

# Nucleus

SCHOOL OF PHARMACY, OFFICE OF RESEARCH

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

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## SPECIAL POINTS OF INTEREST:

- Updates on Centers for Research Excellence
- Research Days 2004, & 2005 is coming
- Guest Speaker Tom Davis, Ph.D.
- Receptor Logic, Ltd.
- Policy on Equipment Usage Fees

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## Office of Research e-Newsletter

The Office of the Associate Dean for Research strives to promote and facilitate clinical and basic science research at the School of Pharmacy. In an effort to not only publicize the research accomplishments of our faculty, but to also stimulate future endeavors, the Office is launching this newsletter.

This newsletter will be published quarterly and is intended to highlight recent developments in research at the School.

From specific information about events, programs, and services provided by the Office to features on each of the School's Research Centers, the newsletter will attempt to provide a general overview of research activities and opportunities.

Please provide feedback – about this newsletter as well as the broader topic of the SOP's research program overall and the



School of Pharmacy,  
Amarillo

role of the Office of Research – to Melissa Lockman, Research Administrator, Room 217 SOP, (806)356-4000, 326 or

[melissa.lockman@ttuhscc.edu](mailto:melissa.lockman@ttuhscc.edu) .

Because this newsletter is so new, the Office of Research welcomes your input. We hope that this will be useful to investigators, rather than just another piece of paper cluttering desks and lining trash cans. Please let Ms. Lockman know what regular items would be of interest and helpful to you in this quarterly publication.

To include information in the April edition of this newsletter, please submit materials to Ms. Lockman by 5 p.m. on Friday, March 11, 2005.

## Cancer Biology Research Center

The mission of the Cancer Biology Research Center (CBC) is to advance understanding, prevention, diagnosis, and treatment of cancer by generating new knowledge in normal and cancer cell biology and by participating in the application of this knowledge to

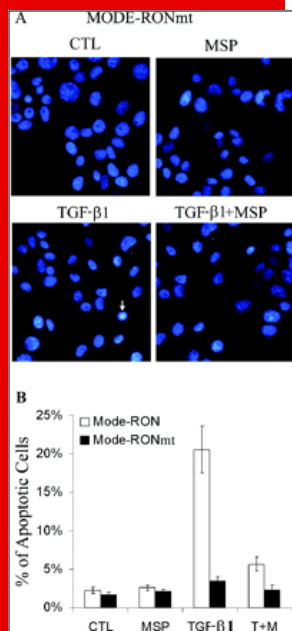
translational and clinical investigation.

Currently, the CBC is directed by Dr. M.-H Wang with five members including Drs. J. Gunaje, M. Moridani, K.S. Srivenugopal, M.-H. Wang, and J.

Weidanz. They are all from the School of Pharmacy.

The CBC was formed in 1999 with common interests and goals shared by several faculty members in the School of Pharmacy. Since its establishment, the CBC has matured significantly, with

## Cancer Biology Research Center (continued from page 1)



“Through collaborative and intensive research, the members of the CBC have published more than 50 articles in highly peer-reviewed journals.”

notable visibilities in the field of cancer research. Armed with different backgrounds and areas of expertise, members of the CBC work together with a clear objective: to understand the oncogenic mechanisms that lead to normal cell transformation and malignant progression.

Since 1998, the members of the CBC have obtained 11 research grants:

- three NIH R01 grants,
- one NIH R21 grant,
- two NIH R43 grants,
- one grant from the American Heart Association,
- one research grant from the Pediatric Tumor Foundation, Amarillo Area Foundation,

- one endowment from the Chung Kung Scholars Program of Chinese Ministry of Education, and
- one research grant from the Chinese National Sciences Foundation.

Through collaborative and intensive research, the members of the CBC have published more than 50 articles in highly peer-reviewed journals, including *Oncogene*, *JBC*, *Carcinogenesis*, *Cancer Letter*, *Protein Science*, and *Experimental Cell Research*.

