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Mission of the Office of Research

The Mission of the Office of the Associate Dean for Research is to promote and facilitate both clinical and basic science research for the faculty of the School of Pharmacy (SOP) in conjunction with the School of Medicine, School of Nursing, School of Allied Health, and other health professionals through all phases of research design, procurement of funding, managing the research process, and dissemination of results to the professional community. The Office of the Associate Dean for Research in the SOP (Amarillo campus) is available to all faculty on all campuses. The purpose of this office is to act as a resource for the granting process, facilitate research, and administer internal research programs.

Srivastava Receives R01 Grant

Sanjay Srivastava, PhD (Associate Professor, Pharmaceutical Sciences) was awarded a NIH R01 grant in June for his project titled "Chemoprevention of Pancreatic Cancer by Capsaicin." Dr. Srivastava joined the TTUHSC SOP in 2007 as a NIH funded investigator. He came to Amarillo from the University of Pittsburgh School of Medicine where he was a full member of the Pittsburgh Cancer Institute. His current work with capsaicin shows to be extremely promising.

Pancreatic cancer remains the fourth leading cause of cancer-related death in the United States with a median survival of less than 6 months following diagnosis. It is one of the most aggressive human malignancies with extremely poor prognosis, thus offering an experimental and clinical challenge. Rationale for a detailed pre-clinical evaluation of capsaicin for its efficacy against pancreatic cancer stems from (i) our solid preliminary data from in vitro and xenograft studies and (ii) the previously published reports of selective apoptosis induction and JNK activation by capsaicin (a compound found in chili peppers) in human cancer cells driven by ras-transformation, a frequent initiating lesion in pancreatic tumorigenesis. Dr. Srivastava's lab showed that human pancreatic cancer cell lines AsPC-1 and BxPC -3 are highly sensitive to growth inhibition by capsaicin. Interestingly, the viability of acinar cells derived from normal human pancreas or immortalized normal human pancreatic ductal epithelial (HPDE-6) cells were minimally affected by capsaicin even at concentrations that were highly cytotoxic to pancreatic cancer cells. These results are particularly encouraging because selective killing of cancer cells is a desirable characteristic of a potential cancer preventive or therapeutic agent. Their results also showed that growth inhibitory effect of capsaicin is associated with the (i) elevated levels of intracellular reactive oxygen species (ROS), (ii) increased expression of bax, (iii) leading to mitochondrial depolarization, release of cytochrome c and AIF, down regulation of survivin, and activation of caspase-3 cascade that eventually induces apoptosis in both AsPC-1 and BxPC-3 cells but not in acinar cells. In

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2009 ABRI Program

The summer has come and gone, and with it, the Amarillo Biomedical Research Internship. This year, our program hosted six interns. During the 10 week program, students were able to work closely with their mentors to develop a project that would allow them to become more knowledgeable of laboratory research. This year's interns included:

Joe Bufford: Joe is studying Food Sciences at Texas Tech University in Lubbock. This fall he will begin his Junior year. *Dr. James Stoll* mentored him on his project "Effects of an Anaplerotic Diet on Epileptic Mice."

Brandon Cooper: Brandon will begin is Sophomore year at Southwestern University this fall where he is majoring in Biology. While here, Brandon was mentored by *Dr. Sanjay Srivastava* on his project "Embelin Induces Apoptosis in Pancreatic Cancer Cells by inhibiting ERK Cell Survival Pathways

Mark Dubina: Mark will begin his Sophomore year at West Texas A&M University this fall. He is currently studying Biology and has voiced interest in dentistry. *Dr. Karen Mark* mentored him on his project titled "Inflammatory Effect of Liver Fibrosis on Lipocalin-2 and Interleukin-10."

Gregory Mitchon: Greg is currently a Pharmacy Student with TTUHSC SOP. He is to begin his P3 year this month. Greg has been working with *Dr. Reza Mehvar* this summer on his project titled "Development of an *ex Vivo* Model to Study Local Immunosuppression in the Liver Following Systemic Administration of Macromolecular Prodrugs of Methylprednisolone to rats."

