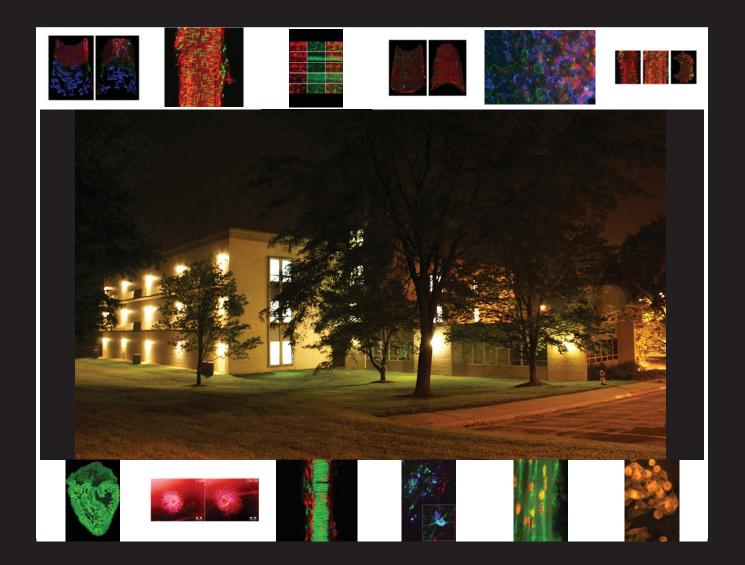


# Dalton Cardiovascular Research Center 2012



Front picture is a nighttime shot of Dalton Cardiovascular Research Center. Images at top and bottom of picture are from Dalton Investigators.

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#### FROM THE DIRECTOR

The Dalton Cardiovascular Research Center (DCRC) supports the objectives of the University of Missouri in its mission of teaching, research and service. Yet it is unique in its commitment to interdisciplinary collaborative research and teaching among various colleges, schools and departments across the Columbia campus. Under the auspices of DCRC, scientists from the fields of biochemistry, biological engineering, biological sciences, biomedical sciences, electrical engineering, medicine, pharmacology, physiology, physics, and veterinary medicine and surgery all come together and apply their particular expertise to research problems.

Our commitment to collaboration is grounded in the belief that interactions among scientists of diverse backgrounds will lead to multidisciplinary research producing meaningful, far-reaching results. Research programs at DCRC include investigations into cardiac functions, cystic fibrosis, exercise, kidney failure, membrane transport, muscular dystrophy, neurohumoral control of the circulation, shock, vascular wall biology, diabetes, hypertension, biomedical engineering, protein-protein interactions, and tumor angiogenesis. Because the mission of DCRC is to promote interaction and collaboration, no single group completely defines the research activity of its members.

The center is committed to excellence in cardiovascular research and in the education of students and fellows. Our investigators provide service to the University, the State of Missouri, and the nation through memberships on committees, peer review panels and editorial boards of scientific journals. During the period of this report, our investigators have \$27.3 million in active research funding, have published 242 manuscripts in nationally recognized journals and books and gave 83 invited presentations.

The Dalton Cardiovascular Research Center is accredited by both the American Association for the Advancement of Laboratory Animal Care and the American Association of Laboratory Animal Sciences.

#### **DCRC** Committees

The Internal Advisory Committee:

Dr. Gerald A. Meininger, Chair Dr. Mike Hill Dr. Alan Jones Dr. Ed Blaine Dr. Virginia Huxley Dr. Ron Terjung Dr. Kevin Gillis

The Appointment and Promotions Committee:

Dr. Salman M. Hyder, Chair Dr. Kevin Gillis Dr. Tzyh-Chang Hwang Dr. Luis A. Martinez-Lemus Dr. David Kline

Scientific Program Committee:

Dr. Michael A. Hill, Chair Dr. Salman M. Hyder Dr. Eileen M. Hasser Dr. Kevin Gillis

Core Facilities Committee:

Dr. Luis A. Martinez-Lemus, Co-Chair Dr. Tzyh-Chang Hwang, Co-Chair Dr. Luis Polo-Parada Dr. Kevin Gillis Dr. Lane Clarke

Safety Committee

Dr. Christopher Baines, Chair Dr. Shinghua Ding Dr. Maike Krenz Dr. Min Li Dr. Luis Martinez-Lemus Laura McClaskey

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#### Interdisciplinary Research Interests Groups

Biomedical Engineering Investigators: M.J. Davis, Ding, Gillis, Gu, Hill, Huxley, Hwang, Jones, Meininger, Milanick, Polo-Parada, Segal, Zou, Sun

Cystic Fibrosis Investigators: Clarke, Hwang, Milanick, Soma, Zou, Bompadre

Exercise/Inactivity Including Atherosclerosis, Muscle Biology, Obesity, Type II Diabetes, and Vascular Biology

Investigators: Booth, Bowles, Hasser, Hill, Huxley, Jones, Korthuis, Laughlin, Martinez-Lemus, Meininger, Polo-Parada, Rubin, Segal, Soma, Terjung, Sun, Fay, Sowers

Membrane Transport Investigators: Clarke, Gillis, Gu, Huxley, Hwang, Milanick, Polo-Parada, Rovetto, Rubin, Zou, Silvia Bompadre

Microcirculation

Investigators: M.J. Davis, Ding, Hill, Huxley, Korthuis, Laughlin, Martinez-Lemus, Meininger, Segal, Sun

Neurohumoral Control of the Circulation Including Ageing, Hypertension, Heart Failure, Respiration and Salt and Water Homeostasis Investigators: Blaine, Ding, Fadel, Hasser, Heesch, Kline, Meininger, Milanick, Segal, Kvochina

Tumor Angiogenesis Investigators: G.E. Davis, Hyder, Liang

Cardiac Muscle, Development & Disease Investigators: Baines, Krenz, Meininger, Sun, Polo-Parada, Rubin

#### Director



Gerald A. Meininger

Office: 138 DCRC Phone: 573-882-9662 E-mail: meiningerg@missouri.edu

Education: PhD University of Missouri-Columbia, MS & BS Central Michigan University

Appointments:Director Dalton Cardiovascular Research Center Margaret Proctor Mulligan Professor in Medical Research Professor, Department of Medical Pharmacology and Physiology Adjunct Professor, Department of Biomedical Sciences Adjunct Professor, Department of Physics

#### Research

Research interests in my laboratory have been focused on vascular physiology and cell biology, with an emphasis on the microvasculature. Currently active areas of research include: 1.) Cell adhesion, extracellular matrix and cell signaling in the vascular wall; 2.) Mechanotransduction in vascular cells; 3.) Regulation of vascular and cardiac responses to tissue injury by extracellular matrix derived signals; 4.) Cellular and molecular mechanisms responsible for mechanotransduction; 5.) Mechanisms of vascular remodeling; 6.) Mechanisms responsible for the myogenic properties of vascular smooth muscle; 7.) Application of fluorescence microscopy and 3D-image analysis for studies of microvascular cell biology and the cyto-architecture and function of the microvessel wall; and 8.) Mechanisms of blood flow autoregulation.

Laboratory models include studies of both the intact microcirculation and of isolated arterioles, freshly dispersed or cultured vascular smooth muscle cells, endothelial cells and cardiac muscle cells. Examples of technical approaches include pharmacology of the intact microvasculature and isolated microvessels; ability to manipulate pressure and flow in isolated microvessels; vessel culture and transfection; immuno-cytochemistry of the microvessel wall and isolated cells; three dimensional fluorescence imaging using confocal, multiphoton or wide field microscopy in combination with deconvolution; atomic force microscopy combined with fluorescence microscopy (TIRF and FRET), and software development for high through-put analysis and display of atomic force microscopy force data.

An emphasis over the last several years has been to understand the role of the extracellular matrix, adhesion molecules and the cytoskeleton in regulation of vascular and cardiac cells, especially in the control of contractile function. A fundamental aim of this work has been to determine to what extent this matrix-adhesion-cytoskeletal axis may be involved in mechanotransduction phenomena that underlie the vascular myogenic response, flow-dependent responses of the endothelium and vascular remodeling. Advances in hybridizing atomic force microscopy with fluorescence microscopy are permitting higher through-put evaluation of cell surface receptors and their interactions with specific ligands.

Our future plans include continuing to study the role of the extracellular matrix and cell adhesion molecules in the regulation of vascular and cardiac cell function. We are extending our studies of mechanotransduction down to the level of single molecular interactions between integrins and extracellular matrix molecules, as well as to the mechanical dynamics of single focal contacts.

#### **Associate Director**



Michael A. Hill

Office: 133A DCRC Phone: 573-884-4601 E-mail: hillmi@missouri.edu

Education: PhD & MS University of Melbourne

Appointment: Professor, Department of Medical Pharmacology and Physiology; Associate Director, Dalton Cardiovascular Research Center

#### Research

Our laboratory has a principal interest in understanding the signaling mechanisms that underlie the vasoconstrictor response of an arteriole following an acute rise in intraluminal pressure (myogenic response). Our studies have examined the roles of a number of vascular smooth muscle signaling molecules including various kinases and intra-cellular Ca2+. More recently these studies have been extended to include approaches aimed at determining the relationships between pressure induced changes in smooth muscle membrane potential and the resulting signaling events that ultimately lead to the contractile response.

In addition to basic studies on myogenic signaling, we are also studying how myogenic tone interacts with other vasoregulatory mechanisms (principally, endothelial-dependent dilation) and how myogenic response is altered in diabetes mellitus.

# **Principal Investigators**



Christopher P. Baines

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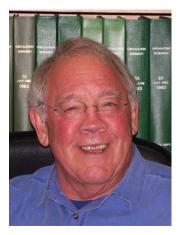
Education: B.Sc. University of Bath, Great Britain PhD University of South Alabama

Appointment: Assistant Professor, Department of Biomedical Sciences

#### Research

Mitochondrial dysfunction is often an underlying cause of myocardial disease. In particular, cardiac pathologies such as ischemia/reperfusion injury, heart failure, diabetic cardiomyopathy, anti-cancer agent-induced cardiotoxicity, etc., are associated with rapid and dramatic increases in mitochondrial permeability.

These changes in permeability lead to ATP depletion, excessive production of reactive oxygen species, and ultimately swelling and rupture of the organelle, thereby instigating a molecular chain of events that leads to cardiomyocyte death. The long-range goal of the lab is to understand how specific mechanisms of mito-chondrial-driven death can be targeted for the prevention of myocardial disease.



Edward H. Blaine

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Education: PhD, MA & AB University of Missouri-Columbia

Appointment: Professor, Department of Medical Pharmacology and Physiology

#### Research

Currently, the primary focus of my laboratory is the underlying cause of hypertension that is associated with an adverse uterine environment. It is well documented that offspring of mothers who have undergone a variety of stressful circumstances during pregnancy may give birth to offspring who suffer from conditions such as hypertension, type II diabetes, and metabolic syndrome as adults. This phenomenon is known as fetal programming or the fetal origin of adult disease. One characteristic of these susceptible offspring is a reduced nephron number and several investigators have suggested that the lack of a full nephron complement is the underlying cause of the adult onset hypertension. How the reduction in nephron number causes or contributes to hypertension is not known. We are presently working on the hypothesis that there is a differential loss of nephrons. Based on inherent heterogeneity, loss of more "salt-losing" nephrons and retention of more "salt-saving nephrons" results in an overall tendency for the kidney of these offspring to retain sodium and, therefore, be more susceptible to hypertension as adults.

Our work involves whole animal studies which detail changes in the kidney's ability to excrete sodium and whether changes in ability to excrete a sodium load is a function of changes in glomerular filtration, sodium reabsorption, or both. These studies are conducted in conscious, freely moving animals to obtain data that is not compromised by anesthesia or restraint. We are also studying changes in renal morphology, especially distribution of the loops of Henle, using immunohistochemistry techniques.

We continue our interest in neuroendocrine regulation of fluid balance and cardiovascular function, with emphasis on hypertension and heart failure. We are particularly interested in the actions of angiotensin II and vasopressin on brain cardiovascular centers. Our recent work has demonstrated two distinct actions of angiotensin on blood pressure regulation: acutely, angiotensin has its primary effect directly on vascular smooth muscle, while chronically, the hypertensive effects of angiotensin are mediated through activation of central nervous system pathways. Not only are the circumventricular organs important, but other brain areas are activated during acute and chronic angiotensin infusion. Our next step is to map the distribution of heightened nervous system activity in the peripheral vascular beds that is associated with chronic angiotensin hypertension. We are also investigating receptor regulation and post receptor signaling associated with angiotensin infusion.

We are also interested in the role of the renin-angiotensin system in diabetic nephropathy and the mechanism by which drugs that inhibit this system are effective in preventing renal damage. 11



Silvia G. Bompadre

Office Location: 359 Office Phone: 573-884-9474 E-mail: BompadreS@missouri.edu

Education: PhD in Physics from University of Washington

Appointment: Assistant Professor, Department of Physics

#### Research

Research in my laboratory focuses on understanding how the CFTR (Cystic Fibrosis Transmembrane conductance Regulator) chloride channel works at the molecular level and how mutations in CFTR cause defective functions. The final goal is to apply the acquired knowledge in therapeutic design for cystic fibrosis . Combining electrophysiology and fluorescence spectroscopy techniques with molecular biology and molecular modeling, studies are set to study CFTR's structure/function which in turn can help design specific compounds for specific disease-associated mutants.



Frank W. Booth

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Education: PhD University of Iowa, BS Denison University

Appointments:Professor, Department of Biomedical Sciences Adjunct Professor, Department of Medical Pharmacology and Physiology

Research

Research interests in my laboratory currently focus on two areas.

The first question being posed is: what are the aging mechanisms of decreased proliferation and differentiation of satellite cells, the adult stem cells in skeletal muscle? Experiments are concerned with regulation of p21Cip1/WAF1, p27Kip1, p53, FoxO3a, Sirt1 and other proteins as they regulate proliferation and differentiation.

The second question being posed is: by what mechanisms does physical inactivity trigger metabolic dysfunction? When rats that have voluntarily ran in wheels cease running, specific intra-peritoneal fat masses increase, insulin sensitivity in specific skeletal muscles falls, and enhanced vasodilatation of the aorta is lost. Research is under way to determine molecules responsible for these inactivity effects.



#### Doug Bowles

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Education: PhD University of Texas-Austin

Appointments:Associate Director of the National Center for Gender Physiology Professor, Department of Biomedical Sciences Adjunct Professor, Medical Pharmacology and Physiology

#### Research

The goal of our lab's research is to understand how ion channels affect the role of coronary smooth muscle (CSM) in vascular pathology, i.e. atherosclerosis and post-angioplasty restenosis. Our major research question is how physical activity/exercise and sex hormones alter ion channel function in coronary smooth muscle to affect the onset and progression of coronary vascular disease.

Currently, the major focus is on two distinct channels, the intermediate-conductance, calcium-activated K channel (IKCa1) and channels underlying store-operated calcium entry, most likely TRPC channels. We are interested on these as they are upregulated during CSM phenotype modulation that occurs during vascular injury. Our lab strives for a molecule to animal approach using cultured and native cells, intact vessels and in vivo models. The primary model is the swine, as its coronary physiology, anatomy and gene expression profile is most similar to human. Experimental techniques include whole-cell and patch clamp, fluorescent based calcium imaging, isometric vessel recordings, cannulated microvessels, immunoblot, real-time RT-PCR, laser capture microdissection and molecular biology (promoter/reporter constructs, etc) to examine gene regulation by ion channels.

Lastly, we have a state-of-the-art, fully digital cath lab exclusively for large animal (e.g. pig) research. With this we can do angiography, intravascular ultrasound, intracoronary flow and pressure. We can also induce coronary injury/ restenosis with balloons and stents. Our goal is to use this to provide direct, in vivo, "translational" endpoints to our cellular/genetic studies.

The results of these experiments will provide novel mechanisms by which a sedentary lifestyle and hormonal status impacts cardiovascular health and well being as well as define potential therapeutic targets for the treatment and prevention of cardiovascular diseases.



Lane Clarke

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Education: PhD North Carolina State University, DVM, MS & AB University of Missouri,-Columbia

Appointments: Associate Professor, Department of Physical Medicine and Rehabilitation. Professor, Department of Biomedical Sciences

#### Research

Our laboratory investigates electrolyte and nutrient transport across epithelial tissues (airway, reproductive and intestinal) during health and disease. The major focus is to understand the role of the cystic fibrosis transmembrane conductance regulator protein (CFTR) in the regulation of acidbase and nutrient transport across alimentary epithelia. CFTR is the protein product of the gene that is mutated in cystic fibrosis (CF) and normally functions in epithelial cells as a cyclic AMP-regulated anion channel. Present studies investigate the role of anion exchange proteins that work with CFTR in promoting bicarbonate transport or that work with Na+ transport proteins for NaCl absorption across intestinal epithelium. Most studies involve either measurements of acidbase or nutrient transporter activity using fluorescent dyes to monitor intracellular pH by microfluorimetry or electrophysiological recordings in Ussing chambers of native mucosa and cell lines derived from gene-targeted ("knockout") mice. In addition to the cystic fibrosis mice, the laboratory maintains colonies of mice with gene-targeted deletion of other acid-base transporting proteins, including Na+/H+ exchangers, Cl-/HCO3- exchangers and Na+/K+/2Cl- cotransporters. Molecular studies in the laboratory involve the measurements of gene expression in the mice (quantitative real-time PCR, Northern blots and microarrays) and cloning of specific murine transporters for functional expression studies in heterologous cell systems. In addition to the above methods, other techniques employed in the laboratory include cell culture, retroviral and adenoviral gene transfer, pH stat/isotopic flux studies, laser capture microdissection and PCR based genotyping.



George E. Davis

Office: MA415 HSC Phone: 573-882-5474 E-mail: davisgeo@missouri.edu

Education: PhD, MD University of California-San Diego, BS Arizona State University

Appointment: Professor, Department of Medical Pharmacology and Physiology

#### Research

My laboratory focuses on the following questions relevant to angiogenesis, wound repair and cancer research: How do endothelial cells form cell-lined tube structures with lumens in three-dimensional (3D) extracellular matrices?

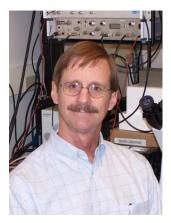
How do endothelial cells and other cell types such as tumor cells invade 3D matrices?

To what extent do endothelial cells directly or indirectly play a role in tumor invasion and metastasis? What molecular events control the process of vascular regression?

How do vascular supporting cells, such as pericytes, stabilize vascular tubes?

How do distinct matrix metalloproteinases and their inhibitors control the processes of vascular morphogenesis versus regression in 3D matrices?

How do extracellular matrix fragments (matricryptins) regulate vascular morphogenesis versus regression in normal versus diseased states (such as diabetes)?



Michael J. Davis

Office: MA415F Lab: 256 DCRC Phone: 573-882-5181 Email: davismj@missouri.edu

Education: PhD University of Nebraska BS University of California, Davis

Appointments: Associate Department Head and Professor, Department of Medical Pharmacology and Physiology

#### Research

My general area of research is on the mechanisms of mechano-transduction by blood vessels: How does the smooth muscle layer of a blood vessel detect changes in pressure? What cellular proteins and signaling pathways are involved in this process? Currently, our focus is on a signaling axis linking the extracellular matrix with integrin receptors, the cytoskeleton, and ion channels. We focus on two ion channels: the L-type, voltage-gated calcium channel and the large-conductance, calcium-activated (BK) potassium channel that are acutely regulated by integrin signaling in vascular cells.

The experimental approaches used in my laboratory include isolated, perfused microvessel methods and singlecell electrophysiology. We combine these with a variety of imaging methods, including confocal, atomic force, and TIRF microscopy. We also use molecular analyses, such as site-directed mutagenesis and co-immunoprecipitation, to identify and test which integrin-associated proteins are involved in modulation of ionic channels. A related research interest is the role that collecting lymphatic vessels play in the regulation of extracellular fluid balance.

These vessels exhibit spontaneous, phasic contractile behavior that propels lymph centrally. Lymphatic function is dramatically different than that of arterioles and venules and they express isoforms of contractile proteins that suggest lymphatic smooth muscle is a hybrid between cardiac muscle and vascular smooth muscle. We investigate their mechanical properties using servo-controlled systems to study isolated lymphatics from rats and mice under isobaric, isometric and isotonic conditions.



#### Shinghua Ding

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Education: PhD & MS State University of New York, BS Zhejiang University of Technology

Appointment: Assistant Professor, Department of Biological Engineering

#### Research

Cerebral ischemia (ischemic stroke) is a leading neural disorder that causes brain damage and human death, and has a major impact on public health. Though various mechanisms by which ischemia induce brain damage have been proposed, clinically there is limited therapeutic approach that is effective to brain recovery after ischemia. Therefore, my research generally focuses on seeking and identifying new mechanisms that can reduce brain injury and improving long-term outcomes after stroke. My research focuses on two distinct but related areas: 1) Glial function and role in stroke; 2) Neuronal mechanisms in brain protection in stroke. We use mice (in vivo) and primary cultured cells (in vitro) including neurons and astrocytes isolated from mouse brains as experimental preparations. We use both in vivo and in vitro ischemic models for ischemic study. Approaches including molecular biology, fluorescent imaging including 2-in vivo two-photon (2-P) microscopy, confocal and epi-fluorescent microscopy, biochemistry, electrophysiology, cell culture, and immunocytochemistry are integrated in our research.



Paul J. Fadel

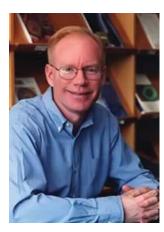
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Education: PhD University of North Texas, MS Northeastern University, Health Science Center, BS Brooklyn College

Appointments: Associate Professor, Department of Medical Pharmacology and Physiology

#### Research

Our laboratory's research focus entails the investigation of neural cardiovascular control at rest and during exercise in humans with a specific emphasis on the sympathetic branch of the autonomic nervous system. Ongoing studies involve assessing sympathetic responses during various physiological manipulations including isometric and aerobic forms of exercise, lower body negative pressure to simulate the effect of gravity when one stands up, and infusions of pharmacological agents. Studies are performed in normal healthy subjects as well as in patients with various pathophysiological conditions such as heart failure and hypertension. Our laboratory obtains direct measures of sympathetic neural firing using the technique of microneurography. This measurement allows for the assessment of moment-to-moment as well as long-term changes in sympathetic nerve activity. Also, with the application of partial autospectral and time series analyses to muscle sympathetic neurograms we are beginning to investigate the central origin(s) and pattern(s) of sympathetic discharge in humans. Our current research focus is on the neural mechanisms that contribute to exercise-induced sympathoexcitation as well as the peripheral modulators of sympathetically medicated vasoconstriction in contracting skeletal muscle with a particular emphasis on the potential roles of free radicals and changes in nitric oxide signaling in altering these responses. Considering the continually increasing population of elderly individuals, we are beginning to examine agerelated alterations in neural cardiovascular control during exercise. Research in this area has been limited and is extremely important considering that an exaggerated blood pressure response to exercise increases the risk for mortality in otherwise healthy adults.



William P. Fay, M.D.

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Education: BS, MD, University of Illinois

Appointments: Professor of Internal Medicine and Medical Pharmacology & Physiology

**Research Interests** 

- Role of leukocyte-derived tissue factor in thrombosis
- Role of plasminogen activator inhibitor-1 (PAI-1) in the proliferative response to vascular injury
- Mechanisms by which C-reactive protein (CRP) modulates thrombosis
- Role of heme oxygenase-1 in thrombosis
- Regulation of fibrinolysis by thrombin activatable fibrinolysis inhibitor (TAFI)
- Techniques / Methodology:
- Mouse gene targeting
- Rodent models of human vascular disease
- Structure-function studies of blood coagulation proteins
- Thrombosis models

#### **Research** Description

Our research laboratory focuses on the roles of the blood coagulation and fibrinolytic systems in vascular disease. We are interested in the molecular processes that determine acute thrombus formation after vascular injury, as well as those that regulate subsequent thrombolysis. We also are interested in how components of the blood clotting and fibrinolytic systems contribute to the pathogenesis of chronic vascular disorders, such as atherosclerosis and restenosis after percutaneous coronary interventions. We study these issues by a variety of experimental approaches, ranging from in vitro studies with purified proteins to intact animal studies. In particular, we rely heavily on murine models of vascular injury and thrombosis, since they enable us to examine the impact of specific genes on complex biologic processes within the living animal.



Gabor Forgacs

George H. Vineyard Professor office: 420 Physics Building phone: 573-882-3036 email: forgacsg@missouri.edu

education: Ph.D., Eotvos Roland University Budapest, 1978

Appointment: Departments of Physics and Astronomy

#### **Research Interests**

My research is focused on the physical mechanisms in cell and development biology. In particular we study (both experimentally and by computer modeling) the biomechanical (i.e. viscoelastic) properties of cells and tissues and their relevance to morphogenetic shape transformations. Current activity is concentrated on the application of these physical mechanisms to "organ printing" a fundamentally new approach to tissue engineering, whereby, spherical cell aggregates with composition appropriate for the particular organ (the bioink) are delivered (with a modified ink-jet printer) according to the organ's anatomical blueprint into biocompatible scaffolding gels (the paper).



Shubra Gangopadhyay Office Location: 243 Engineering Building West Office Phone: 573-882-4070 Email: GangopadhyayS@missouri.edu

Education: PhD in physics, Indian Institute of Technology, Kharagpur MSc in physics, Jabalpur University, Jabalpur BSc, Jabalpur University, Jabalpur

Appointment: LaPierre Chair and Joint Professor, Departments of Electrical Engineering, Biological Engineering and Physics

#### Research

Gangopadhyay, an acclaimed researcher in the fields of material science and physics, heads the group. The group has set up a high class research facility — the first of its kind in Missouri — with plans to upgrade and expand the facilities over the next two years.

#### **Research** Description

The Gangopadhyay Research Group is an electrical engineering and materials science research facility at the University of Missouri Columbia's College of Engineering and is associated with the International Center for Nano/Micro Systems and Nanotechnology. It is dedicated to expanding the realm of science and technology through optimization of existing techniques and exploration of new dimensions of knowledge. The group's research includes discovering, integrating, and optimizing new materials, processing methods, and character-ization techniques. By promoting an interdisciplinary approach, our unique and modern research facility was designed to train, educate and prepare students to join and lead the workforce in innovative solutions to scientific challenges



#### Kevin D. Gillis

Office: 222B DCRC Phone: 573-884-8805 E-mail: gillisk@missouri.edu

Education: DSc, MSEE & BSEE Washington State University, BA St. Louis University

Appointment: Professor Biological Engineering, Professor Medical Pharmacology and Physiology

#### Research

My main area of interest is understanding the final steps of cell secretion and the modulation of these steps by protein kinases. We are presently using multiple biophysical approaches to assay dynamic aspects of secretion from individual adrenal chromaffin cells. We have found that activation of protein kinase C (PKC) enhances depolarization-induced exocytosis many fold while actually decreasing the calcium current which triggers release. Using several different protocols, we have shown that PKC enhances secretion by increasing the size of the "readily releasable pool" of secretory granules. On the other hand, our experiments with caged Ca2+ show that PKC does not shift the Ca2+-sensitivity of the final step in secretion. Since protein kinases play a central role in regulating both secretion of hormones and release of neurotransmitter at synapses, the results of our research have an impact on understanding such diverse phenomena as the "fight or flight" response and the formation of short-term memory. In the future, we plan on further characterizing the kinetic steps modulated by protein kinases. For example, does PKC increase the size of the readily releasable pool by increasing the "filling" rate or does it stabilize vesicles in the "readily releasable" state? We also plan to examine the targets of kinase action at the molecular level.