They also serve in various national committees, as NIH Study Section members, journal ad-hoc reviewers, and conference organizer and chair.

The CBC has helped faculty members establish close relationships with various biotechnology companies, including

Eurgene, Biosources Internationals, and others, and has resulted in the licensing of several research products to these companies.

As an academic entity, the CBC has gained a significant reputation in the cancer research areas, including:

- chemical carcinogenesis,
- signaling pathways,
- DNA repair mechanisms,
- growth factor oncogenesis, and
- T cell malignancy.

These activities also increase the visibility of TTUHSC and the SOP in the nation and world. The increased ranking of the School of Pharmacy in the nation (from ranking 60 to 42) is an excellent example.

## Pathophysiology & Treatment of Stroke Center

The PATOS Center is dedicated to reducing the burden of stroke by encouraging and supporting innovative interdisciplinary research of the highest scientific standard among TTUHSC School of Pharmacy faculty into the pathophysiology of stroke to identify drug targets and develop strategies and drugs for its prevention and/or treatment.

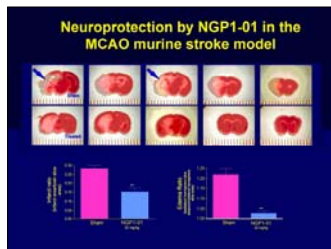
The current members include: Dr. Ulrich Bickel (Director), Dr. Tom Abbruscato, Dr. Jochen Klein, Dr. Neels Van der Schyf (all TTUHSC School of Pharmacy).

The PATOS-Center was formed less than two years ago by faculty members in the Department of Pharmaceutical Sciences as a nucleus for col-

laborative basic research in the field of ischemic brain disease.

The founding members of the Center (Drs. Abbruscato, Bickel, Klein, Weidanz) came from different areas (neurovascular and endothelial biology, neuropharmacology, immunology) but built a strong collaborative program. They were joined in 2003 by Dr. Van

# Stroke Center (continued from page 2)



der Schyf, a medicinal chemist who contributes to the interdisciplinary character of the Center.

The Center's "core facility" consists of a research lab for the "Middle Cerebral Artery Occlusion" (MCAO) method, a standard model in experimental stroke research. The Center members chose the mouse as the species, because it offers better versatility, due to the multitude of transgenic and gene knockout models available. The technical setup of the Stroke lab was complemented by hiring a collaborator with long-time experience in animal models (Dr. A. Mdzinarishvili). As a result, the MCAO model was established within less than 6 months. In the short period of its existence, the Center has taken major steps towards establishing itself as a re-

search endeavor with long-term perspective.

**Future Goals:** 1) Establish novel experimental methods to further boost competitiveness. These include synthesis of drug derivatives, perfection of existing stroke models (e.g. by microdialysis), and the addition of an ischemia/reperfusion model and a model for traumatic brain injury.

2) The Center members will enhance visibility and their work in publications and presentations on scientific congresses. We expect that the Center will give rise to a minimum of three publications by its members each year. At least one of these publications will come from collaborative projects and will be co-authored by at least two members of the Center.

3) P.I.s will strive to obtain extramural funding for individual projects within three years of membership in the Center. After successful funding of several Center members is obtained, an application for a NIH Program Project will be pursued.

### Grants Activity — Funded:

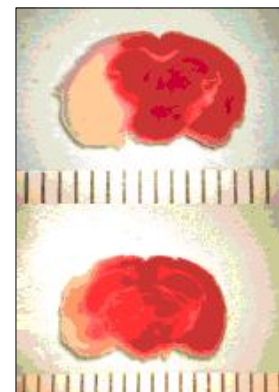
"Tobacco Smoke Chemicals and Stroke Alter Brain K<sup>+</sup> Efflux" I R01 NS 046526-01 (Abbruscato) 07/01/04 – 03/31/09, NIH NINDS \$250,000/year

