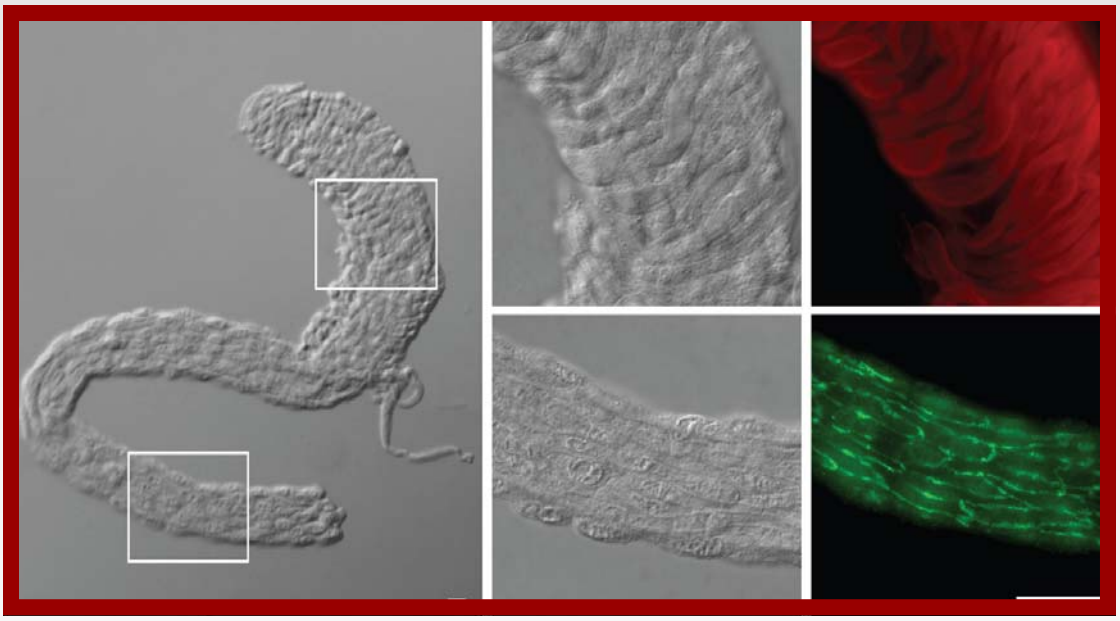
Dalton Cardiovascular Research Center



Annual Report FY 08

"Committed to Interdisciplinary Collaboration in Research and Teaching"

Front cover:

Hakim, C.H., W.F. Jackson and S.S. Segal. Connexin Isoform Expression in Smooth Muscle Cells and Endothelial Cells of Hamster Cheek Pouch Arteries and Retractor Feed Arteries. *Microcirculation* 15(6):503-514, 2008.

Partial dissociation and immunolabeling of a feed artery from the hamster retractor muscle. Differential Interference Contrast images (left and center panels) show partially dissociated microvessel with enlarged regions of interest enclosing 'loosened' smooth muscle cells that remain in register along vessel wall (top) and underlying endothelial tube following smooth muscle cell dissociation (bottom). Right panels show immunoreactivity of respective regions for smooth muscle α-actin (top, red) and for connexin43 (bottom, green). Scale bars = 20 μm; 4 enlarged panels are at equal magnification.

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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 were awarded 4.8 million in research funding and published 58 manuscripts in nationally recognized journals and books and gave 106 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.

The Internal Advisory Committee:

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

The Appointment and Promotions Committee:

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

Scientific Program Committee:

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

Core Facilities Committee:

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

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Interdisciplinary Research Interests Groups

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

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, Sowers, Davis M.J.

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

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, Sun Schadt, Segal

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

Publications and Presentations

- Articles published: 58
- Invited Presentations: 106

Awards and Peer Review

- Forty awards/contracts were active during FY08.
- Nine research awards/contract proposals were awarded.
- Sixty-two grant/contract proposals.
- Twelve graduate students were supported by R90/T90 training grants.
- Seven investigators served as editors or were on editorial boards of nine scientific journals.
- Forteen investigators reviewed articles for forty-nine scientific journals.
- Eight investigators reviewed grant applications for ten granting agencies.
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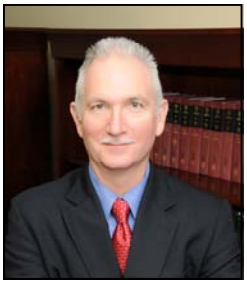
Education and Training

- Resident Investigators-Tenure/Tenure Track: 24
- Resident Research Track: 6
- Non-resident Investigators: 15
- Research Staff: 36
- Post Doctoral Fellows: 20
- Graduate Students: 35
- Undergraduate Students: 29
- Administrative Staff: 5
- Building Support Staff: 5
- Visiting Scholars: 7

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
Margaret Proctor Mulligan Professor in Medical Research
Professor, Department of Medical Pharmacology and Physiology
Adjunct Professor, Department of Biomedical Sciences

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

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Education:
PhD & MS University of Melbourne

Appointment: Professor, Associate 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

Edward H. Blaine

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

Appointment: Professor, Department of Medical Pharmacology and Physiology

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

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

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

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

Frank W. Booth

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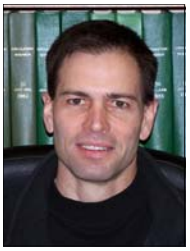
Appointments: Professor, Department of Biomedical Sciences
Adjunct Professor, Department of Medical Pharmacology and Physiology

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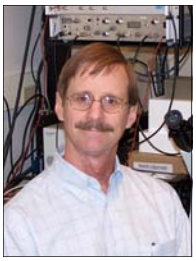
Education:
PhD, MD University of California-San Diego,
BS Arizona State University

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.

Kevin D. Gillis

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

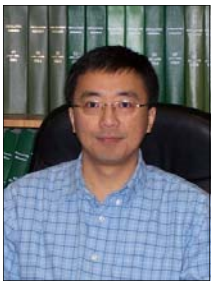
Appointments: Professor, Department of Biological Engineering Adjunct Professor, Department of Medical Pharmacology and Physiology

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.

Marc Hamilton

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

Appointment: Assistant Professor, Department of Biomedical Sciences

Research

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

metabolic responses to normal non-exercise physical activity to more intense and structured exercise. These studies are leading to the emerging school of thought that sitting too much (non-exercise activity deficiency) is a unique stimulus from exercising too little (exercise deficiency), while both types of physical activity can produce potent cellular signals important for combating the metabolic problems associated with metabolic syndrome, coronary artery disease, Type II diabetes, and obesity.

Eileen M. Hasser

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Education:
PhD University of Oklahoma, BA Gettysburg College

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

Research

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

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

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

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Education:
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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.

Virginia Huxley

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

Research Interests: Microvascular transport, *in vivo* imaging/microscopy, in vivo mass transfer, tissue engineering, mathematical modeling

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

Solute and water transfer results from "passive" and "cell mediated" mechanisms. Most have studied the passive mechanisms fewer study the cellular processes. From engaging in research in both arenas we find the exchange barrier to be a dynamic structure whose properties vary in time and space over time scales of seconds to days. Our global intent is to use this understanding of transport through pathways of microscopic geometry to investigate the relationship between blood supply and metabolic demand.

