

BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY

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Chair's Message

Following the torrential rains of October, we seem to be drying out in time for the beginning of the November holiday, the family gathering time to give thanks (with some football thrown in.)

Yes, we are still in the throes of adapting to the newest PeopleSoft changes, this time in the area of salaries and grant reconciliation. But fear not, we are "staying the course" on this one, which means that our staff struggle to try to get it right using a system that has not precisely won our hearts and minds over the years.

Big changes, the first I can remember, in the submission dates for NIH grants. Please make sure to contact our staff or David Konkel if you think that your particular flavor of grant has NOT been affected. Chances are it has. It's bad enough that funding levels

are depressingly low. Do not miss the deadline.

On Wednesday, November 8th, we had a reception at the Faculty Club in Old Red for our three new Assistant Professors, (Drs. Marc Morais, Kay Choi, and Junji Iwahara) who visited here to see their labs, look for housing, etc. As an aside, do drop by and visit the 6th floor space that has been renovated. Our plan is to eventually redo all of the Basic Science Building to the same standard.

We now have a new Dean of the Medical School in place. To those who do not know Dr. Anderson personally and might wonder about his views on research, it is interesting to note that when he took over the department of ObGyn it ranked in the 60s nation wide in terms of research and this last year it ranked 4th nationally. I look forward to working with him on our future faculty recruitment efforts

and departmental plans for growth and stability.

Speaking of stability, our faculty salary compensation committee is making good progress. Also, this week a newly-appointed Space Committee will be charged with the task of developing a three-year plan. The challenges ahead spring from the expected increases in research within the same space, our need to renovate space (requiring "swing" space during renovations) and growth in the research programs of some of our faculty.

Don't overdo the turkey!

regino

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Special Items of Interest

- [New- Faculty Focus](#)
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Graduate Program News



The [Biological Chemistry Student Organization \(BCSO\)](#) is an active and growing student organization in the department of [Biochemistry & Molecular Biology](#). With the support of our graduate program, we organize events that enhance personal & professional development and activities that foster cohesiveness among our students, like the student-hosted Pioneering Biological Discovery seminar series, field trips to professional sport games and surrounding areas, the Christmas Toy Drive and other charity events, and social parties

Our students are actively involved in different committees within the BMB program and the Graduate School, and in other student organizations on campus. This year our BCSO officers are Andy Chen (Chair), Sergio Santa Maria (Vice Chair), Raghavendran Kulasegaran (Treasurer) and Julie Hou (Secretary). The BCSO has just elected a new faculty advisor, Dr. Stan Watowich. We would like to thank Dr. James Lee for being our faculty advisor from the beginning and helping to make the BCSO a well-organized and independent organization.

We have started accepting nominations for the Pioneering Biological Discovery seminar series. This is a great opportunity for us to invite a high-caliber scientist to meet with BMB students and faculty. If there is someone in your field that you would really like to have come speak, please do not hesitate to nominate him or her.

With generous support from many faculty members and alumni, we have recently established the BCSO student award. This unique and prestigious award honors a BMB student who has made significant contributions to the growth and advancement of our organization and our graduate department. The first ever BCSO student award was given to Rodrigo Maillard, student in Dr. James Lee's Laboratory. If you are interested in making a donation to help establish the BCSO endowment fund, please contact Ann Anderson at (409) 747-1233 or at ananders@utmb.edu.

If you have any suggestions for new activities or ideas for this upcoming year, do not hesitate to contact any of our officers or members. We will be glad to help.

Please visit our [website](#) for more information.

Awards and Announcements

Congratulations to the following 16th Annual Keck Center Research Conference poster award winner:

⇒ 2nd Place: **Jason Vertrees**, Graduate Student in the Lab of [Dr. Vincent J. Hilser](#)



Faculty Focus: Vicente A. Resto, M.D., Ph.D.

Dr. Resto's joint appointment as Assistant Professor in the Department of Otolaryngology and the Department of Biochemistry and Molecular Biology began in July 2006. He received both the MD and PhD in Human Genetics from The Johns Hopkins University. Dr. Resto came to UTMB after completing advanced clinical fellowship training in Head and Neck Oncology, Skull Base, and Microvascular Reconstructive Surgery at the Massachusetts Eye and Ear Infirmary in Boston.



