Upcoming Events

**August 8, 2007** Seminar – Dr. Fariba Behbod from Baylor College of Medicine Molecular & Cellular Biology Dept. will present “Role of Stem/Progenitor Cells in Malignant Progression of Human Breast Cancer Cells”

**August 20** Seminar – Dr. Christie Sayes from DuPont Haskell Laboratory for Health & Environmental Sciences will present “Responsible Nanotechnology: How Material Structure Dictates Toxicological Effects”

Gulf Coast Chapter Society of Toxicology Meeting (GCSOT), **October 18-19, 2007**, College Station, TX.

21st Lost Pines Conference on Cellular and Molecular Biology. **November 2-4, 2007**, Science Park campus, University of Texas M.D. Anderson Cancer Center, Smithville, TX

American College of Toxicology Annual Meeting, **November 11-14, 2007**, Westin Hotel, Charlotte, NC.

Group Spotlight

The Liver Toxicologic-Pathology Laboratory

From left to right: Dr. Shashi Ramaiah, Atrayee Banerjee, Mary Wallace, Nivedita Banerjee, Xin-Shen Wu and Jin-Hyung Lee. See page 2 for their research profile.

(Group Spotlight will be a new feature in the newsletter)
Research Spotlight

The research theme in Dr. Ramaiah’s laboratory is centered on “Liver Toxicologic Pathology”. The current research focus is on “Liver Inflammation”. The participation of Polymorphonuclear neutrophils (PMN) in the inflammatory response provides a first line of defense against invading organisms and liver toxic chemicals. However, inflammation has been called “double edged sword” as PMN can cause damage to surrounding tissues and a prolonged inflammatory response can contribute to a variety of pathological conditions. Inflammation is a complex reaction to injurious agents such as microbes and damaged, usually necrotic cells that consists of vascular responses, migration and activation of leukocytes and systemic reactions. The unique feature of the inflammatory process is the reaction of blood vessels leading to the accumulation of fluid and leukocytes in extravascular tissue.

The liver owing to its anatomic location and dual blood supply provides the first line of defense against microbes and toxins crossing the intestinal barrier. Although Kupffer cells (resident macrophages) are highly phagocytic and are able to remove microorganisms, they are also responsible for orchestrating an inflammatory response leading to effective recruitment of inflammatory cells (mostly neutrophils, monocytes, and T and B lymphocytes) to the liver. Inflammatory mediators such as tumor necrosis factor alpha, interleukins (IL-1, and IL-6), chemokines and reactive oxygen species (ROS) are considered to be major culprits for inflammatory cell recruitment into liver. These inflammatory mediators will prime and activate neutrophils in the hepatic microvasculature (sinusoids and postsinusoidal venules) leading to events in a sequential fashion culminating in hepatocyte death mostly by oncotic necrosis. Although these mechanisms have been well investigated in other neutrophil-mediated liver injury models such as with hepatic ischemia-reperfusion and obstructive cholestasis, the mechanisms behind inflammatory cell recruitment in alcoholic liver injury (ALI) during alcoholic steatohepatitis (ASH) and non alcoholic steatohepatitis (NASH) has not been thoroughly studied. Currently, the research in our laboratory is aimed at identifying precise mechanisms by which inflammatory cells infiltrate the liver during ASH and NASH which are important life-style related metabolic diseases involving the liver. This laboratory was the first to identify the relationship between matricellular protein Osteopontin (OPN) induction and hepatic neutrophil infiltration during ALI. Similar induction of OPN and its relevance in ALI has since been reported in human alcoholic hepatitis patients. Osteopontin, is a secreted phosphoprotein induced within hepatocytes, Kupffer cells and biliary epithelium. The role of OPN mediated regulation of neutrophil and lymphocyte integrins, mechanisms of hepatic OPN up-regulation and the role of ethanol metabolism on OPN induction are few of the ongoing projects in the laboratory.

Recent relevant publications:

Role of osteopontin (OPN)-mediated multi-integrin signaling in hepatic neutrophil infiltration. Alcohol (EtOH) ingestion results in elevated biliary epithelial cell (BEC) OPN expression which appear to have several effects. First, circulating OPN upregulates neutrophil β2 (Mac1) integrins resulting in higher neutrophil activation. Second, hepatic OPN upregulation results in elevated levels of neutrophil α9β1 (VLA9) and α4β1 (VLA4) integrins. In addition, thrombin mediated cleavage of OPN results in higher β1 integrin effects most likely mediated by SVVYGLR motif of OPN. RGD motif of OPN appear to have minimal effects on neutrophil migration. Finally, hepatic neutrophil infiltration results in increased hepatocyte damage.
Graduates
Kathy Vanderlaag (Safe lab) received her PhD in May and is now doing postdoctoral research for Schering-Plough in Palo Alto, CA.

