Dalton Cardiovascular Research Center

2014

Front picture is a nighttime shot of Dalton Cardiovascular Research Center.

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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 Resident and Non-Resident Investigators have over $35 million in active research funding, have published 165 manuscripts in nationally recognized journals and books and gave 71 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.

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Dr. Kevin Gillis

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Interdisciplinary Research Interests Groups

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

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

Exercise/Inactivity Including Atherosclerosis, Muscle Biology, Obesity, Type II Diabetes, and Vascular Biology
Investigators: Booth, Bowles, Hasser, Hill, Huxley, Jones, Korthuis, Laughlin, Martinez-Lemus, Meininger, Polo-Parada, Rubin, Segal, Soma, Terjung, Sun, Fay, Sowers

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

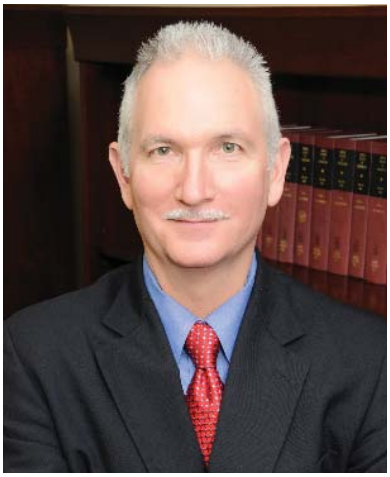
Microcirculation
Investigators: M.J. Davis, Ding, Hill, Huxley, Korthuis, Laughlin, Martinez-Lemus, Meininger, Segal, Sun, Hong

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

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

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

Director



Gerald A. Meininger

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Education:
PhD University of Missouri-Columbia,
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Appointments:Director Dalton Cardiovascular Research Center
Margaret Proctor Mulligan Professor in Medical Research
Professor, Department of Medical Pharmacology and Physiology
Adjunct Professor, Department of Biomedical Sciences
Adjunct Professor, Department of Physics

Research

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

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

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

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

Associate Director

Michael A. Hill

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Education:
PhD & MS University of Melbourne

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

Research

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

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

Resident Investigators

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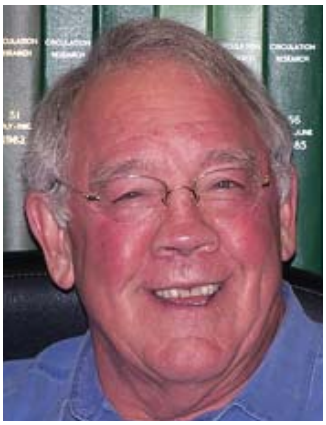
PhD University of South Alabama

Appointment: Assistant Professor, Department of Biomedical Sciences

Research

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

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



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Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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

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

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

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Education:
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Appointment: Assistant Professor, Department of Physics

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

Lane Clarke

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Education:
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Appointments: Professor, Department of Biomedical Sciences

Research

Our laboratory investigates abnormalities of acid-base transporters in cystic fibrosis and other genetic diseases that contribute to epithelial hyperproliferation and dysfunction of secretory cells in the intestinal crypts, i.e., the site of stem cell activity and cell differentiation. Studies of mice with gene-targeted deletion of CFTR (the cystic fibrosis gene) or other acid-base transporters employ in vivo, ex vivo or primary murine or human organoid culture. Mechanistic studies of molecular interactions are performed using cell lines. Functional activity of acid-base or nutrient transporters is measured in real time using fluorescence confocal or conventional microscopy and electrophysiological methods. Gene or protein expression is measured using quantitative real-time PCR, microarrays, immunoblots, immunofluorescence and laser capture microdissection. Currently, three major projects in the laboratory are funded by NIDDK or the Cystic Fibrosis Foundation. The first project investigates the role of CFTR in down-regulating the cell cycle dynamics and Wnt/β-catenin signaling in intestinal stem cells (ISCs). Loss of this regulation in cystic fibrosis (CF) results in intestinal hyperproliferation which likely contributes to the six-fold increase in the incidence of gastrointestinal cancer in the relatively young population of CF patients. The second project investigates the acid-base transporters expressed in ISCs that determine intracellular pH (pHi). Manipulation of pHi is used to control proliferation in a timed manner to offset the "bystander" damage to ISCs resulting from therapeutic doses of chemotherapeutic reagents and radiation during cancer treatment. The third project investigates goblet cell (mucus secreting) dysfunction in the CF intestine, i.e., mucoviscidosis. The goals are to investigate the factors contributing to hyperplasia of goblet cells and the causes of abnormal exocytosis. To facilitate the translational potential of the above projects, our laboratory is developing a human CFTR "rescue" mouse model in which murine CFTR is replaced by the human ortholog of the gene. This humanized CFTR mouse will also enable pharmacological testing of reagents designed to correct defective function CFTR in CF patients and pharmacological/probiotic strategies designed to combat infectious diarrheal diseases in humans.

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Education:
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Appointment: Assistant Professor, Department of Biological Engineering

Research

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

Kevin D. Gillis

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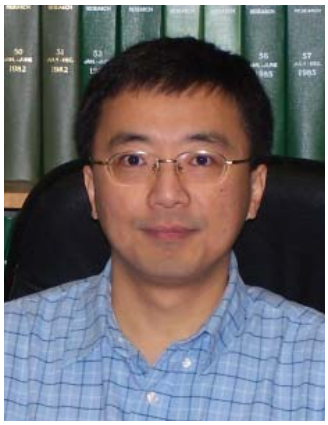
Education:
DSc, MSEE & BSEE Washington University,
BA St. Louis University

Appointment: Professor Biological Engineering, Professor Medical Pharmacology and Physiology

Research

My main area of interest is understanding the final steps of cell secretion and the modulation of these steps by calcium and second messengers. We use multiple biophysical approaches to assay dynamic aspects of secretion from individual adrenal chromaffin cells. Since calcium and second messengers 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.

Our research also has a strong engineering component with particular emphasis on developing or refining electrical and optical techniques for studying secretion. In particular, we have been developing microchips with arrays of transparent electrochemical electrodes to measure secretion of catecholamines from individual cells simultaneously with optical measurements. Other techniques in use in the lab include patch-clamp electrophysiology with membrane capacitance measurements as an assay of exocytosis/ endocytosis, photometric measurement of the intracellular Ca2+ concentration with indicator dyes, and photo- release of intracellular Ca2+ from caged compounds.



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Appointment: Associate Professor, Department of Biological Engineering

Research

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

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

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

Eileen M. Hasser

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

Research

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

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

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

Cheryl M. Heesch

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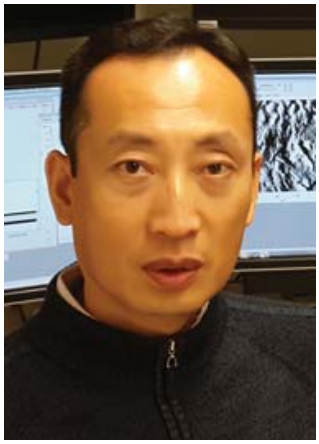
Education:
PhD University of Texas Health Science Center,
BS New Mexico State University

Appointment: Professor, Department of Biomedical Sciences

Research

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

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



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Education:
PhD: Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, China
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Appointment: Medical Pharmacology & Physiology

Research

Altering extracellular matrix protein substrates and substrate elasticity has variable effects on vascular smooth muscle cell stiffness and adhesion to fibronectin.

Tzyh-Chang Hwang

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Education:
PhD Johns Hopkins University, MD National Yang-Ming Medical School,
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Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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

Salman M. Hyder

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Education:
PhD University of Glasgow, BS University of Kent

Appointment: Professor, Department of Biomedical Sciences

Research

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

David D. Kline

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Education:
PhD Case Western Reserve University, BA Miami University

Appointment: Associate Professor, Department of Biomedical Sciences

Research

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

Several techniques are used to elucidate these mechanisms. These include 1) radiotelemetry in conscious animals to measure respiration, blood pressure or heart rate; 2) immunohistochemical localization of ion channels and neurotransmitter receptors to specific regions of the nervous system and individual neurons; 3) patch clamp techniques in isolated neurons for recording current flow through ion channels and 4) electrical recording of synaptic transmission in brainstem slices.
Using these techniques, we have recently discovered that chronic intermittent hypoxia, a model for obstructive sleep apnea, elicits a form of neural adaptation or plasticity in the brainstem. This includes changes in neurotransmitter release from presynaptic chemoreceptor afferent neurons as well as postsynaptic action potential firing. We are currently determining the mechanism of this altered neurotransmitter release.

Maike Krenz

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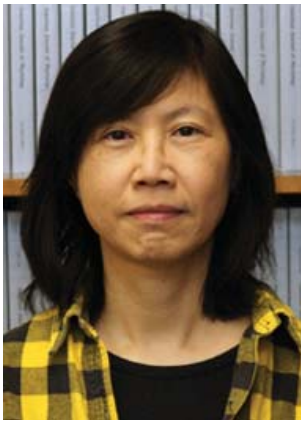
Education:
MD Germany

Appointment: Assistant Professor, Department of Medical Pharmacology and Physiology

Research

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

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



Min Li, Phd

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Education:

PhD: University of Pennsylvania, Philadelphia, PA
MS: National Taiwan University, Taipei, Taiwan
BS: Taipei Medical College, Taipei, Taiwan

Research

Vascular smooth muscle cell elasticity.

Yayun Liang

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Education:

PhD Beijing Medical University

Research

The concept of specific molecular targeting has been applied to the development of innovative cancer-treatment strategies. At present, two main approaches are available for use in clinical practice: therapeutic monoclonal antibodies and small-molecule agents. Both antibodies and small-molecule compounds are therefore promising tools for target-protein-based cancer therapy. Mutations in p53 or the p53 pathway are thought to play a key role in promoting tumor cell survival and tumor cell resistance to chemotherapeutic drugs. Therefore restoring p53 function in tumors has been pursued as a promising strategy for cancer therapy. Furthermore, Tumor cell survival, growth, and metastasis require persistent blood vessel growth or angiogenesis. A tumor cannot grow beyond the size of about 1mm in diameter without acquiring new blood vessels to nurture it. Hence, targeting tumor blood vessels and tumor angiogenesis has been as a new strategy for treatment cancer.

The aims of Liang's research are to 1) Develop innovative cancer-treatment strategies targeting mut-p53, tumor angiogenesis, and tumor blood vessels with novel antibodies and small molecules in advanced breast cancer models; 2) Define molecular signaling pathways involved in inhibition of tumor angiogenesis and induction of tumor cell apoptosis; and (c) Define the role of VEGF in tumor angiogenesis, growth, metastasis, and drug resistance.

Luis Martinez-Lemus

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

Appointment: Associate Professor, Department of Medical Pharmacology and Physiology

Research

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

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

Luis Polo-Parada

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

Appointment: Assistant Professor, Department of Medical Pharmacology and Physiology

Research

The heart is the first organ to form during embryogenesis, and its function is critical for the proper development and survival of the embryo. Although some information on ion-transport genes and their protein products in normal and diseased myocardial tissue is available, little is known about the role of cardiac extracellular matrix (ECM) proteins during cardiac development or in healthy and diseased adult hearts. My interest is to elucidate the role of the ECM in the ionic-transport proteins and molecular basis of cardiac regional electrical specialization during development and in the adult heart.
My recent studies of neural cell adhesion molecule (NCAM) null mice have indicated that NCAM plays a fundamental role in the transmitter release mechanism in neuroendocrine cells through mediation of granule recruitment. Other studies have shown that NCAM plays a functional role in the proper segregation of cell during development of islets of Langerhans in the pancreas. My interest is to elucidate whether NCAM or other cell adhesion molecules, are directly involved in the proper organization of the islets of Langerhans and in glucose-mediated insulin secretion. I also intend to investigate, whether the expression of any of these cell adhesion molecules is affected in diabetic type II patients and animal models of the disease.

Zhe Sun

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Education:
BS in chemical engineering, Chengdu University of Science & Technology, China
MS in chemical engineering, Sichuan Union University, China
PhD in bioengineering, University of Toledo, Ohio

Appointment: Medical Pharmacology & Physiology

Research

Sun's primary interest is in development of novel techniques towards understanding the dynamics of cellular interactions with the extracellular matrix (ECM). The goal is to access the cellular dynamics from both biochemical and biophysical perspectives in real-time, for example to monitor the intracellular signaling, cell adhesion with extracellular matrix proteins and the cellular mechanical activities etc.

The approaches used include live cell fluorescence imaging and FRET to monitor cellular signaling events and specific molecular interactions, and atomic force microscopy (AFM) methods to monitor the cellular mechanical activities and the interaction force between cell and ECM (usually falls in pN~nN range). As an integrated part of these studies, Sun is also interested in developing software for image processing, data analysis and computational modeling of the cellular force transmission. By integrating these techniques together, the understanding of the nature of the cell-ECM interactions will be furthered.

Xiaoqin Zou

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

Appointment: Associate Professor, Department of Biochemistry

Research

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

Non Resident Investigators

Frank W. Booth

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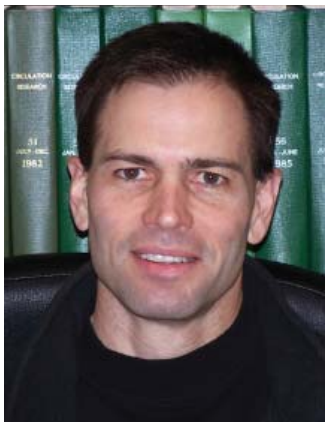
Education:
PhD University of Iowa, BS Denison University

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

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

First, we are addressing the question: what is the identity of genes in the nucleus accumbens that motivate rats that were bred to be "born-to-run" to have long distances of voluntary running in wheels, as compared to other rats that were bred to mimic "couch potato" behavior by having low distances of voluntary running?

Second, we are tackling the questions: 1) does voluntary running in wheels produce higher peak lifetime aerobic capacities than in rats without wheels for voluntary running; 2) does voluntary running attenuate primary aging-induced loss of aerobic capacity; and 3) which genes are responsible for the previous two questions?



Doug Bowles

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Education:
PhD University of Texas-Austin

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

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

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

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

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

George E. Davis

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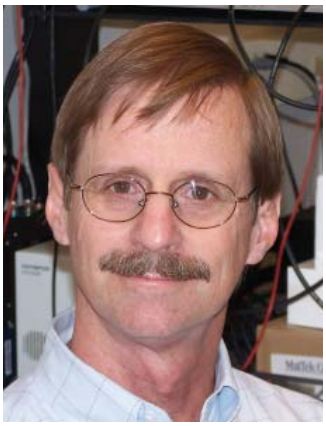
Education:
PhD, MD University of California-San Diego,
BS Arizona State University

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

My laboratory focuses on the following questions relevant to angiogenesis, wound repair and cancer research:
How do endothelial cells form cell-lined tube structures with lumens in three-dimensional (3D) extracellular matrices?
How do endothelial cells and other cell types such as tumor cells invade 3D matrices?
To what extent do endothelial cells directly or indirectly play a role in tumor invasion and metastasis?
What molecular events control the process of vascular regression?
How do vascular supporting cells, such as pericytes, stabilize vascular tubes?
How do distinct matrix metalloproteinases and their inhibitors control the processes of vascular morphogenesis versus regression in 3D matrices?
How do extracellular matrix fragments (matricryptins) regulate vascular morphogenesis versus regression in normal versus diseased states (such as diabetes)?



Michael J. Davis

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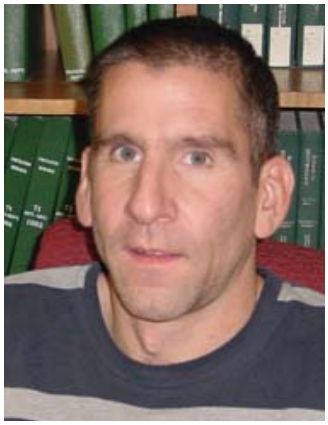
Education:
PhD University of Nebraska
BS University of California, Davis

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

Research

Current research in my laboratory focuses on the ionic mechanisms controlling contraction/pumping of lymphatic vessels. We use mouse models to address questions about the ion channels that normally control pacemaking in lymphatic muscle as well as the underlying causes of lymphatic dysfunction associated with genetic mutations in human patients with primary lymphedema. Methods used in our studies include sharp-electrode and patch-clamp electrophysiology, small vessel pressure myography, confocal microscopy, molecular biology and transgenic mouse models.

My laboratory is supported by the NIH NHLBI to investigate: 1) the ionic basis of pacemaking in lymphatic smooth muscle, 2) the pathophysiology of lymphatic muscle and valves in various models of lymphedema, and 3) the role of smooth muscle and endothelial cell connexins in controlling how electrical signals are conducted and coordinated within and along the lymphatic wall. We also collaborate with other laboratories around the world to investigate the nature of the contractile and valve defects that result in several types of primary lymphedema, including lymphedema distichiasis, Noonan syndrome and Cantu syndrome.