We are developing methods to extend these quantitative studies to mammalian microvessels in skeletal muscle, heart, gut, and brain in collaboration with colleagues in DCRC, MPP, Biomedical Sciences at MU and the University of Rochester. Knowing that microvascular exchange is subject to regulation under normal and pathological situations, we collaborate with clinical colleagues (Nephrology, Surgery, Anesthesia, Cardiology, Pulmonary Medicine, Infectious Disease, and Critical Care Medicine) to elucidate the cellular and molecular mechanisms involved in structuring and restructuring the barrier under conditions of peritoneal dialysis, following endurance exercise training, in coronary occlusive vessel disease, neurogenic edema, diabetes, cancer metastasis, and conditions of remote organ (brain) injury following burn. The combined clinical and basic science expertise provides the possibility of realizing our goal of designing and implementing treatments of permeability dysfunction. Consequent to the collaborative interactions at MU and in light of fundamental sex-related differences in physiological function and pathophysiology observed by us and others, we established the National Center for Gender Physiology. This virtual center is acting as a focus for research scientists at MU and collaborating institutions and augments the services provided by DCRC.

Tzyh-Chang Hwang

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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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Appointment: Professor, Department of Biomedical Sciences

Research

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

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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.

Ronald J. Korthuis

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Professor, Department of Medical Pharmacology and Physiology

Research

Our research focuses on the mechanisms underlying the inflammatory responses to ischemia and reperfusion (I/R) and how blood vessels in the microcirculation (arterioles, capillaries and venules) can be preconditioned to resist the deleterious proinflammatory effects of I/R. When the blood supply is reduced (ischemia) and then subsequently reestablished (reperfusion), the ability of arterioles to regulate the distribution of blood flow is impaired, many capillaries fail to perfuse (capillary no-reflow), and white blood cells and platelets become adherent to and emigrate across the walls of postcapillary venules. Once in the tissues, these inflammatory phagocytes attack

parenchymal cells, thereby exacerbating injury induced by ischemia. In addition, the permeability of the cells lining capillaries and postcapillary venules is increased, leading to edema formation. We are studying how white blood cells which adhere to and emigrate across the walls of postcapillary venules, alter vasoregulatory function in arterioles, cause no-reflow in capillaries, and increase permeability in postcapillary venules.

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

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

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

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

Research

I focus my research on cardiorespiratory effects of exercise. The primary goal is understanding of the effects of exercise training on the coronary circulation and skeletal muscle vascular beds. Exercise training produces increases in the capacity of myocardial and skeletal muscle vascular beds to transport oxygen and other nutrients. The training induced changes in vascular transport capacity are associated with growth of new capillaries, enlargement of arteries and veins, and alterations in factors 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
There are two major research efforts in our laboratory:
One effort is devoted to determining how proteins located in cell membranes move molecules across the membrane. This includes elucidating some of the mechanisms of transport, determining how changes of the

cytoplasmic mileau modulate transport, determining how changes in the rate of transport regulate cell function, and understanding the relationship between protein structure and transporter function. Our studies are currently focused on two transport systems: the plasma membrane calcium pump and the Na/K pump. Our recent work is devoted to examining the movement of the Na pump protein from plasma membrane to endosomes and back. We are determining the molecular basis for the integration of hormonal responses, e.g., what happens when one hormone signals increased endocytosis and another hormone signals exocytosis-who wins? We have also worked on zinc transporters, sodium/ calcium exchanges, and anion exchangers. We use biophysical, bioengineering, biochemical, and optical approaches to studying the relevant physiology and pharmacology of these transport systems, including the development of a molecular mechanistic view of their function and an integrated view of how regulation of cellular transport related to cell, tissue, organ and organism function and pathophysiology.

Another effort is the development of sensors for molecules of biological interest in collaboration with Sheila Grant in Bioengineering and Josh Millspaugh in Fisheries and Wildlife. We are designing sensors that can be used in vivo for continuous monitoring and also sensors that can be used in the field for monitoring wildlife or at home using saliva, urine, or sweat for measurement of pet or human samples. We are currently developing approaches for the measurement of glucose, cortisol, aldosterone and sex steroids. Our techniques include absorbance, fluorescence, FRET and lanthanide luminescence.

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

Research

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

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

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

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

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

Leona Rubin

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Education:
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PhD University of Colorado Health Science Center

Appointments: Associate Professor, Department of Biomedical Sciences
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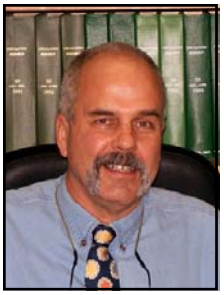
Research

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

Appointment: Associate Professor, Department of Biomedical Sciences

Research

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

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

Steven S. Segal

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PhD University of Michigan,
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Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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

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

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

Ronald Terjung

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BS Wheaton College

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

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

Cuihua Zhang

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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

NOTABLE NEWSMAKERS

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Clarke, Lane

Poster:
Walker, NM, Nalluri, S, Hwang, T-C, Milanick, MA, Zou, X and **Clarke, LL**. Functional assay for correctors of ΔF508 CFTR processing using native murine epithelium. 21st Annual North American Cystic Fibrosis Conference, Anaheim, CA, Oct. 3-6, 2007.

Liu, H-Y, Li, M, **Clarke, LL**, Milanick, MA, Zou, X and Hwang, T-C. Fluroescence-based quantification of CFTR surface expression in living cells. 21st Annual North American Cystic Fibrosis Conference, Anaheim, CA, Oct. 3-6, 2007.

Rigsby, EV, Walker, NM and **Clarke, LL**. Physiolgoical model system for testing pharmacological correctors of DF508 CFTR processing in native murine epithelium. 21st Annual North American Cystic Fibrosis Conference, Anaheim, CA, Oct. 3-6, 2007.

Bradford, E, Gawenis, LR, **Clarke, LL** and Shull, GE. Reduced absorption counters the cystic fibrosis intestinal phenotype and increases survival. EB 2008, April 5-9, 2008.

Oral:
Functional interactions among CFTR, down-regulated in adenoma (DRA, SLC26A3) and Na^+/H^+ exchange in the villous epithelium of murine duodenum. FASEB Summer Research Conference, Gastrointestinal Tract XII: The molecular and integrative basis for GI development, homeostasis and disease. Snowmass Village, Co August 11-16, 2007.

Evidence against electrogenicity of Slc26a3 (down regulated in adenoma) Cl^-/HCO_3^- exchange in murine large intestine. 109th Annual Meeting of the American Gastroenterological Association, Digestive Disease Week, San Diego, CA. May 24, 2008

Acid-base transporters of the villous apical membrane. Dept. of Medicine, University of Illinois-Chicago, Chicago, IL., April 30, 2008.

Davis, George

Cardiovascular Research Center, University of North Carolina School of Medicine, "Molecular control of endothelial cell tube assembly and disassembly in three-dimensional extracellular matrices"

Department of Pathology, Columbia University School of Medicine, "Molecular control of endothelial cell lumen formation and tube assembly in three-dimensional extracellular matrices"

Angiogenesis and Microcirculation Gordon Conference, Newport, RI, Invited speaker, "Cdc42, MT1-MMP and vascular guidance tunnels in EC lumenogenesis"

8th World Congress on Microcirculation, Milwaukee, WI, Invited speaker, "Molecular control of EC lumen formation in 3D extracellular matrices"

Matrix Metalloproteinases Gordon Conference, Il Ciocco, Italy, Invited Speaker, "Matrix metalloproteinases in vessel formation versus regression"

Department of Pharmacology, University of Illinois, Chicago, IL, "Molecular control of capillary tube formation versus regression by matrix metalloproteinases and pericytes"

Vascular Biology Gordon Conference, Ventura, CA, Invited speaker, "ECM and vascular morphogenesis" and discussion leader in session on Endothelial lumen formation.

