BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

JULY 2006 NO. 216

Chairman's Message

JThis is a difficult time for the Department as we restructure ourselves to allow for a new way of doing business, as part of the UTMB transformation effort. We are shifting from deficit budgeting to investment budgeting. While this is a necessary step if we wish to be able to invest in our mission the necessary resources, the initial process does involve loss of jobs and reductions in compensation for many. We are working hard to be able to finish the process promptly and let everybody affected know what the consequences will be. This interregnum period is stressful to all in the Department and is not conducive to a good work environment.

Moving beyond the negative and building towards the future, I will appoint a faculty committee to develop a three-year strategic plan for BMB. As an initial step, I will ask them to organize a one day mini-retreat similar to the ones we have had in the last two years to provide input from the faculty. Their charge will be to use the outcomes from the retreat to develop a white paper that will help me in successfully increasing our research revenues, fulfill our educational goals and establish a solid financial basis to our future growth. Once the individuals in the committee agree to participate, I will let all know what the next steps will be.

In the last week or so, I received assurances from both the Dean and the CFO of the SOM that our faculty recruitment project is to continue on course. I will be contacting our recruits over the next few weeks to make sure that we are on tract and will inform the faculty of the outcomes of those discussions. As I see it, once we have reconfigured, we will be in a strong position to resume our efforts to make our department an outstanding one.

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Administrator's Notes

FIRST "SPACEWALK" to be FRIDAY, JULY 7

Margie Wronski and I will be setting off on our first "Spacewalk" on Friday, July 7 from 9:00 am to 12:00 noon. We will be doing a walk-through of each of BMB's locations, and we plan to visit each lab, core facility, and office location. The primary purpose of the walk-through is for us to learn about any facilities issues that need to be addressed or followed-up on. (Given the weather Galveston has had

Inside this issue:

Special points of interest:

- Dr. Konkel's column can be found online at www.bmb.utmb.edu/department/rcc/
- Featured abstracts can be seen on pages 4-5 in this edition.

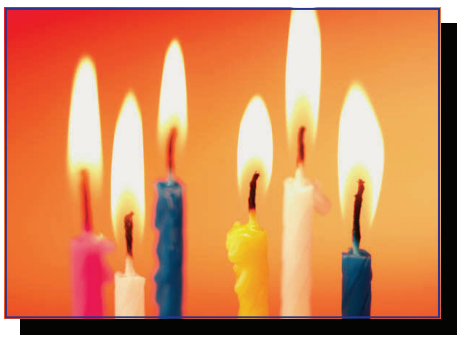
recently, we anticipate seeing the results of roof leaks in certain areas.) We are also hoping this will give us an opportunity to become more familiar with the work being done in all the department's areas which will, in turn, help us gain a greater understanding of support requirements and potential space issues. For the future, we expect to be making a similar Spacewalk on the first Friday of each month. Please gather together any information you may want to point out or pass along to us relating to any issues or problems you are encountering in your areas.

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

JULY BIRTHDAYS

Bindu Aramati – 23rd
Dr. Yogesh Awasthi – 13th
Dr. Werner Braun – 24th
Sanjeev Choudhary – 25th
Sai Hari Gandham – 20th
Beth Gerhardt – 16th
Dr. Vince Hilser – 27th
Aditya Hindupur – 8th
Tieying Hou – 17th
Warna Kaluarachchi – 29th
Raghavendran Shylini – 17th
Julieann Lee– 30th
Marianne Miller – 14th
Eloisa Mitchell – 16th
Surendra Negi – 1st

Dr. Ana Pajor – 13th
J. Justin Robert – 25th
Sergio Sanat Maria Guerra – 6th
Payal Sheth – 2nd
Dr. Satish Srivastava – 21st
Shriram Srivastava – 14th
Corey Theriot – 9th
Dr. Steven Whitten – 14th
Lee Wiederhold, III – 23rd
Dr. Min Zhang – 26th
Xu Zhao – 17th



FACULTY ON THE ROAD

Dr. Yogesh C. Awasthi
- June 06-08, 2006, Washington, DC to attend the Xenobiotic and Nutrient Disposition and Action Study Section at the National Institutes of Health to review grant applications.

- June 14-20, 2006, Genova, Italy to attend the 4-HNE (4-Hydroxynonenal) meeting and present the abstract entitled, ""Role of 4-hydroxynonenal and its Metabolites in Signaling".

Dr. Lee-Nien Lillian Chan
- June 01-02, 3006, Baltimore, MD to attend the American Society of Gene Therapy 09th Annual Meeting and present the abstract entitled, "Recombinant Adeno-Deaminase Deficiency in a Mouse Model".

Dr. Bruce A. Luxon
- June 16-21, 2006, San Francisco, CA to attend the Biomarker Data Analysis Meeting

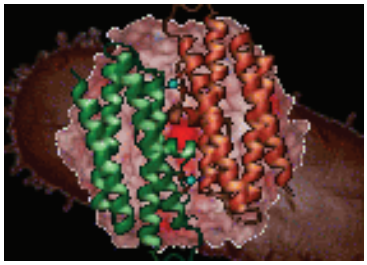
Dr. Olivera Nesic-Taylor
- June 24-28, 2006, Boston, MA to attend the American Spinal Injury Association & International Spinal Cord Society Meeting, "A Global Spinal Cord Injury Conference" and to present the talk entitled, "Chronic Glial Activation After Spinal Cord Injury".

