



NUCLEUS

The newsletter of the School of Pharmacy's Office of Research

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Another Success Story



Dr. Majid Moridani recently received an NIH R15 for his project "A tyrosinase-targeted design for the treatment of melanoma drug." Malignant melanoma is one of the lethal cancers

known to man. Every year approximately 60,000 new melanoma patients are diagnosed in the USA of which ~8,000 die from this disease. Systemic chemotherapy is an important and essential modality for

treatment of advanced melanoma. However, intolerable hepatotoxicity is a major drawback for successful chemotherapy of melanoma. Therefore, a clear need exists for developing novel and improved chemotherapeutics for melanoma.

Generally, drug development has high rate of failure and it is very costly. The current strategy is to identify problems at an earlier stage in drug development rather than at clinical trials where the costs of drug testing [continues on page3]

SOP Pharmaceutical Sciences Welcomes Two New Faculty to Amarillo

The School of Pharmacy is honored to welcome two new faculty members to the Department of Pharmaceutical Sciences.

Dr. Thiruma (Garrie) Arumugam received his Bachelor's of Medical Science (Hons) from the University of Sydney, Australia, and his Ph.D. in Pharmacology from the University of Queensland, Australia. In 2003, Dr. Arumugam was offered a Post Doctoral fellowship at the Louisiana State University Health Sciences Center in Shreveport. He studied the role of the T cells in stroke under Professor Neil Granger. He then moved to the National Institute on Aging, NIH, where he studied novel mechanism of ischemic stroke injury under Dr. Mark P Mattson. Dr. Arumugam's research interest include



revealing the molecular mechanisms responsible for neuronal death after a stroke

and developing novel therapeutic strategies for improving outcome in stroke patients. His recent finding showed that cleavage of the presenilin substrate Notch after ischemic brain injury contributes to neuron death. His future research interests include how Notch-1 activation following ischemic condition influences and NFkappaB activity that may affect neuronal vulnerability and influences glial inflammatory response.

[continues on page 4]

NAMES IN THE NEWS



Dr. Kalkunte Srivenugopal, Associate Professor, was invited to speak at the 2nd International Conference on MGMT and Alkylating Drug Resistance June 13-16th, 2007. He presented his lecture entitled "Antioxidant Upregulation and Unexpected Roles for MGMT in DNA Replication." The conference was held in Mainz, Germany.

ABRI Program 2007

Blake Higley:

Dr. US Rao's lab is currently studying the rnf2 protein. Blake's project will include extracting this protein from insect and mammal cells. He will then run 2D electrofloryses and western blots on the samples in hopes of finding cites that are phosphorlated and how they relate to drug resistance in Breast Cancer. Blake will be returning to the University of Oklahoma as a senior this fall.



Siva Koganti:

Dr. Thomas Thekumkara's lab has shown that high levels of glucose induces cellular depth in human proximal tubal cells. Siva's study

will focus on identifying these factors and determining their effects in kidney cells. The goal of this study is to determine the

expression of these factors and their effects respectively which could help lead the lab to understand the renal damages associated with diabetes and allow them to propose a way to prevent diabetic complications. Siva received his Masters in Sciences from Bangalore University, India and will be joining the TTUHSC SOP Graduated School of Biomedical Sciences this fall.

Jennifer Markley:

Jennifer is working in **Dr. Margaret Weis's** lab. She is studying Human endothelial long chain fatty acyl Co-A synthesase in an effort to find the expression patterns of the different isofoms of eLCFACoAS in the human cardiovascular system. Her method will include Northern Blot analysis. These finding could specify a gene which is responsible for eNOS regulation. Jennifer will be returning to UT at Austin as a senior this fall.



[continues on page 3]

Dr. Weidanz



Jon Weidanz, Ph.D. participated in the international meeting of the Biotechnology Industrial Organization: Bench to Products Meeting. The meeting took place in Boston on May 6-9, 2007. The objectives

included bringing light to the possible reasons that most vaccines fail, to discuss the scientific tools needed to further study

mechanisms of vaccine failure and to offer alternative approaches to vaccine design to improve success rates. Dr. Weidanz presented "Vaccine Development: What we Don't Know."

He also attended the Federation of Clinical Immunology Societies meeting. The meeting took place in San Diego, CA on June 7-11, 2007. He presented "Improving Targeted Immunotherapy Through Direct Validation of Peptide-MHC Epitopes Using TCRm Antibodies."

Dr. Holly Hoffman-Roberts Joins Pharmacy Practice



The Department of Pharmacy Practice welcomes Holly Hoffman-Roberts, an Assistant Professor in the Clinical Research and Sciences Division in Dallas. Dr.

