



Nucleus

SCHOOL OF PHARMACY, OFFICE OF RESEARCH

<http://www.ttuhschool.edu/sop/research/>

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SPECIAL POINTS OF INTEREST:

- Research Days 2005
- New Faculty Researcher
- Faculty & Student Recognized
- Research Success at SOP

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Research Days 2005

The 2005 Research Days event was held July 28-29. Milton Packer, M.D. delivered the keynote speech. Dr. Packer is a Professor at Southwestern Medical School in Dallas. He also serves as the Gayle & Paul Stoffel Distinguished Chair in Cardiology and as the Director of the Center for Biostatistics and Clinical Science.

In addition to Dr. Packer's keynote presentation, four School of Pharmacy faculty members (two from each department) gave podium presentations: Margaret Weis, Ph.D., Pharmaceutical Sciences. "Long chain fatty acyl CoA synthetases as therapeutic targets in brain and heart;" Michael Veronin, R.Ph., Ph.D., Pharmacy Practice. "'URL 404 File Not Found': Internet Reference Disappearance;" Kalkunte Srivenugopal, Ph.D., Pharmaceutical Sciences. "Discovery of MGMT as a New Player in the CDT1-Geminin Axis that Prevents Rereplication of Human Chromosomal DNA;" and Anthony Busti, Pharm.D., BCPS, Pharmacy Practice. "A prospective evaluation of the effect of atazanavir on the QTc-interval and QTc-dispersion in HIV-positive patients."

Numerous faculty members, post-doctoral research associates, graduate students, residents, pharmacy students, and summer interns also presented posters during the event. The Office of Research was pleased to highlight the work of the nine Amarillo Biomedical Research Internships summer interns, each of whom entered posters into the competition.

A total of forty-eight posters were presented during Research Days; of these, forty-four were entered into the competition. Poster award winners were:

"Efficacy of Fluconazole Prophylaxis in Autologous Peripheral Blood Stem Cell Transplantation: Results of a Prospective, Randomized, Controlled, Multicenter, Open-Label Study." **Sachin Shah, PharmD¹**, Tracey L Walsh, PharmD², Carlos Bachier, MD³, Paul Shaughnessy, MD³, Cesar O Freytes, MD², Natalie Callander, MD², C Fred LeMaistre, MD³, Michael Grimley, MD³ and Patrick Bradshaw, MS². ¹Texas Tech University HSC – School of Pharmacy, Dallas, Texas, ²Bone Marrow Transplantation, University of Texas Health Science Center, San Antonio and ³Bone Marrow Transplantation, Texas Transplant Institute, San Antonio, Texas USA.

"The Accumulation of Forskolin in Cysts of Patients with Polycystic Kidney Disease." **William C. Putnam¹**, Sarah M. Swenson¹, Gail Reif², Darren Wallace² and Jared J. Grantham² ¹School of Pharmacy, Texas Tech University Health Sciences Center, Dallas, TX 75216. ²School of Pharmacy, Texas Tech University Health Sciences Center, Dallas, TX 75216; ³University of Kansas School of Medicine, Kansas City, KS 66160.

"Interaction Between Hyperleptinemia and Hypertension in Obese Aged Rats." **Eugene W. Shek**, Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX 79106.

Milton Packer, M.D.



Amarillo Biomedical Research Internships Winning Poster

"Method Development: Analysis of DIM in Human Plasma by LC/MS" **Karl Kashi** and William Putnam, Amarillo Biomedical Research Internship & Texas Tech University Health Sciences Center, School of Pharmacy, Dallas, TX. The Graduate Student Association at Amarillo also recognized outstanding graduate student posters and presented scholarships to the top three:

First Place Graduate Student Poster – Haritha Mandula "Kinetic Analysis of Factors Influencing Restrictive vs. Nonrestrictive Plasma Protein Binding Effects on Brain Uptake."

Second Place Graduate Student Poster – Katie Bennett "Characterization of the low-affinity choline transporter and identification of two novel transporters, BOCT1 and BOCT2."

Third Place Graduate Student Poster – Nikhil Vad "Structure-toxicity relationship of phenolic analogues as anti-melanoma agents: a drug metabolism drug design approach."

Thanks also to Levi Kirwin & VWR International for the Roasters coffee!

New Faculty Researcher - U.S. Rao, Ph.D.