Davis, Mike

Sept. 2007, Keynote speaker, Texas A&M Cardiovascular Research Institute Retreat
August 2007, invited speaker 8th World Congress for Microcirculation
Feb. 2008, Co-chair, ISRA meeting, Hamilton Island, Australia; Session: Ion Channels
Feb. 2008, seminar Dept. of Physiology, Univ. of Newcastle, Australia
March 2008, invited speaker, Lymphatic Gordon Conference, Ventura, CA

Ding, Shinghua

Interdisciplinary Neuroscience Program in MU**.** "Glia-mediated neuronal excitotoxicity". INP Seminar Series, University of Missouri-Columbia, July 10, 2007.

Tiannan Wang, Wenju Cui, and Shinghua Ding. Astrocytic role in neuronal excitotoxicity following photothrombosis induced focal ischemia. Life Science Week, University of Missouri-Columbia. April 13-19, 2008.

Tiannan Wang, Wenju Cui, and Shinghua Ding. Astrocytic role in neuronal excitotoxicity following photothrombosis induced focal ischemia. Brain Awareness Week, University of Missouri-Columbia. March 14, 2008.

Tiannan Wang, Wenju Cui, and Shinghua Ding. Characterization of ischemic lesion following photothrombosis. Cardiovascular Day, University of Missouri-Columbia. March 17, 2008

Gu, Liqun

Gao C. and Gu L.Q. Pharmaceutical detections with a molecular adapter non-covalently implanted in a hand-held nanopore. 52th Biophysical Society Annual Meeting. February 2-6, 2008, Long Beach CA.

Shim J.W. and Gu L.Q. Biosensing on a modular and portable chip containing a single ion channel. 52th Biophysical Society Annual Meeting. Februrary 2-6, 2008, Long Beach CA.

(BeachTalk) Shim J.W. and Gu L.Q. A guest-nanocavity supramolecular system for non-covalent single-molecule manipulation. 52th biophysical Society annual Meeting. February 2-6, 2008 Long Beach CA.

Shim J.W. and Gu L.Q. Single-molecule detection of folding and unfolding of the G-Quadruplex using a protein nanocavity. 52th Biophysical Society Annual Meeting. February 2-6, 2008, Long CA.

(Talk) Gao C. and Gu L.Q. Pharmaceutical detections with a molecular adapter non-covalently implanted in a hand-held nanopore. Institute of Biological Engineering Annual Conference. March 6-9, 2008, Chapel Hill, NC.

(Talk) Shim J.W. and Gu L.Q. Biosensing on a modular and portable chip containing a single ion channel. Institutue of Biological Engineering Annual Conference. March 6-9, 2008, chapel Hill NC.

(Talk) Shim J.W. and Gu L.Q. A guest-nanocavity supramolecular system for non-covalent single-molecule manipulation. Institute of Biological Engineering Annual Conference. March 6-9, 2008, chapel Hill NC.

Shim J.W. and Gu L.Q. In vitro synthesis, tetramerization and single-channel recording of virus-encoded potassium channel KCV. Life Science Week, University of Missouri, April 2007.

Shim J.W. and Gu L.W. biosensing on a modular and portable chip containing a single ion channel. Life Science Week, University of Missouri, April 2007.

Hasser, Eileen

FASEB Summer Research Conference/International Society for Autonomic Neuroscience meeting, Australia
Invited Lecture: Central Nitric Oxide Mechanisms in Cardiovascular Decondtioning

Heesch, Cheryl

The following abstract was presented at 2007 FASEB summer Research Conference, "Neural Mechanisms in Cardiovascular Regulation," in Bondi Beach, Sydney, Australia, July 18 -23, 2007

Heesch, C.M., S.M. Burcks, Y. Ueta, D. Murphy & J.E. Stern. Laser capture microscopy (LCM) and real time RT-PCR: Evaluation of Gene expression in PVN of transgenic vasopressin-enhanced green fluorescent protein rats.

Hwang, T.C.

Biophysical Meeting, Long Beach, CA
Department of Biophysics and Integrative Physiology, University of Illinois, Urbana-Champaign
Department of Pharmacology, National Yang-Ming Medical University
Department of Physiology, Osaka Medical College, Japan
Department of Internal Medicine, Taichun Veteran General Hospital
Osaka University of Pharmatheutical Science, Japan

Hyder, S.

MU Reproductive Biology Group, Nov 14th, 2007, Animal Sciences Dept.

Carroll, C. E., Benakanakere, I., Ellerseick, M. and Hyder, S. M. (2008). Curcumin Inhibits Secretion of Progestin-induced Vascular Endothelial Growth Factor from Human Breast Cancer Cells. University of Missouri, Cardiovascular Day. Abst #9.

Liang, Y., Besch-Williford, C., Benakanakere, I., Brandt, S., Thorpe, P. E. and Hyder, S. M. (2008) Targeting mutant p53 protein and tumor vasculature: an effective combination therapy for advanced breast tumors. MU Life science Week.

Carroll, C. E., Benakanakere, I., Besch-Williford, C., Ellersieck, M. and Hyder, S. M. (2008) Curcumin: A Potential Chemopreventive Agent for Progestin-Dependent Breast Tumors. MU Life Science Week.

Liang Y., Besch-Williford C., , Benakanakere, I., Brandt, S., Thorpe, P. E. and Hyder, S. M. (2008) Targeting mutant p53 protein and tumor vasculature: an effective combination therapy for advanced breast tumors. 98th Annual American Association of Cancer Research Meeting.

Hyder, S. M., Liang, Y., Wu, J. and Welbern, V. (2008) Estrogen Regulation of *Thrombospondin-1 in Normal and Neoplastic Mammary Cells* *98th Annual American* Association of Cancer Research Meeting.

Benakanakere, I., Besch-Williford, C., Ellerseick, M. and Hyder, S. M..(2008) Regression of MPA-accelerated 7, 12-dimethylbenz[a]anthracene (DMBA)-induced mammary tumors in Sprague-Dawley rats by PRIMA-1: A pilot study. 90th Annual Endocrine Society Meeting, San Diego, CA. Abstract P1-97.

Liang Y., Besch-Williford C., , Benakanakere, I., Brandt, S., Thorpe, P. E. and Hyder, S. M. (2008) A novel and effective combination targeting therapy for advanced breast tumors. Dept of Defense Breast Cancer Era of Hope meeting.

Hyder, S. M., Liang, Y., Benakanakere, I. and Besch-Williford, C. (2008) Suppression of breast cancer growth by re-activation of endogenous mutant p53 protein by PRIMA-1. Dept of Defense Breast Cancer Era of Hope meeting.

Anti-Angiogenesis as a Therapeutic Strategy in Cancer-Guest Lecturer in Oncology Course, Biomedical Engineering

Liang Y., Besch-Williford C., , Benakanakere, I., Brandt, S., Thorpe, P. E. and Hyder, S. M. (2008) A novel and effective combination targeting therapy for advanced breast tumors. Dept of Defense Breast Cancer Era of Hope meeting.

