



A Quarterly Report of the Vascular Biology Center of Excellence

## Vascular Biology Turns Out in Full Force to Benefit Heart Research in the Mid South



Staff and students from the Vascular Biology Center of Excellence participated in the American Heart Association's Ninth Annual Heart Walk to raise money for research and education in the Mid South. This is the second year for the 26 Vascular Biology walkers who joined the UTHSC group of 300 to complete the three-mile walk through downtown Memphis.

The American Heart Association is the nation's largest voluntary health agency fighting heart disease, stroke and other cardiovascular diseases. The mission of the National American Heart Association is to reduce disability and death from cardiovascular disease and stroke. Its goal is to reduce coronary heart dis-

ease and stroke risk by 25% before the year 2010. To accomplish this goal, the AHA sponsors special events across the country each year. In 2001-2002, these events generated approximately \$183 million of the total \$532.5 million raised by the AHA that year.

The 2002 Heart Walk realized a record number of walkers across the country, a total of 750,000 people, who raised 68.3 million dollars. Many of these walkers participated in remembrance of the victims of the September 11 tragedy.

Last year alone, the AHA awarded \$134 million to investigators across the country to fund research initiatives related to heart disease and stroke. This

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is in addition to the \$213 million it invests in public health education and professional education and training.

Faculty and students on the UTSHC campus who are recipients of this funding include: Lisa K. Jennings, Ph.D., Celia Longhurst, Ph.D., Xin Zhang, M.D., Ph.D., Jonathan H. Jaggar, Ph.D., Kafait Malik, Ph.D., D.Sc., Daniel Baker, Ph.D., Ziyun Du, Ph.D., Polly A. Hoffman, Ph.D., Yao Sun, M.D., Ph.D., Suleiman Bahouth, Ph.D., Keith English, M.D., Mohammad Kiani, Ph.D., Roderick Hori, Ph.D., Don-

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## New Faculty Member Joins the Vascular Biology Center of Excellence

**T**he Vascular Biology Center welcomes new faculty member Rennolds Ostrom, Ph.D. to the University of Tennessee Health Science Center.

Dr. Ostrom is an Assistant Professor in the Department of Pharmacology with a joint appointment in the Vascular Biology Center of Excellence. He joins the UTHSC from The University of California, San Diego where he was an Assistant Project Pharmacologist. Dr. Ostrom brings with him a long list of accomplishments which includes a grant funded by the National Institutes of Health (NIH).

Dr. Ostrom's lab seeks to understand how cells "pre-arrange" multiple signaling components in GPCR signal

transduction cascades. His focus is on caveolae and lipid rafts as centers for such organization. "Our long-term goal is to understand how such compartmentation impacts cellular response in a physiological setting."

Using molecular cloning, expression of cloned signaling proteins, and a variety of cell biological and biochemical approaches,

Dr. Ostrom will examine signaling mechanisms of G protein-coupled receptors. He is interested in the organization of signaling microdomains in the plasma membrane, especially in lipid raft/caveolin-rich regions, in which various receptors, G-proteins and effectors, particularly certain isoforms of adenylyl cyclase, localize. Dr. Ostrom seeks to elucidate the impact of compart-



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mentation on cellular responses with the goal of developing novel gene therapy strategies to modulate cellular responses through changes in expression of limiting components in the signaling pathways. Adenylyl cyclase is one such limiting component. Currently, he studies cardiac myocytes and fibroblasts, airway smooth muscle cells and pulmonary fibroblasts.

In other studies, Dr. Ostrom is accessing the release of nucleotides and activation of P2Y receptors in

various cultured cell lines. He has found that virtually all cells are capable of releasing ATP in response to mild mechanical stimuli or other forces that cause membrane deformation. The mechanism of this release appears to be due, in part, to membrane channel conductance. The goal is to understand the physiological role of the autocrine/paracrine signaling that is initiated by cellular release of ATP.

## Research Grants Awarded to VBCE Collaborating Investigators

Xin A. Zhang, M.D., Ph.D. University of Tennessee Cancer Institute. Pilot Grant. Identification of the Functional Partners of Cancer Metastasis Suppressor KAI1/CD82. 10/01/03-09/30/04. 40,000.

Yi Lu, Ph.D. Elsa Pardee Foundation. P16 Suppresses Breast Cancer Metastasis by Inhibiting Angiogenesis. 08/1/03-07/31/05. 130,000.

Xin Zhang, M.D., Ph.D. Department of Defense. Idea Development Award. EW12/PGRL, a partner of prostate cancer metastasis suppressor KAI1/CD82. 01/01/04-12/31/06. 507,664.

## Medical Students Devote Their Summer to the Lab

**E**very summer the Vascular Biology Center sponsors UTHSC Medical students to work with research and clinical preceptors on the UTHSC campus. The internships are paid through grants awarded to the Vascular Biology Center by the American Heart Association (AHA) and the American Society of Hematology (ASH).

Three outstanding first year medical students from the UTHSC interned in laboratories this past summer honing their research knowledge and skills. The students included: James Friedenstein, ASH Fellow and Michael Steiner and Brock Lanier, AHA Fellows.