Hoffman-Roberts received her Doctor of Pharmacy from the University of Illinois at Chicago. Afterwards, she became a Pharmacy Practice Resident at the University of Nebraska Medical Center/Nebraska Health System in Omaha. Before joining the Texas Tech

School of Pharmacy, she studied at the University of Iowa in an Infectious Diseases Pharmacotherapy Research Fellowship. Dr. Hoffman-Roberts research is focused on infectious diseases: more specifically centers on Gram-positive pathogens. Her previous work has focused on microbial genetic and antibiotic resistant *Streptococcus pneumoniae*. Her research objects are to apply the results of these previous studies and identify specific human genetic factors for colonization of this pathogen. She is also involved in a study evaluating the epidemiology of community associated methicillin-resistant *Staphylococcus aureus*.

Dr. Moridani [continued from page 1]

are extremely high. The major causes of drug development failure include; 1) drug metabolism, 2) pharmacokinetics, 3) toxicity, 4) clinical efficacy, and then 5) financial and marketing strategies. In our research group, we are using drug metabolism, pharmacokinetic and toxicological approach for lead optimization of a group of novel phenolic agents with anti-melanoma effect in order to tackle the first three causes of drug development failure in our anti-melanoma discovery program. We use tyrosinase, an enzyme found abundantly in melanoma, as a molecular target to activate phenolic agent to a cytotoxic agent that can selectively kill the melanoma cells without harming other cells such as hepatocytes. These phenolic agents are prodrugs that are targeted to tyrosinase by which is activated selectively to anti-cancer agent but not by P450 enzymes that

are found in liver. Therefore, the degree of liver toxicity is expected to be minimal. This strategy leads to a selective and significant intracellular GSH depletion in melanoma cancer cells, which makes the cancer cells weak and leaky, therefore, making it easier for immune system to wipe them out. We use a rationale drug design approach to design and synthesize novel phenolic agents and test them for their mechanism of toxicity in melanoma cell lines and in rat liver hepatocytes, for in vitro metabolism, in vivo toxicity in mice, and in vivo efficacy studies in animal models of mouse skin and metastasis melanoma tumor. A secondary goal of the project is to find ways to predict drug toxicity based on a number of metabolic assays that are used in this study and the drug chemical structures. Such tools are extremely valuable in drug discovery and development projects.

RESEARCH DAYS

The Sixth Annual Research Days is just around the corner. The event will be held in the Amarillo, School of Pharmacy on August 2nd and 3rd. If you are planning to attend and have not yet sent your **RSVP** to the Office of Research, please do so. For those who plan to attend here are some deadlines that should be kept in mind: Posters are due **Wednesday July 18th**. Abstracts are due to the Office of Research Friday, **July 13th**.

Seed Grants Applications

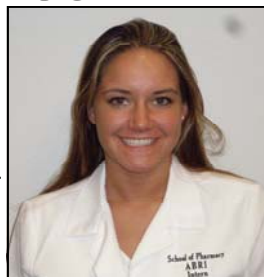
The Office of Research is accepting Seed Grant Application through July 20, 2007. The mission of the Seed Grants Program is to provide a modest level of "seed" funding for faculty to initiate research programs and obtain preliminary data. Faculty will gain experience in grant writing, project design, and project execution. Applications can be found on the Office of Research web page.

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Pablo Rodriguez:
Dr. Jon Weidanz has assigned Pablo a project that focuses on concentrating and purifying antibodies from the supernatant: more specifically for NY-

ESO-1 (a marker found on human tumor cells). These characterization may lead to their use as diagnostic or therapeutic agents. Pablo will be entering his junior year at UT Austin this fall.



Mandy Whiteside:
Mandy is working with **Dr. Majid Moridani** on a project where she will administer controlled benzyl alcohol series of drugs to cultured melanoma cells.

She will then administer Caffeic Acid Phenol Ester (CAPE) and run MTT assay for each to see how well they killed the melanoma cells. Mandy recently graduated from West Texas A&M with a DBL BS in Biology/Biochemistry

SOP Pharm Sci Welcomes Two New Faculty [continued from 1]



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Dr. Sanjay Srivastava joined Texas Tech in June as an Associate Professor in Cancer Biology for the Department of Pharmaceutical Science.

He received his Bachelors of Sciences in Physics, Chemistry & Math and a Masters of Science in Biochemistry from Lucknow University, India. His Ph.D. is in Biochemistry and Toxicology from Industrial Toxicology Research Center, Lucknow and Kanpur University, Kanpur, India. In 1997, he joined the Mercy Cancer Institute in Pittsburg where he served as a Research Scientist. In 2000,

he became an Assistant Professor for the Department of Pharmacology at the University of Pittsburg School of Medicine. Dr. Srivastava was also a full member of the University of Pittsburg Cancer Institute. He is currently a member of the American Association of Cancer Research and Society of Toxicology. His research interest include molecular mechanisms of dietary chemopreventive agents, such as isothiocyanates, organosulfur compounds, capsaicin and curcumin against pancreatic, ovarian and prostate cancer. Environmental carcinogen-induced cell signaling pathways, DNA-adduct formation and chemical carcinogenesis.

Graduating Students



Chaitanya Chimalakonda defended his dissertation “Plasma and liver disposition of a dextran prodrug of the antiviral drug lamivudine in rats” On May 21, 2007. Chaitanya studied under Dr. Mehvar and has co-authored several scientific papers. Chaitanya received his Masters from the TTUHSC School of Biomedical Sciences, and will be joining the Ph.D. program in the Pharmacology Department at the University

of Arkansas this fall.