What path has brought you to UTMB?

I went into the job market towards the end of my clinical fellowship year looking for a position as a clinician-scientist. Because I wanted to remain clinically active, I sought positions within clinical departments across the country. I was very specifically looking for an opportunity that would recognize and integrate my research as part of the package. This was more challenging than I initially thought, as most places want you to be very busy clinically and then "buy" your time back as grants get funded. It seemed to me this approach put my ability to do research at risk. Notwithstanding this, I was able to connect with several departments that had interest in developing their research portfolios, and thus were interested in my research. The Department of Otolaryngology at UTMB was one of them. In the end, it was UTMB that had the best job for me. Several places put together strong financial packages, but it was my exposure to Dr. Shawn Newlands and Dr. Regino Perez-Polo that convinced me they would provide the right environment within which to progress as a clinician scientist.

What is your current research and what are the research goals you are pursuing?

My research work focuses on the study of lymphatic metastasis in cancer. Specifically, I study the role adhesion molecules that are active under conditions of shear stress play in mediating interaction between cancer cells and lymph node constituent elements. These include lymph node constituent cells, such as lymphocytes, as well as lymph node extracellular elements, such as fibronectin, laminin, and collagen. I believe these molecules are important in mediating lodgement of tumor cells within the lymph node microenvironment, a process that is requisite to the formation of clinical lymphatic metastasis. Molecules important for these interactions are prime candidates for early diagnosis of the metastatic phenotype, a feature of tumors that strongly affects disease outcomes.

I also believe that tumor cell-lymph node interactions may be important for the establishment of tumor tolerance. There is strong evidence in support of the fact that our immune system is able to specifically see tumor antigens. Effector cells against said tumor antigens, however, are also known to be ineffective in killing tumor cells. Many approaches have been undertaken to try and activate this specific immune response. Some success has been documented in animal models, but by en large, all approaches have failed in humans. Given the role the lymph node plays as the switch of the immune system, it seems reasonable to think that tumor cells within this important location may interfere with appropriate antigen presentation and activation of effector cells. That is, tumor cells within the lymph node microenvironment may drive tolerance. With this thought in mind, the adhesion molecules that drive tumor cell lodgement within lymph nodes are also candidate molecules that may be important in driving the process of tumor tolerance. Time will tell whether this is a crazy idea or not.

How do your research and your clinical activities dovetail?

I consider them inseparable. Every hypothesis I construct is rooted in clinical experience and driven by clinical questions. More concretely, many of our experiments use tumor tissues as well as donated blood, thus keeping us close to "the patient" at all times. In the end, I hope to have the opportunity to bring back to the clinic something from the laboratory that furthers patient care.

[Dr. Resto's Department of Otolaryngology Webpage](#)

Spotlight: Transgenic Mouse Facility

Dr. Maki Wakamiya was recently appointed Director of the Transgenic Mouse Core Facility, succeeding Dr. Jeffrey Ceci. She had been Interim Director since March 2006. Dr. Wakamiya holds a joint appointment as Assistant Professor in the Department of Neurology and the Department of Biochemistry and Molecular Biology. For the Research Spotlight, Dr. Wakamiya has provided a description of the services offered by the Facility.

The mission of the Transgenic Mouse Core Facility is to facilitate the advancement of animal model studies at UTMB. Our primary functions are: 1) to generate transgenic and knockout mice that can serve as *in vivo* models for addressing a wide variety of biological questions, and 2) to preserve valuable mouse strains as safeguards against accidental loss due to natural disaster, human error, or infection.

The Transgenic Mouse Core Facility is supported by the [Sealy Center for Cancer Cell Biology](#), along with the Department of Neurology and the Department of Biochemistry and Molecular Biology, and is available for use by all UTMB scientists. The facility is located inside the Animal Resource Center within the Medical Research Building and is currently staffed by Research Associate San F. Yang and myself.

The major services offered in the past will be continued, including the generation of transgenic mice, identification of knockout embryonic stem cell lines, generation of knockout mice, cryopreservation of mouse embryos and sperm, recovery of cryopreserved mouse embryos and sperm, and rederivation of mouse stocks (<http://www.utmb.edu/scccb/mouse/services.htm>) We are currently implementing certain operational changes in pursuit of higher quality, better pricing, and greater flexibility in the services offered.