Paul J. Fadel

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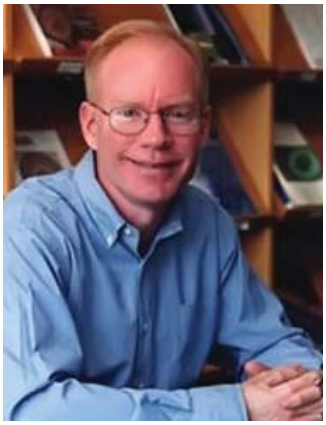
Education:
PhD University of North Texas,
MS Northeastern University, Health Science Center, BS Brooklyn College

Appointments:Associate Professor, Department of Medical Pharmacology and Physiology

Research

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



William P. Fay

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Education: BS, MD, University of Illinois

Appointments: Professor of Internal Medicine and Medical Pharmacology & Physiology

Research

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

Techniques / Methodology:

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

Research Description

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

Gabor Forgacs

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forgacsg@missouri.edu

Education:
Ph.D. Eotvos Lorand University, Budapest Hungary and Landau Institute for Theoretical Physics, Moscow, Russia

Appointments: George H Vineyard Professor of Theoretical Physics

Research

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

Shubra Gangopadhyay

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

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

Research

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

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

Kenneth A. Gruber

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

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

Research

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

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

Virginia Huxley

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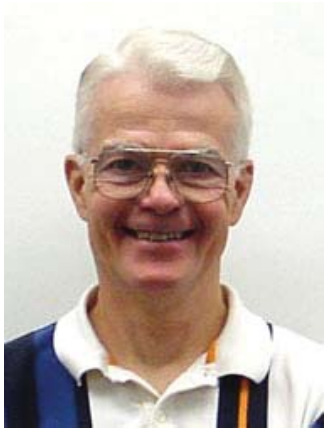
Education:
PhD University of Virginia, BA Hollins University

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

Research

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

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



Allan Jones

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Education:
PhD University of Pennsylvania

Appointments: Professor Emeritus, Medical Pharmacology & Physiology

Research

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

Ronald J. Korthuis

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Education:
PhD & BS from Michigan State University

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

Research

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

Laboratory models include study of the intact microcirculation using intravital microscopy coupled with computerized image analysis, examination of vasomotor responses in isolated arterioles, assessment of cell adhesion and permeability in single postcapillary venules, and evaluation of cell signaling mechanisms in cultured endothelial cells. A wide variety of mutant mouse models (gene knockout and transgenic 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.

M. Harold Laughlin

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Education: PhD University of Iowa, BA Simpson College

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

Research

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

Mark Milanick

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

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research Interests

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

Research Description

Erythrosensors
Our long term goal is to encapsulate glucose sensitive near infrared fluorescent dye inside red blood cells (erythrocytes). Return red cells to patient. Patient can monitor glucose levels non-invasively using a pulse oximeter type of detector for half of the lifetime of the red cells. Since the red cells live about 100 days, this means the erythrosensors only need to be made and injected about every 2 months.
This project is being done in collaboration with Tim Glass, Xiaole Shao, and Nick Cooley (Chemistry, MU) and Ken Meissner and Sarah Ritter (Bioengineering, Texas A&M).
Engineering erythrocytes to be erythrosensors: first steps. Milanick MA, Ritter S, Meissner K.
Blood Cells Mol Dis. 2011 Aug 15;47(2):100-6.
Encapsulation of FITC to monitor extracellular pH: a step towards the development of red blood cells as circulating blood analyte biosensors. Ritter SC, Milanick MA, Meissner KE. Biomed Opt Express. 2011 Jul 1;2(7):2012-21.

Approaches for resource poor areas

1. Soymilk: an effective and inexpensive blocking agent for immunoblotting. Galva C, Gatto C, Milanick M. Anal Biochem. 2012 Jul 1;426(1):22-3.
2. We are developing dipsticks for measuring levels of stress markers, including salivary cortisol and amylase for home use, as well as for detection of pesticides.
3. We have developed an educational laboratory exercise examining enzyme activity using acetylcholinesterase activity from grocery store frozen fish.
Why is that dog paralyzed? A problem-based case & laboratory exercise about neuromuscular transmission. Milanick, M., Graham, K. & Wessel, M. (2013). American Biology Teacher, 75, 36–39.

Educational innovations

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

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

2. We have developed novel interactive course offerings, including

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

Membrane Transport Kinetics

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

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

Leona J. Rubin

Office Location: E102 Veterinary Medicine
Office Phone: 573-882-5903
RubinL@missouri.edu

Education:
BA Temple University.
MS Rutgers University.
PhD University of Colorado Health Sciences Center.

Appointment: Associate Vice Chancellor for Graduate Studies & Associate Vice President of Academic Affairs & Graduate Education

Research

Dr. Rubin is a basic scientist whose research has always focused on understanding cellular signaling pathways. She began her research career at MU exploring second messenger signaling involved in control of cardiovascular function. Rodent models were employed to explore how immune mediators, released during inflammatory conditions (endotoxemia/sepsis) cause myocardial failure and/or vascular dysfunction through modulation of the activity of specific cellular targets such as potassium and calcium channels or contractile proteins. More recent work explored the signaling mechanism impacted by specific therapeutic modalities such as the anesthetic, ketamine which appears able to protect cardiovascular function during inflammatory states. Related studies utilized a swine model of atherosclerosis and the influence of gender to determine whether exercise had beneficial effects on receptor mediated signaling pathways and function of coronary smooth muscle. Studies that explored cellular signaling pathways involved in vascular metabolic vasodilation which is essential to match blood flow to tissue energy demands during exercise or disease impairment led the research to examine the role of AMP kinase, then a novel signaling pathway. Dr. Rubin's studies were the first to explore the role of AMPK in vascular smooth muscle function and metabolic vasodilation. These studies continue in the laboratory with the addition of the AMPK knock out mouse model. A serendipitous finding for this model was an interaction between AMPK alpha-1 KO and the C57Bl6 mouse strain which presents with significant cardiac hypertrophy that resembles physiologic hypertrophy. Current and future studies are directed at understanding the signaling pathway impacted by this interaction to better understand the cellular pathways that underlie exercise and disease-induced cardiac hypertrophy.

Steven S. Segal

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

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

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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

Jim R. Sowers

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

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

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

Research

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

Ronald Terjung

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

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

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

Research

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

International Investigators

Nicola J. Brown, Ph.D.

Adjunct Dalton Investigator
Office Location: Department of Oncology, University of Sheffield, S10 2RX
Office Phone: 0114 2712789
N.J.Brown@sheffield.ac.uk

Education:
PhD: University of Sheffield
BS: University of Sheffield

Appointments: Professor of Microcirculation Biology, Head of Academic Surgical Oncology Unit, Head of Microcirculation Research Group, Department of Oncology, Faculty of Medicine Dentistry and Health

Research

My research interests are mechanisms of physiological and pathophysiological angiogenesis in wound healing and tumour progression and the role of anti-angiogenic and anti-vascular strategies for the treatment of angiogenesis dependent disorders.
The principal objective and research strategy of the Microcirculation Research Group is to investigate the mechanisms regulating tumour angiogenesis in preinvasive to invasive cancer progression and how this may be targeted for therapy. The facility contains state-of-the-art specialised fluorescent in vivo microscopy and multiphoton microscopy which allows real-time imaging of blood vessel development, blood flow, leucocyte-endothelial and tumour-endothelial interactions, in a variety of preclinical in vivo models, in addition to a panel of in vitro angiogenesis assays. The clinical study of human tissue, both normal and breast cancer are complemented by laboratory based modeling, both basic and applied.

Yoshiro Sohma

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

Education:
PhD and MD Osaka Medical College

Appointment: Visiting Professor, Department of Medical Pharmacology & Physiology

Research

I have a broad research interest that covers the molecular physiology and biophysics of ion channels and transporters, and their role in the physiological function of cells/tissue. I have studied the permeation and gating of a large-conductance, Ca2+-activated, voltage-dependent potassium (BKCa) channel. BKCa channels are ubiquitously expressed in many different tissues and are known to be sensitive to membrane potential, intracellular calcium, magnesium, pH. These channels are also activated by CO and sensitive to O2 associated with heme-oxygenase2 and, moreover, some slice-variants respond to membrane stretch. Based on these findings, BKCa channels are suggested to play an important role in integrating cell signals, a recently proposed new function of an ion channel. I am also involved in a Japanese-based collaborative project undertaking a comprehensive study of the GABAergic system in peripheral tissues (not the central nervous system) and work on GABAA receptor channels and GABAB-mediated modulation of K+ and Ca2+ channels in peripheral tissues. In the Dalton Cardiovascular Research Center, I study the molecular mechanism of gating and permeation of the CFTR chloride channel, a member of the ATP-Binding Cassette (ABC) transporter superfamily, in collaboration with Dr. Tzyh-Chang Hwang. Our work has made a significant contribution to the recent advances in the biophysical understanding of the ATP-dependent gating mechanism in CFTR, and has provided great insight into a possible common functional mechanism that can be applied to the whole ABC transporter superfamily. The structure of the membrane spanning domain (MSD) in CFTR is known to be similar to that in the P-glycoprotein drug efflux pump. We therefore believe that understanding MSD structure/function in CFTR will lead to a better understanding of multi-drug resistance (MDR) proteins. In addition to investigating the biophysics of the CFTR molecule itself, I am also interested in studying the functional interactions of CFTR with other membrane proteins and lipids. This should help in our understanding of the complicated regulatory mechanisms that underlie physiological functions in cell membrane. I have also employed computer modeling to simulate ion transport processes in epithelial cells (e.g., bicarbonate transport in pancreatic duct cells). This approach is very useful to bridge information from molecular biophysics and cell/tissue physiology to the research field of epithelial transport. I believe that by taking such a general and comprehensive approach to the study of different channels/transporters and channel/transporter-mediated physiological systems, induces a 'positive cooperative effect' which accelerates each research project, and which also gives us a novel scientific standing point of view for the channel sciences.

APPENDICES

PUBLICATIONS

PRESENTATIONS

SEMINARS

ACTIVE GRANTS & CONTRACTS

PROFESSIONAL SERVICE ACTIVITIES

Christopher Baines

Publications:

Brown DA, Hale SL, Baines CP, del Rio CL, Hamlin RL, Yueyama Y, Kijtawornrat A, Yeh ST, Frasier CR, Stewart LM, Moukdar F, Raza Shaikh S, Fisher-Wellman KH, Neufer PD Kloner RA. Reduction of early reperfusion injury with the mitochondria-targeting peptide Bendavia. J Cardiovasc Pharmacol Ther. 2014; 19:121-32.

Marshall KD, Edwards MA, Krenz M, Davis JW, Baines CP. Proteomic mapping of the proteins released during necrosis and apoptosis from cultured neonatal cardiac myocytes. Am J Physiol Cell Physiol. 2014; 306:C634-5.

Kwong JQ, Davis J, Baines CP, Sargent MA, Karch J, Wang X, Huang T, Molkentin JD. Genetic deletion of the mitochondrial phosphate carrier desensitizes the mitochondrial permeability transition pore and causes cardiomyopathy. Cell Death Differ. 2014; 21:1209-17.

Gutierrez-Aguilar M, Douglas DL, Gibson AK, Domeier TL, Molkentin JD, Baines CP. Genetic manipulation of the mitochondrial phosphate carrier does not affect mitochondrial permeability transition in the heart. J Mol Cell Cardiol. 2014; 72:316-325.

Kalogeris TJ, Baines CP, Korthuis RJ. Adenosine prevents TNF□-induced decrease in endothelial mitochondrial mass through activation of eNOS-PGC1□ regulatory axis. PLoS One. 2014; 9:e98459.

Hiemstra JA, Gutierrez-Aguilar M, Marshall KD, McCommis KS, Zgoda P, Cruz-Rivera N, Jenkins N, Krenz M, Domeier TL, Baines CP, Emter CA. A new twist on an old idea part 2: cyclosporine preserves normal mitochondrial but not cardiomyocyte function in mini-swine with compensated heart failure. Physiol Rep. 2014; 2:e12050. (Co-corresponding Author).

Douglas DL, Baines CP. PARP1-mediated necrosis is dependent on parallel JNK and Ca2+/calpain pathways. J Cell Sci. 2014; 127:4134-45.

Marshall KD, Baines CP. Necroptosis: is there a role for mitochondria? Front Physiol. 2014. 5:323.

Gutierrez-Aguilar M, Baines CP. Structural mechanisms of cyclophilin D-dependent control of the mitochondrial permeability transition pore. Biochim Biophys Acta. 2014; doi:10.1016/j.bbagen. 2014.11.009

Presentations

"How to Successfully Transition From Your SDG/BGIA Early Investigator Award to the Coveted R01." Basic Cardiovascular Sciences 2014 Scientific Sessions. Las Vegas, NV. July 15th.

"An Achy Breaky Heart: heart disease in humans and animals." CVM Open House, University of Missouri-Columbia, Columbia, MO. April 12th.

"Defining Components of the Mitochondrial Pore: what is, what isn't, and what might be." Resuscitation Institute, Rosalind Franklin University of Medicine and Science, Chicago, IL. June 10th.

"Defining Components of the Mitochondrial Pore: what is, what isn't, and what might be." Department of Medical Pharmacology and Physiology, University of Missouri-Columbia, Columbia, MO. November 11th.

Active Grants:

R01HL094404 (PI: Baines) 12/2013-11/2018
NIH/NHLBI $1,250,000 direct costs
"Molecular Identity of The Cardiac Mitochondrial Pore"
Role: PI

Prostate Cancer Development Award (PI: Baines) 9/2012-9/2014
US Department of Defense $75,000 direct costs
"Inhibiting Mitophagy as a Novel Mechanism to Kill Prostate Cancer Cells"
Role: PI

Young Investigator Award (PI: Baines) 1/2013-2/2015
National Ataxia Foundation $35,000 direct costs
"Development of a new model of Friedreich's Ataxia."
Role: PI

AHA Postdoctoral Fellowship (PI: Gutierrez-Aguilar) 1/2013-12/2014
AHA Midwest Affiliate $90,722 direct costs
"The role of the mitochondrial protein C1qbp in cardiac function and disease"
Role: Sponsor

Research Contract 0035484: (PI: Emter) 1/2014–12/2014
Bristol-Myers Squibb/AstraZeneca $677,599 direct costs
"Saxagliptin attenuates cardiac hypertrophy and remodeling induced by hypertrophic stimuli"
Role: Co-I

Professional Services
Professional Activities (Study Section, Moderator, Reviewer, Committee Service, Editor, Consultant, Service to Professional Societies, etc.)

Department/Center:
Chair, Dalton Cardiovascular Research Center Safety Committee
Member, Biomedical Sciences Graduate Program Advisory Committee
Member, Biomedical Sciences Research Advisory Committee

College:
Co-Director, Veterinary Research Scholars Program, College of Veterinary Medicine
Member, Curriculum Committee, College of Veterinary Medicine
Member, Research Committee, College of Veterinary Medicine
Member, VOLUM Committee, College of Veterinary Medicine
Facilitator, VET orientation for incoming veterinary students
Grant Reviewer, Phi Zeta

National/International:
Editorial Boards: American Journal of Physiology, Heart and Circulatory Physiology
Frontiers in Physiology
Journal of Applied Physiology
Journal of Biological Chemistry
Journal of Molecular and Cellular Cardiology

Journal Reviewer: Basic Research in Cardiology
Biochimica Biophysica Acta
Circulation Research
Mitochondrion
Molecular Nutrition and Food Research
Science Translational Medicine

Study Section: NIH ZRG1 CVRS-Q Special Emphasis Panel for Member Conflicts.
NIH ZGM1 CBB-0 (MI) Competing Revisions for Macromolecular Interactions in Cells.
NIH Myocardial Ischemia and Metabolism (MIM) Study Section, Ad Hoc Reviewer.
NIH ZRG1 CB-L (55) Special Emphasis Panel on Adverse Drug Reactions in Children.

Society Service: Member, Council of the North American Section of the
International Society for Heart Research.
Member, Early Career Investigator Committee, North American Section of the International Society for Heart Research.
Chair, Ischemia, Cardioprotection & Mitochondria Interest
Group, North American Section of the International Society for Heart Research.
Judge, Senior Young Investigator Award, North American Section of the International Society for Heart Research Annual Meeting.
Abstract Grader, American Heart Association Scientific Sessions.
Member, Cardiovascular Disease Student Scholarship Committee, American Heart Association.
Member, Early Career Committee, Basic Cardiovascular Sciences Council, American Heart Association.

Edward Blaine

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

Problem-based Learning Curriculum

Continuous teaching contributions since 1992

Microcirculation (Graduate Course)

Renal Physiology (Graduate Course)

Neurohumoral Control of the Circulation (Graduate Course)

Salt and Water Homeostasis (Undergraduate Course)

Herpetology, Physiological Ecology (Undergraduate Course)

Silvia Bompadre

Publications
Combined effects of VX-770 and VX-809 on several functional abnormalities of F508del-CFTR chan-nels. Z. Kopeikin, Z. Yuksek, and S.G. Bompadre. J Cyst Fibros. 13: 508-514 (2014).

Presentations
Interaction of the isolated nucleotide binding domains of CFTR channels. Palmier M.O. and Bompadre S.G. 58th Biophysical Society Meeting. San Francisco, CA. February 2014.

Active Grants
Single-molecule studies of CFTR channels
$14,500 (5/1/2013-4/30/2015)
PI: Silvia G. Bompadre
MU Summer Research Fellowship

Fluorescence microscopy studies of CFTR channels
$23,000 (9/1/2012 – 8/31/2014)
PI: Silvia G. Bompadre
MU Research Board Grant

Professional Service
Spring 2014: : Introduction to Modern Physics (Phys 3150). Writing intensive.
Fall 2014: : Introduction to Modern Physics (Phys 3150). Writing intensive.

