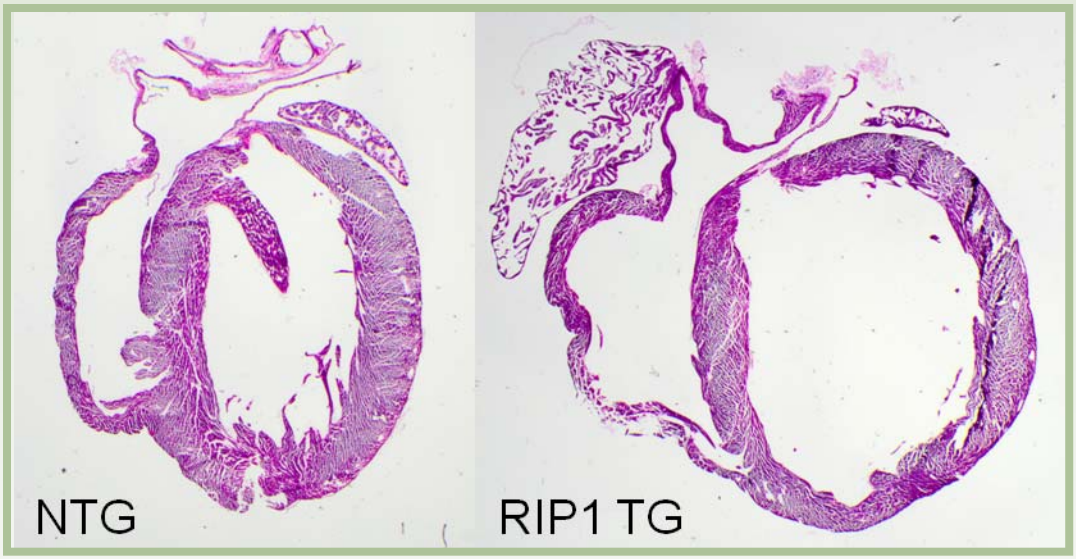
Dalton Cardiovascular Research Center



Annual Report FY 10

"Committed to Interdisciplinary Collaboration in Research and Teaching"

Front Cover: courtesy of Dr. Christopher Baines:
Overexpression of the kinase RIP1 induces heart failure in mice: we overexpressed RIP1, a critical signalling molecule, in the hearts of mice (RIP1 TG). This resulted in an enlarged heart that was less efficient at pumping blood than hearts from normal mice.

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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 37.4 million in active research funding, have published 130 manuscripts in nationally recognized journals and books and gave 72 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

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Dr. Mike Hill
Dr. Alan Jones
Dr. Ed Blaine
Dr. Virginia Huxley
Dr. Ron Terjung
Dr. Kevin Gillis

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Interdisciplinary Research Interests Groups

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

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

Exercise/Inactivity Including Atherosclerosis, Muscle Biology, Obesity, Type II Diabetes, and Vascular Biology
Investigators: Booth, Bowles, 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: 130
- Invited Presentations: 72

Awards and Peer Review

- Fifty-seven awards/contracts were active during FY10.
- Eighteen research awards/contract proposals were awarded.
- Thirty-nine grant/contract proposals.
- Eleven graduate students were supported by R90/T90 training grants.
- Fourteen Investigators served as editors or were on editorial boards of thirty-one scientific journals.
- Eleven Investigators reviewed articles for twenty-two scientific journals.
- Seven Investigators reviewed grant applications for seventeen granting agencies.

Education and Training

- Resident Investigators-Tenure/Tenure Track: 21
- Resident Research Track: 5
- Non-resident Investigators: 16
- Research Staff: 19
- Post Doctoral Fellows: 6
- Graduate Students: 27
- Undergraduate Students: 22
- Administrative Staff: 11
- Visiting Scholars: 10

Director

Gerald A. Meininger

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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

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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

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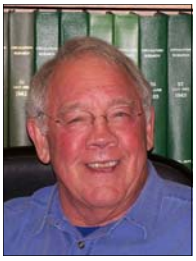
Education:
B.Sc. University of Bath, Great Britain
PhD University of South Alabama

Appointment: Assistant Professor, Department of Biomedical Sciences

Research

Mitochondrial dysfunction is often an underlying cause of myocardial disease. In particular, cardiac pathologies such as ischemia/reperfusion injury, heart failure, diabetic cardiomyopathy, anti-cancer agent-induced cardiotoxicity, etc., are associated with rapid and dramatic increases in mitochondrial permeability. These changes in permeability lead to ATP depletion, excessive production of reactive oxygen species, and ultimately swelling and rupture of the organelle, thereby instigating a molecular chain of events that leads to cardiomyocyte death. The long-range goal of the lab is to understand how specific mechanisms of mitochondrial-driven death can be targeted for the prevention of myocardial disease.



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

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

Currently, the primary focus of my laboratory is the underlying cause of hypertension that is associated with an adverse uterine environment. It is well documented that offspring of mothers who have undergone a variety of stressful circumstances during pregnancy may give birth to offspring who suffer from conditions such as hypertension, type II diabetes, and metabolic syndrome as adults. This phenomenon is known as fetal programming or the fetal origin of adult disease. One characteristic of these susceptible offspring is a reduced nephron number and several investigators have suggested that the lack of a full nephron complement is the underlying cause of the adult onset hypertension. How the reduction in nephron number causes or contributes to hypertension is not known. We are presently working on the hypothesis that there is a differential loss of nephrons. Based on inherent heterogeneity, loss of more "salt-losing" nephrons and retention of more "salt-saving nephrons" results in an overall tendency for the kidney of these offspring to retain sodium and, therefore, be more susceptible to hypertension as adults.
Our work involves whole animal studies which detail changes in the kidney's ability to excrete sodium and whether changes in ability to excrete a sodium load is a function of changes in glomerular filtration, sodium reabsorption, or both. These studies are conducted in conscious, freely moving animals to obtain data that is not compromised by anesthesia or restraint. We are also studying changes 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.

Silvia G. Bompadre

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Education:
PhD in Physics from University of Washington

Research Description
The Cystic Fibrosis Transmembrane conductance Regulator (CFTR) is a chloride channel that is regulated by phosphorylation and gated by ATP binding and hydrolysis. Mutations in the gene coding for CFTR result in the genetic disease cystic fibrosis (CF), the most common lethal autosomal recessive disorder in white populations. CF is manifested by a defective chloride transport across the epithelial cells in various tissues such as respiratory, gastrointestinal, hepatobiliary, and reproductive tracts.

Frank W. Booth

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Education:
PhD University of Iowa, BS Denison University

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

Research
Research interests in my laboratory currently focus on two areas.

The first question being posed is: what are the aging mechanisms of decreased proliferation and differentiation of satellite cells, the adult stem cells in skeletal muscle? Experiments are concerned with regulation of $p21^{Cip1/WAF1}$, $p27^{Kip1}$, 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

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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

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

Appointments: Associate Professor, Department of Physical Medicine and Rehabilitation
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

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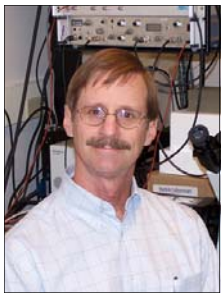
Education:
PhD, MD University of California-San Diego,
BS Arizona State University

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

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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

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

Appointment: Assistant Professor, Department of Biological Engineering

Research
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

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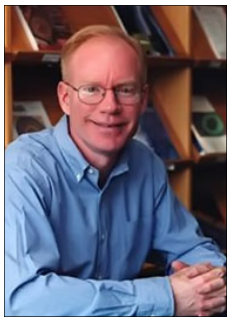
Education:
PhD University of North Texas,
MS Northeastern University, Health Science Center,
BS Brooklyn College

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.