If you have decided to generate a mouse model, please take advantage of the facility. We can help you choose the best possible experimental approach, design your transgene/knockout construct and provide certain materials to make the construct. We are very happy to provide advice and technical assistance to any UTMB investigator on many aspects of animal research, and we can also help with grant proposal and animal protocol writing. Please call or send us an email for more information or to set up a consultation.

[Maki Wakamiya, PhD](#)

Director, Transgenic Mouse Core Facility

Sealy Center for Cancer Cell Biology

UTMB Comprehensive Cancer Center

409-772-2811



Administrator's Notes

This week, the Office of Sponsored Projects (OSP) announced the decision to postpone the implementation of InfoED, the program intended to be the UTMB "front-end" to the NIH system for electronic submission of grants. For the January (AIDS-related), February, and March deadlines for proposal submission, all proposal materials must be entered into "Grants.gov" using the NIH system, PureEdge. OSP will provide three single-session classes on features of "Grants.gov" and the use of PureEdge on Wednesday, November 29 (1:00 to 3:00), Monday, December 4 (9:00 to 11:00), and Thursday, January 4 (9:00 to 11:00.) All BMB support staff members who assist faculty with proposal preparation will attend one of the earlier OSP classes if they have not already received the training. We are fortunate to have several staff members who already have significant experience using PureEdge. We will ask these staff members to provide a "get acquainted" session with the system for any Department members who would like to get started looking at the system before the first OSP class. We also expect to take advantage of the experienced staff's expertise by asking them to function as "superusers" who can provide overall advice as well as problem-solving assistance when other users get stuck. The experienced users have related that learning PureEdge is not as daunting as first reported, and the system, while not necessarily user-friendly, is definitely manageable once certain "tricks" are noted. Moving to completely electronic proposal submission will be a challenge for us all, but sharing of knowledge and tactics can promote our collective success. Getting started on proposals as early as possible will also be important.

Marianne



New Employees

Yow-Jiun Jeng, Ph.D. - Sr. Res. Assoc. working with Cheryl Watson.

Shakuntala Kondraganti, Ph.D. - Postdoctoral Fellow working with Shakeel Ansari.

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

Publications & Grant Awards

Tao Geng, Patricia Seitz, Mary Thomas, Bo Xu, **Soman KV**, Alexander Kurosky, Bruce A. Luxon, and Kathryn A. Cunningham: *Use Of Surface Enhanced Laser Desorption/Ionization Time Of Flight Mass Spectrometry (SELDI-TOF-MS) To Study Protein Expression In A Rat Model Of Cocaine Withdrawal*, J. Neurosc. Meth., **2006**, 58:1-12.

Meltzer, RH., Thompson E., **Soman KV**, Song XZ, Wensel TG, Briggs JM, Pedersen, SE: *Electrostatic Steering at Acetylcholine Binding Sites*, Biophys. J., **2006**; 91:1302-1314.

Grants

Darrell Carney has been awarded a Pilot Project grant entitled "Reversing Endothelial Dysfunction" by the ICTR Novel Technology Core. The funding period is 10/01/2006 - 08/31/2007.

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.

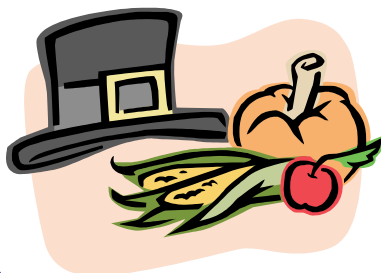
Faculty on the Road

Sankar Mitra was at the University of California, San Diego on October 19, 2006 to give a seminar entitled "Complex Repair Pathways for Oxidative Damage in Mammalian Genomes".



Kizhake Soman:

- ⇒ Participated in the Symposium "Advances in Proteomics and its Impact on Cancer Research" at M.D. Anderson Cancer Center, Houston on Sept. 19, 2006.
- ⇒ Participated and judged posters at the "2006 Keck Center Annual Research Conference", in Houston, Oct. 13, 2006.
- ⇒ Attended the "2006 Welch Conference on Chemical Research—Exploring the Complexity of Signaling Pathways" in Houston, Oct. 23-24, 2006.