Dr. John Papaconstantinou
- June 15, 2006, Houston, TX to attend a seminar at the University of Houston Health Science Center.

Dr. E. Brad Thompson
- June 15, 2006, Houston, TX to attend the Polish Biotech Collaboration and Showcase Program.

WELCOME NEW EMPLOYEES

Sai Hari Gandham, Graduate Assistant



Stay Alert Hurricane Season is Here

PUBLICATIONS, GRANTS & AWARDS

Publications:
Nowak K, Lange-Dohna C, Zeitschel U, Günther A, Lüscher B, Robitzki A, Perez-Polo R, Rossner S. The transcript factor Yin Yang 1 is an activator of BACE1 expression. J. Neurochemistry 96:1696-1707, 2006.
Grants:
Effect of "Decoy" Intervention on NF-kB Activation. Principal Investigator: Dr. Danny Rafati; Agency - Ruth L. Kirschstein National Research Service Award; Type: NS046136-03, Period: 05/22/2006 - 05/21/2007.

Featured Abstracts by Our Faculty

An Incoming Nucleotide Imposes an anti to syn Conformational Change on the Templating Purine in the Human DNA Polymerase-i Active Site

Deepak T. Nair, Robert E. Johnson, Louise Prakash, Satya Prakash and Aneel K. Aggarwal1
Substrate-induced conformational change of the protein is the linchpin of enzymatic reactions. Replicative DNA polymerases, for example, convert from an open to a closed conformation in response to dNTP binding. Human DNA polymerase-i (hPoli), a member of the Y family of DNA polymerases, differs strikingly from other polymerases in its much higher proficiency and fidelity for nucleotide incorporation opposite template purines than opposite template pyrimidines. We present here a crystallographic analysis of hPoli binary complexes, which together with the ternary complexes show that, contrary to replicative DNA polymerases, the DNA, and not the polymerase, undergoes the primary substrate-induced conformational change. The incoming dNTP ‘‘pushes’’ templates A and G from the anti to the syn conformation dictated by a rigid hPoli active site. Together, the structures posit a mechanism for template selection wherein dNTP binding induces a conformational switch in template purines for productive Hoogsteen base pairing.

Stochastic Regulation in Early Immune Response

Tomasz Lipniacki, Pawel Paszek, Allan R. Brasier, Bruce A. Luxon and Marek Kimmel

Living cells may be considered noisy or stochastic biochemical reactors. In eukaryotic cells, in which the number of protein or mRNA molecules is relatively large, the stochastic effects originate primarily in regulation of gene activity. Transcriptional activity of a gene can be ini-

Featured Abstracts by Our Faculty

tiated by transactivator molecules binding to the specific regulatory site(s) in the target gene. The stochasticity of activator binding and dissociation is amplified by transcription and translation, since target gene activation results in a burst of mRNAs molecules, and each copy of mRNA then serves as a template for numerous protein molecules. In this article, we reformulate our model of the NF-kappaB regulatory module to analyze a single cell regulation. Ordinary differential equations, used for description of fast reaction channels of processes involving a large number of molecules, are combined with a stochastic switch to account for the activity of the genes involved. The stochasticity in gene transcription causes simulated cells to exhibit large variability. Moreover, none of them behaves like an average cell. Although the average mRNA and protein levels remain constant before tumor necrosis factor (TNF) stimulation, and stabilize after a prolonged TNF stimulation, in any single cell these levels oscillate stochastically in the absence of TNF and keep oscillating under the prolonged TNF stimulation. However, in a short period of approximately 90 min, most cells are synchronized by the TNF signal, and exhibit similar kinetics. We hypothesize that this synchronization is crucial for proper activation of early genes controlling inflammation. Our theoretical predictions of single cell kinetics are supported by recent experimental studies of oscillations in NF-kappaB signaling made on single cells.

Thioredoxin-ASK1 complex levels regulate ROS-mediated p38 MAPK pathway activity in livers of aged and long-lived Snell dwarf mice.
Ching-Chyuan Hsieh and John Papaconstantinou

We have proposed that the age-associated increase of reactive oxygen species (ROS) by electron transport chain (ETC) dysfunction may cause the elevated basal level of p38 MAPK stress response pathway activity. However, the mechanism by which ROS activates this pathway is not clear. Here we propose that activation of the p38 MAPK pathway by complex I (CI) generated ROS, in response to rotenone (ROT) treatment, is based on the ability of reduced Trx to bind to and inhibit ASK 1 and its release from the complex upon oxidation. This balance of free vs. bound ASK1 regulates the level of p38 MAPK pathway activity. To support this mechanism we demonstrate that the production of ROS by ROT treated AML12 hepatocyte cells dissociates the Trx-ASK1 complex, thereby increasing p38 MAPK pathway activity. This mechanism is supported by the ability of N-acetyl cysteine (NAC) to prevent dissociation of Trx-ASK1 and activation of the p38 MAPK pathway. We also demonstrated that the ratio of ASK1/Trx-ASK1 increases in aged mouse livers and that this correlates with the increased basal activity of the p38 MAPK pathway. The longevity of Snell dwarf mice has been attributed to their resistance to oxidative stress. A comparison of the levels of Trx-ASK1 in young and aged dwarfs showed a higher abundance of the complex than in their age-matched controls. These results, which are indicative of a decreased level of oxidative stress,

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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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