BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

JUNE 2006 NO. 215

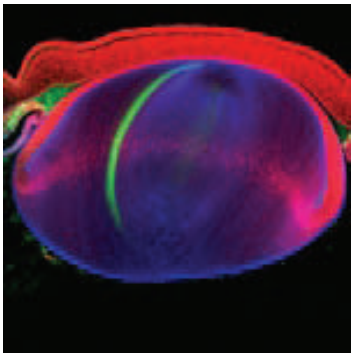
Chairman's Message

June 1 marks the first day of hurricane season. A good time to review laboratory and personal plans and preparations from batteries to canned goods and the battery operated radio. A lesson from last year is that it might be a good idea for every Departmental student, post-doc, staff or faculty member to have access to a non-UTMB server over the summer. Although I am sure most of us have one for our personal internet usage, it might be a good idea if you do not to think of this option. If you do, please send Margie your non-UTMB email address. We will compile an in house listing for emergencies only.

Not surprisingly, the Structural Biology Symposium was a success. This has now become a truly important national meeting for biophysicists and such. Up on the horizon is the SCMS Forum, again this year a joint venture with the SCCCB. Please mark your calendars as you receive the announcements and ask your fellows and student so submit posters to this one-day event.

As the pace of summer sets in, we are winding up our faculty recruitment for this year. I should have a full report soon to the faculty.

As you are all aware, the Navigant Consultant group is in town making recommendations to the administration as to how improve our financial standing and accomplish our goals. It is a certainty that there will be some



Administrator's Notes

Construction Update: 6th Floor BSB: Construction of the new labs and offices in the northwest area of the 6th floor of BSB is beginning on June 5 and will continue through October 2006. The contractor will be setting up a construction barrier to enclose the site. The barrier will be located so that there will still be access to the men's room on the 6th floor but there will not be access to the northwest stairway for the duration of the project. After the construction barrier is in place, the contractor will begin demolishing the concrete block walls behind the barrier. This work will begin on Thursday, June 8 and continue through Saturday, June 10.

Inside this issue:

Special points of interest:

- Dr. Konkel's column can be found online at www.bmb.utmb.edu/department/rcc/
- New this month, Featured abstracts, see page 10.

Chairman's Message (cont.)

impact on Basic Science departments. We will discuss this issue at the next faculty meeting on June 8th. Please do plan to attend. In terms of our performance this year as compared to last year, we have done very very well. Well in terms of awards to our faculty and students. Good science published. A more quantitative metric is that we increased our extramural funding by 12% from last year and our faculty commitment to teaching medical students for next year is over 25% more than it was at this time last year. Our graduate program is going great guns and I am certainly proud of our aggregate performance.

I can also report that great progress is being made in the development of a research strategic plan for the medical school. First drafts are now being written and I predict that by mid-summer the Dean will be able to share the plan with all of us.

After all the warnings from last month about electronic submissions, it appears that the R21 grants being submitted for the June 1 deadline are proceeding well. I guess the extra efforts of our staff working closely with OSP paid off. Lessons being learned will be most valuable when R01 s are submitted in this format in February of '07.

I believe the new BMB Web site is about to be unveiled. Hope you like it. Lisa and Lillian did a great job with their committees to try and satisfy all points of view.

This Saturday June 3 will be SOM graduation at Moody Gardens. If it is your turn to represent the Department, see you there.

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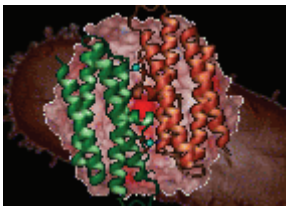


WELCOME NEW EMPLOYEES

Tina Brown, College Intern with Dr. Naseem Ansari

Swapna Sarkar, Postdoctoral Fellow with Dr. Bruce Luxon

Alex Torres, College Intern with Dr. Naseem Ansari

Jade Truong, College Intern with Dr. Naseem Ansari

Administrator's Notes (cont.)

There will be some noise involved in this work, but the dust should be contained within the space. During the wall demolition, the freight elevator will be in continuous use by the contractor for removal of debris. Please contact me if there are any questions about the construction work.

Hurricane Preparedness: Specific information about departmental contingency plans and preparations will be coming after the campus-wide research-oriented hurricane preparedness meeting on Friday, June 9 from 8:30 to 11:30. We encourage each lab group to send a representative to the meeting, if possible. One item we will be reviewing in each lab is the equipment requiring connection to the emergency power system. Each lab should evaluate the equipment placed on the existing emergency circuits to confirm that the total amperage the equipment draws upon starting up does not exceed the capacity of the circuit.

