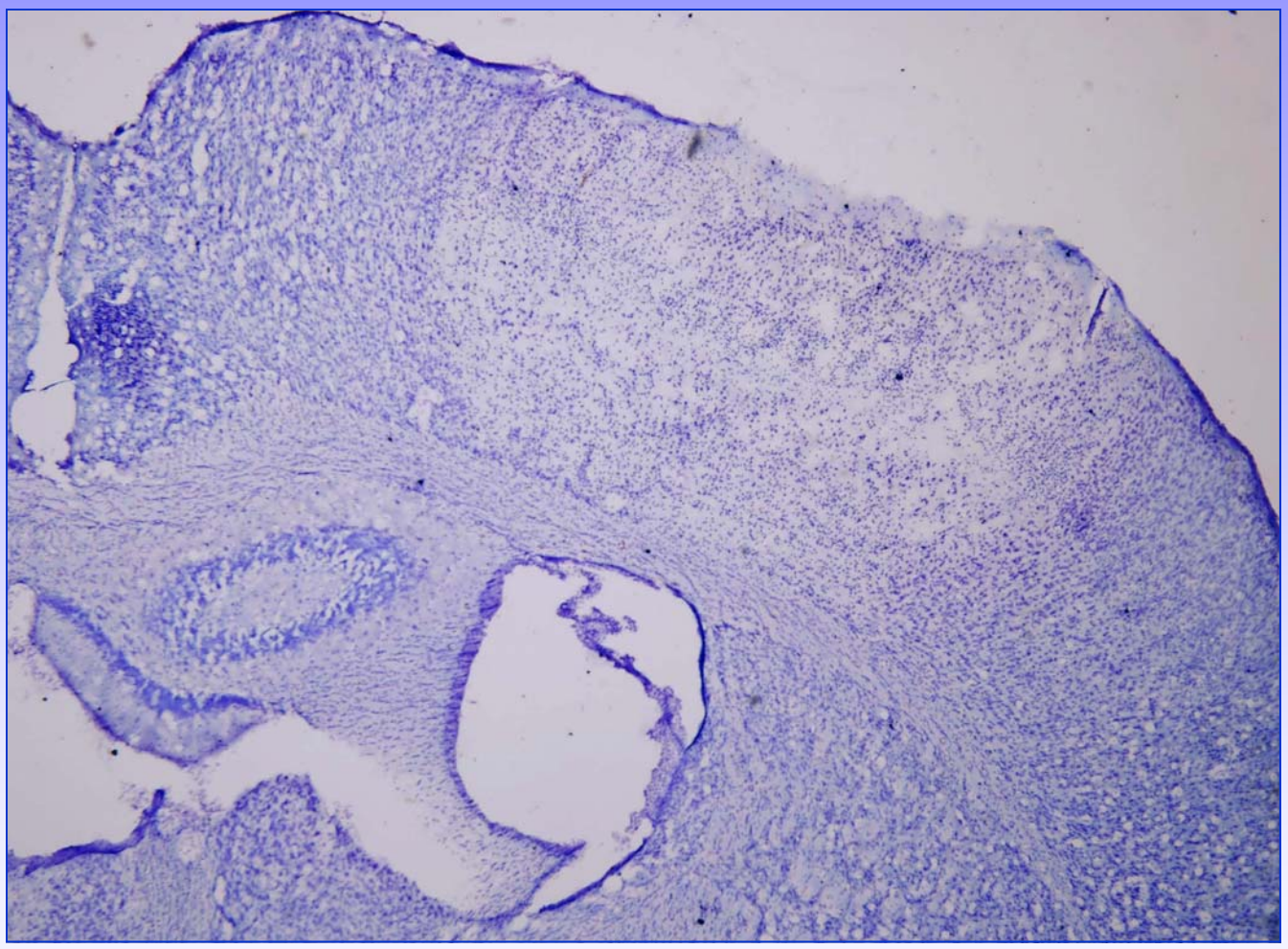
Dalton Cardiovascular Research Center



Annual Report FY 09

"Committed to Interdiscplinary Collaboration in Research and Teaching"

See front cover:

On the cover of the journal (Glia vol 57, 767-776, 2009). It shows the damage of mouse brain after photothrombosis-induced ischemia-Shinghua Ding, PhD.

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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 11.7 million in active research funding, have published 109 manuscripts in nationally recognized journals and books and gave 70 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

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. Maike Krenz
Dr. Min Li
Dr. Luis Martinez-Lemus
Laura McClaskey

Director's Office and Administrative Contacts

Director
Dr. Gerald Meininger
Phone: 573-882-9662 E-mail: meiningerg@missouri.edu

Associate Director
Dr. Michael Hill
Phone: 573-884-4604 E-mail: hillmi@missouri.edu

Development
Dr. Edward Blaine
Phone: 573-882-9014 E-mail: blainee@missouri.edu

Business Manager
Nancy Alton
Phone: 573-882-7587 E-mail: altonn@missouri.edu

Administrative Associate
Bin Ke
Phone: 573-882-9502 E-mail: keb@missouri.edu

Grants and Contracts Specialist (Pre/Post Awards)
Cynthia Haydon
Phone: 573-882-7433 E-mail: haydonc@missouri.edu

Executive Staff Assistant/Building Coordinator
Laura McClaskey
Phone: 573-882-9482 E-mail: mclaskeyl@missouri.edu

Administrative Assistant (Purchasing, etc.)
Karen McVay
Phone: 573-882-7588 E-mail: mcvayk@missouri.edu

Systems Support Administrator
Jason Lee
Phone: 573-882-6348 E-mail: leejb@missouri.edu

User Support Analyst
John Donahue
Phone: 573-882-3546 E-mail: donahuejt@missouri.edu

Animal Facility Manager
Mark Baepler
Phone: 573-884-2318 E-mail: baeplerm@missouri.edu

Assistant Lab Animal Technician
Stacey Mathes
Phone: 573-884-2318 E-mail: mathess@missouri.edu

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, Hamilton, Hasser, Hill, Huxley, Jones, Korthuis, Laughlin, Martinez-Lemus, Meininger, Polo-Parada, Rubin, Segal, Soma, Terjung, Zhang, Sun, Fay, Sowers

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

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

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, Zhang, Kvochina

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

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

Publications and Presentations

- Articles published: 109
- Invited Presentations: 70

Awards and Peer Review

- Sixty-nine awards/contracts were active during FY09.
- Eighteen research awards/contract proposals were awarded.
- Twelve grant/contract proposals.
- Twelve graduate students were supported by R90/T90 training grants.
- Fourteen Investigators served as editors or were on editorial boards of thirty-one scientific journals.
- Nine Investigators reviewed articles for thirty-two scientific journals.
- Six Investigators reviewed grant applications for twelve granting agencies.

Education and Training

- Resident Investigators-Tenure/Tenure Track: 21
- Resident Research Track: 5
- Non-resident Investigators: 17
- Research Staff: 19
- Post Doctoral Fellows: 10
- Graduate Students: 20
- Undergraduate Students: 8
- Administrative Staff: 12
- Visiting Scholars: 6

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
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). 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 throughput 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, Assistant Director, Department of Medical Pharmacology and Physiology

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 Ca^{2+}. 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

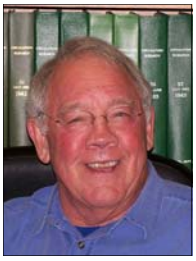
Christopher P. Baines

Office Location: 323 DCRC
Office Phone: 884-8767
Bainesc@missouri.edu

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 mitochondrial-driven death can be targeted for the prevention of myocardial disease.



Edward H. Blaine

Office: 355 DCRC
Phone: 573-882-9014
E-mail: blainee@missouri.edu

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 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.

Frank W. Booth

Office: W145 VMED
Phone: 573-882-6652
E-mail: boothf@missouri.edu

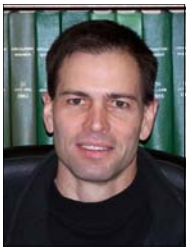
Education:
PhD University of Iowa, BS Denison University

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 $p21^{Cip1/WAF1}$, $p27^{Kip1}$, 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

Office: W124 VMED
Phone: 573-882-7193
E-mail: bowlesd@missouri.edu

Education:
PhD University of Texas-Austin

Appointments: Associate Director of the National Center for Gender Physiology
Associate 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, antatomy 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

Office: 324D DCRC
Phone: 573-882-7049
E-mail: clarkel@missouri.edu

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

Appointments: Associate Professor, Department of Physical Medicine and Rehabilitation
Associate 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 acid-base 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 acid-base 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^-/HCO_3^- 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

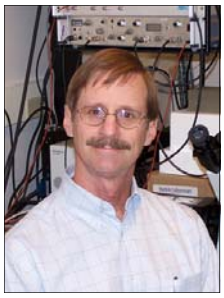
Education:
PhD, MD University of California-San Diego,
BS Arizona State University

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

My laboratory focuses on the following questions relevant to angiogenesis, wound repair and cancer research:

1. How do endothelial cells form cell-lined tube structures with lumens in three-dimensional (3D) extracellular matrices?
2. How do endothelial cells and other cell types such as tumor cells invade 3D matrices?
3. To what extent do endothelial cells directly or indirectly play a role in tumor invasion and metastasis?
4. What molecular events control the process of vascular regression?
5. How do vascular supporting cells, such as pericytes, stabilize vascular tubes?
6. How do distinct matrix metalloproteinases and their inhibitors control the processes of vascular morphogenesis versus regression in 3D matrices?
7. How do extracellular matrix fragments (matricryptins) regulate vascular morphogenesis versus regression in normal versus diseased states (such as diabetes)?