Back Row (left to right): Greg Mitchon, Mark Dubina, Brandon Cooper. Second Row (left to right): Nick Muro, Joe Bufford. Front: Asha Rao

Nick Muro: Nick is also a Pharmacy Student here at the TTTUHSC SOP and is about to begin his P3 year. Nick was mentored by *Dr. Majid Moridani* on his project titled "*In Vitro* Evaluation of Tannic Acid as an Antimelanogenic Agent."

Asha Rao: Asha will begin her Sophomore year at the University of Texas at Austin this fall where she is studying Biochemistry. During her internship, she was mentored by *Dr. Quentin Smith* on her project titled "Cytotoxicity and Cell Uptake of Doxorubicin."

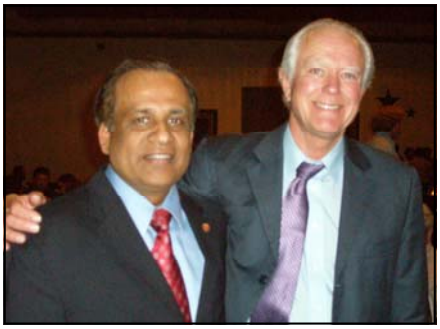
The internships ended July 31st with a symposium for the ABRI interns; students were able to present posters to faculty, family, and lab personnel from the School of Pharmacy and School of Medicine. The Office of Research would like to thank all those that helped make this program such a success this year. ♦

CAB Bond Scholarship Fund

On June 8th, the TTUHSC School of Pharmacy lost one of its beloved faculty members, CAB Bond, PharmD, of the Pharmacy Practice Department. In his memory, the CAB Bond Scholarship fund has been established. Once the funds have reached $10,000, an endowed account will be created. The Office of Research donated all proceeds from the Research Day's vendor show to this scholarship. If you would like to donate, contact Linda Goldstein in School of Pharmacy Student Services. ♦

2009 Marsh Lectureship

The SOP welcomed Fulton Crews, Ph.D. as the 2009 Wendy & Stanley Marsh 3 Endowed Lecturer in Pharmacology & Neurochemistry of Substance Abuse/Addiction. Dr. Crews is Professor of Pharmacology & Psychiatry and Director of the Skipper Bowles Center for Alcohol Studies at the University of North Carolina. He gave 2 lectures during his stay in Amarillo; Tuesday, June 16th he presented "The Neurobiology of Alcohol: Good, Bad, and Ugly" and Wednesday, June 17th "Mechanisms of Brain Degeneration and Regeneration in Alcohol Dependence and Recovery" for the School of Medicine Medical Grand Round. Dr. Crews also had the chance to meet with several of the Medical Residents and SOP faculty and students during Research Days events. The Office of Research would like to thank Dr. Crews for his time and efforts as well as Mr. & Mrs. Stanley Marsh 3 for their continued support of this program. ♦