### Pending:

"Modulation of Brain-to-Blood Potassium Flux by Nicotine and Stroke Conditions" External Research Program (Abbruscato) 06/01/04 - 05/31/07, Phillip Morris \$186,000/year

"Chloride channel blockers as a possible target for neuroprotection: studies with bilobalide as model compound" Submitted to American Heart Association, Texas Affiliate (Grant-in-Aid) 01/06/04 P.I.: Jochen Klein, PhD, Total amount: \$124,000 (for two years)

"Novel Neuroprotective Cage Amines in Cerebral Ischemia" Submitted to American Heart Association, Texas Affiliate (Grant-in-Aid) 01/08/04. P.I.: Neels Van der Schyf, PhD Total amount: \$124,000 (for two years)



**Middle cerebral artery occlusion (MCAO) in the mouse**

*"In the short period of its existence, the Center has taken major steps towards establishing itself as a research endeavor with long-term perspective."*

# Pediatric Pharmacology Research & Development Center

Researchers from the TTUHSC School of Pharmacy have collaborated with the Department of Pediatrics at the University of Texas Southwestern Medical Center (UTSWMC) to support their NIH proposal for establishing a Pediatric Pharmacology Research Unit (PPRU) at the Children's Medical Center of Dallas. This proposal

was funded January, 2004, and UTSWMC's PPRU is part of a nationwide network to conduct clinical research for pediatric pharmaceutical labeling.

Development of pediatric pharmaceuticals requires both preclinical and clinical research. The capability for preclinical research was not part of the PPRU network. As a

result, the School of Pharmacy developed a proposal with the collaboration of UT-Southwestern and Children's Medical Center to establish a preclinical research group to support the PPRU network and conduct industrially-



**Dallas/Fort Worth**

## Pediatric Center (continued from page 3)



### Analytical Equipment

*“The PPRDC is the first TTUHSC initiative to stimulate pharmacy research in D/FW and serves as a significant resource to D/FW-based pharmacy faculty for research support.”*

and federally sponsored research. Such a capability will provide added value to pediatric pharmaceutical clinical research and clearly differentiate UTSWMC's PPRU.

Funding for the Pediatric Pharmacology Research & Development Center (PPRDC) was obtained in part from the School of Pharmacy Center for Research Excellence Awards (October, 2003).

The primary function of the PPRDC is to conduct preclinical research that is required for pediatric pharmaceutical labeling. The Center's early stage analytical laboratory will support such research and development.

The PPRDC is the first TTUHSC initiative to stimulate pharmacy research in D/FW and serves as a significant resource to D/FW-based pharmacy faculty for research support. It represents a significant collaboration between UT Southwestern, Children's Medical Center, and TTUHSC to facilitate pediatric research and product development. The combined preclinical and clinical pediatric research capabilities are unique to the D/FW-

based collaboration. We anticipate that the Center will be self-funding with enhanced research avenues. The training of pharmacy students, post-graduate residents and fellows will be enhanced in the area of pediatric pharmacotherapy. We speculate that graduates will pursue more careers in pediatric pharmacy.

**PPRDC Program Director:** Richard Leff, PharmD, Professor & Regional Dean, TTUHSC School of Pharmacy – D/FW

**PPRDC Laboratory Director:** Trey Putnam, PhD, Assistant Professor, TTUHSC School of Pharmacy – D/FW

**PPRDC Pharmaceutical Consultant:** Reza Mehvar, PhD, Professor, TTUHSC School of Pharmacy – Amarillo

**PPRDC Research Associate:** Sarah Swenson TTUHSC School of Pharmacy – D/FW

**PPRU Principal Investigator:** George McCracken, MD, Professor of Pediatrics, Glaxo-SmithKline Distinguished Professor of Pediatric Infectious Disease, The Sarah M. and Charles E. Seay Chair in Pediatric Infectious Disease, U

