



Nucleus

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

Volume 2, Issue 4

GRANTS AWARDED

See who got grants and for which projects. Page 2

GRADUATE STUDENTS

Future plans for Julie Gaasch & Cornelia Kiewert. Page 2

5th ANNUAL RESEARCH DAYS

Poster winners & Keynote speaker. Page 3

NAMES IN THE NEWS

Page 3

NIH ELECTRONIC SUBMISSION

Page 4

INVITED TALKS, PUBLICATIONS & SEMINARS

Beginning on page 4

MORIDANI CHAIR-ELECT

Page 5

LOOK FOR

Dr. A Busti and his new book

Page 5

Submit your feedback **HERE.**

Drs. Smith & Lockman Receive DOD Grant

The U.S. Department of Defense (DOD) has awarded \$3 million in extramural grant funding to School of Pharmacy investigators **Quentin Smith, PhD**, and **Paul Lockman, PhD**, as part of a 2006 Breast Cancer Center of Excellence Research award. Drs. Smith and Lockman will work with a team of scientists from eight other universities under the direction of Patricia Steeg, PhD of the National Cancer Institute in Bethesda, Maryland.

The Center of Excellence (COE) brings together highly qualified investigators to develop novel drug strategies to treat brain metastases of breast cancer. Brain metastasis of breast cancer is a devastating disease which occurs in 10-16% of metastatic breast cancer patients and is associated with a one-year survival after diagnosis of <20%.

The award was the only one of 38 applications funded this year by the DOD. Drs. Smith and Lockman will each receive approximately \$1.5 million over the next five years and have planned out their research for this grant.

Jointly, Drs. Smith and Lockman will be setting up and standardizing the brain metastasis of breast cancer rodent model. Dr. Smith will evaluate the pharmacokinetics of chemotherapeutic drug deliv-

ery across the blood-brain barrier (BBB) and blood-tumor barrier (BTB). His lab will measure the pharmacokinetics in brain, metastatic brain tumor, brain adjacent to tumor (BAT), and plasma of ten standard breast cancer chemotherapeutics following systemic administration to the brain metastasis of breast cancer rodent model. Also as part of this grant, Dr. Smith will assess the systemic pharmacokinetics, BBB and BTB penetration, and integrated tumor exposure of 10 preclinical therapeutic lead compounds developed by the COE. A particularly intriguing aspect of the grant will be Dr. Smith's



Quentin Smith, PhD



Paul Lockman, PhD

[continued on page 3]

Grant Writing Workshop



David Morrison, PhD

During the 5th Annual Research Days, David C. Morrison, PhD, Co-Founder and Member of the Grant Writers' Seminars and Workshops, LLC, presented an all-day grant-writing workshop to faculty on Thursday, August 3rd, 2006. Attendees praised his instruction, complimenting his ability

to keep a dry subject matter interesting for an entire day.

Dr. Morrison's lecture entitled "Write Winning Grants" held a plethora of helpful information. He covered everything from the development of fundable ideas to the proper preparation for the NIH,

NSF, USDA, and other major agencies. While discussing the review process, Dr. Morrison said, "The key to success in grant writing is to engender enthusiasm in the reviewer—who then becomes an advocate for the applicant's proposal. Therefore *always* write your application for the reviewer, NOT for yourself"

There were a total of 45 attendees, several of which found the presentation so helpful, they requested that Dr. Morrison return for future grant writing seminars. His approach helped the faculty feel more confident and knowledgeable of the subject matter, and his presentation was very proficient.

Faculty had the privilege of a Q&A session afterwards. Due to lack of time, only a few had the opportunity to speak with Dr. Morrison one on one. So much was taken away from this experience. If you would like more information, please contact the Office of Research. ■



Grants Awarded

The School of Pharmacy is pleased to announce the following grant approvals for the past quarter. These grants have a grand total \$1.1 million which further cements our status as an up and coming research institution. Please congratulate the following Drs for their achievements.

Dr. Paul Lockman: DOD/FDN grant for SC: *Breast Cancer Blood-Tumor Barrier Char/Nanoparticle*

Dr. Quentin Smith: DOD/FDN grant for *Chemotherapy Drug uptake/Distribution Pharmacokinetics in Brain Metastasis of Breast Cancer*

Dr. Karin Borges: FDN Grant for *Poly-Unsat*

Fatty Acid in Anticonvulsant in the Anticonvulsant and neuroprotective mechanisms of the ketogenic diet.