Kline, David

"Plasticity of the hypoxic reflex pathway: from carotid bodies to NTS". Experimental Biology 2007, Washington D.C. *Invited presentation*

"Kv1.1 Deletion Augments the Afferent Hypoxic Chemosensory Pathway and Respiration", Winter Conference for Brain Research. *Invited presentation*

Korthuis, Ronald

"Preconditioning with ethanol requires activation of 5'-AMP-activated protein kinase to prevent postischemic leukocyte endothelial cell interactions in murine postcapillary venules". Poster presentation at the World Congress for Microcirculation, Milwaukee, WI, August 2007

"Antecedent Ethanol Prevents Microvascular Dysfunction in Ischemia/Reperfusion". Symposium on Protective Effects of Ethanol, Alcohol Research Society of America annual meeting. Chicago, IL July 2007.

"Postcapillary venular leukocyte adhesion is required for arteriolar vasoregulatory dysfunction in ischemia/ reperfusion". 9th Annual International Conference on Resistance Arteries, Hamilton Island, Australia, February 2008.

Anti-inflammatory mechanisms in ischemia/reperfusion. Children's Memorial Research Center, Northwestern University, June 26, 2007, Chicago, IL.

Gaskin FS, T Yamaguchi, K Kamada, M Yusof, RJ Korthuis. Ethanol preconditioning prevents postischemic leukocyte-endothelial cell adhesive interactions: Role of nitric oxide. FASEB J 21:A1220, 2007.

Yusof M, K Kamada, FS Gaskin, RJ Korthuis. Angiotensin II promotes postischemic leukocyte/endothelial interactions in murine small intestine: role of chymase and ACE, AT1 and AT2 receptors, CGRP, and NADPH oxidase. FASEB J 21:A1236, 2007.

Wang Q, AY Sun, A Simonyi, KD Tompkins, JJ Guo, GY Sun, RJ Korthuis. Ethanol preconditioning protects against ischemia/reperfusion-induced brain damage: Role of NADPH oxidase-derived ROS. FASEB J 21:A1389, 2007.

Kalogeris T, M Wang, FS Gaskin, M Yusof, Q Wang, and RJ Korthuis. Activation of calcium-activated potassium (BK_{Ca}) channels prevents ischemia-reperfusion-induced leukocyte-endothelial adhesive interactions. FASEB J 21:A1220, 2007

Liang, Yayun

Invited an oral presentation (as a symposium platform presentation). Title: **"**A novel and effective combination targeting therapy for advanced human breast tumors" by the U.S. Army Medical Research and Material Command's in the DOD Breast Cancer Research Program (BCRP) Era of Hope Meeting at Baltimore, MD in June 26, 2008.

Poster presentation, title **"** Targeting mutant p53 protein and tumor vasculature: An effective combination therapy for advanced breast tumors" at Annual Meeting of the
American Association for cancer Research, in San Diego, CA in April 14, 2008.

Martinez-Lemus, Luis

Martinez-Lemus, L.A. Vascular smooth muscle cell plasticity and vascular remodelin*g.* In the symposium ""The Role of Hemodynamic Factors in Angioadaptation." 8th World Congress for Microcirculation, Milwaukee, Wisconsin (August, 2007).

Jackson, T.Y., L.A. Martinez-Lemus, M.A. Hill, and G.A. Meininger. 2007. A role for cadherins in arteriolar myogenic responsiveness. 8th World Congress for Microcirculation. Milwaukee. Wisconsin, USA, August, 2007.

Jackson, T.Y., L.A. Martinez-Lemus, M.A. Hill, and G.A. Meininger. 2008. A role for cadherins in vascular myogenic response. International Symposium on Resistance Arteries, Hamilton Island, Australia, published in Journal of Vascular Research, February 2008.

Bosanquet, J.P., V.G. DeMarco, K.C. Dellsperger, and L.A. Martinez-Lemus. 2008. Angiotensin II induces reactive oxygen species formation and augments 5-HT-induced vasoconstriction in isolated pulmonary arterioles. Cardiovascular Day XV, Universiry of Missouri-Columbia, Columbia, MO, March 2008.

Jackson, T.Y., L.A. Martinez-Lemus, M.A. Hill, and G.A. Meininger. 2008. The role of cadherins in arteriolar myogenic responsivness. Cardiovascular Day XV, Universiry of Missouri-Columbia, Columbia, MO, March 2008.

Jackson, T.Y., L.A. Martinez-Lemus, M.A. Hill, and G.A. Meininger. 2008. Cadherins play a role in arteriolar myogenic responsivness. Annual Meeting of the Societies for Experimental Biology. San Diego, CA, April 2008. Published in FASEB J., 2008.

Bosanquet, J.P., V.G. DeMarco, K.C. Dellsperger, and L.A. Martinez-Lemus. 2008. Angiotensin II induces reactive oxygen species formation and augments 5-HT-induced vasoconstriction in isolated pulmonary arterioles. Annual Meeting of the Societies for Experimental Biology. San Diego, CA, April 2008. Published in FASEB J., 2008.

Martinez-Lemus, L.A., Z. Guiling, J.P. Bosanquet. 2008. Matrix metalloproteinaseinhibition prevents the acute inward remodeling induced by prolonged vasoconstriction in isolated arterioles. Annual Meeting of the Societies for Experimental Biology. San Diego, CA, April 2008. Published in FASEB J., 2008.

Meininger, Gerald

Meininger, G.A. "Atomic Force Microscopy for Studies of the Microcirculation" an invited Plenary Lecture at the World Congress for Microcirculation, Milwaukee, WI, July 2007

Jackson T.Y., Martinez-Lemus L.A., Hill M.A. and Meininger G.A. A role for cadherins in arteriolar myogenic responsiveness. 8th World Congress for Microcirculation, Milwaukee, WI, August 2007.

Huang S., Sun Z., Meininger G.A. Involvement of integrin linked kinase in cell adhesion of rat vascular smooth muscle cells. 8th World Congress for Microcirculation, Milwaukee, WI, August 2007.

Meissner K., Sun Z., Fan X., Cot'e G. and Meininger G.A. Combining AFM a FRET for studies at the cellular level. SPIE, 2007.

Jackson T.Y., L.A. Martinez-Lemus, M.A. Hill, G.A. Meininger. A role for cadherins in the vascular myogenic response. International Symposium on Resistance Arteries, Hamilton Island, Australia, published in Journal of Vascular Research, February 2008.

Michael A. Hill, Zhe Sun, Srikanth R. Ella, and Gerald A. Meininger. New imaging approaches for understanding the arteriolar myogenic response. International Symposium on Resistance Arteries, Hamilton Island, Australia, published in Journal of Vascular Research, February 2008.

Ella S.R., M.J. Davis, K.A. Dora, G.A. Meininger, M.A. Hill. Effect of intraluminal pressure and tone on smooth muscle Ca^{2+} oscillations in cremaster muscle arterioles. International symosium on Resistance Arterties, Hamilton Island, Australia, February 2008.

Ella S.R., M.J. Davis, G.A. Meininger, K.A. Dora M.A. Hill. Effect of myogenic tone on smooth muscle Ca^{2+} oscillations in cremaster muscle arterioles. Experimental Biology, San Diego, April 2008.

Askarova S., Sun Z., Sun G.Y., Meininger G.A., J.C-M. Lee. Oligomeric amyloid-b peptide on sialyl $Lewis^x$-selectin bonding at the cerebral endothelial cell surface. International Conference on Alzheimer's Disease, Chicage, July 2008.

