MENTORS DIRECTORY

2019 AMERICAN HEART ASSOCIATION UNDERGRADUATE SUMMER INTERNSHIP RESEARCH PROGRAM

to be held at

The Joan C. Edwards School of Medicine
at Marshall University

Dr. Jung Han Kim
Professor
Department of Biomedical Sciences
Marshall University School of Medicine
kimj@marshall.edu
(304) 696-3873

Genetics of Obesity and Type 2 Diabetes

My research interest is in understanding the etiology and pathogenic mechanisms underlying type 2 diabetes and obesity, concomitantly related diseases. Type 2 diabetes is the most common form of human diabetes, accounting for over 90% of cases and obesity at such epidemic proportions creates serious public health problems. There is substantial evidence demonstrating that genetic factors are strongly involved in the development of type 2 diabetes and obesity, and I have focused my attention on the link between gene dysfunction and these diseases and its interaction with diets. As an internship project in our laboratory for the WV-INBRE Summer Research Program, I propose to study candidate genes for diabetes and obesity loci identified in a genetic mouse model of obesity and type 2 diabetes and their interactions with diets. This study will ultimately provide ready targets for diabetes and obesity therapies in humans. Experimental methods involved in this internship research will include enzyme-linked immunosorbent assay, colorimetric assay, polymerase chain reaction (PCR), western blot analysis, and real-time quantitative PCR. DNA, RNA and protein will need to be isolated from mouse tissues. Instruments involved in this project include gel electrophoresis, western blotting apparatus, microplate readers, spectrophotometer, imaging system, thermal cyclers, EchoMRI, and comprehensive lab animal monitoring system.

Wei Li, MD, PhD

Associate Professor
Department of Biomedical Sciences
Joan C. Edwards School of Medicine
Marshall University
1 John Marshall Drive, Huntington WV 25701
Phone: 304 - 696 - 7342
Fax: 304 - 696 - 7207
Email: liwe@marshall.edu
https://jcesom.marshall.edu/research/office-of-research-and-graduate-education/research-faculty/biomedical-sciences/wei-li/

Projects summary

Dr. Wei Li' laboratory is studying thymidine phosphorylase (TYMP), an intracellular enzyme, on development of cardiovascular diseases. **Project #1** is to study the role of TYMP on activation of platelets, one type of small circulating cells, which prevent blood loss when skin is cut or injured; but in diseased conditions, they form clots, and induce vessel occlusion. The clotted vessel is the cause of some life-threating diseases, such as ischemic stroke or heart attack. Dr. Li is studying how this enzyme affects the activation of platelet surface receptors, and thus induces clot formation, which is also called thrombosis. **Project #2** is to study the role of TYMP on the development of atherosclerosis. Atherosclerosis is induced by deposition of lipid (fat) in the vessel wall, which leads to formation of a buildup called atherosclerotic plaque. The plaque can narrow the vessel lumen and thus reduce blood flow through the diseased portion. Severe obstruction or rupture of the plaque also can lead to clot formation, and thus induce stroke and heart attack . By using genetic modified mice, in which it is easy to induce the atherosclerotic plaque in their vessel wall, Dr. Li is studying whether deletion of TYMP in mice can prevent the atherosclerotic plaque formation.

Description of student training:

The AHA summer student who joins Dr. Li 's laboratory will be assigned a mentor, a Research Assistant Professor in the lab, to perform a mentored, but independent scientific project. The student will be guided to a considerable extent and focus, so she/he can understand the biological concepts and grasp the complexity of the project in which she/he is involved. The student will be taught the research techniques and skills that are necessary for the project. This will be either western blot or immunohistochemical staining, or both. The student also will be trained for equipment usage, software usage, data collection and analysis, data interpretation, etc. The student will also be taught to access sources of the scientific information, such as using Pubmed, Scopus etc. The student will be guided to prepare a 15 to 20 minutes oral presentation to summarize the work and data harvested in the lab, and give a presentation in the lab meeting during her/his last week in the lab.

Dr. Joseph Shapiro
Dean, Joan C Edwards School of Medicine
One John Marshall Drive
Huntington, WV

Dr. Jiang Liu
Associate Professor
Department of Pharmacology, Physiology & Toxicology
Joan C Edwards School of Medicine at Marshall University
LiuJ@Marshall.edu
(304) 696-7359

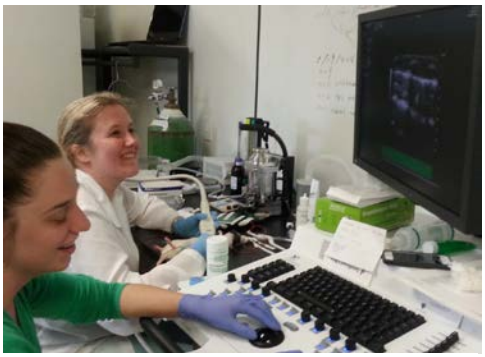
The major research interest is renal physiology, focusing on understanding the molecular mechanism of cardiotonic steroids (CTS)/Na/K-ATPase-mediated signal transduction in the regulation of renal sodium handling. The long-term goals are to understand the role of endogenous CTS and the Na/K-ATPase signaling in salt retention/salt-sensitive hypertension as well as heart/kidney function and remodeling.