Dr. Margaret Weis: AHAT grant for *Inhibitors of Endothelial LCFOACoAS Inhibitors as Anti-Hypertensive agents: defining the eLCFAoAS resaction mechanism.*

Dr. Richard Leff: NIH/ORG for *SC:13-Week Oral Toxicity Studies of Diindoyl Methane-BRNG in Dogs*

Dr. Thomas Thekkumkara: NIH grant for *Role of Glucose in hATI Gene Expression*
[continues on Page 3]

Up Coming Graduates

■ **Julie Gaasch** defended her dissertation “Iron-overload toxicity in central nervous system-associated cells and its attenuation by calcium channel blockers” Monday, October 9th. Since fall of 2002, Julie has studied in the labs of Dr. Suzanne Lindsey, Dr. David Allen as well as her current mentor, Dr. Neels Van der Schyf. She was fortunate enough to work in several different areas with each mentor including osteoporosis, an in vitro subarachnoid hemorrhage model and finally the central nervous system. While working with Dr. Lindsay on osteoporosis, Gaasch earned the publication *Hepatocyte growth factor-regulated genes in differentiated RAW 264.7 osteoclast and undifferentiated cells*. *Gene*. 2006 Mar 15;369: 142-52.

While grateful for her experiences with each lab, Julie commented on Dr. Van der Schyf gusto for science with, “...a wonderful experience. His enthusiasm as a researcher and a teacher is definitely contagious!”

Julie was the recipient of the American Foundation for Pharmaceutical Education (AFPE) pre-doctoral fellowship in 2004 and 2005. Last year, she was selected to give a podium presentation at the Society for Neuroscience meeting in Washington D.C. and again this year in Atlanta, Georgia.

As for future plans, Julie has planned to become a post-doc in Dr. Quentin Smith’s lab.

■ **Cornelia Kiewert** defended her dissertation “Mechanism of action and protective effect of bilobalide, a constituent of *Ginkgo biloba*, in models of brain ischemia and edema” on Friday, October 27th. Connie has studied under Dr. Jochen Klein since the summer of 2002. She joined the doctoral program in January of 2003, and has since co-authored several scientific papers and presented her findings at regional, national and international conferences (AAPS, EB and Neuroscience). She also had the privilege of working with Dr. Alexander Mdzinarishvili and the PATOS center in collaboration with a project concerning “Monitoring of Stroke markers by microdialysis.”

TTUHSC Amarillo was Connie’s first exposure to the United States. Prior to her joining the Health Sciences Center, Kiewert studied at Johannes Gutenberg University of Mainz, Germany where she became a registered German pharmacist. Since she’s been in the US, she has researched several projects in neuropharmacology and the neuroprotective compound bilobalide and still found time to become a frequent traveler and a passionate photographer.

Connie intends to work in Europe, preferably in hospital pharmacy, but has also considered the option of working in the pharmaceutical industry. Connie said, “I definitely plan to visit the US again for vacation. My stay in the US has been an experience of a lifetime, and thanks to all who made it possible.” ■



Julie Gaasch



Cornelia Kiewert

Drs. Smith & Lockman Receive DOD Grant

[continued from page 1]

evaluation of BBB penetration of MDA-MB-231BR cells. In *in vivo* antitumor efficacy studies, Dr. Smith will also measure serum and tissue levels of preclinical compounds. Dr. Smith's lab will provide drug analysis support to other COE investigators to determine brain, metastatic brain tumor, and plasma concentrations of drug delivered by novel nanoparticle, carrier-mediated influx, inhibition of active efflux, or other investigational mechanisms to improve chemotherapeutic drug delivery to tumor within brain. Dr. Smith will also determine serum and tissue pharmacokinetics in animals treated with osmotic BBB disruption to ascertain trastuzumab levels in the brain. Finally, Dr. Smith will measure chemotherapeutic drug levels in resected human brain and tumor tissue for comparison and analysis with the animal model.