Stay Alert Hurricane Season is Here

Faculty on the Road

Dr. Werner Braun

- April 30-May 02, 2006, Shreveport, LA as an invited speaker presenting "In Silico Detection of B- and T-Cell Epitopes" at the North Louisiana Partnership for Innovation (NLPI) at the CERT Institute for Biomedical Informatics Symposium/BioResearch Day at Louisiana Tech University.

Dr. Darrell H. Carney

- May 14-16, 2006, Scottsdale, AZ to attend the Wound Healing Society 16th Annual Meeting & Exhibition and to participate in the ulcer clinical trial data discussions.

- May 19, 2006, Austin, TX to attend a meeting with Dr. Brent Iverson and the Texas Institute for Drug & Diagnostic Development (TI-3D).

Dr. Robert O. Fox

- May 08, 2006, Houston, TX to attend the Keck meeting at Rice University.

- May 20-22, 2006, Berkeley, CA to attend the Conference on Synthetic Biology.

Dr. Elena Frolova

- April 29-May 04, 2005, Fort Lauderdale, FL to attend the 2006 Association for Research in Vision and Opthalmology (ARVO) meeting and to present a paper entitled, "WNT Signaling Plays a Critical Role in Lens Morphogenesis".

Dr. David G. Gorenstein

- May 17, 2006, Houston, TX to attend the Gulf Coast Consortia Symposium at Baylor College of Medicine.

- May 19-20, 2006, Galveston, TX to attend the Sealy Center for Structural Biology Symposium.

Dr. Jason A. Hall

- May 22-23, 2006, Kent, OH to visit Kent State University and present the seminar entitled, "Characterization of a Sodium-Coupled Dicarboxylate Carrier Protein from *S. aureus".*

Dr. Olivera Nesic-Taylor

- May 12, 2006, Houston, TX to attend the Texas Institute Rehabilitation Research (TIRR) meeting to work on collaborative efforts with UT-Houston and Baylor College of Medicine.

Dr. J. Regino Perez-Polo

- May 20-24, 2006, San Juan, Puerto Rico to attend the Specialized Neuroscience Research Projects Advisory Meeting.

Dr. Satish K. Srivastava

- May 01-04, 2006, Fort Lauderdale, FL to attend the 2006 Association for Research in Vi-

Faculty on the Road (cont.)

sion and Opthalmology (ARVO) meeting and present the abstract entitled, "Aldose Reductase Inhibition Prevents Bacterial Lipopolysaccharides (LPS)-Induced Cytotoxic Signals in Human Lens Epithelial Cells".

- May 06-10, 2006, Louisville, KY to attend an annual collaborators meeting at the University of Louisville.

Dr.Stanley J. Watowich

- May 10, 2006, Austin, TX to do research collaboration at United Devices.

Dr. Cheryl S. Watson

- May 17, 2006, Houston, TX to attend the Academic Strategies for High Throughput and High Content Pathway Analaysis meeting at Baylor College of Medicine.

Dr. John Wiktorowicz

- May 23-25, 2006, Sacramento, CA to attend the Golden Capitol Network Conference and present the paper entitled, "Protein ProFiler^{TM} : An Innovative Discovery Platform for Proteomics.

June Birthdays

Dr. Naseem Ansari – 7th

Wendy Baker – 28th

Terry Campbell – 19th

Christopher Chin – 5th

Jennifer Crawford – 15th

Diana Ferrari – 29th

Deborah Greer – 25th

Dr. Jason Hall – 6th

Olga Kololoitsova – 26th

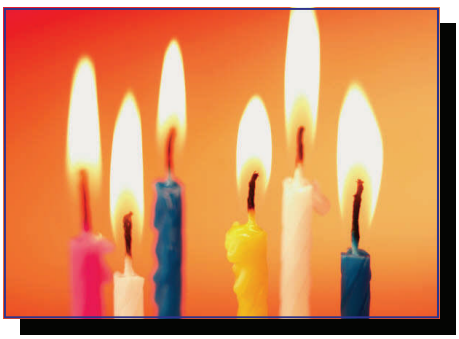
Dr. Jie Li – 6th

C.J. Orlea – 3rd

Kathleen Randolph– 28th

Ravinder Tammali – 25th

Dr. Yuan Xu – 4th



CONGRATULATIONS!!

TO Dr.John Papaconstantinou on being selected as the subject of a featured article in the UTMB Magazine. Please enjoy it at http://www.utmb.edu/utmbmagazine/schoolnews/gsbs/default.htm.

TO the following employees who have reached an anniversary milestone between March 01st, 2006 through August 31 st, 2006

30 Years of Service:

Dr. Ghulam A. S. Ansari

20 Years of Service:

Elizabeth Gerhardt

15 Years of Service:

Bi-Hung Peng

10 Years of Service:

Jonghoon Kang David Volk

5 Years of Service:

Jennifer Crawford

Elena Frolova

Xiaoming Hu

Ovidiu Ivanciuc

Olga Kolokoltsova

Michael Meador

Naomi Oshiro

T. David Power

Payal Sheth

Michael Webb

PUBLICATIONS, GRANTS & AWARDS

Publications:

Boylston WH, DeFord JH and Papaconstantinou J (2006) Identification of Longevity-associated Genes in Long-lived Snell and Ames Dwarf Mice. AGE (In press).