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Education: BS, MD, University of Illinois

Appointments: Professor of Internal Medicine and Medical Pharmacology & Physiology

Research Interests

- Role of leukocyte-derived tissue factor in thrombosis
- Role of plasminogen activator inhibitor-1 (PAI-1) in the proliferative response to vascular injury
- Mechanisms by which C-reactive protein (CRP) modulates thrombosis
- Role of heme oxygenase-1 in thrombosis
- Regulation of fibrinolysis by thrombin activatable fibrinolysis inhibitor (TAFI)

Techniques / Methodology:

- Mouse gene targeting
- Rodent models of human vascular disease
- Structure-function studies of blood coagulation proteins
- Thrombosis models

Research Description

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

Shubra Gangopadhyay

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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

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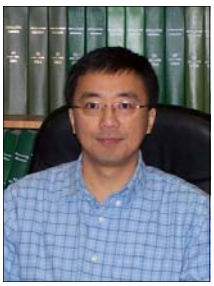
Education:
DSc, MSEE & BSEE Washington State University,
BA St. Louis University

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

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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.

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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.

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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.

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Education:
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Appointments: Director of the National Center for Gender Physiology
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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.

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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.

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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.

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

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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.

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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

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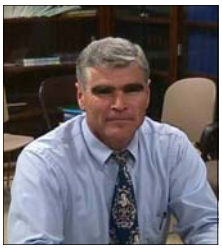
Research

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

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Research

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

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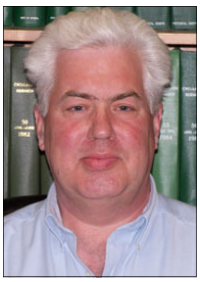
Research

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

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



Mark Milanick

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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

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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.

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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

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Education:
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Appointments: Associate Professor, Department of Biomedical Sciences
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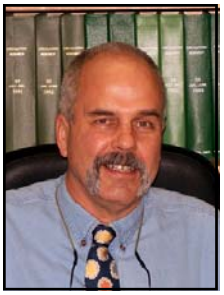
Research

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.



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Research

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

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

Steven S. Segal

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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.

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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

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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.

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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.

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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

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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

Baines, C.

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Changes in skeletal muscle mitochondria in response to the development of type 2 diabetes or prevention by daily wheel running in hyperphagic OLETF rats. Rector RS, Uptergrove GM, Borengasser SJ, Mikus CR, Morris EM, Naples SP, Laye MJ, Laughlin MH, Booth FW, Ibdah JA, Thyfault JP. Am J Physiol Endocrinol Metab. 2010 Jun;298(6):E1179-87. Epub 2010 Mar 16.

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New discovery of Netrin-1 in cardioprotection. Zhang H, Zhang C. J Mol Cell Cardiol. 2010 Jun;48(6):1033-5. Epub 2009 Dec 28. No abstract available. PMID: 20036673

Bariatric Surgery to Correct Morbid Obesity Also Ameliorates Atherosclerosis in Patients with Type 2 Diabetes Mellitus. Wang Y, Zhang C. Am J Biomed Sci. 2009 Jan 1;1(1):56-69.PMID: 19915685

Zou, X.

Multiscale generalized born modeling of ligand binding energies for virtual database screening. Liu HY, Grinter SZ, Zou X. J Phys Chem B. 2009 Sep 3;113(35):11793-9.PMID: 19678651

Inclusion of solvation and entropy in the knowledge-based scoring function for protein-ligand interactions. Huang SY, Zou X. J Chem Inf Model. 2010 Feb 22;50(2):262-73.PMID: 20088605

Baines, C.

"Digging For Holes: molecular dissection of the mitochondrial pore." Department of Pharmacology, Medical College of Wisconsin, Milwaukee, WI, January 5th.

"The Molecular Basis of Programmed Necrosis" Division of Cardiology, Second Department of Internal Medicine, Sapporo Medical University, Sapporo, Japan, February 15th.

"Identifying New Components of the Mitochondrial Pore." Department of Medical Pharmacology and Physiology, University of Missouri-Columbia, Columbia, MO, March 23rd.

"Identifying New Components of the Permeability Transition Pore." Charleston Conference on Mitochondrial Physiology and Pathobiology, Charleston, SC, November 16th.

"Identifying New Components of the Mitochondrial Permeability Transition Pore." Department of Biochemistry and Molecular Biology, St. Louis University, St. Louis, MO, October 2nd.

"Digging For Holes: molecular dissection of the mitochondrial pore." Department of Biochemistry and Molecular Biology, Wright State University, Dayton, OH, October 12th.

"New Component of the Mitochondrial Permeability Transition Pore." American Heart Association Basic Cardiovascular Sciences Conference 2009: Molecular Mechanisms of Cardiovascular Disease. Lake Las Vegas, NV, July 2009

"Mitochondrial Permeability Transition in Ischemia/Reperfusion." International Society for Heart Research World Congress, Kyoto, Japan, May 13th.

"Role of Mitochondria in Cardiomyocyte Death." Friedreich's Ataxia Research Alliance Cardiac Summit, Philadelphia, PA, June 11th.

"RIPing holes in mitochondria: understanding necrotic cell death." Department of Molecular Biology and Biotechnology, Florida Atlantic University, Boca Raton, FL, April 15th.

Booth, F.

Satellite Meeting of International Union of Physiological Sciences, Nagaro, Japan, July 2009

International Union of Physiological Sciences, Kyoto, Japan, July 2009

Free Radical Meeting of Europe, Rome, August 2009

Central States American College of Sports Meetings, Columbia MO , November 2009

Clarke, L.

Clarke, LL. Regulation of Dra Cl^-/HCO_3^- exchange in the lower villous epithelium of murine duodenum. Acta Physi ologica International Symposium. Uppsala University, Upsala, Sweden, August 12, 2009.

Clarke, LL, Horak, RZ, Simpson,JE, and Walker, NM. Electrophysiological changes in Slc26a3 (down-regulated in adenoma, Dra) knockout intestine are associated with epithelial cell alkalinity. Experimental Biology 2009, New Orleans, April 18-22, 2009

Clarke, LL and Walker, NM. Proportion of down-regulated in adenoma (Dra, Slc26a3) Cl^-/HCO_3^- exchange activity coupled with Na^+/H^+ exchange in the lower villous epithelium of murine duodenum. Experimental Biology 2009, New Orleans, April 18-22, 2009.

Hoover, EE, Brazill, JM, Walker, NM and Clarke, LL. Oxygenation of gallbladder mucosa prevents loss of cAMP stimulated anion secretion in organ culture. Digestive Diseases Week 2009, Chicago, IL, May 30-June 4, 2009.