“Dr. Rao and his team are trying to stop the pump action of Pgp in cancer cells.”

U.S. Rao, Ph.D.



In other recent SOP publications (Dean's Newsletter, email on new faculty from Mark Hendricks) we have already seen some biographical information on Dr. Rao. Even so, we wanted to offer him the same opportunity as with other new faculty to discuss his research program for inclusion in our newsletter. Little did I know that after I'd met with him, I'd emerge from his office with a much better understanding of things like P-glycoprotein (Pgp), RING finger proteins, and galectins.

Dr. Rao gleefully welcomed me into his office, dubbing me his “victim” and began to teach me about what he studies. He explained that he likes to describe his science in such a way that even lay people can understand, so with me as his lay person “victim,” he got his marker ready, stood before his dry/erase board and began my education.

He started by taking me back to a motivating factor in his career development – when he read an article published around 1989 in *Scientific American*. In that article, he read about Susan, a woman who had gone through rounds of chemotherapy to be “cured” of the cancer, only to have the cancer relapse and remain unaffected by additional chemotherapy. Susan's cancer cells had developed resistance to the drugs, and she died. Reading about this real-life cancer struggle prompted Dr. Rao to recognize that while the study of basic science is certainly important, translating that study into clinical understanding that could save lives is essential.

Dr. Rao explained to me that

most cancer cells are killed by the first treatment(s) of chemotherapy, but those few that survive are unaffected by the treatment and often remain undetected, resulting in determinations that the patient has been cured. These surviving cancer cells express other genes, which protect them from the drugs. On their plasma membranes, they express Pgp, also called MDRI-protein. The Pgp acts as a pump, immediately pumping out from the cell the cancer medications that have entered. Because the medications do not have time or adequate accumulation within the cancer cell to effect cell death, chemotherapy is ineffective in treating cancer cells with Pgp. After initial chemotherapy treatments, the cancer cells with Pgp adapt by multiplying the number of Pgp proteins on the cell surfaces, further increasing the resistance to the drugs. As a result, future chemotherapy treatments are even less effective on the now more-resistant cancer cells.

The study of Pgp is further complicated by the fact that Pgp is not always detrimental. In endometrial cells, Pgp functions to protect the fetus, and in the brain, Pgp keeps harmful intruders from causing damage. While some researchers have focused on attempting to inhibit Pgp in cancer cells, Dr. Rao and his team are trying to identify the mechanisms that regulate Pgp expression and function in cancer cells.

Dr. Rao's idea, which received NIH funding, was that cancer cells and healthy cells differ because of additional proteins present on cancerous cells. These other, additional proteins cause the Pgp to function

differently on cancer cells than on healthy cells. The proteins regulate Pgp in different ways in the two environments of healthy cells and cancer cells. Dr. Rao and his team employ the yeast two-hybrid analysis to identify the proteins that possibly associate with and affect the behavior of Pgp. Using that technique, they isolated a new RING finger protein. Under the awarded NIH grant, they are now trying to figure out what exactly this RING finger protein does to cause Pgp to behave as it does in cancer cells.

The Department of Defense also awarded Dr. Rao with a grant – a Concept Award, a one-year grant supporting data collection. For this grant, Dr. Rao and his team are investigating why cancer cells metastasize (why they, unlike healthy cells, migrate to other areas of the body). Galectin, a protein that coats cells and functions almost like a glue, (binding cells together and creating organs), is found in higher quantities on cancer cells. Cancer cells excrete too many galectins, decreasing the ability of the cancer cells to solidly bind together. With too much “glue” and not enough effective cell cohesion, the cancer cells break away and migrate to other areas of the body, resulting in the cancer's spread.

Dr. Rao's enthusiasm for his research and his eagerness to apply his findings to real-world clinical applications is clear. And his eagerness is infectious. Undoubtedly Dr. Rao would welcome you to his office, to share his research interests with you – just come ready to set off on an adventure in learning!

Names in the News: Faculty & Student Recognized

Ulrich Bickel, M.D. and **Jochen Klein, Ph.D.** each received a seed grant for \$125,000 as part of the Cardiovascular Seed Grant Program. The Lubbock-based Center for Cardiovascular Disease and Stroke provides these seed grants for basic and applied research related to cardiovascular disease. The funds will be awarded July 1.



Dr. Bickel



Dr. Klein

ive is to enhance availability of labeled products for infants and children.