Gunaje Receives NIH Funding

Jayarama Bunaje, PhD (Associate Professor, Pharmaceutical Sciences) was recently awarded a NIH R03 grant for his project titled "p53 Acetylation as a Mechanism in Chemoprevention by Aspirin." A vast amount of epidemiological, preclinical and clinical studies have revealed aspirin as a promising chemopreventive agent, particularly in epithelial carcinogenesis. Despite the wide attention inhibition of cyclooxygenases has received, it is clear that aspirin elicits a myriad of molecular effects that counteract the carcinogenic episodes. In preliminary studies, Dr. Gunaje has obtained the first and strong evidence for a dose- and time-dependent acetylation of p53 tumor suppressor protein by aspirin in human breast cancer cells, several cancer cells belonging to different tumor types and also in normal liver cells. In these cells, aspirin induced the levels of p53 target genes namely $p21^{CIP1}$, a protein involved in cell cycle arrest, and Bax, a proapoptotic protein; however, p21 induction was transient (1-12h); whereas, induction of Bax was sustained (24 h). Interestingly, in DNA damaged cells (induced by camptothecin), aspirin treatment (24 h) inhibited the p21 induction, while the Bax induction was unaffected. Built on these findings, the central hypothesis of this RO3 pilot project is that aspirin-induced muti-site acetylation of p53 alters its transcription factor function by shifting the gene expression spectrum from those that elicit cell cycle arrest / prosurvival properties to those that promote and drive cell death. The studies proposed in this application will determine the mechanisms by which aspirin regulates apoptosis in DNA damaged cells via inhibition of p21. In addition to camptothecin, all studies will be extended to include doxorubicin and cisplatin, to determine if aspirin also modulates p21 / Bax expression by these DNA damaging drugs. These studies will provide a novel mechanism by which aspirin may exert anticancer effects in DNA damaged cells via acetylation of p53, induction of Bax and inhibition of p21. ♦

Names in the News

Graduate Student, Arun Satelli of Dr. US Rao's lab, was recently awarded two scholarships. He received a $1,000 Dean's Recognition Award; also, Arun was given a GSBS Travel Scholarship for $525. The GSBS Award was used for him to attend the April 18-22 American Association of Cancer Research Meeting in Denver, CO. ♦

Eighth Annual Research Days

The School of Pharmacy and Office of Research were proud to host the Eighth Annual Research Days event which took place June 16-17. This year's event was packed full of research from both Pharmaceutical Sciences and Pharmacy Practice faculty, students, residents, and post docs. The event was kicked off with a welcome by Dean Nelson and Dr. Thekkumkara, followed by podium presentations. This year, the Research Advisory Committee decided to give the Graduate Students and Residents the opportunity to showcase their current research projects. Five Graduate Students and five

Residents presented 30 minute presentation which were judged by audience members. Katie Hazelwood, Snehal Padhye, Lauren Snodgrass, Russell Snyder and Monique Lopes-Serro were the first days podium presentations. Afterward, attendees enjoyed this year's Vendor Show; vendors such as Fisher Scientific, BioTek, Eppendorf, etc had the newest laboratory equipment for attendees to see. The SOP 2nd floor was full of attendees both presenting and viewing posters. The first day of activities ended with a lovely dinner at the Ambassador Hotel where attendees relaxed and mingled with colleagues and friends.

On the second day, podium presentations from Vinay Rudraraju, Katura Thomas, Zhuzhu Li, Alison O'Brien, and Qi Ma were given. Afterwards, the final group of poster presentations were given and, the closing ceremonies commenced. Dean Nelson recognized Drs. Bickel, Lyte, Mehvar, Smith, Srivastava, Thekkumkara, and Wang with the Citation Laureate Award. These faculty members have received over a 1,000 citations on previous research. Dr. Thekkumkara then announced the first, second, and third

place winners for the Pharmacy Practice and the Pharmaceutical Sciences podium presentations. Pharmacy Practice: *First – Alison O'Brien: Second – Monique Lopes-Serrao: Third – Katura Thomas*. Pharmaceutical Sciences: *First – Vinay Rudraraju: Second – Snehal Padhye: Third – Russell Snyder*. The Pharmacy Practice Resident Program awarded the top three poster presentations: *First – Young Ran Lee: Second – Lauren Snodgrass: Third – Katie Hazelwood*. The GSBS

presented travel awards to the two highest scoring posters: *Venki Chithambarampilai and Hussaini Syed Sha Qhattal*.