Brazill, JM, Simpson, JE, Walker, NM and Clarke, LL. Increased transepithelial anion current in the Slc26a3 (down-regulated in adenoma, Dra) knockout jejunum is not associated with loss of electrogenic Cl^-/HCO_3^- exchange. Digestive Diseases Week 2009, Chicago, IL, May 30-June 4, 2009.

N.M. Walker, J. Liu, and L.L. Clarke Nhe3 is not required for cAMP inhibition of Cl^-/HCO_3^- exchange in the murine small intestine, FASEB Summer Research Conference, Gastrointestinal Tract XIII, Snowmass, CO, August 8-11, 2009.

Hoover, EE, Walker, NM, Li,M, Hwang,T-C, and Clarke, LL. Evaluation of publicly available correctors of DF508 CFTR in Physiological Testing Systems, 2009 North American Cystic Fibrosis Conference, Minneapolis, MN, October 15-17, 2009.

Hwang, T.C.

Biophysical Meeting, San Francisco, Feb. 20, 2010

Heesch, C

"CNS Plasticity in Control of Sympathetic Outflow in Pregnancy," Symposium Speaker, International Society for Autonomic Neuroscience (ISAN), Sydney, Australia 09/01/09

"Enhanced Angiotensin II Sympathoexcitation in Pregnant Rats," Symposium Speaker, ISAN Satellite Meeting, Newcastle University, New Castle, Australia, 09/09

Experimental Biology 2009 Meeting;New Orleans, LA; April 2009 (see abstracts above)

Huxley, V.

Cardiovascular Research Center/Physiology Department of Temple University School of Medicine, "*Regulation of microvascular exchange: Contribution of sex (lessons learned from juveniles & exercise).*" January 21, 2010.

Hyder, S.

Mafuvadze B, Benakanakere I and Hyder, S. M. (2010) Apigenin inhibits progestin-induced VEGF at both mRNA and protein secretion level in T47-D human breast cancer cells. 92nd Annual Endocrine Society Meeting, San Diego, June 2010, Abstract P2−55.

Lopez, F.R., Besch-Williford C., Liang, Y. and Hyder, S. M. (2010) Differential expression of fibroblast growth factor family members in a progestin-dependent BT-474 human breast cancer cell xenograft model. 92nd Annual Endocrine_Society Meeting, San Diego, June 2010.

Liang Y., Benakanakere, I., Hyder, R. S. and Hyder, S. M. (2009) Role of natural and synthetic progestins in progresssion of breast cancer cells in nude mice. MidWest Breast Cancer Research Symposium, Iowa City, IA, July 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)-induced mammary tumors in Sprague-Dawley rats. MidWest Breast Cancer Research Symposium, Iowa City, IA, July 2009.

Korthuis, R.

"Venular-arteriolar communication in inflammation." Department of Medicine, Division of Cardiology, University of Louisville, Louisville, KY, 2010.

"Venular-arteriolar communication in inflammation." Symposium on Cell Signaling in Smooth Muscle, 16th International Vascular Biology Meeting, University of California, Los Angeles, June 2010.

AMP-activated protein kinase activation stimulates heme oxygenase-1 gene expression to promote human endothelial cell survival. Experimental Biology Meeting, Anaheim, CA, April 2010.

Manipulation of smooth muscle BKCa using subunit-directed siRNA. Experimental Biology Meeting, Anaheim, CA, April 2010.

Krenz, M.

Poster presentation CV Day Feb 16th 2010

Talking about double-edged swords: how opposite mutations in SHP-2 inflict the same damage to the heart. Nov 12 2009, Department of Biomedical Sciences Seminar Series, College of Veterinary Medicine, University of Missouri.

Liang, Y.

Liang Y, Besch-Williford C, Thorpe P, and Hyder, S.M. (2010) Targeting mutant p53 protein and tumor vasculature: An effective combination therapy for advanced breast tumors. *Breast Cancer Research and Treatment,* in press.

Role of Natural and Synthetic Progestins in the Progression of Human Breast Tumor Xenografts in Nude Mice. *Midwest breast cancer research symposium,* Iowa City, Iowa, on July 17-19-2009, Abstract 37.

Martinez-Lemus, L.

Zhao G. and Martinez-Lemus, L.A. 2010. Rho kinase inhibition prevents acute vasoconstriction-induced in ward remodeling in isolated arterioles. Presented at the XVII Cardiovascular Day meeting. Columbia, MO, February 16 2010.

Zhao G. and Martinez-Lemus, L.A. 2009. Rho kinase inhibition prevents acute vasoconstriction-induced in ward remodeling in isolated arterioles. Presented at the meeting of the Microcirculatory Society entitled "Frontiers in Microcirculation: Control Processes and Clinical Applications. Columbia, MO, October 16-17 2009. Published in Microcirculation, 2009.

Clifford P.S., S.R. Ella, L.A. Martinez-Lemus, K.A. Dora, Y. Yang, M.J. Davis, G.A. Meininger, and M.A. Hill. 2009. Adventitial elastin fibers longitudinally contrain arteriolar smooth muscle cells. Presented at the meeting of the Microcirculatory Society entitled "Frontiers in Microcirculation: Control Processes and Clinical Applications. Columbia, MO, October 16-17 2009. Published in Microcirculation, 2009.

Jackson T.Y., L.A. Martinez-Lemus, M.A. Hill, and G.A. Meininger. 2009. Cadherin and integrin blockade inhibit myogenic responses while not preventing pressure induced increases in Ca2+. Presented at the meeting of the Microcirculatory Society entitled "Frontiers in Microcirculation: Control Processes and Clinical Applications. Columbia, MO, October 16-17 2009. Published in Microcirculation, 2009.

Martinez-Lemus, L.A., and G. Zhao. 2010. Vasoconstriction-induced inward remodeling of isolated arterioles Involves reactive oxygen species-dependent activation of matrix metalloproteinases. Annual Meeting of the Societies for Experimental Biology. Anaheim, CA, April 2010. Published in FASEB J., 2010.

Martinez-Lemus, L.A. 2010. Small artery plasticity and smooth muscle length regulation. Invited presentation at the 2010 Annual Meeting of the Societies for Experimental Biology for the Symposium entitled "Regulation of Vascular Caliber and Contractility." Anaheim, CA, April 28, 2010.

Sun, Z., S. Huang, Z. Li, L.A. Martinez-Lemus, and G.A. Meininger, 2010. Modulation of microvascular smooth muscle adhesion and mechanotransduction by integrin-linked kinase. Annual Meeting of the Societies for Experimental Biology. Anaheim, CA, April 2010. Published in FASEB J., 2010.

Meininger, G.

"Investigating the role of integrin-extracellular matrix interactions in vascular regulation: Studies enabled with atomic force microscopy" to the Academic Surgical Oncology Unit, Section of Oncology, School of Medicine and Biomedical Sciences, University of Sheffield 02/19/10

Milanick, M.

Wanted: Red Cells: Dead or Alive. Saturday Morning Science, MU 9/19/09

Polo-Parada, L.

Universidad de Guanajuato. Division de Ciencias e Ingenierias, Campus Leon. Invited talk and Workshop Centro de Investigacions en Optica AC. Leon Guanajuato. Mexico

Escuela Superior de Fisica y Matematicas. Instituto Politecnico Nacional. Mexico City

International Bio Electric Symposium. University of Missouri

Department of Chemical Engineering. University of Missouri

Segal, S.