C.A. (CAB) Bond, Pharm.D., F.A.S.H.P., F.C.C.P. has been named the 2005 Russell R. Miller Award winner by the American College of Clinical Pharmacy. This award is given to ACCP members who have advanced both clinical pharmacy practice and rational pharmacotherapy by making substantial contributions to the literature of clinical pharmacy. The award is named for Russell Miller, who was the founding editor of *Pharmacotherapy*, which is the ACCP journal. Dr. Bond will receive the award at the annual ACCP meeting in San Francisco on October 23.



Sachin Shah,

Pharm.D. has received a \$4,500 unrestricted educational grant from Amgen, Inc. to support Dallas/Fort Worth student and resident education.



Haritha Mandula, Graduate Student, Pharmaceutical Sciences has received the Graduate Student Award from the Society for Neuroscience chapter. She will receive a \$750 travel award and complimentary registration to the SfN Annual Meeting. SfN is a nonprofit membership organization of basic scientists and physicians who study the brain and nervous system with the primary goal of promoting the exchange of information among researchers. SfN is also devoted to education about the latest advances in brain research and the need to make neuroscience research a funding priority.

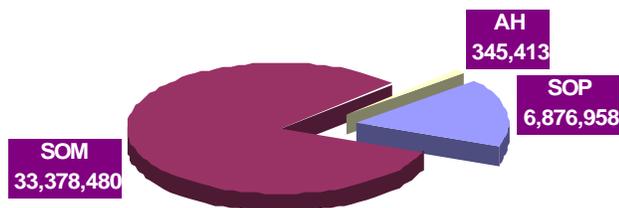


Richard Leff, Pharm.D. has been appointed to the NIH Scientific, Technical, and Regulatory Working Group for the Pediatric Formulations Initiative. The goal of this initia-

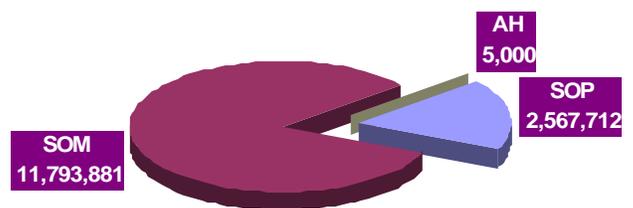
Continued Research Success at the SOP

Within the TTUHSC system, the School of Pharmacy plays a significant role in the overall research of the University. As can be seen by the graphs below and on the next page, School of Pharmacy researchers continue to excel in their pursuit of extramural research dollars.

2005 HSC Total Dollars in Submitted Applications



2005 HSC Total Awards Received in Dollars

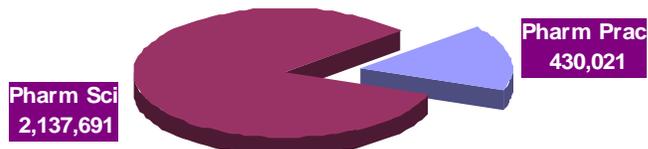


Continued Research Success (continued from page 3)

2005 SOP Total Dollars in Submitted Applications



2005 SOP Total Awards Received in Dollars



Faculty Publications (July-September 2005)

Akins RL, Haase KK. Gram-positive resistance: pathogens, implications, and treatment options. *Pharmacotherapy* 2005;25:1001-10.

Allen DD, Geldenhuys WJ. Molecular modeling of blood-brain barrier nutrient transporters: In silico basis for evaluation of potential drug delivery to the central nervous system. *Life Sci.* 2005 Aug 26; [Epub ahead of print]

Bond CA, Raehl CL. Clinical and economic outcomes of pharmacist-managed aminoglycoside or vancomycin therapy. *Am J Health Syst Pharm.* 2005 Aug 1;62(15):1596-605.

Fischer D, Bhattacharya R, Osburg B, Bickel U. Inhibition of monocyte adhesion on brain-derived endothelial cells by NF-kappaB decoy/polyethylenimine complexes. *J Gene Med.* 2005 Aug;7(8):1063-76.

Frédéric, R., Ooms, F., Castagnoli, N., Jr., Petzer, J.P., Feng, J.-F., Schwarzschild, M.A., Van der Schyf, C.J., and Wouters, J. (E)-8-(3-chlorostyryl)-3-dimethyl-7-methyl-xanthine, a caffeinyl derivative acting both as antagonist of adenosine A2A receptors and inhibitor of MAO-B *Acta Crystallographica*, 2005, C61, 531-532.

