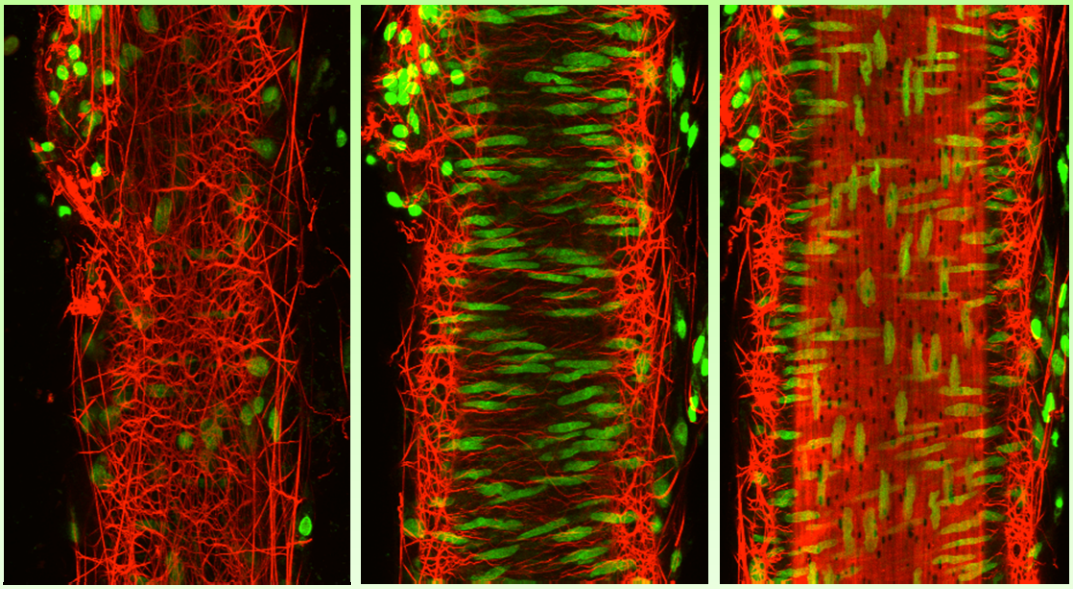
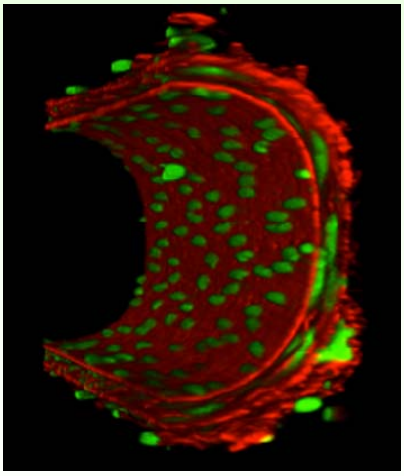
Dalton Cardiovascular Research Center

Research Directory
FY2011





"Committed to Interdisciplinary Collaboration in Research and Teaching"

Pictures on front cover courtesy of Dr. Michael Hill

Spatial distribution and mechanical function of elastin in resistance arteries: a role in bearing longitudinal stress.
Clifford PS, Ella SR, Stupica AJ, Nourian Z, Li M, Martinez-Lemus LA, Dora KA, Yang Y, Davis MJ, Pohl U, Meininger GA, Hill MA. Arterioscler Thromb Vasc Biol. 2011 Dec;31(12):2889-96

Z-section image stacks of a cannulated mesenteric artery stained with Alexa 633- hydrazide (red) to highlight the extracellular matrix protein, elastin. Cell nuclei are shown in green. The individual panels (left to right) show the the vessel at the adventitial surface; through the media; and at the level of the intima.

3D reconstruction of a z-series image stack showing an end-on view of a segment of mesenteric artey. Elastin protein stained with Alexa 633 hydrazide (red) and cell nuclei counterstained green.

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FROM THE DIRECTOR

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

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

The center is committed to excellence in cardiovascular research and in the education of students and fellows. Our investigators provide service to the University, the State of Missouri, and the nation through memberships on committees, peer review panels and editorial boards of scientific journals. During the period of this report, our investigators have 71.3 million in active research funding, have published 183 manuscripts in nationally recognized journals and books and gave 83 invited presentations.

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

DCRC Committees

The Internal Advisory Committee:

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

The Appointment and Promotions Committee:

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Dr. Kevin Gillis
Dr. Tzyh-Chang Hwang
Dr. Luis A. Martinez-Lemus
Dr. David Kline

Scientific Program Committee:

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

Core Facilities Committee:

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

Safety Committee

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Dr. Shinghua Ding
Dr. Maike Krenz
Dr. Min Li
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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, Zhang, Sun, Fay, Sowers

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

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

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

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

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

Director

Gerald A. Meininger

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

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

Research

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

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

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

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

Associate Director

Michael A. Hill

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Education:
PhD & MS University of Melbourne

Appointment: Professor, Assistant Director, Department of Medical Pharmacology and Physiology

Research

Our laboratory has a principal interest in understanding the signaling mechanisms that underlie the vasoconstrictor response of an arteriole following an acute rise in intraluminal pressure (myogenic response). Our studies have examined the roles of a number of vascular smooth muscle signaling molecules including various kinases and intra cellular Ca^{2+}. More recently these studies have been extended to include approaches aimed at determining the relationships between pressure-induced changes in smooth muscle membrane potential and the resulting signaling events that ultimately lead to the contractile response.

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

Principal Investigators

Christopher P. Baines

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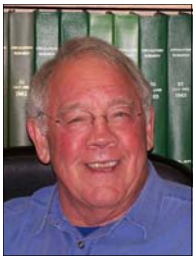
Education:
B.Sc. University of Bath, Great Britain
PhD University of South Alabama

Appointment: Assistant Professor, Department of Biomedical Sciences

Research

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



Edward H. Blaine

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

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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

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

Silvia G. Bompadre

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Education:
PhD in Physics from University of Washington

Appointment: Assistant Professor, Department of Physics

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

Frank W. Booth

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Education:
PhD University of Iowa, BS Denison University

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

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

The first question being posed is: what are the aging mechanisms of decreased proliferation and differentiation of satellite cells, the adult stem cells in skeletal muscle? Experiments are concerned with regulation of $p21^{Cip1/WAF1}$, $p27^{Kip1}$, p53, FoxO3a, Sirt1 and other proteins as they regulate proliferation and differentiation.

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

Doug Bowles

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Education:
PhD University of Texas-Austin

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

Research

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

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

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

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

Lane Clarke

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

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

Research

Our laboratory investigates electrolyte and nutrient transport across epithelial tissues (airway, reproductive and intestinal) during health and disease. The major focus is to understand the role of the cystic fibrosis transmembrane conductance regulator protein (CFTR) in the regulation of acid-base and nutrient transport across alimentary epithelia. CFTR is the protein product of the gene that is mutated in cystic fibrosis (CF) and normally functions in epithelial cells as a cyclic AMP-regulated anion channel. Present studies investigate the role of anion exchange proteins that work with CFTR in promoting bicarbonate transport or that work with Na^+ transport proteins for NaCl absorption across intestinal epithelium. Most studies involve either measurements of acid-base or nutrient transporter activity using fluorescent dyes to monitor intracellular pH by microfluorimetry or electrophysiological recordings in Ussing chambers of native mucosa and cell lines derived from gene-targeted ("knockout") mice. In addition to the cystic fibrosis mice, the laboratory maintains colonies of mice with gene-targeted deletion of other acid-base transporting proteins, including Na^+/H^+ exchangers, Cl^-/HCO_3^- exchangers and $Na^+/K^+/2Cl^-$ cotransporters. Molecular studies in the laboratory involve the measurements of gene expression in the mice (quantitative real-time PCR, Northern blots and microarrays) and cloning of specific murine transporters for functional expression studies in heterologous cell systems. In addition to the above methods, other techniques employed in the laboratory include cell culture, retroviral and adenoviral gene transfer, pH stat/isotopic flux studies, laser capture microdissection and PCR-based genotyping.

George E. Davis

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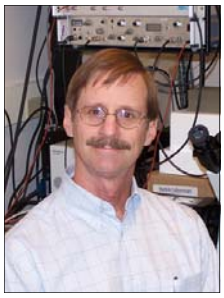
Education:
PhD, MD University of California-San Diego,
BS Arizona State University

Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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



Michael J. Davis

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

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

Research

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

The experimental approaches used in my laboratory include isolated, perfused microvessel methods and single-cell electrophysiology. We combine these with variety of imaging methods, including confocal, atomic force, and TIRF microscopy. We also use molecular analyses, such as site-directed mutagenesis and co-immunoprecipitation, to identify and test which integrin-associated proteins are involved in modulation of ionic channels.