Our current project is to understand the intrinsic relationship between the receptor Na/K-ATPase/Src complex and ROS generation/signaling, and the molecular basis of ROS/Na/K-ATPase interaction and its role in renal salt handling and organ remodeling. Specific projects that we are currently working on are:

1. The involvement of ROS/carbonylation in the Na/K-ATPase signaling.
2. The structure determinant(s) and effect of carbonylation of the Na/K-ATPase in Na/K-ATPase signaling.
3. The role of Na/K-ATPase signaling and salt sensitivity.
4. Animal (mouse) models of renal insufficiency mediated heart/kidney fibrosis

Dr. Sandrine V. Pierre
Associate Scientific Director
Marshall Institute for Interdisciplinary Research
304.696.3505
pierres@marshall.edu

Dr. Zijian Xie
Investigator and Director
Marshall Institute for Interdisciplinary Research 304.696.3549
xiez@marshall.edu



Echocardiographic assessment of rodent cardiac function by Dr. P. Marck and undergraduate fellow A. Bryant.

The Pierre lab studies specific intracellular pathways involved in the integrated response of the myocardium to hemodynamic and metabolic disturbances. Our goal is to develop new paradigms to therapeutically address cardiovascular diseases based on the Na/K-ATPase signaling complex. We examine these issues by combining techniques of molecular and cell biology with *ex-vivo* (biochemistry and cell physiology, isolated heart perfusion, primary cardiac cell cultures, histology) and *in-vivo* assessments of cardiac function in genetically altered mice (echocardiography, measurement of blood pressure by tail-cuff and telemetry, cardiac and vascular catheterization). In the interdisciplinary environment provided by MIIR, interns are exposed to the pre-clinical models and key techniques that are currently available to cardiac and vascular physiologists and pharmacologists.

Project 1. Cardioprotection by Na/K-ATPase ligands in acute myocardial infarction
Rationale: In addition to pumping ions, Na/K-ATPase interacts with neighboring membrane proteins and takes part in signaling complexes to send messages to various intracellular organelles. We believe that understanding these pathways and targeting the Na/K-ATPase receptor function will lead to novel interventions for the treatment and prevention of ischemia and reperfusion injury.
Method: the INBRE fellow will learn the isolated Landendorff-perfused mouse heart preparation and expose it to novel compounds targeting the Na/K-ATPase cardioprotective signaling pathway. This includes analysis of contractile function in real time and assessments of activation of the Na/K-ATPase cardioprotective pathway biochemically. The effectiveness of promising compounds will be further tested *in vivo* following experimentally-induced acute myocardial infarction (AMI). Mice will be subjected to an acute occlusion of the left descending anterior artery (LAD) for 30 min, and cardiac function and remodeling will be monitored after 1 and 2 weeks of reperfusion. In addition to functional echocardiographic assessments, the fellow will conduct morphometric and histological studies as well as biochemical (western blot) and qPCR evaluation of fibrosis, inflammation, and hypertrophy markers.

Project 2. Role of α1 Na/K-ATPase in adverse cardiac remodeling and heart failure
Rationale: Heart failure (HF), a chronic incurable illness, is the common end-stage of heart diseases caused by an array of highly prevalent conditions such as hypertension and coronary heart diseases. A greater and broader protection must be achieved to face the unmanageably high HF morbidity and mortality rates amidst the exploding incidence and prevalence of the condition worldwide. Targeting the Na^+/K^+-ATPase receptor function may lead to novel interventions
Method: Using our newly developed model of cardiac-specific KO of Na^+/K^+-ATPase α1, we will assess the role of Na^+/K^+-ATPase α1 in the development of hypertrophy, fibrosis and heart failure in mice subjected to Angiotensin II infusion by osmotic minipumps. In addition to functional echocardiographic assessments, the students will conduct morphometric and histological studies as well as biochemical (western blot) and qPCR evaluation of fibrosis, inflammation, and hypertrophy markers.

Nalini Santanam, PhD, MPH, FAHA
Professor
Department of Biomedical Sciences
Department of Cardiology (Medicine)
Cardiovascular Disease Research Cluster Coordinator,
Joan C Edwards School of Medicine at Marshall University
1700 3rd Ave, 435S BBSC
Huntington, WV 25755
Tel: (304) 696-7321
Email: santanam@marshall.edu

My laboratory is interested in studying how various organs (gut-brain-adipose) cross-talk in reducing risk to cardiometabolic diseases in all age groups. We are interested in studying lifestyle changes (diet and exercise) on metabolic outcomes.

The following projects are available in my laboratory:

Project 1: Aging, Gut microbiome and risk to cardiometabolic diseases: The microbes that live within the gut play an important role in metabolism. These microbes can release factors that affect the host's metabolic function. In our laboratory we are studying changes in gut microbiome after exercise or dietary modifications and its effect on cardiometabolic function.

Project 2: Behavior and appetite regulation: Energy balance is key to maintaining body weight. Hypothalamic regulation of appetite maintains energy balance. Stress, anxiety and depression may lead to changes in appetite. Our laboratory is interested in studying the interplay between behavioral stress (such as anxiety or depression) and appetite regulation. We are investigating the effect of dietary modification or exercise on behavioral changes in rodent models.