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

Aldose Reductase Regulates Growth Factor-Induced Cyclooxygenase-2 Expression and Prostaglandin E₂ Production in Human Colon Cancer Cells

Ravinder Tammali¹, Kota V. Ramana¹, Sharad S. Singhal², Sanjay Awasthi² and Satish K. Srivastava¹

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Inhibition of prostaglandin E₂ (PGE₂) and cyclooxygenase (COX)-2 by nonsteroidal anti-inflammatory drugs reduces the progression of colon cancer. Inhibition of aldose reductase (AR; EC. 1.1.1.21.) by sorbinil or by antisense ablation prevented fibroblast growth factor-induced and platelet-derived growth factor-induced up-regulation of PGE₂ synthesis in human colon cancer cells, Caco-2. AR besides reducing aldo-sugars efficiently reduces toxic lipid aldehydes and their conjugates with glutathione. Inhibition of AR prevented growth factor-induced COX-2 activity, protein, and mRNA and significantly decreased activation of nuclear factor- κ B and protein kinase C (PKC) and phosphorylation of PKC- β 2 as well as progression of Caco-2 cell growth but had no effect on COX-1 activity. Cell cycle analysis suggests that inhibition of AR prevents growth factor-induced proliferation of Caco-2 cells at S phase. Treatment of Caco-2 cells with the most abundant and toxic lipid aldehyde 4-hydroxy-trans-2-nonenal (HNE) or its glutathione-conjugate [glutathionyl-HNE (GS-HNE)] or AR-catalyzed product of GS-HNE, glutathionyl-1,4-dihydroxynonane (GS-DHN), resulted in increased COX-2 expression and PGE₂ production. Inhibition of AR prevented HNE- or GS-HNE-induced but not GS-DHN-induced up-regulation of COX-2 and PGE₂. More importantly, *in vivo* studies showed that administration of AR-small interfering RNA (siRNA), but not control siRNA, to nude mice bearing SW480 human colon adenocarcinoma cells completely arrested tumor progression. Collectively, these observations suggest that AR is an obligatory mediator of growth factor-induced up-regulation of COX-2, PGE₂, and growth of Caco-2 cells, indicating that inhibition of AR may be a novel therapeutic approach in preventing the progression of colon cancer. (Cancer Res 2006; 66(19): 9705-13)

Aldose Reductase Mediates the Lipopolysaccharide-induced Release of Inflammatory Mediators in RAW264.7 Murine Macrophages*

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Abnormal production of inflammatory cytokines and chemokines is a key feature of bacterial endotoxin, lipopolysaccharide (LPS)-induced inflammation, and cytotoxicity; however, the mechanisms regulating production of inflammatory markers remain unclear. Herein, we show that inhibition of the aldehyde-metabolizing enzyme aldose reductase (AR; AKR1B3) modulates NF- κ B-dependent activation of inflammatory cytokines and chemokines in mouse serum, liver, heart, and spleen. Pharmacological inhibition or small interfering RNA ablation of AR prevented the biosynthesis of tumor necrosis factor- α , interleukin 1 β , interleukin-6, macrophage-chemoattractant protein-1, and cyclooxygenase-2 and prostaglandin E₂ in LPS-activated RAW264.7 murine macrophages. The AR inhibition or ablation significantly attenuated LPS-induced activation of protein kinase C (PKC) and phospholipase C (PLC), nuclear translocation of NF- κ B, and phosphorylation and proteolytic degradation of I κ B in macrophages. Furthermore, treatment of macrophages with 4-hydroxy-trans-2-nonenal (HNE), and cell-permeable esters of glutathionyl-4-hydroxynonanal (GS-HNE) and glutathionyl-1,4-dihydroxynonane (GS-DHN) activated NF- κ B and PLC/PKC. Pharmacological inhibition or antisense ablation of AR that catalyzes the reduction of GS-HNE to GS-DHN prevented PLC, PKC, IKK/ α β , and NF- κ B activation caused by HNE and GS-HNE, but not by GS-DHN, suggesting that reduced GS-lipid aldehydes catalyzed by AR propagate LPS-induced production of inflammatory markers. Collectively, these data provide evidence that inhibition of AR may be a significant therapeutic approach in preventing bacterial endotoxin-induced sepsis and tissue damage.

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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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