Michael J. Davis

Office: M451f Medical Sciences Bldg
Lab: 256 DCRC
Phone: 573-884-5181
E-mail: 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 single-cell electrophysiology. We combine these with 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

Office: 324E DCRC
Phone: 573-884-2489
E-mail: dings@missouri.edu

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

Appointment: Assistant Professor, Department of Biological Engineering

Research
My current research focuses on glial cell function and neuron-glia interactions in the central nervous system using state-of-the-art *in vivo* two photon fluorescent imaging and electrophysiology. My research also involves stem cell differentiation and transplantation.

Paul J. Fadel

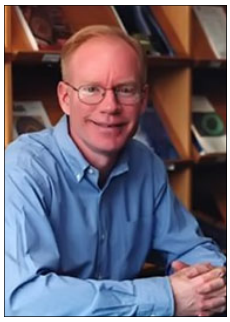
Office: MA415 HSC
Phone: 573-884-5181
E-mail: fadelp@health.missouri.edu

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

Appointments: Assistant 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 age-related 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.

Office Location: 306 Cs&E
Office Phone: 882-2296
E-mail: fayw@missouri.edu

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. We also are conducting human genetic studies. These projects address the role of plasminogin activator inhibitor-1 as a risk factor for myocardial infarction, and the molecular basis of the variable sensitivity of patients to anticoagulation with warfarin.

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 Interests
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 characterization 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

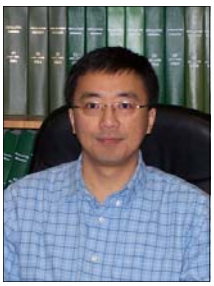
Education:
DSc, MSEE & BSEE Washington State University,
BA St. Louis University

Appointments: Professor, Department of Biological Engineering Adjunct Professor, Department of 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.



Liqun (Andrew) Gu

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

Education:
PhD Nankai University

Appointment: Assistant 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.

Marc Hamilton

Office: 23 VMED
Phone: 573-882-6527
E-mail: hamiltonm@missouri.edu

Education:
PhD University of South Carolina,
MA University of Texas

Appointment: Assistant Professor, Department of Biomedical Sciences

Research
Dr. Hamilton studies the molecular and physiological mechanisms by which physical inactivity causes chronic metabolic diseases related to poor plasma lipid metabolism (coronary artery disease, Type II diabetes, obesity). A focus of the research in our laboratory is on translational research. In so doing, studies of humans, animal, and cell cultures are performed with the goal of integrating fundamental new insights regarding molecular processes while seeking solutions to practical clinical outcomes for metabolic diseases caused by physical inactivity. Multidisciplinary work exposes lab members to a diversity of modern research techniques. Studies have sought to discover the genes and signals linking physical inactivity to disease, especially those processes related to lipoprotein metabolism and skeletal muscle metabolism. A major question we are addressing is the underlying role of lipid metabolism in signaling for adaptations within vascular cells as one explanation for why exercise prevents atherosclerosis. This work largely involves pigs, isolated blood vessels in culture, and primary endothelial cell cultures. Rat and human work is also performed to understand regulation of processes controlling muscle metabolism and plasma lipids. Using microarray methodologies, our laboratory has been characterizing the response of a large percentage of the genome to exercise training, inactivity, and identifying both the transcriptional and post-transcriptional events influenced by lipids. In both human and animal studies, we have been testing the new paradigm of "inactivity physiology." Studies are partly focused on comparing and contrasting the underlying metabolic responses to normal non-exercise physical activity to more intense and structured exercise. These studies are leading to the emerging school of thought that sitting too much (non-exercise activity deficiency) is a unique stimulus from exercising too little (exercise deficiency), while both types of physical activity can produce potent cellular signals important for combating the metabolic problems associated with metabolic syndrome, coronary artery disease, Type II diabetes, and obesity.

Eileen M. Hasser

Office: 351 DCRC
Phone: 573-882-6125
E-mail: hassere@missouri.edu

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

Office: 324C DCRC
Phone: 573-882-2359
E-mail: heeschc@missouri.edu

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

Office: M404 HSC
Phone: 573-882-8069
E-mail: huxleyv@missouri.edu

Education:
PhD University of Virginia, BA Hollins University

Appointments: Director of the National Center for Gender Physiology
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

Office: 222C DCRC
Phone: 573-882-2181
E-mail: hwangt@missouri.edu

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. State-dependent 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

Office: 133B DCRC
Phone: 573-882-1261
E-mail: hyders@missouri.edu

Education:
PhD University of Glasgow, BS University of Kent

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 rele vant 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.

Allan Jones

Office Location: MA 415 Medical Sciences
Office Phone: 573-882-8029
E-mail: JonesA@missouri.edu

Education:

PhD University of Pennsylvania

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

Office: 354 DCRC
Phone: 573-884-0505
E-mail: klinedd@missouri.edu

Education:
PhD Case Western Reserve University, BA Miami University

Appointment: Assistant 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

Office: MA415 HSC
Phone: 573-882-8059
E-mail: korthuisr@missouri.edu

Education:
PhD & BS. from Michigan State University

Appointment: Chair Medical Pharmacology and Physiology
Professor, Department of Medical Pharmacology and Physiology

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 overexpression), 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

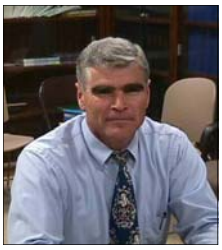
Office Location: 355 Dalton Cardiovascular Research Center
Office Phone: 884-8761
krenzm@missouri.edu

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.



M. Harold Laughlin

Office: E102VMED
Phone: 573-882-7011
E-mail: laughlinm@missouri.edu

Education: PhD University of Iowa, BA Simpson College

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.

Luis Martinez-Lemus

Office: 222A DCRC
Phone: 573-882-3244
E-mail: martinezlemusl@missouri.edu

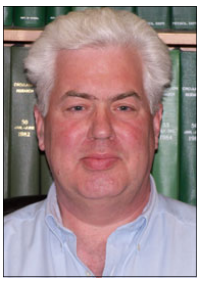
Education:
PhD Texas A&M, MS Auburn University,
DVM from Universidad Nacional Autonoma de México

Appointment: Assistant 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

Office Location: 360 Dalton Cardiovascular Research Center
Office Phone: 573-882-8055
E-mail: MilanickM@missouri.edu

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research Interests
Membrane physiology and biophysics, ion pumps and exchangers in cardiovascularly relevant cells

Research Description
Milanick's efforts are devoted to determining how cell membrane proteins transport molecules across the cell surface. Studies are currently focused on three transport systems: the plasma membrane calcium pump, the Na/K pump and zinc transporters.

One of the issues in determining the molecular mechanism of transport proteins is to identify the amino acid sequences most important for function. Hypotheses about transporter structure-function relationships can more confidently be tested by engineering changes in protein structure that lead to an operating transporter with novel features than by doing biochemical autopsies on defective transporters. Cells that contain transporters with novel features are identified by a selection procedure that kills all cells that do not express transporters with the novel feature from a population of cells which contain randomly mutated transporter genes.

Cells are placed in artificial environments and these stresses kill the cells expressing wild type or inactive transporters. Clearly, a thorough understanding of normal cellular transport physiology is required to design appropriate selection procedures. By learning how transporters adapt to stressful environments, a better understanding of the relationship between structure and function of normal transporters can be gained. This understanding of how the transporter works will elucidate some of the mechanisms for regulation of transport which are important for healthy cell function.

Luis Polo-Parada

Office: 302 DCRC
Phone: 573-884-4599
E-mail: poloparadal@missouri.edu

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.

Michael Rovetto

Office: MA 415 HSC
Phone: 573-882-8773
E-mail: rovettom@missouri.edu

Education:
PhD University of Virginia

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

Myocardial ischemia caused by inadequate blood flow to the heart muscle leads to purine loss from cells. The extent to which they are lost is directly related to recovery of mechanical function upon restoration of blood flow to the heart. Thus, decreased purine levels and decreased ability of the heart to perform useful work are coupled. I am interested in determining what controls rates of transport of purines into and out of cells and how this process can be altered to enhance the energy state of the heart.

Related to these studies are investigations of how the cardioprotective substance, fructose phosphate crosses heart cell membranes. These studies are done in collaboration with Dr. Christopher Hardin.

Membrane transport of glucose also is of interest and of naturally occurring and genetically-induced animal models that lead to diabetes and/or hypertension are used to understand the role of the renin-angiotensin system in the pathologic consequences of diabetes & hypertension. These studies are done in association with Drs. James Sowers and Craig Stump, Department of Medicine and the Truman V.A. Hospital.

A model of hypothyroidism is used to alter the contractile activity of myocardial muscle in order to determine how specific changes in the contractile protein myosin affect the rate of force development by isolated muscle cells and intact heart. This is a collaborative research project with Dr. Kerry McDonald.

A similar investigation to that in hypothyroidism, but in hearts from genetically altered mice that exhibit traits of an inherited form of muscular dystrophy, are being carried out in collaboration with Drs. Joe Kornegy and Casey Childers College Veterinary Medicine and Department of Physical and Rehabilitation Medicine.

Leona Rubin

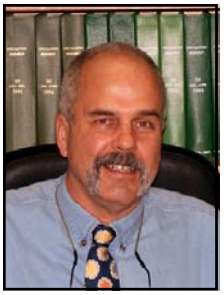
Office: E102 VMED
Phone: 573-882-5903
E-mail: rubinl@missouri.edu

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

Office: 323 DCRC
Phone: 573-882-7366
E-mail: schadtj@missouri.edu

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

Office: MA 415 HSC
Phone: 573-882-2553
E-mail: segalss@health.missouri.edu

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 Soma

Office: 263 DCRC
Phone: 573-882-0938
E-mail: somay@missouri.edu

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, Ca^{2+}-activated, voltage-dependent potassium (BK_{Ca}) channel. BK_{Ca} 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 O_2 associated with hemeoxygenase-2 and, moreover, some slice-variants respond to membrane stretch. Based on these findings, BK_{Ca} 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 $GABA_A$ receptor channels and $GABA_B$-mediated modulation of K^+ and Ca^{2+} 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 metabol.ism 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.