Huang S., Z. Sun, Z. Li and G.A. Meininger. Zyxin is involved in regulation of cell adhesion and mechanotransduction in microvascular smooth muscle cells. Annual Cardiovascular Day Symposium, University of Missouri, Columbia, Missouri, March 2008.

"Using Atomic Force Microscopy as a Tool to Study Extracellular Matrix Adhesive Interactions in Microvascular Cell Types" to the 2007 McLaughlin Symposium-First Symposium on "The Microcirculation in Acute Viral and Bacterial Infections", November 15-17, 2007.

"Applying Atomic Force Microscopy for Studies of Cell Biology" to the Department of Electrical and Computer Engineering, College of Engineering, University of Missouri, April 25, 2008.

Polo-Parada, Luis

Nanoparticle based drug delivery and biosensor detection. St Louis University. Dept. of Rheumatology. Sept. 24

"The Extracellular Matrix Modulates Action Potential Phenotype During Heart Development"
7th Annual Spring Symposium of the medical University of South Carolina. Cardiovascular Developmental Biology Center.

"The use of shockwaves generated b y nanothermites fro cardiac transfection."
Steve J. Apperson, Venumadhav Korampally, Sangho Bok, Gangopadhyay Keshab, Gangopadhyay Shubhra and Luis Polo-Parada. Weinstein Cardiovascular Development Conference. Houston TX.

"The Cardiac Cushions Modulate Action Potential Phenotype During Heart Development"
Luis Polo-Parada, Amol Modgi, Xialoin Zhang. Weinstein Cardiovascular Development Conference. Houston

" The Role of the NCX-1 on the Cardiac Action Potential During Development"
Amol Modgi, Xialoin Zhang and Luis Polo-Parada. Weinstein Cardiovascular Development Conference. Houston TX.

Segal, Steven

"Protein kinase G promotes dilation of hamster cheek pouch arterioles" (Poster)
8th World Congress in Microcirculation – Milwaukee, WI; 8/18/07

"Blood Flow Control in the Microcirculation: Role of Cell-to-Cell Signaling" Mason Eye Institute, EC150, Department of Ophthalmology (MU)

Propagation of Calcium Waves Along Endothelium of Resistance Vessels, San Diego CA (Experimental Biology 2008), 4/8/08

Integrating Electrical and Calcium Signaling in Microvascular Resistance Networks,
Michigan Sate University, 6/18/08

Blood Flow Control in the Microcirculation, MU Department of Dermatology, 5/9/08

Soma, Yoshira

Shimizu H, Sohma Y, Li M, Kubota T, Kono K, Hwang T-C.
Missfiring mechanism in NBD gating engine of CFTR chloride channel.
85th Annual Meeting of Physiological Society of Japan. March 25 – 27, 2008; Shinjyuku, Tokyo, Japan

Mori Y, Inui T, Sohma Y, Miyamoto M, Tashiro-Yamaji J, Yoshida R, Takenaka H, Kubota T. Contribution of Ca^{2+}-permeable channels to the regulation of endocochlear potential in guinea pigs. 85th Annual Meeting of Physiological Society of Japan. March 25 – 27, 2008; Shinjyuku, Tokyo, Japan

Computer Simulation of Bicarbonate-Rich Fluid Secretion in Exocrine Pancreas, 4th International Symposium of Cell/Biodynamics Simulation Project, Kyoto University, Kyoto, Japan, Nov 13 2007

Zhang, Cuihua

Title to present: Feed-forward signaling of TNF and NFkB produces endothelial dysfunction in coronary arterioles in type 2 diabetic mice. Hamilton Island/Australia. Symposium Speaker at the 9th international symposium on resistance arteries (ISRA). Feb 20th, 2008

Title to present: Effect of sodium salicylate on insulin resistance and endothelial dysfunction of coronary arterioles in type 2 diabetes. Cardiovascular Day at University of Missouri-Columbia. March 17th, 2008.

The role of inflammatory cytokines in vascular dysfunction. Invited by Vascular Biology Center/ Physiology, Medical College of Georgia

Yoonjung Park, Darcey Klaahsen, and Cuihua Zhang. Role of PAR2 in Type 2 Diabetes-induced Endothelial Dysfunction. FASEB J. 2008 22:1226.30

Hanrui Zhang, Minga Sellers, Zoltan Ungvari, and Cuihua Zhang. Resveratrol Protects against Oxidative Stress-Induced Endothelial Dysfunction in Type II Diabetes. FASEBJ. 2008 22:lb42

PRESENTATIONS

Jiyeon Yang, Yoonjung Park, and Cuihua Zhang. Effect of Sodium Salicylate on Insulin Resistance and Endothelial Dysfunction of Coronary Arterioles in Diabetic Mice. FASEBJ. 2008 22:lb45

Darcey Lynn Klaahsen, Hanrui Zhang, Yoonjung Park, Sewon Lee, Christopher Hardin and Cuihua Zhang. EXTRA VIRGIN OLIVE OIL AND VASCULAR Health. FASEB J. 2008 22:lb63
Zoltan Ungvari, Nazar Labinskyy, Pal Pacher, Cuihua Zhang, Andrej Podlutsky, andAnna Csiszar. Resveratrol attenuates cigarette smoking-induced pro-inflammatoryalterations in the endothelial phenotype. FASEB J. 2008 22:747.4

Cuihua Zhang. Role of Inflammatory Cytokines in Vascular Dysfunction. Symposium
Oral Presentation at ATVB Spring Annual meeting in Atlanta. April, 2008

INVITED SEMINAR SPEAKERS

July 16, 2007	**Dirk F van Helden, PhD** School of Biomedical Sciences, University of Newcastle, Australia, "*Rythmicity and synchronicity in smooth muscle"*
November 16, 2007	**David Adams, PhD** School of Biomedical Sciences University of Queensland Australia *"Novel peptide toxins and protein modulators of voltage-gated ion channels"*
December 6, 2007	**David Braun, PhD** Department of Pharmacology and Therapeutics, University of Calgary, Calgary, Canada *"Distinct signaling pathways underlie agonist evoked nitric oxide production in single human endothelial cells"*
February 21, 2008	**Jianmin Cui, PhD** Biomedical Engineering & Cell Biology & Physiology Washington University in St. Louis *"Molecular mechanism of Mg2+ dependent activation of BK channels-an interaction between the cytosolic domain and the voltage sensor"*
April 24, 2008	**Richard Horn, PhD** Thomas Jefferson University Jefferson Medical College Department of Molecular Physiology and Biophysics Professor Appointed 1992 *"Plugging the Pore: Hoodwinking Ion Channels with Cationic Blockers"*