Irons BK, Kroon LA. Lipid management with statins in type 2 diabetes mellitus. *Ann Pharmacother.* 2005 Oct;39(10):1714-8. Epub 2005 Aug 23.

Klein J. Functions and pathophysiological roles of phospholipase D in the brain. *J. Neurochem.* 94 (6): 1473-1487.

Leff RD. COPD: clinical significance of early diagnosis. *J Manag Care Pharm.* 2005 Jul;11(6 Suppl A):S8-11; quiz S20-2.

Lockman PR, Van der Schyf CJ, Abbruscato TJ, Allen DD. Chronic nicotine exposure alters blood-brain barrier permeability and diminishes brain uptake of methyllycconitine. *J. Neurochem.* 94, 37-44.

Moridani MY, Moore M, Bartsch RA, Yang Y, Heibati-Sadati S. Structural toxicity relationship of 4-alkoxyphenols' cytotoxicity towards murine B16-F0 melanoma cell culture. *J. Pharm. Pharm. Sci.*, 2005; 8(2):348-360.

Paulson JR, Roder KE, McAfee G, Allen DD, Van der Schyf CJ, Abbruscato TJ. Tobacco Smoke Chemicals Attenuate Brain-to-Blood Potassium Transport Mediated by the Na,K,2Cl-Cotransporter During Hy-

poxia-Reoxygenation. *J Pharmacol Exp Ther.* 2005 Sep 20; [Epub ahead of print]

Shah S. Pharmacy consideration for the use of IGIV therapy. *Am J Health Syst Pharm* 2005;62(Suppl 3):S5-11.

Shah S. Practical consideration for the use of IGIV therapy: Introduction: *Am J Health Syst Pharm* 2005;62(Suppl 3):S3-4.

Shah, S. Guest editor: Practical consideration for the use of IGIV therapy. *Am J Health Syst Pharm* 2005;62(Suppl 3).

Sleeper RB. Antipsychotic dose-sparing effect with addition of memantine. *Ann Pharmacother.* 2005 Sep;39(9):1573-6. Epub 2005 Aug 2.

Stanford BL, Shah SR, Ballard EE, Jumper CA, Rabinowitz I, Dowell JE, Hunt WC, Kriger JA. A randomized trial assessing the utility of a test dose program with taxanes. *Curr Med Res Opin* 2005;21(10):1611-1616.

Young, L.H., Balin, B.J., Weis, M.T. Gö 6983: A fast acting protein kinase C inhibitor that attenuates myocardial ischemia/reperfusion injury. *Cardiovascular Drug Reviews.* 23:262-279, 2005.

Research Seminars

Every Monday during the school year, faculty and graduate students present research seminars. The Office of Research sponsors one of these monthly presentations, which is health-netted, and the other seminars are provided by the Pharmaceutical Sciences Department. Below is a summary of the seminars that took place in the last few months.

8/29/05-John Stallone, Ph.D., Associate Professor, Department of Veterinary Physiology & Pharmacology, College of Veterinary Medicine, Texas A&M University, College Station, TX. "Vascular Effects of Estrogen: Challenging the Dogma."

9/12/05-Raktima Bhattacharya, Post Doctoral Research Associate, Department of Pharma-

ceutical Sciences. "Anti-Inflammatory Effects of Targeted Delivery of a NF-kB Decoy to Brain Endothelial Cells."

9/19/05-Majid Moridani, Ph.D., Assistant Professor, Department of Pharmaceutical Sciences. "Clinical Application of Pharmacogenetics in Personalized Medicine."

New Developments in SOP Research

The Office of Research, with the ad hoc Research Advisory Committee, recently developed a policy for a new faculty bridge program. The Executive Committee has reviewed and approved the plan — please refer to OP 73.P.02 at: <http://www.ttuhs.edu/sop/administration/policies/>.

To briefly explain the program, in order to fund the bridge program, the allocations of the indirect return to the School were adjusted to the following formula: 25% of the annual return will go to the Office of the

Associate Dean for Research bridge fund account. The remaining 75% of the indirect returns will be divided into three equal portions and awarded: directly to the PI for the enhancement of his/her research program, to the Department Chair in support of departmental research programs, and to the Office of the Associate Dean for Research in support of School-wide research enhancement programs and the School's research infrastructure.