Cuihua Zhang

Office Location: 324B Dalton Cardiovascular Research Center
Office Phone: 573-882-2427
E-mail: zhangcu@missouri.edu

EDUCATION**:**
M.D., Jin Zhou Medical College, Liao Ning, China, 1985
Ph.D., Peking Union Medical College, Beijing, China, 1995
Postdoctoral Training: Department of Physiology, Texas A&M University, 1998

Appointment: Associate Professor, Departments of Internal Medicine, Medical Pharmacology & Physiology and Nutritional Sciences

Research
Research in this laboratory is focused on regulation of coronary microvascular function; endothelium and vascular smooth-muscle biology; physiology and pathophysiology of coronary microcirculation; metabolic regulation of microvascular blood flow; nitric oxide and microvascular function; influence of antioxidants/oxidative stress on microvascular vasomotor function.

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: Assistant 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

CHARTS/GRAPHS

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Akamatsu K, Shibata MA, Ito Y, Sohma Y, Azuma H, Otsuki Y (2009) riluzole induces apoptotic cell death in human prostate cancer cells via endoplasmic reticulum stress. Anticancer Res. 29(6): 2195-2004

Tsai MF, Shimizu H, Sohma Y, Li M, Hwang TC (2009) State-dependent modulation of CFTR gating by pyrophosphate. J. Gen. Physiol. 133: 405-419

Mio K, Ogura T, Mio M, Shimizu H, Hwang TC, Sato C, Sohma Y. (2008) Three-dimensional reconstruction of human cystic fibrosis transmembrane conductance regulator chloride channel revealed an ellipsoidal structure with orifices beneath the putative transmembrane domain. J. Biol. Chem. 283: 30300-30310

Sowers, J.

Bakris GL, Sowers JR; on behalf of the American Society of Hypertension Writing Group. Treatment of hypertension in patients with diabetes-an update. J Am Soc Hypertens. 2009 March - April;3(2):150 -155.

Terjung, R.

Yang HT, Prior BM, Lloyd PG, Taylor JC, Li Z, Laughlin MH, Terjung RL. Training-induced vascu lar adaptations to ischemic muscle. J Physiol Pharmacol. 2008 Dec;59 Suppl 7:57-70.

Lai Y, Thomas GD, Yue Y, Yang HT, Li D, Long C, Judge L, Bostick B, Chamberlain JS, Terjung RL, Duan D. Dystrophins carrying spectrin-like repeats 16 and 17 anchor nNOS to the sarcolemma and enhance exercise performance in a mouse model of muscular dystrophy. J Clin Invest. 2009 Mar;119 (3):624-35. doi: 10.1172/JCI36612. Epub 2009 Feb 23.

Zhang, C.

Zhang H. and Zhang C**.** Regulation of Microvascular Function by Adipose Tissue in Obesity and Type 2 Diabetes: Evidence of an Adipose-Vascular Loop. American Journal of Biomedical Sciences (AJBMS). 1(2):133-142, 2009.

Park Y, Wu J, Zhang H, Wang Y, and Zhang C**.** Vascular dysfunction in type 2 diabetes: emerging tar gets for therapy. Expert Rev. Cardiovasc Ther. 7(3):209-213, 2009.

Xiuping Chen, Bradley T. Andresen, Michael Hill, Jing Zhang, Frank Booth and Cuihua Zhang. Role of Reactive Oxygen Species in Tumor Necrosis Factor-alpha Induced Endothelial Dysfunction. Current Hypertension Reviews**.** 4:245-255, 2008

Xue Gao, Hanrui Zhang, Ann Marie Schmidt and Cuihua Zhang. AGE/RAGE Produces Endothelial Dysfunction in Coronary Arterioles in Type II Diabetic Mice. Am J Physiol Heart Circ Physiol. 295 (2):H491-498. 2008.

Yoonjung Park, Stefano Capobianco, Xue Gao, John R. Falck, Kevin C. Dellsperger and Cuihua Zhang. Role of EDHF in Type 2 Diabetes-induced Endothelial Dysfunction. AJP-Heart, 295(5):H1982 -8. 2008.

Xue Gao, Souad Belmadani, Hanrui Zhang, Junxi Wu, Xiangbin Xu, Howard Elford, Barry J. Potter and Cuihua Zhang. Role of TNF-a-induced Reactive Oxygen Species in Endothelial Dysfunction Dur ing Reperfusion Injury. AJP-Heart, 295(6):H2242-9; 2008

Zhang H, Zhang J, Ungvari Z and Zhang C. Resveratrol Improves Endothelial Function: Role of TNFa and Vascular Oxidative Stress. Arterioscler Thromb Vasc Biol. 2009 (in press)

Yang J, Park Y, Zhang H, Xu X, Laine GA, Dellsperger KC and Zhang C. Feed-forward Signaling of TNFa and NFkB via IKKb Pathway Contributes to Insulin Resistance and contributes to Coronary Ar teriolar Dysfunction in Type 2 Diabetic Mice. AJP-Heart, 2009 (in press)

Zhang H, Zhang J, Ungvari Z and Zhang C. Resveratrol Improves Endothelial Function: Role of TNFa and Vascular Oxidative Stress. Arterioscler Thromb Vasc Biol. 2009 (in press)

PUBLICATIONS

Wang Y and Zhang C. Bariatric surgery to correct morbid obesity also ameliorates atherosclerosis in patients with type 2 diabetes mellitus. American Journal of Biomedical Sciences (AJBMS). 2009, 1, 56 - 69

Zhang H. and Zhang C**.** Regulation of Microvascular Function by Adipose Tissue in Obesity and Type 2 Diabetes: Evidence of an Adipose-Vascular Loop. American Journal of Biomedical Sciences (AJBMS). 1(2):133-142, 2009

Baines, C.

"Mitochondrial Permeability Transition and Cell Death." Experimental Biology 2009, New Orleans, 4/21/09.

"RIPing holes in mitochondria: understanding necrotic cell death." International Society for Heart Research North American Section Meeting, Baltimore, 5/26/09.

"Identifying Novel Components of The Mitochondrial Pore." Biophysical Society 53rd An nual Meeting, Boston, MA, February 2009

Booth, F.

Life Sciences Program seminar, Brigham Young University, Provo Utah, January 10, 2009

Keynote speaker at Northwest chapter of American College of Sports Medicine meeting, February 29, 2009

Symposium speaker at Experiment Biology, San Diego, 9 April, 2009

Two symposium talks at the American College of Sports Medicine, Indianapolis, 28-30 May, 2009

Lindhard Symposium, Copenhagen, January 2009

Annual Meeting of American College of Sports Medicine, may 2009

Ding, S.

Lin Sun, Jinglu Tan, Shinghua Ding, Modeling of ATP-induced Calcium Kinetics in Glial Cells. Biomedical Engineering Society (BMES) Annual Fall Meeting. October 1-4, St. Louis, 2008.

"Astrocytic Ca^{2+} mediated neurotoxicity". Dept. of Medical Physiology and Pharmacology, Uni versity of Missouri-Columbia, Oct 14, 2008

Hwang, T.C.

Symposium speaker, Joint meeting of the Physiological Society, the Chinese Association for Physiological Societies, and the American, Australian and Canadian Physiological Societies, Beijing China

Department of Physiology, Chinese University of Hong Kong
Harbin Medical University

14th Annual Conference of the Biophysical Society of ROC, Taiwan
European Cystic Fibrosis Conference, Portugal

Department of Biology, Hong Kong University of Science and Technology
Institute of Biomedical Sciences, Academia Sinica, ROC, Taiwan

Heesch, C.

Cheryl M. Heesch, Korryn Shoge, Terese M. Zidon, and Eileen M. Hasser. Vasopressin and neuronal nitric oxide synthase in hypothalamic paraventricular nucleus (PVN) of pregnant rats. FASEB Journal, 22:1228.4, 2008

Lyudmyla Kvochina, Glenn Phaup, Eileen M. Hasser, and Cheryl M. Heesch. Sympathoexci tation due to Angiotensin II in the subfornical organ is increased by pregnancy and requires I onotropic glutamate receptors in the rostral ventrolateral medulla. FASEB Journal, 22: 1169.5, 2008

Terese M. Zidon, James R. Austgen, Cheryl M. Heesch, and Eileen M. Hasser. Neuronal nitric oxide synthase and vasopressin in the paraventricular nucleus of hindlimb unloaded rats. FASEB Journal, 22: 739.15, 2008

Terese M. Zidon, Angelina Y. Fong, C. Michael Foley, Patrick J. Mueller, Cheryl M. Heesch, Eileen M. Hasser. Neuronal Nitric Oxide Synthase in the Rostral Ventrolateral Medulla of Hindlimb Unloaded Rats. FASEB Journal 22: 1169.12, April 2008

James R. Austgen, Sarah A. Friskey, Cheryl M. Heesch, and Eileen M. Hasser. Increase and decreases in arterial pressure result in the activation of phenotypically different populations of neurons in the nucleus of the solitary tract (NTS). FASEB Journal 22: 1171.18, 2008

Hyder, S.