Grants:

"Helicase Mechanisms in DNA Replication". Principal Investigator: Dr. Wlodek Bujalowski; Agency - NIH, National Institute of General Medical Sciences; Type: 5 RO1 GM046679-14, Period: 05/01/05 - 04/30/09.

"Role of chemokine monomer-dimer equilibrium in innate immunity and inflammation". Principal Investigator: Dr. Krishna Rajarathnam; Agency - National Institute of Allergy and Infectious Diseases (NIAID); Type: 1 R01 A1069152-01, Period: 05/01/2006 – 04/30/2011.

Abstracts:

James H. DeFord, Kashyap B. Choksi, Don "T.J." Tjernlund and John Papaconstantinou, Adding Character to Protein Fractionaton: A High Throughput Method of Multiple Analysis. Presented at the Sealy Center for Molecular Science, Sealy Center for Cancer Cell Biology Annual Science Forum, June 7, 2006, Galveston, Texas.

K.B. Choksi, W.H. Boylston III and J. Papaconstantinou, Age-Related Increase in Oxidatively Damaged Proteins of Mouse Kidney Mitochondrial Electron Transport Chain Complexes Leads to Decline in Mitochondrial Function. Presented at the Sealy Center for Molecular Science, Sealy Center for Cancer Cell Biology Annual Science Forum, June 7, 2006, Galveston, Texas.

J.E. Nuss, J.K. Amaning, J.P. Rabek and J. Papaconstantinou, Ascertaining the Structural and Functional Consequences of the Age-Associated Oxidation and Nitration of Creatine Kinase. Presented at the Sealy Center for Molecular Science, Sealy Center for Cancer Cell Biology Annual Science Forum, June 7, 2006, Galveston, Texas.

Graduate Program Notes — Lillian Chan

Congratulations to our four BMB students, Tieying Hou, Anthony Manson, Weiming Ni and Suzanne Tomlinson, who have successfully passed their Qualifying Exams. Our students within the BSCB tract will be taking their Oral Exams this month and we wish them the best of luck. We sincerely appreciate our entire faculty and the time they have given serving on the Written and Oral Examination and Evaluation Committees.

One of Stan Watowich's students, Payal Sheth, will be presenting her final dissertation June 23 at 1pm in the Old Red Amphitheater 2.214. She has been a wonderful student and a great help in developing our Program. Please come and support her.

Our curriculum is being expanded to reflect the changing needs of our students. We will be offering a number of new courses this upcoming academic year. This fall we will be adding a special topics course on Biological Applications in Statistical Physics taught by Joerg Roesgen as well as an annual course on Introduction to Bioinformatics taught by Bruce Luxon. The DNA Repair & Mutagenesis course taught by Louise Prakash will be moving to the spring term and the Hormone & Cancer course taught by Brad Thompson will be moving to the fall term. Next summer, we will be offering a new course on Single Molecule Detection and Manipulation taught by Andres Oberhauser.

There are a number of new course topics being discussed by the BMB & BSCB Curriculum Committees and as they are created, we will send out announcements.

Please keep in mind tuition costs will be increasing starting in the fall term. For a complete overview of these new fees, visit the Office of the Registrar website, http://www.utmb.edu/enrollmentservices/PDF/GSBSFees0607-other.pdf . Also, please be reminded that starting this coming August, the BBSC will be paying the new incoming BBSC students ALL their assessed tuition and fees, which add up to $1,194 per term, and $3,582 per year.

14TH ANNUAL SCIENCE FORUM

The Sealy Center for Molecular Science and the Sealy Center for Cancer Cell Biology presents:

MICHAEL KARIN, Ph.D.

Professor, Department of Pharmacology University of California at San Diego La Jolla, California

Founder and Consultant

Celgene Pharmaceuticals

San Diego, California

JUNE 07, 2006

KEYNOTE ADDRESS: "THE IKK COMPLEX: LINKING INFLAMMATION & CANCER" 11:30 a.m. - 12:30 p.m.

Levin Hall Auditorium South

Reception to follow in Levin Hall Dining Room

POSTER SESSION:

08:00 - 11:00 a.m.

01:30 - 04:30 p.m.

Levin Hall Dining Room

JUDGING/AWARDS: 04:30 - 04:45 p.m.