Our research also has a strong engineering component with particular emphasis on developing or refining electrical and optical techniques for studying secretion. Techniques in use in the lab include patch-clamp electro-physiology with membrane capacitance measurements as an assay of involved with is investigating the effects of cardiovascular deconditioning which occurs after a period of bed rest or spaceflight. Deconditioning is associated with several changes in cardiovascular regulation including increased incidence of orthostatic hypotension, which is the inability to maintain blood pressure when a person stands up, and a reduced ability to maintain blood pressure during hemorrhagic events. Since females have higher incidence of problems following bed rest or spaceflight, we are evaluating gender differences in autonomic control of the circulation following cardiovascular deconditioning. Defining the central nervous system mechanisms that account for the changes in autonomic nervous system function during these states will increase our understanding and enhance our ability to treat problems associated with pregnancy and cardiovascular deconditioning, exocytosis/ endocytosis, amperometric detection of catecholamine secretion with carbon fiber electrodes, photometric measurement of membrane turnover and intracellular Ca2+ concentration with indicator dyes, and photo- release of intracellular Ca2+ from caged compounds.



Kenneth A. Gruber Office: MU Life Sciences Business Incubator Phone: 909-210-1441 E-mail: gruberke@missouri.edu

Education: B.A. & Ph.D., New York University

Appointment: Adjunct Professor, Department of Medical Pharmacology and Physiology. CEO/President: Tensive Controls, Inc.

#### Research:

Our current interests involve two classes of peptides with therapeutic potential: melanocortins and RFamides. Melanocortins are a family of peptides that have a pivotal role in the regulation of vertebrate food intake and metabolism. Drugs with melanocortin receptor activity (agonists or antagonists) show therapeutic potential in obesity and disease-induced cachexia. Cachexia, the focus of our current melanocortin drug development efforts, is a hyper-metabolic state that produces preferential loss of lean body mass and multi-organ failure. Development of melanocortin drugs has been inhibited by the persistent presence of cardiovascular side-effects. We showed that an overlapping RFamide pharmacophore is the cause of melanocortin cardiovascular activity: the melanocortin pharmacophore (HFRW) contains a "synonym" (RW) of the RFamide pharmacophore. We are currently developing anti-cachexia melanocortin-based drugs free of side-effects. As a consequence of this work we have developed new concepts for the detection and regulation of overlapping pharmacophores in drug development.

An unanticipated outcome of our melanocortin research was the observation that RFamides produce electrocardiogram abnormalities resembling the clinical presentation of "sick sinus syndrome." Increasing RFamide peptide doses evoke other arrhythmic predictors of sudden cardiac death, and eventually produce sudden cardiac arrest. Our current goal is to use RFamide ligands to produce experimental models of cardiac arrhythmias, an important medical problem that has eluded model development. Eventually, our goal is to develop RFamide-based anti-arrhythmic drugs.



#### Liqun (Andrew) Gu

Office: 229 DCRC Phone: 573-882-2057 E-mail: gul@missouri.edu

Education: PhD Nankai University

Appointment: Associate Professor, Department of Biological Engineering

#### Research

We are a newly established nano-biotech laboratory focusing on application of lab-in-hand nanotechnology to the exploration of life science problems and practical biomedical detection. Currently, we utilize various nanopores as receptive probes for single molecule detections. Nanopore refers to a pore structure adopting dimension from one to hundreds nanometer, which can either be formed by naturally-occurred self-assembled protein pore or fabricated by fashion nanotechnology on solid substrates. With the nanopore probe, any analyte, whether it is a single molecule, a molecular complex, or a single viral particle, can reversibly bind to a receptor which is pre-engineered in a properly sized nanopore, and be identified by recognizing the characteristic blocks to the nanopore conductance.

Our laboratory is initially supported by the University of Missouri Startup Fund, Research Board and Research Council. Recently, this laboratory successfully got a National Science Foundation (NSF) Career Award grant in support of a new direction focusing on single molecular protein-oligonucleotide interaction and molecular folding in a nanopore. Specifically, we apply the nanopore technology to the single molecule investigation of dynamic aptamer-protein interactions and related folding processes involved in molecular recognition. Aptamers are engineered DNA/RNA that can specifically recognize broad species of proteins with high affinities, such as HIV-1 Integrase. Upon binding, these powerful molecules can form complex three-dimensional structures and possess sophisticated functions to inhibit pathogen protein, catalyze chemical reactions, control gene expression, and regulate cellular functions, therefore potentially be applied as tools for exploring biological systems. A complete understanding of dynamic processes in aptamer-target interactions and molecular folding is not only important to application-driven rational design, but also gives deep insight into the complexity of various nucleic acid-protein interactions in living cells.

Our research will be significant in the quantitative characterization and precise control of molecular scale components or nanomachinery of living cells by employing fashioning tools that allow us to manipulate complex biological processes in unique ways. Research using nanopore technology can be broadly applied to the study of diverse nucleic acid-protein and protein-protein interactions, which is essential for rational design of small organic molecules that block malfunctions of the cellular machinery, or act as new therapeutic reagents and products for biotechnology and bioengineering applications. This research will also greatly expand the capability of nanopore as the new generation of detection technology for analysis, high-throughput screening, bio-defense, and environmental engineering. In a broader impact, nanopore research will shed light on nanobiotechnology, an interdisciplinary and collaborative area related to biomolecular science, biotechnology, chemical engineering and nanotechnology.



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Education: PhD University of Oklahoma, BA Gettysburg College

Appointments:Professor, Department of Biomedical Sciences Adjunct Professor, Medical Pharmacology and Physiology

#### Research

The primary interest of the laboratory is in central nervous system control of the sympathetic nervous system and blood pressure, and how these reflex systems are modulated under physiological and pathophysiological conditions. Currently, the laboratory is involved in three primary projects.

The primary goal of the first project is to determine the neurotransmitter/receptor mechanisms involved in altered regulation of blood pressure in acute and chronic hypertension. The second project examines potential changes in both cardiovascular regulation and vascular function which may be responsible for cardiovascular deconditioning following prolonged exposure to spaceflight or bedrest. The focus here is on plasticity in specific brain regions that influence cardiovascular control. The third area of investigation focuses on the reflex effects of circulating humoral factors which act in the central nervous system to alter cardiovascular regulation. This project examines the central nervous system neurotransmitters and pathways involved in these effects. These questions are examined utilizing conscious animals which are chronically instrumented for recording of blood pressure, blood flow and sympathetic nerve activity. In addition, anesthetized preparations are utilized for experiments involving electrical and chemical stimulation of specific brain regions, microinjections of neurotransmitter agonists and antagonists, and central neurophysiological recording.

The overall goal of this work is to understand the central nervous system mechanisms underlying cardiovascular regulation in normal and disease states.



#### Cheryl M. Heesch

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Education: PhD University of Texas Health Science Center, BS New Mexico State University

Appointment: Professor, Department of Biomedical Sciences

#### Research

Our laboratory's major focus is to understand how the central nervous system controls arterial blood pressure and how blood pressure is modulated in physiological and pathophysiological states. We evaluate basic mechanisms involved in central nervous system control of autonomic outputs, particularly in brainstem regions which are critical for providing tonic drive to the sympathetic nervous system. We also study how ovarian hormones modulate these basic control mechanisms. Ongoing projects in the laboratory are focused on elucidating the role of central nervous system effects of ovarian hormones and progesterone metabolites in the alterations in control of sympathetic outflow associated with term pregnancy. Once we understand the mechanisms for attenuated sympathoexcitation in normal pregnancy, it may be possible to determine the mechanisms for elevations of arterial blood pressure in hypertensive disorders, where sympathoexcitatory responses are exaggerated. Also, women are generally protected from heart disease and hypertension until the onset of menopause. Understanding the mechanisms for the protective role of ovarian hormones could have important implications for treatment and prevention of cardiovascular disorders.

The possibility that a metabolite of progesterone, 3 -OH-dihydroprogesterone, may play a major role in suppression of sympathoexcitatory responses is especially intriguing. 3 -OH-dihydroprogesterone is the most potent endogenous positive modulator of central nervous system GABAA receptors and physiologically significant levels have been reported in the central nervous systems of both males and females. Experimental approaches include: 1.) measurement of sympathetic nerve activity; 2.) CNS microinjection of putative transmitters and modulators; 3.) extracellular single unit neuronal recording; and 4.) evaluation of neurotransmitter receptor expression in relevant brain regions.



#### Virginia Huxley

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Education: PhD University of Virginia, BA Hollins University

Appointments:Director of the National Center for Gender Physiology, J.O. Davis Chair of Cardiovascular Research, Professor, Department of Medical Pharmacology and Physiology, Adjunct Professor, Department of Biomedical Sciences

#### Research

Research Interests: Microvascular transport, in vivo imaging/microscopy, in vivo mass transfer, tissue engineering, mathematical modeling. We focus on the mechanisms controlling solute, water, and gas transfer between circulating blood and metabolizing tissue. Knowledge of the barriers to transport in living tissue is essential for elucidating the processes providing moment-to-moment regulation organ function and the etiology of dysfunctional states. These data facilitate design and implementation of rational strategies for treating diseases with the progressive goals of abating, arresting, and ultimately reversing disease processes.

Solute and water transfer results from "passive" and "cell mediated" mechanisms. Most have studied the passive mechanisms fewer study the cellular processes. From engaging in research in both arenas we find the exchange barrier to be a dynamic structure whose properties vary in time and space over time scales of seconds to days. Our global intent is to use this understanding of transport through pathways of microscopic geometry to investigate the relationship between blood supply and metabolic demand. We are developing methods to extend these quantitative studies to mammalian microvessels in skeletal muscle, heart, gut, and brain in collaboration with colleagues in DCRC, MPP, Biomedical Sciences at MU and the University of Rochester. Knowing that microvascular exchange is subject to regulation under normal and pathological situations, we collaborate with clinical colleagues (Nephrology, Surgery, Anesthesia, Cardiology, Pulmonary Medicine, Infectious Disease, and Critical Care Medicine) to elucidate the cellular and molecular mechanisms involved in structuring and restructuring the barrier under conditions of peritoneal dialysis, following endurance exercise training, in coronary occlusive vessel disease, neurogenic edema, diabetes, cancer metastasis, and conditions of remote organ (brain) injury following burn. The combined clinical and basic science expertise provides the possibility of realizing our goal of designing and implementing treatments of permeability dysfunction. Consequent to the collaborative interactions at MU and in light of fundamental sex-related differences in physiological function and pathophysiology observed by us and others, we established the National Center for Gender Physiology. This virtual center is acting as a focus for research scientists at MU and collaborating institutions and augments the services provided by DCRC.



#### Tzyh-Chang Hwang

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Education: PhD Johns Hopkins University, MD National Yang-Ming Medical School, MS National Tawain University School of Medicine

Appointment: Professor, Department of Medical Pharmacology and Physiology

#### Research

CFTR (Cystic Fibrosis Transmembrane conductance Regulator) is a chloride channel that plays a critical role in secretion and absorption of water and electrolytes across epithelia. Since CFTR channels are also expressed in cardiac myocytes and are found to shorten action potential duration and induce repetitive activity, they are implicated to be arrhythmogenic. One unique feature of the CFTR protein as an ion channel is that the free energy of ATP hydrolysis is harvested to drive the conformational changes that open and close the channel. Studies using mutant CFTR and various ATP or phosphate analogs have suggested a model that ATP hydrolysis at two nucleotide binding sites is tightly coupled to the opening and closing of the channel pore. Our understanding of the molecular basis of the coupling mechanism, however, remains primitive. Unresolved questions include: What is the stoichiometry of ATP binding/ hydrolysis to gating transitions? How are the biochemical states in ATP hydrolysis cycles translated to the open and closed states in the gating transitions? Which part of the protein forms the aqueous pore? What is the relationship between the gate and the pore? These are the fundamental questions that interest a broad spectrum of physiologists.

A combinational approach is being adopted to tackle the molecular physiology of CFTR chloride channels. Different configurations of the patch-clamp techniques will be used to record CFTR channel activity so that both the cytoplasmic and extracellular sides of the channel are accessible to channel blockers, modifiers, or channel openers. Structure-guided mutagenesis approaches will be employed to study the functional consequences of single amino acid substitutions on gating and permeation/blocking. Statedependent chemical modifications of engineered cysteines allow us to explore the dynamic protein conformational changes during gating transitions. The aims of our ongoing research are: 1. To understand the role of ATP binding and hydrolysis in controlling the opening and closing transitions of CFTR. 2. To probe the CFTR pore with permeant and impermeant anions. 3. To explore the structure/function relationship between the gate and the pore of CFTR. 4. To characterize how CFTR activators act to increase the activity of CFTR. 5. To apply structure-based drug design to identify chemicals that can correct trafficking defects in CF-associated mutations. A clear understanding of the molecular mechanism of CFTR function will aid in the design of pharmacological agents for therapeutic intervention in cystic fibrosis, secretory diarrhea and cardiac arrhythmia.



Salman M. Hyder

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Appointment: Professor, Department of Biomedical Sciences

#### Research

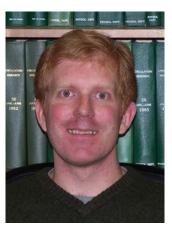
The main aim of our laboratory is to identify steroid hormone dependent molecular targets that can be utilized for anti-angiogenic therapy of endocrine dependent disease such as the breast, uterine, and prostate cancer. Formation of new blood vessels, or angiogenesis, is crucial for normal processes such as embryonic development, wound healing, and endometrial regeneration following menstruation. Angiogenesis is also essential for tumor growth, and metastasis. An emerging field in cancer therapeutics is the targeting of new blood vessels to curtail tumor growth. Our laboratory is currently focusing on the role of steroid hormones, clinically relevant anti-hormones, and endocrine-disruptors to understand the basic mechanisms involved in hormone driven angiogenesis in breast, and uterine tissue. We are currently focusing on the role of estrogens, progestins, and their nuclear receptors in controlling the expression of potent angiogenic growth factors (e.g. VEGF and its receptors) at both molecular and cellular level. Another focus of the laboratory is to investigate the molecular mechanisms of steroid hormone action at the level of gene transcription. We are especially interested in the role of natural and synthetic ligands that have diverse biological effects in different target tissues (e.g. SERMS such as tamoxifen). Many synthetic ligands (agonists/antagonists) are consumed by millions of women all over the world for oral contraception, hormone replacement therapy, or treatment of breast cancer. Consumption of some of these ligands lead to increased risk of breast and/or uterine abnormalities, including cancer. We anticipate that understanding the molecular basis/pharmacology of ligand-nuclear receptor interactions will allow development of better therapeutic modalities for treatment of hormone dependent tumors, as well as endometriosis, osteoporosis and infertility.



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#### **Research** Description

Jones' research program currently focuses on mechanisms of membrane regulation and vascular smooth muscle function leading to abnormalities associated with hyper-lipidemia as well as adaptative mechanisms during exercise training. He is studying mechanisms of adenosine transport and adenosine regulation of smooth muscle responses to acute metabolic depression in porcine coronary arteries. These studies have shown a novel mechanism by which smooth muscle generated adenosine has an autocoid function during an ischemic response. Mechanisms being pursued relate to adenosine interaction with receptors and subsequent cellular events causing relaxation, as well as adenosine interaction with a target enzyme, AMP kinase, which in turn regulates both cell metabolism and functional responses. It has been observed that exercise training may alter the sensitivity of vascular smooth muscle in the porcine coronary arteries especially in males. Gender studies have also been initiated.



David D. Kline

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Education: PhD Case Western Reserve University, BA Miami University

Appointment: Associate Professor, Department of Biomedical Sciences

#### Research

Our laboratory focuses on the autonomic nervous system, in particular the cardiovascular and respiratory system. These vital systems operate to keep our bodies within "normal" physiological limits to preserve homeostasis. When challenged acutely or chronically with low environmental oxygen levels (hypoxia) respiration, blood pressure and heart rate compensate to maintain arterial blood gas levels. This can happen during high altitude assent or disease states such as sleep apnea by activation of the chemoreceptor reflex. Additionally, arterial blood pressure is maintained during swings in pressure by the baroreceptor reflex. Both reflex pathways result from activation of neurons in the peripheral and central nervous system. Determining the mechanism of action of these reflex pathways during health and disease is the focus of the laboratory.

Several techniques are used to elucidate these mechanisms. These include 1) radiotelemetry in conscious animals to measure respiration, blood pressure or heart rate; 2) immunohistochemical localization of ion channels and neurotransmitter receptors to specific regions of the nervous system and individual neurons; 3) patch clamp techniques in isolated neurons for recording current flow through ion channels and 4) electrical recording of synaptic transmission in brainstem slices.

Using these techniques, we have recently discovered that chronic intermittent hypoxia, a model for obstructive sleep apnea, elicits a form of neural adaptation or plasticity in the brainstem. This includes changes in neurotransmitter release from presynaptic chemoreceptor afferent neurons as well as postsynaptic action potential firing. We are currently determining the mechanism of this altered neurotransmitter release.



#### Ronald J. Korthuis

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Education: PhD & BS from Michigan State University

Appointment: Chair Medical Pharmacology and Physiology Professor, Department of Medical Pharmacology and Physiology George L. and Melna A. Bolm Distinguished Professor in Cardiovascular Health

#### Research

Our research focuses on the mechanisms underlying the inflammatory responses to ischemia and reperfusion (I/R) and how blood vessels in the microcirculation (arterioles, capillaries and venules) can be preconditioned to resist the deleterious proinflammatory effects of I/R. When the blood supply is reduced (ischemia) and then subsequently reestablished (reperfusion), the ability of arterioles to regulate the distribution of blood flow is impaired, many capillaries fail to perfuse (capillary no-reflow), and white blood cells and platelets become adherent to and emigrate across the walls of postcapillary venules. Once in the tissues, these inflammatory phagocytes attack parenchymal cells, thereby exacerbating injury induced by ischemia. In addition, the permeability of the cells lining capillaries and postcapillary venules is increased, leading to edema formation. We are studying how white blood cells which adhere to and emigrate across the walls of postcapillary venules, alter vasoregulatory function in arterioles, cause no-reflow in capillaries, and increase permeability in postcapillary venules.

Laboratory models include study of the intact microcirculation using intravital microscopy coupled with computerized image analysis, examination of vasomotor responses in isolated arterioles, assessment of cell adhesion and permeability in single postcapillary venules, and evaluation of cell signaling mechanisms in cultured endothelial cells. A wide variety of mutant mouse models (gene knockout and transgenic over-expression), coupled with pharmacologic approaches, immunocytochemistry of the microvessel wall and cultured cells, western blotting and RT-qPCR to measure protein and mRNA expression, quantitative assessment of adhesion molecule expression using a dual radiolabeled monoclonal antibody technique, and three-dimensional fluorescence imaging using confocal microscopy are used to explore signaling mechanisms cultured cells, isolated microvessels, and intact microcirculatory networks in vivo.

A major area of emphasis over the last several years has been to understand how exposing tissues to preconditioning stimuli such as nitric oxide donors, calcitonin gene-related peptide, or by ingestion of ethanol (at doses equivalent to drinking one to two alcoholic beverages) 24 hours prior to the onset of prolonged ischemia followed by reperfusion prevents postischemic microvascular and parenchymal cell dysfunction. A fundamental aim of this work is to determine the signaling mechanisms that are activated in response to these preconditioning stimuli to upregulate gene expression for proteins that mediate the development of the anti-inflammatory and anti-thrombogenic phenotype in postischemic tissues.

Our future plans include continuing the examination of the mechanisms whereby microvascular function is protected in preconditioned states by focusing on the role of the extracellular matrix and cell adhesion molecules, ion channel function and extravascular constituents such as mast cells in these responses. In addition, we are exploring how leukocytes, which adhere almost exclusively in postcapillary venules in our models, alter the function of upstream arterioles in tissues exposed to ischemia and reperfusion.



#### Maike Krenz

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Appointment: Assistant Professor, Department of Medical Pharmacology and Physiology

#### Research

Congenital heart defects remain the most common birth defect, occurring in about 1% of live births and constituting the leading cause of infant deaths in the US. Over the past decade, genetic analyses of families with congenital heart disease have directed us to the molecular causes of certain defects. In particular, gain-of-function mutations in the protein tyrosine phosphatase Shp2 have recently been discovered in families with Noonan syndrome. In the majority of cases, NS follows autosomal dominant inheritance and is characterized by short stature, facial dysmorphia, skeletal anomalies, and congenital heart disease. Among the heart defects, pulmonary valve stenosis and hypertrophic cardiomyopathy are most prominent. Understanding the exact cellular mechanism(s) by which dysfunction of Shp2 causes valve malformation may provide the basis for future development of novel therapeutic approaches in congenital heart disease.

To study the pathomechanisms of heart malformations, we have been creating genetically altered mouse models that recapitulate human congenital heart disease. In particular, our mouse models are designed to express the mutant proteins in a time- and tissue-specific manner. These models can then be used to study in detail which developmental steps in the heart play a role in the disease process. Subsequently, we can dissect the downstream signaling pathways through which mutant Shp2 mediates its effects in vivo. For example, we were recently able to show that the ERK pathway is both necessary and sufficient for the development of valve defects in a Noonan Syndrome mouse model. Furthermore, we use tissue culture approaches to investigate the effects of Shp2 mutations on the cellular and biochemical level to complement the in vivo mouse studies.



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Appointments: Chair of the Department of Biomedical Sciences, Professor, Department of Biomedical Sciences, Adjunct Professor, Department of Medical Pharmacology & Physiology

#### Research

I focus my research on cardiorespiratory effects of exercise. The primary goal is understanding of the effects of exercise training on the coronary circulation and skeletal muscle vascular beds. Exercise training produces increases in the capacity of myocardial and skeletal muscle vascular beds to transport oxygen and other nutrients. The training induced changes in vascular transport capacity are associated with growth of new capillaries, enlargement of artieries and veins, and alterations in factos that control blood flow in the heart and skeletal muscle. The laboratory is currently investigating the mechanisms responsible for these changes. Studies are conducted with: isolated hearts, isolated muscle tissue, single blood vessels and in conscious, chronically instrumented animals during exercise. To allow examination of the relationships among vascular adaptations and the response of the myocytes to training induced increases in the functional demands of the muscles, the effects of training on biochemical and histological characteristics of the muscles are also measured. The biochemical systems examined include: the metabolic pathways involved in supplying the myocytes with ATP, the contractile proteins, the systems responsible for controlling intracellular Ca++ levels and endothelin nitric oxide synthase. Most of our current experiments are focused on endothelial cell biology. We are determining the effects of physical activity on endothelial phenotype in normal animals and in models of vascular disease. We are also using genetically modified pigs to examine the role of endothelial nitric oxide synthase in the impact of endothelial cell phenotype on vascular health.



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Appointment: Associate Professor, Department of Medical Pharmacology and Physiology

#### Research

My research is focused on the mechanisms responsible for the architectural transformation of blood vessels also known as vascular remodeling. Vascular remodeling is a hallmark for numerous cardiovascular diseases, yet numerous questions remain to be answered regarding this process. What stimuli drive the remodeling process? How do blood vessels detect those stimuli? What are the mechanisms initiating the remodeling and under which conditions are they counterproductive participating in disease states?

Currently funded research in my laboratory is focused at determining the changes in the position and function of cells within the intact blood vessel wall that occur in response to common mechanical and vasoactive biochemical stimuli. Our studies indicate that cells within the vascular wall rapidly change their position in response to stimulation in as little as four hours. This adaptive cell behavior appears to allow the vessel to maintain a reduced diameter for extended periods of time with reduced levels of activation and energy expenditure. An additional goal is focused at determining the changes in the structure and compliance of the extracellular matrix that occur during the initial stages of the remodeling process.



Mark Milanick

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Education: Swarthmore College, Pennsylvania B.A. Physics University of St. Andrews, Scotland Math/Pharmacology University of Chicago, Illinois Ph.D. Biophysics Yale University, Connecticut postdoctoral Physiology

Appointment: Professor, Department of Medical Pharmacology and Physiology

#### **Research Interests**

Erythrosensors, Approaches for resource poor areas, Educational Innovations, Membrane Transport kinetics

**Research** Description

#### Erythrosensors

Our long term goal is to encapsulate glucose sensitive near infrared fluorescent dye inside red blood cells (erythrocytes). Return red cells to patient. Patient can monitor glucose levels non-invasively using a pulse oximeter type of detector for half of the lifetime of the red cells. Since the red cells live about 100 days, this means the erythrosensors only need to be made and injected about every 2 months. This project is being done in collaboration with Tim Glass, Xiaole Shao, and Nick Cooley (Chemistry, MU) and Ken Meissner and Sarah Ritter (Bioengineering, Texas A&M).

Engineering erythrocytes to be erythrosensors: first steps. Milanick MA, Ritter S, Meissner K. Blood Cells Mol Dis. 2011 Aug 15;47(2):100-6.

Encapsulation of FITC to monitor extracellular pH: a step towards the development of red blood cells as circulating blood analyte biosensors. Ritter SC, Milanick MA, Meissner KE. Biomed Opt Express. 2011 Jul 1;2(7):2012-21.

Approaches for resource poor areas

1. Soymilk: an effective and inexpensive blocking agent for immunoblotting. Galva C, Gatto C, Milanick M. Anal Biochem. 2012 Jul 1;426(1):22-3.

2. We are developing dipsticks for measuring levels of stress markers, including salivary cortisol and amylase for home use, as well as for detection of pesticides.

3. We have developed an educational laboratory exercise examining enzyme activity using acetylcholinesterase activity from grocery store frozen fish.

Why is that dog paralyzed? A problem-based case & laboratory exercise about neuromuscular transmission. Milanick, M., Graham, K. & Wessel, M. (2013). American Biology Teacher, 75, 36–39. Educational innovations

1. We have published several education articles that use novel approaches to interest students in various scientific activities.

- Fact or Fiction? General Chemistry Helps Students Determine the Legitimacy of Television Program Situations. Mark A. Milanick\* and Ruth L. Prewitt J. Chem. Educ., April 19, 2013
- Units, Jargon, G-forces and Squirting Blood. Milanick, MA. The Physics Teacher 50, 410, 2012.
- Changes of membrane potential demonstrated by changes in solution color. Milanick M. Adv Physiol Educ. 2009 Sep;33(3):230.
- Fluorescence Using Turmeric Mark A. Milanick J. Chem. Educ., 2011, 88 (3), pp 260.