PRINCIPAL INVESTIGATOR *TITLE* AGENCY	AMOUNT PERIOD
Bompadre, S.	
"Molecular physiology and pharmacology of CFTR"	$107,258
National Institute of Diabetes and Digestive and Kidney Diseases	9/07-8/08
Clarke, LL.	
"CFTR and Intestinal Acid-Base Transporters"	$800,000
National Institute of Health	8/06- 7/10
"Structure-Guided Physiological Screening of DF508 CFTR Correctors"	$1,349,781
Cystic Fibrosis Foundation Therapeutics, Inc.	12/06–11/09
Davis, G.	
"Molecular control of EC lumen formation by MT1-MMP"	$250,000
National Institute of Health/National Heart Blood and Lung Institute	1/08-12/11
"Tissue engineering of dermal blood and lymphatic microvascular networks"	$110,000
Defense Advanced Research Projects Agency	10/07-6/08
"Pericyte proteinase inhibitors and EC tube stabilization"	$200,000
National Institute of Health/National Heart Blood and Lung Institute	2/05-12/08
"Genes regulating capillary morphogenesis and apoptosis"	*$200,000*
National Institute of Health/National Heart Blood and Lung Institute	7/04-6/08
Davis, M.	
"*Regulation of Vascular Tone and Ca Channels by Integrins"*	$1,000,000
National Institute of Health	2003-2007
"*Regulation of Arteriolar Tone and K Channels by Integrins"*	$1,000,000
National Institute of Health	2003-2007

"Pericyte Proteinases and EC Tube Stabilization"	$800,000
National Institute of Health	2005-2009
"Molecular Control of EC Lumen Formation by MT-1 MMP"	$1,250,000
National Institute of Health	3/08-2/12
"Mechanisms of Reperfusion-induced Endothelial Injury"	$1,250,000
National Institute of Health	5/06-4/11

Ding, S.

"*Scientist Development Grant"*	$260,000
American Heart Association	7/07-6/11
"*An Optical and Genetic Strategy to Study Glutamate Release from Astrocytes in vivo*"	$10,000
Ralph E. Powe Junior Faculty Enhancement Awards through the Oak Ridge Associated Universities	6/08-5/09

Gu, L.

"Single molecule study of oligonucleotide-protein interaction and folding in a nanopore"	
National Science Foundation	7/06-6/11
"Programmable multi-target detection using an aptamer-integrated nanopore"	
National Institute of Health	2/7-1/12

Hasser, E.

"*Cardiovascular Regulation in Hindlimb Unweighted Rats"*	$900,000
National Institute of Health	4/7-3/11
"*BDNF and MeCP2 in autonomic dysfunction"*	
National Institute of Health	10/7-9/11
"Neural Circulatory Control: Pregnancy & Ovarian Hormones"	
National Institute of Health	4/4-3/09
"Sympathetic premotor neuron alterations in cardiovascular control"	$33,696
University of Missouri Research Board	2007

Heesch, C.

"Differential neurotransmitter modalities of CNS presympathetic neurons,"	$29,500
University of Missouri Research Board Grant	3/07-3/08
No cost extension to 6/30/09	

"Neural Circulatory Control: Pregnancy & Ovarian Hormones," $142,227
National Institute of Health 3/07-2/08
No cost extension to 02/29/09

"Effects of Pregnancy on Hypothalamic Neurosecretory Neurons," $17,887
University of Missouri, college Veternary Medicine
Research Award 1/06-12/07

"*Cardiovascular regulation in hindlimb unweighted rats,*" $225,000
National Institute of Health 4/07-3/11

Adaptation of brainstem circuits to chronic hypoxia," $1,000,000
National Institute of Health Co PI (Kline) 4/08-3/13

Hwang, T.C.

"Confocal equipment for biomedical and nanomedicine research" $402,030
National Institute of Health, NIHS10 2006-2007

"Molecular pathophysiology of cystic fibrosis" $640,000
National Institute of Health, NIHR01, NIDDK 2003-2007

"Gating of CFTR chloride channels by ATP hydrolysis" $933,056
National Institute of Health, NIHR01, NHLB 2006-2010

"*Structure-guided physiological screening of AF508 CFTR correctors"* $482,764
Cystic Fibrosis Foundation Therapeutics 2006-2007

Hyder, S. M.

"Development of a novel progestin-dependent model to identify therapeutics" $275,000
National Institute of Health 4/08-03/10

"A novel progestin-dependent model of human breast cancer for the development of anti-tumor therapeutics" $18,000
College of Veterinary Medicine 1/08-12/08

"Inhibition of Progestin-Dependent Angiogenesis in $60,000

Breast Cancer" Mentor-Candace Carroll
National Institute of Health/National Cancer Institute 5/08-4/10
Ruth L. Kirschstein NRSA Fellowship

"Development and characterization of a novel progestin-dependent human breast cancer model" $300,000
Department of Defense Breast Cancer Program 1/08-12/10

"Re-activation of tumor suppressor p53 as a therapeutic approach for breast cancer" $100,000
Elsa U Pardee Foundation 1/08-12/08

Kline, D.

Adaptation of brainstem circuits to chronic hypoxia," $1,000,000
National Institute of Health 4/08-3/13

Korthuis, R.

"Ethanol prevents microvascular dysfunction" $225,000
National Institute of Health 7/06-6/11

"Venular leukocyte adhesion, impaired arteriolar vasoreactivity, and intestinal I/R" $250,000
12/06-1/11
National Institute of Health

"Ethanol prevents microvascular dysfunction" $225,000
National Institute of Health 7/06-6/11

Liang, Y.

"A novel progestin-dependent model of human breast cancer for the development of anti-tumor therapies." $18,000
1/08-2/08
College of Veterinary Medicine

Martinez-Lemus, L.

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

"A Confocal/ Multiphoton Microscopy System." $53,000
University of Missouri-Columbia PRIME fund 2007

Meininger, G.

"*Atomic Force FRET Microscopy Using Quantum Dot for Cell Mechanobiology"*	$555,529
National Institute of Health	9/06-8/09
"*Microvascular Control: A Role for Integrins"*	$1,455,000
National Institute of Health	2/06-11/07

Segal, S.

"Microcirculation in Aging Skeletal Muscle"	$1,934,108
National Institute of Health	9/07-8/12
"Unit Control of Muscle Blood Flow"	$1,250,000
National Institutes of Health	8/04 -7/09
qRT-PCR machine for MPP Molecular Core	$39,313
MU PRIME Fund	9/07

Zhang, C.

"Role of Cytokine-Induced Inflammation in Endothelial Dysfunction in Diabetes"	$1,226,000
National Institute of Health	2/08-11/11
"Mechanisms of Reperfusion-induced Endothelial Injury"	$715,577.61
National Institute of Health	6/08-3/11

Blaine, E.

Dalton development Coordinator
Dalton Advisory Committee
Campus Planning Committee
Graduate Education Committee
Campus Grievance Committee
MS Reviews for AJP

Bompadre, S.

Moderator of 2 roundtables at the 21st annual Cystic Fibrosis Conference, Anaheim CA, October 6 2007
Reviewer for the American Journal of Physiology
Reviewer for Telethon, Italy.

Clarke, LL.

Cystic Fibrosis Foundation, Research and Training Committee, Regular Member
Abstract reviewer, Airways Pathophysiology/ Airways Defense, Cystic Fibrosis Foundation
Abstract reviewer, Intestinal Disorders Section, Am. Gastroenterological Assoc.
National Institutes of Health – Clinical and Integrative Gastrointestinal Physiology (Ad Hoc Member)
Moderator, Ion Transport and Mucosal Biology Workshop, North American Cystic Fibrosis Conference
Journal Reviews: American Journal of Physiology
Gastroenterology
American Journal of Respiratory and Critical Care Medicine
University Promotion and Tenure Committee, Member College of Veterinary Medicine - Space Allocation Committee, Member
Director of Graduate Studies, Biomedical Sciences Area Graduate Program

Davis, G.

Research Council- participated on subcommittee to select Spurgeon Award.
MD/PhD program Executive committee

Davis, M.