Texas Southwestern Medical Center at Dallas

**Chief of Pathology – Children's:** Beverly Rogers, MD, Professor of Pathology U Texas Southwestern Medical Center at Dallas

### Specific PPRDC Aims

The aims of the PPRDC parallel the aims of the PPRU to:

- Conduct studies of: Bioavailability, Formulations, Drug Metabolism, Pharmacokinetics/ dynamics
- Gather and promote accrual of clinical data for pediatric age-specific labeling of drugs
- Conduct research on novel and innovative approaches in pediatric pharmacology
- Develop and apply pharmacogenomic tools for conducting pharmacology clinical trials
- Develop proteomic tools in clinical studies
- Provide training in clinical and developmental pharmacology

## Faculty Publications (October-December 2004)

**Busti AJ, Bussey HI.** *“The Role of Oral Direct Thrombin Inhibitors in the Treatment of Venous Thromboembolism.”* *Pharmacother* 10/2004.

**Thomas BE, Thekkumkara TJ.** *“Glucose Mediates Transcriptional Repression of the Human Angiotensin Type-I Receptor Gene: Role for a Novel CIS-Acting Element.”* *Mol Biol Cell* 10/2004.

# Faculty Publications (continued from page 4)

**Bhat GJ**, Samikkannu T, **Thomas JJ**, **Thekkumkara TJ** "alpha-thrombin Rapidly Induces Tyrosine Phosphorylation of a Novel, 74-78-kDa Stress Response Protein(s) in Lung Fibroblast Cells." *J Biol Chem*, 11/2004.

Borst SE, Lee Y, Conover CF, **Shek EW**, Bagby GJ. "Neutralization of Tumor Necrosis Factor-Alpha Reverses Insulin Resistance in Skeletal Muscle but not Adipose Tissue." *Am J Physiol Endocrinol Metab* 11/2004.

**Brouse SD**, Wiesehan VG "Evaluation of Bleeding Complications Associated with Glycoprotein IIb/IIIa Inhibitors" *Ann Pharmacother*, 11/2004.

Gopalachar A, **Akins RL**, Davis WR, Siddiqui AA. "Urinary Tract Infection Caused by Aerococcus Viridans, a Case Report." *Med Sci Monit*, 11/2004.

Hawkins BT, **Abbruscato TJ**, Egleton RD, Brown RC, Huber JD, Campos CR, Davis TP. "Nicotine

Increases in vivo Blood-Brain Barrier Permeability and Alters Cerebral Microvascular Tight Junction Protein Distribution." *Brain Res*, 11/2004.

Keller DM, Ogoh S, **Greene S**, Olivencia-Yurvati A, Raven PB. "Inhibition of KATP Channel Activity Augments Baroreflex-Mediated Vasoconstriction in Exercising Human Skeletal Muscle." *J Physiol*, 11/2004.

**Yang T**, **Mustafa F**, **Bai S**, **Ah-san F**. "Pulmonary Delivery of Low Molecular Weight Heparins." *Pharm Res* 11/2004.

**Busti, AJ**. "Additional Antiretroviral and Immunosuppressive Drug-Drug Interactions." *Kidney Int*, 12/2004.

**Busti AJ**, **Hall RG**, Margolis DM. "Atazanavir for the Treatment of Human Immunodeficiency Virus Infection." *Pharmacother* 12/2004.

**Irons BK**, **Tsikouris JP**, Thomas AA. "The Use of Angiotensin Re-

ceptor Blockers in the Treatment of Chronic Heart Failure." *J Cardiovasc Pharmacol*, 12/2004.

**Lockman, PR**, **McAfee JH**, **Geldenhuys WJ**, **Van der Schyf CJ**, **Allen DD**. "Cation Transport Specificity at the Blood-Brain Barrier." *Neurochem Res* 12/2004.

**Vuppugalla R**, **Mehvar R**. "Short-Term Inhibitory Effects of Nitric Oxide on Cytochrome P450-Mediated Drug Metabolism: Time Dependency and Reversibility Profiles in Isolated Perfused Rat Livers." *Drug Metab Dispos*, 12/2004.