Reviewer for the University of Missouri Research Board
Reviewer for the Research Grants Council (Hong Kong), Telethon Italy, Frontiers in Pharmacology, Computational Biology, Journal of General Physiology, American Journal of Physiology, Science Signaling
Member of the Arts & Sciences Diversity Committee (2012-present).
Member of Department of Physics and Astronomy Personnel Committee (2014-2016)

Frank Booth

Publications

Post-dinner resistance exercise improves postprandial risk factors more effectively than pre-dinner resistance exercise in patients with type 2 diabetes. Heden TD, Winn NC, Mari A, Booth FW, Rector RS, Thyfault JP, Kanaley JA. J Appl Physiol (1985). 2014 Dec 24:jap.00917.2014. doi: 10.1152/japplphysiol.00917.2014. [Epub ahead of print] PMID:25539939

Physiology of Sedentary Behavior and Its Relationship to Health Outcomes. Thyfault JP, Du M, Kraus WE, Levine JA, Booth FW. Med Sci Sports Exerc. 2014 Sep 12. [Epub ahead of print] PMID:25222820

Timing and intensity of exercise for glucose control. Reply to Chacko E. [letter]. Booth FW, Thyfault JP. Diabetologia. 2014 Nov;57(11):2427. doi: 10.1007/s00125-014-3359-9. Epub 2014 Aug 23. No abstract available. PMID:25149071

Nucleus accumbens neuronal maturation differences in young rats bred for low versus high voluntary running behaviour. Roberts MD, Toedebusch RG, Wells KD, Company JM, Brown JD, Cruthirds CL, Heese AJ, Zhu C, Rottinghaus GE, Childs TE, Booth FW. J Physiol. 2014 May 15;592(Pt 10):2119-35. doi: 10.1113/jphysiol.2013.268805. Epub 2014 Mar 24. PMID:24665095

Unique transcriptomic signature of omental adipose tissue in Ossabaw swine: a model of childhood obesity. Toedebusch RG, Roberts MD, Wells KD, Company JM, Kanosky KM, Padilla J, Jenkins NT, Perfield JW 2nd, Ibdah JA, Booth FW, Rector RS. Physiol Genomics. 2014 May 15;46(10):362-75. doi: 10.1152/physiolgenomics.00172.2013. Epub 2014 Mar 18. PMID:24642759

Exercise biology and medicine: innovative research to improve global health. Bamman MM, Cooper DM, Booth FW, Chin ER, Neufer PD, Trappe S, Lightfoot JT, Kraus WE, Joyner MJ. Mayo Clin Proc. 2014 Feb;89(2):148-53. doi: 10.1016/j.mayocp.2013.11.013. No abstract available. PMID:24485128

Comparing serum responses to acute feedings of an extensively hydrolyzed whey protein concentrate versus a native whey protein concentrate in rats: a metabolomics approach. Roberts MD, Cruthirds CL, Lockwood CM, Pappan K, Childs TE, Company JM, Brown JD, Toedebusch RG, Booth FW. Appl Physiol Nutr Metab. 2014 Feb;39(2):158-67. doi: 10.1139/apnm-2013-0148. Epub 2013 Jul 30. PMID:24476471

Combining metformin and aerobic exercise training in the treatment of type 2 diabetes and NAFLD in OLETF rats. Linden MA, Fletcher JA, Morris EM, Meers GM, Kearney ML, Crissey JM, Laughlin MH, Booth FW, Sowers JR, Ibdah JA, Thyfault JP, Rector RS. Am J Physiol Endocrinol Metab. 2014 Feb;306(3):E300-10. doi: 10.1152/ajpendo.00427.2013. Epub 2013 Dec 10. PMID:24326426

Active Grants

Dalton Investigator Frank Booth, PhD made a 1 Million Dollar donation to MU to fund exercise research.

Booth contintued

Professional Services
Editorial Board, Journal of Applied Physiology, 1980-1993; 1996-1999; 2005-present
Editorial Board, American Journal of Physiology: Cell Physiology, 1994-present

SERVICE ON DEPARTMENTAL COMMITTEES
Departmental Faculty Promotions and Tenure Committee 2008-present
Editorial Board, American Journal of Physiology: Regulatory, integrative and Comparative Physiology
Editorial Board, Physiological Genomics, 2005-present
Editorial Board, Section III: Health and Disease, Scandinavian Journal of Medicine and Science in Sports, 2006-present

SERVICE ON COLLEGE OF VETERINARY MEDICINE (1999-PRESENT) COMMITTEES
Faculty Responsibility Committee, 2005-present

SPONSORSHIP OF CANDIDATES FOR POSTGRADUATE DEGREE

SPONSORSHIP OF POSTDOCTORAL FELLOWS

Douglas Bowles

Publications

Bender, S., V.J. de Beer, D.L. Tharp, E.D. van Deel, D.K. Bowles, D.J. Duncker, M.H. Laughlin and D. Merkus. Reduced contribution of endothelin to the regulation of systemic and pulmonary vascular tone in severe familial hypercholesterolaemia. J. Physiol. 592(Pt 8):1757-69, 2014. PMID: 24421352

Kilroy, J.P., A.L. Klibanov, B.R. Wamhoff, D.K. Bowles and J.A. Hossack. Localized in vivo model of drug delivery with intravascular ultrasound and microbubbles. Ultrasound in Medicine and Biology 40(10):2458-67, 2014. PMID:25130449

Gole, H.K.A., D.L. Tharp and D.K. Bowles. Upregulation of intermediate-conductance Ca2+-activated K+ channels (KCNN4) in porcine coronary smooth muscle requires NADPH oxidase 5 (NOX5). PLoS OnePLoS ONE 9(8): e105337, 2014. PMID:25144362

Active Grants

R44 HL097485-01 (Chen, PI; Bowles, Co-I) 9/1/11-7/31/14 8%
NIH/NHLBI: SBIR $237,000 ADC
Improved long-term biocompatibility of coronary stents by plasma coating process
Major goals: Develop a superior plasma coating for stents

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

RO1 (Fay, PI; Bowles, Co-I) 10/1/10-7/31/14 5%
NIH/NHLBI $250,000 ADC
Roles of Plasminogen Activator Inhibitor-1 and Vitronectin in Failure of Coronary Revascularization

T32 RR007004 (Franklin, PI; Bowles, Mentor) 7/1/11-6/30/16 *2%
NIH/NCRR $321,084 ADC
Postdoctoral Training in Comparative Medicine
Major goals: The major goal of this project is to provide graduate research training in comparative medicine

CVM/COR Faculty Research Grant (Bowles, PI) 1/1/14-12/31/14 *2%
$18,000 ADC
Role of KCa3.1 in plaque formation and vascular remodeling
Major goals: Use partial carotid ligation in a KCa3.1/ApoE double knockout mouse to study the role of KCa3.1 in atherosclerosis.

Professional Service
National
Manuscript Review

Reviewer, Biology Open
Reviewer, PLOSOne
Reviewer, BioMed Research International
Reviewer, Hypertension
Reviewer, Atherosclerosis, Thrombosis and Vascular Biology
Reviewer, Circulation Research
Reviewer, Journal of Applied Physiology
Reviewer, Applied Physiology, Nutrition, and Metabolism

2011-14 Nominating Committee, Cardiovascular Section, American Physiological Society

International
Editorial boards

Editorial Board of Scientifica

Nicola Brown

Publications

Atorvastatin reduces endotoxin-induced microvascular inflammation via NOSII. McGown CC, Brookes ZL, Hellewell PG, Ross JJ, Brown NJ. Naunyn Schmiedebergs Arch Pharmacol. 2015 Feb 14. [Epub ahead of print] PMID:25678054

Professional Service

Medical Research Council Clinical Training & Fellowship Panel 2006 –
Editorial Board Journal of Vascular Research 2005 -
Photochemistry and Photobiology 2003-

Current Projects

Mechanisms of angiogenesis in preinvasive and invasive breast cancer
Role of neural guidance molecules in physiological and pathophysiological angiogenesis
Vascular targeting in breast cancer and sarcomas - funded by the Breast Cancer Campaign and Yorkshire Cancer Research
Role of angiogenesis in bone metastasis - funded by EU Framework VI consortium PROMET and Yorkshire Cancer Research
Vascular targeting and imaging - funded by Cancer Research UK/EPSRC/DOH
Role of stress proteins in the breast tumour microenvironment - funded by the Breast Cancer Campaign

Lane Clarke

Publications

Liu, J, Walker, NM, Ootani, A, Strubberg, AM, Clarke, LL. Defective goblet cell exocytosis contributes to murine cystic fibrosis-associated intestinal disease. J. Clin. Invest. doi: 10.1172/JCI73193. [Epub ahead of print], 2014.

Walker, NM, Stein, SR, Williams, AM, Liu, J, Clarke, LL. Increased Functional AE2 activity does not compensate for increased pHi in Cftr knockout enteroids. Gastroenterology 146: S-50, 2014.

Liu, J, Walker, NM, Williams, AM, Clarke, LL. Abnormal exocytosis by goblet cells in the Cystic Fibrosis mouse intestine. Gastroenterology 146: S-787, 2014.

Williams, AM, Liu, J, Walker, NM, Clarke, LL. Loss of CFTR results in intestinal stem cell hyperproliferation. Gastroenterology 146: S-517, 2014.

Walker, NM, Stein, S, Williams, AM, Liu, J, Clarke, LL. Intracellular Cl- accumulation prevents pHi normalization by anion exchanger 2 (Ae2) in Cftr KO intestinal epithelium. Pediatr. Pulmonol. Suppl. 38: 242, 2014.

Liu, J, Walker, NM, Williams, AM, Clarke, LL. Ectopic degranulation within goblet cells of the Cftr knockout intestine. Pediatr. Pulmonol. Suppl. 38: 255, 2014.

Williams, AM, Liu, J, Walker, NM, Clarke, LL. Cftr negatively regulates intestinal stem cell proliferation. Pediatr. Pulmonol. Suppl. 38: 413, 2014.

Presentations

Increased Functional AE2 Activity Does Not Compensate for Increased pHi in Cftr Knockout Enteroids, 115th Annual Meeting of the American Gastroenterological Association, Digestive Disease Week, Chicago, IL. May 3, 2014

Annetti, K, Williams, A, Walker, NM, Clarke, LL. Minimizing chemotherapy-induced intestinal damage by targeting cell pH and volume. 25th Annual Merial Veterinary Scholars Symposium, Washington, DC - July 30-Aug. 1, 2014

Active Grants

National Institutes of Health R01 DK48816 – Years 15-19; "CFTR and Acid-Base Transporters in Regenerating Intestinal Crypts", 04/01/12-03/31/16 $1,518,290, PI.

Cystic Fibrosis Foundation; "Defective Goblet Cell Degranulation in Cystic Fibrosis Enteroids"; 04/01/2013-03/31/2015; $86,600, Sponsor.

Mizzou Advantage (Round 4); "Targeting Cell pH/Volume to Minimize Chemo-/Radiotherapy-Induced Intestinal Damage", 07/01/14-06/30/14, $58,000, Seed Grant, PI.

CVM COR, Faculty Research Grant; "Abnormal goblet cell biology in the cystic fibrosis intestine", 1/28/14-4/30/14, $18,000, PI.

Phi Zeta Research Grant; "The Effect of High Bicarbonate on Small Intestinal Nutrient Absorption in a Cystic Fibrosis Mouse Model", 12/18/14-11/30/15, $1000, Sponsor.

Professional Services
International

2004 - present: Cystic Fibrosis Foundation - Research and Research Training Committee (grant reviews), Regular member

2014 - Cystic Fibrosis Foundation - Genetics and Model Systems, Cystic Fibrosis Foundation, Abstract reviewer

Moderator, Cell, Organoid & Animal Models workshop, 28th North American Cystic Fibrosis Conference, Atlanta, GA, October 8-11, 2014.

Manuscript Reviews: American Journal of Physiology: Gastrointestinal and Liver Physiology
Gastroenterology
Stem Cell Research and Therapy
European Journal of Oral Sciences

National

2011-present: National Institutes of Health – Clinical, Integrative and Molecular Gastroenterology study section, Regular member

National Institutes of Health - Special Emphasis Review Panel: RFA-DK-12-012: Intestinal Stem Cell Consortium Research Projects (U01), Member

Department

Biomedical Sciences Graduate Policy Advisory Committee, member
Biomedical Sciences Promotion and Tenure Advisory Committee, member
Biomedical Sciences Reprod/Endocrine Faculty Search Committee, chair
Biomedical Sciences Pharmacology Faculty Search Committee, member

George Davis

Publications
Outside in: inversion of cell polarity controls epithelial lumen formation. Davis GE, Cleaver OB. Dev Cell. 2014 Oct 27;31(2):140-2. doi: 10.1016/j.devcel.2014.10.011. PMID:25373773

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

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

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

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

Ad hoc reviewer for the following journals:
American Journal of Physiology
Cancer
Experimental Cell Research
Journal of Virology
Clinical and Experimental Metastasis
Journal of Cell Biology
Science
Brain Research
Developmental Brain Research
Journal of Leukocyte Biology
Trends in Cardiovascular Medicine
FASEB Journal
Molecular Biology of the Cell
Developmental Dynamics
Development
Proc. Natl. Acad. Sci. USA
Microcirculation
Blood
Current Biology
Arthritis and Rheumatism
BBA-Cancer
Cancer Research
Journal of Vascular Biology
Molecular and Cellular Biology
American Journal of Pathology Journal of Cell Science
Atherosclerosis, Thrombosis and Vascular Biology

Michael J. Davis

Publications
Dougherty PJ, Nepiyushchikh ZV, Chakraborty S, Wang W, Davis MJ, Zawieja DZ, Muthuchamy M: PKC activation increases calcium sensitivity of permeabilized lymphatic muscle via myosin light chain 20 phosphorylation dependent and independent mechanisms. Am J Physiol HCP 306(5):H674-H683, 2014.

Active Grants
NIH P01 HL-095486, Mechanisms of Microvascular Control in Health and Disease:
Project 2, Regulation of vascular smooth muscle Ca2+ and BK channels by the ECM-integrin-cytoskeletal axis;
Davis MJ, Project Leader, $265,000/yr, 4/1/10-3/31/15, 25% effort

NIH P01 HL-095486, Mechanisms of Microvascular Control in Health and Disease
Project 1, Regulation of Microvascular Smooth Muscle Contraction by the ECM-Integrin-Cytoskeletal Axis;
Davis MJ, Co-I (G. Meininger, P.I.), $256,000/yr, 4/1/10-3/31/15, 5% effort

NIH R01 HL-120867, Mechanisms of lymphatic valve and pump dysfunction in lymphedema;
Davis MJ, P.I., $250,000/yr, 8/1/14-7/31/18, 30% effort

NIH R01 HL-122608, Conduction within and along the lymphatic vascular wall; Davis MJ, P.I., $270,000/yr, 12/24/14 - 12/23/18, 25% effort

NIH U01 HL-123420, Transport Phenomena in the Lymphatic System; (D. Zawieja and J. Moore, Co-P.I.), $250,000/yr, 6/1/14-5/31/19, Davis MJ, Co-I; 5% effort

NIH R01 HL-117487, Lymphatic Vessel Abnormalities in CM-AVM; (Philip King, P.I.), $250,000/yr, 12/24/14 - 12/23/18, Davis MJ, Co-I; 5% Effort

Presentations
2014 Lymphatic Gordon Conference, Il Chiocco, Italy
2014 SMUG 2014/EB 2014, San Diego, CA
2014 Children's Discovery Institute Symposium, Washington University, St. Louis
2014 ISRA, Banff, Alberta, Canada
2014 NIH Lymphatics Investigators Meeting, Bethesda, MD

Professional Services
2004- Associate Member, Smooth Muscle Research Group, University of Calgary, Alberta, Canada
2005- Margaret Proctor Mulligan Professor of Medical Research, Dept. of Medical Pharmacology & Physiology, University of Missouri, Columbia, MO

Vice-chair, Dept. of Medical Pharmacology & Physiology;
Adjunct Professor, Dept. of Internal Medicine;
Adjunct Professor, Dept. of Veterinary Biomedical Sciences;
Adjunct Professor, Dept. of Biological Engineering;
Investigator, Dalton Cardiovascular Research Center, University of Missouri

Microcirculatory Society: Member, 1983-
American Physiological Society: Member, 1986-
Biophysical Society: Member, 1990-
American Society for Biochemistry and Molecular Biology: Member, 2001-
North American Vascular Biology Organization: 1997-98, 2010-
The Physiological Society: 2011-

Editorial Boards:
American Journal of Physiology: Heart & Circulatory Physiology, 1991-99; 2001-10; 2013-
Journal of Vascular Research, 2001-
Frontiers in Vascular Physiology, 2010-

Shinghua Ding

Publications

Dynamic reactive astrocytes after focal ischemia. Ding S. Neural Regen Res. 2014 Dec 1;9(23):2048-52. doi: 10.4103/1673-5374.147929. Review. PMID:25657720

Imaging of mitochondrial Ca2+ dynamics in astrocytes using cell-specific mitochondria-targeted GCaMP5G/6s: mitochondrial Ca2+ uptake and cytosolic Ca2+ availability via the endoplasmic reticulum store. Li H, Wang X, Zhang N, Gottipati MK, Parpura V, Ding S. Cell Calcium. 2014 Dec;56(6):457-66. doi: 10.1016/j.ceca.2014.09.008. Epub 2014 Sep 30. PMID:25443655

The effects of NAD+ on apoptotic neuronal death and mitochondrial biogenesis and function after glutamate excitotoxicity. Wang X, Li H, Ding S. Int J Mol Sci. 2014 Nov 7;15(11):20449-68. doi: 10.3390/ijms151120449. PMID:25387075

Ca(2+) signaling in astrocytes and its role in ischemic stroke. Ding S. Adv Neurobiol. 2014;11:189-211. doi: 10.1007/978-3-319-08894-5_10. PMID:25236730

Histological, cellular and behavioral assessments of stroke outcomes after photothrombosis-induced ischemia in adult mice. Li H, Zhang N, Lin HY, Yu Y, Cai QY, Ma L, Ding S. BMC Neurosci. 2014 May 2;15:58. doi: 10.1186/1471-2202-15-58. PMID:24886391

Active Grants

13GRANT17020004 (Grant-in-aid) SHINGHUA DING (PI) 07/01/2013-06/30/2015
American Heart Association-Midwest Affiliate Title: Mechanistic study of neuronal protective role of PBEF in cerebral ischemia The goal of this project is to study the mechanism of PBEF in neuronal protection in ischemia with focus on the role of PBEF in mitochondrial function and biogenesis. Role: PI R01NS069726

SHINGHUA DING (PI) 05/15/2010-04/30/2015 NINDS/NIH Title: The Role of Gliotransmission in Cerebral Ischemia The goal of this project is to determine whether astrocytes play a role through gliotransmission in neuronal excitotoxicity and brain damage after ischemia using two-photon (2-P) microscopy, electrophysiology and immunocyto- and histo- chemistry. Role: PI

Professional Service

June 15, 2009-present: Member of safety committee of Dalton Cardiovascular Research Center.
August 18, 2009-present: Member of safety committee of College of Engineering.
September 2011- present: Member, Library Committee, College of Engineering.
Member of Membership Committee, American Society for Neurochemistry. March 2011-March 2015.