Intercellular Coordination of Blood Flow Control, Case Western Reserve University (Cleveland, OH) 12/14/2009

"Regulation of Microcirculatory Flow: Conducted vasodilation" (Copenhagen, Denmark at the Danish Royal Academy of Sciences: August Krogh Symposium; June 1, 2010)

Sohma, Y.

"Getting images of functional membrane molecules during their functioning—from still photos to movies—2009", National Institute of Physiological Sciences, Okazaki, Japan 09/09

Laboratory Seminar, Department of Frontier Materials, Nagoya Institute of Technology, Nagoya, Japan 11/09

Molecular mechanism of a multi-functional Cl^- channel CFTR. Symposium "Regulation of various physiological functions by chloride-transporting proteins", 87th Annual Meeting, The Physiological Society of Japan, Morioka, Ja pan, May 19 – 21, 2010

Zhang, C.

Yoonjung Park, Yong Wang, Sewon Lee, Cuihua Zhang. Bariatric Surgery Treats Morbid Obesity and Type 2 Diabetes: Mechanisms of Improved Endothelial Function. AHA Scientific Meeting. Circulation, Nov 2009; 120: S444. Orlando, FL.

Hanrui Zhang and Cuihua Zhang. IFN induced Adipose Inflammation Linked to Impairment of Vascular Function. AHA Scientific Meeting. Circulation, Nov 2009; 120: S1038 - S1039. Orlando, FL.

Role of Inflammation in atherosclerosis. October 1, 2009: Invited by the Department of Physiology, 4th Military Medical College, Xi'an, China.

Role of Inflammation in Vascular Dysfunction. November 12, 2009: Invited by the Department of Pharmacology & Physiology; UMDNJ - New Jersey Medical School; Medical Sciences Building, H609/H648; 185 S. Orange Avenue; Newark, NJ 07103.

Zou, X.

A hierarchical approach to protein-protein docking," 4th CAPRI(Critical Assessment of Prediction of Interactions) Meeting, Xiaoqin Zou, Sheng-You Huang, Barcelona, Spain, December 2009.

This is a bi-annual meeting held by CAPRI for international competition on predicting protein-protein complex structures. The selection of oral presentations is highly competitive. I was chosen to give the first oral presentation because of our excellent performance in the competition (despite being a new member in the field) and because of our well-written abstract on the new method we've developed.

"Structure-based predictions on protein-ligand & protein-protein interactions for rational drug design," "Function and Dynamics of Biomolecules" advanced workshop, Kevli Institute for Theoretical Physics China at the Chinese Academy of Sciences, Beijing, China, July 2009.

"A scoring framework for selecting structural models," Telluride Meeting: "Method Development for Protein Structure Prediction", Xiaoqin Zou, Telluride, CO, June 2009.

"Structure-based prediction on protein-ligand and protein-protein interactions for rational drug design," Departmental seminar, Dept of Chemistry, University of Memphis, TN, April 2009.

"Development of novel iterative knowledge-based scoring functions for protein-ligand and protein-protein interactions," 237th American Chemical Society National Meeting, Xiaoqin Zou, Salt Lake City, UT, March 2009.

"Structure-based prediction on protein-ligand and protein-protein interactions for rational drug design," Departmental seminar, Dept of Chemistry, University of Memphis, TN, April 2009.

Invited Speakers

Dr. Richard Gumina, Ohio State University, Seminar: "Cardiac Injury – Where Do I Go From Here"

Dr. Chuanyu Gao, Department of Cardiology Henan Provincial People's Hospital Seminar:"Structural and Functional Approaches to Myocardial Repair"

Dr. James Moore , Texas A&M, Seminar: "Multi-Scale Modeling of Lymphatic System Pumping"

Dr. Jesse Procknow, St. Louis University, Seminar: "Effect of Gender and ACE Inhibition in a Mouse Model of Atherosclerosis"

Dr. Santiago Lorenzo, University of Oregon, Seminar: "Mechanisms of Heat Acclimation and Exercise Performance."

Dr. Ruth Stornetta, University of Virginia, Seminar: "Brainstem mechanisms of cardio-respiratory control in the age of enlightenment."

Dr. Ligio Toro, University of CA, Los Angeles

Dr. Frank Yin, Professor Washington University, Seminar: "Role of Zyxin in Endothelial Cell Response to Cyclic Stretching"

PRINCIPAL INVESTIGATOR **AGENCY** ***TITLE***	**PERIOD** **AMOUNT**
Baines, Christopher	
AHA Scientist Development Grant (PI: Baines) AHA National Center *"Mechanisms of Mitochondrial-Dependent Myocyte Death"*	07/06-06/10 $118,282
R21HL092327 (PI: Baines) NIH/NHLBI *"Identifying Novel Components of The Cardiac Necrotic Program"*	07/08-04/10 $275,000
R01HL094404 (PI: Baines) NIH/NHLBI *"Molecular Identity of The Cardiac Mitochondrial Pore"*	12/08-11/13 $1,250,000
P01HL52490 (PI: Laughlin) NIH/NHLBI *"Vascular Biology: Exercise Training and Coronary Disease"*	01/10-12/10 $104,856
Bompadre, Sylvia	
K01 DK075408 NIDDK *"Molecular physiology and pharmacology of CFTR."*	09/06-08/10 $102,542
Booth, Frank	
5 P01 HL052490 *"Vascular biology: exercise training and coronary disease"*	01/10-12/11 $13,400

Clarke, Lane

NIH (R01 DK48816 – Years 10-13); PI *"CFTR and Intestinal Acid-Base Transporters"*	08/06-07/10 $800,000
Cystic Fibrosis Foundation Therapeutics, Inc. *"Structure-Guided Physiological Screening of DF508 CFTR Correctors";* PI	12/06–01/10 $1,349,781

Davis, M.

NIH R01 HL-089784 *"Cellular Mechanisms of Lymphatic Muscle Contractility"*	05/08-04/13 $1,100,000
NIH R01 HL-072989 *"Regulation of Vascular Tone and Ca Channels by Integrins"*	04/09-3/13 $1,000,000
NIH R01 HL-087308 *"Molecular Control of EC Lumen Formation by MT-1 MMP"*	12/08-11/12 $1,250,000
NIH R01 HL-077566 *"Mechanisms of Reperfusion-induced Endothelial Injury"*	05/06-04/11 $1,250,000
NIH R01 AG-030578 *"Mechanisms of age-related alterations in lymphatic pumping"*	06/08-05/13 $1,000,000
NIH R01 HL-092241 *"Signaling Mechanisms for Myogenic Tone in Skeletal Muscle Arterioles: Role of* BK_{Ca}*"*	*0*7/09-06/13 $1,250,000
NIH R01 HL-079460 *"Pericyte Proteinases and EC Tube Stabilization"*	09/09-08/13 $1,250,000
National Institutes of Health *"Mechanisms of Microvascular Control and Coordination in Health and Disease."*	2010-2014 $8,450,000

Davis, G.