With the conclusion of the awards ceremony, the 2009 Research Days ended. The Office of Research would like to thank everyone who helped make this year's event such a success. We also invite any comments or suggestions to help us improve this event for next year. ♦

Restructuring of the Sciences Department

The Board of Regents has approved two new Science Departments at the School of Pharmacy: the Department of Biomedical Sciences and the Department of Pharmaceutical Sciences. In the past, Pharmaceutical Sciences has greatly contributed to the growth of biomedical research. With the development of the two departments, the Office of Research hopes that they will continue their collaborative and successful tradition. We wish both departments great success. ♦

(Continued from pg 1)
addition, they found that capsaicin significantly reduces glutathione and thioredoxin levels and activates JNK in pancreatic cancer cells, reflecting the potent alterations in intracellular redox triggered by the chili pepper compound. Furthermore, they found that orally feeding capsaicin significantly retarded the growth of AsPC-1 pancreatic tumor xenograft in nude mice with no discernible toxicity. Tumors obtained from capsaicin treated mice exhibited increased Bax expression, cytoplasmic cytochrome c, cleavage of caspase-3, reduced mitototic activity and increased apoptosis. Dr. Srivastava's results also showed that capsaicin enhances the growth suppressive effects of gemcitabine in pancreatic cancer cells. *Building on this promising data, we hypothesize that capsaicin can effectively retard pancreatic carcinogenesis, and also exert potent anticancer effects against this tumor type, through a differential induction and modulation of oxidative stress leading to JNK activation and mitochondrial death pathway of apoptosis.* To test this hypothesis his lab will: (1) Elucidate the mechanisms by which capsaicin triggers oxidative stress in pancreatic cancer cells, (2) Investigate the activation of mitogen- and stress-regulated signal transduction pathways in response to the oxidative imbalance induced by capsaicin, (3) Determine the effect of capsaicin on the activation of mitochondrial death pathway, and (4) Investigate the preventive and therapeutic effect of capsaicin in athymic nude mice and $Kras^{G12D}$ transgenic mice models of pancreatic intraepithelial neoplasia (PanINs) respectively and its bioavailability and pharmacokinetics. Successful completion of this project will support the development and clinical application of capsaicin for the chemoprevention of pancreatic cancer. ♦

Dr. Moridani Appointed as Consultant

Dr. Majid Moridani (Assistant Professor, Department of Pharmaceutical Sciences) has been given a 4 year appointment as a consultant for the Clinical Chemistry & Clinical Toxicology Devices Panel. This panel reviews and evaluates data concerning the safety and effectiveness of marketed and investigational *in vitro* devices for use in clinical laboratory medicine. This includes clinical toxicology, clinical chemistry, endocrinology and oncology. The panel makes recommendations to the Commissioner of the FDA-USA according to the devices performance. Dr. Moridani will also provide serves for the Medical Devices Advisory Committee and Center for Devices & Radiological Health.

Dr. Moridani has also been presenting at several meetings. He presented both "The application of pharmacogenetics in personalized treatment" and "Vitamin B12 deficiency and its laboratory investigation" at the American

Association for Clinical Chemistry (AACC) in Chicago, IL. Also, he presented "Office Applications of Clinical Chemistry" for the TTUHSC SOM summer OB/Gyn Grand Rounds. ♦

Dr. Hall Finishes Master's Program

Ronald Hall II, Pharm.D. (Assistant Professor of Pharmacy Practice), graduated in June from the NIH Clinical Scholars program at UT Southwestern Medical Center. The three year program is structured to help develop successful independent clinical researchers. Students work in both laboratory and clinical settings. Dr. Hall's project was titled "Effect of body mass index on the pharmacokinetic variability of antifungals and antimycobacterials" and was submitted as part of the Clinical and Translational Sciences pilot award program at the UT Southwestern Medical Center. With the completion of this program, Dr. Hall has received a Master's of Science in Clinical Sciences with distinction. Dr. Hall would like to thank Milton Packer, M.D., NIH Clinical Scholars program director at UT Southwestern & Chair of the Department of Clinical Sciences as well as his mentors, Tawanda Gumbo, MD (UT Southwestern), Richard Leff, PharmD, FCCP, and Reza Mehvar, PharmD, PhD for the guidance and mentorship during the NIH Clinical Scholars program. ♦

Dissertation Defenses

Ph.D. Candidate, Lloyd Alfonso of Dr. Jayarama Gunaje's lab, presented "Acetylation-Medated Modulation of p53 Target Gene Expression by Aspirin: Implications for Chemotherapy" as his doctoral dissertation defense. The presentation took place May 8th; the seminar was tech-linked to each distant campus.