Reviewers for multiple Journals
2013-Peer review study section member for BRAIN 5, American Heart Association (AHA).
2013-2016: Chair of the Membership Committee for American Society of Neurochemistry (ASN).
2011-2013: Member of the Membership Committee for American Society of Neurochemistry (ASN).

Paul J. Fadel

Publications
Keller DM, Fadel PJ, Harnsberger MA, Remington GM, Frohman EM, Davis SL. Reduced spontaneous sympathetic nerve activity in multiple sclerosis patients. J Neurol Sci. 2014 Sep 15;344(1-2):210-4.

Horiuchi M, Fadel PJ, Ogoh S. Differential effect of sympathetic activation on tissue oxygenation in gastrocnemius and soleus muscles during exercise in humans. Exp Physiol. 99(2):348-58, 2014.

Ives SJ, Fadel PJ, Brothers RM, Sander M, Wray DW. Exploring the vascular smooth muscle receptor landscape in vivo: ultrasound Doppler versus near-infrared spectroscopy assessments. Am J Physiol Heart Circ Physiol. 306(5):H771-6, 2014. 12)

George KP, Fadel PJ, Taylor NA. Thematic reviews. Series III: Blood pressure regulation outside the comfort zone. 114(3):443-4, 2014.

Presentations
Vascular Consequences of Physical Inactivity. Department of Physiology, Penn State University, State College, Pennsylvania (11/14).

Methodological Considerations for Microneurographic Recordings of Sympathetic Outflow in Humans. American College of Sports Medicine Annual Meeting, Orlando, Florida (6/14)

Active Grants
"Impaired insulin-stimulated blood flow in diabetic patients: Underlying mechanisms", American Heart Association, Midwest Affiliate Grant in Aid, 10% effort, PI: Paul Fadel, 7/14-8/16, $143,000.

"Aging, Sex, and Neural Cardiovascular Control during Dynamic Exercise," National Institutes of Health, R01 HL093167, 30% effort, PI: Paul Fadel, 8/08-8/14, $1,250,000.

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

Professional Services
Associate Professor- Department of Medical Pharmacology and Physiology, University of Missouri, Columbia, MO (9/11-present)
Assistant Director for Research Training- MU Institute for Clinical and Translational Science (MU-iCATS), University of Missouri, Columbia, MO (9/11-present)

TEACHING EXPERIENCE:
Associate Professor- University of Missouri, Columbia, MO (9/05-present) Graduate Courses: Neural Control of the Circulation- 12 contact hours; Advanced Exercise Physiology- 3 contact hours; Skills in Biomedical Research- 6 contact hours, Respiratory Physiology Section of Veterinary Physiology- 3 contact hours.
Medical Courses: Problem Based Learning Tutor- Block 8.

PEER REVIEW EXPERIENCE:
Ad-hoc Manuscript Reviewer- Medicine and Science in Sports and Exercise (6/01-present)
Experimental Physiology (2/03-present)
AJP: Regulatory, Integrative and Comparative Physiology (8/03-present)
Journal of Applied Physiology (12/03-present)
European Journal of Applied Physiology (9/04-present) AJP: Heart and Circulatory Physiology (12/04-present)
Journal of Physiology (5/05-present)
Experimental Biology and Medicine (10/06-present)
Hypertension (5/07-present)
Brain Research (8/09-present)
Annals of Neurology (12/09-present)
Expert Review of Cardiovascular Therapy (2/13-present)

Editorial Board- Experimental Physiology (11/12-present)
Journal of Applied Physiology (1/11-present)
AJP: Heart and Circulatory Physiology (1/11-present)
European Journal of Applied Physiology (1/10-present)
Frontiers in Exercise Physiology (7/10-present)

Ad-hoc Grant Reviewer- Alberta Heritage Foundation for Medical Research
University of Missouri Research Board
Natural Sciences & Engineering, Research Council of Canada

Director, Medical Pharmacology and Physiology Seminar Program- University of Missouri, Columbia (6/10-present). Coordinate and manage the selection and invitation of intramural and extramural speakers with the MPP seminar committee.

Director, MU Institute for Clinical and Translational Science (MU-iCATS) Seminar Series- University of Missouri, Columbia (9/11-present). Coordinate and manage the selection and invitation of intramural and extramural speakers for monthly MU-iCATS seminars.

COMMITTEES:
American Physiological Society, Neural Control & Autonomic Regulation Section Steering Committee (7/12-present)
University of Missouri, School of Medicine Scientific Peer Review Committee (1/08-present)
Medical Pharmacology and Physiology Seminar Committee (9/08-present)
Medical Pharmacology and Physiology Graduate Education Committee (9/13-present)

TRAINEES
Current:
Seth Holwerda, PhD student, 1/2011-present, Robert Restaino, PhD student, 8/2013-present,
Leryn Boyle, PhD student, 8/2009-5/2014, Current Position: Post-Doctoral Fellow- University of Kentucky
Daniel Credeur, Post-Doctoral Fellow, 1/2012-7/2014, Current Position: Assistant Professor, School of Human Performance and Recreation, University of Southern Mississippi

William Fay

Publications

Acute isolated right ventricular myocardial infarction masquerading as acute anterior myocardial infarction. Sidhu MS, Aggarwal K, Fay WP. BMJ Case Rep. 2014 Feb 13;2014. pii: bcr2012008087. doi: 10.1136/bcr-2012-008087. No abstract available. PMID:24526191

Active Grants

NIH R01
"Roles of Plasminogen Activator Inhibitor-1 and Vitronectin in Failure of Coronary Revascularization"
PI: W. Fay (25% effort) 9/1/10-8/31/14. $250,000 annual direct costs. Impact/Priority Score: 12; %ile score: 1.0

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

NIH R44
"Improved long-term biocompatibility of coronary stents by plasma coating process"
PI: M. Chen. Dr. Fay is Co-Investigator (10% effort) 09/01/2011-02/28/2014.

Professional Services

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

Vice-Chair of Department, 2006-present
Administrative Advisory Committee, 2005-present
Space Committee, 2005-present
RIF Committee, 2005-present

Journal Review

American Journal of Physiology: Advances in Physiology Education
American Journal of Physiology: Cell Physiology
American Journal of Physiology: Heart and Circulatory Physiology
American Journal of Physiology: Regulatory, Integrative, and Comparative Physiology
Circulation Research
Journal of Applied Physiology
Journal of Vascular Research
Microcirculation
PLoS ONE

Gabor Forgacs

Publications

Predictive modeling of post bioprinting structure formation. McCune M, Shafiee A, Forgacs G, Kosztin I. Soft Matter. 2014 Mar 21;10(11):1790-800. PMID:24800270

Shubra Gangopadhya

Publications

Haisheng Zheng, Yang Zhou and Shubhra Gangopadhyay, "Size-dependent work function and single electron memory behavior of pentacene non-volatile memory with embedded sub-nanometer platinum nanoparticles", Journal of Applied Physics, 117, 024504, 2015

Francisco Ramirez-Perez, Gerardo Gutiérrez-Juárez, Sangho Bok, Keshab Gangopadhyay, Shubhra Gangopadhyay, Gary A Baker, Luis Polo-Parada "Dye-doped organosilicate nanoparticles as cell preserving labels for photoacoustic signal generation", Journal of Biomedical Nanotechnology, vol. 10, no. 11, pp. 3337–3350, 2014.

Roli Kargupta, Sangho Bok, Charles M. Darr, Brett D. Crist, Keshab Gangopadhyay, Shubhra Gangopadhyay, Shramik Sengupta, "Coatings and surface modifications imparting antimicrobial activity to orthopedic implants", Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, Volume 6, Issue 5, pages 475–495, 2014

Lei Sun, Fei Cheng, Cherian J Mathai, Shubhra Gangopadhyay, Jie Gao, Xiaodong, Yang, "Experimental Charactarization of Optical Nonlocality in Metal-Dielectric Mulitlayer Metamaterials", Optics Express 22 (19), 22974-22980, 2014

Somik Mukherjee, Balavinayagam Ramalingam, Keshab Gangopadhyay, and Shubhra Gangopadhyay, "Stability of Sub—2 nm Pt Nanoparticles on Different Support Surfaces", Journal of The Electrochemical Society 161 (4), F493-F499, 2014.

Balavinayagam Ramalingam, Haisheng Zheng, and Shubhra Gangopadhyay, "Layer-by-Layer Charging in Non-Volatile Memory Devices using Embedded Sub-2 nm Platinum Nanoparticles", Applied Physics Letters, 104 (14), 143103, 2014

Charles M. Darr, Venumadhav Korampally, Biyan Chen, Keshab Gangopadhyay, and Shubhra Gangopadhyay, "Plasmonic-Enhanced Conjugated Polymer Fluorescence Chemosensor for Trace Nitroaromatic Vapors", Sensors & Actuators: B. Chemical, 202, 1088–1096, 2014.

Steven C. Hamm, Jacob Waidmann, Joseph C. Mathai, Keshab Gangopadhyay, Luke Currano and Shubhra Gangopadhyay, "Characterization and versatile applications of low hydrogen content SiOCN grown by plasma-enhanced chemical vapor deposition", Journal of Applied Physics 116, 104902, 2014.

Rajagopalan Thiruvengadathan, Stephen W. Chung, Sagnik Basuray, Balamurugan Balasubramanian, Clay S. Staley, Keshab Gangopadhyay, and Shubhra Gangopadhyay, "A Versatile Self-Assembly Approach toward High Performance Nanoenergetic Composite using Functionalized Graphene", Langmuir, 30, pp 6556–6564, 2014.

Clay S. Staley, Kristofer E. Raymond, Rajagopalan Thiruvengadathan, Jackson J. Herbst, Sean M. Swaszek, Robert J. Taylor, Keshab Gangopadhyay, and Shubhra Gangopadhyay, "Effect of nitrocellulose gasifying binder on thrust performance and high-g launch tolerance of miniaturized nanothermite thrusters", Journal and Propellants, Explosives and Pyrotechnics, 39, 374–382, 2014.

Francisco I. Ramirez-Perez, Gerardo Gutiérrez-Juárez, Sangho Bok, Keshab Gangopadhyay, Shubhra Gangopadhyay, Gary A. Baker and Luis Polo-Parada, ,"Dye-doped Organosilicate Nanoparticles as Cell-preserving Labels for Photoacoustic Signal Generation", Journal of Biomedical Nanotechnology, 10, 3337-3350, 2014.

Roli Kargupta, Sangho Bok, Charles M. Darr, Brett D. Crist, Keshab Gangopadhyay, Shubhra Gangopadhyay and Shramik Sengupta, "Coatings and surface modifications imparting antimicrobial activity to orthopedic implants", Nanomedicine and Nanobiotechnology, 6,475–495, 2014.

Somik Mukherjee, Balavinayagam Ramalingam, and Shubhra Gangopadhyay, "Hydrogen Spillover at sub-2 nm Pt Nanoparticles by Electrochemical Hydrogen Loading", Journal of Materials Chemistry A, 2 (11), 3954-3960, 2014.

Steven C. Hamm, Sagnik Basuray, Somik Mukherjee, Shramik Sengupta, Joseph C. Mathai, Gary A. Baker, and Shubhra Gangopadhyay, "Ionic conductivity enhancement of sputtered gold nanoparticle-in-ionic liquid electrolytes", Journal of Materials Chemistry A, 2 (3), 792-803, 2014.

Ankur Gupta, Abhinav Srivastava, Cherian J. Mathai, Keshab Gagnopadhyay, Shubhra Gangopadhyay, Shantanu Bhattacharya, "Nano Porous Palladium Sensor for Sensitive and Rapid Detection of Hydrogen", Sensor Letters, 22, 1-7, 2014.

Presentations
Inexpensive Plasmonic and Photonics for Sensor and Solar Cell Applications, Missouri State University, April 24, 2014
Insensitive Nanoenergetic Materials for Microthrusters and Guided Munitions, 2014 Triservice Energetic materials Basic Science Review, Arlington, VA, September 15, 2014
Materials Genome Initiative, Western Regional Workshop, Los Angeles, CA, April 2014
University of Michigan lecture, April 2014
Missouri State University lecture on plasmonics, Springfield, MO, April 2014
Association for Research in Vision and Ophthalmology (ARVO), Orlando, FL, May , 2014

Active Grants
IREX, $32,500: "Developing the concepts of entrepreneurship, technology transfer and curriculum development of a course in entrepreneurship in a university setting at UoT," Award period 8/1/2014-2/28/2015 Role Co-I

IREX, $39,500: "Training of professors from UoT in nanotechnology projects and equipment," Award period 8/1/2014-2/28/2015 Role: PI

Coulter Translational Partnership, $141,306: "Cost Effective Plasmonic Grating Platform for Detection of Mycobacterium Tuberculosis", Award period 7/1/2014-6/30/2015. Role: PI.

Professional Service
Worked with U.S. Army Armament Research, Development and Engineering Center (ARDEC) to secure $15M in appropriations for the NanoTechnology Enterprise Consortium (NTEC)

Editorial Board of the Journal of Materials Science: Material and Electronics.

NSF Panel

Kevin Gillis

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

NIH, SBIR (to ExoCytronics LLC), $671,743 (subcontract to MU: $212,101), "Development of a prototype system for assaying exocytosis from individual cells", PI, 09/11 – 05/14.

NIH, RO1, $1,016,600, "Programmable multi-target detection using an aptamer-integrated nanopore", co-I (PI: L.-Q. Gu), 02/07 – 01/14

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

Undergraduate Graduate Student Advisor

Kenneth Gruber

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

2004-Present Lytmos Group, Inc

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

Li-Qun Gu

Publications

Probing molecular pathways for DNA orientational trapping, unzipping and translocation in nanopores by using a tunable overhang sensor. Wang Y, Tian K, Hunter LL, Ritzo B, Gu LQ.Nanoscale. 2014 Oct 7;6(19):11372-9. doi: 10.1039/c4nr03195d.PMID:25144935

Single molecule investigation of Ag+ interactions with single cytosine-, methylcytosine- and hydroxymethylcytosine-cytosine mismatches in a nanopore. Wang Y, Luan BQ, Yang Z, Zhang X, Ritzo B, Gates K, Gu LQ. Sci Rep. 2014 Aug 8;4:5883. doi: 10.1038/srep05883. PMID:25103463

Programming nanopore ion flow for encoded multiplex microRNA detection. Zhang X, Wang Y, Fricke BL, Gu LQ. ACS Nano. 2014 Apr 22;8(4):3444-50. doi: 10.1021/nn406339n. Epub 2014 Mar 26. PMID:24654890

Active Grants

R01 GM079613 02/01/07-01/31/14 $1,263,152
"Programmable multi-target dete"
National Institutes of Health

NIH, SBIR (subcontract from ExoCytronics LLC), 09/20/11-05/31/14 $100,629
"Development of a prototype system for assaying exocytosis from individual cells"

NIH, SBIR (subcontract from ExoCytronics LLC), 07/13/12-05/31/14 $111,472
"Development of a prototype system for assaying exocytosis from individual cells"

Eileen Hasser

Publications

Depressed GABA and glutamate synaptic signaling by 5-HT1A receptors in the nucleus tractus solitarii and their role in cardiorespiratory function. Ostrowski TD, Ostrowski D, Hasser EM, Kline DD. J Neurophysiol. 2014 Jun 15;111(12):2493-504. doi: 10.1152/jn.00764.2013. Epub 2014 Mar 26. PMID:24671532

H_2O_2 induces delayed hyperexcitability in nucleus tractus solitarii neurons. Ostrowski TD, Hasser EM, Heesch CM, Kline DD. Neuroscience. 2014 Mar 14;262:53-69. doi: 10.1016/j.neuroscience.2013.12.055. Epub 2014 Jan 4. PMID:24397952

Active Grants

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

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

Professional Service

Committees

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

Manuscript Review

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

Grant Review

Research Board, University of Missouri

Cheryl Heesch

Publications
Ostrowski, TD, EM Hasser, CM Heesch, DD Kline. H2O2 induces delayed hyperexcitability in nucleus tractus solitarii neurons. Neuroscience, 262: 53 -69 (2014). http://dx.doi.org/10.1016/j.neuroscience.2013.12.055

Presentations:
Tim D Ostrowski, Eileen M Hasser, Cheryl M Heesch, David D Kline. Hydrogen peroxide modulates barium-sensitive K+ currents of nucleus tractus solitarii neurons. FASEB J: 28: 686.14, 2014.

Daniela Ostrowski, Brian Ruyle, Allison Kleiber, David Kline, Cheryl Heesch, Eileen Hasser. Nucleus tractus solitarii reactive oxygen species contribute to acute intermittent hypoxia-induced long-term facilitation of phrenic and splanchnic sympathetic nerve activity. FASEB J: 28: 686.26, 2014.

K Max Coldren, Charles M Berka, David D Kline, Eileen M Hasser, Cheryl M Heesch. Corticotropin releasing hormone neurons in the paraventricular nucleus of the hypothalamus co-labeled with nNOS are activated by acute hypoxia. FASEB J: 28: 710.8, 2014.