Carroll, C E., Benakanakere, I., Besch-Williford, C., Liang, Y. and Hyder S. M. (2009). HIF-1alpha is required for both progestin-induced VEGF secretion by breast cancer cells and in vivo progression of progestin-dependent mammary tumors. 100th Annual American Association of Cancer Research Meeting, Denver, CO. *Abst#4069.*

Benakanakere, I., Carroll, C. E., Besch-Williford, C., Ruhlen, R. L. and Hyder, S. M. (2009). The synthetic progestin Norgestrel prevents the progression of pre-neoplastic lesions in a rat model of DMBA-induced breast cancer. 91st Annual Endocrine Society Meeting, Washington DC, June 2009.

Benakanakere, I., Besch-Williford, C., Ellersieck, M. R. and Hyder, S. M. (2009) PRIMA-1 dependent regression of progestin-accelerated 7, 12-dimethylbenz[a]anthracene (DMBA)-I nduced mammary tumors in Sprague-Dawley rats. 91st Annual Endocrine Society Meeting, Washington DC, June 2009.

Liang Y., Benakanakere, I., Hyder, R. S. and Hyder, S. M. (2009) Role of natural and syn thetic progestins in progression of breast cancer cells in nude mice. 91st Annual Endocrine So ciety Meeting, Washington DC, June 2009.

Grinter, S. Z., Liang, Y, Huang, S-Y, Hyder, S. M. and Zou, X. (2009) Developing anti-tumor agents by investigating the action mechanism of PRIMA-1. National Library of Medicine In formatics Training Conference 2009, Portland, OR., June 2009.

Kline, D.

All presented in poster form at Experimental Biology April 2009

James R Austgen, Heather A Dantzler, and David D Kline
Anatomical location and electrophysiological properties of the serotonin receptors type 2 (5-HTR2) in the nucleus of the solitary tract (nTS).
FASEB J. 23: 1011.8

David D. Kline, Gabriel Hendricks, Gerlinda E. Hermann, Richard C. Rogers, and Diana L. Kunze Dopamine inhibits N-type channels in chemosensory afferents to reduce synaptic transmit ter release under normoxic and chronic intermittent hypoxic (CIH) conditions
FASEB J. 23: 1011.2

Luise T King, Cheryl M Heesch, David D Kline, and Eileen M Hasser
Effects of Hypoxia on Fos Expression in RVLM-Projecting Neurons in the Nucleus of the Solitary Tract (NTS)
FASEB J. 23: 1011.4

Catharine Grace Clark, Eileen M. Hasser, Diana L. Kunze, David M. Katz, and David D. Kline Brain Derived Neurotrophic Factor (BDNF) blunts neural activity in the nu cleus tractus solitarius (nTS)
FASEB J. 23: 1011.5

M Cathleen Kuehl-Kovarik, David D Kline, and Eileen M Hasser Properties of Dissoci ated Paraventricular Nucleus (PVN) Neurons following Hindlimb Unloading (HU) in Rats *FASEB J.* 23: 792.5

Poster # 382.10/RR53 Title: Mecp2 null mice exhibit enhanced excitatory postsynaptic currents (EPSCs) in the brainstem nucleus tractus solitarius (NTS) Location: Washing ton Convention Center: Hall A-C Presentation Time: Monday, Nov 17, 2008, 9:00 AM - 10:00 AM Authors: *D. D. KLINE[1], E. M. HASSER[1], C. G. CLARK[1], D. L. KUN ZE[2,3], D. M. KATZ

Program#/Poster#: 676.7/QQ31 Title: The role of brain derived neurotrophic factor on autonomic and cardiovascular function Location: Washington Convention Center: Hall A-C Presentation Time: Tuesday, Nov 18, 2008, 3:00 PM - 4:00 PM Authors: **C. G.** CLARK[1], D. D. KLINE[1], D. L. KUNZE[2,3], D. M. KATZ[3], *E. M. HASSER[1];

Korthuis, R.

"Microvascular dysfunction in ischemia/reperfusion." Department of Physiology, Tu lane University School of Medicine, New Orleans, LA, August 2008

"Neutrophil-mediated arteriolar vasoregulatory dysfunction in ischemia/reperfusion." Cardiovascular Research Center, St Louis University School of Medicine, St Louis, MO, September 2008

Postischemic arteriolar dysfunction is dependent on venular leukocyte adhesion and mast cells: Role of cell-cell communication, Keystone Conference on Dissecting the Vasculature: Function, Molecular Mechanisms, and Malfunction, Vancouver, BC, Can ada, February 2009

Plenary Session Chair: Keystone Conference on Complications of Diabetes and Obe sity, Vancouver, BC, Canada, February 2009

AMP-activated protein kinase activation stimulates heme oxygenase-1 gene expression in human vascular endothelium. Experimental Biology ’09 Meeting; New Orleans, April 2009.

Adenosine stimulates mitochondrial biogenesis in microvascular endothelial cells. Experimental Biology ’09 Meeting; New Orleans, April 2009.

Antecedent ethanol attenuates cerebral ischemia/reperfusion-induced leukocyte-endothelial adhesive interactions: Role of large conductance, Ca^{2+}-activated K^+ channels (BK_{Ca}). Experimental Biology ’09 Meeting; New Orleans, April 2009.

Hydrogen sulfide preconditioning attenuates ischemia/reperfusion-induced mitochondrial dysfunction in rat intestine by a BK_{Ca} channel-dependent mechanism. Experimental Biology ’09 Meeting; New Orleans, April 2009.

Role of proteases in ischemia/reperfusion-induced arteriolar endothelium-dependent vasodilatory dysfunction. Experimental Biology ’09 Meeting; New Orleans, April 2009.

Role of mast cells in ischemia/reperfusion-induced arteriolar endothelium-dependent vasodilatory dysfunction. Experimental Biology ’09 Meeting; New Orleans, April 2009.

Relative lack of b1-subunit-mediated regulation of BK_{Ca} in cremaster arteriolar smooth muscle. Experimental Biology ’09 Meeting; New Orleans, April 2009.

.

Liang, Y.

Role of Natural and Synthetic Progestins in the Progression of Human Breast Tumor Xenografts in Nude Mice, at 91st ENDO-Annual Meeting, in Washington, DC on June 10, 2009

Martinez-Lemus, L.

Martinez-lemus, L.A., Z. Sun, M.A. Hill and G.A. Meininger. “he Role of Integrins on the Control of Skeletal Muscle Arteriolar Diameter.” The Integrative Biology of Exercise-V. Hilton Head, S.C. September 24-27, 2008. Guest Speaker

Martinez-Lemus. “Remodeling of the resistance Microvasculature: Early Mechanisms.” American Heart Association, Research Symposium. New Orleans Louisiana, November 7, 2008.

Martinez-Lemus. “Veterinary Spanish in a Diverse World.” School of Veterinary Medicine, University of Missouri-Columbia. Columbia, MO. October 27, 2008

"Mechano-responsive behavior of Vascular Smooth Muscle Studied using Atomic Force Microscopy" to the Department of Integrative Physiology, University of North Texas Health Science Center, Octo ber 9, 2008

Meininger, G.

"Atomic Force Microscopy as a Biological Research Tool". International Bioelectrics Sympo sium, Columbia, Missouri, June 25-26, 2009"Micro-Myogenic Events induced in vascular smooth muscle by Mechanical force applied to a single fibronectin focal adhesion". 25th Conference of the European Society for Microcirculation, Budapest, Hungary, August 26-29, 2008.

"Mechano-responsive behavior of Vascular Smooth Muscle Studied using Atomic Force Microscopy" to the Department of Integrative Physiology, University of North Texas Health Science Center, Octo ber 9, 2008.

Mechanosensation in Vascular Smooth Muscle Cells Utilizes Unique Extracellular Matrix Proteins and Integrins" to the Department of Systems Biology and Translational Medicine, Texas A&M University Health Science Center, January 29, 2009.

Milanick, M.

"Atomic Force Microscopy as a Biological Research Tool". International Bioelectrics Symposium, Columbia , Missouri, June 25-26, 2009.

Polo-Parada, L.

Division of Cardiology. University of Missouri. Hospital and Clinics
Department of Chemical Engineering. University of Missouri
International Bio Electric Symposium. University of Missouri
Escuela Superior de Fisica y Matematicas. Instituto Politecnico Nacional. Mexico City
Centro de Investigacions en Optica AC. Leon Guanajuato. Mexico
Universidad de Guanajuato. Divison de Ciencias e Ingenierias, Campus Leon. Invited talk and Work shop

Segal, S.

"Integrating Electrical and Calcium Signaling in Microvascular Resistance Networks",
Budapest, Hungary 08/27/08 (European Society for Microcirculation)

"Role for Endothelial Calcium Waves in Conducted Vasodilatation", Budapest, Hungary
08/28/08 (European Society for Microcirculation)

Integral Roles of Cell-to-Cell Signaling in Blood Flow Control to Skeletal Muscle, Slovak Academy of Sciences, Bratislava, Slovakia 08/24/08

"Electrical and Calcium Signaling Along Microvascular Endothelium: Integral Roles in Blood Flow Control", Rush University, Dept. Molecular Biophysics & Physiology (10/16/08)

President's Symposium and Workshop, the Microcirculatory Society, Inc.; New Orleans, LA; 04/18/2009 (Organized and Chaired; Introductions and Discussion)

Electrical and Calcium Signaling in the Resistance Microvasculature;
University of Virginia, 05/15/09

Zhang, C.

Park Y, Lee S, Booth FW, Laye MJ, and Zhang C. Physical activity prevents endothelial dysfunction induced by sedentary life style and high fat diet in murine coronary microcirculation. *FASEB J*. 23:952.4. 2009

Lee S, Park Y, and Zhang C. Exercise Training Improves Endothelial Dysfunction in Type 2 Diabe tes. *FASEB J*. 23:594.4. 2009.