Boyeon Lee (Dees lab) received her PhD in May and is seeking postdoctoral work in the area.

Xinsheng Gu (Tian lab) receives his PhD in August. He is joining the laboratory of Dr. Jose Manautou at the University of Connecticut, Storrs, CT for postdoctoral research.

Tanya Gustafson (Porter lab), our first DVM-PhD student, defended for her PhD and will now return to complete her final two years of vet school.

Fei Wu (Safe lab) recently defended for her PhD and is seeking postdoctoral work in the Boston, MA area.

Congratulations
Dr. Tim Phillips was honored at the Office of Technology Commercialization’s Patent and Innovation 2007 Awards Luncheon in February as one of five individuals whose research exemplifies the spirit of innovation of TAMUS.

At the 2007 CVM Graduate Student Association’s Research Symposium held April 23, 2007, Sabitha Papineni and Elizabeth Wellberg tied for 3rd place with their platform presentations, and Atrayee Banerjee and Sabitha Papineni placed 2nd and 3rd respectively in the poster competition.

Kathy Vanderlaag and Tanya Gustafson each received the George T. Edds Award for Excellence in Toxicology at the CVM Convocation, March 23, 2007.

New Arrivals
Dr. Jin-Hyung Lee, Post Doctoral Research Associate joined Dr. Ramaiah’s lab in June 2007. Jin-Hyung finished her PhD in Dr. Sydney Pestka’s lab (Rutger’s University) on a project to identify, clone and characterize human and yeast protein arginine methyltransferases.

Mary Wallace started student study work in Dr. Ramaiah’s laboratory since June 2007. She plans to enter the graduate program in Spring 2008.

Laura Quilivan is a research technician in Dr. Mirkes laboratory and will be involved in transgenic mice experiments.

Rui Xu is a doctoral student in Biochemistry & Biophysics who recently joined the Safe laboratory.

Claudia Cordero is a visiting student from Columbia who is conducting research on plant toxicants in the Safe laboratory.

New IFT Faculty Members
Clint Allred – Nutrition & Food Sciences
Michelle Pine – Veterinary Integrative Biosciences
Susanne Talcott – Vet. Physiology & Pharmacology
Alice Villalobos – Nutrition & Food Sciences

Travel
Brian Laffin and Dr. Weston Porter traveled to Whistler, British Columbia, from March 17-24, 2007 to attend the Structure-Based Drug Discovery Keystone Symposium. Brian presented “Singleminded-2 is a Transcriptional Barrier to EMT and Metastasis.”

Dr. Sudhakar Chintharlapalli, Sabitha Papineni, Dr. Sung-Dae Cho and Ping Lei (Safe Lab) attended the AACR annual meeting in Los Angeles, CA, April 13-18, 2007. Each presented an abstract at the meeting.

Fei Wu (Safe Lab) attended the Endocrine Society Annual Meeting in Toronto, Ontario from June 2-5, 2007. She presented “Hormone-Responsiveness of Transgenic Animlas Expressing a GC-Rich Promoter-Luciferase Construct.”

Atrayee Banerjee (Ramaiah Lab) attended the Annual Society of Toxicologic Pathology Meeting in Vancouver, Canada from June 17-22, 2006. She received a travel award from the society to attend.

Dr. Weston Porter, Dr. Rick Metz, Brian Laffin and Elizabeth Wellberg traveled to Newport, RI from June 10-15, 2007 to attend the Gordon Research Conference on Mammary Gland Biology. Dr. Porter presented “Transcriptional Regulation of Singleminded 2’s.” Dr. Metz presented “Role of Per 1 and Per 2 in Mouse Mammary Gland Development.” Brian presented “SIMZs is a Transcriptional Barrier to Invasion and EMT,” which won first prize. Elizabeth presented “The Role of Singleminded 2s in Mammary Gland Biology.”

Dr. Phil Mirkes, Donna Mirkes, Dr. Marianne Barrier and Hiromi Hosako attended the 47th Annual Teratology Society Meeting in Pittsburgh, PA from June 22-28, 2007. Dr. Barrier presented two abstracts, “A Genomic Approach to Hyperthermia-Induced Neural Tube Defects” and “MicroRNA Expression Changes in Response to Hyperthermia During Early Postimplantation Mouse Development.”