Active Grants

"Central nervous system plasticity in Sympathoinhibition in pregnancy NIH (R01 HL091164) (Principal Investigator, 20% effort)	06/01/09- 03/31/15 (no cost extension)	~$250,000 (annual direct)
"Adaptation of brainstem circuits to chronic hypoxia" NIH R01 HL085108 (D.D. Kline, P.I.) (Co-Investigator, 1person/month effort)	04/15/08-04/14/15 (no cost extension)	$250,000 (annual direct)
"The role of gliotransmission in cerebral Ischemia" NIH-R01-NS069726 (Shinghua Ding, P.I.) (Co-Investigator, 3% effort, 0.36 person/month)	04/01/10-03/31/15	$250,000 (annual direct)
"Plasticity of nTS output neurons in acute and chronic hypoxia" NIH-R01-HL098602-A1 Multi-Investigator PD/PI = E.M. Hasser, D.D. Kline, C.M. Heesch (1.8 Calendar months/ each)	07/01/10-12/24/14	$491,679 (annual direct)
"CNS role of the ovarian hormone Relaxin In maintenance of sympathetic outflow In pregnancy." Univ. of Missouri, Research Council, #8008 PI	03/14 – 03/15	$7,500

Professional Service
Departmental:
02/06- present: Junior Faculty Mentoring Committees, Dept. Biomed ScI.
2013 - 14 Col of Vet Med Faculty Honor Code Com (3 hearings), University of Missouri, Chair 2013

College:
12/10 – present CVM COR Grant Review Committee
8/11 – 7/14 CVM Faculty Policy Committee (Ex Officio)

1985- current -(Member)American Physiological Society

2000-2014 (Wtr.) Vet. Pharmacol. VBmS 508 (VBSCI 5508) – Course Director, Autocoid, antihistamine lectures (32 contact hours total)
2012-14 (Wtr) VBmS 9467 (MPP 9437): Neural Cardio-respiratory Control (team taught) (15 lecture/contact hours)

2/2014 (Wtr Sem) PBL 3: School of Medicine--Neuro-humoral Control – 1 hr lecture

Undergraduate & Graduate Advisor

Journal Reviews:

1985-2014 Heart & Circulatory Physiology
1986-2014 Regulatory, Integrative, and Comparative
1988-2014 Hypertension
2014 Neuroscience Letters

5/09/2014 "Control of Sympathetic Nerve Activity in Pregnancy: CNS Effects of Ovarian Hormones," Grand Rounds, OB-Gyn, Univ. Missouri

Michael Hill

Publications

Large conductance Ca2+-activated K+ channel (BKCa) α-subunit splice variants in resistance arteries from rat cerebral and skeletal muscle vasculature. Nourian Z, Li M, Leo MD, Jaggar JH, Braun AP, Hill MA. PLoS One. 2014 Jun 12;9(6):e98863. doi: 10.1371/journal.pone.0098863. eCollection 2014. PMID:24921651

N-cadherin, a vascular smooth muscle cell-cell adhesion molecule: function and signaling for vasomotor control. Sun Z, Parrish AR, Hill MA, Meininger GA. Microcirculation. 2014 Apr;21(3):208-18. doi: 10.1111/micc.12123. Review. PMID:24521477

Vasoactive agonists exert dynamic and coordinated effects on vascular smooth muscle cell elasticity, cytoskeletal remodelling and adhesion. Hong Z, Sun Z, Li M, Li Z, Bunyak F, Ersoy I, Trzeciakowski JP, Staiculescu MC, Jin M, Martinez-Lemus L, Hill MA, Palaniappan K, Meininger GA. J Physiol. 2014 Mar 15;592(Pt 6):1249-66. doi: 10.1113/jphysiol.2013.264929. Epub 2014 Jan 20. PMID:24445320

Grants

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

NIH RO1HL085119 – 3/31/2016
Role of Cytokine-induced Inflammation in Endothelial Dysfunction in Diabetes Total Award (Current Period): $1,000,000 (Direct Costs) The major focus of this proposal is on vascular dysfunction in a rodent model of type 2 diabetes. Specifically focusing on how cytokines and immune cells contribute to abnormal function of endothelial cells and alter vasomotor responsiveness. Principal Investigator; Michael A. Hill, Ph.D., Effort 22.5%

Professional Service

2006 – present Associate Director
Dalton Cardiovascular Research Center
University of Missouri

2006 – present Professor of Physiology (Tenured)
Dalton Cardiovascular Research Center
Department of Medical Pharmacology and Physiology
University of Missouri

2007 – present Adjunct Professor
Department of Biological Engineering
University of Missouri

2011 – present Distinguished Research Fellow
RMIT University
Melbourne, Vic 3083.

External Joint Appointments (Current):

2011 – present Visiting Professor
Luzhou Medical College
Luzhou, China

Postdoctoral/Research Fellow Trainees Supervised

Associate Editor:
- Frontiers in Vascular Physiology (2010 – present)

Editorial Boards:
- American Journal of Physiology: Heart and Circulatory Physiology (1/96 - 12/98; 1/13 - present)
- Microcirculation (1/2002 – present)
- Journal of Vascular Research (2007 – present)
- Frontiers in Vascular Pharmacology (2010 – present)
- Frontiers in Vascular Physiology (2010 – present)

Professional Societies

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

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

TEACHING, SUPERVISION AND RELATED ACTIVITIES

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

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

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

Virginia Huxley

Publications

The P2Y2 Receptor Interacts with VE-Cadherin and VEGF Receptor-2 to Regulate Rac1 Activity in Endothelial Cells. Liao Z, Cao C, Wang J, Huxley VH, Baker O, Weisman GA, Erb L. J Biomed Sci Eng. 2014 Dec 1;7(14):1105-1121. PMID:25657827

Multi-focus image fusion using epifluorescence microscopy for robust vascular segmentation. Pelapur R, Surya Prasath VB, Bunyak F, Glinskii OV, Glinsky VV, Huxley VH, Palaniappan K. Conf Proc IEEE Eng Med Biol Soc. 2014 Aug;2014:4735-8. doi: 10.1109/EMBC.2014.6944682. PMID:25571050

Active Grants

Current:
NIH R01 DK095501-01A1 "Insulin as a Regulator of Microvascular Exchange Score 20; 9th percentile
06-01-2013 through 05-31-2017; $1,250,000 total direct

Professional Service

1996 - Director, Microvessel Core Facility
1999 - Adjunct Professor, Veterinary Biomedical Sciences, UM-Columbia School of Veterinary Medicine
2003 - Professor, Department of Medical Pharmacology & Physiology, UM-Columbia
2003 - Senior Investigator, Center for Diabetes and Cardiovascular Health
2005 - Director, National Center for Gender Physiology, UM-Columbia
2011 - Director, Pulmonary/Critical Care & Physiology Research Partnership
2011 - Professor, Department of Internal Medicine, UM-Columbia

PRIZES, AWARDS, FELLOWSHIPS:
2012-2015 Associate Editor, Journal of Physiology (London)
2010- Associate Editor, Frontiers in Vascular Physiology
Monthly Division Research Meeting/Journal Club (2011-)

Faculty of 1000, Integrative Physiology	2010-present
Associate Editor	
Frontiers in Vascular Physiology	2010-present

Editorial Board	
American Journal of Physiology: Heart & Circulatory Physiology	2011-2014
Journal of Vascular Research	1998-present
Asian Biomedicine	2007-present

Guest Reviewer	
American Journal of Physiology:	1983-present
Circulation Research	1986-
Biorheology	1989-
Biophys. Biochem. Acta	1989-
Journal of Applied Physiology	1991-
Journal of Physiology (London)	1991-
Hypertension	1996-

Microcirculation	2004 –
Cardiovascular Research	2005 –
Journal of Pharmacology and Experimental Therapeutics	2007 -
Arteriosclerosis, Thrombosis and Vascular Biology	2008 -
Journal of General Physiology	2009 -

Extra-mural Advisory Boards	
University of Arizona Training Grant Advisory Committee	2006-present
Center for Gender Physiology, Johns Hopkins University	2008-present

Tzyh-Chang Hwang

Publications

Wen-Ying Lin, Kang-Yang Jih, and Tzyh-Chang Hwang. (2014). A single amino acid substitution converts ATP into an inhibitory ligand. J. Gen. Physiol.144:311-320.

Han-I Jeh, Juinn-Tyng Yeh, and Tzyh-Chang Hwang. (2015). Modulation of CFTR gating by permeant ions. J. Gen. Physiol. 145:47-60.

Yoshiro Sohma, and Tzyh-Chang Hwang. (2015). Cystic fibrosis and the CFTR chloride channel. In: "Handbook of Ion Channels", in press.

Tzyh-Chang Hwang. (2014). CFTR: A missing link between exocrine and endocrine pancreas. Sci. China Life Sci. 57:1044-1045

Presentations

2014 International Symposium on Frontiers in Life Sciences 2014, Chongqing, China
Cystic Fibrosis in Asia from Basics to Clinics, Nagoya, Japan

Active Grants

2013 – 2015 Cystic Fibrosis Foundation, $125,000
2013 – 2015 University of Missouri, School of Medicine Bridge Fund, $38,960
2014 – 2018 NIHR01, NIDDK, "Molecular pathophysiology of cystic fibrosis", $920,000
2014 – 2016 Vertex Pharmaceuticals, $134,012
2014 – 2015 AbbVie, $35,000

Professional Service

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

2010 – present Associate Editor, Frontier in Pharmacology of Nature Products
2003 - present Editorial Board, Journal of General Physiology
2010 – present Member of College of CSR Reviewers, NIH
2014 – present Ad hoc member, ZRG1 F10A (Physiology and Pathobiology of Cardiovascular and Respiratory Systems) Study Section, NIH

Graduate and PostDoctoral Student Supervisor

Journal Reviewer: Journal of General Physiology
Grant Reviewer: Cystic Fibrosis Foundation, Italian Telethon Foundation, NIH (ZRG1 F10A, ad hoc reviewer).

Salman Hyder

Publications

Liang, Y., Mafuvadze, B/., Besch-Williford, C., Thorpe, P. and Hyder, S. M. (2014) Mutant p53 targeting compound APR-246 alone and in combination with a vascular disrupting antibody suppresses growth and metastasis of human breast cancer. 16th International p53 Workshop, Karolinska Institute, Stockholm, Sweden. Abst #0059,

Mafuvadze, B., Liang, Y., Hyder, S. M. (2014) Oxidosqualene Cyclase Inhibitor Suppresses Transcriptional Activity of Estrogen Receptor-α in Human Breast Cancer Cells. 96th Annual Endocrine Society/ICE Meeting, Chicago, IL. Abst. SAT 0279

Cook, M. T., Liang, Y., Mafuvadze, B., Besch-Williford, C. and Hyder, S. M. (2014) The Nutraceutical Luteolin Inhibits Progestin-Dependent VEGF Induction in Breast Cancer Cells and Blocks Tumor Progression in a Xenograft Model. 96th Annual Endocrine Society/ICE Meeting, Chicago, IL. Abst. PP38-1

Cook, M. T., Liang, Y., Mafuvadze, B., Zhang, J., Goyette, S. and Hyder, S. M. (2014) Therapeutic and preventive potential of nutraceutical luteolin against progestin-dependent breast cancer. Proceedings of the 19th World Congress on Advances in Oncology, Athens, Greece. Int J. Molecular Medicine 34: Abstract #118 (Oral Presentation)

Cook, M. T., Mafuvadze, B., Besch-Williford, C.; Ellersieck, M., Goyette, S. and Hyder, S. M. Luteolin Prevents Development of Progestin-accelerated 7,12- dimethylbenz(a)anthracene (DMBA)-induced Mammary Tumors in Sprague-Dawley Rats. 97th Annual Endocrine Society Meeting, San Diego, In press

Liang, Y., Mafuvadze, B., Zou, X., Besch-Williford, C., and Hyder , S. M. Inhibition of oxidosqualene cyclase blocks proliferation and survival of prostate cancer cells. 105th Annual American Association of Cancer Research Meeting, Philadelphia, USA, submitted

Goyette, S., Mafuvadze, B., Cook, M. T., Liang, Y., Hyder, S. M. Enrichment of CD44high stem-cell-like cells as a possible mechanism of progestin-dependent progression of human breast cancer. 105th Annual American Association of Cancer Research Meeting, Philadelphia, USA, submitted

Cook, M. T., Liang, Y., Goyette, S., Mafuvadze, B., Besch-Williford, C. and Hyder, S. M. Therapeutic Effects of Luteolin Against Progestin-Dependent Breast Cancer Involves Induction of Apoptosis, and Suppression of both Stem-Cell-Like Cells and Angiogenesis. 105th Annual American Association of Cancer Research Meeting, Philadelphia, USA, submitted

Cook, M. T., Liang, Y., Mafuvadze, B., Goyette, S. and Hyder, S. M. Therapeutic and preventive potential of nutraceutical luteolin against progestin-dependent breast cancer. Proceedings of the St. Jude Children Hospital Symposium. Submitted

Liang, Y., Besch-Williford, C., Aebi, J. D., Mafuvadze, B., Cook, M, T., Zou, X. and Hyder, S. M. (2014) Cholesterol biosynthesis inhibitors as potent novel anti-cancer agents: suppression of hormone-dependent breast cancer by the oxidosqualene cyclase inhibitor RO 48-8071. Breast Cancer Res Treat. 146:51-62.

Mafuvadze, B., Liang, Y. and Hyder, S. M. (2014) Cholesterol synthesis inhibitor RO 48-8071 suppresses transcriptional activity of human estrogen and androgen receptor. Oncol Rep. 32:1727-1733.

Active Grants

Hyder, S.M. (PI)
"Treatment and prevention of breast cancer using multi-functional inhibitors of cholesterol biosynthesis"
Dept of Defense Breast Cancer Pgm
$500,000-direct cost
6/1/12-5/31/15

Hyder, S. M. (PI)
"Blocking androgen receptor activity with an inhibitor of cholesterol synthesis: a novel means of suppressing prostate cancer"
Dept of Defense Prostate Cancer Pgm
$75,000 (direct cost)
9/2014-8/2015

Hyder, S. M. (PI)
"Targeting drug-resistant ovarian cancer cells using cholesterol synthesis inhibitors"
College of Veterinary Medicine, University of Missouri-Columbia (1/14-12/14)
$18,000

Hyder, S. M. (Mentor)
Franklin, C (PI)
NIH T32 RR07004 "Post-doctoral Comparative Medicine Training Grant"
Date: 07/11-06/16 (Direct cost: $169, 266/yr)

Hyder, S.M. (consultant) (Clarke, L PI)
"CFTR and acid-base transporters in regenerating intestinal crypts"
NIH-RO1 $1, 250, 000/direct cost (3/12-2/16)

University/College/Departmental Committees

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

National/International Service

National/International Service

Invited, Scientific Advisory Board International Foundation for Science (IFS) (Natural Products), Sweden,

April 2014 Manuscript Review
- BBA-Molecular Cell Research
- Carcinogenesis
- Endocrine Related Cancer
- Environmental Health Perspective
- J Agriculture & Food Chemistry
- J Clinical Endocrinology & Metabolism
- Oncogene

Ad-hoc reviewer for the following journals in 2014
- Chemical Research in Toxicology
- Drug and Chemical Toxicology
- Environmental Health Perspective
- Nutrition and Cancer
- Oncotargets

Editorial Board: Histology & Histopathology (2002-present)

Honorary Visiting Professorship, Luzhou Medical College, China (2011-2016)

Abstract Reviewer for Annual Endocrine Society Meeting 2014

Judge, Health Sciences Research Day, MU School of Medicine (2014

Recognized for discoveries at the University of Missouri in 2014 http://news.missouri.edu/2014/a-year-of-discovery/

David Kline

Publications

Moore BM, Jerry Jou C, Tatalovic M, Kaufman ES, Kline DD, Kunze DL. The Kv1.1 null mouse, a model of sudden unexpected death in epilepsy (SUDEP). Epilepsia. 2014 Nov;55(11):1808-16. doi: 10.1111/epi.12793. Epub 2014 Nov 6. PubMed PMID:25377007.

Ostrowski TD, Ostrowski D, Hasser EM, Kline DD. Depressed GABA and glutamate synaptic signaling by 5-HT1A receptors in the nucleus tractus solitarii and their role in cardiorespiratory function. J Neurophysiol. 2014 Jun 15;111(12):2493-504. doi: 10.1152/jn.00764.2013. Epub 2014 Mar 26. PubMed PMID: 24671532; PubMed Central PMCID: PMC4044435.