Hanrui Zhang, Brandon Morgan, Barry J Potter, Lixin Ma, Kevin C. Dellsperger and Cuihua Zhang. Resveratrol Alleviates Cardiac Dysfunction in Type 2 Diabetes by Inhibiting Oxidative/ Ni trative Stress: in vivo Demonstration with Magnetic Resonance Imaging. American Diabetes Asso ciation Scientific meetings in New Orleans. 2009
http://www.sino-meetings.com/sfrr/index.html

Yong Wang, Jing Zhang and Cuihua Zhang. Role of gastric bypass surgery in treating morbid obesity and type 2 diabetes in db/db mice. American Diabetes Association Scientific meetings In New Orleans. 2009

Hanrui Zhang and Cuihua Zhang. The Interactive Balance Between Adiponectin and TNFa in the Regulation of Aortic and Coronary Endothelial Function in Type 2 Diabetic Mice. Atherosclerosis, Thrombosis and Vascular Biology Annual Meeting in Washington DC, April 2009.

Cuihua Zhang, Yoonjung Park, Hanrui Zhang, Xiuping Chen, William P. Fay. Endothelial Dilation in ApoE KO Mice: An Interactive Balance Among TNF-α, Adiponectin and LOX-1. *Circulation*. 2008. Annual Scientific American Heart Association meetings in New Orleans, 11/2008

Invited Symposium Speaker: ROS-dependent Endothelial Dysfunction in Diabetes and the Metabolic Syndrome. AHA Annual Scientific Sessions. November 7-12, 2008.

Invited speaker for XIV Biennial Meeting of the Society for Free Radical Research Interna tional.

Jiuhua Spa and Resort, Beijing, China. October 18-22, 2008. Orla Presentation title: ROS-de pendent Endothelial Dysfunction in Type 2 Diabetes

Cuihua Zhang: Role of Gastric Bypass Surgery in Treating Obesity and Type 2 Diabetes in db/db mice. Atherosclerosis, Thrombosis and Vascular Biology Annual Meeting in Washington DC, April 2009

Role of Inflammatory Cytokine in Vascular Dysfunction. The University of Texas Health Science Center – Houston on June 22nd, 2009

Role of Inflammatory Cytokine in Vascular Dysfunction. Ground Rounds at the Department of Internal Medicine, University of Missouri-Columbia on July 9th, 2009

Chikara Sato — 8/29/08

"Three-dimensional structures of ion channels revealed By electron microscopy"

Group Leader, Structual Physiology Group of Neuroscience Institute, Tsukuba, Japan

Stephen Vatner — 09/11/08

"*Adrenergic regulation in heart failure-last half century*"

Chair, Department of Cell Biology & Molecular Medicine & Director, Cardiovascular Research Institute UMDNJ-NJ Medical School

John Yang — 01/15/09

"*Bcl3: its potential roles in cardiac stress response"*

Assistant Professor of Internal Medicine, Washington University School of Medicine in St. Louis, MO

PRINCIPAL INVESTIGATOR *TITLE* AGENCY	AMOUNT PERIOD
Baines, Christopher	
"Mechanisms of Mitochondrial-Dependent Myocyte Death" American Heart Association Scientist Development Grant American Heart Association National Center	$260,000 7/06-6/10
"Identifying Novel Components of The Cardiac Necrotic Program" National Institute of Health/National Heart Lung and Blood Institute	$275,000 7/08-4/10
"Molecular Identity of The Cardiac Mitochondrial Pore" National Institute of Health/National Heart Blood and Lung	$1,250,000 12/08-1/13
"Mechanisms of Mitochondrial-Dependent Myocyte Death" American Heart Association National Center	$260,000 7/06-6/10
"Indentifying novel components of the cardiac necrotic program" National Institute of Health	$368,250 3/09-4/11
Bompadre, Sylvia	
"*Molecular physiology and pharmacology of CFTR"* National Institute of Diabetes and Digestive and Kidney Diseases	$101, 542 9/08-8/09
"Physiology and pharmacology of G551D mutations" Cystic Fibrosis Foundation	$175,375 4/06-3/09
"Molecular physiology and pharmacology of CFTR" National Institute of Health	$322,923 9/06-8/10
Booth, Frank	
"Satellite Cell Biology" National Institute of Health RO1 AG18780	$177,000 Ends 2009
"Exercise training and coronary disease" 5 P01 HL052490	$13,400

"Role of physical inactivity in weight regain from weight loss; *and do epigenetic changes with physical activity exist?"*	$18,000 Ends 2009
College of Veterinary Medicine	
Epigenetic regulation of genes by exercise	$5,000
American College of Sports Medicine	
Physical activity induced methylation of key CVD-related genes in mouse skeletal muscle	$25,000
American Heart Association	

Clarke, Lane

"Parion Sciences Materials Transfer and Testing"	$50,237
Parion Sciences, Inc	12/08-06/10
"Structure-guided physiological screening for DeltaF508 C"	$1,349,781
Cystic Fibrosis Foundation	12/06-11/10
"CFTR & acid-base transporters of intestinal epithelia"	$1,148,473
National Institute of Health	7/06-6/11

Davis, M.

"Cellular Mechanisms of Lymphatic Muscle Contractility"	05/08-04/13
National Institute of Health	$1,100,000
"Regulation of Vascular Tone and Ca Channels by Integrins"	$1,000,000
National Institute of Health	04/09-03/13
"Molecular Control of EC Lumen Formation by MT-1 MMP"	$1,250,000
National Institute of Health	12/08-11/12
" Mechanisms of Reperfusion-induced Endothelial Injury"	$1,250,000
National Institute of Health	5/06-4/11
"Mechanisms of age-related alterations in lymphatic pumping"	$1,000,000
National Institute of Health	6/08-5/13

Ding, Shinghua

"Astrocyte-mediated neuronal excitation"	$260,000
American Heart Association-National Center,	7/07-6/11
Scientist development grants	

"*An Optical and Genetic Strategy to Study Glutamate Release from Astrocytes in vivo"* Ralph E. Powe Junior Faculty Enhancement Awards through the Oak Ridge Associated Universities	$10,000 6/08-6/09
"*Optical and Genetic Strategy to Study Astrocyte-Neuron Interaction"* Research Board	$44,527 7/09-6/10

Gillis, Kevin

"Microchip devices to assay quantal exocytosis" National Insitute of Health-Institute of Neurological Disorder"	$2,056,842 9/04-7/10

Gu, Liqun

"Programmable multi-target detections with aptamer-integr National Institute of Gen Med Sci	$1,014,059 2/07-1/11
"Single molecule study of oligonucleotide-protein" National Science Foundation	$526,349 7/06-6/11

Hasser, Eileen

"Cardiovascular Regulation in Hindlimb Unweighted Rats" National Institute of Health	$1,327,459

Heesch, Cheryl

"Differential neurotransmitter modalities of CNS presympathetic neurons," University of Missouri Research Board Grant	$29,500 3/07-06/09
"*Neural Circulatory Control: Pregnancy & Ovarian Hormones,"* National Institiute of Health	$700,000 3/07-2/09
"Cardiovascular regulation in hindlimb unweighted rats," National Institute of Health	$225,000 4/07-3/11
"Adaptation of brainstem circuits to chronic hypoxia," National Institute of Health	$250,000 7/07-6/12
"Central nervous system plasticity in sympathoinhibition" National Institute of Health	$897,096 6/09-3/11

Hyder, Salman

"*p53-activating Compunds as Therapeutic Tools for progress"*	$135,000
Susan G Komen Breast Cancer Foundation	5/06-4/09
"*Estrogen and Progestin Regulation of Thrombospondin-1 in"*	$250.000
Susan G Komen Breast Cancer Foundation	5/06-4/09
"*Inhibition of Progestin-Dependent Angiogene"*	$55,955
National Institute of Health	5/08-4/10
"*Recovery of functional p53 as a therapeutic approach"*	$311,187
National Institute of Health	8/08-7/10

Hwang, T.C.

"Gating of CFTR chloride channels by ATP hydrolysis"	$933,056
National Institute of Health/National Heart Lung Blood	2006-2010
"Molecular pathophysiology of cystic fibrosis"	$1,014,155
National Institute of Health/National Institute of Diabetes and Digestive and Kidney Diseases	2008-2013
"*Molecular Pathophysiology of Cystic Fibrosis"*	$638,724
National Institute of Health National Institute of Diabetes and Digestive and Kidney Diseases	9/08-8/10

Kline, David

"*BDNF and MeCP2 in autonomic dysfunction"*	$304,388
Case Western University	4/07-3/10
"Adaptation of brainstem circuits to chronic hypoxia"	$1,122,225
National Institute of Health	4/08-3/13

Korthuis, Ronald

"Ethanol prevents microvascular dysfunction",	$225,000
National Institute of Health	6/06-5/11
"*Venular leukocyte adhesion, impaired arteriolar vasoreactivity, and intestinal I/R"*	$250,000 12/06-11/10
National Institute of Health	

Krenz, Maike

"*Defective Valvulogenesis in Noonan Syndrome"*	$118,658
American Heart Association	11/08-06/10

Li, Min

"Search for CFTR Mutations in Dogs" $4320
University of Southern Alabama 12/08-03/09

Liang, Yayun

"Therapeutic Targeting of Human Breast Tumors by Reactivation of p53 Activity" $400,000
1/09-1/12
Susan G Komen Breast Cancer Foundation

"Simultaneous targeting of mutant p53 and the angiogenic pathway to treat and prevent primary and metastatic breast cancer" $18,000
1/09-12/09
MU Veterinary Medicine

Martinez-Lemus, Luis

"Remodeling of the Resistance Vasculature: Early Mechanisms." $260,000
American Heart Association National Grant 2005-2008

"Oxidative Stress and Vascular Remodeling." $49,698
University of Missouri, Research Board 2009-2010