Levin Hall Dining Room

Contact: Jeannie Rice-Osburn at (409) 772-1253

Featured Abstracts by Our Faculty

PTP-PEST couples membrane protrusion and tail retraction via VAV2 and p190RhoGAP Sarita K. Sastry , Zenon Rajfur, Betty P. Liu, Jean-Francois Cote, Michel Tremblay, and Keith Burridge

Cell motility is regulated by a balance between forward protrusion and tail retraction. These phenomena are controlled by a spatial asymmetry in signals at the front and the back of the cell. We show here that the protein tyrosine phosphatase, PTP-PEST is required for the coupling of protrusion and retraction during cell migration. PTP-PEST null fibroblasts, which are blocked in migration, exhibit exaggerated protrusions at the leading edge and long, unretracted tails in the rear. This altered morphology is accompanied by changes in the activity of Rho GTPases, Rac1 and RhoA, which mediate protrusion and retraction, respectively. PTP-PEST null cells exhibit enhanced Rac1 activity and decreased RhoA activity. We further show that PTP-PEST directly targets the upstream regulators of Rac1 and RhoA, VAV2 and p190RhoGAP. Moreover, we demonstrate that the activities of VAV2 and p190RhoGAP are regulated by PTP-PEST. Finally, we present evidence indicating the VAV2 can be regulated by integrin-mediated adhesion. These data suggest that PTP-PEST couples protrusion and retraction by acting on VAV2 and p190RhoGAP to reciprocally modulate localized Rac1 and RhoA activity.

The crystal structure of the cis-proline to glycine variant (P114G) of ribonuclease A. David A. Schults, Alan M. Friedman, Mark A. White and Robert O. Fox

Replacement of a cis-proline by glycine at position 114 in ribonuclease A leads to a large decrease in thermal stability and simplifies the refolding kinetics. A crystallographic approach was used to determine whether the decrease in thermal stability results from the presence of a cis glycine peptide bond, or from a localized structural rearrangement caused by the isomerization of the mutated cis 114 peptide bond. The structure was solved at 2.0A $^{\circ}$ resolution and refined to an R-factor of 19.5%and an Rfree of 21.9%. The overall conformation of the protein was similar to that of wild-type ribonuclease A; however, there was a large localized rearrangement of the mutated loop (residues 110–117—a 9.3 A $^{\circ}$ shift of the Ca atom of residue 114). The peptide bond before Gly114 is in the trans configuration. Interestingly, a large anomalous difference density was found near residue 114, and was attributed to a bound cesium ion present in the crystallization experiment. The trans isomeric configuration of the peptide bond in the folded state of this mutant is consistent with the refolding kinetics previously reported, and the associated protein conformational change provides an explanation for the decreased thermal stability.

Proteomic analysis of colonic myofibroblasts and effect on colon cancer cell proliferation. Andy L. Chen, Kizhake V. Soman, Piotr G. Rychahou, Bruce A. Luxon and B. Mark Evers **Background.** The stromal microenvironment influences many steps of tumor progression through the elaboration of signals from myofibroblasts. The phosphatidylinositol 3-kinase (PI3K)/Akt pathway transduces signals initiated by growth factors and is involved in colonic epithelial proliferation. The purpose of this study was to determine (1) the influence of myofibroblasts on colon cancer cell proliferation and PI3K activity, and (2) the protein alterations associated with myofibroblasts derived from polyp versus normal margins. **Methods.** Myofibroblasts were derived from polyps and corresponding normal mucosa. Myofibroblasts were cocultured with colon cancer cells HT29 stably transfected with green fluorescent protein and KM20 cells. Proliferation was quantitated by green fluorescent protein count and cytokeratin enzyme-linked immunosorbent assay. HT29 cells were incubated with conditioned medium from myofibroblasts, and the effect on proliferation and PI3K activity was determined by 5-bromo 2-deoxyuridine incorporation and Akt kinase assay, respectively. Protein profiles were obtained by SELDI-TOF MS analysis. **Results.** In coculture experiments, all myofibroblasts significantly enhanced HT29 and KM20 cell proliferation. However, polyp myofibroblasts enhanced proliferation of the cancer cells to a greater extent than normal myofibroblasts. Conditioned medium from all myofibroblasts stimulated Akt kinase activity. SELDI-TOF MS profiles showed more than 40 protein peaks for each isolate. One protein was differentially expressed in polyps versus normal cells. **Conclusions.** Utilizing a novel proteomic approach, we identify distinct protein profiles in myofibroblasts of polyps compared with stromal cells of normal mucosa. Moreover, myofibroblasts can stimulate indirectly PI3K activity and enhance colon cancer cell proliferation. These findings suggest that targeted therapy to signaling pathways in myofibroblasts may be useful in colorectal cancer chemoprevention and possible treatment.

JUNE 2006 NO. 215

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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.

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The University of Texas Medical Branch