2. We have developed novel interactive course offerings, including

- Ethics Education through Enactment, Engagement and Empowerment (Graduate)
- The Science of Sex, Drugs, and Rock'n'Roll (Undergraduate, non-majors)
- Clinical Biodetection (Graduate)

#### Membrane Transport Kinetics

We were funded for about 18 years by NIH for studies on membrane transport. Some of the highlights include

- Eosin, a Potent Inhibitor of the Plasma Membrane Ca Pump, Does Not Inhibit the Cardiac Na-Ca Ex changer
- Kinetic characterization of tetrapropylammonium inhibition reveals how ATP and Pi alter access to the Na+-K+-ATPase transport site
- Extracellular protons regulate the extracellular cation selectivity of the sodium pump.
- Probing the extracellular release site of the plasma membrane calcium pump.
- Na-Ca exchange: evidence against a ping-pong mechanism and against a Ca pool in ferret red blood cells.
- Proton fluxes associated with the Ca pump in human red blood cells.
- Na-Ca exchange in ferret red blood cells.
- Proton inhibition of chloride exchange: asynchrony of band 3 proton and anion transport sites?
- Proton-sulfate co-transport: mechanism of H+ and sulfate addition to the chloride transporter of human red blood cells.



Luis Polo-Parada

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Education:

PhD Case Western Reserve University, MS University of Connecticut, BS School of Physics and Mathematics, National Polytechnic Institute

Appointment: Assistant Professor, Department of Medical Pharmacology and Physiology

#### Research

The heart is the first organ to form during embryogenesis, and its function is critical for the proper development and survival of the embryo. Although some information on ion-transport genes and their protein products in normal and diseased myocardial tissue is available, little is known about the role of cardiac extracellular matrix (ECM) proteins during cardiac development or in healthy and diseased adult hearts. My interest is to elucidate the role of the ECM in the ionic-transport proteins and molecular basis of cardiac regional electrical specialization during development and in the adult heart.

My recent studies of neural cell adhesion molecule (NCAM) null mice have indicated that NCAM plays a fundamental role in the transmitter release mechanism in neuroendocrine cells through mediation of granule recruitment. Other studies have shown that NCAM plays a functional role in the proper segregation of cell during development of islets of Langerhans in the pancreas. My interest is to elucidate whether NCAM or other cell adhesion molecules, are directly involved in the proper organization of the islets of Langerhans and in glucose-mediated insulin secretion. I also intend to investigate, whether the expression of any of these cell adhesion molecules is affected in diabetic type II patients and animal models of the disease.



#### Leona Rubin

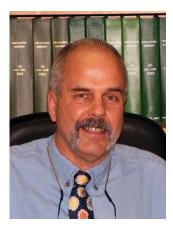
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Education: BA Temple University, MS Rutgers University, PhD University of Colorado Health Science Center

Appointments: Associate Professor, Department of Biomedical Sciences Adjunct Professor, Dept of Medical Pharmacology and Physiology

#### Research

Dr. Rubin's research is focused on understanding cellular pathways that regulate cardiovascular function during health and disease states. There are three major projects within the laboratory: 1.) How do immune mediators, released during inflammatory conditions (endotoxemia/sepsis, atherosclerosis) cause myocardial and/or vascular failure? Investigations focus on alterations in second messenger system(s) and cellular targets such as potassium and calcium channels. Therapeutic modalities also are probed as a means to identify affected pathways. 2.) What are the cellular pathways that mediate vascular hypoxic vasodilation? Matching of blood flow to meet tissue substrate needs is a fundamental property of the vasculature. However, the signals and vascular mechanisms responsible for dilation are unknown. We have targeted three sites for involvement in hypoxic vasodilation, AMP-activated kinase, Akt and voltage-dependent potassium channels. 3.) What is the role of sex hormones in modulating cardiovascular function? Specifically, do sex hormones alter expression of voltage-dependent potassium channels in either vascular smooth muscle or the myocardium? Myocardial studies examine both intrinsic (potassium currents of cardiac myocytes) and extrinsic (heart rate variability) control of heart rate. Methodologies include those needed to: 1.) measure contraction, Ca2+, and ionic currents of isolated ventricular myocytes; 2.) measure intracellular second messenger molecules, their substrates and products (gel electrophoresis ion chromatography, high performance liquid chromatography, gas chromatography and mass spectrometry), 3.) in vitro physiology of vascular function and 4.) in vivo assessment of heart rate variability. Our animal models include a swine model of sex hormone replacement (estrogen or testosterone), guinea pig and rat models of endotoxemia and genetically modified mouse models lacking components of signaling pathways that regulate cardiovascular function.



James C. Schadt

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Education: PhD Texas Tech University, MS Indiana State University, MS & BS Northern Illinois University

Appointment: Associate Professor, Department of Biomedical Sciences

Research

Traumatic injury is the leading cause of death for individuals under 40 years of age. While head trauma is the most common cause of death, blood loss is number two, and the effects of head injury are exacerbated by blood loss.

The goal of my research is to learn more about how the brain and endocrine systems control the heart and blood vessels during traumatic blood loss.



Steven S. Segal

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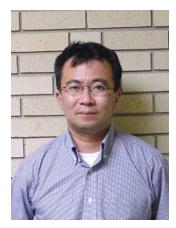
Education: PhD University of Michigan, MA & BA University of California, Berkley

Appointment: Professor, Department of Medical Pharmacology and Physiology

#### Research

Our research is focused on understanding how oxygen delivery increases in response to metabolic demand. During exercise, the recruitment of skeletal muscle fibers (motor units) generates electrical and chemical signals in endothelial cells and smooth muscle cells of the microvessels that control the distribution and magnitude of muscle blood flow. Our experiments center on elucidating the cellular and molecular events which initiate these signals, how such signals are transmitted from cell to cell to orchestrate vasodilation and vasoconstriction in microvascular networks, and how these integrative processes are governed by the nervous system. Intravital video microscopy enables direct observations of blood flow control in the mammalian microcirculation. Histochemistry and vascular casting are used to quantify the architecture of neural and microvascular networks. Intracellular recording with dye labeling reveals cell-specific electrical signals which determine the contractile status of smooth muscle and its regulation by the endothelium. Calcium imaging provides unique insight into cellular responses which reflect the activity of ion channels and key regulatory enzymes. Complementary studies of isolated microvessels and their constitutive cells enable even greater resolution of specific regulatory processes. Pharmacology, immunolabeling, and Real-Time Polymerase Chain Reaction are used to resolve the functional expression of proteins which mediate cell-to-cell coupling through gap junctions and electrical signaling through ion channels.

Collaborative studies using transgenic mice afford unique insight into how particular signaling pathways affect control processes within the microcirculation. In turn, these basic relationships are athways affect control processes within the microcirculation. In turn, these basic relationships are being explored in light of how aging affects microvascular structure and function. Opportunities for graduate and postdoctoral training include: molecular physiology of vascular cells, electrical and optical monitoring of cell signaling, microsurgery and microdissection, intravital video microscopy, conventional and immunohistochemistry, evaluation of gene expression, and modeling the biophysical properties of cells and tissues.



#### Yoshiro Sohma

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Education: PhD and MD Osaka Medical College

Appointment: Visiting Professor, Department of Medical Pharmacology & Physiology

#### Research

I have a broad research interest that covers the molecular physiology and biophysics of ion channels and transporters, and their role in the physiological function of cells/tissue. I have studied the permeation and gating of a large-conductance, Ca2+-activated, voltage-dependent potassium (BKCa) channel. BKCa channels are ubiquitously expressed in many different tissues and are known to be sensitive to membrane potential, intracellular calcium, magnesium, pH. These channels are also activated by CO and sensitive to O2 associated with hemeoxygenase2 and, moreover, some slice-variants respond to membrane stretch. Based on these findings, BKCa channels are suggested to play an important role in integrating cell signals, a recently proposed new function of an ion channel. I am also involved in a Japanese-based collaborative project undertaking a comprehensive study of the GABAergic system in peripheral tissues (not the central nervous system) and work on GABAA receptor channels and GABAB-mediated modulation of K+ and Ca2+ channels in peripheral tissues. In the Dalton Cardiovascular Research Center, I study the molecular mechanism of gating and permeation of the CFTR chloride channel, a member of the ATP-Binding Cassette (ABC) transporter superfamily, in collaboration with Dr. Tzyh-Chang Hwang. Our work has made a significant contribution to the recent advances in the biophysical understanding of the ATP-dependent gating mechanism in CFTR, and has provided great insight into a possible common functional mechanism that can be applied to the whole ABC transporter superfamily. The structure of the membrane spanning domain (MSD) in CFTR is known to be similar to that in the P-glycoprotein drug efflux pump. We therefore believe that understanding MSD structure/function in CFTR will lead to a better understanding of multi-drug resistance (MDR) proteins. In addition to investigating the biophysics of the CFTR molecule itself, I am also interested in studying the functional interactions of CFTR with other membrane proteins and lipids. This should help in our understanding of the complicated regulatory mechanisms that underlie physiological functions in cell membrane. I have also employed computer modeling to simulate ion transport processes in epithelial cells (e.g., bicarbonate transport in pancreatic duct cells). This approach is very useful to bridge information from molecular biophysics and cell/tissue physiology to the research field of epithelial transport. I believe that by taking such a general and comprehensive approach to the study of different channels/transporters and channel/transporter-mediated physiological systems, induces a 'positive cooperative effect' which accelerates each research project, and which also gives us a novel scientific standing point of view for the channel sciences.



#### Jim R. Sowers

Office: D109 Diabetes Center UHC Phone: 882-0999 E-mail: sowersj@missouri.edu

Education: MD University of Missouri-Columbia, BS Central Missouri State University

Appointment: Director of the MU Diabetes and Cardiovascular Center, Professor, Department of Medicine, Professor, Department of Medical Pharmacology and Physiology

#### Research

Fifty million people have high blood pressure and are prone to developing Type 2 diabetes. Dr. Sowers, directs the MU Diabetes and Cardiovascular Center and is associate dean for clinical research. His work addresses the link between high blood pressure and diabetes to better understand how to prevent and cure the diseases, which are growing problems in the United States.



Ronald Terjung

Office: E101VMED Phone: 882-2635 E-mail: terjungr@missouri.edu

Education: PhD University of Iowa, MA San Jose State College, BS Wheaton College

Appointment: Associate Dean of Research, Department of Biomedical Sciences, Professor, Department of Biomedical Sciences, Adjunct Professor, Department of Medical Pharmacology and Physiology

#### Research

Adenine nucleotide (And = ATP + ADP + AMP) metabolism occupies a pivotal role in cell regulation, particularly for skeletal muscle where contractile activity increases ATP hydrolysis rate manyfold. The control of [ATP] in contracting muscle depends upon: 1.) the control of energy supply pathways; 2.) And degradation reactions; 3.) And synthesis reactions from precursors; and 4.) contractile activity which determines the rate of ATP hydrolysis. He is evaluating differences in And metabolism among skeletal muscle fiber types, critical responses to exercise, and adaptations induced by chronic exercise. Enhanced physical activity represents an important treatment for persons with peripheral arterial insufficiency and leads to meaningful adaptations that increase exercise tolerance. These adaptations include neovascular development to improve a) blood/tissue exchange properties within muscle (enhanced capillarity) and b) flow capacity to active muscle (collateral vessel expansion). The exercise-induced increase in collateral blood flow likely involves the angiogenic growth factors (e.g. bFGF, VEGF). These potent cytokines stimulate neovascularization in experimental ischemia in vivo. His working hypothesis is that neovascularization occurs in response to tissue "need" established by flow deficits (ischemia) and/or by increased demands for vascular support (exercise). His research is evaluating: 1.) the interactions between ischemia, exercise and exogenously infused recombinant angiogenic growth factors; 2.) the functional significance of the vascular adaptations; and 3.) the tissue events related to neovascularization.



Xiaoqin Zou

Office: 222D DCRC Phone: 573-882-6045 E-mail: xiaoqinz@missouri.edu

Education: PhD University of California, San Diego, BS Wuhan University

Appointment: Associate Professor, Department of Biochemistry

#### Research

The molecular interactions that drive ligand-protein binding are a key to quantitatively understanding the basis of molecular recognition and to designing therapeutic interventions through rational drug design. Drug molecules usually act by binding to specific target proteins. Drug candidates that have high binding affinities can be identified by their geometric and chemical complementarity to the target in a process analogous to solving a "jigsaw puzzle," if the target structure is known. An energy model that can give rapid and accurate evaluation of the molecular interaction strength is thus essential for selecting plausible candidate compounds from a chemical database consisting of hundreds of thousands of molecules. We are developing novel and efficient algorithms to calculate binding free energies for ligand-receptor complexes. The derived energy models will be applied to protein-substrate interactions, protein-protein interactions, and structure-based drug design. We are also developing new docking algorithms to account for protein flexibility. Methods used in our laboratory include computer modeling, simulation and graphics display. A second line of research in the laboratory is quantitative studies on structure-function relationship of membrane proteins. Structures of membrane proteins will be predicted using homology modeling and structure alignment techniques. Structural information often suggests mechanisms of protein function, which will be experimentally tested in collaboration with other Dalton Investigators.

# APPENDICES

# PUBLICATIONS

## PRESENTATIONS

# **SEMINARS**

# ACTIVE GRANTS & CONTRACTS

# PROFESSIONAL SERVICE ACTIVITIES

### **Christopher Baines**

#### **Publications:**

Peer-Reviewed:

Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Cell biology of ischemia/reperfusion injury. Int Rev Cell Mol Biol. 2012; 298:229-317.

McGee AM, Baines CP. Phosphate is not an absolute requirement for the inhibitory effects of cyclosporin A or cyclophilin D deletion on mitochondrial permeability transition. Biochem J. 2012; 443:185-91.

McCommis KS, Baines CP. The role of VDAC in cell death: Friend or foe? Biochim Biophys Acta. 2012; 1818:1444-50.

#### **Book Chapters:**

Baines CP. Fractionation of cardiomyocytes and isolation of mitochondria. In: Ardehali H, Bolli R, Losordo D, eds. Manual of Research Techniques in Cardiovascular Medicine. Hoboken, NJ: Wiley-Blackwell; In Press

Abstracts:

McCommis KS, Baines CP. Hexokinase-2-Mediated Protection Against Cell Death is Dependent Upon Voltage-Dependent Anion Channels 2 & 3. Presented at the AHA Scientific Sessions meeting, November 2012.

Gutierrez-Aguilar M, Baines CP. Mapping the Role of the Mitochondrial Phosphate Carrier in Cardiomyocyte Life and Death. Presented at the AHA Scientific Sessions meeting, November 2012.

Kalogeris TJ, Wang M, Jones A, Baines CP, Korthuis RJ. Ethanol preconditioning augments increase in cardiac mitochondrial mass elicited by ischemia/reperfusion. FASEB J. 2012; 26:888.3. Presented at Experimental Biology, April 2012.

Nourian Z, Li M, Clifford PS, Stupica A, Krenz M, Baines CP, Meininger GA, Hill MA. Age-related changes in the expression of elastin in small cerebral and mesenteric arteries. FASEB J. 2012; 26:861.4. Presented at Experimental Biology, April 2012.

Lee S, Park Y, Zuidema MY, Laughlin MH, Bowles DK, Baines CP, Hannink M, Hill MA, Dellsperger KC, Zhang C. Exercise training improves coronary microvascular arteriolar function in familial hypercholesterolemia porcine model via Nrf2. FASEB J. 2012; 26:1138.24. Presented at Experimental Biology, April 2012.

#### Presentations

"Role of Mitochondrial Permeability Transition in Cardiomyocyte Death." Friedreich's Ataxia Research Alliance Symposium, Los Angeles, CA. 11/4/12.

"Basic Mechanisms of Cell Death." Cardioprotection Colloquium, UCLA, Los Angeles, CA. 11/2/12.

"RIPing Holes in Mitochondria: trying to decipher programmed necrosis." Cardiovacular Center, University of Iowa, Iowa City, IA. 10/12/12.

Baines continuted:

"Regulation of the Mitochondrial Permeability Transition Pore." International Society for Heart Research, North American Section Annual Meeting, Banff, Canada. 5/28/12.

"Complement 1q Binding Protein, Or Why a Cardiac Guy is Looking at Cancer." Center for Translational Medicine and Department of Pathology and Cell Biology, Thomas Jefferson University, Philadelphia, PA. 4/12/12.

#### **Active Grants:**

Current: R01HL094404 (PI: Baines) NIH/NHLBI "Molecular Identity of The Cardiac Mitochondrial Pore" Role: PI	12/2008-11/2013 \$1,250,000 direct costs	
AHA Predoctoral Award (PI: McCommis) AHA Midwest Affiliate "Investigating Hexokinase-2-mediated cardioprotection" Role: Sponsor	7/2011-6/2013 \$52,000	
MU-iCATS Pilot Grant (PI: Emter) 1/2012-12/2012 University of Missouri \$50,000 direct costs "The Effects of Cyclophilin Inhibition on Cardiomyocyte Cell Death and Ventricular Remodeling in Heart Failure" Role: Co-PI		
Prostate Cancer Development Award (PI: Baines) US Department of Defense "Inhibiting Mitophagy as a Novel Mechanism to Kill Prosta Role: PI	9/2012-9/2013 \$75,000 direct costs te Cancer Cells"	
Research Council Award (PI: Baines)4/2012-3/2013University of Missouri\$7,500 direct costs"Identifying C1qbp binding drugs as potential anti-cancer agents"Role: PI		
Sponsored Research Agreement (PI: Baines) Stealth Peptides, Inc. "Mechanisms of Cytoprotection by SPI-20 and MTP-131 p Role: PI	7/2012-6/2013 \$17,765 eptides"	

Baines continued

#### **Professional Service**

Department/Center:

Chair, Dalton Cardiovascular Research Center Safety Committee

Director, Biomedical Sciences Seminar Series

Member, Biomedical Sciences Graduate Program Admissions Committee

Member, Biomedical Sciences Assistant/Associate Professor Search Committee

College:

Member, Research Committee, College of Veterinary Medicine

Member, VOLUM Committee, College of Veterinary Medicine

University:

Panel member, Summer Faculty Grant Writing Institute

National/International:

Editorial Boards: American Journal of Physiology, Heart and Circulatory Physiology Bioenergetics

### **Edward Blaine**

#### **Professional Service**

Committee on Committees, 2009-, Chair 2010-present

Faculty Grievance Oversight Committee, 2009-present

Honorary Degree Committee, University of Missouri, 2008-present

Graduate Education Committee, Dept. Med. Pharm./Phys, 2004-present

Campus Planning Committee, University of Missouri, 2005-present

Health Outcomes in Athletes, 2009-

Problem-based Learning Curriculum Continuous teaching contributions since 1992

- 2011-2012 Tutor Blocks 2,3,4,5,7, M4 mentor
- 2012-2013 Tutor Blocks 1,2,3,5,8, M4 mentor

Microcirculation (Graduate Course)

Renal Physiology (Graduate Course)

Neurohumoral Control of the Circulation (Graduate Course)

Salt and Water Homeostasis (Undergraduate Course)

Herpetology, Physiological Ecology (Undergraduate Course)

### Silvia Bompadre

#### **Active Grants**

Fluorescence microscopy studies of CFTR channels \$23,000 (9/1/2012 – 8/31/2013) PI: Silvia G. Bompadre MU Research Board Grant

Single-molecule studies of CFTR channels \$14,500 PI: Silvia G. Bompadre MU Summer Research Fellowship

#### **Professional Service**

Reviewer

University of Missouri Research Board Research Grants Council (Hong Kong) Frontiers in Pharmacology Computational Biology

Member of the Arts & Sciences Diversity Committee (2012-present).

### **Frank Booth**

#### Publications

Mikus CR, Oberlin DJ, Libla JL, Taylor AM, Booth FW, Thyfault JP. Lowering Physical Activity Impairs Glycemic Control in Healthy Volunteers. Med Sci Sports Exerc. 44:225-231, 2012.

Roberts MD, Childs TE, Brown JD, Davis JW, Booth FW. Early depression of Ankrd2 and Csrp3 mRNAs in the polyribosomal and whole-tissue fractions in skeletal muscle with decreased voluntary running. J Appl Physiol. 2 J Appl Physiol. 2012 Apr;112(8):1291-9, 2012.

Zwetsloot KA, Nedergaard A, Gilpin LT, Childs TE, Booth FW. Differences in transcriptional patterns of extracellular matrix, inflammatory, and myogenic regulatory genes in myofibroblasts, fibroblasts, and muscle precursor cells isolated from old male rat skeletal muscle using a novel cell isolation procedure. Biogerontol-ogy. 2012 Aug;13(4):383-98.

Brown JD, Naples SP, Booth FW. Effects of voluntary running on oxygen consumption, RQ, and energy expenditure during primary prevention of diet-induced obesity in C57BL/6N mice. J Appl Physiol. 2012 Aug;113(3):473-8.

Toedebusch RG, Childs TE, Hamilton SR, Crowley JR, Booth FW, Roberts MD. Postprandial leucine and insulin responses and toxicological effects of a novel whey protein hydrolysate-based supplement in rats. Journal of the International Society of Sports Nutrition 2012, J Int Soc Sports Nutr. 2012 Jun 6;9(1):24.

Park Y, Booth FW, Lee S, Laye MJ, Zhang C. Physical Activity Opposes Coronary Vascular Dysfunction Induced during High Fat Feeding in Mice. J Physiol. 2012 2012 Sep 1;590(Pt 17):4255-68.

Padilla J, Jenkins NT, Roberts MD, Arce-Esquivel AA, Martin JS, Laughlin MH, and Booth FW. Differential changes in vascular mRNA levels between rat iliac and renal arteries produced by cessation of voluntary running. Exp Physiol 2012 Jun 18. [Epub ahead of print]

Morris EM, Meers GM, Booth FW, Fritsche KL, Hardin CD, Thyfault JP, Ibdah JA. PGC-1a Overexpression Results in Increased Hepatic Fatty Acid Oxidation withReduced Triacylglycerol Accumulation and Secretion. Am J Physiol GastrointestLiver Physiol. 2012 Aug 16.

Booth FW, Neufer PD. Exercise Genomics and Proteomics. In ACSM's Advanced Exercise Physiology 2nd Ed. Editors, Farrell PA, Joyner, MJ, Caiozzo VJ. Wolters Kluwer, Philadelphia, PA, 2012, pp 669-698.

Booth FW, Roberts CR, Laye MJ. Lack of exercise is a major cause of chronic diseases. Comprehensive Physiol 2: 1143-1211, 2012.

Roberts MD, Company JM, Brown JD, Toedebusch RG, Padilla J, Jenkins NT, Laughlin MH, Booth FW. Potential clinical translation of juvenile rodent inactivity models to study the onset of childhood obesity. Am J Physiol Regul Integr Comp Physiol. 2012 Aug;303(3):R247-58.

#### Active Grant

National Institutes of Health. Vascular biology: exercise training and coronary disease. P01 HL52490-12. Co-PI on project 1 of program project. 51

### **Douglas Bowles**

#### Publications

Laughlin, M.H., D.K. Bowles and D. Duncker. The Coronary Circulation in Exercise Training. Am. J. Physiol. (Heart Circ. Physiol) 302(1): H10-23, 2012. PMID: 21984538

O'Connor, E.K., J.R. Ivey and D.K. Bowles. Differential effects of androgens on coronary blood flow regulation and arteriolar diameter in intact and castrated swine. Biol. Sex Differences. 3(1):10, 2012. PMID:22620281

Masseau, I., M.J. Davis and D.K. Bowles. Carotid Inflammation Is Unaltered by Exercise in Hypercholesterolemic Swine. Med. Sci. Sport Med., 44(12):00, 2012.

#### Presentations

Tharp, D.L., J. Ivey and D.K. Bowles. Exercise alone attenuates reductions in intimal smooth muscle K+ current in a swine model of coronary artery disease. FASEB J. 21(5): 2012.

Lee. S, Y. Park, M.Y. Zuidema, M. H. Laughlin, D. K. Bowles, C. Baines, M. Hannink, M. A. Hill, K. C. Dellsperger and C. Zhang. Exercise Training Improves Coronary Microvascular Arteriolar Function in Familial Hypercholesterolemia Porcine Model via Nrf2. FASEB J. 21(5): 2012.

De Beer, V.J., D. Merkus, S.B. Bender, D.L. Tharp, D.K. Bowles, D.J. Duncker and M.H. Laughlin. Reduced NO bioavailability hampers exercise induced vasodilation in Familial Hypercholesterolemic swine. FASEB J. 21(5): 2012.

Bender, S.B., De Beer, V.J., D.L. Tharp, D.K. Bowles, D.J. Duncker, M.H. Laughlin and D. Merkus. Blunted exercise-induced vasodilation in familial hypercholesterolemic swine does not involve enhanced ET-1-mediated vasoconstriction. FASEB J. 21(5): 2012.

Invited Symposium for AALAS Conference on "Swine models of atherosclerosis", Minneapolis, Minnesota, November, 2012

#### **Active Grants**

CVM/COR Faculty Research Grant (Bowles, PI) 1/1/12-12/31/12 \*2% NIH/NHLBI: SBIR \$17,953 ADC Role of KCa3.1 in driving coronary smooth muscle phenotype Major goals: Perform loss-of-function/gain-of-function experiments of KCa3.1 in porcine coronary arteries.

R44 HL097485-01 (Chen, PI; Bowles, Co-I) 9/1/11-7/31/13 10% NIH/NHLBI: SBIR \$237,000 ADC Improved long-term biocompatibility of coronary stents by plasma coating process Major goals: Develop a superior plasma coating for stents

P01 HL52490 (Laughlin, PI; Bowles, Project Leader) 1/1/06-12/31/12 (NCE) 25% NIH/NHLBI\$187,472 ADC(Project 1) Ion channel regulation of coronary smooth muscle phenotype.\$187,472 ADC

Major goals: Determine the role of ion channels in coronary smooth muscle regulation of tone following exercise training. Treadmill endurance exercise and dietary high fat interactions are studied in miniature swine P01

HL52490 (Laughlin, PI; Bowles, Core Leader) 1/1/06-12/31/112 (NCE) 5% NIH/NHLBI \$167,681 ADC (Core C)Vascular Biochemistry and Molecular BiologyMajor goals: Provide investigators with access to routine as well as state-of-the-art molecular and biochemical tools, expertise, and techniques.