Milanick, Mark

"From Clinic to Bench & Back: Clinincal biodetective Training" $622,919
National Institute of Health-National Institute of Diabetes and Digestive and kidney diseases 9/04-7/08

"From Clinic to Bench & Back: Clinical Biotective" 687,382
National Institute of Health-National of Diabetes and Digestive and kidney diseases 9/04-7/08

"From Clinic to Bench & Back: Clinical Biodetective" $458,829
National Institute of Health-National Institute of Diabetes And Digestive and kidney diseases 8/08-7/10

Meininger, Gerald

"Hybrid atomic force - optical imaging system to investigate prenatal exposure to nicotine." $150,000
National Institutes of Health-National Institute 12/08-1109

"Hybrid atomic force-optical imaging system to investigate prenatal exposure to nicotine." $74,750
9/08-9/10
University of North Texas

EACR Travel Fellowship for Kimberley J Reeves €2000
03/09

BACR Travel Fellowship for Kimberley J Reeves £2717
03/09

"Acute mechanisms of vascular remodeling", $1,250,000
National Institutes of Health - National Heart, Lung and
Blood Institute, Public Health Service Grant 7/09-6/14

"Plasma surface modification to improve $30,000
neo-endothelialization of ePTFE grafts" 12/08-11/09
National Institute of Health

"Atomic Force-Fret Microscopy" $555,529
National Institute of Health 9/06-8/09

Polo-Parada, Luis

"Role of the Cardiac Cushions" $220,245
American Heart Association 2/06-1/09

Segal, Stephen

"Intercellular Coordination of Blood Flow Control" $1,807,558
National Institutes of Health/National Heart Lung 7/08-8/13
and Blood Institute

"Frontiers in Microcirculation" $12,500
National Institute of Health/National Heart Lung and 9/09-8/10
Blood Institute

Sohma, Yoshiro

"Gating of CFTR C1 Channels by ATP Hydrolysis"
National Institute of Health-collaborator 2006-2011

Terjung, Ronald

"*Vascular Biology: Exercise Training and* $11,550,565
Vascular Disease" 12/05-11/10
National Institute of Health/National Heart Lung
And Blood Institute

"Factors Controlling Peripheral Vessel Development $1,135,539
in a Large Mammal" 12/5-12/10
National Institute of Health/National Heart Lung
And Blood Institute

7/07-6/09

Zhang, Cuihua

"*Role of TNF alpha in Endothelial Dysfunction in the Meta"* $132,408
American Heart Association 1/08-6/10

"*Role of Cytokine-Induced Inflammation in Endothelial"* $1,032,150
National Institute of Health 7/08-11/10

"*Mechanisms of Reperfusion-induced Endothelial"* $1,335,914
National Institute of Health 6/08-3/11

Zhe, Sun

"*Integrin-mediated mechanotransduction"* $143,000
American Heart Association 7/07-6/09

"Integrin-mediated mechanotransduction" $77,000
American Heart Association 7/08-6/12

Zou, Xiaoqin

"*Molecular mechanisms and rational design of CFTR potenti"* $43,200
Cystic Fibrosis Foundation

PROFESSIONAL SERVICE ACTIVITIES

Baines, C.

Editorial Boards:
American Journal of Physiology, Heart and Circulatory Physiology
Journal of Molecular and Cellular Cardiology
Reviewer:
American Journal of Physiology, Heart and Circulatory
Journal of Cardiovascular Pharmacology
Journal of Molecular and Cellular Cardiology
Journal of Pharmacology and Experimental Therapeutics
Journal of Applied Physiology
Journal of Vascular Research

Blaine, E. H.

Reviewer for various journals, esp. AJP
UM Research Board
Campus Planning Committee (Chairman)
Faculty Grievance Oversight Committee
Honorary Degrees Committee
Dalton Development Committee
Dalton Internal Advisory Committee
MPP Graduate Education Committee

Booth, F.

Chair of Search Committee for Department of Nutrition and Exercise Physiology
Director, Health Activity Center
Three American College of Sports Medicine Committees
Health and Science Policy
Activity and Health Policy Network
FASEB relationship
Director, Researchers Against Inactivity Related Disorders
Research Group of the International Biochemistry of Exercise

Davis, M.

Microcirculatory Society: Member,
Website Committee
Publications Committee
Communications Committee
American Physiological Society: Member
Biophysical Society: Member
American Society for Biochemistry and Molecular Biology: Member
The Physiological Society: Member

Editorial Boards
Editorial Board Member:
American Journal of Physiology: Heart & Circulatory Physiology, 1991-99; 2001-
Journal of Vascular Research, 2001-
Microcirculation, 1994-2009

Grant Review

National:
NHLBI P01 and R01 Special Emphasis Panels (ad hoc), 1991, 1996, 1999, 2004, 2005, 2008, 2009

Ding, S.

Serve on a Dalton Safety Committee since Jun 15, 2009.
Member of thesis's committee (PhD) for Youghong Bai (July 9, 2008-, Dr. Hwang's lab).
Member of thesis's committee (PhD) for Srikanth Ella (June 6, 2008-, Dr. Michael Hill's lab).
Member of thesis's committee (PhD) for Shopan Askarova (Jan, 2007-, Dr. James Lee lab).
Member of thesis's committee (PhD) for Xiaoguang Yang (June 7, 2007-, Dr. James Lee lab).
Coordinator of Membrane Journal Club since July, 2008.

Fay, W.

Editorial Board
ATVB Journal
Member National Research Committee, AHA
Chair, Annual Scientific Meeting, ATVB Council of AHA

Heesch, C.

Manuscript Reviews
Clinical & Experimental Pharmacology and Physiology (1)
American Journal of Physiology (4)
Experimental Neurology (1)
Hypertension in Pregnancy (1)
University of Missouri, College Vet. Med. Honor Code Revision Committee
University of Missouri, Interdisciplinary Neuroscience Program, Executive Committee
University of Missouri, Dept. Biomed. Sci., Chair Promotion & Tenure Committee

University of Missouri, Dept. Biomed. Sci., Junior Faculty Mentoring Committees for:
Ileana Constantinescu (Committee Chair)
Kathy Kuel-Kovarik (Committee Member)

Huxley, V.

Editorial Boards
American Journal of Physiology
Microvascular Research
Microcirculation
Reviewer
National and International Journals and National Institute of Health

Hwang, T.C.

Consultant for Cystic Fibrosis Foundation
Editorial board member, JGP &BJ

Hyder, S.

Invited Reviewer 2008 Israel Science Foundation
Grant Reviewer 2008 International Union Against Cancer (UICC) Review Panel
Invited Reviewer 2008 Austrian Science Fund
Invited Reviewer 2008 American Medical Association
Reviewer, Technology Transfer grant, International Union Against Cancer, Switzerland.
Session Chair (Tumor and Cell Biology), International Bioelectrics '09 conference, MU, June 26-27.

Kline, D.

Animal Resources Committee, CVM
Service-APS Communications Committee, APS Hypoxia Interest Group
Journal Reviewer Brain Research, J Physiology, J Neuroscience Research
Member, Research Advisory Committee (RAC)
Member, Graduate Program Advisory Committee (GPAC)
Coordinator, Department of Biomedical Sciences Seminar Series
Member, Appointment and Promotions Committee, DCRC
Member, Committee on Research

Member, Animal Issues Response Team (AIRT)Office of Research
Hypoxia Interest Group Steering Committee, American Physiological Society
Communications Committee, American Physiological Society
Journal Review Service
Journal of Physiology (London)
Journal of Neurophysiology
Journal of Neuroscience
Journal of Applied Physiology
Brain Research
American Journal of Physiology
Journal Neuroscience Research
Reviewer, National Science Foundation (NSF)

Korthuis, R.

NIH, Vascular Cell and Molecular Biology Study Section, February 2009
Health Research Board of Ireland, March 2009
American Physiological Society, Finance Committee
Microcirculatory Society, Liaison Committee
American Heart Association, Peer Review Steering Committee
Editorial Board: American Journal of Physiology: Heart and Circulatory Society
Editorial Board: Cardiovascular Research
Editorial Board: Microcirculation
American Physiological Society Finance Committee Meeting;
American Physiological Society Joint Programming Committee
Meeting

Krenz, M.

Reviewer, Journal of Applied Physiology

Laughlin, H.

Editorial boards
Journal of Applied Physiology
American Journal of Physiology: Heart and Circulatory Physiology
Association Editor for Journal of Applied Physiology & Medicine & Science in Sports & Exercise

Liang, Y.

Invited to review BMIC-2009 on May 2009
Invited Peer Reviewer by University of Missouri Research Board to process a peer review for a proposal submitted to the University of Missouri Research Board in Nov. 2008.

Martinez-Lemus, L.

Reviewer for:
Journal of Vascular Research
Arteriosclerosis, Thrombosis, and Vascular Biology
American Journal of Physiology
Editorship:
Associate Editor for the Physiology and Reproduction section of Poultry Science
Microcirculatory Society: Program Committee (2007-2010)
American Physiological Society: Awards Committee
Member, Committee for Appointment and Promotion of Non-Tenure Research Track Faculty. Dalton Cardiovascular research Center. University of Missouri-Columbia.
Member, MPP Program Assessment Committee.
Extramural Grant Reviewer for:
American Heart Association – National. Member, Vascular Biology and Blood Pressure / Regulation, 2006-2010. (October 20, 2008)
Member, Gender and Racial Diversity Equity Council Representation.
CV-Day 2009. Session Moderator. University of Missouri-Columbia
Member, Dalton Cardiovascular research center Safety Committee.

Meininger, G.

US Co-Editor for Journal of Vascular Research.
Associate Editor for American Journal of Physiology: Heart and Circulatory Physiology.
Grant review for Innovation fund of Canada Foundation for Innovation, July 2001.
Grant reviewer (ad hoc) for Canadian Institutes of Health Research, July 2008.
Attended Section Advisory Committee for American Physiological Society as Chair of the Cardiovascular Section

Milanick, M.