For bridge fund application procedures and

eligibility requirements, please contact the Research Office or visit our website: <http://www.ttuhs.edu/sop/research/InternalGrants/Bridgefunds.aspx>.

The Office of Research has also drafted a policy for SOP research laboratory volunteers (including minors) that has gone to the Executive Committee for review. This policy will be disseminated to the faculty after it has been reviewed, amended as needed and given final approval.

Open Forum

The Office of Research and ad hoc Research Advisory Committee would like to seek opinions from all faculty on the issues that affect the overall research program at the School and/or individual faculty researchers. This new "Open Forum" column will be regularly featured in this quarterly newsletter. Please share your opinions with Melissa Lockman, Research Administrator, via email (melissa.lockman@ttuhsc.edu) or by phone (806-356-4000, 326).

- **Upkeep of Equipment Maintenance Contracts.** The School has acquired expensive, valuable equipment that must be properly maintained. The maintenance contracts with equipment such as the LC-MS/MS are high-dollar. Ensuring

that the costs of these contracts are covered from year to year is also a priority of the ad hoc Research Advisory Committee. Funding sources are difficult to identify. Again, if you have any feedback on this issue, please share with Ms. Lockman.

- **Research Infrastructure.** The faculty survey conducted by the Faculty Development Committee identified a perceived weakness among the faculty of the School's and the University's research infrastructure. As the Office of Research and ad hoc Research Advisory Committee attempt to address this concern and to strengthen the research programming, more specific information from the faculty regarding the individual

elements that are weak/need improvement would be helpful. Please provide Ms. Lockman with additional information and ideas for improvement.

- **Mentoring Program.** Many of you have already offered opinions on how to structure a research mentoring program in the School. We appreciate all recommendations; however, the ad hoc Research Advisory Committee is still evaluating how best to implement a research mentoring program and would welcome additional suggestions/comments. Particularly if you participating in programs at other institutions, please share your recommendations with Ms. Lockman.

Upcoming Events/Deadlines

2006 Wendy & Stanley Marsh 3 Endowed Lectureship in Pharmacology and Neurochemistry of Substance Abuse/Addiction

The 2006 Marsh lecture will be scheduled for two days in March. Specific announcements will be made as soon as the speaker is confirmed. As always, the speaker will be a rec-

ognized research expert in the pharmacologic area of substance abuse and the neurochemistry that precipitates this behavior.

Upcoming NIH Deadlines

T series grants-Cycle I-January 10; Cycle II-May 10; Cycle III-September 10.

R15 grants-Cycle I-January 25; Cycle II-May 25; Cycle III-September 25.

P series grants-Cycle I-February 1; Cycle II-June 1; Cycle III-October 1.

New Research grants (R01, R03, R21)-Cycle I-February 1; Cycle II-June 1; Cycle III-October 1.

Renewing Research grants (R01, R03, R21)-Cycle I-March 1; Cycle II-July 1; Cycle

III-November 1.

New K series grants-Cycle I-February 1; Cycle II-June 1; Cycle III-October 1.

Renewing K series grants-Cycle I-March 1; Cycle II-July 1; Cycle III-November 1.

New Education grants (R25)-Cycle I-February 1; Cycle II-June 1; Cycle III-October 1.

Renewing Education grants (R25)-Cycle I-March 1; Cycle II-July 1; Cycle III-November 1.

SBIR & STTR grants (R41, R42, R43, R44)-Cycle I-April 1; Cycle II-August 1; Cycle III-December 1.

Individual Kirschstein Awards (F30, F31, F32, F33)-Cycle I-April 5; Cycle II-August 5; Cycle III-December 5.

Conference Grants/Agreements (R13, U13)-Cycle I-April 15; Cycle II-August 15; Cycle III-December 15.

AIDS grants-Cycle I-May 1; Cycle II-September 1; Cycle III-January 2.

OFFICE OF RESEARCH

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Nucleus is a quarterly newsletter published by the SOP Office of the Associate Dean for Research.

To include information in the January edition of this newsletter, please submit materials to:

Melissa Lockman, melissa.lockman@ttuhsc.edu OR fax 806-356-4643 by 5 p.m. on Friday, December 16, 2005.