Microcirculatory Society Website Committee
Dept. RIF committee
Dept. Seminar committee
Dept. Promotion & Tenure committee
Dept. Post-Doc subcommittee
Dept. Curriculum subcommittee
Dept. Space committee
Faculty Mentor (G. Sowa, Fadel, Martinez-Lemus, C. Zhang, A. Gashev (TAMU), C. Quick (TAMU))
Dept. Vice-Chair

Ding, S.

Reviewing a paper for Journal of Vascular Research
Teaching course of Biomedical Imaging (BE4570/7570)
Seminar host in Dalton: April 23, Speaker: Dr. Richard Horn, University of Jefferson.
Member of thesis's committee (PhD) for Yonghong Bai (July 9, 2008-, Dr. Hwang's lab).

Gu, L.

Reviewers of these journals, Nano Letters, the Journal of American Chemical Society and Clinic Chemistry.

Organizer of the Dalton Center Membrane Journal Club, a weekly academic seminar for campus-wide faculties, postdocs and students to present new papers, introduce their research progresses and discuss new grant proposals.

Hasser, E.

American Physiological Society – Publications Committee
FASEB Publications Committee
National Space Biomedical Research Institute - Board of Scientific Councillors
Manuscript review
Grant Review – NIH (ad hoc)
Grant Review - NSF

Heesch, C.

Manuscript Reviews 07/07/07 – 09/30/07: Amer. J. Physiol. Regulatory, Integrative & Comp. – 1 Manuscript
University of Missouri, Interdisciplinary Neuroscience Program, Executive Committee
University of Missouri, Dept. Biomed. Sci., Chair Promotion & Tenure
01/08 – 03/08: University of Missouri, College Vet. Med. Honor Code Revision Committee

Hyder, S.

Ad hoc Manuscript Reviewer: Clinical Cancer Research
Ad hoc Manuscript Reviewer: Molecular Endocrinology
Ad hoc Manuscript Reviewer: Endocrinology
Ad Hoc Reviewer MU-Institute of Clinical and Translation Research.
Ad Hoc Reviewer: Israel Science Foundation grants
Ad Hoc Reviewer J Pharmacology and Experimental Therapeutics
Ad Hoc Reviewer Endocrinology

Hwang, T.-C.

Wellcome Trust, grant review
Ad hoc member, Board of Scientific Counselors Meeting, NIH.
Editorial, Biophysical Journal
Manuscript review, Bioorganic and medicinal chemistry
Ad hoc reviewer for JGP

Kline, D.

University/College/Departmental
Coordinator, Biomedical Sciences, UM CVM Seminar Series
Judge, Phi Zeta Research Day, March 23, 2007
Graduate Program Advisory Committee (GPAC); member
College of Veterinary Medicine Research Committee; member
Reviewer, Research Board Grants, Feb cycle
Reviewer, Scientific Journals:*Journal of Physiology (London) , Journal of Neurophysiology, Journal Applied Physiology, Brain Research*
Co-Chair. Neural Plasticity of the hypoxic reflex: carotid bodies, NTS and pons. Experimental Biology 2007

Korthuis, R.

Editorial Boards for American Journal of Physiology: Heart and Circulatory Physiology; Microcirculation; Pathophysiology, AHA, Cardiovascular Research

Appointed as Charter Member, Vascular Cell and Molecular Biology Study Section, National Institutes of Health

Member of the Joint Programming Committee, Cardiovascular Section Steering Committee, and Finance Committee for the American Physiogical Society

Member, Peer Review Steering Committee, American Heart Association, National Center

Vascular Cell and Molecular Biology Study Section member, NIH, Feb 2007

Martinez-Lemus, L.

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

Editorship: Associate Editor for the Physiology and Reproduction section of Poultry Science.
Co-Chairman of the session entitled "The Role of Hemodynamic Factors in Angioadaptation" held at the 8th World Congress for Microcirculation, Milwaukee, Wisconsin, August 15-19, 2007.

Microcirculatory Society: Program Committee (2007-2010)
Member, Committee for Appointment and Promotion of Non-Tenure Research Track Faculty. Dalton Cardiovascular research Center. University of Missouri-Columbia.
Member of the Curriculum Committee for the Department of Medical Pharmacology and Physiology, University of Missouri-Columbia (2007).

Member of the Structure and Function of the Graduate Education Committee for the Department of Medical Pharmacology and Physiology, University of Missouri-Columbia (2007).
American Physiological Society: Awards Committee

Meininger, G.

Cardiovascular Section Chair of American Physiological Society
US Co-Editor for Journal of Vascular Research.
Associate Editor for American Journal of Physiology: Heart and Circulatory Physiology.

Chair, Session on "Vascular Cell Mechanobiology" at the 9th International Resistance Artery Meeting, Hamilton Island, Australia, February 17-21, 2008.
Proposal reviewer for a Croucher Foundation Award, February 2008.

Chair, Vascular Wall Biology 2 Review Committee, American Heart Association - National, October, 2007.

Internal PPG advisory committee member, meeting June 2008.
University of Missouri Research Board Grant Review, University of Missouri-Columbia, 2008.

Chair, Vascular Wall Biology 2 Review Committee, American Heart Association - National, April, 2008

PROFESSIONAL SERVICE ACTIVITIES

Polo-Parada, L.

Journal of Neuroendocrinology. Reviewer.
AHA. Reviewer
NSF. Reviewer
Journal of Neurosciences Methods. Reviewer
Journal of Neuroendocrinology. Reviewer
Journal of Applied Physiology. Reviewer

Schadt, J.

Dalton Science Teacher's Symposium, 9-20-07.
Dalton Science Teacher's Symposium, 11-26-07.
Dalton Science Teacher's Symposium, 2-20-08.

Segal, S.

Associate Editor for *Microcirculation*
Reviewer for: *Am. J. Physiol. Heart Circ. Physiol., J. Physiol., J. Vasc. Research*
Planning Committee Member, Specialty Meeting of the American Physiological Society: "Integrative Biology of Exercise" (to be held 09/08)
President-Elect, The Microcirculatory Society, Inc. (planning, advisory roles)
MPP committees: Member: RIF, Space, Dissertation; Chair: Postdoctoral Trainee Guidelines
Associate Editor: *Microcirculation*
Reviewer for: *Circulation Research; Am. J. Physiol. Heart Circ. Physiol.*; J. Va*sc. Research,*
Planning Committee Member, Specialty Meeting of the American Physiological Society: "Integrative Biology of Exercise" (to be held 09/08)
President-Elect, The Microcirculatory Society, Inc. (planning, advisory roles)
MPP committees: RIF, Space & Renovation for MPP Molecular Core,
Associate Editor: *Microcirculation*
Reviewer for: *Circulation Research; Am. J. Physiol. Heart Circ. Physiol.*; J. Va*sc. Research,*
Planning Committee Member, Specialty Meeting of the American Physiological Society: "Integrative Biology of Exercise" (to be held 09/08)
President-Elect, The Microcirculatory Society, Inc. (planning, advisory roles)
MPP committees: RIF, Space & Renovation for MPP Molecular Core,
Associate Editor: *Microcirculation*
Member, Search Committee: Nutritional Science/MPP
Member, MPP Assessment Committee on Research and Graduate Student and Postdoctoral Education
Reviewer, British Heart Foundation (Senior Fellowships)
Moderator, President's Symposium, Annual meeting of The Microcirculatory Society, Inc

Soma, Y.