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

Shinghua Ding

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

Appointment: Assistant Professor, Department of Biological Engineering

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

Paul J. Fadel

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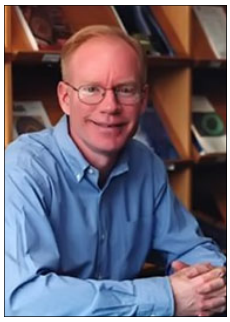
Education:
PhD University of North Texas,
MS Northeastern University, Health Science Center,
BS Brooklyn College

Appointments: Assistant Professor, Department of Medical Pharmacology and Physiology

Research
Our laboratory's research focus entails the investigation of neural cardiovascular control at rest and during exercise in humans with a specific emphasis on the sympathetic branch of the autonomic nervous system. Ongoing studies involve assessing sympathetic responses during various physiological manipulations including isometric and aerobic forms of exercise, lower body negative pressure to simulate the effect of gravity when one stands up, and infusions of pharmacological agents. Studies are performed in normal healthy subjects as well as in patients with various pathophysiological conditions such as heart failure and hypertension. Our laboratory obtains direct measures of sympathetic neural firing using the technique of microneurography. This measurement allows for the assessment of moment-to-moment as well as long-term changes in sympathetic nerve activity. Also, with the application of partial autospectral and time series analyses to muscle sympathetic neurograms we are beginning to

investigate the central origin(s) and pattern(s) of sympathetic discharge in humans. Our current research focus is on the neural mechanisms that contribute to exercise-induced sympathoexcitation as well as the peripheral modulators of sympathetically medicated vasoconstriction in contracting skeletal muscle with a particular emphasis on the potential roles of free radicals and changes in nitric oxide signaling in altering these responses. Considering the continually increasing population of elderly individuals, we are beginning to examine age-related alterations in neural cardiovascular control during exercise. Research in this area has been limited and is extremely important considering that an exaggerated blood pressure response to exercise increases the risk for mortality in otherwise healthy adults.



William P. Fay, M.D.

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Education: BS, MD, University of Illinois

Appointments: Professor of Internal Medicine and Medical Pharmacology & Physiology

Research Interests

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

Techniques / Methodology:

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

Research Description

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

Shubra Gangopadhyay

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

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

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

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

Kevin D. Gillis

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

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

Research

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

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

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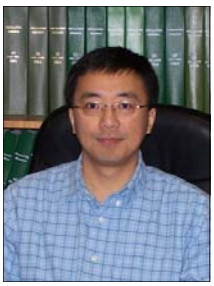
Education:
B.A. & Ph.D., New York University

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.



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Education:
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Appointment: Assistant Professor, Department of Biological Engineering

Research

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

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

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

Eileen M. Hasser

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Appointments: Professor, Department of Biomedical Sciences
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Research

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

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

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

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Research

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

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

Virginia Huxley

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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.

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Research

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

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

Principal Investigators

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

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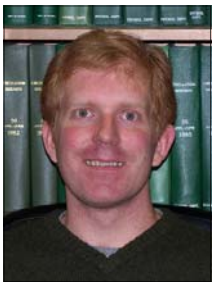
Research Description
Jones' research program currently focuses on mechanisms of membrane regulation and vascular smooth muscle function leading to abnormalities associated with hyper-lipidemia as well as adaptative mechanisms during exercise training. He is studying mechanisms of adenosine transport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



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Research

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

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

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

Ronald J. Korthuis

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

Research

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

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

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

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

Maike Krenz

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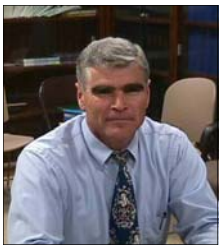
Appointment: Assistant Professor, Department of Medical Pharmacology and Physiology

Research

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

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



M. Harold Laughlin

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Adjunct Professor, Department of Medical Pharmacology Physiology

Research

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

Luis Martinez-Lemus

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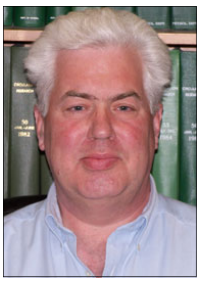
Appointment: Assistant Professor, Department of Medical Pharmacology and Physiology

Research

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

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



Mark Milanick

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Appointment: Professor, Department of Medical Pharmacology and Physiology

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

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

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

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

Luis Polo-Parada

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

Research

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

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

Michael Rovetto

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Research

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

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

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

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

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

Leona Rubin

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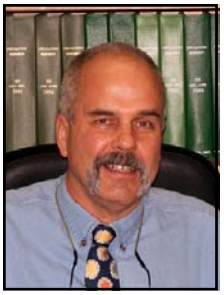
Research

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



James C. Schadt

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

Appointment: Associate Professor, Department of Biomedical Sciences

Research

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

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

Steven S. Segal

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Appointment: Professor, Department of Medical Pharmacology and Physiology

Research

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

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

Yoshiro Soma

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Education:
PhD and MD Osaka Medical College

Appointment: Visiting Professor, Department of Medical Pharmacology & Physiology

Research

I have a broad research interest that covers the molecular physiology and biophysics of ion channels and transporters, and their role in the physiological function of cells/tissue. I have studied the permeation and gating of a large-conductance, Ca^{2+}-activated, voltage-dependent potassium (BK_{Ca}) channel. BK_{Ca} channels are ubiquitously expressed in many different tissues and are known to be sensitive to membrane potential, intracellular calcium, magnesium, pH. These channels are also activated by CO and sensitive to O_2 associated with hemeoxygenase-2 and, moreover, some slice-variants respond to membrane stretch. Based on these findings, BK_{Ca} channels are suggested to play an important role in integrating cell signals, a recently proposed new function of an ion channel. I am also involved in a Japanese-based collaborative project undertaking a comprehensive study of the GABAergic system in peripheral tissues (not the central nervous system) and work on $GABA_A$ receptor channels and $GABA_B$-mediated modulation of K^+ and Ca^{2+} channels in peripheral tissues. In the Dalton Cardiovascular Research Center, I study the molecular mechanism of gating and permeation of the CFTR chloride channel, a member of the ATP-Binding Cassette (ABC) transporter superfamily, in collaboration with Dr. Tzyh-Chang Hwang. Our work has made a significant contribution to the recent advances in the biophysical understanding of the ATP-dependent gating mechanism in CFTR, and has provided great insight into a possible common functional mechanism that can be applied to the whole ABC transporter superfamily. The structure of the membrane spanning domain (MSD) in CFTR is known to be similar to that in the P-glycoprotein drug efflux pump. We therefore believe that understanding MSD structure/function in CFTR will lead to a better understanding of multi-drug resistance (MDR) proteins. In addition to investigating the biophysics of the CFTR molecule itself, I am also interested in studying the functional interactions of CFTR with other membrane proteins and lipids. This should help in our understanding of the complicated regulatory mechanisms that underlie physiological functions in cell membrane. I have also employed computer modeling to simulate ion transport processes in epithelial cells (e.g., bicarbonate transport in pancreatic duct cells). This approach is very useful to bridge information from molecular biophysics and cell/tissue physiology to the research field of epithelial transport. I believe that by taking such a general and comprehensive approach to the study of different channels/transporters and channel/transporter-mediated physiological systems, induces a 'positive cooperative effect' which accelerates each research project, and which also gives us a novel scientific standing point of view for the channel sciences.

Jim R. Sowers

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

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

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

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

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

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

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

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

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

Appointment: Assistant Professor, Department of Biochemistry

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

APPENDICES

PUBLICATIONS

PRESENTATIONS

SEMINARS

ACTIVE GRANTS & CONTRACTS

PROFESSIONAL SERVICE ACTIVITIES

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Gillis, K.

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Gruber, K.

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Effects of Different Levels of Hypoxia on Fos Expression in PVN-Projecting Neurons in the Nucleus of the Solitary Tract (nTS). Luise T King, David D Kline, Cheryl M Heesch, Eileen M Hasser. *FASEB Journal. 2010*

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National Institutes of Health, 2010 Angiogenesis Course, Invited Speaker

Department of Pathology, University of North Carolina School of Medicine

Center for Vascular Biology Research, Beth Israel Deaconess Medical Center, Harvard Medical School

Developmental Vascular Biology Workshop IV, Invited speaker, Monterey, CA

Department of Pathology and Anatomical Sciences, University of Missouri School of Medicine

Ding, S.

40*th Annual Meeting on Neuroscience*. Nov 13-17, 2010, San Diego.

10 Alzheimer's Association International Conference on Alzheimer's Disease 2010. July 10-15, 2010.

41st Annual meeting of American Society for Neuronchemistry. March 06-10, 2010, Santa Fe, New Mexico.

Cardiovascular Day, University of Missouri-Columbia. Feb 16, 2010.

Life Science Week, University of Missouri-Columbia. University of Missouri-Columbia. April 12-16, 2010.

Wenting Chang[1,2], Nannan Zhang, Shinghua Ding[1,2]. AAV transduction reduces adult neurogenesis in hippocampus in mice. *ASGCT 14th Annual Meeting*, May 18-21, 2011, Seattle, WA. *Molecular Therapy 19: 1392, 2011.*

Yicheng Xie, Nannan Zhang, Hailong Li Shinghua Ding* Spontaneous Calcium activities in astr cytes in vivo are not mediated by IP3 receptors *Gordon Research Conference on Glial Biology.* March 06-11, 2011, Ventura, CA.

Jing Bi, Hailong Li, Yicheng Xie Shui Qing Ye, Shinghua Ding. The role of PBEF in neuronal protection after ischemia. 42nd *Annual ASN meeting*. St Louis, March 19-23, 2011.

Yicheng Xie, Hailong Li, Shinghua Ding. The role of astrocytic Ca^{2+} signaling in brain damage after ischemia. 42nd *Annual ASN meeting*. St Louis, March 19-23, 2011.

"Ca^{2+} signaling in astrocytes and its role in neurotoxicity" Missouri University of Science and Technology, Rolla, MO. April 11, 2011.

"Astrocyte-mediated neurotoxicity" Medical School of Wuhan University, China, Aug 4, 2010.