Mizzou Advantage (Fay, PI; Bowles, Co-I) 4/1/10-3/31/15 2.5% MU \$50,000 ADC Targeting Plasminogen Activator inhibitor-1 to Inhibit Neointimal Hyperplasia Major goals: Develop a novel DES

MU Life Sciences Trust Fund Research Grant (Fay, PI; Bowles, Co-PI) 1/1/09-11/30/12 (NCE) 10% Missouri Life Sciences Research Board \$\$815,625 ADC Targeting Plasminogen Activator Inhibitor-1 to Inhibit Restenosis

#### **Professional Service**

Appointments	
1998-present	Graduate Faculty, University of Missouri-Columbia
1998-present	Doctoral Faculty, University of Missouri-Columbia
1998-present	Biomedical Sciences Faculty, College of Veterinary Medicine, UMC
2006-present	Medical Pharmacology and Physiology Faculty, College of Medicine, UMC

\*Course Director, Veterinary Cell Biology 5506/7333 Faculty evaluator, Veterinary Physiology 8420 Course Director, Multidisciplinary Approaches to Biomedical Sciences 8085

WS 2004-06, 2008, FS 2008, 2010-12

Graduate Committee Member

Kurt Marshall, 2011-pres. Department of Biomedical Sciences, University of Missouri Ashlee Williams, 2011-2012, Department of Biomedical Sciences, University of Missouri Zeev Swartz, DVM, 2011-pres. Departments of Surgery, Biomedical Sciences, University of Missouri Joe Company, 2008-pres. Department of Biomedical Sciences, University of Missouri Kyle McCommis, 2008-pres. Department of Biomedical Sciences, University of Missouri Luise King, 2009-pres. Department of Biomedical Sciences, University of Missouri

- 2012-pres. Chair, Biomedical Sciences Doctoral Faculty Nomination Committee
- 2010-pres. Biomedical Sciences Faculty Mentoring Committee (Dr. Emter)
- 2012-2015 CVM Promotion and Tenure Committee
- 2012 Chair, Associate Dean for Academic Affairs Search Committee
- 2011-2012 Chair, CVM Faculty Policy Committee
- 2009-2013 CVM Faculty Policy Committee
- 2010-2012 Chair, CVM Administrator Evaluation Committee
- 2005-present CVM Graduate/Resident Training Committee
- 2003-present Research Mentor, Comparative Medicine Training Program
- 2012 Member, Professional Science Masters Task Force
- 2012-2015 Member, Graduate Faculty Senate

Bowles continued

2012-2013	Graduate Faculty Senate Awards Committee
2012-pres.	Member, Life Sciences Fellowship Awards committee
2006-pres.	Trustee, Health Activity Center M. Harold Laughlin Scholarship Fund

#### Manuscript Review

2009-pres.	Reviewer, Hypertension
2009-pres.	Reviewer, Atherosclerosis, Thrombosis and Vascular Biology
2007-pres.	Reviewer, Circulation
2000-pres.	Reviewer, American Journal of Physiology: Cell
1995-pres.	Reviewer, Circulation Research
1995-pres.	Reviewer, Journal of Applied Physiology
1993-pres.	Reviewer, American Journal of Physiology: Heart and Circ. Physiology
1998-pres.	Reviewer, Medicine & Science in Sports & Exercise
2011-14	Nominating Committee, CV Section, American Physiological Society
2012	Sponsor for Visiting Professor, Dr. David Fisher, University of Western Cape, Capetown, South
	Africa during October/November. Purpose of Dr. Fisher's visit was to continue collaborative proj
	ect on cellular mechanisms of herbal-based medical therapies.

#### Grant Review Board

2012	Dunhill	Medical	Trust Review	(London)
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#### Editorial boards

2012-pres. Editorial Board of Scientifica

#### Manuscript Review

- 2006-pres. Reviewer, Journal of Vascular Research
- 2003-pres. Reviewer, Journal of Physiology
- 2001-pres. Reviewer, Cardiovascular Research

### Lane Clarke

#### Publications

**Professional Journals** 

Liu, J, Walker, NM, Cook, MT, Ootani, A, Clarke, LL. Functional Cftr in crypt epithelium of organotypic enteroid cultures from murine small intestine. Am. J. Physiol. Cell Physiol. 302: C1492-C1503, 2012.

Published Abstracts

Liu, J, Walker, NM, Clarke, LL. Hyperproliferation is an intrinsic property of the intestinal epithelium in Cftr-null mice. Gastroenterology 142 (Suppl. 1): S334, 2012.

Liu, J, Walker, NM, Clarke, LL. Intracellular pH is normal in CF goblet cells but not in adjacent epithelial cells of murine intestinal organoids. Pediatr. Pulmonol. Suppl. 35: 266, 2012.

#### Presentations

\*Cftr and the Biology of Regenerating Crypts in Intestinal Organoids. St. Jude Children's Research Hospital, Memphis, TN – April 5, 2012

\*Breaking GI Research in Cystic Fibrosis, Plenary Session II, North American Cystic Fibrosis Conference, Orlando, FL, October 12, 2012. Presented by Dr. D. Borowitz, MD, Plenary Speaker.

\*Epithelial-Specific Pathology Revealed in Intestinal Organoids from the Cystic Fibrosis Mouse, West Virginia University Health Sciences Center, Morgantown, WV – October 18, 2012

Poster presentations

Liu, J, Walker, NM, Clarke, LL. Hyperproliferation is an intrinsic property of the intestinal epithelium in Cftr-null mice. Digestive Diseases Week, San Diego, CA, May 20, 2012.

Liu, J, Walker, NM, Clarke, LL. Intracellular pH is normal in CF goblet cells but not in adjacent epithelial cells of murine intestinal organoids. 26th North American Cystic Fibrosis Conference. Orlando, FL – October 11-13, 2012.

#### **Active Grants**

01/12-11/12 MU Research Board, Modulation of Cftr to minimize crypt damage during chemotherapy", \$50,000, PI

01/12-12/12 Mizzou Advantage, "Regenerating Intestinal Crypts for Biomedical Research", \$50,000, PI.

04/11 - 3/13 Cystic Fibrosis Foundation; "Abnormal Regulation of Goblet Cells in the Cystic Fibrosis Intestine", \$194,400, PI.

#### Clarke continued

07/11-06/12 National Institutes of Health; "CFTR and Acid-Base Transporters in Regenerating Intestinal Crypts", \$74,946, NIH R56, PI.

05/12-04/16 National Institutes of Health; "CFTR and Acid-Base Transporters in Regenerating Intestinal Crypts", \$1,619,473, R01 DK48816–14-17, PI.

#### **Professional Service**

National/International

-Cystic Fibrosis Foundation, Research and Training Committee (Grant Reviews), Charter Member

-CIMG NIH Study Section, Charter Member

-South Carolina INBRE Bioinformatics Pilot Projects

-Manuscript reviewer for Journal of Clinical Investigation, Gastroenterology, Journal of Physiology, American

-Journal of Physiology and Fish Physiology and Biochemistry.

College

NAVMEC/Education Committee, Member

Department

Graduate Policy Advisory Committee, Biomedical Sciences - Member

### **George Davis**

#### Publications

Sacharidou, A., Stratman, A.N., and Davis, G.E. (2012) Molecular mechanisms controlling vascular lumen formation in three-dimensional extracellular matrices, Cells Tissues Organs (special issue), 195:122-143.

Stratman, A.N., and Davis, G.E. (2012) Endothelial cell-pericyte interactions stimulate basement membrane matrix assembly: Influence on vascular tube remodeling, maturation and stabilization, Microscopy and Micro-analysis, 18:68-80.

Pan, W., Pham, V.N., Stratman, A.N., Castranova, D., Kamei, M., Kidd, K.R., Lo, B.D., Shaw, K.M., Torres-Vasquez, J., Mikelis, C.M., Gutkind, J.S., Davis, G.E., and Weinstein, B.M. (2012) CDP-diacylglycerol synthetase-controlled phosphatidylinositol 4,5-bisphosphate availability limits VEGFa signaling and vascular morphogenesis, Blood, 120:489-498.

Davis, G.E. (2012) Molecular regulation of vasculogenesis and angiogenesis: Recent advances and future directions. In Molecular and Translational Vascular Medicine, Eds. J.W. Homeister and M.S. Willis, Springer, pgs. 169-206.

Yuan, L., Le Bras, A., Sacharidou, A., Itagaki, K., Zhan, Y., Kondo, M., Carman, C., Davis, G.E., Aird, W.C., and Oettgen, P. (2012) ETS-related gene (Erg) controls endothelial cell permeability via transcriptional regulation of the claudin-5 (CLDN5) gene, J. Biol. Chem., 287:6582-6591.

Schrimpf, C., Xin, C., Campanholle, G., Gill, S.E., Stallcup, W., Lin, S-L., Parekh, D.J., Venkatachalam, M., Davis, G.E., Gharib, S.A., Humphreys, B.D., and Duffield, J.S. (2012) Pericyte-derived TIMP-3 and ADAMTS1 regulate vascular stability after kidney injury, J. Amer. Soc. Nephrol., 23:868-883.

Stratman, A.N., Kim, D. J., Sacharidou, A., Speichinger, K.R., and Davis, G.E. (2012) Methodologic approaches to investigate vascular tube morphogenesis and maturation events in 3D extracellular matrices in vitro and in vivo. In The Textbook of Angiogenesis and Lymphangiogenesis: Methods and Applications, Eds. E. Zudaire and F. Cuttitta, Springer, pgs. 101-125.

Zheng, X., Xu, C., Smith, A.O., Stratman, A.N., Zou, Z., Kleaveland, B., Yuan, L., Didiku, C., Sen, A., Liu, X., Skuli, N., Zaslavsky, A., Chen, M., Cheng, L., Davis, G.E., and Kahn, M.L. (2012) Dynamic regulation of the cerebral cavernous malformation pathway controls vascular stability and growth, Dev. Cell, 23:342-355.

#### **Invited Lectures/ Presentations**

2012 (October) Developmental Vascular Biology Workshop V- Navbo Conference, Monterey, CA, Invited Speaker

2012 (August) 5th Mayo Clinic Angiogenesis Conference, Minneapolis, MN, Invited Speaker

2012 (July) Signal Transduction by Engineered Extracellular Matrices-Gordon Conference, Biddeford, ME, Invited Speaker

#### George Davis continued

2012 (June) International Vascular Biology Meeting 2012, Wiesbaden, Germany, Invited Speaker
2012 (April) UCLA Vascular Biology Seminar Series, Los Angeles, CA
2012 (March) Program in Genomics of Differentiation Seminar Series, National Institutes of Health, Bethesda, MD
2012 (March) Harvard Medical School Vascular Biology Seminar Series, Boston, MA

#### Active Grants

NIH-NHLBI - R01 G.E. Davis- PI, B. Weinstein- Coll. Investigator, S.C. Peck, Coll. Investigator, "Genes regulating capillary morphogenesis and apoptosis" 7/01/08- 6/30/13, \$250,000/ yr.

NIH-NHLBI- R01 G.E. Davis- PI, "Hematopoietic stem cell cytokine control of developmental vascularization" 1/01/11- 12/31/14. \$250,000/ yr.

NIH- NHLBI- R01 G.E. Davis- PI, M.J. Davis Coll. Investigator, "Pericyte proteinase inhibitors and EC tube stabilization" 1/12/10- 11/30/13, \$250,000/ yr.

NIH- NHLBI- R01 G.E. Davis- PI, M.J. Davis Coll. Investigator, D.C. Zawieja- Coll. Investigator, "Molecular control of EC lumen formation by MT1-MMP" 1/01/08- 12/31/12, \$250,000/ yr.

NIH-NHLBI- R01 R.T. Tranquillo-PI, G.E. Davis Coll. Investigator, "Biopolymer-guided human stem cell assembly for engineered myocardium. 9/05/11- 5/31/15., \$65,000/ yr.

#### **Professional Service**

Professional Society Memberships American Society for Investigative Pathology American Association for the Advancement of Science American Society for Cell Biology North American Vascular Biology Organization

Ad hoc reviewer for the following granting agencies: American Cancer Society Spinal Cord Research Foundation National Institutes of Health, Pathology A Study Section American Heart Association, Western States Affiliate ZRG1 CVRS-L Special Emphasis Panel ZRG1 CVRS-B Special Emphasis Panel (Challenge grants) ZRG1 VH C (02) Special Emphasis Panel

#### Ad hoc reviewer for the following journals:

American Journal of Physiology Cancer Experimental Cell Research Journal of Virology Clinical and Experimental Metastasis

#### George Davis continued

Journal of Cell Biology Science Brain Research Developmental Brain Research Journal of Leukocyte Biology American Journal of Pathology Journal of Cell Science Trends in Cardiovascular Medicine Atherosclerosis, Thrombosis and Vascular Biology Journal of Vascular Biology **FASEB** Journal Molecular and Cellular Biology Cancer Research **BBA-Cancer** Arthritis and Rheumatism Current Biology Blood Microcirculation Proc. Natl. Acad. Sci. USA Development **Developmental Dynamics** Molecular Biology of the Cell

### Michael J. Davis

#### Publications

Davis MJ: Perspectives: Physiological roles of the vascular myogenic response. Microcirculation 19(2):99-114, 2012.

Liu Y, Kalogeris T, Wang M, Zuidema M, Wang Q, Davis MJ, Hill MA, and Korthuis RJ: Hydrogen sulfide preconditioning or neutrophil depletion attenuates ischemia/reperfusion-induced mitochondrial dysfunction in rat small intestine. Am J Physiol 302(1):G44-G54, 2012.

Gashev AA, Zhang R-Z, Muthuchamy M, Zawieja DC and Davis MJ: Regional heterogeneity of length-tension relationships in rat lymphatic vessels. Lymphatic Res Biology 10(1):14-19, 2012.

Dongaonkar RM, Quick CM, Vo JC, Meisner JK, Laine GA, Davis MJ, Stewart RH: Blood flow augmentation by intrinsic venular contraction in vitro. Am J Physiol 302(12):R1436-1442, 2012.

Rahbar E, Weimer J, Davis MJ, Zawieja DC, Moore JE Jr: Passive pressure-diameter relationship and structural composition of rat mesenteric lymphangions. Lymphatic Res Biology, Nov. 12, 2012.

Masseau I, Davis MJ, Bowles DK: Effects of chronic exercise on carotid inflammation and endothelial dependent relaxation in Familial Hypercholesterolemic swine. Med Sci Sports Ex 44(12): 2277-2289, 2012.

Davis MJ, Wolpers HJ, Muthuchamy M, Gashev AA, Zawieja DC: Intrinsic increase in lymphatic muscle contractility in response to elevated afterload. Am J Physiol 303(7):H795-H808, 2012.

Scallan JP, Wolpers HJ, Muthuchamy M, Zawieja DC, Gashev AA, Davis MJ: Independent and interactive effects of preload and afterload on the lymphatic pump. Am J Physiol 303(7):H809-H824, 2012.

#### **Manuscripts in Press**

Fairfax ST, Padilla J, Vianna LC, Davis MJ, Fadel PJ: Spontaneous bursts of muscle sympathetic nerve activity decrease femoral vascular conductance in resting humans (Am J Physiol: HCP, 2012) (Cited by Faculty 1000)

Scallan JP, Wolpers HJ, Davis MJ: Rapid lymphatic constriction in response to elevated output pressure is conducted across inter-lymphangion valves (J Physiology, Dec. 10, 2012) (Highlighted article)

#### **Book Chapters**

Hill MA and Davis MJ: Local Control of Blood Flow, In: Systems Physiology—From Molecule to Function, Eds. Granger DN and Granger JP, Morgan & Claypool, Princeton, 2012.

Muller-Delp J, Dick GM, Davis MJ, Chilian WM: The coronary microcirculation in health and disease. In: The Heart in Biology and Disease, ed. Bittar EE, Springer, 2012

### Shinghua Ding

#### Publications

Li Qin Zhang, Dilyara Cheranova, Margaret Gibson, Shinghua Ding, Daniel P. Heruth, Deyu Fang4 and Shui Qing Ye1,2. RNA-seq reveals novel transcriptome of genes and their isoforms in human pulmonary microvascular endothelial cells treated with thrombin. PloS ONE 7:e31229, 2012.

Jing Bi3, Hailong Li2, Shui Qing Ye, Shinghua Ding<sup>\*</sup>. PBEF exerts a neuronal protection through its enzymatic activity and the reduction in mitochondrial dysfunction in vitro ischemic models. Journal of Neurochemistry 120:334-346, 2012.

Shinghua Ding. In vivo imaging of Ca2+ signal in astrocytes using two-photon laser scanning fluorescent microscopy. Methods in Molecular Biology 814:545-554, 2012.

#### Presentations

Knockout of type 2 IP3 receptor (IP3R2) enhances cell proliferation in the subgranular zone (SGZ) in dentate gyrus of hippocampus. 42th Annual Meeting of Society for Neuroscience, October 13-17, 2012, New Orleans. Wenting Chang, Hailong Li, Nannan Zhang, Shinghua Ding.

The effect of inhibition of group 1 mGluRs on brain damage after ischemia. 43nd Annual Meeting of American Society for Neurochemistry. Baltimore, March 3-7, 2012. Hailong Li, Nannan Zhang, Shinghua Ding.

Astrocytic Ca2+ signaling and its role in ischemia 43nd Annual Meeting of American Society of Neurochemistry. Baltimore, March 3-7, 2012. Shinghua Ding (Symposium talk)

Evaluation of transduction patterns of novel serotypes of adenoassociated virus (AAV) in retina. Life Science Week, University of Missouri-Columbia. April 16-20, 2012.

Xiaozhen Wang, Hailong Li, Jinglu Tan, Shinghua Ding Knockout of type 2 IP3 receptor (IP3R2) enhances neuronal proliferation. Life Science Week, University of Missouri-Columbia. April 16-20, 2012.

Wenting Chang, Hailong Li, Nannan Zhang The effect of inhibition of group 1 mGluRs on brain damage after ischemia. Life Science Week, University of Missouri-Columbia. April 16-20, 2012. Hailong Li, Nannan Zhang, Shinghua Ding.

Knockout of type 2 IP3 receptor (IP3R2) enhances neuronal proliferation. Cardiovascular Day, University of Missouri-Columbia. February 21, 2012. Wenting Chang, Hailong Li, Nannan Zhang, Shinghua Ding.

Knockout of type 2 IP3 receptor (IP3R2) enhances neuronal proliferation. Cardiovascular Day, University of Missouri-Columbia. February 21, 2012. Wenting Chang, Hailong Li, Nannan Zhang

"PBEF plays a critical role in brain protection after ischemia". Cardiovascular Day, University of Missouri-Columbia, February 21, 2012. Shinghua Ding (Invited talk)

#### Ding continued

Brain protection by PBEF in cerebral ischemia. Children's Mercy Hospitals and Clinics, School of Medicine, University of Missouri-Kansas City, January 6, 2012.

#### **Active Grants**

Astrocyte-mediated neuronal excitation (0735133N)\* AHA (National SDG grant) \$260,000 7/1/2007-6/30/2012 PI 24% effort Non-cost extension for the year 7/01/2011-6/30/2012

Role of Gliotransmission in ischemia (R01NS069726) NIH \$1,591,689 5/15/2010- 4/30/2015 PI 40% effort

#### **Professional Service**

June 15, 2009-present: Member of safety committee of Dalton Cardiovascular Research Center.

August 18, 2009-present: Member of safety committee of College of Engineering.

September 2011- present: Member, Library Committee, College of Engineering.

Member, Organizing Committee; Cardiovascular Day 2012; University of Missouri-Columbia. February 21, 2012.

Judge, Undergraduate Research & Creative Achievements Forum; University of Missouri. April 24, 2012

Member of Membership Committee, American Society for Neurochemistry. March 2011-March 2015.

Reviewers for multiple Journals

Session chair on the Colloquium titled "Glial dysfunction and role in brain ischemia" at 43rd Annual American Society for Neurochemistry (ASN) meeting in Baltimore, March 3-7, 2012.

### Paul J. Fadel

#### Publications

Deo SH, Fisher JP, Vianna LC, Kim A, Chockalingam AC, Zimmerman MC, Zucker IH, Fadel PJ. Statin therapy lowers muscle sympathetic nerve activity and oxidative stress in patients with heart failure. AJP (Heart Circ Physiol), 303(3):H377-85, 2012.

Fadel PJ, Farias III M, Gallagher KM, Wang Z, Thomas GD. Oxidative stress and enhanced sympathetic vasoconstriction in contracting muscles of nitrate-tolerant rats and humans. J Physiol, 590(Pt 2):395-407, 2012.

Vianna LC, Hart EC, Fairfax ST, Charkoudian N, Joyner MJ, Fadel PJ. Influence of age and sex on the pressor response following a spontaneous burst of muscle sympathetic nerve activity. AJP (Heart Circ Physiol), 302(11):H2419-27, 2012.

Kim A, Deo SH, Fisher JP, Fadel PJ. Effect of sex and ovarian hormones on carotid baroreflex resetting and function during dynamic exercise in humans. J Appl Physiol, 112(8):1361-71, 2012.

Fadel PJ, Raven PB. Human investigations into the arterial and cardiopulmonary baroreflexes during exercise. Exp Physiol, 97(1):39-50, 2012.

#### Presentations

Impaired Nitric Oxide Signaling in the Brain, Not the Periphery, Contributes to Increased Cardiovascular Risk. APS Conference, Omaha, Nebraska (7/12).

Influence of Sex and Ovarian Hormones on Arterial Baroreflex Control during Exercise in Humans. Brazil Control of the Sympathetic Nervous System in Humans: A Role for Insulin. Department of Biomedical Sciences-Veterinary Medicine, University of Missouri, Columbia (2/12).

#### Active Grants

"Aging, Sex, and Neural Cardiovascular Control during Dynamic Exercise," National Institutes of Health, R01 HL093167, 30% effort, PI: Paul Fadel, 8/08-8/13, \$1,250,000.

"Exercise and Health: Integration from molecule to patient," National Institutes of Health, T32-AR048523, PI: Ronald Terjung, Mentor: Paul Fadel, 7/09-6/14, \$1,000,000.

"Sympathetic Control in Heart Failure: A Role of Statins," National Institutes of Health, R01 ARRA 34-5170-2059-02, 20% effort, PI: Irving Zucker, Co-I: Paul Fadel, 8/09-8/12, \$353,993.

"Age- and sex- related alterations in arterial baroreflex control of blood pressure during dynamic exercise," American College of Sports Medicine Foundation Research Grant, PI: Areum Kim (Graduate Student), Advisor: Paul Fadel, 7/10-3/12, \$5,000.

#### Fadel continued

Professional Services

Ad-hoc Manuscript Reviewer- Medicine and Science in Sports and Exercise (6/01-present)

Experimental Physiology (2/03-present)

AJP: Regulatory, Integrative and Comparative Physiology (8/03-present)

Journal of Applied Physiology (12/03-present)

European Journal of Applied Physiology (9/04-present)

AJP: Heart and Circulatory Physiology (12/04-present)

Journal of Physiology (5/05-present)

Experimental Biology and Medicine (10/06-present)

Hypertension (5/07-present)

Brain Research (8/09-present)

Annals of Neurology (12/09-present)

Editorial Board- Experimental Physiology (11/12-present)

Journal of Applied Physiology (1/11-present)

European Journal of Applied Physiology (1/10-present)

Frontiers in Exercise Physiology (7/10-present)

Ad-hoc Grant Reviewer- Alberta Heritage Foundation for Medical Research

University of Missouri Research Board

Natural Sciences & Engineering, Research Council of Canada

University of Missouri, School of Medicine Scientific Peer Review Committee (1/08-present)

Medical Pharmacology and Physiology Seminar Committee (9/08-present)

### William Fay

#### Publications

Ji Y, Strawn TL, Fay WP, Chen R. Systemic administration of an optimized human apyrase inhibits acute thrombosis and neointima formation in vein grafts. Arterioscler Thromb Vasc Biol 2012.

A dominant negative mutant of plasminogen activator inhibitor-1 does not inhibit intimal hyperplasia after balloon coronary angioplasty in pigs. Strawn TL, Ivey JR, Lawrence DA, Bowles DK, Fay WP. Arterioscler Thromb Vasc Biol 2012.

Mittal M, Strawn T, Fay W: Novel Tiplaxtinin Eluting Stent Inhibits the Migration of Vascular Smooth Muscle Cells but not Endothelial Cells. Circulation. 2012

#### Presentations

Dept. of Cellular and Molecular Physiology, Univ. of Nevada Reno (Sept. 2012); Topic: Regulation of ion channels by integrin-ECM signaling (Ion Channel Regulation course

March 2012	Cardiovascular Day, University of Missouri, Columbia, MO
May 2012	Dept. of Toxicology & Pharmacology, University of Mississippi, Jackson, MS
October 2012	Dept. of Physiology & Cell Biology, University of Nevada, Reno
November 2012	Dept. of Anatomy & Physiology, Kansas State University, Lawrence, KS
2012	Co-chair, MCS-BMS meeting, Oxford, UK

#### **Active Grants**

#### NIH R01

"Roles of Plasminogen Activator Inhibitor-1 and Vitronectin in Failure of Coronary Revascularization" PI: W. Fay (25% effort)
9/1/10-8/31/14. \$250,000 annual direct costs.
Impact/Priority Score: 12; %ile score: 1.0

NIH/NHLBI Program Project Grant "Molecular Genetics of Coagulation Disorders" PI: D. Ginsburg Dr. Fay is Co-Investigator (10% effort) on Project 3: ("Thrombosis and Hemostasis in Host Defense from Bacterial Infection", PI: H. Sun) 4/1/09-3/31/14 (\$223,863 annual direct costs of Project 3)

#### NIH R44

"Improved long-term biocompatibility of coronary stents by plasma coating process" PI: M. Chen. Dr. Fay is Co-Investigator (10% effort) 09/01/2011-02/28/2014. Fay continued

#### NIHR44 "Prevention of Vein Graft Intimal Hyperplasia with Human Apyrase" PI: R. Chen. Dr. Fay is Co-Investigator (10% effort) 0/1/12-9/30/13

#### **Professional Services**

#### **Specialty Board Review**

Fay WP: Pathophysiology of Arterial Thrombosis, in Baliga R (Ed), Specialty Board Review: Cardiology. Mc-Graw-Hill, New York, NY; 2012; 999-1004.

Garg R, Kuppuswamy S, Webel R, Fay WP: Treatment of Arterial Thrombosis, in Baliga R (ed), Specialty Board Review: Cardiology. McGraw-Hill, New York, NY; 2012; 1005-1012.

- 2010- School of Medicine Advisory Committee on Research Space
- 2011- Blue Ribbon Commission, School of Medicine
- 2012-2013 Research Portfolio Taskforce Committee

Vice-Chair of Department, 2006-present

Administrative Advisory Committee, 2005-present

Space Committee, 2005-present RIF Committee, 2005-present

2012 FASEB Summer Research Conference: Smooth Muscle, Snowmass, CO-Session Chair

#### Journal Review

American Journal of Physiology: Advances in Physiology Education

American Journal of Physiology: Cell Physiology

American Journal of Physiology: Heart and Circulatory Physiology

American Journal of Physiology: Regulatory, Integrative, and Comparative Physiology

**Circulation Research** 

Journal of Applied Physiology

Journal of Vascular Research

Microcirculation

PLoS ONE

### Shubra Gangopadhya

#### Publications

K Bhatnagar, A Pathak, D Menke, P V Cornish, K Ganopadhyay, V Korampally, and S Gangopadhyay "Fluorescence enhancement from nanogap embedded plasmonic gratings by a novel fabrication technique with HD-DVD", Nanotechnology, in press (2012).

Somik Mukherjee, Balavinayagam Ramalingam, Lauren Griggs, Steven C. Hamm, Gary A. Baker, Phil Fraundorf, Shramik Sengupta, Shubhra Gangopadhyay, "Ultrafine sputter-deposited Pt nanoparticles for triiodide reduction in dye-sensitized solar cells: impact of nanoparticle size, crystallinity and surface coverage on catalytic activity", Nanotechnology, in press (2012).

