. Newly identified water-borne protein pheromones interact with attractin to stimulate mate attraction in Aplysia. Peptides 27(3):597-606, 2006.

Agnieszka Pladzyk, Aramati B.M. Reddy, Umesh C.S. Yadav, Ravinder Tammali, **Kota V. Ramana**, and **Satish K. Srivastava.** Inhibition of aldose reductase prevents lipopolysaccharide-induced inflammatory response in human lens epithelial cells. Invest. Opthalmol. & Vis. Sci. 47(12): 5395-5403, 2006.

Kota V. Ramana and **Satish K. Srivastava**. Mediation of aldose reductase in lipopolysaccharide-induced inflammatory signals in mouse peritoneal macrophages. Cytokine (in press).

Zivadinovic D, Gametchu, B, and **Watson, CS** Membrane estrogen receptor levels in MCF-7 breast cancer cells predict cAMP and proliferation responses. Breast Can Res **7:**R130-R144, 2005.

Zivadinovic D and **Watson, CS** Membrane estrogen receptor levels in MCF-7 breast cancer cells predict MAP kinase (ERK) activation and cell proliferation. Breast Cancer Res 7:R130-R144, 2005.

Bulayeva NN, Wozniak AL, Lash L, and **CS Watson.** Mechanisms of membrane estrogen receptor-α-mediated rapid estrogenic stimulation of Ca^{2+} and prolactin release in a pituitary cell line. American Journal of Physiology – Endocrinology & Metabolism 288: E388-E397, 2005.

Wozniak, A, Bulayeva, N, and **Watson, CS.** Xenoestrogens trigger membrane-estrogen receptor-α mediated calcium fluxes and prolactin release in GH3/B6 pituitary tumor cells. Env Health Perspectives, 113:431-439, 2005.

CS Watson, NN Bulayeva, AL Wozniak, CH Campbell Signaling from the membrane via membrane estrogen receptor-α: estrogens, xenoestrogens, and phytoestrogens. Steroids 70:364-371, 2005.

CS Watson and CA Lange. Steadying the boat: Integrating mechanisms of membrane and nuclear steroid signaling. EMBO Reports 6:116-119, 2005.

Watson, CS, Alyea, RA, Hawkins, BE, Reed, T, Thomas, ML, Cunningham, KA, and Jakubas, AA Estradiol effects on the dopamine transporter -- protein levels, subcellular location, and function. J. Molecular Signaling. in press, December, 2006

Zaitsu M, Narita S, Lambert KC, Grady JJ, Curran EM, Estes DM, Brooks EG, **Watson CS**, Goldblum RM, Midoro-Horiuti T. Estradiol activates mast cells via a nongenomic estrogen receptor-α and calcium influx. Molecular Immunology. in press, November, 2006.

Narita, S-I., Goldblum R.M., Brooks E.G., **Watson C.S**, Estes, DM, Curran, EM, and Midoro-Horiuti, T. Environmental estrogens induce mast cell degranulation and enhance IgE-mediated release of allergic mediators Env. Health Perspectives. in press, December 2006.

CS Watson, NN Bulayeva, AL Wozniak, and RA Alyea. Xenoestrogens are potent activators of nongenomic estrogenic responses. Steroids, in press, December 2006.

Nesic O, Lee J, Ye Z, Unabia GC, Rafati D, Hulsebosch CE and **Perez-Polo, JR.** Acute and chronic changes in aquaporin 4 expression after spinal cord injury. Neuroscience Dec 13;143(3):779-92, 2006.

Grants

Principal Investigator: Dr. Cheryl S. Watson

American Institute for Cancer Research- "Phytoestrogen-induced Nongenomic Signaling Cascades and their Functional Consequences in Pituitary Cancer". Jan. 2007-Dec. 2009.

NIH (NIEHS) – R01 - "Nongenomic Signaling Mechanisms of Environmental Estrogens". Dec. 2006-Nov. 2010

To have your publication or award included in the monthly newsletter, please send the information directly to Lisa Pipper (lpipper@utmb.edu) by the 1st of each month.

Administrator's Notes

Special Training in PureEdge for BMB Faculty

Kelly Lee of the Office of Sponsored Projects will present a special one-hour training session for BMB faculty in the use of the PureEdge system for electronic submittal of NIH grant proposals. For faculty members who will be working directly in PureEdge only as required, this session will convey the essentials of the electronic grant submission process for investigators. This special session is provided as an alternative to OSP's standard three-hour training session in the use of PureEdge. The session will be held in the 2nd Floor Auditorium of the Basic Science Building and will be offered on two dates: **Thursday, December 14 at 10:00 am and Tuesday, January 9, 2007 at 10:00 am**. *Please e-mail Margie Wronski if you plan to attend one of the two special sessions.*

Administrative staff are welcome to attend the special session, but all staff who will be working on preparation of grant proposals should attend the standard OSP training. Post-doctoral fellows and other researchers who may be preparing proposals for future submission are also encouraged to attend one of the standard three-hour training sessions conducted by OSP. The schedule for these sessions is provided on the OSP website.