Fay, W.

"Plasminogen Activator Inhibitor-1 and Vascular Remodeling," Cardiovascular Research Seminar Series, Mayo Clinic, Rochester, MN, April 14, 2011.

44. "Blood Clotting Factors and Atherosclerosis," Cardiovascular Disease Grand Rounds, Mayo Clinic, Rochester, MN, April 15, 2011.

Gangopadhyay, S.

Cost Effective Optical Sensing Platforms for medical diagnostics Indo Global Education Summit, Aurangabad, India December 2010 Shubhra Gangopadhyay

Sub-2nm metal nanoparticle-based nonvolatile memory devices and applications in sensingIndo Global Education Summit, Aurangabad, India December 2010 Shubhra Gangopadhyay

Session Chair 4th International Conference on Optical, Optoelectronic and Photonic Materials and Applications (ICOOMPA) Conference, Budapest, Hungary August 16, 2010 Shubhra Gangopadhyay

Session Chair – S. Gangopadhyay Plus Five Presentations International Symposium on Spectral Sensing Research (ISSSR), "Bridging the Gap from Emerging Technology to Warfighter", Springfield, MO June 20, 2010 Shubhra Gangopadhyay Charles Darr Craig Weilbaecher Venu Korampally Keshab Gangopadhyay

Nanostructured Modular Platform Encompassing Fluorescent Nanoparticles, Nanostructured Microarrays and Metal Nanoislands for Biological Agent Detection 27th Army Science Conference Orlando, FL December 2010 Korampally, V.; Bok, S.; Harris, B. C.; Mamidi, V. K.; Mukherjee, S.; Darr, C. M.; Gangopadhyay, K.; Folk, W.; Parada, L. P.; Gangopadhyay, S.

Single Step Surface Energy Assisted Patterning of Nanoporous Organosilicate Films for Sensor Applications International Symposium on Spectral Sensing Research (ISSSR), "Bridging the Gap from Emerging Technology to Warfighter", Springfield, MO June 20, 2010 V.R Korampally, Charles Darr, Luis P. Parada, Keshab Gangopadhyay and Shubhra Gangopadhyay

Novel Nanostructured Platform and Nanoparticles for Sensitive Detection of Biological Materials
IEEE Sensors 2010 Conference Waikoloa, Hawaii November 2010 Sangho Bok

Invited speaker BAE Systems, Picatinny, NJ July 9, 2010 Shubhra Gangopadhyay

Sub-2 NM Size Tunable High Density Pt Nanoparticle Embedded Non-Volatile Memory CMOS Emerging Technologies Conference, Whistler, BC May 20, 2010 Shubhra Gangopadhyay

Invited speaker and panel chair Center for Nanoscience & Technology, Champaign, IL May 6, 2010 Shubhra Gangopadhyay

Imprinted polymer particles labeled with quantum dots for detection of nitroaromatic explosives R. Cody Stringer, Shubhra Gangopadhyay, Sheila A. Grant

Fluorescent imprinted polymers for the detection of explosive nitroaromatic compounds SPIE Defense Security and Sensing, Orlando, FL, April 6, 2010 R. Cody Stringer, Shubhra Gangopadhyay, Sheila A. Grant

Invited speaker Los Alamos National Laboratory, Albuquerque, NM March 19, 2010 Shubhra Gangopadhyay
Invited speaker Army Research Lab, Adelphi, MD, February 26, 2010 Shubhra Gangopadhyay

Hasser, E.

Experimental Biology, New Orleans LA, April 2010
FASEB Summer Research Conference, July 2010
Oklahoma State University, February 2010
Wayne State University, November 2010

Heesch, C

4/2010: Experimental Biology 2010; New Orleans, LA; April 2010 (see abstracts above)

3/10/2010: "Pregnancy: CNS Plasticity in Control of Sympathetic Outflow," Dept. of Physiology, Medical College of Georgia, Augusta, Georgia

7/21/2010: "Baroreflex Impairment During Pregnancy: Plasticity of GABAA receptors in the RVLM," Symposium SpeakerFASEB Summer Research Conference, Saxtons River, VT

10/11/2010: "Pregnancy: Brain Region Specific Changes in GABAA and AT1 Receptor Mechanisms," Department of Physiology, Kansas State University, Manhattan, Kansas

Huxley, V.

2010 Cardiovascular Research Center/Physiology Department of Temple University School of Medicine, "*Regulation of microvascular exchange: Contribution of sex (lessons learned from juveniles & exercise).*" January 21, 2010. APS Cross Section Symposium APS History group and WEH symposium in honor of Starling.

"What Starling did not know about sex and its role in the regulation of volume homeostasis." Experimental Biology, April 27, 2010 Anaheim CA

2011"*Physiology, Pharmacology, and Pathology of Tissue Fluid Exchange*" Symposium sponsored by Journal of Physiology at the 31st International Symposium on Intensive Care and Emergency Medicine (ISICEM), Session Moderator and speaker" *Lymphatic fluid exchange: mechanisms and regulation*" Square – Brussels Conference Center, Glass Entrance, rue Mont des Arts, 1000 Brussels, Belgium, March 22-25

Hyder, S.

Mafuvadze, B., Benakanakere, I., Lopez, F., Besch-Williford, C., Ellersieck, M. R. and Hyder, S. M. (2011) Apigenin: A potential natural angio-preventive compound inhibits progestin-accelerated 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumors in Sprague-Dawley rats. 18th Annual Cardiovascular Day, University of Missouri, MO. (Feb 2011)

Mafuvadze, B., Benakanakere, I., Lopez, F., Besch-Williford, C., Ellersieck, M. R. and Hyder, S. M. (2011) Apigenin prevents development of progestin-accelerated 7,12- dimethylbenz(a)anthracene (DMBA)-induced mammary tumors in Sprague-Dawley rats. 101st Annual American Association of Cancer Research Meeting, Orlando, FL. submitted. In Press Abstract #1844

Kline, D.

FASEB Summer Conference "Neural Mechanisms in Cardiovascular Regulation", Saxton's River, VT on July 18-23, 2010. Title: *Opening the gates to reflex control of the cardiorespiratory system: Importance of the nucleus tractus solitarius and its plasticity*

Iowa Physiological Society Meeting, Des Moines University, IA on October 9th, 2010. Title: *Plasticity of nTS neurotransmission*

Emory University, Department of Physiology, Atlanta, GA. Title: "Regulating the gateway of cardiorespiratory reflexes: BDNF and H2S in synaptic and neuronal activity in the nucleus tractus solitarii (nTS)"

FASEB Summer Conference "Neural Mechanisms in Cardiovascular Regulation", Saxton's River, VT. Title: "Plasticity of nTS neurotransmission "

Iowa Physiological Society Meeting, Des Moines University, IA. Title: "Opening the gates to reflex control of the cardiorespiratory system: Importance of the nucleus tractus solitarius and its plasticity"

Korthuis, R.

"Matrix-metalloproteinase-dependent arteriolar dysfunction in ischemia/reperfusion". Symposium on Protease-dependent Vascular Dysfunction, Experimental Biology '11, Washington, DC, April 2011.

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

"Matrix-metalloproteinase-dependent mast cell chymase release as mediator of microvascular inflammation". Symposium on Extracellular Proteases in Microvascular Disease, 9th World Congress for Microcirculation, Paris, France, September 2010.

"Venular-arteriolar communication in inflammation." Department of Pharmacology, Temple University, Philadelphia, September 2010.

Liang, Y

I was invited to give a speech by the Organizing Committee of BIT' 3rd Annual International Congress of Antibodies-2011 (ICA-2011) in Track 3-28: MAbs against Cardiovascular Diseases in Beijing, China.

Martinez-Lemus, L.

Galiñanez E.L., and L.A. Martinez-Lemus, 2011. Visualization of G-Actin Dynamics in Isolated Arterioles. Cardiovascular Day. Columbia, MO. February 15, 2011.

Beig, M.I., A. Dolan, G. Zhao, E. Hoover, E.L. Galiñanez, and L.A. Martinez-Lemus, 2011. Role of actin cytoskeleton and microtubules in passive diameter and viscoelastic charectistics of rat cremaster arterioles. Cardiovascular Day. Columbia, MO. February 15, 2011.

Meininger, G.

Invited, "Do changes in integrin adhesion accompany excitation-contraction coupling in vascular smooth muscle? – Insights using Atomic Force Microscopy" 10th International Symposium on Resistance Arteries, Rebild, Denmark May 8–12, 2011.

"Atomic Force Microscopy as an investigative tool in Cardiovascular Research" to the Diabetes Center, School of Medicine, University of Missouri, Mom July 2010.

"Optics and biology at the tip of an AFM" to the Department of Bioengineering, Research Day, Texas A&M University, August 2010.

"Biology and Optics at the tip of an AFM" to the Department of Physics, University of Missouri, Columbia, Missouri, 2011.

Polo-Parada, L.

Universidad Autónoma de México. Centro de Ciencias Aplicadas y Desarrollo Tecnológico.

Escuela Superior de Física y Matemáticas. Instituto Politécnico Nacional. México City.

Universidad de Guanajuato. División de Ciencias e Ingenierías. Campus León.

Segal, S.