Minseong Yun, Balavinayagam Ramalingam, and Shubhra Gangopadhyay, "Multi-layer Pt nanoparticle embedded high density non-volatile memory devices", Journal of The Electrochemical Society, in press, 2012. Sangho Bok, Venumadhav Korampally, Charles M. Darr, William R. Folk, Luis Polo-Parada, Keshab Gangopadhyay, Shubhra Gangopadhyay "Femtogram-level Detection of Clostridium botulinum Neurotoxin Type A by Sandwich Immunoassay Using Nanoporous Substrate and Ultra-bright Fluorescent Suprananoparticles", Biosensors and Bioelectronics, in press (2012).

Wei-Ning Wang, Woo-Jin An, Balavinayagam Ramalingam, Somik Mukherjee, Dariusz M. Niedzwiedzki, Shubhra Gangopadhyay, and Pratim Biswas, "Size and Structure Matter: Enhanced CO2 Photoreduction Efficiency by Size-Resolved Ultrafine Pt Nanoparticles on TiO2 Single Crystals" J. Am. Chem. Soc. (in press), 2012.

Madhuri Korampally, Steven J. Apperson, Clay S. Staley, Jorge A. Castorena, Rajagopalan Thiruvengadathan, Keshab Gangopadhyay, Rajiv R. Mohan1, Arkasubhra Ghosh, Luis Polo-Parada, and Shubhra Gangopadhyay, "Transient pressure mediated intranuclear delivery of FITC-Dextran into chicken cardiomyocytes by MEMS-based nanothermite reaction actuator", Sensors & Actuators: B. Chemical, in press, 2012.

An, Woo-Jin; Wang, Wei Ning; Ramalingam, Balavinayagam; Mukherjee, Somik; Daubayev, Batyrbek; Gangopadhyay, Shubhra; Biswas, Pratim, "Enhanced Water Photolysis with Pt Metal Nanoparticles on Single Crystal TiO2 Surfaces", Langmuir, in press (2012).

Steven C. Hamm, Ravi Shankaran, Venu Korampally, Sangho Bok, Snigdha Praharaj, Gary A. Baker, J. David Robertson, Byung Doo Lee, Shramik Sengupta, Keshab Gangopadhyay and Shubhra Gangopadhyay, "Sputter-deposition of silver nanoparticles into ionic liquid as a sacrificial reservoir in antimicrobial organosilicate nano-composite coatings, ACS Appl. Mater. Interfaces, 4, 178–184, 2012.

Sangho Bok, Venumadhav Korampally, Luis Polo-Parada, Vamsi Mamidi, Gary A. Baker, Keshab Gangopadhyay, William R. Folk, Purnendu K. Dasgupta and Shubhra Gangopadhyay, "Confeito-like assembly of organosilicate-caged fluorophores: ultrabright suprananoparticles for fluorescence imaging", Nanotechnology (accepted), 2012.

Kassandra Kisler, Brian N. Kim, Xin Liu, Khajak Berberian, Qinghua Fang, Cherian J. Mathai, Shubhra Gangopadhyay, Kevin D. Gillis, and Manfred Lindau, "Transparent electrode materials for simultaneous amperometric detection of exocytosis and fluorescence microscopy", Journal of Biomaterials and Nanobiotechnology, in press, 2012. Trenkmann, I.; Bok, S.; Korampally, V.; Gangopadhyay, S.; Graaf, H\*.; Borczyskowski, C.V.; "Determination of single dye molecules in luminescent organosilicate nanoparticle markers" Chemical Physics, Accepted, 2012.

Bryant C. Harris, Venumadhav Korampally, Craig Weilbaecher, Sheila Grant, Luis Polo-Prada, and Shubhra Gangopadhyay, "Protease Sensing on Novel High Surface Area Organosilicate Nanoporous Films", Sensors and Actuators: B. Chemical, (in press), 2012.

Thiruvengadathan R, Gianetta M Belarde, Andrey Bezmelnitsyn, Maxim Shub, Wendy Balas-Hummers, Keshab Gangopadhyay, and Shubhra Gangopadhyay "Combustion characteristics of silicon-based nanoenergetic formulations with reduced Electrostatic discharge sensitivity" Propellants, Explosives, Pyrotechnics, in press, 2012. Collin R. Becker, Steven Apperson, Christopher J. Morris, Shubhra Gangopadhyay, Luke J. Currano, Wayne A.

#### **Active Grants**

NSF ECCS-123217, \$ 360,000:"Trace Vapor Detection of Explosives using Molecularly Imprinted Organic Field Effect Transistors and Metal Nanoparticles", Award Period: 9/1/2012-5/31/2015. Role: PI.

THE BOEING COMPANY \$70,000:"Window repair", Award Period:5/1/2012-7/31/2012.

NSF ECCS-1102070 \$ 359,350: Nanostructured High Surface Area Sensor Systems for Enhanced Detection, Award Period: 6/1/2011-5/31/2014. Role: Co-PI.

NANOTECHNOLOGY ENTERPRISES INC/US Army \$779,000: Integration and Commercialization of Sensor Nanotechnology for Explosive Detection 08/01/2011-07/30/2012 Role: Co-I

NANOTECHNOLOGY ENTERPRISES INC/US Army \$299,712: Large scale production of advanced nanoenergetics materials as primer for propellant ignition 08/01/2011-07/30/2012 Role: Co-I

NEMS/MEMS Works, LLC./NANOTECHNOLOGY ENTERPRISES INC/US Army \$150,000: Prototype development of remote memory disruption systems for portable electronics 08/01/2011-07/30/2012 Role: PI

LEONARD WOOD INSTITUTE/US Army \$200,000: Gangopadhyay, S, Multi-functional Nanocomposite Fibers with Antimicrobial and Flame Retardant Properties for Fabrication of Smart Defense Fabrics 06/15/2011-12/31/2012 Role: PI

CROSSLINK , LLC., NTEC/US Army \$100,000: Solid State High Power and Energy Density Supercapacitors Using Nanostructured Conductive Polymer Composites 08/01/11-07/30/2012 Role: PI

NEMS/MEMS Works, LLC ARMY SBIR PHASE II \$145K: Fast Impulse Solid Fuel Miniature Thruster, Award Period: 6/11-5/13. Role: PI.

NEMS/MEMS Works, LLC/US Army \$85K: MEMS Based Systems Development for Contaminant Analysis Role: PI. Award Period: 8/09-8/12. The objective of this research is experimentation with PDMS fiber and nanoporous particulate films for efficient contaminant analysis with specificity.

NSF ECCS-0901566 GOALI \$372K: Nanothermite Based Micro Shockwave Generators and Nanoparticles for Targeted and Efficient Gene/Drug Delivery Role: PI. The objective of this research is to develop a novel digitally controlled micro shockwave generator by integrating nanothermites with MEMS. Award Period: 8/09-7/13.

NSF ECCS-0801753 \$324K: Collaborative Research: High Density Metal and Semiconductor Nanoparticles for Memory and Photonic Applications. Role: PI. The major goal of this project is to prepare high density metal and semiconductor nano-particles for fabricating memory and photonic devices. Award Period: 6/08-NEMS/MEMS Works, LLC US Army \$50K: Development of a Micro-Device for Remote Disruption of Electronic Hardware. Role: PI Award Period: 11/10-09/11

Leonard Wood Institute-US Army: \$150K: Trace Vapor Phase Detection of Explosives using Platinum Nanoparticle Embedded Organic Transistors. Award Period: 09/10-09/12. Role: Co-I.

Office of Naval Research N00014-11-C0392 \$1.6M: University of Missouri Railgun Program. Role: Co-I. Award Period: 03/11-03/13

#### **Professional Service**

American Physical Society

Institute of Electronics and Electrical Engineers

Material Research Society

American Chemical Society

- Sep. 2003 present LaPierre Chair Professor, Department of Electrical and Computer Engineering, Uni versity of Missouri, Columbia, Missouri (MU)
- Sep. 2003 present Joint Professor, Department of Physics and Astronomy, MU
- Sep. 2003 present Joint Professor, Department of Biological Engineering, MU
- April 2006 present Director, International Center for Nano/Micro Systems and Nanotechnology, MU

### Kevin Gillis

#### Publications

Yao, J., and Gillis, K.D. Quantification of noise sources for amperometric measurement of quantal exocytosis using microelectrodes. Analyst 137: 2674-2681, 2012.

Kisler, K., Kim, B.N., Liu, X., Berberian, K., Fang, Q., Mathai, C.J., Gangopadhyay, S., Gillis, K.D., and Lindau, M. Transparent electrode materials for simultaneous amperometric detection of exocytosis and fluorescence microscopy. Journal of Biomaterials and Nanobiotechnology 3: 243-253, 2012.

Misler, S., and Gillis, K.D. Modes of exocytosis and electrogenesis underlying canine biphasic insulin secretion. Frontiers in Bioscience E4: 669-676, 2012.

Research Funding (all dollar amounts indicate direct costs)

Present

NIH, SBIR (to ExoCytronics LLC), \$671,743 (subcontract to MU: \$212,101), "Development of a prototype system for assaying exocytosis from individual cells", PI, 09/11 – 05/13.

NIH, R01, \$543,546 (MU portion), "A scalable nxn electrochemical detector array platform with on-chip amplifiers for massively parallel recordings of quantal transmitter release events.", co-I (PI: M. Lindau, Cornell Univ.), 09/11-04/15

NIH, RO1, \$1,016,600, "Programmable multi-target detection using an aptamer-integrated nanopore", co-I (PI: L.-Q. Gu), 02/07 – 01/12

#### Completed

University of Missouri Research Board, \$40,000, "Combined optical and electrical measurement of exocytosis from single vesicles", PI, 9/10 – 2/12.

#### **Professional Service**

**Journal Reviewer:** Nature, Science, Neuron, EMBO Journal, Biophysical Journal, Journal of Theoretical Biology, Journal of Neuroscience

#### **Current graduate students:**

Jia Yao, PhD student in BE, 08/06 – present Jaya Ghosh, PhD student in BE, 08/07 – present

### Kenneth Gruber

#### **Professional Service**

Current: Founder and CEO/President, Tensive Controls, Inc., a biotech pharmaceutical company supported by grants from the NIH/NCI SBIR program, North Carolina State SBIR matching funds, and the IRS/HHS Qualifying Therapeutic Discovery Project program. Professor Emeritus of Biological Sciences, California State Polytechnic University, Pomona, CA; Adjunct Professor, Dalton Cardiovascular Research Center and Department of Medical Pharmacology and Physiology, University of Missouri, Columbia, MO

2004-Present Lytmos Group, Inc

American Physiological Society Association Pour les Exchanges Scientifique Internationaux (Honorary Member)

### Li-Qun Gu

#### Publications

Shim,J. & Gu,L.Q. Single-molecule investigation of G-quadruplex using a nanopore sensor. Methods 57, 40-46 (2012).

Gu,L.Q., Wanunu,M., Wang,M.X., McReynolds,L., & Wang,Y. Detection of miRNAs with a nanopore single-molecule counter. Expert Review in Molecular Diagnostics. 12, 573-584 (2012).

Tan,Q., Ritzo,B., Tian,K., & Gu,L.Q. Tuning the tetraethylammonium sensitivity of potassium channel Kcv by subunit combination. J. Gen. Physiol. 139, 295-304 (2012).

(News and View) Gu,L.Q., Ritzo,B., & Wang,Y. Biosensing: When less is more in a nanopore. Nature Nanotechnology. 7, 212-213 (2012)

Tian, K; Gu,L.Q., Ritzo,B. and Wang,Y. Biosensing: Designing a polycationic probe for simultaneous enrichment and detection of nucleic acids in a nanopore. ACS Nano (accepted) (Impact factor 11).

Gu, L.Q.; Wang, Y. Nanopore single-molecule detection of circulating microRNAs. Circulating MicroRNAs: Methods and Protocols. Ed. Nobuyoshi Kosaka. Method in Molecular Biology series (in press), published by Humana Press, USA (part of the Springer publishing group)

#### Presentations

(Invited student talk in Nanoscale Biophysics Symposium) Wang,Y. and Gu,L.Q. Nanopore-based detection of circulating microRNAs in lung cancer patients. Biophysical Society 56th Annual Meeting, February, 2012, San Diego.

Tian,K. and Gu,L.Q. A polycationic probe for noise-free detection of microRNA fragments in a protein nanopore. Biophysical Society 56th Annual Meeting, February, 2012, San Diego.

(Invited talk) Gu, L.Q. A nanopore sensor for detection of circulating microRNAs in lung cancer patients. Pre-conference webinar on microRNA Detection and Profiling Approaches for Cambridge Healthtech Institute's microRNA in Human Disease and Development meeting, March, 2012, in Cambridge, MA.

(Talk) Gu,L.Q. Aptamer-based biosensing of single protein molecules in a protein nanopore. 2012 International Conference on Engineering and Applied, July 2012, Beijing, China

(Invited speech) Gu,L.Q. Nanopore in personalized medicine –from Sequencing to Epigenetics Biophotonics Workshop, University of Missouri, 2012

(Elevator pitch presentation as a featured technology) Gu,L.Q. and Wang,Y. Nanopore microRNA detection in cancer patients. Missouri Technology Expo-2012, Columbia, MO.

Gu continued

#### **Active Grants**

Programmable multi-target detection using aptamerintegrated nanopore NIH \$1,270,750 02/01/2007 –1/31/2012 (non-cost extension) PI

Coulter Foundation Bridging Fund at MU Coulter Foundation \$111,800 (+\$25,000 for commercialization strategy) 07/01/2012-06/30/2013 PI

## **Eileen Hasser**

## Publications

Regulation of arterial pressure by the paraventricular nucleus in conscious rats: interactions among glutamate, GABA, and nitric oxide. Martins-Pinge MC, Mueller PJ, Foley CM, Heesch CM, Hasser EM. Front Physiol. 2012 PMID: 23316170

Hypoxia activates nucleus tractus solitarii neurons projecting to the paraventricular nucleus of the hypothalamus. King TL, Heesch CM, Clark CG, Kline DD, Hasser EM. Am J Physiol Regul Integr Comp Physiol. 2012; 302(10):R1219-32.

## Presentations

Activation of nucleus tractus solitarii (nTS) neurons that project to the rostral ventrolateral medulla (RVLM) or hypothalamic paraventricular nucleus (PVN): Role of acute hypoxia (AH). Ruyle BC, Heesch CM, King TL, Kline DD, Hasser EM. FASEB J., 2012

Caudal ventrolateral medulla (CVLM) activation by acute hypoxia (AH) is independent of changes in arterial blood pressure (ABP). King, TL, Heesch CM, Friskey SA, Ruyle BC, Kline DD, Hasser EM

Cardiovascular deconditioning augments baseline breathing as well as peripheral and central chemoreflex responses. Zhou Z, King TL, Kline DD, Heesch CM, Hasser EM

Hydrogen peroxide (H2O2) modulates membrane properties in second-order nucleus tractus solitarii (nTS) neurons. Ostrowski TD, Hasser EM, Heesch CM, Kline DD

Expression of ROS catabolic enzymes in the medial nucleus tractus solitarii (nTS) of rats and upregulation during acute hypoxia. Ostrowski TD, Barr SL, Dantzler HS, Hasser EM, Kline DD, Heesch CM

## **Active Grants**

RO1 HL55306 04/01/07-03/31/11 No-cost extension Cardiovascular Regulation in Hindlimb Unweighted Rats National Institutes of Health Annual: \$225,000/yr. Total: \$900,000 Role: PI

RO1 HL098602 07/15/2010-06/30/2014 Plasticity of nTS output neurons in acute and chronic hypoxia National Institutes of Health Role: (Multi PI with Cheryl M. Heesch and David D. Kline) Annual: \$491,679 Total Direct/yr (\$163,283.00-EMH Direct): Total: 2,830,531

R01 HL091164 (Cheryl M. Heesch, PI) Central nervous system plasticity in sympathoinhibition in pregnancy National Institutes of Health Role: Co-I Annual: \$250,000 Direct costs

### **Professional Service**

Committees

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- Departmental GPAC New Faculty Mentoring Committee Outreach Committee
- College
  - Promotion and Tenure Committee
- University
  - Animal Care and Use Committee
  - Cardiovascular Day Organizing Committee
- National

Manuscript Review

American Journal of Physiology (Heart Circulatory Physiology) American Journal of Physiology (Regulatory Comp & Integ Physiology) Journal of Physiology Brain Research Journal of Applied Physiology Experimental Physiology Journal of Neuroscience Neuroscience

Grant Review

Research Board, University of Missouri

# **Cheryl Heesch**

## Publications

King,T.Luise; Heesch,Cheryl M.; Friskey,Sarah; Ruyle,Brian; Kline,David D.; Hasser,Eileen M. Caudal ventrolateral medulla (CVLM) activation by acute hypoxia (AH) is independent of changes in arterial blood pressure (ABP). FASEB J. 26: 702, 2012.

Brown,Randall J.; Phaup,J.Glenn; Hasser,Eileen M.; Heesch,Cheryl M. Relaxin in the subfornical organ (SFO) increases arterial pressure and lumbar sympathetic nerve activity in female rats: Role of Angiotensin II. FASEB J. 26: 891, 2012.

Zhou,Zijin; King,T.Luise; Kline,David D.; Heesch,Cheryl M.; Hasser,Eileen M. Cardiovascular deconditioning augments baseline breathing as well as peripheral and central chemoreflex responses. FASEB J. 26: 702, 2012.

Ruyle,Brian C.; Heesch,Cheryl M.; King,T.Luise; Kline,David D.; Hasser,Eileen M. Activation of nucleus tractus solitarii (nTS) neurons that project to the rostral ventrolateral medulla (RVLM) or hypothalamic paraventricular nucleus (PVN): Role of acute hypoxia (AH). FASEB J. 26: 702, 2012.

Ostrowski,Tim Daniel; Hasser,Eileen M.; Heesch,Cheryl M.; Kline,David D. Hydrogen peroxide (H2O2) modulates membrane properties in second-order nucleus tractus solitarii (nTS) neurons. FASEB J. 26: 701, 2012.

Ostrowski, Tim Daniel; Barr, Stacy L.; Dantzler, Heather A.; Hasser, Eileen M.; Kline, David D.; Heesch, Cheryl M. Expression of ROS catabolic enzymes in the medial nucleus tractus solitarii (nTS) of rats and upregulation during acute hypoxia. FASEB J. 26: 702, 2012.

Coldren,Kevin Max; Brown,Randall J.; Kline,David D.; Hasser,Eileen M.; Heesch,Cheryl M. Colocalization of estrogen receptor {beta} (ER{beta}) with spinally projecting and vasopressinergic neurons in the hypothalamic paraventricular nucleus (PVN) during pregnancy. FASEB J. 26: 891, 2012.

Tim D. Ostrowski, Stacy L. Barr, Heather A. Dantzler, Eileen M. Hasser, David D. Kline, Cheryl M. Heesch. Expression of ROS catabolic enzymes in the medial nucleus tractus solitarii (nTS) of rats and upregulation during acute hypoxia. Presented American Physiological Society Meeting, Omaha, Nebraska, Fall 2012

King, TL, CM Heesch, CG Clark, DD Kline, EM Hasser. Hypoxia activates nucleus tractus solitarii neurons projecting to the paraventricular nucleus of the hypothalamus. Amer. J. Physiol. (Regulatory, Integrative, & Comparative Physiol.), 302 (10): R1219 – R1232, 2012

## Active Grants

"Central nervous system plasticity in 06/01/09- 03/31/13 Sympathoinhibition on pregnancy" National Institutes of Health (R01 HL091164) (Role: Principal Investigator, 20% effort) ~\$250,000 (annual direct) Heesch continued

"Plasticity of nTS output neurons in acute and chronic hypoxia" 07/01/10-06/30/15 \$491,679 National Institutes of Health (R01 HL098602) Multi-Investigator Role: PD/PI = E.M. Hasser, C.M. Heesch, D.D. Kline [CMH direct \$163,512] (1.8 Calendar months/ each)

"Cardiovascular regulation in hindlimb unweighted Rats" 04/01/07-03/31/13 \$225,000 (no cost extension) NIH-R01-HL53306 (E. Hasser, P.I.) (Role: Co-Investigator, 10% effort)

"Adaptation of brainstem circuits to chronic hypoxia" NIH R01 HL085108-01 04/15/08-04/14/13 \$250,000 (annual direct) (D.D. Kline, P.I.) (Role: Co-Investigator, 1person/month effort)

## Presentations (\*) invited presentations

4/2012: Experimental Biology 2012; San Diego, CA; April 2012 (see abstracts above)

\* 8/2012: Tim D. Ostrowski, Stacy L. Barr, Heather A. Dantzler, Eileen M. Hasser, David D. Kline, Cheryl M. Heesch. Expression of ROS catabolic enzymes in the medial nucleus tractus solitarii (nTS) of rats and upregulation during acute hypoxia. Presented American Physiological Society Conference, Omaha, Nebraska, Fall 2012

### **Professional Service**

Departmental:
02/06- present: Junior Faculty Mentoring Committees, Dept. Biomed ScI. Ileana Constantinescu (Committee Chair) Kathy Kuel-Kovarik (Committee Member)
2012 Biomedical Science: Conflict of Interest Committee
College:
01/09 – 9/30/12 Committee on Faculty Responsibility
12/10 – present CVM COR Grant Review Committee
8/11 – 7/14 CVM Faculty Policy Committee (Ex Officio)

Heesch continued

University: 09/03-present Executive Committee, Interdisciplinary Neuroscience Program 8/11 – 7/14 College of Vet Med Representative to Faculty Council 8/11 – 7/14 Faculty Affairs Committee, Univ. of Missouri Faculty Council

Manuscript Peer Review: American Journal of Physiology/ Heart & Circ. Physiol (1), Autonomic Neuroscience: Basic & Clinical (1), Brazilian J Med. (1), Experimental Physiology (1), Journal of Applied Physiology (1), Journal Neurophysiology (1)

Editorial Board: 06/10- present: Review Editor, Frontiers in Physiology: Frontiers in Integrative Physiology

Grant Application Reviews: 3/ 2012 External Consultant, "Sex and Gender in Women's Cardiovascular Disease," University of California, Davis.

Committee/mentorship li Dept. Vet. Biomed. Sci, U 8/2011 – present 2008 present	
L.	cology & Physiology, School of Medicine, Univ. of Missouri Areum Kim (Ph.D., Adviser, Dr. Paul Fadel) Shenghua Yuan (Ph.D., Adviser, Dr. Steven Segal)
Dept. of Physics, University of Missouri 9/11 – present Chris Owens (Ph.D.,Adviser, Dr. Gabor Forgacs)	
Interdisciplinary Neuroscience Program 7/2010 – present Randall Brown (M.S., Adviser, Dr. Cheryl Heesch)	
Honors College, Senior H 1/2012 – present 8/2012 – present	
Veterinary Research Sum 4/2012 – 8/2012	mer Program (VRSP) Lance Serbousek (Adviser, Cheryl Heesch)
Teaching Activity:	
course (14 contact hrs) Wtr 2012 VE lec/contact hrs.)	3SCI 9467 (MPP 9437): Neural Control of the Circulation, 3 credit hr. 3SCI 400: Multipisciplinary Problems Course 1 credit hr. course (2 3SCI 5508: Veterinary Pharmacology, Course Director, 2 credit hr.
Fall 2012 VE	BmS 5507: Veterinary Pharmacology (Diuretics, 2 lec/contact hrs) t Neuroscience 5100: Autonomic Nervous System (1 lec/contact hr)

## **Michael Hill**

## Publications

Yu, X., Stavrakis, S., Huang, S., Patterson, E., Hill, M.A., Hamlett, S., Lazarra, R., Cunningham, M.W. and Kem, D.C. Autoantibody activation of beta-adrenergic and muscarinic receptors contributes to an "autoimmune" postural hypotension. J. Am. Hypertension Soc 6:40-47, 2012.

Liu, Y., Kalogeris, T., Wang, M., Zuidema, M., Wang, Q., Dai, H., Davis, M.J., Hill, M.A. and Korthuis, R.J. Hydrogen sulfide preconditioning or neutrophil depletion attenuates ischemia/reperfusion-induced mitochondrial dysfunction in rat small intestine. Am. J. Physiol. Gastrointest Liver Physiol. 302:G44-54, 2012.

Li, H., C. Kem, D.C., Reim, S., Khan, M., Vanderlinde-Wood, M., Zillner, C., Collier, D., Liles, C., Hill, M.A., Cunningham, M.W., Aston, C.E. and Yu, X. Agonistic autoantibodies as vasodilators in orthostatic hypotension: a new mechanism. Hypertension 59:402-408, 2012.

Zhu, Y., Qiu, H., Trzeciakowski, J.P., Sun, Z., Hill, M.A., Depre, C., Hunter, W.C., Vatner, D.E., Vatner, S.F. and Meininger, G.A. Atomic force microscopy measurements reveal time-dependent oscillations in vascular smooth muscle elasticity and adhesion that differ with aging. Aging Cell 11:741-750, 2012.

Hill, M.A. and Meininger, G.A. Arteriolar vascular smooth muscle cells: Mechanotransducers in a complex environment. Int. J. Biochem. Cell Biol. (Cells in Focus), 44:1505-1510, 2012.

Burch, M.L., Osman, N., Getachew, R., Al-aryahi, S., Poronnik, P., Zheng, W., Hill, M.A. and D; Little, P. G Protein Coupled Receptor Transactivation: extending the paradigm to include serine/threonine kinase receptors. Int. J. Biochem. Cell Biol. (Signaling Networks in Focus Review), 44:722-727, 2012.

Lee, S. Zhang, H., Chen, J., Dellsperger,, K.C. Hill, M.A. and Zhang, C. Adiponectin abates diabetes-induced endothelial dysfunction by suppressing oxidative stress, adhesion molecule formation, and inflammation in type 2 diabetic mice. Am. J. Physiol. (Heart and Circ.), 303:H106-115, 2012.

Rahbar, E., Weimer, J., Gibbs, H., Yeh, A.T., Bertram, C.D., Davis, M.J., Hill, M.A., Zawieja, D.C. and Moore Jr., J.E. Passive Pressure-Diameter Relationship and Structural Composition of Rat Mesenteric Lymphangions. 10:152-163, 2012.

Amy McCurley, Paulo W. Pires, Shawn B. Bender, Mark Aronovitz, Michelle J. Zhao, Daniel Metzger, Pierre Chambon, Michael A. Hill, Anne M. Dorrance, Michael E. Mendelsohn and Iris Z. Jaffe. Direct regulation of blood pressure by smooth muscle cell mineralocorticoid receptors. Nature Medicine 18:1429-1433, 2012.

Zhang, Z., Yan Yang, Y., Hill, M.A. and Wu, J. Role of CRP in ROS generation in atherothrombosis. Frontiers in Vascular Physiology 3:433 - , 2012.

Moreno-Dominguez, A. Colinas, O., El-Yazbi, A., Walsh, E.J., Hill, M.A., Walsh, M.P. and Cole, W.C. Role of calcium sensitization and dynamic cytoskeletal reorganization in the myogenic response of skeletal muscle resistance arteries to intravascular pressure. J. Physiol. 591:1235-1250, 2012.