Jennifer Paulson defended her dissertation “Nicotine’s effects on brain edema and ion movement during stroke” on June 21, 2007. Jennifer worked in Dr. Abruscato’s. She will be returning to the TTUHSC Pharm.D. program this fall. When finished, she will graduate with a Pharm.D./Ph.D.

Seminars and Invited Talks

Sharanya Vemula. “Metabolic adaptation of brain endothelial cells subjected to mild to severe conditions of stroke.” Graduate Seminar. SOP room 107, April 2, 2007.

Fancy Thomas. “Anticancer drug delivery to the brain.” Graduate Seminar. SOP room 107, April 2, 2007.

Ridhi Parasrampur. “Hepatobiliary disposition of Rhodamine 123 in isolated perfused rat liver model.” Graduate Seminar. SOP room 107, April 9, 2007.

Rachita Sumbria. “Effect of Bilobalide on Ischemia Induced Release of Amino Acids.” Graduate Seminar. SOP room 107, April 9, 2007.

Kaci Bohn. “Microvascular Density in a Metastatic Model.” Graduate Seminar. SOP room 107, April 23, 2007.

Venkateswaran Chithambaram Pillai. “Endothelial long chain fatty acyl CoA synthase inhibitors as antihypertensive agents.” Graduate Seminar. SOP room 107, April 23, 2007.

Sunny Guin. “Designing a RON specific mAb Zt/cl-Doxorubicin Immunoliposome for colon cancer therapy.” Graduate Seminar. SOP room 107, April 30, 2007.

Ramakrishna Samala. “Effect of Ketogenic Diet on Brain Extracellular Fluid Composition.” Graduate Seminar. SOP room 107, May 7, 2007.

Kunal Taskar. “Studies in Support of Metastatic Breast Cancer Brain-Tumor Model.” Graduate Seminar. SOP room 107, May 7, 2007.

US Rao, Ph.D. “On the development of P-glycoprotein-mediated multidrug resistance in breast cancer.” Graduate Seminar. SOP room 107, May 14, 2007.

Chaitanya Chimalakonda. “Plasma and liver disposition of a dextran prodrug of the antiviral drug lamivudine in rats.” Graduate Seminar. SOP room 107, May 21, 2007.

Arun Satelli. “Toward elucidating the role of Galectin-1 in Cancer.” Graduate Seminar. SOP room 107, May 21, 2007.

SOP Consultation in Dallas

The School of Pharmacy Pharmaceutical Sciences and Pharmacy Practice Departments are having a consultation in Dallas on July 31st. Dr. Ken Miller, Senior Vice President of the AACP, Dr. Robert Blouin, Dean of University of North Carolina and Dr. Barry Carter, Professor of Pharmacy and Family Medicine at the University of Iowa. The goal is to obtain information to better our School of Pharmacy and to define the future institutional relationship between UT Southwestern and TTUHSC.

Publications

- Gaasch JA, Geldenhuys WJ, **Lockman PR**, Allen DD, Van der Schyf CJ. Voltage-gated Calcium Channels Provide an Alternate Route for Iron Uptake in Neuronal Cell Cultures. *Neurochem Res.* 2007 Apr 3.
- Mehvar R**, Elliott K, Parasrampur R, Eradiri O. Stereospecific high-performance liquid chromatographic analysis of tramadol and its O-demethylated (M1) and N,O-demethylated (M5) metabolites in human plasma. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2007 Jun 1;852(1-2):152-
- Velu CS, Niture SK, Doneanu CE, Pattabiraman N, **Srivenugopal KS**. Human p53 Is Inhibited by Glutathionylation of Cysteines Present in the Proximal DNA-Binding Domain during Oxidative Stress(.). *Biochemistry.* 2007 Jun 8.
- Chiriva-Internati M, Grizzi F, **Weidanz JA**, Ferrari R, Yuefei Y, Velez B, Shearer MH, Lowe DB, Frezza EE, Cobos E, Kast WM, Kennedy RC. A NOD/SCID tumor model for human ovarian cancer that allows tracking of tumor progression through the biomarker Sp17. *J Immunol Methods.* 2007 Apr 10;321(1-2):86-93.
- Bond CA, Raehl CL**. Clinical pharmacy services, pharmacy staffing, and hospital mortality rates. *Pharmacotherapy.* 2007 Apr;27(4):481-93.
- Patry RA**, Eiland LS. Addressing the shortage of pharmacy faculty and clinicians: the impact of demographic changes. *Am J Health Syst Pharm.* 2007 Apr 1;64(7):773-5.
- Hedges SJ, Dehoney SB, Hooper JS, Amanzadeh J, **Busti AJ**. Authors' response to "Tranexamic acid and uremic bleeding: evidence-based treatment recommendations" *Nat Clin Pract Nephrol.* 2007 Jun;3(6):E3.

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