Bagher P, Davis MJ and Segal SS. "Macrozoom imaging of endothelial cell calcium signaling in arteriolar networks of Cx40BAC-GCaMP2 transgenic mice." (*9th World Congress of Microcirculation; Paris 09/27/10*)

Segal, SS. "Intercellular coordination of blood flow control". Plenary Lecture, American College of Sports Medicine - Integrative Physiology of Exercise. (09/22/10; Miami Beach)

Moore, A.W., W. F. Jackson and S. S . Segal. Functional adrenorecptor distribution in arteriolar networks of mouse gluteus maximus muscle. FASEB J. 24:976.5,2010.

Socha, M. J. and S. S. Segal. Distinquishing receptor—versus store-operated calcium entry in arteriolar endothelium. FASEB J. 24:777.7, 2010.

Aarhus University Institute of Physiology and Biophysics, International Society of Resistance Arteries (05/11, Rebild Bakker, Denmark) "Intercellular signaling along resistance artery endothelium"

Opening Plenary Lecture for ACSM's Integrative Physiology of Exercise (09/10; Miami Beach)

University of Colorado Boulder, Department of Integrative Physiology (03/11)

Behringer EJ, L Polo-Parada, WF Jackson and **SS Segal**. Glycyrrhetinic acid derivatives block hyperpolarization concomitant with intercellular coupling along microvascular endothelial tubes. *FASEB J.* 25:817.5, 2011

Socha MJ, TL Domeier, P Bagher and **SS Segal**. Coordinated calcium signaling within isolated microvascular endothelial celubes. *FASEB J.* 25:817.18, 2011.

Behringer EJ, MJ Socha, WF Jackson and **SS Segal**. IK_{Ca}/SK_{Ca} channels modulate electrical conduction along microvascular ewndothelial tubes. *International Society of Resistance Arteries (Rebild Bakker, Demark; 05/11).*

Westcott EB, **SS Segal** and WF Jackson. Inositol (1,4,5) trisphosphate receptor type 1 underlies Ca^{2+} waves and contributes to myogenic tone in murine arterioles. *International Society of Resistance Arteries (Rebild Bakker, Demark; 05/11).*

Sohma, Y.

Sohma Y. Direct measurement and simulation of water movement: a novel approach to water transport physiology. The Gordon Research Conference "Salivary Glands & Exocrine Biology", February 6-11, 2011; Galveston, TX, USA.

Zhang, C.

November 17-20, 2010: Endothelial Progenitor Cells as Factors in Endothelial Repair in Type 2 Diabetes. 14th Scientific Meeting of the Chinese Diabetes Society in Su Zhou, PR China.

November 22, 2010: Dendritic Cell Depletion Reduces Ischemic Reperfusion Injury. Peking Union Medical College. Beijing, PR China.

November 25, 2010: Bariatric Surgery Reduces Adipose Inflammation and Improves Vascular Function in Type 2 Diabetic Mice. Department of Surgery, China Medical College in Shen Yang, PR China.

David C. Kem, MD Regent's Professor of Medicine Division of Endocrinology and Diabetes University of Oklahoma Health Sciences Center *"Activating Autoantibodies and the Cardiovascular System"* Date: Tuesday, May 24, 2011 Time: 3:00 pm

Jessica Wagenseil, DSc Assistant Professor Saint Louis University Department of BioMedical Engineering *"Cardiovascular Mechanics: Postnatal Development and Elastin Amounts"* Date: Friday, April 22, 2011 Time: 2:00 pm

Philip S. Tsao, PhD Division of Cardiovascular Medicine, Stanford University School of Medicine *"Molecular Pathways Approach to Abdominal Aortic Aneurysm Disease"* DCRC Library room 132 3:00 pm Thursday, December 16th, 2010

Shu Chien, PhD, Department of Bioengineering, University of California, San Diego, *"Effects of shear flow on interactions between endothelial cells and smooth muscle cells"*, April 19, 2011, Acuff Auditorium, 9:00 am. Franklin Endowed Lecture Series

Baljit S. Khakh Ph.D Associate Professor UCLA ***"****Imaging astrocyte calcium signals in health and disease"* 2010 December 7, 2010, 3:00 PM, DCRC

David Adams, PhD Professor and Director Health Innovations Research Institute RMIT University Melbourne, Australia *"Analgesic Conotoxins: Modulation of Voltage Gated Ion channels in Pain"* Date: Thursday, November 11, 2010 Time: 10:00 am

Kenneth Gruber, President Tensive Controls, Inc is a private company categorized under Laboratories-Research and Development and located in Greensboro, NC. *"Cardiovascular Mechanisms of Melanocortin Ligands."* Date: Thursday, October 14, 2010 Time: 2:00 pm

Yoram Rudy, PhD The Fred Saigh Distinguished Professor of Engineering Professor of Biomedical Engineering, Medicine, Cell Biology & Physiology, Radiology, and Pediatrics, Director, Cardiac Bioelectricity and Arrhythmia Center (CBAC) Member of the National Academy of Engineering Washington University in St. Louis *"Modeling and Imaging Cardiac Repolarization and Arrythmias"* When: Wednesday, September 1, 2010 Time: 2:00 pm

Melissa Collins, PhD Texas A&M, Department of Biomedical Engineering. "A Structurally Based Investigation of Abdominal Aortic Aneurysms in Mouse Models", Thursday, September 22, 2011, 3:00 pm, DCRC Library.

PRINCIPAL INVESTIGATOR AGENCY *TITLE*	PERIOD AMOUNT
Baines, Christopher	
AHA Scientist Development Grant (PI: Baines) AHA National Center "Mechanisms of Mitochondrial-Dependent Myocyte Death"	7/06-6/10 $260,000
R21HL092327 (PI: Baines) NIH/NHLBI "Identifying Novel Components of The Cardiac Necrotic Program"	7/08-4/10 $275,000
R01HL094404 (PI: Baines) NIH/NHLBI "Molecular Identity of The Cardiac Mitochondrial Pore"	12/08-11/13 $1,250,000
Booth, F.	
NIH "Aerobic fitness, mitochondrial dysfunction, and fatty liver disease."	04/11-03/16 $2,073,038
NIH "Muscle blood flow and capillary dynamics"	05/10-04/14 $1,498,520
Bowles, D.	
P01 HL52490 NIH/NHLBI "Ion channel regulation of coronary smooth muscle phenotype"	1/06-12/11 $187,472
P01 HL52490 NIH/NHLBI "Vascular Biochemistry and Molecular Biology "	1/06-12/11 $167,681
Mizzou Advantage MU "Targeting Plasminogen Activator inhibitor-1 to Inhibit Neointimal Hyperplasia"	4/10-3/15 $50,000
MU Life Sciences Trust Fund Research Grant Missouri Life Sciences Research Board "Revascularization Targeting Plasminogen Activator Inhibitor-1 to Inhibit Restenosis"	1/09-12/11 $362,500

RO1 — 7/10-6/14
NIH/NHLBI — $250,000
"Roles of Plasminogen Activator Inhibitor-1 and Vitronectin in Failure of Coronary Revascularization"

Cardiometabolic Disease Research Foundation — 10/08-9/11
"Epicardial Adipose Tissue (EAT) Study" — $127,000

T32 AR048523 — 7/09-6/14
NIH/NIAMS — $243,386
"Exercise and Health: Integration from Molecule to Patient "

T32 RR007004 — 7/05-6/10
NIH/NCRR — $321,084
"Postdoctoral Training in Comparative Medicine "

Clarke, Lane

Bridge Funding; — 9/10-8/11
Department of Biomedical Sciences RAC; — $45,000

MU Research Board, PI — 2/11-1/12
"Modulation of Cftr to minimize crypt damage during chemotherapy" — $50,000

CVM Faculty Research Award, PI. — 1/11-12/11
"Validation of Intestinal Crypts in 3D Gel Culture as a Model for In Vivo Intestine", — $18,000

Mizzou Advantage, PI. — 2/11-12/12
"Regenerating Intestinal Crypts for Biomedical Research" — $50,000

CFF — 4/11 - 3/13
"Abnormal Regulation of Goblet Cells in the Cystic Fibrosis Intestine" — $194,400

Davis, G.

NIH-NHLBI - R01 — 7/08- 6/12
"Genes regulating capillary morphogenesis and apoptosis" — $250,000

NIH-NHLBI- R01 — 1/11- 12/14
"Hematopoietic stem cell cytokine control of developmental vascularization" — $250,000

NIH- NHLBI- R01 — 1/10- 11/13
"Pericyte proteinase inhibitors and EC tube stabilization" — $250,000

NIH- NHLBI- R01 — 1/08- 12/11
"Molecular control of EC lumen formation by MT1-MMP" — $250,000

Ding, S.