#### Presentations

Hill, M.A. Keynote Address, Combined meeting of the British Microcirculatory Society and the Microcirculatory Society, Oxford, UK (July 2012).

Hill, M.A. Mechanotransduction in arterioles. Australian Vascular Biology Society, Sanctuary Cove, Qld, Australia (September 2012).

### **Active Grants**

"Signaling Mechanisms Underlying Myogenic Tone in Arterioles of Skeletal Muscle: Role of BKCa" Total Award: \$1,000,000 (Direct Costs) Period: 7/2009 – 6/2013. This project focuses on the role of the large conductance K+ channel (BKCa) in regulation myogenic tone in skeletal muscle arterioles. Specific emphasis is placed on heterogeneity in BKCa regulation in differing vascular beds. Principal Investigator: Michael A. Hill, Ph.D., Effort 27.5%

National Institutes of Health 1 P01 HL095486-01A1 Project Title: Mechanisms of Microvascular Control and Coordination in Health and Disease Period: 5/2010 – 4/2015 Principal Investigator: Gerald A. Meininger, PhD. Co-Investigator Project 1 (10% time) Michael A. Hill, Ph.D. Co-Investigator Project 2 (5% time) Michael A. Hill, Ph.D. Director of Core C (10% time) Michael A. Hill, Ph.D.

#### **Professional Service**

## **External Joint Appointments (Current):**

2011 – present Visiting Professor Luzhou Medical College Luzhou, China

2006 – present Lecturer/discussion leader in Microcirculation graduate course (topics relating to endothelial cell/smooth muscle interactions)

2008 – present Problem Based Learning Facilitator (University of Missouri) for medical student education (Years 1 and 2). Block content related to metabolism, endocrinology, cell biology and cardiovascular.

2009 - present Advanced Imaging Techniques, Skills in Biomedical Research graduate course

Graduate Students/Residents Supervised

Srijita Dhar	2010 – present (University of Missouri)
Tanyi Qui	2012 – present (University of Missouri)
Kwangseok He	ong 2012 – present (University of Missouri)

Michael Hill continued

Postdoctoral/Research Fellow Trainees Supervised

Yan Yang (M.D., Luzhou Medical College, China)	2008 - present
Zahra Nourian (Ph.D., Aarhus University, Denmark)	2010 – present
Mozow Zuidema (M.D., Ph.D., University of Missouri)	2011 – present
Sewon Lee (Ph.D., University of Missouri)	2011 - present
Melissa Collins (Ph.D., Texas A&M University)	2012 - present

Associate Editor:

• Frontiers in Vascular Physiology (2010 – present)

**Editorial Boards:** 

- American Journal of Physiology: Heart and Circulatory Physiology (1/96 12/98; 1/13 present)
- Microcirculation (1/2002 present)
- Journal of Vascular Research (2007 present)
- Frontiers in Vascular Pharmacology (2010 present)
- Frontiers in Vascular Physiology (2010 present)
- Member of the organizing committee for the combined British and US Microcirculatory Societies Meet ing, Oxford, July 2012.
- Planning group for combined Microcirculatory Society/NAVBO Meeting (October 2013).

Professional Societies Microcirculatory Society American Physiological Society Australian and New Zealand Microcirculatory Society Australian Physiological Society Australian-American Fulbright Alumni American Association for the Advancement of Science

**Biophysical Society** 

2012 – present	University of Missouri, Research Council
2011 – present	Coordinator of MOU/Exchange agreement between Suzhou Medical College,
	China and DCRC, University of Missouri.
2007 – present	Seminar Committee, Dep't of Medical Pharmacol. and Physiol.
	University of Missouri
2006 – present	Internal Review Committee, Dalton Cardiovascular Research Ctr
2012 - present	Joint Programming Committee Representative (APS, CV Section)
2012 - present	International Committee, American Physiological Society.
2012 - 2013	President, Microcirculatory Society, USA (effective 5/2012).
2011 - 2012	President-elect, Microcirculatory Society, USA.
2011 – present	International Liaison Committee, Microcirculatory Society, USA.
2011 – present	Long Range Planning Committee, Chair, Microcirculatory Society, USA.
2010 - present	Steering Committee, CV Section, American Physiological Society
2010 – present	Development Committee, Microcirculatory Society, USA.
2009 - 2012	Nominating Committee, American Physiological Society (CV Section), USA.
	Chairperson, 2010 - present

# Virginia Huxley

## Publications

Lu X, Huxley VH, Kassab GS. 2012. Endothelial Barrier Dysfunction in Diabetic Conduit Arteries: A Novel Method to Quantify Filtration. Am J Physiol In Press

#### Presentations

2012

Gordon Conference on Molecular Mechanisms in Lymphatic Function & Disease "Natriuretic peptide modulation of lymphatic exchange: coupling of barrier and contractile function?" Ventura Beach, CA, March 2012

2013

Department of Pharmacology and Toxicology Seminar Series, Medical College of Georgia,

#### Active Grants

Current:

NIH R21 HL093068-01A2 "Sexual Dimorphism of Skeletal Muscle Microvascular Function"; Score 22; 10th percentile July 1, 2010 - June 30, 2012; \$275,000 total direct No-cost extension through June 30, 2013

NIH R01 HL103151-01

"Sexual dimorphism in microvascular and lymphatic function: a role for insulin"; Score 29; 17th percentile 04-01-2010 through 03-31-2015; \$ 1,250,000 total direct NIH R01 HL103425-01

" Sexual Dimorphism of Collecting Lymphatic Permeability" Score 28; 17th percentile 07-01-2010 through 06-30-2015 \$ 1,250,000 total direct NIH R01 HL105328-01

"Integration of vascular network structure and function by quantitative microscopy analysis"; Multi PI; Palaniappan, Kannappan and Virginia H. Huxley Score 39 06/01/2010-05/31/2015; \$3,199,806.46 total direct

## **Professional Service**

<ul> <li>1996 - Director, Microvessel Core Facility</li> <li>1999 - Adjunct Professor, Veterinary Biomedical Sciences, UM-C</li> <li>2003 - Professor, Department of Medical Pharmacology &amp; Physic</li> <li>2003 - Senior Investigator, Center for Diabetes and Cardiovascula</li> <li>2005 - Director, National Center for Gender Physiology, UM-Col</li> <li>2008 - MPP Journal Club</li> <li>2008 - MPP Graduate student Skills</li> <li>2011 - Director, Pulmonary/Critical Care &amp; Physiology Research</li> <li>2011 - Professor, Department of Internal Medicine, UM-Columbia</li> </ul>	logy, UM-Columbia ar Health umbia Partnership
<ul> <li>PRIZES, AWARDS, FELLOWSHIPS:</li> <li>2012-2015 Associate Editor, Journal of Physiology (London)</li> <li>2010- Associate Editor, Frontiers in Vascular Physiology</li> <li>2008-12 Member NIH Hypertension &amp; Microcirculation (HM) Stof the PBL curriculum):</li> <li>Respiration (3 lectures) (2011-)</li> <li>Monthly Division Research Meeting/Journal Club (2011-)</li> </ul>	tudy Section Medical Students (since inception
Faculty of 1000, Integrative Physiology	2010-present
Associate Editor	
Frontiers in Vascular Physiology	2010-present
Editorial Board American Journal of Physiology: Heart & Circulatory Physiology Journal of Vascular Research Asian Biomedicine	1989-2005, 2011-2014 1998-present 2007-present
Guest Reviewer	
American Journal of Physiology:	1983-present
Circulation Research	1986-
Biorheology	1989-
Biophys. Biochem. Acta	1989-
Journal of Applied Physiology	1991-
Journal of Physiology (London)	1991-
Hypertension	1996-
Microcirculation	2004 -
Cardiovascular Research	2005 -
Journal of Pharmacology and Experimental Therapeutics	2007 -
Arteriosclerosis, Thrombosis and Vascular Biology	2008 -
Journal of General Physiology	2009 -
NIH Hypertension and Microcirculation (HM) Study Section	2008-2012
Fritze margal Advisory Decards	
Extra-mural Advisory Boards University of Arizona Training Grant Advisory Committee	2006 present
Center for Gender Physiology, Johns Hopkins University	2006-present 2008-present
Senter for Gender i hysiology, joints Hopkins Oniversity	83

# **Tzyh-Chang Hwang**

### Publications

Kang-Yang Jih, Yoshiro Sohma, Min Li, and Tzyh-Chang Hwang. (2012). Identification of a post-hydrolytic state in CFTR gating. J. Gen. Physiol.39:359-370.

Kang-Yang Jih, Yoshiro Sohma, and Tzyh-Chang Hwang. (2012). Non-integral stoichiometry in CFTR gating revealed by a pore-lining mutation. J. Gen. Physiol. 140:347-359.

Xiaolong Gao., Yonghong Bai, and Tzyh-Chang Hwang. (2013). Cysteine scanning of CFTR's first transmembrane segment reveals its plausible roles in gating and permeation. Biophys. J. 104:786-797.

Kang-Yang Jih, and Tzyh-Chang Hwang. (2013). Vx-770 potentiates CFTR function by promoting decoupling between the gating cycle and ATP hydrolysis cycle. Proc. Nat. Acad. Sci. USA.110:4404-4409.

Kangyang Jih, and Tzyh-Chang Hwang. (2012). Non-equilibrium gating of CFTR on an equilibrium theme. Physiology 27:351-361.

Tzyh-Chang Hwang and Kevin Kirk. (2013). The CFTR ion channel: gating, regulation, and anion permeation. Cold Spring Harbor Perspective in Medicine. In press.

Yoshiro Sohma, Yin-Jun Yu, and Tzyh-Chang Hwang. (2013) Curcumin and genistein: the combined effects on disease-associated CFTR mutants and their clinical implications. Curr. Pharm. Des. In press.

## **Active Grants**

2008 – 2013 NIHR01, NIDDK, "Molecular pathophysiology of cystic fibrosis", \$1,014,155

2011 – 2012 Cystic Fibrosis Foundation, \$75,000

#### **Professional Service**

2004 – present Member, Graduate Educational Committee, Medical Pharmacology and Physiology 2004 - present Member, Tenure and Promotion committee, Dalton Cardiovascular Research Center 2011 – present, Member, Tenure and Promotion committee, School of Medicine

2010 – present Associate Editor, Frontier in Pharmacology of Nature Products

2003 - present Editorial Board, Journal of General Physiology

# Salman Hyder

## Publications

Li, R., Ren, M., Chen, Ni., Hyder, S. M. And Wu, J. (2012) Depletion of platelets in B16/F10 melanoma tumor bearing mice prevents maturation of newly formed tumor blood vessels. 19th Annual Cardiovascular Day, University of Missouri, MO. (Feb 2012)

Mafuvadze, B., Liang, Y., Besch-Williford, C. And Hyder, S. M. (2012) Apigenin: an anti-angiogenic nutraceutical with preventive and therapeutic potential against progestin-dependent breast cancer. 19th Annual Cardiovascular Day, University of Missouri, MO. (Feb 2012)

Mafuvadze, B., Manguvo, A., Jiaxin, H., Whitney, S. D. and Hyder, S. M. (2012) Breast Cancer Knowledge and Awareness among High School and College Students in Mid-Western USA. American Educational Research Association Annual Conference. Vancouver, Canada.

Mafuvadze, B., Manguvo, A., Jiaxin, H., Whitney, S. D. and Hyder, S. M. (2012) Breast Cancer Knowledge and Awareness among High School and College Students in Mid-Western USA. 102nd Annual American Association of Cancer Research Meeting, Chicago, IL, USA, Abstract # 4460

Mafuvadze, B., Liang, Y., Besch-Williford, C. and Hyder, S. M. (2012) Apigenin blocks medroxyprogesterone acetate-dependent progression of BT-474 human breast tumor xenografts by inducing apoptosis. 102nd Annual American Association of Cancer Research Meeting, Chicago, IL, USA, Abstract # 578

Mafuvadze, B., Liang y., Besch-Williford, C. and Hyder, S. M. (2012) Preventive and Therapeutic Potential of Apigenin Against Progestin-Dependent Breast Cancer. 94th Annual Endocrine Society Meeting, Houston, TX. Abstract Sun-255.

Neubauer, H., Schneck, H., Seeger, H., Cahil, M. A., Fehm, T, Liang, Y., Mafuvadze, B., Hyder, S. M. and Mueck, A.O (2012) Membrane-initiated effects of progestogens alone and in combination with estradiol on the proliferation of human breast cancer cells. 94th Annual Endocrine Society Meeting, Houston, TX. Late Breaking Abstracts. Abstract Sat-LB11.

Hyder, S. M., Mafuvadze, B., Liang, Y. and Besch-Williford, C. (2012) Apigenin: a plant derived nutraceutical with preventive and therapeutic potential against progestin-dependent breast cancer. 17th World Congress on Advances in Oncology. Crete, Greece.

Mafuvadze, B, Cook, M, Zhang, X, Besch-Williford, C and Hyder, S.M. (2012) Complex effects of dietary apigenin on prevention of MPA-accelerated DMBA-induced mammary tumors in Sprague-Dawley rats. 103rd Annual American Association of Cancer Research Meeting, Washington DC, USA. submitted

Liang, Y., Zou, X., Besch-Williford, C., Johnnes, A. and Hyder, S. M. (2012) Synthetic inhibitors of the cholesterol biosynthetic enzyme oxidosqualene cyclase block proliferation and survival of breast cancer cells. 103rd Annual American Association of Cancer Research Meeting, Washington DC, USA. submitted

Hyder, S. M., Mafuvadze, B and Besch-Williford, C. (2012) Novel Anti-Angiogenic Therapies using Naturally-Occuring and Synthetic Drugs to Combat Progestin-Dependent Breast Cancer. To be published in Cell and Molecular Biology of Breast Cancer, Humana Press, In Press

#### Hyder continued

Lopez, F.R., Liang, Y., Besch-Williford C., Mafuvadze, B. and Hyder, S. M. (2012) Differential expression of fibroblast growth factor family members in a progestin-dependent BT-474 human breast cancer xenograft model. Histology and Histopathology, 27: 337-345.

Mafuvadze, B., Manguvo, A., He, J., Whitney, S.D. and Hyder, S.M. (2012) Breast Cancer Knowledge and Awareness among High School and College Students in Mid-Western USA. International Journal of Science Education. International Journal of Science Education; Part B: 1-15.

Mafuvadze, B., Liang, Y., Besch-Williford, C. and Hyder, S. M. (2012) Apigenin induces apoptosis and blocks growth of medroxyprogesterone acetate-dependent BT-474 xenograft tumors. Hormones and Cancer, 3:160–171

Carroll, C., Benakanakere, I., Liang, Y., Besch-Williford, C and Hyder, S.M. (2012) An anticancer agent YC-1 suppresses progestin-stimulated VEGF in breast cancer cells and arrests breast tumor development. Int. J. Oncology, 42: 179-187.

Neubauer, H., Schneck, H., Seeger, H., Cahill, M. A., Liang, Y., Mafuvadze, B., Hyder, S. M., Fehm, T and Mueck, A. O. (2012) Overexpression of PGRMC1 - possible mechanism for increased breast cancer risk using norethisterone in hormone therapy. Menopause, In press

*Presentations:* Indicate invited presentations with an asterisk (\*)

\*Invited Presentation UMKC, Department of Pharmacology and Toxicology: VEGF: A therapeutic molecular target for treatment and prevention of hormone-dependent breast cancer

\*Invited presentation at the 17th World Congress on Advances in Oncology. Crete, Greece. Title: Apigenin: a plant derived nutraceutical with preventive and therapeutic potential against progestin-dependent breast cancer.

\*Mafuvadze, B., Manguvo, A., He, J., Whitney, S.D., & Hyder, S. M. (2012, April). Breast cancer knowledge and awareness among high school and college Student in the Midwestern United States. American Educational Research Association Annual Meeting (AERA), Vancouver, B.C., Canada.

Mafuvadze, B., Manguvo, A., Jiaxin, H., Whitney, S. D. and Hyder, S. M. (2012) Breast Cancer Knowledge and Awareness among High School and College Students in Mid-Western USA. 102nd Annual American Association of Cancer Research Meeting, Chicago, IL, USA, Abstract # 4460

Mafuvadze, B., Liang, Y., Besch-Williford, C. and Hyder, S. M. (2012) Apigenin blocks medroxyprogesterone acetate-dependent progression of BT-474 human breast tumor xenografts by inducing apoptosis. 102nd Annual American Association of Cancer Research Meeting, Chicago, IL, USA, Abstract # 578

Mafuvadze, B., Liang y., Besch-Williford, C. and Hyder, S. M. (2012) Preventive and Therapeutic Potential of Apigenin Against Progestin-Dependent Breast Cancer. 94th Annual Endocrine Society Meeting, Houston, TX. Abstract Sun-255

Neubauer, H., Schneck, H., Seeger, H., Cahil, M. A., Fehm, T, Liang, Y., Mafuvadze, B., Hyder, S. M. and Mueck, A.O (2012) Membrane-initiated effects of progestogens alone and in combination with estradiol on the proliferation of human breast cancer cells. 94th Annual Endocrine Society Meeting, Houston, TX. Late Breaking Abstracts. Abstract Sat-LB11

#### Hyder continued

#### Awards & honors

Editorial Board: Histology & Histopathology (2002-present) International Journal of Oncology (elected to editorial board, 2005) Honorary Visiting Professorship, Luzhou Medical College, China (2011-2016)

#### University/College/Departmental Committees

Chancellor's Advisory Committee (MU, Chancellor Brady Deaton) Member, Promotion and Tenure Committee, Dept of Biomedical Sciences, University of Missouri-Columbia Chair, Appointment and Promotion Committee, DCRC Member, Dalton Cardiovascular Research Center Scientific Programs Committee Faculty Responsibility Committee (member), College of Vet Med, MU Chair, 2013 Cardiovascular Research Day Program Committee Judge, Health Sciences Research Day, MU School of Medicine (2012)

#### National/International Service

Grant Review

Invited Reviewer, Florida Health Grants (Bankhead-Coley Cancer Research Program) (Follows NCI process for review) Invited Reviewer, American Medical Association (Neoplastic Study Section) Reviewer, Fellowship, International Union Against Cancer Reviewer (ad hoc) University of Missouri Botanical Center Pilot Projects Reviewer (ad hoc), University of Missouri internal LOIs to select one for Mary Kay

Foundation grant submission

Manuscript Review BBA-Molecular Cell Research Carcinogenesis Endocrine Related Cancer Environmental Health Perspective J Agriculture & Food Chemistry J Clinical Endocrinology & Metabolism Oncogene

# David Kline

## Publications

Austgen JR, Dantzler HA, Barger BK, Kline DD (2012) 5-hydroxytryptamine 2C receptors tonically augment synaptic currents in the nucleus tractus solitarii. J Neurophysiol. 108(8):2292-305. doi: 10.1152/jn.00049.2012. Epub 2012 Aug 1. PubMed PMID: 22855775; PubMed Central PMCID: PMC3545023.

Cui F, Gao L, Yuan F, Dong ZF, Zhou ZN, Kline DD, Zhang Y, Li DP (2012) Hypobaric intermittent hypoxia attenuates hypoxia-induced depressor response. PLoS One. 7(7):e41656. doi: 10.1371/journal.pone.0041656. Epub 2012 Jul 27. PubMed PMID: 22848558; PubMed Central PMCID: PMC3407201.

King TL, Heesch CM, Clark CG, Kline DD, Hasser EM (2012) Hypoxia activates nucleus tractus solitarii neurons projecting to the paraventricular nucleus of the hypothalamus. Am J Physiol Regul Integr Comp Physiol. 2012 May 15;302(10):R1219-32. doi: 10.1152/ajpregu.00028.2012. Epub 2012 Mar 7. PubMed PMID: 22403798; PubMed Central PMCID: PMC3362152.

Book Chapter.

1. Kline DD, Mendelowitz D (2012) Intermittent hypoxia alters central control of cardiorespiratory function in the brainstem. In: Intermittent Hypoxia and Human Diseases. Editors: Xi and Serebrovskaya, Springer.

## Abstracts.

King TL, Heesch CM, Friskey S, Ruyle BC, Kline DD, and Hasser EM (2012) Caudal ventrolateral medulla (CVLM) activation by acute hypoxia (AH) is independent of changes in arterial blood pressure (ABP). FASEB J March 29, 26:702.6

Zijin Zhou, King TL, Kline DD, Heesch CM, and Hasser EM (2012) Cardiovascular deconditioning augments baseline breathing as well as peripheral and central chemoreflex responses. FASEB J March 29, 26:702.14

Ruyle BC, Heesch CM, King TL, Kline DD, and Hasser EM (2012) Activation of nucleus tractus solitarii (nTS) neurons that project to the rostral ventrolateral medulla (RVLM) or hypothalamic paraventricular nucleus (PVN): Role of acute hypoxia (AH). FASEB J March 29, 26:702.15

Ostrowski TD, Hasser EM, Heesch CM, and Kline DD (2012) Hydrogen peroxide (H2O2) modulates membrane properties in second-order nucleus tractus solitarii (nTS) neurons. FASEB J March 29, 26:701.7

Ostrowski TD, Barr SL, Dantzler HA, Hasser EM, Kline DD, and Heesch CM (2012) Expression of ROS catabolic enzymes in the medial nucleus tractus solitarii (nTS) of rats and upregulation during acute hypoxia. FASEB J March 29, 26:702.4

Coldren KM, Brown RJ, Kline DD, Hasser EM, and Heesch CM (2012) Colocalization of estrogen receptor {beta} (ER{beta}) with spinally projecting and vasopressinergic neurons in the hypothalamic paraventricular nucleus (PVN) during pregnancy. FASEB J March 29, 26:891.9

Austgen JA and Kline DD (2012) Serotonin 2A receptors augment synaptic transmission in the nucleus tractus solitarii (nTS).FASEB J March 29, 26:702.17

Kline continued

Active Grants

1R01 HL085108-01 (Kline DD) 4/01/2008-03/30/2013 NIH/NHLBI \$250,000 direct/yr Adaptation of brainstem circuits to chronic hypoxia Role: PI

R01HL098602 (Kline DD) 04/01/2010 –03/31/2015 NIH/NHLBI Direct: \$499,999 Plasticity of nTS output neurons in acute and chronic hypoxia Role: PI (MultiPI: Kline/Hasser/Heesch)

12POST11670002 (Ostrowski) 07/01/2012-06/30/2014 American Heart Association \$46,000/yr Reactive Oxygen Species in Nucleus Tractus Solitarii Output Neurons: Neuronal Properties Following Intermittent Hypoxia

**Professional Service** 

Committee/mentorship listing	
Michael P. Matott, PhD Post-doctoral mentor	
Tim D. Ostrowski, PhD Post-doctoral mentor	
T. Luise King	Committee member, Dept. of Biomedical Sciences
Kevin "Max" Coldren Committee member, Dept. of Biomedical Sciences	
Randall Brown	Committee member, Interdisciplinary Neuroscience Program
Nicholas P. Cooley	Committee member, Dept. of Chemistry
Tim Pale	Committee member, Dept. of Biological

Teaching Activity: Didactic and Clinical Teaching

Veterinary Physiology 5504, Co-Course Director

Veterinary Physiology 5504, Didactic teaching, 11 lecture hours, 18 laboratory hours, 12 examination hours, 4 review hours, 45 total contact hours, 126 students

Neural Control of the Circulation 9467 (Co-listed MPP 9437), Course Director Neural Control of the Circulation 9467 (Co-listed MPP 9437), Didactic teaching, 5 lecture hours, 10 presentation hours, 4 examination hours, 19 total contact hours, 5 students

# **Ronald Korthuis**

### Publications

Krenz M and RJ Korthuis. Moderate Ethanol Ingestion and Cardiovascular Protection: From Epidemiologic Associations to Cellular Mechanisms. J Mol Cell Cardiol 52: 93-104, 2012.

Korthuis RJ and T Kalogeris. TRPing up reperfusion: neutrophil TRPM2 channels exacerbate necrosis and contractile dysfunction in postischemic myocardium. Cardiovasc Res 2012 doi: 10.1093/cvr/cvs365.

Kalogeris T, Baines CP, Krenz M, Korthuis RJ. Cell biology of ischemia/reperfusion injury. Int Rev Cell Mol Biol. 2012;298:229-317.

Korthuis RJ. Skeletal Muscle Circulation. Integrated Systems Physiology: Molecules to Function eBook series, edited by Granger DN and Granger JP, Morgan-Claypool, 2012.

### Presentations

"Molecular signaling pathways triggered by preconditioning inflammatory stimuli". Symposium on Inflammation, Immune Cell Modulation, and Microvascular Dysfunction, Experimental Biology '12, San Diego, CA April 2012.

"Ethanol, immune cells, and prevention of stroke-induced cerebral injury". Symposium on Ethanol in Moderation: Cerebrovascular Protection. Research Society on Alcoholism Meeting, San Francisco, CA June 2012.

"Molecular signaling pathways in ethanol preconditioning". Department of Pharmacology, Tulane University, New Orleans, LA February 2012.

## **Active Grants**

NIH; HL-095486, Program Project Grant, "Mechanisms of Microvascular Control and Coordination in Health and Disease"; Project Director, Project 3, "Microvascular Dysfunction: Impact of Ischemia-Reperfusion on ECM-Vascular Cell Interaction"; \$262,000 per year, April 2010- March 2015.