Dr. Weston Porter, Dr. Rick Metz, Brian Laffin and Elizabeth Wellberg attended the Mammary Gland Workshop at Baylor College of Medicine on July 20, 2007.
National Bioassay Network

Dr. K.C. Donnelly was recently funded by the NIEHS to coordinate the Development of a National Bioassay Network to Assess Ecological Toxicity of Environmental Mixtures. This project complements ongoing research within the TAMU Superfund Project which has been focused on development and application of bioassays for risk assessment of chemical mixtures. The mixtures will be obtained from extracts of various sediment samples from polluted environments. The unique nature of this project is its multidisciplinary approach which will use scientific expertise of scientists/institutions throughout the nation and they include the following.

1. Aquatic toxicity bioassays - Baylor University (Dr. Brooks)
2. Embryo development and enzyme activity - Duke University (Dr. DiGiullio)
3. P450 reporter gene assays - University of California - San Diego (Dr. Tukey)
4. Estrogen-responsive assays - Texas A&M University (Dr. Safe)
5. Cell culture studies - Michigan State University (Dr. Upham)
6. CALUX assay - University of California-Davis (Dr. Denison)
7. In situ biomonitoring - Texas A&M University (Dr. Donnelly)

Dr. Donnelly has developed a consortia of Superfund Center investigators and other colleagues to carry out these studies and this is an important example of inter-Center collaboration to address a complex environmental problem.

Save the Date

The Texas A&M University Superfund Project has organized and sponsored a series of international symposia entitled “Central and Eastern Europe Conference on Health and the Environment”. The first and second conferences were held in Prague (2004) and Bratislava (2006) and the third meeting is planned for the Fall, 2008, in Istanbul. The finalized details for this conference will be reported in the next Bulletin.
A group of faculty, staff and students traveled to Charlotte, NC for the 46th Society of Toxicology (SOT) Annual Meeting.

Dr. Stephen Safe was awarded the Distinguished Lifetime Achievement Award, the highest award given by the SOT, for his distinguished career and contributions to the field of toxicology including advances in understanding the molecular toxicology of the aryl hydrocarbon receptor, development of the toxic equivalency factor approach for human risk assessment, molecular endocrinology, and development of novel mechanism-based chemotherapeutic drugs.

Graduate student Atrayee Banerjee also received a high award, the Novartis Graduate Fellowship, which is awarded annually to only one student. Several graduate students received numerous travel awards from SOT, Gulf Coast Chapter-SOT, the Burdock Group, the CVM-Graduate Student Association and the IFT.

Other TAMU attendees included Kim Daniel, a member of the Committee on Diversity Initiatives that presents the Undergraduate Education Program annually for students in underrepresented ethnic groups and those from institutions with low amounts of research funding. Dr. Alice Villalobos and Atrayee Banerjee also assisted with this program.

Presenting abstracts at the meeting were:

- Dr. Evans Afriyie-Gyawu
- Gayathri Chadalapaka
- Navada Eagleton
- Natalie Johnson
- Rebecca Lingenfelter
- Dr. Michelle Pine
- Kerry Thuett
- Dr. Alice Villalobos
- Shu Zhang

**SOT 2007 Abstracts**


Role of Estradiol in Secreted Phosphoprotein 1 (Osteopontin) Induction in a Female Rat Model of Alcoholic Steatohepatitis. A. Banerjee, R. Rose and S.K. Ramaiah.

Inhibition of Bladder Cancer Cell Growth by Glycyrrhetinic Acid Derivatives. G. Chadalapaka, S. Chintharlapalli, S. Papineni, I. Jutooru and S. Safe.


Increased Susceptibility of Aging Kidney to Ischemic Injury: Role of Increased MMP Expression. A. Parrish.

The Type II Pyrethroid Pesticide Esfenvalerate Lowers Serum Estradiol and Delays Onset of Puberty. M Pine.


Regulation of Transcriptional Activity of Human Pregane X Receptor by Histone Methyltransferase Prmt1. Y. Xie, X. Gu, S. Ke, D. Liu, M. Bedford and Y. Tian.

IFT External Review and Retreat

An External Review Committee appointed by the Office of Graduate Studies conducted an intensive review of the IFT on May 6-9 and met extensively with Dr. Burghardt (IFT Chair), the Executive Committee, students, staff and University administrators. The Review Committee consisting of Drs. Patricia Hoyer (University of Arizona), Jack Hinson (University of Arkansas Medical Sciences) and Norb Kaminski (Michigan State University) made several helpful suggestions and comments and concluded the review with the following statement:

“Overall, the External Review Committee considers the IFT to be an outstanding program, which has a justly deserved reputation of excellence at the University, National and International levels.”