AHA (National SDG grant) — 7/07-6/11
"Astrocyte-mediated neuronal excitation (0735133N)" — $260,000

NIH — 5/10-4/15
"Role of Gliotransmission in ischemia" — $1,591,689

UM system Research board	9/09-8/10
"An Optical and Genetic Strategy to Study Glutamate Release from Astrocytes *in vivo"*	$44,527

Fay, William

Missouri Life Sciences Trust Fund	1/09–12/11
"Targeting Plasminogen Activator Inhibitor-1 to Inhibit Restenosis"	$725,000
NIH R01	9/10-8/14
"Roles of Plasminogen Activator Inhibitor-1 and Vitronectin in Failure of Coronary Revascularization"	$250,000
NIH/NHLBI Program Project Grant	4/09-3/14
"Molecular Genetics of Coagulation Disorders"	$223,863
NIH R01	9/09-8/11
"C-Reactive Protein and Atherosclerosis"	$250,000

Gruber, Kenneth

Phase I Grant	6/10-6/12
Therapeutic Discovery Project Grant, I.R. S	$199,345

Hasser, Eileen

"National Institutes of Health	4/07-3/11
Cardiovascular Regulation in Hindlimb Unweighted Rats"	$900,000
National Institutes of Health	7/10-6/14
"*Plasticity of nTS output neurons in acute and chronic hypoxia* "	2,830,531

Heesch, Cheryl

National Institutes of Health	6/09- 3/13
"Central nervous system plasticity in Sympathoinhibition on pregnancy"	$250,000
"National Institutes of Health	7/10-6/15
Plasticity of nTS output neurons in acute and chronic hypoxia"	$491,679
NIH	4/07-3/11
"Cardiovascular Regulation in Hindlimb Unweighted Rats"	$225,000
NIH	4/08-4/13
"Adaptation of brainstem circuits to chronic hypoxia"	$250,000
NIH	4/10-3/15
"The role of gliotransmission in Cerebral ischemia"	$250,000

Hill, Michael

NIH/NHLBI	7/09-7/14
"Signalling Mechanisms Underlying Myogenic response"	$1,800,000
NIH/NHLBI	3/10-2/15
"Mechanisms of Microvascular Control and Coordination"	$849,131

Huxley, Virginia

NIH R21 HL093068-01A2 — 7/10-06/12
"Sexual Dimorphism of Skeletal Muscle Microvascular Function" — $275,000

NIH RO1 HL078816-01A1 — 6/05-5/10
"Microvascular Permeability and Sex" — $1,470,000

NNJ05HF37G — 1/05-12/10
"Human Health from Earth to Space: A NASA-MU Partnership for Understanding Sex Differences in Physiology" — $1,480,000

Hyder, Salman

Universitaets-Frauenklinik, Germany — 3/11-6/11
"Progestin Regulation of Breast Cancer Cells in vivo" — $10,057

College of Veterinary Medicine Faculty Award — 1/11-12/11
"Novel breast cancer therapy using an inhibitor of cholesterol biosynthesis" — $18,000

NIH-NIGMS R21 Co-PI — 9/09-7/12
"*A New Scoring Framework for Selecting Structural Models"* — $250,000

NIH T32 RR07004 Mentor Franklin — 7/11-6/16
"Post-doctoral Comparative Medicine Training Grant" — $169,266

College of Veterinary Medicine Faculty Award –Consultant Ray — 1/11-12/11
"Assessment of a novel repressor of transcription to control breast cancer growth"

VA Merit Grant –Consultant-Hoffman — 4/08-3/12
"Targeted Radiotherapy/Chemotherapy for Prostate Cancer Metastases"

Hwang, T.C.

NIH — 8/06 -7/11
"Gating of CFTR CL Channels by ATP Hydrolysis"

Kline, David

NIH/NHLBI — 4/08-03/13
"Adaptation of brainstem circuits to chronic hypoxia" — $250,000

NIH/NHLBI — 4/10 –3/11
"Plasticity of nTS output neurons in acute and chronic Hypoxia" — $499,999

NIH/NIDDK/Case Western Reserve Univ — 4/07-3/11
"DNF and MeCP2 in autonomic dysfunction" — $41,892

NIH/NHLBI — 7/08-6/13
"Central nervous system plasticity in sympathoinhibition in pregnancy" — $394,834

Korthuis, Ronald

NIH	6/06-5/12
"Ethanol prevents microvascular dysfunction "	$225,000
NIH	3/10-2/12
"Mechanisms of Microvascular Control and Coordination in Health and Disease "	$262,000

Krenz, Maike

American Heart Association, National Center	7/06-6/10
"Defective Valvulogenesis in Noonan Syndrome"	$260,000
MU Research Council Grant	11/11-10/12
"Regional microRNA profiling in hypertrophic-obstructiveCardiomyopathy"	$7,319

Liang, Yayun

College of Veterinary Medicine Faculty	1/11-12/11
"Novel breast cancer therapy using an inhibitor of cholesterol biosynthesis"	$18,000
Universitaets-Frauenlininek, Germany,	3/11-6/11
"Progestin regulation of breast cancer cells in vivo.	$10,057

Martinez-Lemus, Luis

NIH	09-14
"Mechanisms of Microvascular Remodeling Progression."	2,250,000
NIH	10-14
"Mechanisms of Microvascular Control and Coordination in Health and Disease."	$8,450,000

Meininger, Gerald

National Institutes of Health-National Heart, Lung and Blood Institute	2010-15
"Mechanisms of Microvascular Control and Coordination in Health and Disease"	$10,096,262
National Institutes of Health - National Heart, Lung and Blood Institute	2009-14
"Acute mechanisms of vascular remodeling"	$1,825,523
NSF	2009-11
"Evanescent Field-Enabled Atomic Force Microscopy for Nanoscale Imaging of Cell Membrane Dynamics"	$200,000
NIH/NHLBI	2009-11
"Amyloid-b peptide on endothelial adhesion with its related cellular pathways."	$397,524

Polo-Parada, Luis

Mo Life Science Research Board	1/09-12/11
"*Photoacoustic detection of circulating melanoma cells in blood (Commercialization) "*	
NSF	6/11-5/14
"Nanostructured High Surface Area Sensor Systems for Enhanced Detection "	

Segal, Steven

NIH/NHLBI — 9/07-8/12
"Microcirculation in Aging Skeletal Muscle " — $1,949,380

NIH — 8/05-7/11
"Unit Control of Muscle Blood Flow " — $885,656

NIH/NHLBI — 9/08-8/11
"Intercellular Coordination of Blood Flow Control " — $1,076,098

NIH/NHLBI — 8/09-7/11
"Fast calcium responses along arteriolar endothelium" — $102,208

Terjung, Ronald

NIAMS — 7/09-6/14
"Exercise and Health: Integration From Molecule to Patient" — $1,309,555

NHLBI — 1/06-12/10
"Vascular Biology: Exercise Training and Vascular Disease." — $11,550,565

NHLBI — 1/06-12/10
"Factors Controling Peripheral Collateral Vessel Development in a Large Mammal" — $1,422,201

Cytokinetics Inc. — 10/09-10/10
"Influence of Muscle Activators on Exercise Performance and Muscle Blood Flow in Rats with Peripheral Arterial Insufficiencey" — $51,287

Zhang, Cuihua

NIH/NHLVI — 4/11-3/15
"Ang II and Aldosterone Effects on Insulin Resistance in Cardiovascular Tissue" — $250,000

1R01 DK085495-01A1 — 7/10-6/14
"Adipose tissue hypoxia and inflammation in obesity" — $250,000

NIH R01 — 6/06-4/12
"Mechanisms of Reperfusion-induced Endothelial Injury" — $1,808,540

NIH/NIDDK RO1 — 2/07-1/12
"Role of Cytokink-Induced Inflammation in Endothelial Dysfunction in Diabetes" — $1,620,440

Mizzou Advantage — 4/11-3/12
"Modeling childhood/adolescent obesity in a pig" — $92,500

2009 Myears Family Research Fellow in Cardiovascular Disease — 7/09-6/12
"Inflammatory Mediators of Atherogenesis in Diabetes" — $5,000

AHA Postdoctoral Fellowship — 7/10-6/12
"Role of Inflammatory Cell Types in Reperfusion-induced Vascualr Injury" — $102,040

AHA Pre-doctoral Fellowship — 7/10-6/12
"Bariatric Surgery Reduces Adipose Inflammation" — $52,000

2010 Myears Family Research Fellow in Cardiovascular Disease — 7/10-6/13
"Role of Dendritic Cells I nIschemia Reperfusion Injury" — $52,000

Zou, Xiaoqin

NIH 9/09-8/12
"ARRA Scoring Framework for structural models"

NSF 8/10-7/12
"A computational approach to template-based structure selection for protein-protein interactions "

Baines, C.

Editorial Boards:
American Journal of Physiology, Heart and Circulatory Physiology
Frontiers in Mitochondrial Physiology
ISRN Cardiology
Journal of Applied Physiology
Journal of Molecular and Cellular Cardiology

Reviewer:
American Journal of Physiology, Heart and Circulatory
Biochimica Biophysica Acta
Circulation Research
International Journal of Cardiology
Journal of Applied Physiology
Journal of Cardiovascular Pharmacology and Therapeutics.
Journal of Molecular and Cellular Cardiology
Journal of Pharmacology and Experimental Therapeutics
Journal of Vascular Biology
Mitochondrion
Stress

Committee Service:
Chair, DCRC Safety Committee
Chair, 2011 Cardiovascular Day Planning Committee
Member, Research Committee, College of Veterinary Medicine
Dissertation committee Advisor: Kyle S. McCommis
Director, Dept. of Biomedical Sciences Seminar Series

Service to Professional Societies:
Member-at-large, Leadership Committee, American Heart Association Basic Cardiovascular Sciences Council

Study Section:
NIH Myocardial Ischemia and Metabolism Study Section, Ad hoc reviewer. February 3rd.

Blaine, E. H.

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

Bompadre, S.

Reviewer for the University of Missouri Research Board

Bowles, D.

