MENTORS DIRECTORY

2017-2018 RESEARCH INTERNSHIP PROGRAM FOR HSTA SCHOLARS

Offered by the

West Virginia IDeA Network of Biomedical Research Excellence (WV-INBRE)

to be held at

The Robert C. Byrd Health Sciences Center of West Virginia University

And

The Joan C. Edwards School of Medicine at Marshall University

Introduction

The WV-INBRE is pleased to offer research internships to HSTA scholars at West Virginia University and Marshall University during the academic year. For the 2017-2018 academic year the internship period will begin as early as October 1, 2017 and extend through April 30, 2018. (End date is flexible). Internees will eventually present the results of their research at the WV-INBRE Research Symposium to be held In July 2018 at West Virginia University. Listed in this directory are faculty members at the West Virginia University Health Sciences Center and the Joan C. Edwards School of Medicine at Marshall University who have agreed to participate as mentors in this internship program. Each mentor has submitted a description of the project(s) that is (are) available to interns in his/her laboratory. Please review these carefully so that you are aware of what is available for research projects. Some descriptions are more comprehensive than others; therefore, you may want to contact certain mentors for more detail or to ask for clarifications about the opportunities in their labs. In any case, it is a good idea to speak with potential mentors to be sure you understand what will be expected if you work in his/her lab for the year.

A listing of mentors with a short description of their research and the general area of their research is presented on pages 3-5. Mentors and project descriptions begin on page 6. Listed for each mentor is an e-mail address, phone number and, where available, a home-page address. The home-page addresses will allow you to learn more about the mentors and their research programs.

Application forms are available on the WV-INBRE web site (http://www.wv-inbre.net) at a link under **Internship Programs, then HSTA**. Applications may be submitted by mail or e-mail; however, **direct electronic submission is available and its use is encouraged.**

For general questions about the internship program, or if you have difficulty reaching a mentor, please contact:

Valerie A. Watson, M.S.
WV-INBRE/HSTA Coordinator
West Virginia University
2073-A Health Sciences North
(304) 293-4120
Email: vwatson@hsc.wvu.edu

Andrew Shiemke
HSTA/Summer program Assistant Coordinator
West Virginia University
(304) 293-2310
Email: ashiemke@hsc.wvu.edu

WV-INBRE website: http://www.wv-inbre.net

Directory of Mentors – Mentors are listed by their location; the first list contains mentors at the West Virginia University Health Sciences Center and the second list contains mentors at Marshall University

Mentors at the West Virginia University Health Sciences Center

Mentor	Description of Research	Page #
Dr. Vagner Benedito	Plant tissue culture for the production of pharmacological compounds	4
Dr. Julie Brefczynski-Lewis	Stress and neural responses to social stimuli and meditation	4
Dr. Paul Chantler	Cardiovascular responses to exercise	5
Dr. Roberta Leonardi	Regulation of CoA levels in diabetes	5
Dr. Bingyun Li	Nanotechnology-based drug delivery for the prevention or treatment of infection, cancer, and intracellular diseases	6
Dr. Paul Lockman	Prevention of brain metastases in breast cancer	6
Dr. Joseph W. McFadden	Discovery of biomarkers associated with the development of insulin resistance	7
Dr. Yon Rojanasakul	Cancer Cell Biology and Nanotechnology	8
Dr. Peter Stoilov	Targeting alternative splicing in cancer therapy	8

Mentors at the West Virginia University Health Sciences Center

Dr. Vagner Benedito
Dr. Julie Brefczynski-Lewis
Dr. Paul Chantler
Dr. Roberta Leonardi
Dr. Bingyun Li
Dr. Paul Lockman
Dr. Yon Rojanasakul
Dr. Peter Stoilov

WVU Mentor Listing According to Area of Research

Cancer Research: Li; Lockman; Rojanasakul; Stoilov
Cardiovascular Research: Chantler
Chemistry/Nanotechnology: Li
Diabetes: Leonardi; McFadden
Drug Development: Benedito; Li
Infectious Disease: Li
Nanotechnology: Li; Rojanasakul
Neuroscience Research: Brefczynski-Lewis
Pulmonary Research: Rojanasakul
Toxicology Research: Li