National Institutes of Health *"Mechanisms of Microvascular Control and Coordination in Health and Disease."*	2010-2014 $8,450,000

Hasser, Eileen

National Institutes of Health	04/07-03/11
"*Cardiovascular Regulation in Hindlimb Unweighted Rats*"	$900,000
National Institutes of Health	10/07– 9/09
Case Western Reserve subcontract to Univ. of Missouri	$240,388
"BDNF and MeCP2 in autonomic dysfunction"	
National Institutes of Health	06/09-03/13
"Central nervous system plasticity in sympathoinhibition in pregnancy"	$250,000

Heesch, Cheryl

NIH (Competitive Renewal R01 HL36245)	04/04-02/09
"Neural Circulatory Control: Pregnancy & Ovarian Hormones"	$700,000
Univ. MO, Research Board Grant	04/07-06/09
"Differential neurotransmitter modalities of CNS pre-sympathetic neurons"	$29,800
NIH (R01 HL091164)	06/09- 03/13
"Central nervous system plasticity in *Sympathoinhibition on pregnancy"*	$250,000
NIH (R01 HL091164)	04/07-03/11
"Cardiovascular Regulation in Hindlimb Unweighted Rats"	$225,000
NIH R01 HL085108-01	04/08-04/13
"Adaptation of brainstem circuits to chronic hypoxia"	$250,000

Hill, Michael

NIH RO1	07/09-06/11
"Signaling Mechanisms Underlying Myogenic Tone in Arterioles of Skeletal Muscle: Role of BKCa."	$719,867
NIH P01	03/10-02/14
"Mechanisms of Microvascular Control and Coordination in Health and Disease"	$8,450,000

Hyder, Salman

College of Veterinary Medicine	1/10-12/10
"*Therapeutic potential of apigenin for treatment and prevention of progestin-accelerated breast cancer"*	$18,000

"

Hwang, T.C.

NIHR01 NHLB, *"Gating of CFTR chloride channels by ATP hydrolysis",*	2006 – 2010 $933,056
NIHR01, NIDDK, *"Molecular pathophysiology of cystic fibrosis",*	2008 – 2013 $1,014,155

Kline, David

1R01 HL085108-01 (Kline DD, P.I.) NIH/NHLBI *"Adaptation of brainstem circuits to chronic hypoxia"*	04/08-03/201 $250,000
1R01NS057398-01 (Kline DD, P.I., Missouri NIH/NIDDK/Case Western Reserve Univ. "*BDNF and MeCP2 in autonomic dysfunction*	04/07-03/11 $41,892
MU College of Vet Med (Kline DD, P.I.) University of Missouri "*Neurobiology of PVN- and RVLM-projecting NTS cells "*	01/08-12/09 $18,000
R01 (Heesch, CM PI; Kline DD, Co-I) NIH/NHLBI "*Central nervous system plasticity in sympathoinhibition in pregnancy"*	07/08-06/13 $274,370
Clark, CG (PI) American Heart Association "*The Role and Mechanism of Brain Derived Neurotrophic Factor on Autonomic and Cardiovascular Function"*	07/08-06/10 $55,000

Korthuis, Ronald

NIH; AA-14945 *"Ethanol prevents microvascular dysfunction"*	06/06 – 05/11 $225,000
NIH; HL-82816 *"Venular leukocyte adhesion, impaired arteriolar vasoreactivity, and intestinal I/R"*	12/06 – 11/10 $250,000
NIH; Program Project Grant, *"Mechanisms of Microvascular Control and Coordination in Health and Disease per year*	04/10– 03/15 $262,000
National Institutes of Health *"Mechanisms of Microvascular Control and Coordination in Health and Disease."*	2010-2014 $8,450,000

Krenz, Maike

Edward Mallinckrodt Jr. Foundation, 01/10-12/12
"Role of PTPN11 mutations in congenital heart disease" $210,000

Liang, Yayun

NIH-R21, 07/09-06/11
"A new scoring framework for selecting structural models." $ 411,125

Martinez-Lemus, Luis

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

National Institutes of Health (NIH) 2009-2014
"Mechanisms of Microvascular Remodeling Progression." $2,250,000

National Institutes of Health 2010-2014
"Mechanisms of Microvascular Control and Coordination in Health and Disease." $8,450,000

Meininger, Gerald

National Science Foundation 9/09-8/11
"Evanescent Field-Enabled Atomic Force Microscopy for Nanoscale Imaging of Cell Membrane Dynamics." $200,000

National Institutes of Health-National Heart, Lung and Blood Institute, R21 12/09-11/11
"Amyloid-b peptide on endothelial adhesion with its related cellular pathways." $275,000

National Institutes of Health 2010-2014
"Mechanisms of Microvascular Control and Coordination in Health and Disease." $8,450,000

Polo-Parada, Luis

National Science Foundation 2009-2011
"Nanothermite Based Micro shockwave generators and nanoaparticles for targeted and efficient Gene/Drug Delivery." *$175,000*

Missouri Life Sciences Trust Fund 2009-2011
"Photoacustic detection of circulation melanoma cells"

National Institute of Health 2009-2010
"Detection of melanoma cells in vitro using an optical detector"

Segal, Stephen

National Institute of Health Postdoctoral Fellowship for Pooneh Bagher, Ph.D 8/09-7/11
"Fast calcium responses along arteriolar endothelium in vivo" $101,764

Sohma, Yoshiro

Japan Society for the Promotion of Science 04/10-3/13
"CFTR-NBD engine based on the ATP-hydrolysis switch hypothesis", $65,000

Keio University Foundation for Research Promotion 04/10-03/11
"Development of new drugs targetting ATP transporter superfamily" $6,000

Terjung, Ronald

National Heart Lung Blood Institute 12/05-11/10
Vascular Biology: Exercise Training and Vascular Disease. $1,135,539

National Institute of Arthritis and Musculoskeletal and Skin Diseases 07/09-061/4
"Exercise and Health: Integration From Molecule to Patient" $1,216,930

Research Grant
"Influence of Muscle Activators on Exercise Performance and Muscle Blood Flow in Rats with Peripheral Arterial Insufficiency." 10/09-10/10 $51,287

Zou, Xiaoqin

NIH 09/04-08/09
"Bench & Back: Clinical Biodetective Training" $611,630

Cystic Fibrosis Foundation 12/06-11/09
"Structure-Guided Physiological Screening of F508 CFTR Processing Correctors" $1,349,781

NLM predoctoral fellowship 09/08-8/12
NIH National Library of Medicine $100,000

University of Missouri Research Council Grant 01/09-12/09
Development of novel energy functions for protein structure prediction $7,500

Arts & Science Alumni Faculty Incentive Grant 02/09-12/09 $1,500

NIH 07/09-06/11
A new scoring framework for selecting structural models $411,125

PROFESSIONAL SERVICE ACTIVITIES

Baines, C.

Editorial Boards:
American Journal of Physiology, Heart and Circulatory Physiology
Frontiers in Mitochondrial Physiology
Journal of Applied Physiology
Journal of Molecular and Cellular Cardiology
Reviewer:
American Journal of Physiology, Heart and Circulatory
British Journal of Pharmacology
Circulation Research
Journal of Applied Physiology
Journal of Pharmacology and Experimental Therapeutics
Rejuvenation Research
Journal of Molecular and Cellular Cardiology
Life Sciences
Committee Service:
Chair, DCRC Safety Committee
Chair, 2011 Cardiovascular Day Planning Committee
Member, Research Committee, College of Veterinary Medicine
Dissertation committee member: Hope Gole (Mentor: Doug Bowles)
Dissertation committee member: Kyle S. McCommis (Mentor: Baines)
Member-at-large, Leadership Committee, American Heart Association Basic Cardiovascular Sciences Council
Poster Judge, 2010 Life Sciences Week
Study Section:
ZRG1 CB-L (50)R Special Emphasis Panel on Developmental Pharmacology.