Michael Steiner worked with Xin Zhang, M.D., Ph.D. on a project designed to elucidate the function of a newly identified protein called ICAP—1a. Steiner helped perform RNA interference (RNAi) which is a relatively new technique that allows downregulation of a specific protein by transfecting cells with short RNA duplexes of the protein to be downregulated. After a few protocol adjustments, he was able to successfully downregulate the expression of ICAP-1a in cos-7 cells. “The experiments that I performed in Dr. Zhang’s lab helped me to gain a greater understanding of basic science and respect for the work that takes place in the laboratories in the medical field.”

James Friedenstein interned in Dr. Lisa K. Jennings’ lab designing a platelet adhesion assay to examine the effects of platelet agonists and platelet receptor antagonists on platelet adherence to fibrinogen and fibronectin. The assay is similar in nature to a direct ELISA and can be used as a template to compare future inhibitors and agonists that play a role in the physiology and pathophysiology of platelet function. The assay represents a relatively simple in-vitro technique for assessing platelet adhesion and the factors that play into platelet function. The long-term goal of this work is to identify new targets for antiplatelet therapies that will be used in the treatment of acute coronary syndromes and acute stroke.

Brock Lanier assisted Dr. Catherine Cagiannos, Trauma Attending, in investigating the new application of a drug that has been used as an immunosuppressant for some time. It is thought that when used locally instead of systemically this drug can decrease the neointimal hyperplasia associated with vascular grafts. Brock assisted with all aspects of the study including obtaining animal certification, study design, animal care and implanting the vascular grafts. Results, which appeared promising, are currently still pending. If the study is successful Brock believes that this technique has great potential for application in humans.

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The American Heart Association will host a Town Hall Meeting on November 20 at 6:30 p.m. at Christian Brothers High School, 5900 Walnut Grove Rd. The purpose for the meeting is to bring together community leaders and policy makers to dialogue issues related to Cardiovascular Disease and Stroke in Memphis and Shelby County.

Health policy issues to be discussed include childhood obesity, physical activity and vending machines in schools, emergency medical services, 9-1-1 issues, tobacco prevention and control, the proposed tobacco excise tax, clean indoor air and repeal of preemption, access to CPR and automated external defibrillators and public policy regarding non-profits.

To RSVP or for more information contact Julie Griffin, American Heart Association Tennessee Advocacy Manager at (615) 340-4114 or email [julie.griffin@heart.org](mailto:julie.griffin@heart.org).

## Published Manuscripts by VBCE Collaborating Faculty

Angiotensin II enhances adenylyl cyclase signaling via Ca<sup>2+</sup>/calmodulin. Gq-Gs cross-talk regulates collagen production in cardiac fibroblasts. Ostrom R, Naugle JE, Gregorian C, Hase M, Swaney JS, Insel PA, Brunton LL and Meszaros JG. *J Biol Chem* 278 (27):24461-8, 2003.

Hypertonic stress co-stimulates T Cell IL-2 expression through a Mechanism that involves ATP release, P2 receptor activation of p38 MAP kinase. Loomis WH, Namiki S, Ostrom RS, Insel PA, Junger WG. *J Biol Chem* 278(7):4590-6, 2003.

Subtype-Selective Antagonists of Lysophosphatidic Acid Receptors Inhibit Platelet Activation Triggered by the Lipid Core of Atherosclerotic Plaques. Rother E, Brandl R, Baker DL, Goyal P, Gebhard H, Tigyi G and Siess W. *Circulation* 108:741-747, 2003.

Emerging Trends in Oral Delivery of Peptide and Protein Drugs. Mahato RI, Narang AS, Thoma L and Miller DD. *Critical Reviews in Therapeutic Drug Carrier Systems* 20(2&3):153-214, 2003.



## TAM Cardiovascular Clinical Research Consortium Notes

The TAM network recently completed the TAM3 study, a comparison of the pharmacodynamic effects of bivalirudin and eptifibatid in patients undergoing balloon angioplasty. The study evaluated the different drug treatments' effects on platelet aggregation in addition to various measures of thrombin generation and clot lysis.

Dr. Larry Spiotta, in conjunction with his study coordinator Kay Sims, RN, MSN, served as the

clinical principal investigator on the study. Results of this study are currently being analyzed, and will be published within the coming months.

Tests that have recently been developed and utilized in the UTHSC core lab include soluble CD40 ligand, Rantes, IL-6, D-dimer, fibrinopeptide A and Prothrombin fragment 1.2.

The UT Core Lab of the TAM Network is currently involved in

several new trials. If you are interested in participating in clinical trials, or if you have an idea for a trial and you would like help in the design or coordination please contact Mary V. Jacoski at 901-448-1597, or email at [mjacoski@utmem.edu](mailto:mjacoski@utmem.edu).

For more information about the Vascular Biology Center of Excellence call (901) 448-4350 or visit us on the Web at [www.utmem.edu/vascular](http://www.utmem.edu/vascular)



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