Installation of New Fire Alarm System in the Basic Science Building

Work on installation of a new fire alarm system in BSB will begin in mid-to-late December. Before the project starts, FOAM will provide information about the schedule and workplan for the replacement effort. The project manager will endeavor to limit disruption to building operations as much as possible. More details will be provided as we receive information from FOAM.

Marianne

FACULTY ON THE ROAD

Dr. Catherine Schein

-presented a poster on October 18-22, 2006 “The Eyes Have It!: Using Positional Information to Select Inhibitors.” Southwest Regional American Chemical Society Meeting, Houston, TX.

- presented a poster on November 16-18. 2006 Texas Branch Meeting of The American Society for Microbiology, The University of Texas Medical Branch, Galveston, TX. Poster “Non-Nucleotide Inhibitors of Anthrax Edema Factor Identified by an ab initio Screening Method. Schein, C.H., Chen, D., Misra, M., Sower, L., Menche, G., Peterson, J.W., Kellogg, G.E.

- presented a poster November 8-10, 2006 at The Changing Landscape of Vaccine Development – Vaccines for Global Health, Moody Gardens Hotel, Galveston, TX . “Flavitrack, an Annotated Database to Compare Flavivirus Sequences”. Misra, M., Tran, V., Zhang, M. and Schein, C.H.

- presented at The 16th Keck Annual Research Conference "Extraction and Integration of Data in Biosystems", October 13, 2006 in Houston, TX.

⇒ Binding Modes for Inhibitors of Beta-amyloid Fibril Formation. Chen, D.*, Marks, G.E., Bryce, R.A., Soto, C. and Schein, C.H.

⇒ Screening for Non-Nucleotide Based Inhibitors of Anthrax Edema Factor Using Molecular Docking. Chen, D., Misra, M., Sower, L., Menche, G., Peterson, J.W., Kellogg, G.E. and Schein, C.H.

Dr. John Papaconstantinou

-gave a keynote speech at the 3rd Symposium on Proteome Fractionation and Biomarker Discovery, held at the Salk Institute in La Jolla, CA on Oct. 26-27.

- attended the Executive Meeting of the Claude D. Pepper Older Americans Independence Centers at the Gerontological Society of America meeting in Dallas on November 17, 2006.

- presented a seminar November 28, 2006 at Texas A & M University in College Station.

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

Featured Abstracts by Our Faculty

Xenoestrogens are Potent Activators of Nongenomic Estrogenic Responses.

CS Watson, NN Bulayeva, AL Wozniak, and RA Alyea. Steroids, in press, December 2006.

Studies of the nuclear transcriptional regulatory activities of nonphysiological estrogens have not explained their actions in mediating endocrine disruption in animals and humans at the low concentrations widespread in the environment. However, xenoestrogens have rarely been tested for their ability to participate in the plethora of nongenomic steroid signaling pathways elucidated over the last several years. Here we review what is known about such responses in comparison to our recent evidence that xenoestrogens can rapidly and potently elicit signaling through nongenomic pathways culminating in functional endpoints. Both estradiol (E_2) and compounds representing various classes of xenoestrogens (diethylstilbestrol, coumestrol, bisphenol A, DDE, nonylphenol, endosulfan, and dieldrin) act via a membrane version of the estrogen receptor-α on pituitary cells, and can provoke Ca^{++} influx via L-type channels, leading to prolactin (PRL) secretion. These hormones and mimetics can also cause the oscillating activation of extracellular regulated kinases (ERKs). However, individual estrogen mimetics differ in their potency and temporal phasing of these activations compared to each other and to E_2. It is perhaps in these ways that they disrupt some endocrine functions when acting in combination with physiological estrogens. Our quantitative assays allow comparison of these outcomes for each mimetic, and let us build a detailed picture of alternative signaling pathway usage. Such an understanding should allow us to determine the estrogenic or antiestrogenic potential of different types of xenoestrogens, and help us to develop strategies for preventing xenoestrogenic disruption of estrogen action in many tissues.

New Employees

Steve Widen, Ph.D., Scientist in Dr. Tom Wood's lab. Dr. Widen will be working on a program to develop aptamers, oligonucleotide sequences that bind to protein targets, for various members of the NF kappa B transcriptional regulatory pathway. This is one of several new initiatives from the Sealy Center for Molecular Medicine.

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

DECEMBER 2006 NO. 220

Department of Biochemistry &
Molecular Biology
301 University Blvd.
Galveston, TX 77555-0625

http://www.bmb.utmb.edu

Our Department is home to a broad spectrum of research activities and expertise. Our most singular quality is a culture of interdisciplinary research and collaboration. We believe that teaching and research are interdependent activities, and so give high priority to the education of our graduate students and postdoctoral fellows.

BMB
Biochemistry & Molecular Biology

UTMB
The University of Texas Medical Branch