Consult with biochemistry about developing new undergraduate laboratory.
Consult with nurses about stress assays-cortisol and amylase in saliva

Polo-Parada, L.

Consultancies/Advising Services:
National Biodefense and Analysis and Countermeasure Center (NBACC). US Department of Homeland Security
Battelle. US Department of Homeland Security
NEMS/MEMS LLC

Dr. Indu Joshi. CNS Pharmacology, PFZIER Global R&D Michigan Laboratories
Dr. Toshido Matsuda. Laboratory of Medicinal Pharmacology. Graduate School of Pharmaceutical Sciences. Osaka University
Dr. Anita Zaremba. Case Western Reserve University
Dr. Michiko Watanbe. Case Western Reserve University
Dr. George Porter. Department of Pediatrics, Division of Cardiology. Yale University., School of Medicine
Dr. Robert H Chow. Zikha Neurogenetic Institute and Dept. Of Physiology and Biophysics. University of Southern California
Dr. M Isabel Dominguez. Hematology-Oncology Section. Department of Medicine. Boston University School of Medicine
Dr. Jill A. Rafael-Fortney. Dept. of Molecular & cellular Biochemistry. The Ohio State University

Advisor Committees:

The National Academies. Advisers to the Nation of Science, Engineering and Medicine (2009)
American Heart Association (2009)
NRC Program Quality Bio-and Medical Informatics and Cybernetics: BMIC 2008

Chair and Co-Chair Services:

Missouri Nano Frontiers Symposium. 2009. Co-Chair.

Study Section Participant:

NSF Instrument Development for Biological Research Panel
Winter. American Heart Association. Peer Review Cardiac biology/Regulation 1 Study Group
NSF Instrument Development for Biological Research Panel
Spring. American Heart Association. Peer Review Cardiac biology/Regulation 1 Study Group

Advisor and Co-advisor:

Amol A Modgi. Department of Biological Engineering. Masters student. Graduated 2008. Advisor.
Riberet Almeida, masters student. Graduated 2008. Co-Advisor
Tsai, Mingfeng. Department of Medical Pharmacology and Physiology. Ph.D. Co-Advisor.
Steven J Apperson. Department of Engineering. Ph.D. Student. Co=Advisor.
Sangho Bok. Department of Engineering. Ph.D. Student. Co-Advisor
Sagar K Gupta. Department of Biological Engineering. Ph.D. Student. Co-Advisor.
Craig R. Weilbaecher. Department of Biological Engineering. Ph.D. Student. Co=Advisor.
Jasenka Memisevic. NSF Graduate Research Fellow. Biological Engineering. Ph.D. Student. Co-Advisor.

Segal, S.

Chair, Organizing Committee for MCS meeting at MU in 11/09
Symposium Chair & Organizer: Integrative Biology of Exercise meeting (APS; 09/08)
Associate Editor/Editor-Elect, Microcirculation
President, International Liaison; The Microcirculatory Society, Inc
Chair, Organizing Committee for MCS meeting at MU in 11/09
Organizing: President's Symposium and Workshop, The Microcirculatory Society, Inc. (to be held February 17, 2009 in New Orleans)
Associate Editor/Editor-Elect, *Microcirculation*
President and International Liaison; The Microcirculatory Society, Inc.
Manuscript reviewer: Am. J. Physiol., Circulation Research, Microcirculation.
Chair, Organizing Committee for MCS meeting at MU in 11/09

Sohma, Y

Editor (Journal of Physiological Society of Japan)
Journal reviewer (J. Physiol)
Manuscript Reviews:
Biochimica et Biophysica Acta
Biophysical Journal
Biology of Reproduction
BIOPHYSICS
Cell biology International
Experimental Physiology
Japanese Journal Physiology
Journal General Physiology
Journal Membrane Biology
Journal Physiological Sciences
Journal of Physiology

Sowers, J.

Editorial Boards:
Hypertension
Endocrinology
Journal of Hypertension
Chief Editor: Journal of Cardiometabolic Syndrome
Reviewer:
Several study sections for the NIH and VA.
Safety and Monitoring committee for the NIH
NIH ACCORD study
Several VA cooperative studies

Terjung, R.

Associate Chair, Biomedical Sciences
Associate Dean for Research and Graduate Studies
2004-Present *Member,* Executive Committee, College of Veterinary Medicine
2004-Present *Member,* Council of Research Advisors, Asst Provost for Re search
2004-Present *Director,* Grant Review Program, College of Veterinary Medicine

Editor-in-Chief, Comprehensive Physiology [On-line published version of the American Physiological Society's *Handbooks of Physiology*], 2008 - 2011
Member, Nominating Committee, American College of Sports Medicine. 2008-2010.

Chair, Book Committee, American Physiological Society, 2007 - 2011.

Member, Hypertension/Microvasc Study Section, NIH, Bethesda, MD, 2007-2010.

Member, Special Emphasis Panel Study Section, NIAMS, Bethesda, April 2009

Zhang, C.

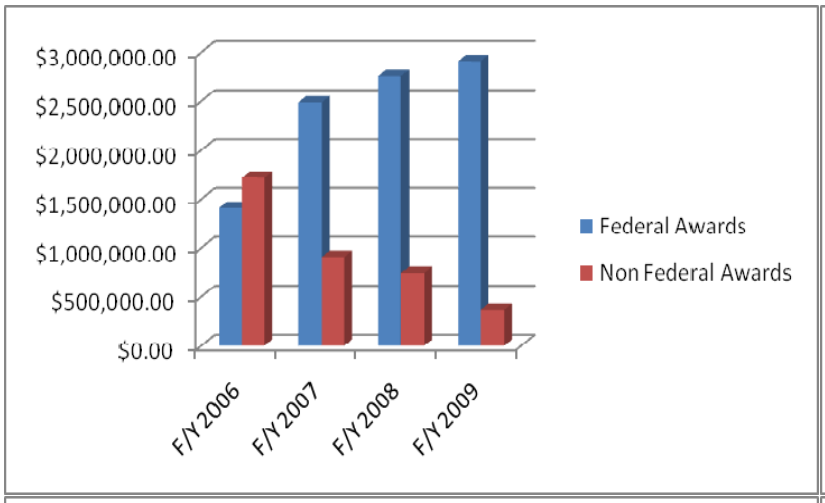
Serve on NIH MIM Study Section on June 11-12th, 2009
Moderator for the Session of Vascular Function for ATVB Spring Conference in Washington DC on April, 2009
Serve on Consultant for Dr. DeWayne Townsend's AHA and NIH grant's submission; Dr. Meng Chen and Dr. Zoltan Ungvari's NIH and ADA's grants' submission.
US Co-Editor for Journal of Vascular Research.
Associate Editor for American Journal of Physiology: Heart and Circulatory Physi ology.

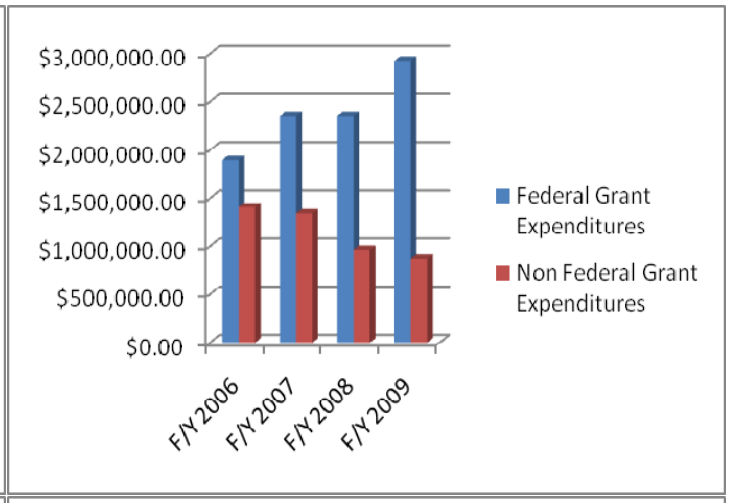
Zou, X.

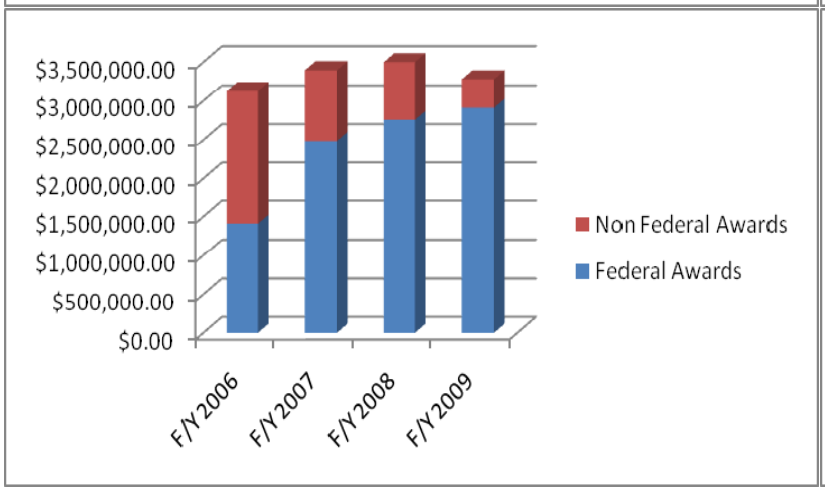
Postdoctoral advisor for Dr. Sheng-You Huang, Diana Bolser, Sam Grinter
Graduate Committee/Student Memberships for Renhao Xue, Yingchu Zhao, Sam Grinter, Jian Yin, Ming-Feng Tsai, Sewon Lee, Haiying Zhou, Mostafa I Abd, Xiaohui Wang
Program committee member for IEEE International Conference on Bioinformatics & Bio medicine, International, 2009-present.
Editorial Advisory Board Member, Current Computer-Aided Drug Design, International, January 2007 - 2011.
Grant review for Kentucky Science & Engineering Foundation, Regional, May 2009.
Interviewing/arranging faculty interviews for Physics Department, Department, May 2009 - June 2009.
Interviewing five Biochemistry faculty candidates, Department, 2009.
Manuscript reviews, International, 2009.