Dr. Lockman will be responsible for characterizing barrier passive permeability at the tumor, brain adjacent to tumor and in brain distant from tumor as well as normal brain using the brain metastasis of breast cancer rodent model with sham injected animals as normal, healthy con-

trols. Dr. Lockman will measure expression of critical anticancer drug efflux transporters at the BTB, BBB and tumor using the brain metastasis of breast cancer rodent model. Efflux carriers that will be examined include p-glycoprotein (P-GP), multi-drug resistance associated protein (MRP-1, -2 and -4), and breast cancer resistance protein (BCRP), all of which have been identified at the BBB and closely linked to chemotherapeutic multidrug resistance. In addition, Dr. Lockman will be responsible for quantifying expression of influx carriers at the BTB, BBB, and tumor using the brain metastasis of breast cancer rodent model. The influx carriers that will be examined include the glucose carrier (GLUT-1), large neutral amino acid carrier (LAT-1), cationic amino acid carrier (CAT-1), and choline transporter. Dr. Lockman's lab will also engineer nanoparticle colloidal drug delivery devices. For nanoparticle/drug formulations that show promise of increased brain distribution *in vitro*, Dr. Lockman will test the colloidal formulations *in vivo*. In addition, brain and tumor uptake will be compared for free drug and for drug incorporated in NP after intravenous or *in situ* perfusion administration. ■

[continued from page 2]

Dr. Fakhrul Ahsan: NIH grant for *Long Circulating Low Molecular Weight Heparins for Pulmonary Delivery*

Dr. Jochen Klein: NIH grant for *Anti-edema and Neuroprotective Effects of Ginkgo Extract Egb761 and Bilobalide*

Dr. Ronald Hall: NIH/UNIV grant for SC: *NIH Clinical Scholars Program*

Dr. Cynthia Raehl: West Texas grant for *Improving Care in West Texas Long term Care Facilities Regarding Outcome Measures and Prescription Practices*

Dr. US Rao: WHRI grant for *Drug Resistant Biomarkers in the Human Breast Cancers* ■

5th Annual Research Days



David Margolis,
MD, FACP

The 5th Annual Research Days was busier than in previous years, stretched to a full three days. But as with previous years, the event was a success.

On Wednesday, August 2, 2006, our keynote speaker, Dr. David Margolis presented his talk entitled "Opportunities in Translational Research: The HIV Pandemic as Paradigm" to an appreciative crowd of SOP and SOM faculty, students, and staff.

Forty-two posters were exhibited during Research Days. Thirty-nine were entered into the competition, and of those, four poster teams were recognized. The winners (first authors/presenters) are listed below:

First place—**Kalkunte Srivenugopal, PhD**
Second place—**Jennifer Paulson**
Third place—**James Egbert**
ABRI best poster—**Brandi Cota**

As always, Research Days attendees enjoyed the time to interact more informally with their peers and complimented the food (lots of good eating!) ■

NAMES IN THE NEWS



Dr. Jeanie
Jaramillo

the managing director of the Texas Panhandle Poison Center was interviewed on KAMR NBC 4, November 11. The interview regarded the acetaminophen recall and the effects of the caplets that had been consumed.

NIH Electronic Submission of Grant Applications

The NIH is shifting to a completely electronic grant system. All grants will have to be submitted via the web at Grants.gov. The change has been planned to happen in intervals which started in December of 2005 and will conclude in October of 2007. To find more information on the dates or the forms that are going electronic, you can go to the NIH.gov website or to get the form schedule go to: http://era.nih.gov/ElectronicReceipt/strategic_timeline.htm#1.



Publications (July-September 2006)

Kumar V, Mdzinarishvili A, Kiewert C, **Abbruscato T**, **Bickel U**, **van der Schyf CJ**, **Klein J**. *NMDA receptor-antagonistic properties of hyperforin, a constituent of St. John's Wort*. J Pharmacol Sci. 2006 Sep;102(1):47-54. Epub 2006 Aug 26.

Bond CA, **Raehl CL**. *Clinical pharmacy services, pharmacy staffing, and adverse drug reactions in United States hospitals*. Pharmacotherapy. 2006 Jun;26(6):735-47.

Niture SK, Velu CS, **Smith QR**, **Bhat GJ**, **Srivenugopal KS**. *Increased expression of the MGMT repair protein mediated by cysteine prodrugs and chemopreventative natural products in human lymphocytes and tumor cell lines*. Carcinogenesis. 2006 Aug 31.

Kumar V, Naik RS, Hillert M, **Klein J**. *Effects of chloride flux modulators in an in vitro model of brain edema formation*. Brain Res. 2006 Sep 30.

McCall KL, Craddock D, Edwards K. *Effect of angiotensin-converting enzyme inhibitors and angiotensin II type 1 receptor blockers on the rate of new-onset diabetes mellitus: a review and pooled analysis*. Pharmacotherapy. 2006 Sep;26(9):1297-306.

Mehvar R. *Interdependency of pharmacokinetic parameters: a chicken-and-egg problem? Not!* J Pharm Pharm Sci. 2006;9(1):113-8.