Walter A, Korth U, Hilgert M, Hartmann J, Weichel O, Hilgert M, Fassbender K, Schmitt A, **Klein J**. "Glycerophosphocholine is Elevated in Cerebrospinal Fluid of Alzheimer's Patients." *Neurobiol Aging*, 11-12/2004.

Please note: If we missed your publication, we apologize! Please send publication announcements to Ms. Lockman, 806-356-4000, 326 or [melissa.lockman@ttuhsc.edu](mailto:melissa.lockman@ttuhsc.edu).

Please send future publication announcements to **Melissa Lockman, Room 217, 806-356-4000, 326 or [melissa.lockman@ttuhsc.edu](mailto:melissa.lockman@ttuhsc.edu)**

## Research Days 2004

Research Days is an interdisciplinary forum designed to showcase the research activities of the School over the past year. It provides an opportunity for faculty, postdoctoral fellows, and students to exchange research ideas and interests to stimulate interdisciplinary collaborations between departments.

The 2004 Research Days event was held July 29-30. TTUHSC President M. Roy Wilson, MD delivered the keynote speech, and Roderick

Nairn, PhD, Dean of the Graduate School of Biomedical Sciences and Executive Vice President for Academic Affairs, closed the event and presented awards.

Sixty-two posters were presented during Research Days; of these, fifty-three were entered into the competition.

Poster winners were as follows: Pharmacy Student – Ajith Pai; Resident – Timothy Mazzolini,

Pharm.D.; Graduate Student – Jennifer Paulson; Post Doctoral Research Associate - Chinavenmani Velu, Ph.D.; Faculty (Pharmacy Practice) – C.A. (CAB) Bond, Pharm.D.; Faculty (Pharmaceutical Sciences) – Paul Lockman, Ph.D.

We look forward to our next Research Days on

**Thursday and Friday,  
July 28-29, 2005.**



## Guest Speaker for Research Workshop



Thomas P. Davis, Ph.D.

*“It puts the School of Pharmacy and Amarillo on the map in terms of beginning to develop a biotechnology industry base.”*



Jon Weidanz, Ph.D.

Thomas P. Davis, Ph.D., Professor of Pharmacology & Program in Physiology & Neurosciences, University of Arizona College of Medicine, presented a special workshop September 7, 2004. Faculty who attended learned about the “Management of Biomedical

Research Laboratories.” Dr. Davis focused on issues such as research integrity, responsible conduct in research, mentoring, and authorship.

The Office of Research was pleased to bring in this guest speaker and hopes to offer

similar such presentations from visiting scientists in the future.

Please contact Ms. Lockman, 806-356-4000, 326 or [melissa.lockman@ttuhsc.edu](mailto:melissa.lockman@ttuhsc.edu) if you have speaker suggestions for future programs.

## SOP's 1st Spin-Off Commercial Company

Faculty member Jon Weidanz, Ph.D., co-founded the spin-off company Receptor Logic, Ltd. based in part on his research for the TTUHSC School of Pharmacy. Rony Tal and Vaughn Wittman are also instrumental to the new venture, which holds great promise in breast cancer research.

In fiscal year 2004, the company was awarded a three-

year, \$2 million award from the Advanced Technology Program (ATP) of the National Institute of Standards & Technology (NIST). The award will fund development of a cancer profiling and immunotherapy platform targeting breast cancer.

According to Dr. Weidanz, “What it means for the School of Pharmacy is that we can

commercialize research by scientists at the school. In other words, we're competitive nationally for that kind of money. It puts the School of Pharmacy and Amarillo on the map in terms of beginning to develop a biotechnology industry base.”