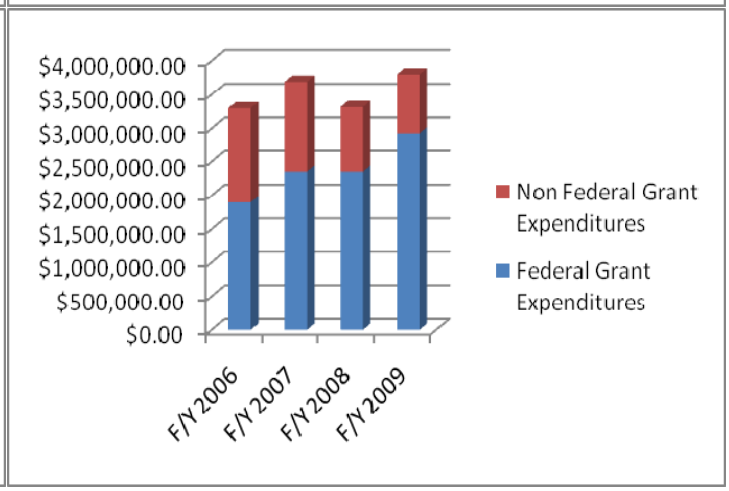
Federal and Non Federal Awards/Federal and Non Federal Grant Expenditures

		F/Y 2006	F/Y 2007	F/Y 2008	F/Y 2009
Federal Awards		$1,409,199.28	$2,485,943.90	$2,756,583.04	$2,911,444.25
Non Federal Awards		$1,719,844.11	$908,701.65	$742,555.01	$368,497.02
Total Awards		$3,129,043.39	$3,394,645.55	$3,499,138.05	$3,279,941.27
Federal Grant Expenditures		$1,895,248.00	$2,354,142.15	$2,354,651.58	$2,928,125.77
Non Federal Grant Expenditures		$1,404,761.82	$1,338,872.74	$962,121.56	$873,751.93
Total Grant Expenditures		$3,300,009.82	$3,693,014.89	$3,316,773.14	$3,801,877.70



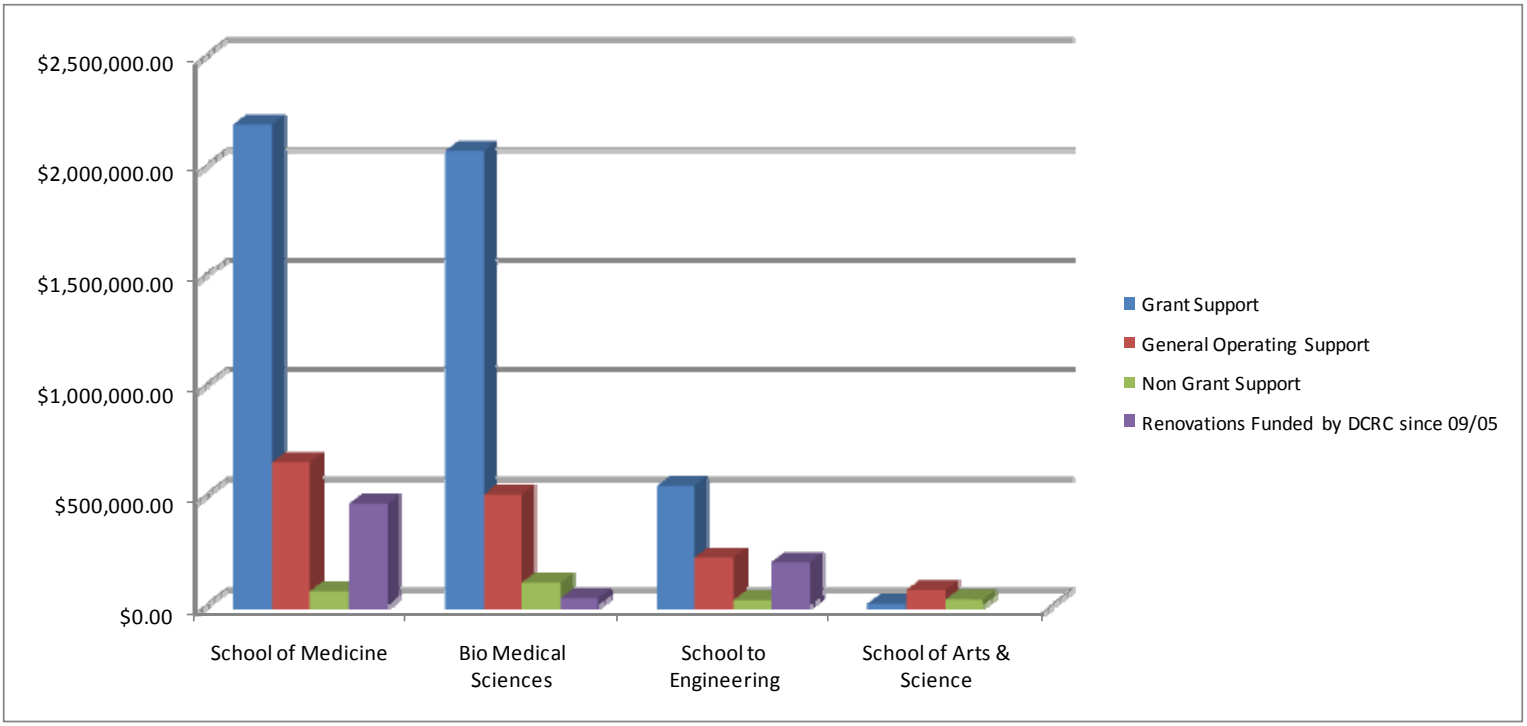






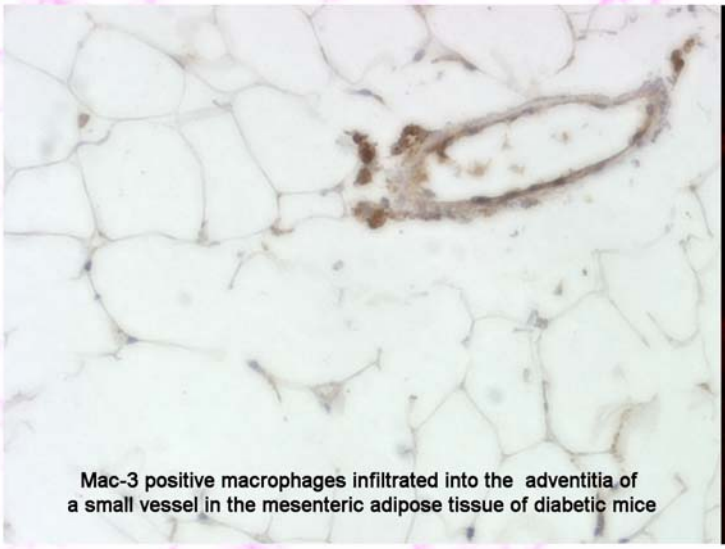
DCRC Support to Collaborating Departments F/Y 09

	School of Medicine	Bio Medical Sciences	School to Engineering	School of Arts & Sci-
Grant Support	$2,186,047.11	$2,067,725.00	$544,026.00	$10,654.00
General Operating Support	$648,838.35	$504,652.05	$216,279.45	$72,093.15
Non Grant Support	$65,538.70	$104,068.36	$27,039.64	$29,267.75
Total DCRC Support	$2,900,424.16	$2,676,445.41	$787,345.09	$112,014.90
Renovations Funded by DCRC since 09/05	$464,323.92	$35,462.54	$195,300.26	

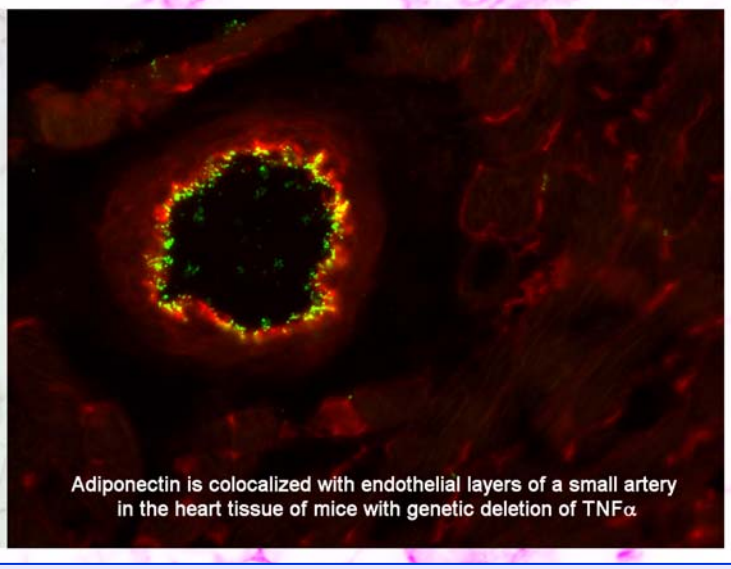


"Magic of Blood Vessels"

Dr. Cuihua Zhang's lab



Mac-3 positive macrophages infiltrated into the adventitia of a small vessel in the mesenteric adipose tissue of diabetic mice



Adiponectin is colocalized with endothelial layers of a small artery in the heart tissue of mice with genetic deletion of TNFα