Presentations

Coldren KM, Berka C, Kline DD, Hasser EM, and Heesch CM (2014) Cortocotropin releasing hormone neurons in the paraventricular nucleus of the hypothalamus co-labeled with nNOS are activated by acute hypoxia. FASEB J April 2014 28:710.8

Ostrowski T, Hasser EM, Heesch CM, and Kline DD (2014) Hydrogen peroxide modulates barium-sensitive K+-currents of nucleus tractus solitarii neurons (686.14) FASEB J April 2014 28:686.14

Matott MP, Schramm C, Dantzler HA, and Kline DD (2014) Sustained hypoxia alters expression and function of excitatory amino acid transporters in the nucleus of the solitary tract (1127.2) FASEB J April 2014 28:1127.2

Ostrowski D, Ruyle B, Allison A, Kline DD, Heesch CM, and Hasser EM (2014) Nucleus tractus solitarii reactive oxygen species contribute to acute intermittent hypoxia-induced long-term facilitation of phrenic and splanchnic sympathetic nerve activity. FASEB J April 2014 28:686.26

Active Grants

1 R01 HL085108-01 (Kline DD) 4/01/2008-03/30/2015
NIH/NHLBI $250,000 direct/yr
Adaptation of brainstem circuits to chronic hypoxia
Role: PI
Currently in no cost extension

R01 HL098602 (Kline DD) 04/01/2010 –12/31/2015
NIH/NHLBI Direct: $499,999 direct/yr
Plasticity of nTS output neurons in acute and chronic hypoxia
Role: PI (MultiPI: Kline/Hasser/Heesch)
Currently in no cost extension

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

Professional Service

Committee/mentorship

Teaching Activity: Didactic and Clinical Teaching Departmental

2013-pres. Director of Graduate Studies (DGS)
2013-2014 Member, Faculty Search Committee, Dept. of Biomedical Sciences
2009-pres. Member, Research Advisory Committee (RAC)

College

2013-pres. Member, Non-Tenure Track Promotion Committee (term ends 2016)
2013-pres. Member, Computer Committee (term ends 2016)
2008-pres. Member, Animal Resources Committee (term ends 2015)
2014 Reviewer, CVM Faculty Research Awards

University

2013-2014 Member, Organizing committee for 2014 Cardiovascular Day
2009-pres. Member, Appointment and Promotions Committee, Dalton Cardiovascular Research Center
2008-pres. Member, Animal Issues Response Team (AIRT), Office of Research

National

2013-pres. Joint Programming Committee (JPC) representative, Hypoxia Interest Group of the American Physiological Society.
2011-pres. Reviewing Editor: Frontiers in Integrative Physiology

International

Journal Review

Reviewing Editor: Frontiers in Integrative Physiology, 2011-pres.

Reviewer: Journal of Physiology (London), Journal of Neurophysiology, Journal of Neuroscience, Neuroscience, Neuroscience Letters, Journal Neuroscience Methods, Journal of Applied Physiology, Brain Research, American Journal of Physiology (Regulatory, Integrative and Comparative Physiology; Cell), Respiration Physiology and Neurobiology, British Journal of Pharmacology, Experimental Physiology, Neurogastroenterology and Motility

Ronald Korthuis

Publications

Kalogeris TJ, Baines C, Korthuis RJ. Adenosine prevents TNF⊠-induced decrease in endothelial mitochondrial mass via activation of eNOS-PGC-1⊠ regulatory axis. PLoS One. 2014 Jun 10;9(6):e98459. doi: 10.1371/journal.pone.0098459

Kalogeris TJ, Y Bao, and RJ Korthuis. Invited review: Mitochondrial reactive oxygen species: A double-edged sword in ischemia/reperfusion versus preconditioning. Redox Biol 2: 702-714, 2014.

Zuidema M and Korthuis RJ. Intravital Microscopic Methods to Evaluate Anti-inflammatory Effects and Signaling Mechanisms Evoked by Hydrogen Sulfide. Methods Enzymol 3-35, 2014.

Presentations

"Emerging concepts in inflammation". Symposium at Experimental Biology 2014 (chaired session).

Adenosine prevents TNF-induced decrease in endothelial mitochondrial mass via activation of eNOS-PGC-1regulatory axis. Poster presentation, Experimental Biology 2014

"Protease-mediated arteriolar dysfunction in ischemia/reperfusion". Seminar, Department of Physiology, Georgia Regents University, September 2014.

Active Grants

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

Professional Service

Editorial Advisory Boards:

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

Associate Editor: Frontiers in Vascular Physiology: 2010 – present
PLoS One; 2013 -- present

Maike Krenz

Publications
Proteomic Mapping of Proteins Released During Cardiac Myocyte Necrosis K Marshall, MA Edwards, M Krenz, CP Baines Am J Physiol Cell Physiology (2014) 306: C639-647

The protein tyrosine phosphatase Shp2 is required for the generation of oligodendrocyte progenitor cells and myelination in the mouse telencephalon L Ehrman, D Nardini, S Ehrman, T Rizvi, J Gulick, M Krenz, B Dasgupta, J Robbins, N Ratner, M Nakafuku, R Waclaw Journal of Neuroscience (2014) 34: 3767-3778

SHP-2 deletion in post-migratory neural crest cells results in impaired cardiac sympathetic innervation JD Lajiness, P Snider, J Wang, GS Feng, M Krenz, SJ Conway Proc Natl Acad Sci (2014) 111: E1374-1382

A new twist on an old idea part 2: Cyclosporine preserves normal mitochondrial but not cardiomyocyte function in mini-swine with compensated heart failure JA Hiemstra, M Gutiérrez-Aguilar, KD Marshall, KS McCommis, PJ Zgoda, N Cruz-Rivera, NT Jenkins, M Krenz, TL Domeier, CP Baines, CA Emter Physiol Reports (2014) Jun 24;2(6). pii:e12050

The Q510E mutation in Shp2 perturbs heart valve development by increasing cell migration MA Edwards, K Crombie, C Schramm, M Krenz J Appl Physiol (2015) Jan 1; 118: 124-131 (ePub ahead of print 10/30/2014)

Presentations
21st Annual Cardiovascular Day, Columbia, February 18, 2014
Electrocardiographic Abnormalities in a Transgenic Mouse Model of Noonan Syndrome with Multiple Lentigines (NSML)

Active Grants
1R01HL116525-01, Research Project Grant (R01), NIH/NHLBI, Krenz (PI)
Title: SHP2 controls cardiac stress adaptation
07/24/2013 – 06/30/2017 (total cost $1,437,357)
Role: PI

0035484, Research Contract, Bristol-Myers Squibb/AstraZeneca, Emter (PI)
Title: Saxagliptin attenuates cardiac hypertrophy and remodeling induced by hypertrophic stimuli
01/01/2013 – 12/31/2014 (total cost $1,370,197)
Role: Collaborator (5% effort = 0.6 calendar months 01/01/2014 – 12/31/2014)

NIH/ NCATS, TRND program
Use of Rapamycin for the Treatment of Hypertrophic Cardiomyopathy in Patients with LEOPARD Syndrome (Key Investigator Kontaridis)
06/01/2013 – 05/31/2017
Role: Co-Investigator, 0% effort

Professional Service
2014 PBL Block 3 Jan – Feb facilitator for 8 M1 Medical Students
2014 PBL Block 3 Jan – Feb mentor for 1 Family Medicine resident

2014 Skills in Biomedical Research: I presented 1 lecture to graduate students focusing on genetic engineering in mice (2 hrs). (6 Students)

2014 Veterinary Physiology (#8420) I was co-director for the Graduate Portion of this class and I taught one 2-hr class on cardiovascular physiology (6 students)
2014, May-July Mentor, Summer Research Fellowship
2014 – present Graduate and Undergraduate Mentor
2012 – present Dissertation Committee Member

2014 "Speed Science" Event, Health Sciences Research Day, MU School of Medicine

2009 – present Member, Dalton Safety Committee

2011 – present Member, Dalton Science Display Committee
2011 – present Member, MPP Graduate Education Committee

2011 – present MPP representative, School of Medicine Faculty Affairs Council
2014 "Speed Science" Event, Health Sciences Research Day, MU School of Medicine

2013 – 2014 Member, Cardiovascular Day Organizing Committee
2014 Session Chair, Cardiovascular Day

1999 – present Member, International Society for Heart Research (ISHR), North American Section
2010 – present Member, American Physiological Society
2010 – present Member, American Heart Association

April 2014 AHA Study Section CVD2, member
August 2014 NIH/NHLBI Special Emphasis Panel ZHL1 CSR-I (F1) 1 (R13/U13), member

ad hoc Reviewer
2000 – present American Journal of Physiology, Heart and Circulation Physiology

Trends in Cardiovascular Medicine	Basic Research in Cardiology
Yonsei Medical Journal	Circulation Research
Pro Natl Acad Sci	Coronary Artery Disease
PLOS ONE	FEBS Letters
Journal of Vascular Research	Frontiers in Integrative Physiology
Journal of Cardiac Failure	Journal of Applied Physiology

Journal of Molecular and Cellular Cardiology
Dec 2014 Congressionally Directed Medical Research Program (CDMRP), Review Panel member
Jan 2015 Congressionally Directed Medical Research Program (CDMRP), Review Panel member (Please note this was a different panel from the Dec 2014 review. The exact names of the panels are classified information.)

Apr 2014 AHA Study Section CVD2, member
Aug 2014 NIH/NHLBI Special Emphasis Panel ZHL1 CSR-I (F1) 1 (R13/U13), member

Harold Laughlin

Publications

Simmons GH, Padilla J, Jenkins NT, and Laughlin MH. Exercise training and vascular cell phenotype in a swine model of familial hypercholesterolaemia: conduit arteries and veins. Exp Physiol. 2014 Feb;99(2):454-65. [PubMed - in process]

Sheldon RD, Roseguini BT, Laughlin MH, and SC Newcomer. New insights into the physiologic basis for intermittent pneumatic limb compression as a therapeutic strategy for peripheral artery disease. J. Vasc Surg 58:1688-1696, 2013. PMID: 24213857

Padilla J, Jenkins NT, Thorne PK, Martin JS, Rector RS, Davis JW, Laughlin MH. Transcriptome-wide RNA sequencing analysis of rat skeletal muscle feed arteries. Part II: Impact of exercise training in obesity. J Appl Physiol 2014; 116(8):1033-1047. PMID:24408995. (PubMed in process)

Bender SB, de Beer VJ, Tharp DL, van Deel ED, Bowles DK, Duncker DJ, Laughlin MH, Merkus D. Reduced contribution of endothelin to the regulation of systemic and pulmonary vascular tone in severe familial hypercholesterolaemia. J Physiol 2014 592(Pt 8):1757-69 PMID: 24421352 (PubMed - as supplied by publisher]

de Beer VJ, Merkus D, Bender SB, Tharp DL, Bowles DK, Duncker DJ, Laughlin MH. Familial hypercholesterolemia impairs exercise-induced systemic vasodilation due to reduced NO bioavailability. J Appl Physiol (1985). 2013 Dec;115(12):1767-76. Epub 2013 Oct 24. PMID: 24157527 [PubMed - in process]

Zhou Z, de Beer VJ, de Wijs-Meijler D, Bender SB, Hoekstra M, Laughlin MH, Duncker DJ, Merkus D. Pulmonary vasoconstrictor influence of endothelin in exercising swine depends critically on phosphodiesterase 5- activity. Am J Physiol Lung Cell Mol Physiol. 2014. 306 (6):H918-27. PMID: 2464751 [PubMed - as supplied by publisher]

McKenney ML, Schultz KA, Boyd JH, Byrd JP, Alloosh M, Teague SD, Arce-Esquivel AA, Fain JN, Laughlin MH, Sacks HS, Sturek M. Epicardial adipose excision slows the progression of porcine coronary atherosclerosis. J Cardiothorac Surg. 2014 Jan 3;9(1):2. PMID: 24387639 [PubMed - as supplied by publisher]

Linden MA, Fletcher JA, Morris EM, Meers GM, Kearney ML, Crissey JM, Laughlin MH, Booth FW, Sowers JR, Ibdah JA, Thyfault JP, Rector RS. Combining Metformin and Aerobic Exercise Training in the Treatment of Type 2 Diabetes and NAFLD in OLETF Rats. Am J Physiol Endocrinol Metab. 2013 Dec 10. [Epub ahead of print] PMID: 24326426 [PubMed - as supplied by publisher]

Jenkins NT, Padilla J, Thorne PK, Martin JS, Rector RS, Davis JW, Laughlin MH. Transcriptome-wide RNA sequencing analysis of rat skeletal muscle feed arteries. Part I: Impact of obesity. J Appl Physiol 2014; 116(8):1017-1032. PMID:24436298. (PubMed in process)

Padilla J, Jenkins NT, Thorne PK, Lansford KA, Fleming NJ, Bayless DS, Sheldon RD, Rector RS, Laughlin MH. Differential regulation of adipose tissue and vascular inflammatory gene expression by chronic systemic inhibition of NOS in lean and obese rats. Physiol Reports 2014; 2(2):e00225 PMID:24744894.

Sheldon RD, Laughlin MH, Rector RS.
Reduced hepatic eNOS phosphorylation is associated with NAFLD and type 2 diabetes progression and is prevented by daily exercise in hyperphagic OLETF rats. J Appl Physiol (1985). 2014 May 1;116(9):1156-64. PMID: 24577062 (Pubmed in Process)

Crissey JM, Jenkins NT, Lansford KA, Thorne PK, Bayless DS, Vieira-Potter VJ, Rector RS, Thyfault JP, Laughlin MH, Padilla J. Adipose tissue and vascular phenotypic modulation by voluntary physical activity and dietary restriction in obese insulin-resistant OLETF rats. Am J Physiol Regul Integr Comp Physiol. 2014 Apr 15;306(8):R596-606. PMID 24523340 [PubMed - indexed for MEDLINE]

Linden MA, Fletcher JA, Morris EM, Meers GM, Laughlin MH, Booth FW, Sowers JR, Ibdah JA, Thyfault JP, Rector RS. Treating NAFLD in OLETF rats with vigorous-intensity interval exercise training. Med & Sci Sport and Ex. In Press 2014. PMID: 2498336. (PubMed as supplied by publisher)

Mortensen SP, McAllister RM, Yang HT, Hellsten Y, and Laughlin MH. The effect of purinergic P2 receptor blockade on skeletal muscle exercise hyperemia in miniature swine. Eur J Appl Physiol 2014; 114(10):2147-55. PMID:249620002. (PubMed as supplied by publisher).

Zhou Z, de Beer VJ, Bender SB, Jan Danser AH, Merkus D, Laughlin MH, Duncker DJ.
Phosphodiesterase-5 activity exerts a coronary vasoconstrictor influence in awake swine that is mediated in part via an increase in endothelin production. Am J Physiol Heart Circ Physiol. 306(6):H918-H927, 2014. PMID: 24464751 [PubMed - indexed for MEDLINE]

Sanzari JK, Billings PC, Wilson JM, Diffenderfer ES, Arce-Esquivel AA, Thorne PK, Laughlin MH, Kennedy AR. Effect of electron radiation on vasomotor function of the left anterior descending coronary artery. Life Sci Space Res. 4(2015) 6-10.

Padilla J, Jenkins NT, Thorne PK, Martin JS, Rector RS, Davis JW, Laughlin MH. Identification of genes whose expression is altered by obesity throughout the arteral tree. Physiol Genomics 2014; 46(22):821-32. PMID: 25271210 (PubMed in process)

Gielen S, Laughlin MH, O'Conner C, Duncker DJ. Exercise training in patients with heart disease: Review of beneficial effects and clinical recommendations. Prog. Cardiovasc. Dis. 2014 PMID 25459973

Credeur DP, Holwerda SW, Restaino RM, King PM, Crutcher KL, Laughlin MH, Padilla J, and Fadel PJ. Characterizing rapid onset vasodilation to single muscle contractions in the human leg. J Appl Physiol In Press. 2014

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

Professional Service
Administrative Activity:
Chair of Biomedical Sciences
Curators' Professor

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

Manuscript Review for Journals:

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

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

Min Li

Publications

Hong Z, Sun Z, Li M, Li Z, Bunyak F, Ersoy I, Trzeciakowski JP, Staiculescu MC, Jin M, Martinez-Lemus L, Hill MA, Palaniappan K, Meininger GA. (2014) Vasoactive agonists exert dynamic and coordinated effects on vascular smooth muscle cell elasticity, cytoskeletal remodelling and adhesion. J Physiol. 592(Pt 6):1249-66.

Nourian Z, Li M, Leo MD, Jaggar JH, Braun AP, Hill MA. (2014) Large conductance Ca2+-activated K+ channel (BKCa) α-subunit splice variants in resistance arteriesfrom rat cerebral and skeletal muscle vasculature. PLoS One. 9(6):e98863.

Yayun Liang

Publications

Liang Y, Besch-Williford C, Aebi J.D., Mafuvadze B, Cook M.T., Zou X, and Hyder, S.M. (2014) Cholesterol biosynthesis inhibitors as potent novel anti-cancer agents: suppression of hormone-dependent breast cancer by the oxidosqualene cyclase inhibitor RO 48-8071. Breast Cancer Research and Treatment, 146:51–62

Mafuvadze, B., Liang, Y, and Hyder, S. M. (2014) Cholesterol synthesis inhibitor RO 48-8071 suppresses transcriptional activity of human estrogen and androgen receptor. Oncology Report, 32:1727-1733.

Presentations

Matthew Cook, Yayun Liang1, Benford Mafuvadze, Cynthia Besch-Williford, Salman M. Hyder (2014) The Nutraceutical Luteolin Inhibits Progestin-Dependent VEGF Induction in Breast Cancer Cells and Blocks Tumor Progression in a Xenograft Model. 96th Annual Endocrine Society Meeting, June 21-24, Chicago, Illinois.

Benford Mafuvadze, Yayun Liang, and Salman M. Hyder (2014) Oxidosqualene Synthase Inhibitor Suppresses Transcriptional Activity of Estrogen Receptor-α (ERα) in Human Breast Cancer Cells. 96th Annual Endocrine Society Meeting, June 21-24, Chicago, Illinois.

Active Grants

Liang, Yayun (Co-I), Hyder, S. M (PI), "Blocking Androgen Receptor Activity with an Inhibitor of Cholesterol Synthesis: A Novel Means of Suppressing Prostate Cancer" Department of Defense Breast Cancer Pgm. Total cost: $151500.00 (6/1/14-5/30/15).

Liang, Yayun (Co-I), Hyder, S. M (PI), "Treatment and prevention of breast cancer using multi-functional inhibitors of cholesterol biosynthesis" Dept of Defense Breast Cancer Pgm $500,000-direct cost (8/1/12-7/31/14).