Mehvar R, Vuppugalla R. *Hepatic disposition of the cytochrome P450 2E1 marker chlorzoxazone and its hydroxylated metabolite in isolated perfused rat livers*. J Pharm Sci. 2006 Jul;95(7):1414-24.

Vuppugalla R, **Mehvar R**. *Selective effects of nitric oxide on the disposition of chlorzoxazone and dextromethorphan in isolated perfused rat livers*. Drug Metab Dispos. 2006 Jul;34(7):1160-6. Epub 2006 Apr 18.

Edwards JM, **Patry RA**. *Pharmacy's changing demographics*. Am J Health Syst Pharm. 2006 Sep 15;63(18):1691.

Busti AJ, Tsikouris JP, **Peeters MJ**, Das SR, Canham RM, Abdullah SM, Margolis DM. *A prospective evaluation of the effect of atazanavir on the QTc interval and QTc dispersion in HIV-positive patients*. HIV Med. 2006 Jul;7(5):317-22.

[continued on page 5]

Invited Talks

Majid Moridani: *The application of pharmacogenetics in personalized treatment*. American Association of Clinical Chemistry (AACC). 2006 Annual Meeting. Chicago, IL, July 2006.

Majid Moridani: *Vitamin B12 deficiency and its laboratory investigation*. American Association of Clinical Chemistry (AACC). 2006 Annual Meeting. Chicago, IL, July 2006.

Busti, AJ: *Improvement in Insulin Sensitivity & Dyslipidemia in Protease Inhibitor-Treated Patients After Switch to Atazanavir/Ritonavir (ATV/RTV): A Prospective Study Using Hyperinsulinemic, Euglycemic Clamp Testing*. San Francisco, CA, September 24, 2006.

Veronin, Michael: *Quality Assessment of Statins Obtained from the Internet*. World Congress on Internet in Medicine (MedNet). Toronto, Canada, October 13-20, 2006.

Veronin, Michael: *Moderator for panel discussion on Online Pharmacies*. World Congress on Internet in Medicine (MedNet). Toronto, Canada. October 13-20, 2006.

Brent Field: *Research funding Opportunities in Texas*. American Heart Association. Amarillo, TX. November 6th, 2006.

Majid Moridani: *Toxicity and metabolism of phenolic agents as anti-melanoma drugs*. Seminar Series for the Cancer Research Initiative. TTUHSC, Lubbock, November 2006. ■

Publications (July-September 2006)

[continued from page 4]

Niture SK, Velu CS, **Smith QR**, **Bhat GJ**, **Srivenugopal KS**. *Increased expression of the MGMT repair protein mediated by cysteine prodrugs and chemopreventative natural products in human lymphocytes and tumor cell lines*. *Carcinogenesis*. 2006 Aug 31.

Geldenhuis WJ, **Van der Schyf CJ**. *Triquinane-based compounds as possible serotonin 5-HT(6) receptor antagonists for the treatment of Alzheimer's disease*. *Med Hypotheses*. 2006 Sep 7.

Van der Schyf CJ, Gal S, Geldenhuis WJ, Youdim MB. *Multifunctional neuroprotective drugs targeting monoamine oxidase inhibition, iron chelation, adenosine receptors, and cholinergic and glutamatergic action for neurodegenerative diseases*. *Expert Opin Investig Drugs*. 2006 Aug;15(8):873-86.

Gressett SM, **Stanford BL**, Hardwicke F. *Management of hand-foot syndrome induced by capecitabine*. *J Oncol Pharm Pract*. 2006 Sep;12(3):131-41.

Yao HP, Luo YL, Feng L, Cheng LF, Lu Y, Li W, **Wang MH**. *Agonistic Monoclonal Antibodies Potentiate Tumorigenic and Invasive Activities of Splicing Variant of the RON Receptor Tyrosine Kinase*. *Cancer Biol Ther*. 2006 Sep 11;5(9).

Wittman VP, Woodburn D, Nguyen T, Neethling FA, Wright S, **Weidanz JA**. *Antibody targeting to a class I MHC-peptide epitope promotes tumor cell death*. *J Immunol*. 2006 Sep 15;177(6):4187-95.

Tsikouris JP, **Cox CD**, Simoni JS, Seifert CF, Peek MC, Meyerrose GE. *Lack of effect on coronary atherosclerotic disease biomarkers with modest dosing of an angiotensin-converting enzyme inhibitor, angiotensin II type-I receptor blocker, and the combination*. *Coron Artery Dis*. 2006 Aug;17(5):439-45.