Journal reviewer (J. Membrane Biology)
Journal reviewer (Biophysical Journal)
Journal Reviewer (Cell Biology International)
Journal Reviewer (Journal of Physiological Sciences Zhang, C.
Serve as the Treasurer for Chinese American Diabetes Association
Moderator and Symposium Co-organizer with Ann Marie Schmidt for Experimental Biology Meetings, 2008: Myriad Mechanisms Underlying the Pathophysiology of Diabetes
Moderator and Invited Concurrent Speaker for Session II C (control of Vascular Tone), 2008 ATVB Annual Conference. The Title is "Mechanisms of Altered Vascular Control in the Pre-diabetic Metabolic Syndrome".

Serve on Award Committee for American Physiological Society Cardiovascular Section

Serve on Membership Committee for Microcirculatory Society

Serve on Planning Program Committee member for ATVB Spring Meeting in 2008

Editorial Board Member for AJP Heart and Basic Research in Cardiology.

Reviewer for: 1. Circulation; 2. Circulation Research; 3. American Journal of Physiology; 4. Basic Research in Cardiology; 5. Journal of the American College of Cardiology; 6. Diabetic Medicine

.Zou, X.

Reviewing articles for the following journals: Proteins (2 articles), Indian Journal of Medical Research
Editorial Advisory Board Member for Current Computer-Aided Drug Design.
Faculty candidate interview: Dr. Svetlana Tikunova of Department of Biomedical Science.
Graduate Admission and Recruitment Committee of the Biochemistry Department.
Position Search Committee for a research scientist position at Dalton.
Graduate Committee for a Chemistry Ph.D. student (Mostafa I Abd Elhamed).
Reviewing manuscripts for the following journals: BMC Structural Biology; Proteins: Structure, Function and Genetics.
Reviewing grants for the following funding agencies: Kentucky Science and Engineering Foundation, and UM Research Board.
Serving in the graduate committee of two PhD students in the Chemistry Department

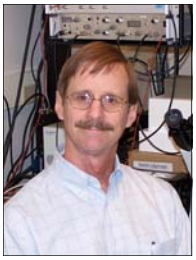
NOTABLE NEWSMAKERS

Margaret Proctor Mulligan a Missouri native and breast cancer survivor was also touched by Cardiovascular disease when her father died of a heart attack. She was a long time supporter of the MU School of Medicine, but upon her death at age 97, her estate gift created more than 10 endowed faculty professors in Medical Research. This gift created the most endowed faculty positions that MU has every had the privilege of receiving.

Of the 10 endowed faculty positions, four are Dalton Investigators:

George E. Davis is a member of the Department of Medical Pharmacology and Physiology. Dr. Davis research examines breast cancer and cardiovascular disease by studying the development of new blood vessels, or angiogenesis and how to control tumor cell migration and invasion at the molecular level.

Gerald A. Meininger is Director of Dalton Cardiovascular Research Center and a member of the Department of Medical Pharmacology and Physiology. Dr. Meininger uses advanced imaging technology to conduct cellular-level studies on how the tiniest blood vessels contribute to cardiovascular health and disease.



Michael J. Davis is a member of the Department of Medical Pharmacology and Physiology. Dr. Davis research is focused on the mechanisms of mechano-transduction by blood vessels.

Steven S. Segal is a member of the Department of Medical Pharmacology and Physiology. Dr. Segal's research is focused on understanding how oxygen delivery increases in response to metabolic demand.

Discovery Channel News Story

The Discovery Channel recently ran a news article about Dr. Shubhra Gangopadhyay and Dr. Polo-Parada's work on Nanoparticle shockwaves and how their device enhances drug delivery.

Because of Dr. Polo-Parada's work with "microshockwave generator integrated with nanoparticle delivery for cell transfection, cell imaging and gene therapy", he was offered to present at the WBT showcase 2008 in Arlington, TX, March 26-28, 2008 as part of an outstanding group of researchers and entrepreneurs representing breakthrough technologies.

NOTABLE NEWSMAKERS

2008 Intel Science Talent Search

Evan Mirts, a high school student from Jefferson City, won 10th place in the Intel Science Talent Search (National Science Fair).

Evan's project was using a Scanning Ion Conductance Microscope to image chloroplasts at ~100 nm resolution.

The research was conducted in the laboratory of **Dr. Kevin Gillis**, a resident Dalton Cardiovascular Research Center Investigator and a Professor in the Department of Biological Engineering.

Evan was the only finalist (among 40) from Missouri and won a $20,000 scholarship and a laptop computer for placing 10th.

Dalton Welcomes a New Investigator

Cuihua Zhang, MD, PhD joined Dalton as an Investigator on January 1, 2008.

Dr. Zhang joins us as a researcher from Texas A&M and holds an Associate Professor position with tenure in Departments of Internal Medicine, Medical Pharmacology & Physiology and Nutritional Sciences.

Dr. Zhang's basic research is in coronary microcirculation and physiology. One of her primary research interests is aimed at understanding a contributing factor to the pathophysiological manifestations of ischemic heart disease by assessing a potential role of the inflammatory cytokine, tumor necrosis factor-alpha in ischemia/reperfusion injury.

Inaugural Franklin Lecture

Dean Franklin, a former Dalton Director from 1980 -1991, passed away May 2, 2007. Plans were made for our Inaugural Franklin Lecture held September 12th, 2008. This was made possible due to the donations of family and friends of Dr. Franklin.

The Franklin lecture will enhance the scholarly environment of the University of Missouri and Dalton Cardiovascular Research Center for faculty and students. The Lecture will be used to invite distinguished speakers of high caliber that are considered to be at the top of their field. Speakers will be selected for their expertise in the cardiovascular sciences and the technologies that drive the field forward.

Stephen F. Vatner, M.D., Chair, Department of Cell Biology & Molecular Medicine Director, Cardiovascular Research Institute, Newark NJ accepted our invitation to be our first speaker.

NOTABLE NEWSMAKERS

International Media Coverage Inactivity Research

Dr. Mark Hamilton's research on inactivity reached global media coverage. UK's, The Earth Times reports: Even exercising for an hour a day isn't sufficient to reverse the effects of sitting the rest of the day, U.S. researchers found.

University of Missouri-Columbia researchers Marc Hamilton and Theodore Zderic found evidence that sitting had negative effects on fat and cholesterol metabolism and that physical inactivity throughout the day stimulated disease-promoting processes.

Hamilton said that there is a misconception that actively exercising is the only way to make a healthy difference in an otherwise sedentary lifestyle but his studies found that standing and other non-exercise activities burn many calories in most adults even if they don't otherwise exercise.

"The enzymes in blood vessels of muscles responsible for 'fat burning' are shut off within hours of not standing," Hamilton said in a statement. "Standing and moving lightly will re-engage the enzymes, and it stands to reason that when people sit much of that time they are losing the opportunity for optimal metabolism throughout the day."

Common non-exercise physical activities include: household chores, shopping, fidgeting and standing while watching a ball game, watching TV or talking on the telephone.

The findings were published and presented at the Second International Congress on Physical Activity and Public Health in the Netherlands.

Explanation of Figures

Back cover:

From Dr Mike Hill: The three dimensional figure shows the spontaneous generation of a Ca2+ wave in a single smooth muscle cell of a small artery. Intensity of the Ca2+ signal is depicted by the height of the peaks and the relative color, with blue representing a low level and red the highest.