Manuscript Review
Reviewer, *American Journal of Veterinary Research*
Reviewer, *American Journal of Physiology: Cell*
Reviewer, *Circulation Research*
Reviewer, *Journal of Applied Physiology*
Reviewer, *American Journal of Physiology: Heart and Circ. Physiology*
Reviewer, *Medicine & Science in Sports & Exercise*
Reviewer, *Journal of Vascular Research*
Reviewer, *American Journal of Physiology: Heart & Circulatory Physiology*
Reviewer, *Journal of Applied Physiology*
Reviewer, *Cardiovascular Research*
Charter Member, NIH Vascular Cell & Molecular Biology (VCMB) Study Section
Internal Advisory Board, NIH PO1 Application, G. Meininger (P.I.)
Supervision of personnel: Darla Tharp, Rebecca Shaw, Jan Ivey, Craig Emter, Hope Gole, Brad Fleenor, Erin O'Connor, Jenna Bilhorn, Jillian Fairchild, Tom Fay, Melissa Morehead, Miles Tanner, Stacy Bruno

Clarke, L.

Cystic Fibrosis Foundation, Research and Training Committee (Grant Reviews), Charter Member
Cystic Fibrosis Foundation – Regional Development Program Review Committee
Digestive Diseases and Sciences, manuscript reviewer
Gastroenterology, manuscript reviewer
American Journal of Physiology, manuscript reviewer
University Promotion and Tenure Committee, sub-committee chair
Graduate Policy Advisory Committee, Biomedical Sciences - Member
Chair, faculty mentor committee for Dr. David Kline
Biomedical Sciences Physiology Search Committee, Chair (Dudeja recruitment)
Supervision of staff
Nancy M. Walker, Res. Spc.
Jen M. Brazill, Sr. Res. Tech.
Erin H. Hoover, Res. Tech.
Graduate students
Matthew Cook (rotation)
Post-doctoral fellows
Jinghua Liu
Undergraduates
Ashley Willingham

Davis, G.

Teaching

2009-current Course Director, MPP Journal Club Course
2006-current Graduate lectures in departmental Microcirculation course, Cell signaling course and Research Skills course
2008-current Medical Student PBL Curriculum Block 3 Mentor (Neurology block)
Postdoctoral Research Fellows Sponsored
Dae Joong Kim, PhD
Amber Straman, PhD
Anastasia Sacharidou, Ph.D
Member on Graduate Student Thesis Committees

Chair of Graduate Thesis Committee
Co-Chair of Graduate Thesis Committee
Sponsored Undergraduate Research Projects
Sponsored Medical Student Research Projects
Sponsored Ph.D. or M.D., Ph.D. Graduate Student Laboratory Rotations
Committees/ Administrative responsibilities
MD/PhD Executive Committee
Tenure and Promotions Committee
Chair, Tenure and Promotions Committee

Ding, S.

Coordinator of Membrane Journal Club (MJC) in Dalton
Member of safety committee of Dalton Cardiovascular Research Center
Invited review for research grant of MRC, UK. Grant title: Physiological role for CO in astrocytes: Link to neuroprotection.
March 2011-2015: Member of the Membership Committee for American Society of Neurochemistry (ASN).
Serving on the Organizing Committee for Cardiovascular Day 2012 in University of Missouri. Feb 23, 2012.
Serving on the Organizing Committee for Translational Neuroscience Symposium in University of Missouri. Feb 27-March 1, 2011. Duty: Find speaker, arrange transportation, schedule.

Fay, W.

SCIENTIFIC ACTIVITIES
Editorial Boards
2010-2012 Heart Insight
Manuscript Reviewer
Arteriosclerosis Thrombosis and Vascular Biology
Blood
Mayo Clinic Proceedings
New England Journal of Medicine
Gene
Circulation
Circulation Research
Journal of Biological Chemistry
Coronary Artery Disease
Trends in Cardiovascular Medicine
Journal of Clinical Investigation
American Journal of Hematology
Hypertension
Thrombosis and Haemostasis
Thrombosis Research
American Journal of Cardiology
Journal of Leukocyte Biology
Journal of Vascular Research
British Journal of Pharmacology
Journal of Histochemistry and Cytochemistry
Bioorganic & Medicinal Chemistry Letters
Journal of Thrombosis and Thrombolysis
American Heart Journal
Journal of Thrombosis and Haemostasis
Nature Medicine

MEMBERSHIPS AND OFFICES IN PROFESSIONAL SOCIETIES
Fellow, American College of Cardiology
Council on Thrombosis, American Heart Association
International Society on Thrombosis and Haemostasis
Central Society for Clinical Research
Fellow, American Heart Association
American Society of Hematology

TEACHING ACTIVITIES
Basic Science Teaching:
Coordinator, Weekly Basic Science/Clinical Lecture Series for Cardiology Fellows
Coordinator, Cardiovascular Research Center Seminar Series
Coordinator, Cardiovascular Research Center Journal Club
Mentorship: Research Fellows:
Yan Ji, M.D., Ph.D.
Neha Goyal, MD
Lakshmi Yaddanapudi, MD

Internal Medicine Residents/Cardiology Fellows:
Poorna Karuparthi, MD
Manavjot Sidhu, MD
Mayank Mittal, MD

Undergraduate Students:
Matthew Rendo

COMMITTEE AND ADMINISTRATIVE SERVICES
National
American Heart Association National Peer Review Steering Committee
American Heart Association Emeritus Member Task Force
Chair, Membership Committee, Atherosclerosis Thrombosis and Vascular Biology Council, American Heart Association
American Heart Association Heartland Affiliate Research Committee
Board of Directors, AHA Midwest Affiliate
AHA National Research Committee (Chair of Peer Review Subcommittee, 2009-2011)
ATVB Editor Search Committee
School of Medicine Advisory Committee on Research Space

Hasser, E.

Committee/Mentorship

Graduate Students - Mentor
T. Luise King, DVM (Ph.D.)
Catharine G. Clark (Ph.D.; co-mentor with David D. Kline)

Graduate Students – Committee Member
Seth T. Fairfax (Ph.D.)

Teaching
Veterinary Physiology 5504 and 8420; Course Director
Cardiovascular Physiology – 13 Lectures
Renal Physiology – 14 Lectures
Total Contact Hours – 41

American Physiology Society Cardiovascular Nomination Committee
Microcirculatory Society Publications Committee

Government Service Peer review
NIH Hypertension and Microcirculation (HM)Study Section
NIH Special Emphasis panel ZRG1 EMNR-B

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

University of Missouri-Columbia School of Medicine (Since 1998

1997-present	Departmental Committee of Research Incentive Funds
2002-present	Internal Advisory Panel: Center for Diabetes and Cardiovascular Health
2004-2010	Departmental Tenure and Promotions Committee, Chair
2010-present	Departmental Tenure and Promotions Committee
2004-present	Departmental Faculty Search Committee
2004-present	Departmental Space Committee
2004-present	Departmental Curriculum Development Committee
2005-present	School of Medicine Council of Chairs
2005-present	School of Medicine Administrators Council
2006-present	MPP Executive Committee
2007-present	Executive Committee of the MD-PhD Program

Graduate student committees:
Joshua Scallan, PhD
Meredith Jean (Jaye) Stevenson
Hanrui Zhang, M.D
Areum Kim, Ph.D.
Chen Cao, Ph.D.

Hwang, T.C.

Editorial Board for Biophysical Journal and the Journal of General Physiology.
Reviewed manuscripts for JGP, JBC, PNAS, BBA and Biochimie.
Reviewed grant proposals for Italian Telethon Foundation and National Science and Engineering Research Council of Canada.
Graduate Educational Committee and Dalton P&T Committee
Block 3 teaching
Committee member: Yong-Hong Bai

Hyder, S.

Reviewer Carcinogenesis
Reviewer Steroids
Endocrinology
Acta Odontologica Scandinavica
Faculty Search Committee (ad hoc), Internal Medicine (GI)

Hill, M.

Editorial Boards
Microcirculation
Journal of Vascular Research
Frontiers in Vascular Physiology
Grant Reviewer
Member of the Medical Review Board for the Sir Edward Dunlop Medical Research fund
American Heart Association

Ad Hoc Reviews
American Heart Association, American Heart Association, Feffress Foundation, Diabetes Australia Research Trust, National Health and Medical Research Council, Cardiovascular Lipid Grants, Clive and Vera Ramaciotti Foundation, Canadian heart and Stroke Foundation, Australian Research Foundation, Wellcome Foundation, Louisiana Board of Regents, Qatar National Research Foundation, National Science Engineering Research Council.

Peer Reviewer
American Journal of Physiology, Journal of Biological Chemistry, Hypertension, Microvascular, Journal of Applied Physiology, Diabetes, Journal of Vascular Research , Journal of Pharmacology and Experimental Therapeutics, Diabetologia, Journal of Laboratory and Clinical Medicine, Australian and New Zealand Journal of Medicine, Biochemica Biophsica Acta, British Journal of Pharmacology, Clinical and Experimental Physiology and Pharmacology, Diabetes Care, Journal of Physiology, Microcirculation, Pflugers Archives, Cardiovascular Research FASEB Journal, Circulation, Expert Option on Therapeutic Targets, Journal of Vascular Pharmacology, Journal of Cellular Physiology, Lipids, Cell Calcium, Circulation Research, Canadian Journal of Physiology and Pharmacology, Arteriosclerosis, Thrombosis and Vascular Biology, Journal of Pharmacy and Pharmacology, Journal of Hypertension, PLOS.
Committee
Nominating Committee for American Physiological Society,

Kline, D.