Tsikouris JP, **Cox CD**, Simoni JS, Seifert CF, Peek MC, Meyerrose GE. *Lack of effect on coronary atherosclerotic disease biomarkers with modest dosing of an angiotensin-converting enzyme inhibitor, angiotensin II type-I receptor blocker, and the combination*. *Coron Artery Dis*. 2006 Aug;17(5):439-45.

Peeters MJ, **Seifert CF**. *The use of combination antimicrobials in critically-ill ventilated patients with pseudomonal pneumonia*. *Hospital Pharmacy* 2006;41:848-54.

Gressett SM, **Stanford BL**, Hardwicke F. *Management of hand-foot syndrome induced by capecitabine*. *J Oncol Pharm Pract*. 2006 Sep;12(3):131-41.

Cole J, **Busti AJ**, KaziH. *The effect of TNF- α inhibitors on the incidence of new heart failure and exacerbation of existing heart failure in patients with rheumatoid arthritis [Original Research]*. *Rheumatol Int* 2006.

MacLaughlin EJ, Sleeper RB, McNatty D, **Raehl CL**. *Management of age-related osteoporosis and prevention of associated fractures*. *Ther Clin Risk Manage*. 2006;2:281-295. ■

Moridani Chair-elect



Dr. Majid Moridani was elected as the Chair-elect of the Pharmacogenomics Focus Group. The group consists of 400 members who promote the study of genetic causes of individual variations in drug responses. It is one of five focus

groups within the Clinical Pharmacology and Translation Section (CPTR) at the American

Association of Pharmaceutical Science (AAPS).

The group organizes discussions and workshops, along with several other outreach programs. They facilitate communications between academia, biotechnology/genomics firms and regulatory agencies as well as provide a forum for information exchange on topics in the pharmacogenetics and pharmacogenomic areas via the internet. The team of scientists generate yearly Theme Issues in Pharmacogenetics-Pharmacogenomics in AAPS PharmSci.

Congratulations Dr. Moridani! ■

Look For:



Anthony Busti,

Assistant Professor, Adult Medicine Division, Dallas, has had several achievements with his publications. Busti, as a contributing author, has another book on the shelves, *Advanced Cardiac Life Support Provider Manual for Professionals*. He also participated in the 8th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV this past September as well as the Annual Scientific Sessions for the Southeast Lipid Association in August.

Research Seminars (July-September 2006)

During the school year, faculty and graduate students present research seminars highlighting their work. Occasionally, guest speakers also present seminars while visiting the school. Below is a summary of the seminars that took place in the last few months.

7/14/06-Xianxin Hua, MD, PhD, Assistant Professor of Cancer Biology, Abramson Family Cancer Research Institute, University of Pennsylvania, Philadelphia. "Menin, a Tumor Suppressor or Tumor Promotor?"

7/25/06-Janette Dufour, PhD, Brandt Schneider, PhD & Simon Williams, PhD, Department of Cell Biology & Biochemistry & Raul Martinez-Zaguilan, PhD, Department of Physiology, TTUHSC, Lubbock. "Development of a cross campus cancer research initiative at TTUHSC."

8/28/06-Richard Bartsch, PharmD, PhD, Organic, Analytical and Polymer Chemistry, TTUHSC, Lubbock. "Metal Ion Complexation and Separation with Calix(4)arene Compounds."

9/11/06-Karin Borges, PhD, Assistant Professor, Department of Pharmaceutical Sciences. "Use of microarrays in the search of Neuroprotective genes & pathways."

9/18/06-Randolph Schiffer, MD, Professor and Chairman, Department of Neuropsychiatry and Behavioral Science, TTUHSC SOM, Lubbock. "A new Sigma-1 agonist and NMDA blocker for the treatment of emotional lability syndromes."

9/25/06-Vamshi Manda, Graduate Student/Research Assistant, Department of Pharmaceutical Sciences. "Active transport of High-Affinity Choline and Nicotine Analogs into the Central Nervous System by the BBB Choline Transporter."

9/25/06-Runa Naik, Graduate Student/Research Assistant, Department of Pharmaceutical Sciences. "Effects of Chloride Flux Blockers in an in vitro model of Brain Edema."

9/27/06-Dr. Suresh Ambudkar, Senior Investigator & Chief, Transport Biochemistry Section, Laboratory of Cell Biology, National Cancer Institute, NIH, "Multidrug resistance in cancer cells and ABC drug transporters." ■

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To include information in the next edition of this newsletter, please submit materials to logan.larue@ttuhsc.edu OR fax 806.356-4643 by 5 p.m. Friday, December 15.

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