Liang, Yayun (Co-I), Hyder, S. M (PI), "Targeting drug-resistant ovarian cancer cells using cholesterol synthesis inhibitors" College of Veterinary Medicine, University of Missouri-Columbia, $18,000, (1/14-12/14)

Professional services

Member of The Science Advisory Board (Since 2014). Editorial Board of Journal of Heart Health (Since 2014)
Editorial Board of Chinese Journal of Clinicians (International) (2011-2014)
Active member of American Association for Cancer Research (1997-present)
Active member of Women in Cancer Research (2002-present)
Active member of Minorities in Cancer Research (2009-present)

Luis Martinez-Lemus

Publications

Hong, Z., Z. Sun, M. Li, Z. Li, F. Bunyak, I. Ersoy, J.P. Trzeciakowski, M.C. Staiculescu, M. Jin, L.A. Martinez-Lemus, M.A. Hill, K. Palaniappan, and G.A. Meininger, 2014. Vasoactive agonists exert dynamic and coordinated effects on vascular smooth muscle elasticity, cytoskeletal remodeling and adhesion. J. Physiol. (In Press, Epub ahead of print Jan. 20, 2014

Active Grants

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

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

Professional Service

- European Society for Microcirculation
- American Physiological Society
- Microcirculatory Society
- Poultry Science Association

- Appointed member of the subcommittee for animal studies at the Harry S. Truman Memorial Veterans Hospital, 800 Hospital Dr. Columbia, MO 65201 (December 2013-2016)
- International Society for Resistance Arteries (ISRA) 2014 Tri-annual Conference Organization Commit tee (2013-2014)
- American Physiological Society-Cardiovascular Section: NIH Liaison Committee (2012-2015)
- Microcirculatory Society: Councilor (2011-2014)
- Appointed member of the Dalton Cardiovascular Research Center Safety Committee (2009-Present).
- Appointed member of the Appointment and Promotions Committee for non-tenure track faculty within the Dalton Cardiovascular Research Center, University of Missouri-Columbia (2006-Present).

Editorship

- Editorial Board Member for "CardioRenal Medicine," 2012-Present.
- Review Editorial Board for "Frontiers in Vascular Physiology," 2010-Present.
- Editorial Board member for "Microcirculation," 2010-2015

Reviewer

- Journal of Vascular Research
- Arteriosclerosis, Thrombosis, and Vascular Biology
- American Journal of Physiology
  - Heart and Circulatory Physiology
  - Regulatory, Integrative and Comparative Physiology
- Clinical and Experimental Medicine
- The Anatomical Record
- Experimental Physiology
- Poultry Science
- BioMed Central Cell Biology
- Hospital Practice
- Microcirculation
- Hypertension
- Clinical and Experimental Pharmacology and Physiology
- Anatomical Record
- PLOS-One

2009-Current Teaching advance imaging techniques (Fuorescence, Confocal and Multiphoton Microcopy) to graduate students at the Department of Medical Pharmacology and Physiology, University of Missouri-Columbia as part of the course entitled "Skills in Biomedical Research" (course # MPP8420).

2010-Current Coordinating the Journal Club for graduate students at the Department of Medical Pharmacology and Physiology, University of Missouri-Columbia (course # MPP9422).

2008-Current Teaching Microvascular Function to graduate students in the Department of Medical Pharmacology and Physiology, University of Missouri-Columbia as part of the course entitled "Microvascular Circulatory Function" (course # MPP9434).

2010-Current Teaching Extracellular Matrix-Dependent signaling to graduate students in the course entitled "Transmembrane Signaling" within the Department of Medical Pharmacology and Physiology, University of Missouri-Columbia (course # MPP9426).

2010-Current Tutor for second year medical students in the Problem Based Learning Course for Endocrinology and the Gastrointestinal Systems, School of Medicine, University of Missouri-Columbia.

Graduate student & PhD advisor and committee member

Gerald Meininger

Publication
Amini, S., Z. Sun, A. Juriani, G.A. Meininger and K.E. Meissner. Characterization of the evanescent field surrounding QD-embedded microspheres supporting whispering gallery modes, The European Physical Journal: Special Topics, 223:2023-2033, 2014 {Shared senior authorship, Co-Corresponding Authors}

Meininger, GA. The central importance of the cytoskeleton for increased cell stiffness in cardiovascular disease. Editorial Focus. American Journal of Physiology-Cell Physiology, 2014. PMID: 25122875 (In press)

Staiculescu M.C., F.I. Ramirez-Perez, J.A. Castorena-Gonzalez, Z. Hong, Z. Sun, G.A. Meininger and L.A. Martinez-Lemus. Lysophosphatidic acid induces integrin activation in vascular smooth muscle cells and alters myogenic vasoconstriction. Frontiers in Vascular Physiology, 2014. (In press)

Sehgel N.L., Z. Sun, Z.Hong, W.C. Hunter, M.A. Hill, D.E. Vatner, S.F. Vatner, G.A. Meininger. Augmented Vascular Smooth Muscle Cell Stiffness and Adhesion when Hypertension is Superimposed on Aging. Hypertension, 65:xx-xx, 2015. (Shared Senior Authorship and Corresponding Author) DOI: 10.1161, PMID: xxx, PMCID: xxx. (Epub)

Sun Z., S. Huang, Z. Li and G.A. Meininger. A mechanotransducing role for N-cadherin in vascular smooth muscle. Journal of Physiology, 2014. (In revision)

Presentations
N.L. Sehgel, Y. Zhu, Z. Sun, W.C. Hunter, J.P. Trzeciakowski, D.E. Vatner, G.A. Meininger, S.F. Vatner. Aortic Smooth Muscle Cell Stiffness Contributes to Increased Aortic Stiffness in Hypertensive Aging. Multi-scale Mechanobiology: From Morphogenesis to Nuclear Mechanotransduction. La Jolla, CA, January 7 - 11, 2014.

N.L. Sehgel, Y. Zhu, Z. Sun, W.C. Hunter, J.P. Trzeciakowski, D.E. Vatner, G.A. Meininger, S.F. Vatner. Intrinsic Aortic Smooth Muscle Cell Stiffness Contributes to Increased Aortic Stiffness in Hypertensive and Aging. 10th Asian Pacific Congress of Hypertension. Cebu, Philippines; February 12-14, 2014.

G.A. Meininger, Z. Hong, Z. Sun, M. Li, Z. Li, F. Bunyak, I. Ersoy, J.P. Trzeciakowski, M. C. Staiculescu, L.A. Martinez-Lemus, M.A. Hill, K. Reeves, K. Palaniappan. Dynamic effects of vasoactive agonists on vascular smooth muscle cell elasticity, cytoskeletal remodeling and adhesion. XVI. Annual Linz Winter Workshop, Linz, Austria, January 31-February 3, 2014.

N.L. Sehgel, Y. Zhu, Z. Sun, W.C. Hunter, J.P. Trzeciakowski, D.E. Vatner, S.F. Vatner, G.A. Meininger. Vascular Smooth Muscle Cell Stiffness: a Novel Mechanism for the Increased Aortic Stiffness in Hypertensive and Aging. Biophysical Society Meeting, San Francisco, February 15-19, 2014.

L. Xie, Z. Sun, Z. Hong, N.J Brown, O.V. Glinskii, V.V. Glinsky, G.A Meininger. Cell confluency affects the cortical stiffness of human bone marrow endothelial cells. Experimental Biology, San Diego, April 26-30, 2014.

Z. Sun, M. Li, Z. Li, M.A. Hill, G.A. Meininger. N-cadherin Adherens Junctions in Rat Cerebral Artery Are Mechano-sensitive. Experimental Biology, San Diego, April 26-30, 2014.

Z. Hong, M. Jin, F. Bunyak, I. Ersoy, Z. Sun, Z. Li, K. Palaniappan, G.A. Meininger. The effect of substrate elasticity on the mechanical and adhesion of vascular smooth muscle cells. Experimental Biology, San Diego, April 26-30, 2014.

K. Hong, G.A. Meininger, M.A. Hill. Exogenous Diacylglycerol Restores Arteriolar Myogenic Constriction Following Candesartan. Experimental Biology, San Diego, April 26-30, 2014.

A.R. Aroor, V. DeMarco, G. Jia, Z. Sun, M. Garro, L.A, Martinez-Lemus, G.A Meininger and J.R. Sowers. Increased endothelial cell stiffness and impaired diastolic function in western diet fed female mice. ICE/Endocrinology Meeting, Chicago, IL June 21-24, 2014.

L. Xie, Z. Sun, Z. Hong, N.J. Brown, O.V. Glinskii, V.V. Glinsky, G.A. Meininger. Elastic properties of human bone marrow endothelial cells analyzed by atomic force microscopy. 21st Annual Cardiovascular Day Meeting, University of Missouri, Columbia, MO February 2014.

M.A. Hill and G.A. Meininger. Mechanisms Underlying the Local Control of Microvascular Blood Flow. Myocardial Ischemia Symposium, Millennium Hilton, Seoul, SOUTH Korea, March 2014.

Z. Hong, M. Jin, F. Bunyak, I. Ersoy, Z. Sun, M. Li, Zhaohui Li, J.P. Trzeciakowski, M.A. Hill, K. Palaniappan, G.A. Meininger. Vasoactive agonists effects on vascular smooth muscle are associated with coordinated changes in cell elasticity, adhesion and cytoskeletal remodeling. World Congress of Biomechanics, Boston, MA, July 2014.

M. Collins, Y. Ji, G.A. Meininger, W. Fay, M.A. Hill. Impact of Arterial Grafting on the Mechanical Properties of Mouse Inferior Vena Cava. World Congress of Biomechanics, Boston, MA, July 2014.

L.A. Martinez-Lemus, M.C. Staiculescu, J. Castorena-Gonzalez, Z. Hong, M.A. Hill, G.A. Meininger. Role of the vascular smooth muscle cytoskeleton on vasoconstriction-induced remodeling of resistance arteries. 11th International Symposia on Resistance Arteries (ISRA 2014), Banff, Canada September 7-11,2014.

G. Jia, A.R. Aroor, V.G. DeMarco, Z.Sun, B.P. Bostick, G.A. Meininger, I. Jaffe and J.R. Sowers. Mineralocorticoid receptors mediate western diet – induced macrophage polarization and vascular stiffness. High Blood Pressure Research Council Meeting, October 2014.

A.R. Aroor, V.G. DeMarco, G. Jia, J. Habibi, Z. Sun, M. Garro, G.A. Meininger and J.R. Sowers. Dipeptidyl peptidase-4 (DPP-4) inhibition decreases cardiac and vascular stiffness and improves cardiac and vascular relaxation in western diet fed mice. High Blood Pressure Research Council Meeting, October 2014.

S. Dhar, G.A. Meininger and M.A. Hill. Advanced glycation of fibronectin converts vascular smooth muscle integrin to RAGE signaling mediated mechanisms. Microcirculatory-NAVBO Meeting, Monterey, CA, October 19-23, 2014.

"Vasoactive agonists exert dynamic and coordinated effects on vascular smooth muscle cell elasticity, cytoskeletal remodeling and adhesion", Department of Bioengineering, Imperial College London, UK, February 2014.

"VSMC Contraction: A coordinated dance between cell elasticity, adhesion and cytoskeletal remodeling", School of Medicine, University of Nottingham, Nottingham, UK, March 2014.

"Coordination of VSMC contraction and VSMC adhesion for efficient contractile function", Magdalan College, Department of Pharmacology, Oxford University, Oxford, UK, June 2014.

"Atomic force microscopy applied to cell biological studies: Emphasis on cardiovascular biology", AFM Users Supergroup on Single Molecule Research, University of Missouri, Columbia, MO, August 20, 2014.

"Efficient coordination of VSMC contraction with extacellular matrix adhesion", Luzhou Medical College, Luzhou, China, September 10-13, 2014.

"Arteriole and VSMC are not what they used to be", Department of Medical Pharmacology and Physiology, University of Missouri, Columbia, MO, November 2014.

Active Grants

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

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

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

National Institutes of Health-National Heart, Lung and Blood Institute, R01, SFRP2, cell survival, and coronary vascular angiogenesis, Principal Investigator, D.E. Vatner (Rutgers University), Co-Investigator, G.A. Meininger (5%), $310,670 for 07/01/2013-08/30/2018.

Professional Service

APS: Conference Committee, Chair, 2011-2013.
Commission II – Circulation/Respiration; Section: Microcirculation; Member 2002-2009; Chair, 2010-2015.
Member, US National Committee to the International Union of Physiological Sciences, 2006-present.

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

Editorial Boards
Editorial Board Member for Frontiers in Cardiovascular and Smooth Muscle Pharmacology, 2010-present.

Editorial Board Member for International Journal of Physiology, Pathophysiology and Pharmacology, 2010-present.

Editorial Board Member for Nanotechnology, Science and Applications, 2007-present.

Editorial Board Member for Microcirculation, 1993-1999; 2003-2009; 2010-2012.

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

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

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

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

Member of Graduate and Doctoral Faculty at the University of Missouri-Columbia, September 2005-Present.

Member Council of Chairs, School of Medicine, University of Missouri-Columbia, September 2005-Present.

Member Center Directors Council, Office of Research, University of Missouri-Columbia, October 2005-Present.

Member Core Imaging Facility, Dalton Cardiovascular Research Center, University of Missouri-Columbia, September 2005-Present.

Mark Milanick

Active Grants
NIH R21 DK09186 Developing a non-invasive monitoring system using NIR dyes inside erythrocytes
233,719 non-competitive renewal.

Professional Services
Graduate Student Committees

Journal Reviewer: Journal of Physiology

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

2010-present Chair, Campus Minority Affairs Committee
2008-present Departmental Doctoral Faculty Review Committee
2012-present MU Status of Women Committee

Luis Polo-Parada

Publications

Sudhir Ravula, Jeremy B. Essner, Wendy A. L, Luis Polo-Parada, Roli Kargupta, Garret J. Hull, Shramik Sengupta, and Gary A. Baker. (2014). Sunlight-assisted route to antimicrobial plasmonic aminoclay catalysts. Nanoscale. In Press. DOI: 10.1039/C4NR04544K.

A., Guadarrama-Santana, A. Garcia-Valenzuela, F Perez-Jimenez and Luis Polo-Parada (2014). Interdigitated capacitance sensor in the mm scale with sub-femto Farad resolution suitable for monitoring processes in liquid films. Revista Mexicana de Fisica. In Press.

Francisco I. Ramirez-Perez, Gerardo Gutiérrez-Juárez, Sangho Bok, Keshab Gangopadhyay, Shubhra Gangopadhyay, Gary A. Baker and Luis Polo-Parada (2014). Dye-doped Organosilicate Nanoparticles as cell-preserving labels for photoacoustic signal generations. Journal of Biomedical Nanotechnology. Volume 10, Number 11, November 2014, pp 3337-3350(14).

Jorge A. Castorena-Gonzalez, Marius C. Staiculescu, Christopher A. Foote, Luis Polo-Parada and Luis A. Martinez-Lemus (2014). The obligatory role of the actin cytoskeleton on inward remodeling induced by dithiothreitol activation of endogenous transglutaminase in isolated arterioles. Am J Physiol Heart Circ Physiolg. Feb 15;306(4):H485-95, doi:0.1152/ajpheart.00557.2013. Epub 2013 Dec 13.

Luis Polo-Parada, Gabriel Mettlack, Lauren Peca, Clinton T. Rubin, Florian Plattner and James A Bibb (2014). Enhancement of neuromuscula dynamics and strenght behavior using extremely low magnitude mechanical signals in mice. Journal of Biomechanics. J Biomech. 2014 Jan 3;47(1):162-7. doi: 10.1016/j.jbiomech.2013.09.024. Epub 2013 Oct 9.

Presentations

Jeniffer England, Luis Polo-Parada, Elisabeth Ehler and Siobhan Loughna (2014). Tropomyosin 1: Multiple roles in the developing heart and in the formation of congenital heart defects. Weinstein Cardiovascular Development Conference. Madrid, Spain.

Active Grants

5/2014-5/2015 $120,000 Mizzolar: A Hub for Research & Training in sustainable Carbon Based Solar Energy. Co-PI, 33% FTE The Mizzou Advantage imitative.

Professional Service

Advisor Ph. D. Students:

Advisor Post-Doctoral:

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

Polo-Parada continued

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

Advisory committee Member of the University of Missouri Doctoral Faculty	2009-2014
Committee on Committees	2013-2016
School of Medicine Research Council.	2012-2015
American Heart Association	2004-present
Society for Neuroscience	1999-present
Biophysical Society	1994-present

Leona J Rubin

Professional Services

Associate Vice Chancellor of Graduate Studies and Associate Vice President of Academic Affairs & Graduate Education

Steven Segal

Publications

Hayoz S, Bradley V, Hayoz S, Bradley V, Boerman, EM, Nourian Z, Segal SS and Jackson WF. Aging increases the size and spontaneous transient outward current amplitude of smooth muscle cells from murine superior epigastric arteries. Am J Physiol Heart Circ Physiol 306: H1512–H1524, 2014.

Domeier TL, Roberts CR, Gibson AK, Hanft LM, McDonald KS and Segal SS. Dantrolene suppresses spontaneous Ca2+ release without altering excitation-contraction coupling in cardiomyocytes of aged mice. Am J Physiol Heart Circ Physiol 307: H818-H829, 2014.

Sinkler S and Segal SS. Aging alters reactivity of microvascular resistance networks in mouse gluteus maximus muscle. Am J Physiol Heart Circ Physiol 307: H830-H839, 2014.