Ph.D. Candidate, Nikhil Vad of Dr. Majid Moridani's lab, presented "Phenolic Compounds as Anti-Melanoma Agents: A Selective Melanoma Targeted Prodrug Approach" as his doctoral dissertation defense. The presentation took place June 19th; the seminar was tech-linked to each distant campus. ♦

Dr. MacLaughlin's CAPTION study

Eric MacLaughlin, PharmD (Associate Professor, Pharmacy Practice) will be participating in a Collaborative Among Pharmacists and Physicians to Improve Outcomes Now (CAPTION) study. This $8.5 million NIH funded study is a prospective, cluster-randomized multicenter clinical trial enrolling up to 2,160 patients with uncontrolled hypertension with the hope of establishing the effectiveness of physician/pharmacist collaborative management (PPCM). The study is based out of the University of Iowa and will have 27 locations across the country participating. Each site will be selected for one of three arms of the study: 1) BP PCM Intervention, 2) BP PPCM Extended Intervention, or 3) Asthma PPCM Intervention/BP Usual Care. Dr. MacLaughlin and SOM Family Medicine Chair, Rodney Young, MD, will be responsible for the site in Amarillo which will be part of the Asthma PPCM Intervention/BP Usual Care group. This portion of the study's objective is to conduct clinical trials with geographic, racial, and ethnic diversity to determine the impact of PPCM on asthma management. They hypothesize that the number of asthma patient visits will decrease during the 9-month study period and that the questionnaire scores will improve. TTUHSC will participate as an NIH subcontract for the next 4 years receiving ~$52,000. ♦

Seminars

Ross McKinnon, Ph.D., Professor, Division of Health Sciences, School of Pharmacy and Medical Sciences, University of South Australia, Friday, April 3, 2009. SOP Room 107. "Personalizing Cancer Treatments – Challenges in the Australian Clinical Setting."

Chris Adkins, Graduate Student/ Research Assistant, Monday, April 6, 2009. AMA – 107/ ABI – 1130. "P-glycoprotein at the blood tumor barrier."

Md. Mamunur, Graduate Student/ Research Assistant, Monday, April 6, 2009. AMA – 107/ ABI – 1130. "Characterization of the non-AT1, non-AT2 Angiotensin Binding Site in Primary Neuronal Cultures."

Russell Snyder, Graduate Student/ Research Assistant, Monday, April 13, 2009. AMA – 107/ ABI – 1130. "Identification and Characterization of Tannic Acid Response Element on the Rat AT1R Promoter."

Hussaini Syed Sha Qhattal, Graduate Student/Research Assistant, Monday, April 13, 2009. AMA – 107/ ABI – 1130. "CD44 mediated tumor targeting using hyaluronan conjugated liposomes."

Dr. Palmer Taylor, Dean, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, Wednesday, April 29, 2009. AMA – 107/ABI – 1130. "Freeze-frame, Click Chemistry – A new approach to structure-guided drug design and application to cholinergic neurotransmission." ♦

Publications

Pharmacogenomics Testing: "Required", "Recommended", or "For Information Only". **Moridani**. *PGx Highlights*, June 2009, 1(1) 6-7.

Genomics in the Development of Vaccines. Thomas, **JA. Weidanz, F. Ahsan, MY. Moridani**. *International Pharmacy Journal*, 2009, in press.

The importance of including topics related to pharmacogenetics, pharmacogenomics and medical genetics in the pharmacy curriculum. Harirforoosh, Fleckenstein, Mahajan, Aruoma, Huang, and **Moridani**. (Letter to Editor) *American Journal of Pharmaceutical Education*, 2009.