#### **Professional Service**

- 1. American Physiological Society, Committee on Committees, 2011-2013
- 2. American Physiological Society, Cardiovascular Section Steering Committee, 2002-2013
- 3. Association of Physiology Department Chairs, 2004 present
- 4. Association of Pharmacology Department Chairs, 2004 present
- 5. National Heart, Lung, and Blood Institute: Special Emphasis Panel, November 2011

Korthuis continued

6. Editorial Advisory Boards:

American Journal of Physiology: Heart and Circulatory Physiology; 2005 – present Cardiovascular Research; 2008 – present Circulation Research; 2010 - present

7. Associate Editor: Frontiers in Vascular Physiology: 2010 - present

## Maike Krenz

## Publications

The PTPN11 loss-of-function mutation Q510E-Shp2 causes hypertrophic cardiomyopathy by dysregulating mTOR signaling C Schramm, DM Fine, MA Edwards, AN Reeb, M Krenz. Am J Physiol Heart Circ Physiol (2012) 302: H231 – H243

Heart Failure with Preserved Ejection Fraction: Chronic Low-Intensity Interval Exercise Training Preserves Myocardial O2 Balance and Diastolic Function K Marshall, B Muller, M Krenz, L Hanft, KS McDonald, K Dellsperger, C Emter J Appl Physiol (2012) Oct 25. [Epub ahead of print]

Moderate ethanol ingestion and cardiovascular protection: from epidemiologic associations to cellular mechanisms M Krenz, RJ Korthuis. J Mol Cell Cardiol (2012) 52: 93 – 104

Cell biology of ischemia/reperfusion injury T Kalogeris, CP Baines, M Krenz, RJ Korthuis. Int Rev Cell Mol Biol (2012) 298: 229 – 317

### **Presentations at Meetings**

Growth signaling in the ventricular wall Experimental Biology April 22nd 2012, San Diego, CA

19th Annual Cardiovascular Day, Columbia, February 21, 2012 A model of hypertrophic cardiomyopathy induced by a protein tyrosine phosphatase Shp2 mutation demonstrates increased myofibrillar function. KS McDonald, LM Hanft, M Krenz

56th Annual Meeting of the Biophysical Society, San Diego, February 25 – 29, 2012 A model of hypertrophic cardiomyopathy induced by a protein tyrosine phosphatase Shp2 mutation demonstrates increased myofibrillar function. KS McDonald, LM Hanft, M Krenz

Myofilament Meeting 'Myofilament proteins as structural scaffolds and mediators of function', Madison, June 2 – 5, 2012. A model of hypertrophic cardiomyopathy induced by a protein tyrosine phosphatase Shp2 mutation demonstrates increased myofibrillar function. LM Hanft, TL Domeier, KS McDonald, M Krenz

## **Active Grants**

RB 12-09, Research Board Grant, Krenz (PI) Title: Role of Akt signaling in heart valve development and disease 02/01/12 – 01/31/13 (total cost \$52,000)

URC 12-011, Research Council Grant, Krenz (PI) Title: Regional microRNA profiling in hypertrophic-obstructive cardiomyopathy 11/1/11 – 10/31/12 (total cost \$7319) Krenz continued

#### **Professional Service**

April 20122012 Experimental Biology Meeting, Chair of Symposium "A Complex Interplay Coming togeth<br/>er to Build the Heart", April 22nd 2012

June 2012 Abstract Grader for Scientific Sessions 2012

June/July 2012 Abstract Session Builder for Scientific Sessions 2012

ad hoc Reviewer

2000 – present Basic Research in Cardiology Circulation Research Coronary Artery Disease FEBS Letters Journal of Applied Physiology Journal of Cardiac Failure Journal of Molecular and Cellular Cardiology Trends in Cardiovascular Medicine Yonsei Medical Journal

Feb / Mar 2012 Netherlands Organization for Scientific Research, Research Council for Earth and Life Sciences

July 2012 Congressionally Directed Medical Research Program (CDMRP), Tuberous Sclerosis Complex Research Program (TSCRP)

2011 - present Review Editor, Frontiers in Integrative Physiology

# Harold Laughlin

## Publications

Laughlin MH, MJ Davis, NH Secher, JJ van Lieshout, AA Arce-Esquivel, GH Simmons, SB Bender, J Padilla, RJ Bache, D Merkus, and DJ Duncker. Peripheral Circulation. Comprehensive Physiology. Published for APS by Wiley-Blackwell, 2012.

Roberts MD, Company JM, Brown JD, Toedebusch RG, Padilla J, Jenkins NT, Laughlin MH, Booth FW. Potential clinical translation of juvenile rodent inactivity models to study the onset of childhood obesity. Am. J. Physiol. Heart Circ Physiol 2012 Aug; 303(3):R247-58. PMC 2269577 [PubMed – in process]

Arce-Esquivel AA, KV Kreutzer, JW Rush, JR Turk, and MH Laughlin. Exercise does not attenuate early coronary artery disease progression in a pig model. Med Sci Sports Exerc. 44(1):27-38, 2012. PMC3286114.

Laughlin MH, DK Bowles, and DJ Duncker. The coronary circulation in exercise training. Am J Physiol Heart Circ Physiol 302(1):H10-H23, 2012. PMID: 2984538

Delaney LE, Arce-Esquivel AA, Kuroki K, Laughlin MH. Exercise training improves vasoreactivity in the knee artery. Int J Sports Med. 2012 Feb;33(2):114-22. PMID:22095322

Sheldon RD, Roseguini BT, Thyfault JP, Crist BD, Laughlin MH, and SC Newcomer. Acute impact of intermittent pneumatic leg compression frequency on limb hemodynamics, vascular function, and skeletal muscle gene expression in humans. J. Appl. Physiol. 112:0-0, 2012. PMID: 22442025, [PubMed - as supplied by publisher]

Jenkins, NT, Martin JS, Laughlin MH, and Padilla J. Exercise-induced Signals for Vascular Endothelial Adaptations: Implications for Cardiovascular Disease. Curr Cardiovasc Risk Rep. Aug 1;6(4):331-346, 2012. PMID: 22844545 [PubMed]

Simmons GH, Padilla J, and Laughlin MH. Heteogeneity of endothelial cell phenotype within and amongst conduit vessels of the swine vasculature. Exp Physiol. 97(9): 1074-1082, 2012. PMID: 22542613 [PubMed - as supplied by publisher]

Fletcher, JA, Meers GM, Laughlin MH, Ibdah JA, Thyfault JP, and Rector RS. Modulating fibroblast growth factor 21 in hyperphagic OLETF rats with daily exercise and caloric restriction. Appl Physiol Nutr Metab. 37(6):1054-1062, 2012. PMID:22891896.

Mikus CR, Rosequini BT, Uptergrove GM, Mossis EM, Rector RS, Libla JL, Oberlin Boengasser SJ, Taylor AM, Ibdah JA, Laughlin MH, Thyfault JP. Voluntary wheel running selectively augments insulin-stimulated vasodilation in arterioles from white skeletal muscle of insulin-resistant rats. Microcirculation. 19(8):729-738, 2012. PMID: 22804760

Roberts MD, Company JM, Brown JD, Toedebusch RG, Padilla J, Jenkins NT, Laughlin MH, Booth FW. Potential clinical translation of juvenile rodent inactivity models to study the onset of childhood obesity. Am J Physiol Regul Integr Comp Physiol. 2012 Aug 1;303(3):R247-58. PMID: 22696577 Laughlin continued

Jenkins, NT, Arce-Esquivel AA, Bayless DS, Martin JS, Leidy HJ, Thyfault JP, Booth FW, R. Rector S, Laughlin MH, and Padilla J. Effects of Endurance Exercise Training, Metformin, and their Combination on Adipose Tissue Leptin and IL-10 Secretion in OLETF Rats. J. Appl Physiol. 2012 Dec;113(12):1873-1883. PMID 23019312.

Jenkins NT, Padilla J, Boyle L J, Credeur, D P, Laughlin MH. Disturbed blood flow acutely induces activation and apoptosis of the human vascular endothelium. Hypertension.2012; in press. PMID: 23319545

Martin JS, Padilla J, Jenkins NT, Crissey JM, Bender SB, Rector Rector RS, Thyfault JP, Laughlin MH. Functional adaptations in the skeletal muscle microvasculature to endurance and interval sprint training in the type 2 diabetic OLETF rat. J Appl Physiol. 2012 Oct 15;113(8):1223-32. PMID: 22923508

#### Presentations

Laughlin, MH: Under Pressure: Is Shear the Principle Mediator of Exercise-Induced Vascular Adaptation. Annual meeting of the American College of Sports Medicine, Baltimore MD, May 29-June 2, 2012.

Laughlin, MH: Exercise for Coronary Artery Health: a Proven Remedy: Basic Science. MU Institute for Clinical and Translational Science. University of Missouri, Columbia MO. November 13, 2012.

#### **Active Grants**

National Institutes of Health, R01; "Training: Muscle Blood Flow and Capillary Dynamics; Annual Direct \$225,000; Duration: 7/15/10-4/20/14; 25% effort; PI.

#### **Professional Service**

Administrative Activity: Chair of Biomedical Sciences Curators' Professor

Service Activity: Member of the Editorial Board, Medicine and Science in Sports & Exercise. 2005 - Present ASSOCIATE EDITOR: Journal of Applied Physiology. March 1, 2008 – Present

Manuscript Review for Journals: 1980-Present Avia. Space Environ. Med 1980-Present J. Applied Physiol 1980-Present Med. Sci. Sports Exercise 1981-Present Am. J. Physiol. 1985-Present Hypertension 1990-Present Microvascular Research 1993-Present Circulation 1993-Present Circulation Research 1994-Present Microcirculation

GRANT REVIEW COMMITTEES: 7/1/1990-Present National Institutes of Health Reviewer reserve

# Yayun Liang

## Publications

- Neubauer H, Schneck H, Seeger H, Cahill M. A., Fehm T, Liang Y, Mafuvadze B, Hyder S.M., and Mueck, A.O. (2012) Overexpression of PGRMC1—possible mechanism for the observed increased breast cancer risk using norethindrone in hormone therapy. Menopause, in press.
- Carroll C Liang Y, Besch-Williford C, Benakanakere I, and Hyder, S.M. (2012) An anticancer agent YC-1 suppresses progestin-stimulated VEGF in breast cancer cells and arrests breast tumor development. International J Oncology, in press.
- Mafuvadze, B., Liang, Y., Besch-Williford, C, Zhang, Xu, and Hyder, S. M. (2012) Apigenin Induces apoptosis and blocks growth of medroxyprogesterone acetate-dependent BT-474 xenograft tumors. Hormones and Cancer, 3:160–171
- Lo'pez P'erez PR, Liang Y, Sesch-williford CL, Mafuvadze B, and Hyder SM. (2012) Differential expression of FGF family members in a progesterone-dependent BT-474 human breast cancer xenograft model. Histol Histopathol, 27:337-345.

#### Presentations

Invited Presentation by the School of Pharmaceutical Sciences, Medical University of Herbei with title "Preclinical targeted therapy for combating advanced breast cancer" in Herbei, China on Oct. 2012

#### **Active Grants**

Liang, Yayun (Co-I), Hyder, S. M (PI), "Treatment and prevention of breast cancer using multi-functional inhibitors of cholesterol biosynthesis" Dept of Defense Breast Cancer Pgm. \$500,000-direct cost (6/1/12-5/31/14).

Liang, Yayun (Co-I), Hyder, S. M (PI), "Treatment of Breast Cancer and its Metastasis with APR-246 (PRIMA-1MET)" APREA AB \$86,205 direct cost (2/1/12-7/31/12).

Liang, Yayun (Co-I), Hyder, S. M (PI), "Treatment and prevention of prostate cancer with novel inhibitors of cholesterol biosynthesis" College of Veterinary COR Award, \$18,000 (2/1/12-12/31/12)

#### **Professional services**

9/2012-Present Adjunct Research Associate Professor, Dept. of Biomedical Sciences, College of Veterinary Medicine, University of Missouri, MO, USA Editorial Board of Chinese Journal of Clinicians (International) (2011-2014)

Invited Presentation by the School of Pharmaceutical Sciences, Medical University of Herbei with title "Preclinical targeted therapy for combating advanced breast cancer" in Herbei, China on Oct. 2012

Active member of American Association for Cancer Research (1997-present) Active member of Women in Cancer Research (2002-present) Active member of Minorities in Cancer Research (2009-present)

# Luis Martinez-Lemus

## Publications

Martinez-Lemus, L.A., 2012. The dynamic structure of arterioles. Basic Clin. Pharmacol. Toxicol. 110:5-11. (Invited Review)

Kim J., H. Jang, L.A. Martinez-Lemus, and J.R. Sowers, 2012. Activation of mTOR/p70S6 Kinase by ANG II Inhibits Insulin Stimulated Endothelial Nitric Oxide Synthase and Vasodilation. Am. J. Physiol. 302:E201-208.

Staiculescu, M.C., E.L. Galiñanes, G. Zhao, M. Li, U. Ulloa, M. Jin. Smooth Muscle Actin Polymerization and Vasoconstriction-Induced Inward Remodeling of Resistance Arteries. Annual Meeting of the Societies for Experimental Biology. San Diego CA, April 2012. Published in FASEB J., 2012.

Martinez-Lemus, L.A., K. Stockard, M. Jin, M.C. Staiculescu, G. Zhao, M.A. Hill and G.A. Meininger. Characteristics of the internal elastic lamina in inwardly remodeled arteries. Joint meeting of The British Microcirculation Society and The Microcirculatory Society. Keble College, University of Oxford, U.K., July 4-6, 2012. Published in Microcirculation.

Schenewerk, A., S.R. Huffman, G. Zhao, L.A. Martinez-Lemus, and R.M. Rivera. The effect of maternal highfat diet and ART on cardiovascular outcome in offspring. Presented at the 45th annual meeting of the Society for the Study of Reproduction and the 18th Ovarian Workshop. State College, PA. August, 2012. Published in Reproduction.

## Presentations

Characteristics of the internal elastic lamina in inwardly remodeled arteries. Joint meeting of The British Microcirculation Society and The Microcirculatory Society. Keble College, University of Oxford, U.K. (July 4-6, 2012).

Acute Adaptations of vascular smooth muscle cells in continuously constricted resistance arteries. Presentation at the symposium "Physiological remodeling of resistance arteries" Experimental Biology 2012, San Diego, CA (April 2012).

## **Active Grants**

National Institutes of Health (NIH) RO1. "Mechanisms of Microvascular Remodeling Progression." Principal Investigator, Luis A. Martinez-Lemus (40% Effort), \$2,250,000.00 for 2009-2014. Scored at 120 (3.5%).

National Institutes of Health (NIH) PO1. "Mechanisms of Microvascular Control and Coordination in Health and Disease." Principal Investigator, Gerald A. Meininger. Core Director, Luis A. Martinez-Lemus (15% Effort), \$8,470,000.00 for 2010-2014

## **Professional Service**

American Physiological Society-Cardiovascular Section: NIH Liaison Committee (2012-2015)

Microcirculatory Society: Councilor (2011-2014)

Microcirculatory Society: Membership Committee (2010-2013)

Appointed member of the School of Medicine Research Council, University of Missouri-Columbia (2009-2012).

Appointed member of the Dalton Cardiovascular Research Center Safety Committee (2009-Present).

Appointed member of the Gender and Racial Diversity Equity Council Representation. School of Medicine, University of Missouri-Columbia (2009-2012).

Appointed member of the Appointment and Promotions Committee for non-tenure track faculty within the Dalton Cardiovascular Research Center, University of Missouri-Columbia (2006-Present).

## **Scientific Journals**

Editorial Board Member for "CardioRenal Medicine," 2012-Present.

Review Editorial Board for "Frontiers in Vascular Physiology," 2010-Present.

Editorial Board member for "Microcirculation," 2010-2015.

Journal of Vascular Research

Arteriosclerosis, Thrombosis, and Vascular Biology

American Journal of Physiology

Heart and Circulatory Physiology

Regulatory, Integrative and Comparative Physiology

Clinical and Experimental Medicine

The Anatomical Record

Experimental Physiology

Poultry Science

BioMed Central Cell Biology

Hospital Practice

Microcirculation

Hypertension

Clinical and Experimental Pharmacology and Physiology

# **Gerald Meininger**

## Publications

Sun, Z., Z. Li and G.A. Meininger. Mechanotransduction through fibronectin-integrin focal adhesions in microvascular smooth muscle cells: Is calcium essential? American Journal of Physiology: Heart Circ. Physiol. 302(10):H1965-H1973, 2012. PMID: 22427509

Zhu Y., H. Qiu, J.P. Trzeciakowski, Z. Sun, A. Li, Z. Hong, M.A. Hill, W.C. Hunter, D.E. Vatner, S.F. Vatner, G.A. Meininger. Temporal analysis of vascular smooth muscle elasticity and adhesion reveals time-dependent oscillations that differ with aging. Aging Cell 1-10, 2012. PMID: 22639979

Hong Z., Z. Sun, W.T. Mesquitta, Z. Li, J.P. Trzeciakowski, G.A. Meininger. Coordination of fibronectin adhesion with contraction and relaxation in microvascular smooth muscle. Cardiovascular Research 96:73-80, 2012. PMID: 22802110 Featured in editorial by G.W. Schmid-Schonbein on September 6,2012.

Reeves, K.J., J. Hou, S. Higham, Z. Sun, J.P. Trzeciakowski, G.A. Meininger and N.J. Brown. Selective measurement and manipulation of adhesion forces between cancer cells and bone marrow endothelial cells using Atomic Force Microscopy (AFM). Nanomedicine Journal, 2012. (In Press)

Clark, C.G., Z. Sun, G.A. Meininger and J.T. Potts. Atomic force microscopy to characterize binding properties of 7-containing nicotinic acetylcholine receptors on NK1-expressing medullary respiratory neurons. Experimental Physiology, 2012. (Epub ahead of print)

Hong, Z., I. Ersoy, M. Sun, F. Bunyak, P. Hampel, Z. Hong, Z. Sun, Z. Li, I. Levitan, G.A. Meininger, K. Palaniappan. Influence of membrane cholesterol and substrate elasticity on endothelial cell spreading behavior. Journal of Biomedical Materials Research - part A, 2012. (In Press)

Sun Z., S. Huang, Z. Li and G.A. Meininger. Zyxin Is involved in regulation of mechanotransduction in arteriolar smooth muscle cells. (In revision for Frontiers in Physiology: Frontiers in Vascular Physiology), 2012.

Staiculescu, M.C., E.L. Galinanes, G. Zhao, U. Ulloa, M. Jin, I. Beig, G.A. Meininger, L.A. Martinez-Lemus. Prolonged vasoconstriction of small resistance arteries involves vascular smooth muscle actin polymerization leading to inward remodeling. (In revision for Cardiovascular Research), 2012.

J.R. Tangney, J.S. Chuang, M.S. Janssen, A. Krishnamurthy, P. Liao, M. Hoshijima, X. Wu, G.A. Meininger, M. Muthuchamy, A. Zemljic-Harpf, R.S. Ross, L. R. Frank, A.D. McCulloch, J.H. Omens. Novel role for vinculin in ventricular myocyte mechanics and heart failure. (Submitted to Biophysical Journal), 2012.

Askarova, S., Z. Sun, G.Y. Sun, G.A. Meininger and J.C.M. Lee. Oligomeric amyloid-β peptide on sialyl-LewisXselectin mediated membrane tether mechanics at the cerebral endothelial surface. Blood, 2012. (Submitted to Journal of Cell Science), 2012.

Amini, S., Z. Sun, A. Juriani, G.A. Meininger and K.E. Meissner. QD embedded microspheres as an evanescent light source for nearfield imaging. (In preparation for Nature Methods), 2012. {Shared senior authorship, Co-Corresponding Authors}

#### Meininger continued

Amini, S., Z. Sun, A. Juriani, K.E. Meissner, and G.A. Meininger. Partnering atomic force microscopy with quantum dot enabled probes for FRET to study integrin-extracellular matrix interactions. (Submitted to Cellular and Molecular Bioengineering), 2012.

Sehgel, N.L., S. Gao, Y. Zhu, X. Zhao, Z. Sun, J.P. Trzeciakowski, Z. Hong, W.C. Hunter, D.E. Vatner, G.A. Meininger, S.F. Vatner, H. Qiu. Increased intrinsic stiffness of aortic vascular smooth muscle cells as a mechanism for increased aortic stiffness in spontaneously hypertensive rats. (Submitted to Hypertension), 2012.

Sun Z., S. Huang, Z. Li and G.A. Meininger. A mechanotransducing role for N-cadherin in vascular smooth muscle. Journal of Physiology, 2012. (In preparation)

Cheng, Q., Z. Sun, G.A. Meininger and M. Almasri. Micromachined PDMS Elastic Post Arrays for Studying Vascular Smooth Muscle Cells, Submitted to Biomedical Device, 2012. (In preparation)

Hill, M.A. and G.A. Meininger. Myogenic tone and mechanotransduction. In: Muscle: Fundamental Biology and Mechanisms of Disease, Eds. J. Hill, E.N.Olson, K.K.Griendling, R.N.Kitsis, J.T.Stull and H.L.Sweeney, Academic Press, Elsevier, 2012.

Hill MA, Meininger G.A. Arteriolar vascular smooth muscle cells: mechanotransducers in a complex environment. Int J Biochem Cell Biol. Sep; 44(9):1505-10. doi: 10.1016/j.biocel.2012.05.021. Epub 2012 Jun 5. 2012.

Hill, M.A. and G.A. Meininger. Smooth muscle cells as the driving force of vascular wall structure: Integrating cytoskeletal and adhesive proteins and tissue engineering concepts. Cardiovascular Research, 2012. (In Preparation)

Stockard, K.A., M.A. Hill, G.A. Meininger and L.A. Martinez-Lemus. The Structure and Function of the Internal Elastic Lamina. Frontiers in Vascular Biology, 2012. (Submitted)

#### Seminars

"Biology at the tip of an atomic force microscope", Annual Experimental Biology Meeting, San Diego, CA, April 2012.

National Institutes of Health-National Heart, Lung and Blood Institute, P01, Program Project Grant, "Mechanisms of Microvascular Control and Coordination in Health and Disease", Project Director and Principal Investigator, G.A. Meininger (30% effort), with MJ Davis, and RJ Korthuis as project leaders, \$5,549,287 direct (\$8,471,385 total) for 04/01/2010-03/31/2015.

#### **Active Grants**

As Co-Investigator National Institutes of Health-National Heart, Lung and Blood Institute, R01, Intrinsic vascular smooth muscle cell stiffness, Principal Investigator, S. Vatner, Co-Investigator, G.A. Meininger (5%), \$213,827 (total for 5 year sub-contract period, direct and indirect), 04/01/10-03/31/15.

National Institutes of Health - National Heart, Lung and Blood Institute, Public Health Service Grant, R01, "Acute mechanisms of vascular remodeling", Principal Investigator, Luis A. Martinez-Lemus, Co-Investigator, G.A. Meininger (10% effort), \$1,250,000 (direct) (\$1,825,523 total) for 07/01/09-06/30/14. Meininger continued

National Science Foundation; Evanescent Field-Enabled Atomic Force Microscopy for Nanoscale Imaging of Cell Membrane Dynamics. Principal Investigator, K Meissner, Co- Investigator, G.A. Meininger (8%), \$200,000 (total) 09/01/2009-08/31/2011. No cost extension until 08/31/12.

#### **Professional Service**

#### **Scientific Journals**

Editorships Editor-in-Chief for Frontiers in Vascular Physiology, January 2010-present. Co-Editor (US) for Journal of Vascular Research, August 1999-Present.

#### **Editorial Boards**

Editorial Board Member for Frontiers in Cardiovascular and Smooth Muscle Pharmacology, 2010-present. Editorial Board Member for International Journal of Physiology, Pathophysiology and Pharmacology, 2010-present. Editorial Board Member for Nanotechnology, Science and Applications, 2007-present. Editorial Board Member for Microcirculation, 1993-1999; 2003-2009; 2010-2012.

Poster Judge at combined meeting of the British and US Societies for Microcirculation, Keble College, Oxford University, June 4-6, 2012.

Member Search Committee for Director of Office of Grant Writing and Publications, January-June 2012.

Member of the Strategic Planning and Resource Advisory Council (SPRAC), Office of the Chancellor, University of Missouri, July 2012-June 2015.

Member of the Internal Medicine Research Council (IMRC), Department of Internal Medicine, School of Medicine, University of Missouri, September 2012-present.

Member of Advisory Committee Meeting for T90/R90 Clinical Biodetective Training Grant, March 2009-present.

Member of School of Medicine Advisory Committee on Research Space, November 2010-present.

# Mark Milanick

## Publications

Milanick, MA. Units, Jargon, G-forces and Squirting Blood. The Physics Teacher 50, 410-11, 2012.

Galva, C, Gatto C, Milanick MA. Soymilk: an effective and inexpensive blocking agent for immunoblotting. Analytical Biochemistry.2012 Jul 1;426(1):22-3.

Fainting Felines and Faulty Physiology (18 chapters, ~ 350 page book) Conversational textbook MU Bookstore Espresso Book Machine. August, 2012

#### **Active Grants**

2012-2014NIH R21 DK09186Developing a non-invasive monitoring system using NIR dyes insideerythrocytes233,719

#### **Professional Services**

Graduate Student Committees

Journal Reviewer: Journal of Physiology

Red Cell Club, 1979-present National Association of Biology Teachers, 2011-present

2010-present Chair, Campus Minority Affairs Committee2008-present Departmental Doctoral Faculty Review Committee2012-present MU Status of Women Committee

## Luis Polo-Parada

## Publications

Korampally M, Apperson SJ, Staley CS, Castorena JA, Thirunvengadathan R, Gangopadhyay K, Mohan RR, Gosh A, Gangopandhyay S, Polo-Parada L. (2012) Transient pressure-mediated intranuclear delivery of FITC-Dextran into chicken cardiomyocytes by MEMS-based nanothermite reaction actuator. Sensors & Actuators: B. Chemical. Volumes 171–172, August–September 2012, Pages 1292–1296.

Tan J, Lee B, Polo-Parada L, Sengupta S. Kinetically Limited Differential Centrifugation in an inexpensive and readily-available alternative to Centrifugal Elutriation (2012). Biotechniques. Aug;53(2):104-8. doi: 10.2144/0000113853.

Bok S, Korampally V, Polo-Parada L, Mamidi V, Baker G, Gangopadhyay K, Folk WR. Dasgupta PK, Gangopadhyay S (2012). Confeito-like Assembly of Organosilicate1caged Fluorophores: Ultrabright Suprananoparticles for Fluorescence Imaging. Nanotechnology. 23, 175601 doi:10.1088/0957-4484/23/17/175601

Pérez-Solano R, Gutiérrez Juárez G,\* Polo-Parada L\* (2012). Modelo esféricamente simétrico de la señal fotoacústica en el dominio temporal producida por objetos micrométricos: el caso de células de melanoma in vitro. Superficies y Vacio. 25(2).

Pérez-Solano, R, Ramirez-Perez FI, Castorena Gonzalez JA, Anell EA; Gutiérrez-Juárez G,\* Polo-Parada, L\* (2012). An Experimental and Theoretical approach to the study of the photoacoustic signal produced by cancer cells. AIP Advances. 2, 011102 (2012); http://dx.doi.org/10.1063/1.3697852

## Active Grants

Nanostructured High Surface Area Sensor Systems for Enhanced Detection. PI-Sheila Grant, Ph D. Co-PI, 10% Responsibility and credit. Funded by NSF. 6/2011-6/2012 \$320,000

Nano thermite Based Micro shockwave generator and nanoparticles for targeted and efficient Gene/Drug Delivery. Co-Investigator, 50% FTE. Co-Investigator, Shubhra Gangopadhyay, Ph. D. Funded by NSF. 6/2009-6/2012 \$375,000 Requested one year extension 6/2013

## **Professional Service**

Problem Based Learning (PBL) Module 5 University of Missouri- Medical School -2012.

## Advisor Ph. D. Students:

- Francisco Ramirez. Department of Biological Engineering Ph. D. Student.
- Jorge Gonzalez Castorena. Department of Biological Engineering. Ph. D. student.

Polo-Parada continued

Advisor Post-Doctoral:

- Dr. Asur Guadarrama Santana. University of Mexico. CYCADET. 2012-2013
- School of Medicine Research Council.
  Hearnes Center Committee.
  MU PREP (Post-baccalaureate Research Education Program.
  2012-2015
  2011-2013
  2008-present

This is a program funded by NIH to increase research skills of BA/BS graduates from underrepresented minority or disadvantaged populations or with disabilities in order to enable them to enter and successfully complete PhD programs in the biomedical sciences.