Blaine, E. H.

Reviewer for various journals, esp. AJP
Committee on Committees
Faculty Grievance Oversight Committee
Honorary Degrees Committee
Dalton Development Committee
Dalton Internal Advisory Committee
MPP Graduate Education Committee
Jefferson Club Trustee
Friends of the Library Committee
Develop research program with Pam Hinton, Brick Johnstone and Neal Dawson on Health Outcomes of Intercollegiate Athletes
Develop research program to rehabilitate overweight intercollegiate athletes at the end of their athletic career

Booth, F.

Graduate course entitled Skeletal Muscle (Medical Pharmacology and Physiology 9435 and Biomedical Sciences Problems 8085)
Course Director
Lectures (each lecture given is 1.5 hrs)
Energy metabolism during exercise – Lecture 1
Energy metabolism during exercise – Lecture 2
Energy metabolism during exercise – Lecture 2
Atrophy

Sarcopenia
Hypertrophy
Fiber type switch
Monitor three student debates (each is 1.5 hrs)
Veterinary Medicine Professional course
Veterinary Molecular and Cellular Biology; Biomed 5506
Lectures given (each is 1 hr)
Gene Therapy
Obesity
Topics in Aging course graduate course
(cross-listed in Medicine, Nursing, Public Health, Architectural Studies, and Human Development)
One lecture (top rated) (2 hrs)
Centre for Inflammation and Metabolism course entitled "Inflammation and Metabolism" (University of Copenhagen) 1 contact hour

Davis, M.

Executive Council, Publications Committee, Communications Committee-Microcirculatory Society Editorial Board: American Journal of Physiology: Heart & Circulatory Physiology, 1991-99; 2001-Journal of Vascular Research, 2001-
Microcirculation, 1994-2009
Journal Review: American Journal of Physiology: Heart and Circulatory Physiology
British Journal of Pharmacology, Circulation Research
Journal of Vascular Research
Journal of Physiology
Microcirculation
Molecular and Cellular Neuroscience
Grant Review: NHLBI P01 and R01 Special Emphasis Panels (ad hoc)
Health Research Board (Ireland)
NMHB – MRC (UK)
Extramural Grant Review: Lymphatic Research Foundation Travel Award Review
Co-chair, Experimental Biology, New Orleans, LA (Cellular mechanisms that initiate and coordinate changes in vascular tone)
Seminars:
Integrated Biomedical Sciences, Loma Linda University, Loma Linda, CA
Center for Perinatal Biology, Loma Linda University, Loma Linda, CA
Dept. of Veterinary Physiology & Pharmacology, Texas A&M University
Dept. of Physiology & Biophysics, Univ. of Nebraska Med. Center, Omaha, NE
Teaching:
Transmembrane Signaling, PBL (first year, Block 2), Skills in Biomedical Science, Veterinary Physiology
Vet. Physiology 8420 literature
Visiting Lecturer:
Bioengineering & Bioinformatics Summer Program, Texas A&M University, College of Veterinary Medicine, College Station, TX (July 2009); Master Lecture: Lymphatic Contractility (undergraduate)
Dept. of Physiology & Biophysics, Univ. of Nebraska Medical Center, Omaha, NE (Dec. 2009); Topic: Vascular Smooth Muscle (CV and Respiratory Physiology graduate course)
Committees:
Promotions & Tenure, 2006-present
Administrative Advisory Committee, 2005-present
Space Committee, 2005-present
RIF Committee, 2005-present

Seminar Committee, 2005-present
Vice-Chair of Department 2006-present
Major Advisor:
John Wolpers (Advisor, Ph.D. student in Med. Pharmacology & Physiology, MU), 2009-
Jyoti Gulia (Advisor, Ph.D. student in Biological Engineering, MU), 2005-
PhD Advisory Committee:
Tim Cornell (Committee member, Ph.D. student in Med Pharm/Phys, MU), 2009-
Bruno Rosenguini (Committee member, Ph.D. student in Vet Med Biosciences, MU), 2009-
Amber Stratman (Committee member, Ph.D. student in Med Pharm/Phys, MU), 2006-
Anastasia Sacharidou (Committee member, Ph.D. student in Med Pharm/Phys, MU), 2007-
Curt Canine (Committee member, M.S. student in Med Pharm/Phys, MU), 2007-2009
Hongyan Dai (Committee member, Ph.D. student in Med Pharm/Phys, MU), 2007-
Srikanth Ella (Committee member, Ph.D. student in Biological Engineering, MU), 2007-
Hope Gole (Committee member, Ph.D. student in Vet Med Biosciences, MU), 2006-
Josh Scallan (Committee member, Ph.D. student in Med Pharm/Phys, MU), 2006-
Cindy Wu (Committee member, Ph.D. student in Med Pharm/Phys, MU), 2006-
Teresa Jackson-Hayes (Committee member, M.S. student in Med Pharm/Phys, MU), 2006-
Patrick Dougherty (Committee member, Ph.D. student in Systems Biology, TAMU), 2005-2009
Postdoctoral Trainees:
Peichun Gui, M.D., 1999-present (Present title: Assistant Research Scientist)
Sherry Chao, Ph.D., 2005-present

Heesch, C.

Teaching Activity: Didactic and Clinical Teaching
Wtr 2009 VBmS 400: Multidisciplinary Problems Course (2 lec/contact hrs.)
Wtr 2009 VBmS 5508: Veterinary Pharmacology, Course Director, 2 credit hr. course
Fall 2009 VBmS 5507: Veterinary Pharmacology (Diuretics, 2 lec/contact hrs)
Dept. Vet. Biomed. Sci, Univ. of Missouri
2008- present Catharine Clark (Ph.D., Advisers, Dr. David Kline/Dr. Eileen Hasser)
2008- present Luise King (Ph.D., Adviser, Dr. Eileen Hasser)
Committee/mentorship listing
Dept. of Medical Pharmacology & Physiology, School of Medicine, Univ. of Missouri
2007 - present Collin Young (Ph.D., Adviser, Dr. Paul Fadel)
2008- present Areum Kim (Ph.D., Adviser, Dr. Paul Fadel)
Undergraduate student, independent research credit
2008- 09 Susanna Jones (Senior research project, Biological Sciences)
Clinical Service: quantify by days of service duty per year and revenue generated (if revenue data is available)
Not Applicable
Department Biomedical Sciences
02/06- present: Junior Faculty Mentoring Committees, Dept. Biomed ScI.
Ileana Constantinescu (Committee Chair)
Kathy Kuel-Kovarik (Committee Member)
01/06 – 12/09 Promotion &Tenure Advisory Committee, Chair
06/09 Grade Appeal Committee, Chair
College
01/09 – 01/10 Committee on Faculty Responsibility
University
09/03-present Executive Committee, Interdisciplinary Neuroscience Program
National
Manuscript Peer Review (2009): American Journal of Physiology/ Regulatory (1)
Circulation Research 1)
Clinical & Experimental Pharmacology and Physiology (1)
Experimental Physiology (1)
Journal of Neurophysiology (1)

Journal of Physiology (1)
Other faculty:
Serve on advisory committee for junior faculty: Ileana Constantinescu, Asst. Prof, Clin. track (Committee Chair)
Kathy Kuel-Kovarik, Asst. Prof., Tenure Track (Committee Member)
Staff:

Ludmyla Kvochina, M.D., Ph.D.	Research Scientist/Academic
J. Glenn Phaup, M.S.	Research Specialist
Shannon Burcks, M.S.	Research Specialist

Undergraduates:
Susanna Jones, part-time student worker
Other
Reorganization of Veterinary Pharmacology Course and Graduate Neural-humoral Control of the Circulation Course

Hill, M.