Teaching Activity: Didactic and Clinical Teaching

Veterinary Physiology 5504, Co-Course Director
Veterinary Physiology 5504, Didactic teaching, 11 lecture hours, 18 laboratory hours, 12 examination hours, 4 review hours, for 45 total contact hours, 127 students
Neural Control of the Circulation 9467 (Co-listed MPP 9437), Course Director
Neural Control of the Circulation 9467 (Co-listed MPP 9437), Didactic teaching, 5 lecture hours, 10 presentation hours, 4 examination hours, for 19 total contact hours, 6 students

Service Activity

Departmental

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

College

2009-2011	Member, Faculty Honor Code Committee
2008-2011	Member, Animal Resources Committee
2007-2010	Member, Committee on Research

University

2010-2011	Organizing committee for 2011 Cardiovascular Day
2009-present	Member, Appointment and Promotions Committee, Dalton Cardiovascular Research Center
2008-present	Member, Animal Issues Response Team (AIRT), Office of Research

National Service

2009-2011	Member, Communications Committee, American Physiological Society
2010-	Member, Respiration Section Advocacy Sub-Committee, American Physiological Society

International Service

2009-2012	Member, Hypoxia Interest Group Steering Committee, Secretary, American Physiological Society
2010	Reviewer, Italian Ministry of Health - Health Research Grant, Italy
2010	Reviewer, National Institute of Academic Anaesthesia Research Grants, London, UK

Journal Review Service

American Journal of Physiology: Regulatory, Integrative and Comparative Physiology
American Journal of Physiology: Cell
Journal of Applied Physiology
Respiratory Physiology and Neurobiology
British Journal of Pharmacology
The International Journal of Neuroscience
BMC Neuroscience
Journal of Neurophysiology
Reviewing Editor: Frontiers in Integrative Physiology

Grant Review Boards Service

Reviewer, National Science Foundation (NSF), Faculty Early Career Development (CAREER) Program
Member, American Heart Association (AHA), Study Section, Grant Review Service, Vascular Biology and Blood Pressure 2 (VBBP2)
Reviewer, Italian Ministry of Health - Health Research Grant (also listed under International Service)
Reviewer, National Institute of Academic Anesthesia Research Grants, London, UK (also listed under International Service
Reviewer, National Institutes of Health (NIH), Respiratory Integrative Biology and Translational Research Study Section (RIBT) – Feb 2011

Supervision of personnel

James R. Austgen- postdoctoral fellow
Brenna Barger- veterinary research assistant
Catharine G. Clark- graduate student
Heather A. Dantzler- technician
Erin Willis- veterinary research assistant

Korthuis, R.

NIH, Vascular Cell and Molecular Biology Study Section, charter member, 2007-1011

Editorial Board

American Journal of Physiology: Heart and Circulatory Physiology; 1987 – 1999; 2005 – present
Cardiovascular Research; 2008 – present
Circulation Research; 2010 - present

Associate Editor

Frontiers in Vascular Physiology: 2010 – present

Service to Professional Societies

Cardiovascular Section Steering Committee, 2002-2011
Committee on Committees, 2011-2013
Association of Physiology Department Chairs, 2004 - present
Association of Medical School Pharmacology Chairs, 2004 - present

Ad hoc reviewer for over 60 journals

Krenz, M.

Dalton Safety Committee
Graduate Committee, Kyle McCommis (Biomedical Sciences)
1999 – present Member, International Society for Heart Research (ISHR), North American Section
2010 – present Member, American Physiological Society
2010 – present Member, American Heart Association

Reviewer *(ad hoc)* *Basic Research in Cardiology, Circulation Research, Coronary Artery Disease, FEBS Letters, Journal of Applied Physiology, Journal of Cardiac Failure, Journal of Molecular and Cellular Cardiology*
Poster Judge CV Day 2010, University of Missouri-Columbia

Editorial Board, Journal of Applied Physiology, Frontiers in Integrative Physiology

Liang, Y.

Invited Reviewer for the journal of Cellular Physiology and Biochemistry for reviewing manuscript **2011MS001.**

An appointment to the Editorial Board of Chinese Journal of Clinicians (International) for Scientific Review. This appointment is for a term beginning on January 2011 and ending on December 2014.

Martinez-Lemus, L.

Extramural Grant Reviewer for:
Editorial Board member for "Microcirculation," 2010-2015.
Review Editorial Board for "Frontiers in Vascular Physiology," 2010-Present
Reviewer for:
Journal of Vascular Research
Arteriosclerosis, Thrombosis, and Vascular Biology
American Journal of Physiology
Clinical and Experimental Medicine
BioMed Central Cell Biology
Hospital Practice
Microcirculation
Microcirculatory Society: Program Committee (2007-2010)
Membership Committee (2010-2013)
American Physiological Society: Fellowship Committee (2008-2011)
Member, Committee for Appointment and Promotion of Non-Tenure Research Track Faculty. Dalton Cardiovascular research Center. University of Missouri-Columbia.
Member, MPP Program Assessment Committee.
Member, Gender and Racial Diversity Equity Council Representation.
Member, Dalton Cardiovascular Research Center Safety Committee.
Appointed member of the School of Medicine Research Council (2009-).

Meininger, G.

American Physiological Society (APS)
- Fellow, Cardiovascular Section of APS
- Member, Splanchnic Circulation Group of APS

Microcirculation Society
Biophysical Society
European Society for Microcirculation
Asian Union for Microcirculation
American Heart Association (AHA)
- Fellow, Council on High Blood Pressure Research of AHA
- Fellow, Council on Circulation of AHA
- Member, Council on Basic Science of AHA

American Society for Cell Biology
North American Vascular Biology Organization
Association of Chairs of Departments of Physiology

Extramural Grant Review: Member American Heart Association Steering Committee, Unified Peer Review Panel representing the Midwest Programs, July 2009-June 2011.

National Committees:

APS: SAC/Nominating Committee: CVS Representative, 2003-2004; 2007-2010

AJP (Heart Circulatory Physiology) Associate Editor 1993-1999; 2007-2010

External Consulting:

Chair, Internal Advisory Committee, for NIH PPG, PI. Harold Laughlin and Doug Bowles, University of Missouri, Columbia, MO, 2010.

Editor Scientific Journal:

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 International Journal of Physiology, Pathophysiology and Pharmacology, 2010-present.
Editorial Board Member for Nanotechnology, Science and Applications, 2007-present.

Reviewer:

American Journal of Physiology: (Heart and Circ. Physiology)
American Journal of Physiology: (Regulatory, Integ. and Comp. Physiology)
American Journal of Physiology: (Renal, Fluid and Elec. Physiology)
American Journal of Physiology: (Gastrointestinal and Liver Physiology)
American Journal of Physiology: (Cell Physiology)
American Journal of Pathology
Arteriosclerosis and Thrombosis and Vascular Biology
Biology of Reproduction
British Journal of Pharmacology

Circulation Research
Diabetologia
European Journal of Physiology
European Journal of Pharmacology
Experimental Cell Research
Hypertension
Journal of Biomechanical Engineering
Journal of Cell Biology
Journal of Fundamental and Clinical Pharmacology
Journal of Applied Physiology
Journal of Cardiovascular Research
Journal of Diabetes and its Complications
Journal of Experimental Pharmacology and Experimental Therapeutics
Journal of Vascular Research
Life Science

Microvascular Research
Nature Methods
Nature Nanotechnology
Pediatric Research
Proceedings of the Society for Experimental Biology and Medicine
Proceedings for the National Academy of Science

Scientific Meetings:
Scientific Committee member, 10th International Symposium on Resistance Arteries, Comwell Rebild Bakker, Skorping, Denmark, May 8-12, 2011.

Intramural:
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.

Polo-Parada, L.

2008-present Member of the MU PREP (Post-baccalaureate Research Education Program) Scholars Program. 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.

EDITORIAL BOARD:

Medical Pharmacology: Current Research.

CONSULTANCIES/ADVISING SERVICES:

National Biodefense and Analysis and Countermeasure Center (NBACC). US Department of Homeland Security.
Battelle. US. Department of Homeland Security.

ADVISOR AND CO-ADVISOR:

Tsai, Mingfeng. Department of Medical Pharmacology and Physiology. Ph.D. Graduated 2010 Co-Advisor.
Steven J Apperson. Department of Engineering. Ph.D. Student. Graduate 2010. Co-Advisor.
Sangho Bok. Department of Engineering. Ph.D. Student. Graduated 2010.Co-Advisor.
Charles M Darr. Department of Biological Engineering. Ph.D. Student. Advisor.

Sagar K Gupta. Department of Biological Engineering. Ph.D. Student. Co-Advisor.
Craig R. Weilbaecher. Department of Biological Engineering. Ph.D. Student. Graduated 2010. Co-Advisor.
Jasenka Memisevic. NSF Graduate Research Fellow. Biological Engineering. Ph.D. Student. Gradauted 2010. Co-Advisor.
Kathy Brown. Department of Biological Engineering. M.E. Student. Graduated 2010. Co-Advisor.
Francisco Ramirez. University of Guanajuato. M.S. Student. Co-Advisor.
Jorge Gonzalez Castorena. Department of Biological Engineering. Ph. D. student. Advisor.
Jih, Kangyang. Department of Medical Pharmacology and Physiology. Ph. D. student Co-Advisor.
Dr. Asur Guadarrama Santana. University of Guanajuato. Pos-Doctoral.

ADVISOR COMMITTEES:
The National Academies. Advisers to the Nation on Science, Engineering and Medicine.
Americana Heart Association.