## New Developments in SOP Research

**Coming Policy on Equipment Usage Fees:** The School of Pharmacy places a high priority on providing superior equipment to School researchers. In the last year, major equipment purchases — such as the confocal microscope and the LC-MS/MS — have been made. The cost of the maintenance contracts for such high-dollar pieces of equipment are significant, however, and the School is attempting to iden-

tify ways in which these contracts can be maintained in future years.

A draft policy is currently under works that will outline an equipment usage fee for the major equipment. These usage fees are not intended to be prohibitory, and new faculty without adequate funding will not be expected to pay exorbitant fees to use needed equipment. The fee structure is instead just one

way to help the School get funding support for the upkeep of research equipment.

The Office of Research urges all investigators submitting new grants to budget for usage fees for equipment like the confocal and LC-MS/MS, as outlined in the new policy. This policy detailing exact rates, etc. is still being developed, but please be looking for future announcements.

# New Faculty Researchers

Eugene W. Shek, Ph.D. has been working for the School of Pharmacy (Pharmaceutical Sciences Department) since August 1, 2004. Dr. Shek joined us from the North Florida/South Georgia Veterans Healthcare System in Gainesville, Florida, where he served as the Research Health Scientist. Prior to that, he served as research faculty at the University of Florida.

Dr. Shek's primary research focus is on understanding the neurohumoral pathways and mechanisms

that are important in regulating the autonomic, cardiovascular, renal, and metabolic functions in aging, obesity, and hypertension.

Currently, Dr. Shek is investigating his hypothesis that in aged animals, there may be resistance to the natriuresis/diuresis and/or vasorelaxation effects of leptin on the kidney and/or blood vessels, respectively, with preservation of the stimulatory effects of leptin on the sympathetic nervous system promoting hypertension. His studies

are primarily directed towards determining the physiologic role of leptin on blood pressure regulation in aging. His laboratory is focused on understanding the etiology of age-related increase in blood pressure, thus enabling him to design and to develop new therapeutic strategies to prevent or reverse the age-related increase in blood pressure in aged rats and eventually in older people.



***“Dr. Shek’s primary research focus is on understanding the neurohumoral pathways and mechanisms that are important in regulating the autonomic, cardiovascular, renal, and metabolic functions in aging, obesity, and hypertension.”***

## Upcoming Events

The Office of Research is proud to offer programming year-round. The following events are coming to Amarillo soon. Please mark your calendars and plan to attend!

- 8th Annual Wendy & Stanley Marsh 3 Endowed Lectureship in Pharmacology & Neurochemistry of Substance Abuse/Addiction. Wednesday, March 15–Friday, March 17, 2005.

Thomas R. Kosten, M.D., Deputy Chief of Psychiatry Research, VA Connecticut Healthcare System, Professor, Department of Medicine & Yale Graduate School, Investigative Medicine Program, West Haven, Connecticut. Dr. Kosten will be lecturing on “Neurobiology of Stimulant Dependence” and offering a

Grand Rounds entitled “Pharmacotherapy of Substance Dependence.”

- 4th Annual Research Days, Thursday, July 28–Friday, July 29.
- This semester, the Research Seminar Series is being offered from 12-1 p.m. on every last Monday of the month.

## Upcoming NIH Deadlines

Institutional National Research Service Awards—Cycle II May 10; Cycle III September 10.

New Research Grant, Conferences, FIRST, and Research Career Awards. ALL Program Project and Center Grants—Cycle I February 1; Cycle II June 1; Cycle III October 1.

Competing Continuation, Supplemental, and Revised Grants—Cycle I March 1; Cycle II July 1; Cycle III November 1.

All AIDS-Related Grants—Cycle I May 1; Cycle II September 1; Cycle III January 2.

Scientific Merit Review—Cycle I June–July; Cycle II October–November; Cycle III

February–March.

Advisory Council Review—Cycle I September–October; Cycle II January–February; Cycle III May–June.

Earliest Project Starting Date—Cycle I December; Cycle II April; Cycle III July.

**OFFICE OF RESEARCH**

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