Editorial Boards: Microcirculation , Journal of Vascular Research, Frontiers in Vascular Physiology
Grant Reviewer: American Heart Association, NIH Special Emphasis Panel on Lymphatic Biology
Memberships: Microcirculatory Society, American Physiological Society, Australia and New Zealand Microcirculatory Society, Australian Physiological Society, Fulbright Alumni, American Association for the Advancement of Science.
Nominating Committee: American Physiological Society (CV Section), Council Member, Microcirculatory Society

Huxley, V.

NIH HM Study Section, San Francisco, CA

Hwang, T.C.

Review articles for JGP, JBC, Biosci. Rep.
Editorial work for BJ

Hyder, S.

Oncogene *(ad-hoc reviewer)*
Cancer Epidemiology: the international journal of cancer epidemiology, detection and prevention. *(ad-hoc reviewer)*
Reviewer, Florida Health Grants (Bankhead-Coley Cancer Research Program)

Kline, D.

Committee/Mentorship listing

Catharine G. Clark	Co-mentor
Luise King	Committee member
Yong Wang	Committee member, MS awarded SP2009
James Austgen, Ph.D.	Post-doctoral mentor

Veterinary Physiology 5504, 11 lecture hours, 28 contact hours, 120 students (2009)

Departmental

2009-2012	Member, Research Advisory Committee (RAC) Committee Function: Review and administer requests from faculty and the Chair for the Departmental Research Incentive Funds (RIF funds)
2007-present	Member, Graduate Program Advisory Committee (GPAC) Committee Function: Review departmental admission applications; provide advisory functions to current students and graduate policies; mediate conflict resolution between students and their mentors.
2007-2010	Coordinator, Department of Biomedical Sciences Seminar Series

College

2009-2010 Member, Faculty Honor Code Committee (10/1/09-09/30/10)
2008-2011 Member, Animal Resources Committee (10/01/08 – 09/30/11)
2007-2010 Member, Committee on Research (10/01/07- 09/30/10)

University

2009-present Member, Appointment and Promotions Committee, Dalton Cardiovascular Research Center
2008-present Member, Animal Issues Response Team (AIRT), Office of Research

National

2009-2012 Hypoxia Interest Group Steering Committee, American Physiological Society
2009-2011 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

Grant Review Boards Service

2009 Reviewer, National Science Foundation (NSF), Faculty Early Career Development (CAREER) Program
2006-2009 Reviewer, Research Board Grants, University of Missouri System
2008-pres Member, American Heart Association (AHA), Study Section, Grant Review Service, Vascular Biology and Blood Pressure 2 (VBBP2)

Supervision of Personnel:

Catharine G. Clark- graduate student
James R. Austgen- postdoctoral fellow
Heather A. Dantzler- technician
Jessica Howard-Summer veterinary research student

Korthuis, R.

Joint Programming Committee, American Physiological Society
Cardiovascular Section Steering Committee, American Physiological Society
Grant review study section member: Vascular Cell and Molecular Biology Study Section member, NIH
Associate Editor: Frontiers in Vascular Physiology
Editorial Board Member: American Journal of Physiology: Heart and Circulatory Physiology
Editorial Board Member: Cardiovascular Research
Editorial Board Member: Microcirculation

Krenz, M.

Moderator and poster judge CV Day 2010
Reviewer: J Appl Physiol, Circulation Research
Dalton Safety Committee,
Organizing Committee CV Day 2010

Liang, Y.

Supervision of students: Ryyan Hyder, Benford Mafuvadze, and Franklin Lopez.
Member of Minorities in Cancer Research

Martinez-Lemus, L.

Extramural Grant Reviewer for:
American Heart Association
Vascular Biology and Blood Pressure /Regulation, 2006-2010.
Editorial Board
"Microcirculation," 2010-2015.
Hospital Practice
Associate Editor for the Physiology and Reproduction section of Poultry Science
Extramural Grant Reviewer for:
American Heart Association – National. Member, Vascular Biology and Blood Pressure / Regulation, 2006-2010.
Reviewer for:
Journal of Vascular Research
Arteriosclerosis, Thrombosis, and Vascular Biology
American Journal of Physiology
Clinical and Experimental Medicine
BioMed Central Cell Biology
Microcirculatory Society: Program Committee (2007-2010)
American Physiological Society: Awards Committee (2008-2011)
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.
Member, Gender and Racial Diversity Equity Council Representation.
CV-Day 2010. Organizing Committee. University of Missouri-Columbia.
Member, Dalton Cardiovascular Research Center Safety Committee.
Appointed member of the School of Medicine Research Council (2009).
Committee on developing guidelines for Joint appointments at the Department of Medical Pharmacology and Physiology (2009).
Served as Judge for the Poster presentations at the 2009 School of Medicine Research Day. November 12, 2009, Columbia, MO.

Meininger, G.

US Co-Editor for Journal of Vascular Research.
Associate Editor for American Journal of Physiology: Heart and Circulatory Physiology.
Grant reviewer for NHLBI Proteomic Centers for heart, lung and blood diseases. September 2009
Problem Base Learning (PBL) tutor
Association of Chairs of Departments of Physiology
The American Physiology Society
Biophysical Society member
American Society for Cell Biology
Microcirculation Section committee member
North American Vascular Biology Organization
Cardiovascular Section committee member
Student mentor: Teresa Jackson, Walatta-Tseyon Mesquitta
Graduate Student committee member: Jyoti Gulia, Shrikanth Ella, Lana Bruney, Rebecca Burkhalter

Milanick, M.

NSF written review
Course Director-Mission Based Management, Jan 1, 2010-June 30, 2010
Lecturer-Clinical Biodetection & Ethics Education Through Enactment, Engagement, Empowerment
PhD committee: Quilin Tan
Grad student advisor: Tim Cornell, Kangyang Jih, John Wolpers, Sewon Lee, Hanrui Zhang

Polo-Parada, L.

Lecturer-Vet Physiology 5504/8420
Skills in Biomedical Research MPP8420
2008-present Member of the MU PREP (Post-baccalaureate Research Education Program) Scholars Program.
Consulting Services: National Biodefense and Analysis and Countermeasure Center (NBACC). US Department of Homeland Security
Battelle. US. Department of Homeland Security
Advisor Committees: The National Academies. Advisers to the Nation on Science, Engineering and Medicine (2009).
Americana Heart Association
Journal of Neuroscience Methods
Journal of Neuroendocrinology
Journal of Applied Physiology
NSF Instrument Development for Biological Research Panel
Winter. American Heart Association. Peer Review Cardiac biology/Regulation 1 Study Group
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.
Charles M Darr. Department of Biological Engineering. Ph.D. Student. 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.
Problem Base Learning (PBL) Tutor Training

Segal, S.