Segal SS. Blood flow restriction without sympathetic vasoconstriction in ageing skeletal muscle during exercise. J Physiol 592.21:4607-4608, 2014

Presentations

West Virginia University, Betschart Symposium Keynote Speaker (05/14/2014)
"Intercellular Signaling Underlying Blood Flow Control in Microvascular Resistance Networks"

University of Kansas (KUMC), Kansas City, KS (10/05/2014)
"Blood Flow Control in Microvascular Resistance Networks: Organization, Integration and Modulation"

Georgia Regents University (GRU), Augusta, GA (11/18/2014)
"Modulation of Intercellular Signaling during Advanced Age: Manifestations in Microvascular Resistance Networks"

University of Tennessee Health Sciences Center, Memphis, TN (11/20/2014)
"Modulation of Intercellular Signaling during Advanced Age: Manifestations in Microvascular Resistance Networks"

Active Grants

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

Mentored Research Support
1K99 AG047198 (Erik Behringer, PhD); NIH/NIA Pathway to Independence Award
Title: Impact of aging on calcium and electrical signaling in microvascular endothelium
Project Period: 04/01/2014-03/31/2016
Role: Research Assistant Professor

F32 HL118836 (Erika Boerman, PhD); NIH/NHLBI Individual Postdoctoral NRSA
Title: Aging and neurovascular regulation of endothelial cell calcium signals
Project Period: 12/01/2013 – 11/31/2015
Role: Postdoctoral Fellow

15PRE22840000 (Shenghua Sinkler); American Heart Association Predoctoral Fellowship
Title: Rapid Onset Vasodilation with Advanced Age: Roles of Adrenergic and Endothelial Signaling
Project Period: 01/01/112015 - 12/31/2015
Role: PhD Candidate; dissertation research

Professional Service
Reviewing Editor: Journal of Physiology

Editorial Boards : American Journal of Physiology: Heart Circulatory Physiology; Journal of Vascular Research

NIH Study Section (ad hoc): CSR IAM meeting 2015/01 ZAI1 TT-M (J1) 1 (2014)

Yoshiro Sohma

Publications

Guo JH, Chen H, Ruan YC, Zhang XL, Zhang XH, Fok KL, Tsang LL, Yu MK, Huang WQ, Sun X, Chung YW, Jiang X, Sohma Y, Chan HC* (2014) Glucose-induced electrical activities and insulin secretion in pancreatic islet β-cells are modulated by CFTR. Nat Commun. 15;5: 4420

Kato J, Takai Y, Hayashi MK, Kato Y, Tanaka M, Sohma Y, Abe Y, Yasui M* (2014) Expression and localization of aquaporin-4 in sensory ganglia. Biochem Biophys Res Commun. 451(4):562 – 7.

Furukawa-Hagiya T, Yoshida N, Chiba S, Hayashi T, Furuta T, Sohma Y, Sakurai M*. Water-meditated forces between the nucleotide binding domains generate the power stroke in an ABC transporter. Chemical Physics Letters in press.

Presentations

A novel method to measure epithelial water permeability using coherent anti-Stokes Raman scattering (CARS) microscopy. The 18th congress of the international federation of associations of anatomists / The 30th congress of Chinese society of anatomical sciences, Beijing China. 2014.8

Structure and fluctuation of single CFTR molecules observed by high-speed atomic force microscopy International symposium"Cystic fibrosis in Asia from basics to clinics", Nagoya, Japan. 2014.9

Let's "See" ATP-dependent gating of CFTR channels The 45th NIPS International Symposium "Cutting-edge approaches towards the functioning mechanisms of membrane proteins", Okazaki, Japan. 2014.11

Mechanism of ATP-dependent gating in CFTR channels Symposium "Frontiers of molecular mechanisms of ligand recognition and activation of receptor channels" Australian Physiological Society Meeting 2014, The University of Queensland, Brisbane, Australia. 2014.12

Active Grants

2013.4 – 2016.3 $160,000., $130,000. Japan Society for the Promotion of Science. Grant-in-Aid for Scientific Research (B): 25293049, PI, "Mechanism of ABC transporters studied by direct observations using high-speed Atomic Force Microscopy".

2013.4 – 2014.3 $15,000., $15,000. Keio Gijuku Fukuzawa Memorial Fund for the Advancement of Education and Research. Research support: PI, "Study for the dynamics of membrane protein complex by high-speed AFM and CARS microscopy".

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

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

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

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

James Sowers

Publications

Jia G, Sowers JR. New Thoughts in an Old Player: Role of Nitrite in the Treatment of Ischemic Revascularization. Diabetes. 2014;63(1):39-41.

Whaley-Connell A, Sowers JR. Implications for Glucose Measures in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study. Diabetes. 2014;63:45–47.

Lastra G, Syed S, Kurukulasuriya LR, Manrique C, Sowers JR. Type 2 diabetes mellitus and hypertension: an update. Endocrinol Metab Clin North Am. 2014;43(1):103-22.

Manrique C, Lastra G, Sowers JR. New insights into insulin action and resistance in the vasculature. Ann N Y Acad Sci. 2014;1311:138-50.

Nair KS, Abel ED, Adler SG, Dyck PJ, Gardner TW, Haskins KM, Hotamisligil G, Jensen MD, Krook A, Mandarino LJ, Mitchell BD, Pessin JE, Sowers JR, Sussel L, Wareham N, Vella A. Time to look back and to look forward. Diabetes. 2014;63(4):1169-70.

Muniyappa R, Sowers JR. Glycogen synthase kinase-3β and cathepsin B in diabetic endothelial progenitor cell dysfunction: an old player finds a new partner. Diabetes. 2014;63(4):1194-7.

Grais IM, Sowers JR. Thyroid and the Heart. Am J Med. 2014 Mar 21.

Nistala R, Habibi J, Lastra G, Manrique C, Aroor AR, Hayden MR, Garro M, Meuth A, Johnson M, Whaley-Connell A, Sowers JR. Prevention of Obesity-Induced Renal Injury in Male Mice by DPP4 Inhibition. Endocrinology. 2014;155(6):2266-76. PMCID: PMC4020930

DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. Nat Rev Endocrinol. 2014;10(6):364-76. doi:10.1038/nrendo.2014.44

Jia G, Aroor AR, Whaley-Connell AT, Sowers JR. Fructose and uric acid: is there a role in endothelial function? Curr Hypertens Rep. 2014;16(6):434. PMCID: PMC4084511

Habibi J, Hayden MR, Ferrario CM, Sowers JR, Whaley-Connell AT. Salt Loading Promotes Kidney Injury via Fibrosis in Young Female Ren2 Rats. Cardiorenal Med. 2014;4(1):43-52. PMCID: PMC4025048

Jia G, Aroor AR, Sowers JR. Arterial Stiffness: A Nexus between Cardiac and Renal Disease. Cardiorenal Med. 2014;4(1):60-71. PMCID: PMC4024508

Yousef I, Siyam F, Layfield L, Freter C, Sowers JR. Cervical neuroendocrine tumor in a young female with Lynch Syndrome. Neuro Endocrinol Lett. 2014;35(2):89-94. PMID: 24878972

Aroor AR, Sowers JR, Jia G, DeMarco VG. Pleiotropic Effects of the Dipeptidylpeptidase-4 Inhibitors on the Cardiovascular System. Am J Physiol Heart Circ Physiol. 2014 Jun 13. pii: ajpheart.00209.2014. [Epub ahead of print]. PMCID: PMC4137125

Bostick B, Habibi J, Ma L, Aroor A, Rehmer N, Hayden MR, Sowers JR. Dipeptidyl peptidase inhibition prevents diastolic dysfunction and reduces myocardial fibrosis in a Mouse model of Western diet induced obesity. Metabolism. 2014 Aug;63(8):1000-11. PMCID: PMC4128682

Linden MA, Fletcher JA, Morris EM, Meers GM, Laughlin MH, Booth FW, Sowers JR, Ibdah JA, Thyfault JP, Rector RS. Treating NAFLD in OLETF Rats with Vigorous-Intensity Interval Exercise Training. Med Sci Sports Exerc. 2014 Jun 30. [Epub ahead of print]. PMID: 24983336

Jia G, Sowers JR. Autophagy: A housekeeper in cardiorenal metabolic health and disease. Biochim Biophys Acta. 2014 Jun 28. pii: S0925-4439(14)00202-6. doi: 10.1016/j.bbadis.2014.06.025. [Epub ahead of print] Review. PMID: 24984281

Nistala R, Habibi J, Aroor A, Sowers JR, Hayden MR, Meuth A, Knight W, Hancock T, Klein T, DeMarco VG, Whaley-Connell A. DPP4 Inhibition attenuates filtration barrier injury and oxidant stress in the zucker obese rat. Obesity (Silver Spring). 2014 Oct;22(10):2172-9. PMCID:PMC4180797

Jia G, Aroor AR, Sowers JR. Estrogen and mitochondria function in cardiorenal metabolic syndrome. Prog Mol Biol Transl Sci. 2014;127:229-49. PMID: 25149220

Whaley-Connell A, Sowers JR. Basic science: Pathophysiology: the cardiorenal metabolic syndrome. J Am Soc Hypertens. 2014 Aug;8(8):604-6. PMCID: PMC4170524

Jia G, Sowers JR. Endothelial Dysfunction Potentially Interacts With Impaired Glucose Metabolism to Increase Cardiovascular Risk. Hypertension. 2014 Sep 15. pii: HYPERTENSIONAHA.114.04348. [Epub ahead of print]. PMID: 25225204

Ren J, Sowers JR. Application of a novel curcumin analog in the management of diabetic cardiomyopathy. Diabetes. 2014 Oct;63(10):3166-8. PMCID: PMC4171654

Jia G, Aroor AR, Martinez-Lemus LA, Sowers JR. Invited Review: Over-nutrition, mTOR Signaling and Cardiovascular Diseases. Am J Physiol Regul Integr Comp Physiol. 2014 Sep 24:ajpregu.00262.2014. doi: 10.1152/ajpregu.00262.2014. [Epub ahead of print]. PMID: 25253086

Active Grants

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

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

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

Professional Service

Professional consultation (other patient care)

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

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

Editorial Board Memberships

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

Editorships - Reviewer
New England Journal of Medicine, Hypertension, Journal of Biological Chemistry, Circulation, Circulation Research, American Journal of Physiology, Diabetes, Journal of Clinical Investigation, Journal of Clinical Endocrinology and Metabolism, Endocrinology, American Journal of Medicine, Archives of Internal Medicine, Annals Internal Medicine, Journal American Medical Association, and others. Other professionally related service

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

National and International Boards and Committees

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

State and Local Boards and Committees

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

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

04/2007-Present	Director, Center for Diabetes and Cardiovascular Research, Columbia, Missouri
04/2007-Present	Director, Division of Endocrinology, Diabetes & Metabolism, University of Mis souri-Columbia, Columbia, Missouri
04/2007-Present	Vice-Chair for Research, Department of Internal Medicine, University of Missouri-Columbia, Columbia, Missouri
04/2007-Present	Professor of Medicine, Physiology & Pharmacology, University of Missouri-Colum bia, Missouri
04/2007-Present	Staff Physician, Medical Service, Truman VA, Columbia, Missouri

Major Professional Societies

American Society Clinical Investigation
Alpha Omega Alpha, Honor Medical Society
American Physiology Society
Society of Vascular Medicine
American Federation of Clinical Research
Fellow, High Blood Pressure Council
American College of Physicians
Endocrine Society
American Diabetes Association
American Society of Hypertension
American College of Physicians (Fellow)
Southern, Western, and Central Society of Clinical Investigation
International Society of Hypertension
International Society of Hypertension in Blacks
Inter-American Society of Hypertension

Zhe Sun

Publications

Lysophosphatidic acid induces integrin activation in vascular smooth muscle and alters arteriolar myogenic vasoconstriction. Staiculescu MC, Ramirez-Perez FI, Castorena-Gonzalez JA, Hong Z, Sun Z, Meininger GA, Martinez-Lemus LA. Front Physiol. 2014 Oct 31;5:413. doi: 10.3389/fphys.2014.00413. eCollection 2014. PMID:25400583

N-cadherin, a vascular smooth muscle cell-cell adhesion molecule: function and signaling for vasomotor control. Sun Z, Parrish AR, Hill MA, Meininger GA. Microcirculation. 2014 Apr;21(3):208-18. doi: 10.1111/micc.12123. Review. PMID:24521477

Vasoactive agonists exert dynamic and coordinated effects on vascular smooth muscle cell elasticity, cytoskeletal remodelling and adhesion. Hong Z, Sun Z, Li M, Li Z, Bunyak F, Ersoy I, Trzeciakowski JP, Staiculescu MC, Jin M, Martinez-Lemus L, Hill MA, Palaniappan K, Meininger GA. J Physiol. 2014 Mar 15;592(Pt 6):1249-66. doi: 10.1113/jphysiol.2013.264929. Epub 2014 Jan 20. PMID:24445320

Active Grants

1P01HL095486 (G. Meininger, PI) $ 1,515,000 04/01/2010~03/31/2015
Project Title: Mechanisms of Microvascular Control in Health and Disease
National Institutes of Health- National Heart, Lung and Blood Institute
Role: Co-Investigator, 20% effort

Professional Service

Assistant Research Professor, Dalton Cardiovascular Research Center, University of Missouri-Columbia, November 2005- present Supervisor: Dr. Gerald A. Meininger

Director of the Atomic Force Microscopy Core, Dalton Cardiovascular Research Center, University of Missouri-Columbia, November 2008- present. Supervisor: Dr. Gerald A. Meininger

Sigma Xi, the Scientific Research Society
Microcirculation Society
American Physiological Society

Ad Hoc Reviewer:
American Journal of Physiology: Heart and Circulatory Physiology
Journal of Vascular Research
Journal of Neuroscience Methods
Nature Nanotechnology
Nano-Medicine

Ronald L. Terjung

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

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

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

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

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

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

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

Xiaoqin Zou

Publications

Sheng-You Huang, Xiaoqin Zou*. ITScorePro – An efficient scoring program for evaluating the energy scores of protein structures for structure prediction. Invited book chapter in Methods in Molecular Biology, Protein Structure Prediction (3rd Edition). Daisuke Kihara (ed.), Chapter 6, 1137:71-81, Springer Science + Business Media, New York, 2014.

Sam Z. Grinter, Xiaoqin Zou*. A Bayesian statistical approach of improving knowledge-based scoring functions for protein-ligand interactions. Journal of Computational Chemistry, 35: 932–943, 2014 (featured in the front cover of the issue).

Sheng-You Huang, Xiaoqin Zou*. A knowledge-based scoring function for protein-RNA interactions derived from a statistical mechanics-based iterative method. Nucleic Acids Research, 1–12, doi:10.1093/nar/gku077, 2014.

Sam Z. Grinter, Xiaoqin Zou*. Challenges, applications, and recent advances of protein-ligand docking in structure-based drug design. Molecules, Special Issue "In-Silico Drug Design and In-Silico Screening" (invited), 19: 10150-10176, 2014.

Min Li, Shan Chang, Jingyi Shi, Kelli McFarland, Longlin Yang, Xiao Yang, Alyssa Moller, Chunguang Wang, Xiaoqin Zou, Chengwu Chi, Jianmin Cui. Conopeptide Vt3.1 preferentially inhibits BK potassium channels containing 4 subunits via electrostatic interactions. Journal of Biological Chemistry, 289: 4735-4742, 2014.

Juan Xu, Xie Jie, Chengfei Yan, Xiaoqin Zou, Dongtao Ren, and Shuqun Zhang. A chemical genetic approach demonstrates that MPK3/MPK6 activation and NADPH oxidase-mediated oxidative burst are two independent signaling events in plant immunity. The Plant Journal, 77: 222–234, 2014.

Yayun Liang, Cynthia Besch-Williford, Johannes D. Aebi, Benford Mafuvadze, Xiaoqin Zou, and Salman M. Hyder. Cholesterol biosynthesis inhibitors as potent novel anti-cancer agents: suppression of hormone-dependent breast cancer by the oxidosqualene cyclase inhibitor RO 48-8071. Breast Cancer Research and Treatment, 146:51-62, 2014.

Marc F. Lensink, et al. Blind Prediction of Interfacial Water Positions in CAPRI. Proteins: Structure, Function and Bioinformatics, 82:620-32, 2014.

Presentations

CASP (Critical Assessment of techniques for protein Structure Prediction) 11/CAPRI, Riviera Maya, Mexico, 2014 (highly selective).

Truman State University, Kirksville, Missouri, 2014

Telluride Meeting: "Coarse-Grained Modeling of Structure and Dynamics of Biomacromolecules", Telluride, Colorado, 2014.

Zhejiang University, Hangzhou, Zhejiang, China, 2014.
Jiangnan University, Wuxi, Jiangsu, China, 2014.

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

Funding Agency: American Heart Association (Midwest Affiliate) Grant # 13GRNT16990076
Project Title: Structure-based screening and discovery of potentiators for KCNQ1 and IKs channels
Funding Period: July 1, 2013 – June 30, 2015 Total Amount: $143,000
Principal Investigator: Xiaoqin Zou

Professional Services
Campus Services - Serve as a member in the Campus Parking and Transportation Committee (2011-present).

NIH study section ad hoc reviewer, 2014.
PhD Mentor
American Physical Society, Biophysical Society, American Chemical Society

Session chair, Telluride Meeting: "Coarse-Grained Modeling of Structure and Dynamics of Biomacromolecules", Telluride, Colorado, 2014

Program Committee member for the 13th Pacific Rim International Conference on Artificial Intelligence (PRICAI-2014), Special track of Big Data in Bioinformatics, 2014

Program Committee member for IEEE International Conference on Bioinformatics & Biomedicine (BIBM), 2009, 2010, 2012-2014

Member of the Advisory committee for Oversea Outstanding Faculty Recruitment, College of Life Sciences, Zhejiang University, 2014-present.

Diabetes UK grant review, 2014

Physics 1100, Science and Inventions (Physics Department). Responsible for course development, organization, grading, and 1 lecture hour per week. Fall 2014, 80 students.

Biochemistry 4970 (Biochemistry Department). This is a capstone course for Biochemistry majors and is a case-based course, which includes written and oral presentations. Spring 2014, two classes (7 and 8 students, respectively).