AAPS-FIP Summary Workshop Report: Pharmacogenetics in Individualized Medicine: Methods, Regulatory and Clinical Applications. **Moridani**, Maitland-van der Zee, Sasaki, McKinnon, Fleckenstein, Shah. *AAPS Journal*, 2009.

The role of STAT-3 in the induction of apoptosis in pancreatic cancer cells by benzyl isothiocyanate (BITC). R. Sahu and **SK. Srivastava.** *J. Natl. Can. Inst.* 101, 176-193**.**

Activation of ATM/Chk1 by curcumin causes cell cycle arrest and apoptosis in human pancreatic cancer cells. R. Sahu, S. Batra, and **SK. Srivastava.** *Br. J. Can.*, 100, 1425-1433**.**

Benzyl isothiocyanate sensitizes human pancreatic cancer cells to radiation therapy. R. Sahu, MW. Epperly and **SK. Srivastava.** *Frontiers in Bioscience* E1, 568-576.

Does Aspirin acetylate multiple cellular proteins? Alfonso, L.F., **Srivenugopal, K.S. and Bhat, G.J.** (Review). *Molecular Medicine Reports 2*, 533-537.

Cationic Liposomes as Carriers for Aerosolized Formulations of an Anionic Drug: Safety and Efficacy Study. Bai S, Gupta V, **Ahsan F**. *Eur J Pharm Sci.* 2009 Jul 15.

Influence of surface charge of PLGA particles of recombinant hepatitis B surface antigen in enhancing systemic and mucosal immune responses. Thomas C, Gupta V, **Ahsan F**. *Int J Pharm*. 2009 Jun 12.

Effects of P-glycoprotein and Mrp2 inhibitors on the hepatobiliary disposition of Rhodamine 123 and its glucuronidated metabolite in isolated perfused rat livers. Parasrampuria R, **Mehvar R**. *J Pharm Sci*. 2009 Jun 4.

Determination of dextra-methylprednisolone conjugate with glycine linker in rat plasma and liver by high-performance liquid chromatography and its application in pharmacokinetics. Zhang SQ, **Mehvar R**. *Biomed Chromatogr*. 2009 Jun 1.

RNF2 is the target for phosphorylation by the p38 MAPK and ERK signaling pathways. Rao PS, Satelli A, Zhang S, **Srivastava SK**, **Srivenugopal KS**, **Rao US**. *Proteomics*. 2009 May; 9(10):2776-87

Brain AT1 angiotensin receptor subtype binding: Importance of peptidase inhibition for identification of angiotensin II as an endogenous ligand. **Karamyan VT**, Gadepalli R, Rimoldi J, Speth R. *J Pharmacol Exp Ther*. 2009 Jul 8.

Benzyl isothiocyanate mediated generation of ROS causes cell cycle arrest and induces apoptosis via activation of MAPK in human pancreatic cancer cells. R. Sahu, R. Zhang, S. Batra, Y. Shi and **SK Srivastava** *Carcinogenesis.* June 2009.

Biochemical mechanism of acetaminophen (APAP) induced toxicity in melanoma cell lines. Vad NM, Yount G, Moore D, **Weidanz J**, **Moridani MY**. *J Pharm Sci*. 2009 Apr;98 (4):1409-25.

Role of TNF-alpha in liver ischaemia-reperfusion injury: new evidence or experimental artefact? **Mehvar R**. *Eur J Clin Invest.* 2009 Jun;39(6):527-8; author reply 529-30.

Efficacy of acetaminophen in skin B16-F0 melanoma tumor-bearing C57BL/6 mice. Vad NM, Kudugunti SK, Graber D, Bailey N, **Srivenugopal K, Moridani MY**. *Int J Oncol*. 2009 Jul;35(1):193-204. ♦

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Nucleus

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