The leadership of Dr. Burghardt in the review process was invaluable, and with the assistance of Mrs. Kim Daniel and the Executive Committee, a comprehensive document was prepared for the review team. One of the highlights of the review was the annual IFT retreat organized by Dr. Weston Porter. The enthusiasm of the 60 attendees made a great impression on the External Review Committee. A summary of the program and presentations are given below. We wish to thank Dr. Larry Johnson and all the graduate student participants for their excellent presentations.

Platform Presentations

1 ROLE OF OSTEOPONTIN IN GENDER DIFFERENCE IN ALCOHOLIC STEATOHEPATITIS. Atrayee Banerjee and Shashi K Ramaiah.


3 ESTIMATION OF GENOTOXIC EXPOSURES IN CHILDREN WITH NEURAL TUBE DEFECTS IN SHANXI, CHINA. ZS Naufal, RH Finnell, GD Zhou, TJ McDonald, Z Li, ZW Li, LJ Pei, and KC Donnelly.

4 MECHANISMS OF SILENCING BREAST TUMOR SUPPRESSOR SINGLEMINDED-2 DURING CANCER PROGRESSION. Tanya Gustafson and Weston Porter.

5 BETULINIC ACID INHIBITS PROSTATE CANCER GROWTH THROUGH INHIBITION OF SPECIFICITY PROTEIN TRANSCRIPTION FACTORS. Sabitha Papineni, Sudhakar Chintharlapalli, and Stephen Safe.

Poster Presentations

1 INHIBITION OF BLADDER CANCER CELL GROWTH BY GLYCYRRETINIC ACID DERIVATIVES. Gayathri Chadalapaka, Sudhakar Chintharlapalli, Sabitha Papineni, Indira Jutooru, and Stephen Safe.


3 CROSS-TALK BETWEEN ARYL HYDROCARBON RECEPTOR AND PREGNANE X RECEPTOR PATHWAYS. Xinsheng Gu, Sui Ke, Tao Sheng, Duan Liu and Yanan Tian.

4 ARSENIC-INDUCED DISRUPTION OF MATERNAL BLOOD GLUCOSE AND BIRTH DEFECTS IN A MOUSE MODEL. Denise Hill, Bogdan Wlodarczyk, and Richard Finnell.

5 TERATOGEN-INDUCED ACTIVATION OF P53 IN EARLY POSTIMPLANTATION MOUSE EMBRYOS. Hiromi Hosako, Sally Little, Marianne Barrier, and Philip E. Mirkes.


7 IN SITU STUDIES OF SEDIMENT TOXICITY AT SUPERFUND SITES: USING BIOMARKERS OF EXPOSURE IN COHO SALMON TO EVALUATE COMPLEX MIXTURES OF PCBS AND PAHS. K.C. Donnelly, Bruce Duncan, Annika Gillespie, G.D. Zhou, Matt Kelley, and Thomas McDonald.

8 ENCAPSULATED ENZYME BIOSCAVENGERS
9 STRUCTURE-DEPENDENT INDUCTION OF ENDOPLASMIC RETICULUM STRESS AND APOPTOSIS IN COLON AND PANCREATIC CANCER CELLS BY 1,1-BIS(3'-INDOLYL)-1-(P-SUBSTITUTEDPHENYL) METHANES. Ping Lei, Sung Dae Cho, Shengxi Liu, Sudhakar Chintharlapalli and Stephen Safe.

10 PAH EXPOSURE AND BIOMARKERS IN HUMAN POPULATIONS. Rebecca Lingenfelter, Ziad Naufal, Leslie Cizmas, Christine Naspinski, Ling-Yu He, Guo-Dong Zhou, Thomas McDonald, Guy Denoux, Robin Autenrieth, Arif Mekhtiev, Arif Islamzadeh, and Kirby Donnelly.

11 SELECTIVE ARYL HYDROCARBON RECEPTOR MODULATORS (SAhRMs) DIRECTLY ACTIVATE ESTROGEN RECEPTOR IN MCF-7 BREAST CANCER CELLS. Shengxi Liu, Maen Abdelrahim, Shaheen Khan, Eric Ariazi, V. Craig Jordan and Stephen Safe.