National Chair and Co-Chair Services Experimental Biology Meeting.	2012
Study Section Participant American Heart Association. Per Review. Cardiac Bio BCT4.	Fall 2012

Advisory committee Member of the University of Missouri Doctoral Faculty (2009-2014).

## Leona Rubin

## **Professional Service**

2011-Pres	Faculty/Provost Task Force on eLearning/Online Academic Programs: Chair. Develop roadmap and policies for development of online courses including issues of quality, intellectual property and impact on face to face courses.
2011-Pres	University of Missouri System Retirement and Staff Benefits Committee: Chancellor appointed.
2011-Pres	Strategic Plan Progress Committee: Tasked with maintaining a "living" web version of the campus strategic plan by identifying and collecting action plan updates and data for plan objectives.
2011-2012	Faculty Grievance process Oversight Committee, Chair
	Service as Part of MU Faculty Council on University Policy
2006-2012	MU Faculty Council on University Policy: College of Veterinary Medicine Elected Representative

# Steven Segal

## Publications

Behringer EJ, Socha MJ, Polo-Parada L and Segal SS. Electrical conduction along endothelial cell tubes from mouse feed arteries: Confounding actions of glycyrrhetinic acid derivatives. Brit J Pharmacol 166:774-787, 2012. PMC3417504

Correa D and Segal SS. Neurovascular proximity in the diaphragm muscle of adult mice. Microcirculation 19: 306–315, 2012. PMC3336045

Westcott EB, Goodwin EL, Segal SS and Jackson WF. Function and expression of ryanodine receptors and inositol 1,4,5 trisphosphate receptors in smooth muscle cells of murine feed arteries and arterioles J Physiol 590.8: 1849-1869, 2012. PMID: 22331418

Behringer EJ and Segal SS. Tuning electrical conduction along endothelium of resistance arteries through Ca2+activated K+ channels. Circ Res 110:1311-1321, 2012. PMC3467972

Socha MJ, Domeier TL, Behringer EJ and Segal SS. Coordination of Intercellular Ca2+ Signaling in Endothelial Cell Tubes of Mouse Resistance Arteries. Microcirculation 19:715-770, 2012. (Cover Illustration) PMC3502682

## Presentations

Behringer E and S Segal. Aging impairs electrical conduction along resistance artery endothelium via enhanced signal dissipation through KCa channels FASEB J 26:861.2, 2012.

Behringer E and S Segal. Tuning electrical conduction along endothelial cell tubes via Ca2+-activated K+ channels. FASEB J 26:1058.12, 2012.

Westcott EB and SS Segal. Differential roles for  $\alpha$ 1- versus  $\alpha$ 2 adrenoreceptor activation of mouse mesenteric arterial networks in vivo. FASEB J 26:853.11, 2012.

Socha MJ, TL Domeier and SS Segal. Manipulating IP3R-mediated calcium release in permeabilized endothelial cell tubes of resistance arteries. FASEB J 26:1058.8, 2012.

Westcott EB, SS Segal and WF Jackson. Aging differentially alters calcium signals and myogenic tone in murine cremaster muscle feed arteries and downstream arterioles. FASEB J 26:861.3, 2012.

Westcott EB and SS Segal. Aging impairs  $\alpha$ 1-adrenergic reactivity and blunts sensory nerve attenuation of sympathetic vasoconstriction in mouse mesenteric arteries in vivo. Joint meeting of British and USA Microcirculatory Societies, Oxford, England, 07/12.

Behringer E and S Segal. Aging impairs electrical conduction along endothelial tubes via activation of KCa channels by reactive oxygen species. Joint meeting of British and USA Microcirculatory Societies, Oxford, England, 07/12.

#### Segal continued

#### Seminars

Physiological Soc. 2012 (07/2012, Edingburg, Scotland; Session: Blood Flow Regulation: From Rest to Maximal Exercise) "Spreading the Signal for Vasodilation"

Joint meeting of the British Microcirculation Society and the Microcirculatory Society, Inc. USA (07/2012; Oxford, England) "Intercellular Coordination of Blood Flow Control"

Symposium celebrating the 20th Anniversary of the Robert M. Berne Cardiovascular Research Center, University of Virginia (11/2012; Charlottesville, VA) "Neuromodulation of Cell-to-Cell Signaling In Resistance Networks"

#### **Active Grants**

R37 HL041026; National Institutes of Health/NHLBI (Segal, PI) Title: "Intercellular Coordination of Blood Flow Control" Current Project Period: 09/01/2008-02/28/2019 (MERIT Award)

R01 HL086483; National Institutes of Health/NHLBI (Segal, PI) Title: "Microcirculation in Aging Skeletal Muscle" Current Project Period: 09/01/2007-02/28/2014 (with 1-year no-cost extension)

#### **Professionsl Service**

Invited Reviews

Socha MJ, Behringer EJ and Segal SS. Calcium and Electrical Signaling along Endothelium of the Resistance Vasculature. Basic Clin Pharmacol Toxicol 110:80-86, 2012. PMC3271116

Behringer EJ and Segal SS. Spreading the signal for vasodilatation: Implications for blood flow control and the effects of aging. J Physiol 590.24: 6277–6284, 2012. (Cover Illustration) PMID: 22890708

Westcott EB and Segal SS. Perivascular innervation: A multiplicity of roles in vasomotor control and myoendothelial signaling. Microcirculation; accepted 10/25/2012) doi:10.1111/micc.12035 PMID: 23289720

# Yoshiro Sohma

## Publications

Jih KY, Sohma Y, Hwang TC Non-integral stoichiometry in CFTR gating revealed by a pore-lining mutation J. Gen. Physiol. 140: 347 – 359, 2012

Hayasaki H, Sohma Y, Kanbara K, Otsuki Y. Heterogeneous GABAB receptor-mediated pathways are involved in the local GABAergic system of the rat trigeminal ganglion: Possible involvement of KCTD proteins. Neuroscience 218: 344 – 358, 2012

Jih KY, Sohma Y, Li M, Hwang TC. Identification of a novel post-hydrolytic state in CFTR gating J. Gen. Physiol. 139: 359 – 370, 2012

## Presentations

Yu YC, Sohma Y, Takimoto S, Miyawaki A. Yasui M. (2012) A direct measurement of water movement across epithelia using CARS microscopy. 89th Annual Meeting, The Physiological Society of Japan, March 29 – 31, 2012; Matsumoto, Japan.

Sohma Y (2012) Application of Two Emerging Measurement Technologies to Epithelial Transport Physiology: CARS Microscopy and High-Speed AFM. International Symposium on Frontiers in Life Sciences. October 18 – 20, 2012; Kusatsu, Japan.

Sohma Y (2012) What two new measurement techniques teach us in epithelial transport physiology: CARS microscopy and high-speed AFM. International Symposium on Frontiers in Life Sciences. October 18 – 20, 2012; Chengdu, China.

Sohma Y, Yu YC, Hwang TC (2012) Fluctuations in function and structure of NBD engine in CFTR channel observed by single channel recording and high-speed AFM. Workshop "Spectrum of functional and structural fluctuations in functional membrane molecules – 2012", National Institute of Physiological Sciences, Sept 6 – 7, 2012; Okazaki, Japan

Nakamura Y, Hanyuda A, Yu YC, Hagiya-Furukawa T, Odera M, Hwang TC, Sakurai M, Yasui M, Sohma Y. Effects of genistein and curcumin on non-hydrolytic CFTR mutants. 56th Biophysical Society Annual Meeting. San Diego, California, USA, February 25-29, 2012

## Active Grants

2009.4 – 2012.3 Grant-in-Aid for Scientific Research (C): 21591990, Co-PI (PI: H. Hayasaki), "Approach toward trigeminal neuralgia based on local GABAergic system hypothesis", funded by the Japan Society for the Promotion of Science.

2010.4 – 2013.3 Grant-in-Aid for Scientific Research (C): 22590212, PI, "ATP-hydrolysis switch hypothesis for mechanism of NBD engine in ABC transporters", funded by the Japan Society for the Promotion of Science.

2010.4 – 2012.3 Individual Research (Special B): PI, "Study for a systematic development of drugs targeting ABC transporters" funded by Keio Gijuku Academic Development Funds.

2011.4 – 2013.3 Research support: PI, "Approach to a novel membrane transport physiology based on a direct observation of water and lipids by a non-linear optical microscopy" funded by Keio Gijuku Fukuzawa Memorial Fund for the Advancement of Education and Research

2011.4 – 2013.3 Grant-in-Aid for Scientific Research on Innovative Areas: 23118714, PI, "Mechanism for utilizing ATP-hydrolysis energy in NBD engine in ABC transporters", funded by the Japan Society for the Promotion of Science.

2012.4 – 2013.3 Individual Research (Special A): PI, "A novel drug developing system based on single molecular live-imaging by high-speed atomic force microscopy" funded by Keio Gijuku Academic Development Funds.

### **Professional Services**

Society of General Physiologist (USA) Biophysical Society (USA) The Physiological Society (UK) Physiological Society of Japan Biophysical Society of Japan The Japanese Pharmacological Society

Editorial Board: 2006.4 – present Member, Editorial Board, Journal of the Physiological Society of Japan.

Co-chairman in Symposium "Motion pictures of the functional membrane molecules in action - What we want to see in the movies and what they will teach us - ", 89th Annual Meeting, The Physiological Society of Japan, Matsumoto, Japan, 2012

Co-chairman in Symposium "Capturing single molecule images of potential drug targets in operation - From stills to movies -", 85th Annual Meeting, The Japanese Pharmacological Society, Kyoto, Japan, 2012

## **James Sowers**

### Publications

Pulakat L, Aroor AR, Gul R, Sowers JR. Cardiac insulin resistance and microRNA modulators. Exp Diabetes Res. 2012;2012:654904.

Whaley-Connell AT, Habibi J, Nistala R, Demarco VG, Pulakat L, Hayden MR, Joginpally T, Ferrario CM, Parrish AR, Sowers JR: Mineralocorticoid receptor-dependent proximal tubule injury is mediated by a redox-sensitive mTOR/S6K1 pathway. Am J Nephrol. 2012;35(1):90-100.

Ofili EO, Zappe DH, Purkayastha D, Samuel R, Sowers JR: Antihypertensive and metabolic effects of angiotensin receptor blocker/diuretic combination therapy in obese, hypertensive african american and white patients. Am J Ther. 2012 Jan 13. [Epub ahead of print]

Kim JA, Jang HJ, Martinez-Lemus LA, Sowers JR. Activation of mTOR/p70S6 Kinase by ANG II Inhibits Insulin Stimulated Endothelial Nitric Oxide Synthase and Vasodilation. Am J Physiol Endocrinol Metab. 2012;302(2):E201-8.

Sowers JR: Role of TRIB3 in diabetic and overnutrition-induced atherosclerosis. Diabetes. 2012;61(2):265-6. Shababi M, Habibi J, Ma L, Glascock J, Sowers JR, Lorson CL: Partial restoration of cardio-vascular defects in rescued severe model of spinal muscular atrophy. J Mol Cell Cardiol. 2012 Jan 17. [Epub ahead of print]

Sofue T, Kiyomoto H, Kobori H, Urushihara M, Nishijima Y, Kaifu K, Hara T, Matsumoto S, Ichimura A, Ohsaki H, Hitomi H, Kawachi H, Hayden MR, Whaley-Connell A, Sowers JR, Ito S, Kohno M, Nishiyama A. Early treatment with olmesartan prevents juxtamedullary glomerular podocyte injury and the onset of microalbuminuria in type 2 diabetic rats. Am J Hypertens. 2012 May;25(5):604-11.

Nistala R, Sowers JR, Whaley-Connell A. Over-nutrition contributes to tubulointerstitial fibrosis by targeting nutrient-sensing kinases: Role for the mTOR/S6K pathway. Cell Cycle. 2012;11(5).

Demarco VG, Johnson MS, Ma L, Pulakat L, Mugerfeld I, Hayden MR, Garro M, Knight WC, Britton SL, Koch LG, Sowers JR. Overweight female rats selectively bred for low aerobic capacity exhibit increased myocardial fibrosis and diastolic dysfunction. Am J Physiol Heart Circ Physiol. 2012;302(8):H1667-82.

Whaley-Connell A, Sowers JR. The kaliuretic impact of cicletanine compared to hydrochlorothiazide. J Hypertens. 2012;30(4):691-2.

Ma L, Gul R, Habibi J, Yang M, Pulakat L, Whaley-Connell AT, Ferrario CM, Sowers JR. Nebivolol improves diastolic dysfunction and myocardial remodeling through reductions in oxidative stress in the transgenic (MRen2) rat. Am J Physiol Heart Circ Physiol. 2012 Jun 1;302(11):H2341-51.

Mandavia CH, Pulakat L, Demarco V, Sowers JR. Over-nutrition and metabolic cardiomyopathy. Metabolism. 2012 Sep;61(9):1205-10.

Whaley-Connell A, Habibi J, Nistala R, Hayden MR, Pulakat L, Sinak C, Locher B, Ferrario CM, Sowers JR. Combination of direct renin inhibition with angiotensin type 1 receptor blockade improves aldosterone but does not improve kidney injury in the transgenic Ren2 rat. Regul Pept. 2012;176(1-3):36-44.

Siyam F, Abdullah O, Gardner M, Brietzke S, Sowers J. A case of carcinoid tumor-associated hypercalcemia. Cardiorenal Med. 2012;2(1):52-56.

Hayden MR, Habibi J, Joginpally T, Karuparthi PR, Sowers JR. Ultrastructure study of transgenic Ren2 rat aorta - part 1: endothelium and intima. Cardiorenal Med. 2012;2(1):66-82.

Whaley-Connell A, Sowers JR. Oxidative stress in the cardiorenal metabolic syndrome. Curr Hypertens Rep. 2012;14(4):360-5.

Whaley-Connell A, Sowers JR. Initial choice of antihypertensive on long-term cardiovascular outcomes in CKD. Clin J Am Soc Nephrol. 2012;7(6):884-6

Aroor AR, Mandavia C, Ren J, Sowers JR, Pulakat L. Mitochondria and oxidative stress in the cardiorenal metabolic syndrome. Cardiorenal Med. 2012;2(2):87-109. dysfunction in diabetes. Life Sci. 2012 Nov 9. [Epub ahead of print].

Hayden MR, Habibi J, Joginpally T, Karuparthi PR, Sowers JR. Ultrastructure study of transgenic Ren2 rat aorta - part 1: endothelium and intima. Cardiorenal Med. 2012;2(1):66-82.

Whaley-Connell A, Sowers JR. Oxidative stress in the cardiorenal metabolic syndrome. Curr Hypertens Rep. 2012;14(4):360-5.

Whaley-Connell A, Sowers JR. Initial choice of antihypertensive on long-term cardiovascular outcomes in CKD. Clin J Am Soc Nephrol. 2012;7(6):884-6

Aroor AR, Mandavia C, Ren J, Sowers JR, Pulakat L. Mitochondria and oxidative stress in the cardiorenal metabolic syndrome. Cardiorenal Med. 2012;2(2):87-109. dysfunction in diabetes. Life Sci. 2012 Nov 9. [Epub ahead of print].

Deedwania PC, Zappe DH, Egan BM, Purkayastha D, Samuel R, Sowers JR. Does response of RAS blockade on serum K+ levels influence its glycemic-mitigating response when combined with hydrochlorothiazide? J Clin Hypertens (Greenwich). 2012 Jul;14(7):415-21.

Zhang Y, Sowers JR, Ren J. Pathophysiological insights into cardiovascular health in metabolic syndrome. Exp Diabetes Res. 2012;2012:320534.

Garcia-Vargas L, Addison SS, Nistala R, Kurukulasuriya D, Sowers JR. Gestational diabetes and the offspring: implications in the development of the cardiorenal metabolic syndrome in offspring. Cardiorenal Med. 2012;2(2):134-142.

Forte V, Pandey A, Abdelmessih R, Forte G, Whaley-Connell A, Sowers JR, McFarlane SI. Obesity, Diabetes, the Cardiorenal Syndrome, and Risk for Cancer. Cardiorenal Med. 2012;2(2):143-162.

Varagic J, Ahmad S, Voncannon JL, Moniwa N, Simington SW Jr, Brosnihan BK, Gallagher PE, Habibi J, Sowers JR, Ferrario CM. Nebivolol reduces cardiac angiotensin II, associated oxidative stress and fibrosis but not arterial pressure in salt-loaded spontaneously hypertensive rats. J Hypertens. 2012;30(9):1766-74.

Muniyappa R, Sowers JR. Endothelial Insulin and IGF-1 Receptors: When Yes Means NO. Diabetes. 2012 Sep;61(9):2225-7.

Sowers continued

Manrique C, Lastra G, Habibi J, Mugerfeld I, Garro M, Sowers JR. Loss of Estrogen Receptor α Signaling Leads to Insulin Resistance and Obesity in Young and Adult Female Mice. Cardiorenal Med. 2012 Aug;2(3):200-210.

Gul R, Demarco VG, Sowers JR, Whaley-Connell A, Pulakat L. Regulation of Overnutrition-Induced Cardiac Inflammatory Mechanisms. Cardiorenal Med. 2012 Aug;2(3):225-233.

Aroor AR, Mandavia CH, Sowers JR. Insulin resistance and heart failure: molecular mechanisms. Heart Fail Clin. 2012;8(4):609-17.

Demarco VG, Ford DA, Henriksen EJ, Aroor AR, Johnson MS, Habibi J, Ma L, Yang M, Albert CJ, Lally JW, Ford CA, Prasannarong M, Hayden MR, Whaley-Connell AT, Sowers JR. Obesity-Related Alterations in Cardiac Lipid Profile and Nondipping Blood Pressure Pattern during Transition to Diastolic Dysfunction in Male db/db Mice. Endocrinology. 2012 Nov 9. [Epub ahead of print]

Mandavia CH, Aroor AR, Demarco VG, Sowers JR. Molecular and metabolic mechanisms of cardiac Nistala R, Sowers JR. Hypertension: Synergy of antihypertensives in elderly patients with CKD. Nat Rev Nephrol. 2012 Nov 27. doi: 10.1038/nrneph.2012.264. [Epub ahead of print]

Pulakat L, Aroor AR, Gul R, Sowers JR. Cardiac insulin resistance and microRNA modulators. Exp Diabetes Res. 2012;2012:654904.

Garcia-Touza M, Sowers JR: Evidence-based hypertension treatment in patients with diabetes. J Clin Hypertens (Greenwich). 2012;14(2):97-102.

Mandavia CH, Aroor AR, Demarco VG, Sowers JR. Molecular and metabolic mechanisms of cardiac Nistala R, Sowers JR. Hypertension: Synergy of antihypertensives in elderly patients with CKD. Nat Rev Nephrol. 2012 Nov 27. doi: 10.1038/nrneph.2012.264. [Epub ahead of print]

Pulakat L, Aroor AR, Gul R, Sowers JR. Cardiac insulin resistance and microRNA modulators. Exp Diabetes Res. 2012;2012:654904.

Garcia-Touza M, Sowers JR: Evidence-based hypertension treatment in patients with diabetes. J Clin Hypertens (Greenwich). 2012;14(2):97-102.

## **Active Grants**

2012-2016 BLR&D, Interactions of the RAAS and a Western Diet on Insulin Metabolic Actions, James R. Sowers (PI), 650,000

2011-2016 NHLBI, Ang II and Overnutrition and Insulin resistance in Cardiovascular Tissue, James R. Sow ers (PI), \$1,250,000.

2009-2014 NHLBI, Ang II and Aldosterone Effects on Insulin Resistance in Cardiovascular Tissue, James R. Sowers (PI), \$1,250,000.

2008-2012 VA Merit Review, Mechanisms of Angiotensin II and Aldosterone Inhibition of Insulin Metabolic Signaling, James R. Sowers (PI), \$650,000.

Sowers continued

#### **Professional Service**

Professional consultation (other patient care)

- Public presentations as an expert in endocrinology, metabolism and hypertension and vascular medicine
- No consulting to public agencies, foundations, or professional associations

Journal Editorial activity Editor In Chief – Cardiorenal Medicine 2010-present Journal Cardiometabolic Syndrome 2006-2010 Associate Editor – Diabetes, Journal of Hypertension 2011-present

#### Editorial Board Memberships

- o 2006-present Journal of Hypertension
- o 2006-present Journal of American Society of Hypertension
- o 2004-present Cardiovascular Drug Reviews
- o 2002-present American Journal Clinical Hypertension
- o 2002-present American Journal Hypertension
- o 1996-2004 Endocrinology, Nutrition, Metabolism and Cardiovascular Diseases, Journal of Clinical Endocrinology & Metabolism
- o 1994-present Journal of Human Hypertension
- o 1991-present Metabolism
- o 1991- present Hypertension

#### Editorships - Reviewer

New England Journal of Medicine, Hypertension, Journal of Biological Chemistry, Circulation, Circulation Research, American Journal of Physiology, Diabetes, Journal of Clinical Investigation, Journal of Clinical Endocrinology and Metabolism, Endocrinology, American Journal of Medicine, Archives of Internal Medicine, Annals Internal Medicine, Journal American Medical Association, and others.

Other professionally related service

- NIH, VA Merit Board, American Heart National Reviews Committees
- Department of Veterans Affairs (VA) Joint Biomedical Laboratory Research and Development and Clinical Science Research and Development Scientific Merit Review Board
- VCMB (Vascular Cell Molecular Biology) Study Section NIH
- Data Monitoring Committee "Combination Angiotensin Receptor Blocker and Angiotensin converting Enzyme Inhibitor for Treatment of Diabetic Nephropathy. Cooperative Studies Program Coordinating Center. VA Connecticut Healthcare System
- Microcirculation Study Section NIH

National and International Boards and Committees

- Positions held in professional associations
- Educational Committee High Blood Pressure Council
- Scientific Awards Committee American Society of Hypertension
- External Advisory Board COBRE grant "Hypertension and Cardiorenal Disease Research Center, John Hall, University of Mississippi

Sowers continued

State and Local Boards and Committees

- University of Missouri Internal Medicine Research Council, Chiar 2011-present
- SOM Administrators Research Council (ARC) 2004-present
- Truman VA Research and Development Committee 2004-present
- R and D committee; ACCORP Truman VA 2004-present
- Chair Brooklyn VA R and D 2001-2004

COMMITTEES AND STUDY SECTIONS Charter Member VCMB Study Section – NIH – 2010-present

HONORS & AWARDS

2012 Irvine Page-Alva Bardley Lifetime Achievement Award in Hypertension

# Ronald L. Terjung

## Publications

Yang, H.T., J-H Shin, C.H.Hakim, X. Pan, R.L. Terjung, and D. Duan. Dystrophin deficiency compromises force production of the extensor ulnaris muscle in the canine model of Duchenne muscular dystrophy. PLoS ONE 7(9): 1-7, e44438, 2012; Doi: 10.1371/journal.pone.0044438.

Roseguini, B.T., A.A. Arce-Esquivel, S.C. Newcomer, H.T. Yang, R.L. Terjung, and M.H. Laughlin. Intermittent pneumatic leg compressions enhance muscle performance and blood flow in a model of peripheral arterial insufficiency. J. Appl. Physiol. 112:1556-1563, 2012.

#### **Active Grants**

NIAMS T32-AR048523-06 through 10: Exercise and Health: Integration From Molecule to Patient, P.I.: R.L.T. Sum: \$1,309,555, 07-01-09 to 06-30-14.

Research Grant: Jesse's Journey. AAV micro-dystrophin therapy in a single intact muscle in GRMD dogs, P.I.: D. Duan. R.L.T: Consultant; Sum: \$294,204. 1/1/2011-12/31/2013.

Muscular Dystrophy Assoc of America. Improving AAV potency for DMD gene therapy P.I.: D. Duan. RLT: Consultant; Sum: \$527,670, 2/1/2011 – 1/31/2014

#### **Professional Service**

2004-Present Member, Executive Committee, College of Veterinary Medicine

2004-Present Member, Council of Research Advisors, Asst Chancellor for Research

2004-Present Director, Grant Review Program, College of Veterinary Medicine

2004-Present Co-Chair, Search Committee, Clinician Scientists-Mission Enhancement, Division of Cardiology, Dept. of Internal Medicine, College of Medicine

1998/2000/02/04/06/08/10/12 Course Director with Dr. C. Hardin, Control of Energy Metabolism (VBMS/MPP 9431), Joint listed: Biomed Sci and Med Pharm & Physiol: Selected lectures (10 3-hr sessions)

# Xiaoqin Zou

### Publications

Tao Yu, Xiao-Qing Wang, Jian-Ping Sang, Chun-Xu Pan, Xian-Wu Zou, Tsung-Yu Chen, Xiaoqin Zou\*. Influences of mutations on the electrostatic binding free energies of chloride ions in Escherichia coli ClC. Journal of Physical Chemistry B, 116, 6431-6438, 2012.

Sam Z. Grinter, Xiaoqin Zou\*. Improving knowledge-based scoring functions for protein-ligand interactions by accounting for sparse data in the training set. Biophysical Journal 102: 409a, 2012.

American Chemical Society National Meeting, Symposium on "The Community Structure Activity Resource (CSAR) Scoring Challenge", Philadelphia, Pennsylvania, 2012.

Telluride Meeting: "Coarse-Grained Modeling of Structure and Dynamics of Biomacromolecules", Telluride, Colorado, 2012.

Telluride Meeting: "Characterizing Landscapes: From Biomolecules to Cell Networks", Telluride, Colorado, 2012.

Medical Research Council, School of Medicine, University of Missouri-Columbia, Missouri, 2012.

### **Active Grants**

Funding Agency: NSF Grant # 0953839 Project Title: CAREER: A computational approach to templatebased structure selection for protein-protein interactions Funding Period: August 1, 2010 to July 31, 2015 Total Amount: \$734,016 Principal Investigator: Xiaoqin Zou

Funding Agency:NIH/ National Institute of General Medical Sciences Grant # 1R21GM088517Project Title:A new scoring framework for selecting structural models Funding Period:September 30, 2012 Total Amount:\$411,125 Principal Investigator:Xiaoqin Zou

#### **Professional Services**

Editorial Advisory Board Member for Current Computer-Aided Drug Design, 2007-2012

Program Committee member for IEEE International Conference on Bioinformatics & Biomedicine (BIBM), 2009, 2010, 2012, 2013

Review Panel member for Annual International IEEE Engineering in Medicine and Biology Society (EMBS) Conference, 2011 & 2012

Served as an International Examiner on PhD thesis for Nanyang Technological University, Singapore, 2009, 2010, 2012

### Photos on back cover courtesy of Christopher Baines:

We have overexpressed cyclophilin-D (CypD) in the hearts of mice (CypD TG). CypD is a critical component of a protein complex in the mitochondria call the mitochondrial pore, that play a role in the death of heart cells during a heart attack and other forms of heart disease.

Overexpression of CypD resulted in an enlarged heart that was less efficient at pumping blood than hearts from normal mice. When we looked at the structure of the heart cells we saw that increased CypD caused a massive enlargement and swelling of mitochondria compared to normal mice. This in turn eventually lead to the death of the heart cells.