Reviewer: Am. J. Physiol.; J. Physiol., Associate Editor: Microcirculation; Past-President: The Microcirculatory Society, Inc., MPP/DCRC Younger faculty advisor
Chairman: Organizing Committee for Fall MCS meeting at MU (Oct 16-17, 2009)
Editor: Abstracts for Fall MCS meeting (above); Past President: The Microcirculatory Society Inc.
Associate Editor: Microcirculation
Past President: The Microcirculatory Society Inc.;
Associate Editor: Microcirculation;
Manuscript reviewer: American Journal of Physiology, Journal of Physiology, Microcirculation;
Chairman: Organizing Committee for MCS meeting at MU (Oct 16-17, 2009)
Ad hoc Study Section: NIH Challenge Grants: 06/2009
Young faculty advisor (preliminary grant review): Maike Krenz.

Sohma, Y

Journal reviewer (BIOPHYSICS, The Biophysical Society of Japan)
Meeting organizer, The International Joint Symposium: Physiology of Anion Transport and Cell Volume Regulation (PAT-CVR 2009), Okazaki, Japan, Aug 3 – 6, 2009
Meeting organizer, The SEIRIKEN workshop "Getting images of functional membrane molecules during their functioning – from still photos to movies –", National Institute of Physiological Sciences, Okazaki, Japan, Sept 3 – 4, 2009;
Session chair, PAT- CVR 2009, Okazaki, Japan, Aug 3 – 6, 2009

Sowers, J.

Editorial board of Hypertension, Endocrinology, Journal of Hypertension
Chief Editor of the Journal of Cardiometabolic Syndrome
Reviewer on study section for NIH and VA
Safety and Monitoring Committee for NIH ACCORD
VA cooperative studies

Terjung, R.

Graduate Committees/Mentorship

Member, Graduate Committee for Seth Jump
Member, Graduate Committee for Catharine Clark
Control of Energy Metabolism (BMS 9431), course director with Dr. C. Hardin and John Thyfault. 8 hr Lecturing; 54 hr/course assisting/discussion;
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/Microvascular Study Section, NIH, Bethesda, MD, 2007-2010.
Member, Special Emphasis Panel Study Section, NIAMS, Bethesda, April 2009

Zhang, C.

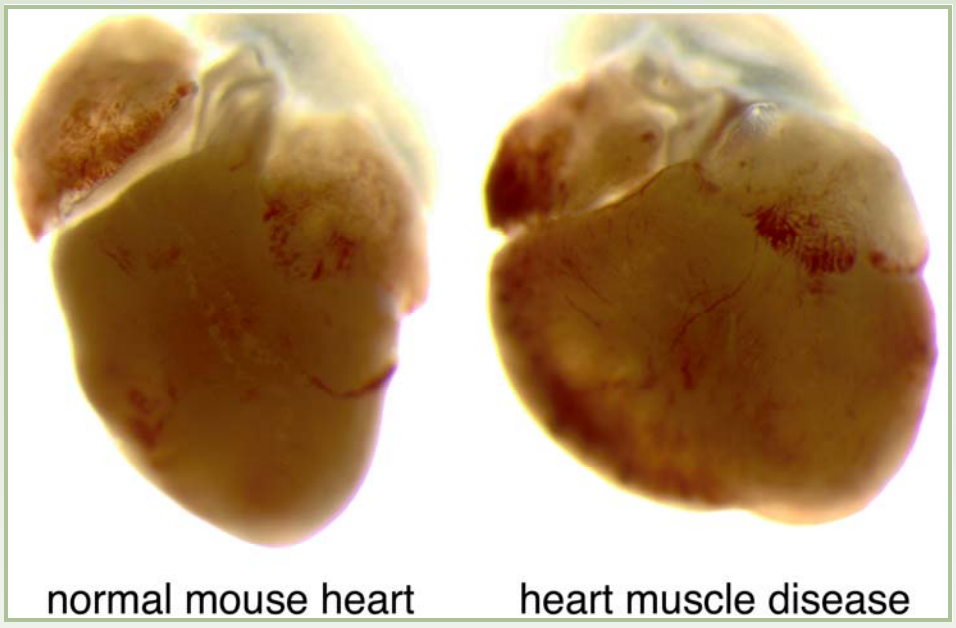
Consultant for Dr. Lu Cai's NIH RO1's submission.

Zou, X.

Saturday Morning Science, Lecture to local community, 10-31-2009.
Manuscript reviews, International, 2009. Review for the following journals: Proteins (1 time), BMC Bioinformatics (1 time), Current Computer-Aided Drug Design (1 time)
Grant review for Kentucky Science & Engineering Foundation, Regional, May 2009
Editorial Advisory Board Member, Current Computer-Aided Drug Design, International, January 2007 - 2011.
Program committee member for IEEE International Conference on Bioinformatics & Biomedicine, International, 2009 -present. Program committee member for 8th International Bioinformatics Workshop (IBW2010), International, 2010.
Committee member, Graduate Admission and Recruitment Committee of the Biochemistry Department, Department, 08-20-2007 to present.
Jian Yin, Member, Ph.D. Committee, 2008 -
Description: Jian is a PhD student of Dr. Rainer Glaser in the Department of Chemistry.
Ming-Feng Tsai, Member, Ph.D. Committee, 2008 -
Description: Ming-Feng is a PhD student of Dr. Tzyh-Chang Hwang in the Department of Medical Pharmacology & Physiology.
Sewon Lee, Member, Ph.D. Committee, 2008 -
Description: Sewon is a PhD student of Dr. Cuihua Zhang in the Department of Medical Pharmacology & Physiology.
Haiying Zhou, Member, Ph.D. Committee, 11-07-2007 -
Description: Haiying is a PhD student of Dr. Kent Gates in the Department of Chemistry.
Mostafa I Abd Elhamed, Member, Ph.D. Committee, 04-25-2007 -
Description: Mostafa is a PhD student of Dr. Kent Gates in the Department of Chemistry.
Xiaohui Wang, Member, Ph.D. Committee, 11-20-2006 - July 2009
Student Achievement: The student has received her Ph.D.
Description: Xiaohui is a Ph.D. student of the Department of Medical Pharmacology and Physiology. I serve as a member of both her Ph.D. Committee and her Ph.D. Exam Committee.
Yingchu Zhao, Member, Ph.D. Committee, 05-20-2009 -
Description: Yingchu is a PhD student of Dr. Steve Van Doren in the Department of Biochemistry.
Sam Grinter, Chair, Ph.D. Committee, 2009 -
Description: Sam is my PhD student at the Informatics Institute.

Back cover: courtesy of Dr. Maike Krenz

To model human diseases of the heart and investigate the underlying mechanisms, genetically altered mice were created that recapitulate a particular form of heart muscle disease found in children with LEOPARD Syndrome. Shown on the left is a normal heart from a newborn mouse. On the right, a newborn heart with heart muscle disease called hypertrophic cardiomyopathy caused by a mutation in the phosphatase Shp2. Shape and function of such hearts are abnormal.


normal mouse heart
heart muscle disease