12 1,1-BIS(3'-INDOLYL)-1-(P-SUBSTITUTEDPHENYL) METHANES INHIBIT GROWTH, INDUCE APOPTOSIS, AND DECREASE THE ANDROGEN RECEPTOR IN LNCAP PROSTATE CANCER CELLS THROUGH PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA-INDEPENDENT PATHWAYS. Sabitha Papineni, Sudhakar Chintharlapalli, and Stephen Safe.


15 IN UTERO EXPOSURE TO METHYLMERCURY CAUSES DELAYED CHANGE IN MITOCHONDRIAL MEMBRANE POTENTIAL OF EARLY POSTNATAL MOUSE CEREBELLAR GRANULE CELLS. Kerry A. Thuett, Devang Ghandi, Tania Kannadan, and Louise C. Abbott.

16 SINGLEMINDED-2S INHIBITS ADIPOKINES BUT MAINTAINS LIPOGENESIS IN 3T3-L1 ADIPOCYTES. Elizabeth Wellberg, Brian Laffin, and Weston Porter.

17 REGULATION OF TRANSCRIPTIONAL ACTIVITY OF HUMAN PREGNANE X RECEPTOR BY HISTONE METHYLTRANSFERASE PRMT1. Ying Xie, Xinshegu Gu, Sui Ke, Duan Liu, Mark Bedford, and Yanan Tian.

18 1,1-BIS(3-INDOLYL)-1-(P-SUBSTITUTEDPHENYL) METHANES INDUCE APOPTOSIS AND INHIBIT RENAL CELL CARCINOMA GROWTH. Melissa York, Maen Abdelrahim, Sudhakar Chintharlapalli, and Stephen Safe.

19 LIGAND-DEPENDENT INTERACTIONS OF THE AH RECEPTOR WITH COACTIVATORS IN A MAMMALIAN TWO-HYBRID ASSAY. Shu Zhang, Craig Rowlands, and Stephen Safe.

**Retreat Participants**

Dr. Patricia Hoyer
Dr. Jack Hinson
Dr. Norbert Kaminski
Dr. Louise Abbott
Dr. Clint Allred
Dr. Bob Burghardt
Dr. Evelyn Castiglioni
Dr. Robb Chapkin
Dr. K.C. Donnelly
Dr. Rick Finnell
Dr. Larry Johnson
Dr. Gladys Ko
Dr. Philip Mirkes
Dr. Tim Phillips
Dr. Suresh Pillai
Dr. Weston Porter

Dr. Shashi Ramaiah
Dr. Steve Safe
Dr. Yanan Tian
Dr. Nancy Turner
Dr. Alice Villalobos
Dr. Emily Wilson
Dr. Evans Afriyie-Gyawu
Dr. Marianne Barrier
Dr. Jeffrey Catania
Dr. Sudhakar Chintharlapalli
Dr. Seung Dae Cho
Dr. Marianne Barrier
Dr. Rick Metz
Kim Daniel
Atrayee Banerjee
Gayathri Chadalapaka

Xinshegu Gu
Tanya Gustafson
Denise Hill
Hiromi Hosako
Natalie Johnson
Indira Jutooru
Matt Kelley
Rory Kern
Brian Laffin
BoYeon Lee
Ping Lei
Rebecca Lingerfelter
Lucy Liu
Shengxi Liu
Alicia Marroquin
Travis Mays

Ziad Naufal
Kristin Newman
Sabitha Papineni
Abraham Robinson
Rohit Senghal
Kyle Spencer
John Taylor
Kerry Thuett
Liz Wellberg
Fei Wu
Ying Xie
Melissa York
Shu Zhang
Grants

Dr. Shashi Ramaiah was recently funded by the NIH (National Institute of Alcohol Abuse on Alcoholism) on “Alcoholic hepatitis: Molecular Mechanisms.”

Atrayee Banerjee, Graduate student in Dr. Shashi Ramaiah’s lab was awarded the “Novartis Corporation Graduate Fellowship” grant for 2007-2008 to investigate the “Role of Osteopontin in the higher female susceptibility to alcoholic liver disease.”

Dr. Gladys Ko was recently awarded an NIH Grant on “Circadian Rhythm in Cone Photoreceptors: Cellular Mechanisms.”

Dr. Robert Chapkin received an NIH grant on “n-3 fatty acids alter T-cell activation and signaling.”

Dr. Thomas Spencer received two NIH grants on “Endogenous Retroviruses and Placental Morphogenesis” and “Genetic Regulation of Postnatal Uterine Morphogenesis and Function.”

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