PROFESSIONAL ASSOCIATIONS:
2004-present Member, American Heart Association.
1999-present Member, Society for Neuroscience.
1994-present Member, Biophysical Society.

INTERNATIONAL MENTORING PROGRAMS:
American Heart Association.

Ad Hoc reviewer:
Journal of Neuroscience Methods.
Journal of Neuroendocrinology.
Journal of Applied Physiology.

STUDY SECTION PARTICIPANT:
2011. Spring. American Heart Association. Peer Review. Cardiac Bio BCT4.
2010 Fall. American Heart Association. Membrane and Subcellular Organelles (MSO), Committee1.

Committees:
2011-2013 Hearnes Center Committee Faculty representative – University of Missouri
2011 Representative to the Graduate Life Sciences & Professionals Programs Summer Expo 2010
2012 Cardiovascular Day - Member of Organizing Committee.

Segal, S.

Manuscript reviewer: Am. J. Physiol. (Heart Circ. Physiol & Regul. Integ. Physiol.), J. Appl. Physiol., J. Physiol.; Promotion and Tenure review committee (MPP)

Editorial Boards: American Journal of Physiology: Heart and Circulatory Physiology, ChronoPhysiology and Therapy, Micro-circulation, Journal of Applied Physiology , Journal of Vascular Research

North American Vascular Biology Organization (NAVBO) 1994 - 2010

Grant reviewer: Swiss National Science Foundation (1998 -), Wellcome Trust (1996 -)

POSTDOCTORAL FELLOWS SPONSORED
Pooneh Bagher, Ph.D. (2007- 2011)
Matthew J. Socha, Ph.D. (2009-)
Erik J. Behringer, Ph.D. (2009-)

Doctor of Philosophy
Shenghua Yuan (University of Missouri, Medical Pharmacology and Physiology; *in progress*)

JUNIOR FACULTY MENTOR/ADVISOR
Timothy L. Domeier, Ph.D.
Paul Fadel, Ph.D.
Maike Krenz, M.D.
Louis Polo-Parada, Ph.D

GRADUATE STUDENT THESIS COMMITTEES SERVED
Josh Scallan (MU, MPP: 2006-2010: Ph.D., 2010)
Erica Boerman (MSU, Toxicology & Pharmacology: 2006-2010; Ph.D. 2010)
Seth Fairfax (MU, Medical Pharmacology & Physiology: Doctorate in progress)
John Wolpers (MU, Medical Pharmacology & Physiology: M.S. in progress)

External Referee for Promotion and Tenure
Baylor College of Medicine (05/11)
University of Virginia (07/2011)

Sohma, Y
Paper reviewer (Journal of Physiological Sciences)

Terjung, R.
Member, Hypertension/Microvasc Study Section, NIH, Bethesda, 2007-2010.
Chair, Book Committee, American Physiological Society, January 2007-2012.
Editor-in-Chief, Comprehensive Physiology (Online Handbooks of Physiology*)* 2009-2012

Zhang, C.
Invited Speaker for Experimental Biology Meetings by the 2011 American Society for Investigative Pathology(ASIP) Programming Committee at the Session of "Metabolic Syndrome: Links Between Insulin Resistance, Inflammation, Vascular Pathobiology" at 8:30 AM on Monday, April 11, 2011 in Washington DC. Title is "Role of inflammatory mediators in insulin resistance and endothelial dysfunction".

Symposium Moderator: AHA Scientific Session. Session Number: ADD.700.04 and Title: Endothelium, Vascular Tone and Nitric Oxide. November, 2010

Symposium Organizer: AHA Scientific Session. Session Number: CVS.172 and Title: Vascular Dysfunction, Regeneration and Repair. November, 2010

Serve on Research Council Committee for Internal Medicine and School of Medicine
National: American Physiological Society, FASEB/EB & American Heart Association
ATVB Program Committee for AHA Scientific Session
AHA Peer Review Committee for National Center (Vascular Biology & Blood Pressure)

Membership Director for Chinese American Diabetes Association (CADA)
Treasurer for CADA
Member of Executive Committee for China Faculty Association (CFA) at Texas A&M University

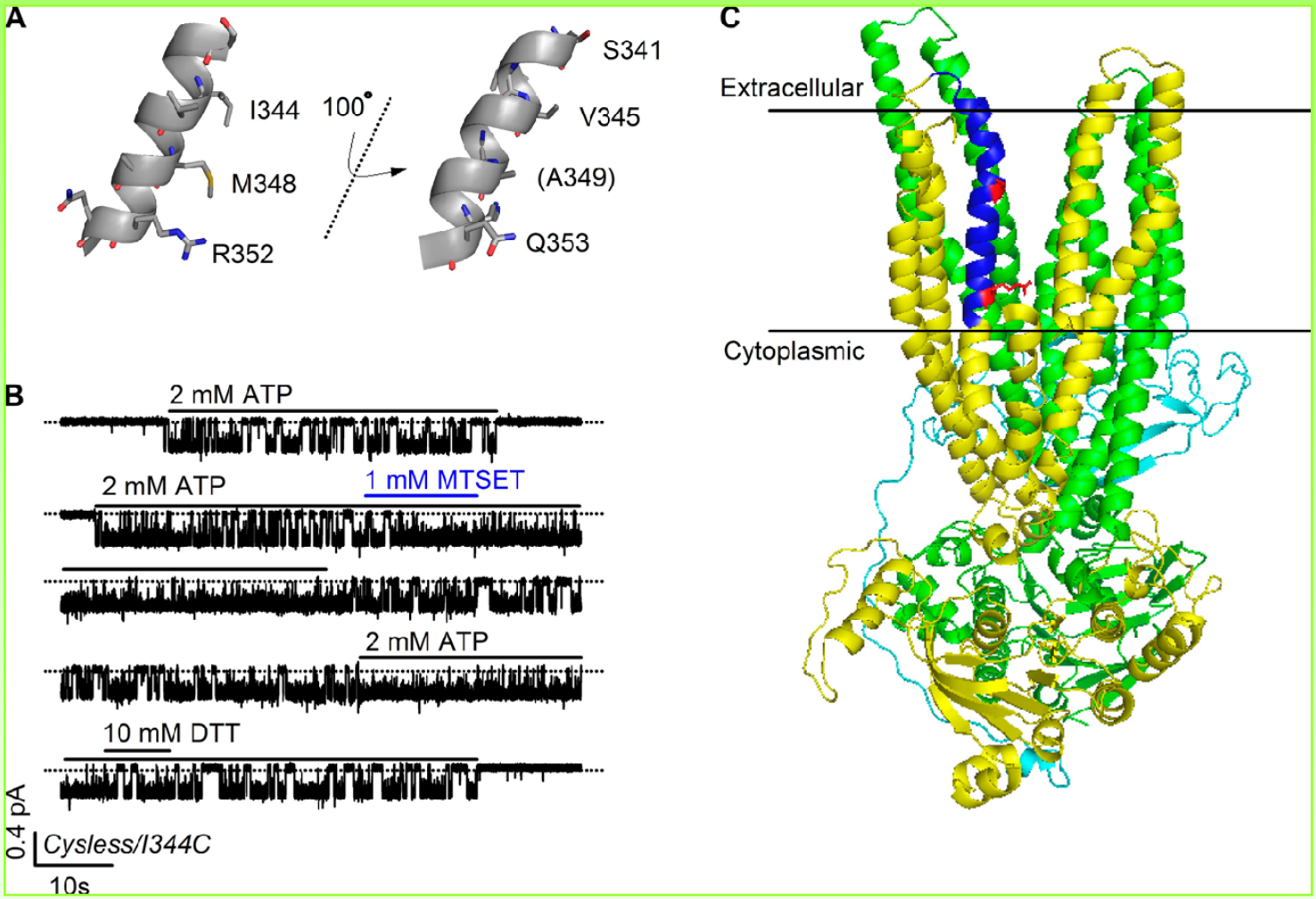
Editorships:
Editorial Board Member, Amer. J. Physiol. - Heart and Circulatory Physiology
Editorial Board Member, Basic Research in Cardiology
World Journal of Cardiology
Circulation Research
Frontiers in Vascular Physiology
Serve on NEP faculty searching committee

Picture on back cover courtesy of Dr. T. C. Hwang

Dual roles of the sixth transmembrane segment of the CFTR chloride channel in gating and permeation.
Bai Y, Li M, Hwang TC.
J Gen Physiol. 2010 Sep;136(3):293-309.
PMID: 20805575

Panel A: Helical structure of the 6th transmembrane segment (TM6) of the CFTR chloride channel.

Panel B: Real time single-channel recording of the CFTR channel with an engineered cysteine at position 344 of TM6. Chemical modification of this cysteine dramatically alters the behavior of the channel: first, significant activity of the channel can be seen even in the absence of ATP; second, in the presence of ATP, the channel almost never closes. These observations indicate, for the first time, that movement of TM6 is intimately involved in CFTR gating.
Panel C. A homology model of the CFTR protein based on the crystal structure of the ABC protein, SAV1866, shows the position of TM6 (colored blue) and positions 341 and 352 are colored red.


A
I344
M348
R352
100°
S341
V345
(A349)
Q353
B
2 mM ATP
2 mM ATP
1 mM MTSET
2 mM ATP
10 mM DTT
0.4 pA
Cysless/I344C
10s
C
Extracellular
Cytoplasmic