MENTORS
At West Virginia University

Vagner A. Benedito, Ph.D.
Assistant Professor of Biochemical Genetics
Genetics and Developmental Biology Program
Division of Plant & Soil Sciences
2090 Agricultural Sciences Building
West Virginia University
Phone: (304) 293-5434
http://plantandsoil.wvu.edu/faculty_staff/vagner_benedito

Plants are very important sources of active compounds related to human health. By using tissue culture techniques and genetic manipulations, pharmaceutical compounds can be produced in vitro or enhanced in vivo, thus increasing production and decreasing costs. Dr. Vagner Benedito's research at WVU include furthering the current understand of secondary metabolite physiology and its regulation by genetic and environmental factors, and how this knowledge can be used to enhance production of pharmaceutical compounds in plants. Specifically, we are interested in 1) understanding how glandular trichomes develop, by using mutants of the dwarf tomato Micro-Tom, 2) understanding how secondary metabolism is regulated by hormones (e.g., jasmonates and brassinosteroids) and stress (e.g., low K, light regimen, drought), and 3) generating herbs with high-yield pharmaceuticals (e.g., the anti-malarial artemisinin by increasing leaf surface in Artemisia annua).

Julie Brefczynski-Lewis, Ph.D.
Research Assistant Professor
Center for Advanced Imaging
Department of Physiology and Pharmacology
Phone: (304) 293-4820
http://medicine.hsc.wvu.edu/radio/Faculty-and-Staff/Faculty/JBLewis

Stress related to difficult personal encounters is very pervasive yet poorly understood. Such stress over time can lead to physical (e.g. cardiovascular) and mental health (e.g. depression/anxiety) issues. Compassion training is a simple and inexpensive way to help decrease the stressful reactions from difficult personal encounters. The project for the summer will be to examine brain responses (using electroencephalography (EEG)) and heart rate variability and cortisol/alpha amylase responses to aversive stimuli (such as pictures of disliked political figures and narratives). The physiological and neural responses to stressful stimuli will be measured before and after compassion meditation or relaxation meditation training (active control).
This project will provide opportunities to learn:
• how to work with human participants,
• how to do measure event related potential (response to stimuli) using EEG
• how to combine physiological, behavioral, and neural measures.

Dr. Paul Chantler
Assistant Professor
Division of Exercise Physiology
Center for Interdisciplinary Research in Cardiovascular Sciences
Robert C. Byrd Health Sciences Center of West Virginia University
Email: pchantler@hsc.wvu.edu
Phone: (304) 293-0646
http://www.hsc.wvu.edu/ccrs/Investigators/chantler.asp

Cardiovascular responses to exercise
INBRE program participants will work in conjunction with laboratory personnel on projects examining cardiovascular responses to exercise in health and disease. Projects in the laboratory are focusing on cardiac and arterial structure and function, and includes exploring the age-associated changes in arterial structure and function, how they interact with aging, lifestyle, and various disease states, in particular the Metabolic Syndrome (MetS), and Heart Failure and how they influence the structure and function of the heart. INBRE participants will interact with graduate students and staff members to answer research questions, using a non-invasive comprehensive approach to examining cardiovascular function that includes cardiac/vascular ultrasound, and radial applanation tonometry. Training provided to the participants will include human CV physiology, ultrasound, and applanation techniques, and biochemical analyses.

Roberta Leonardi, Ph.D.
Assistant Professor
Graduate Program Affiliations
Biochemistry and Molecular Biology
Office: 3143 HSN
Phone: 304-293-7591
Email: roleonardi@hsc.wvu.edu

Coenzyme A (CoA) is an essential and universally distributed cofactor that acts as the major acyl group carrier in the cell. Free CoA and acyl-CoAs are involved in hundreds of metabolic reactions, and are among a selected number of small molecules that have the ability to act as global regulators of cellular metabolism. Consistent with this key function, CoA levels are at the same time tightly regulated and flexible, so that the available supply is sufficiently adaptive to metabolic challenges such as fasting or a high fat diet.
Regulation of CoA levels occurs through coordination of synthesis and degradation. In the liver, modulation of the amount of CoA contributes to the metabolic flexibility of this organ and to its ability to maintain glucose homeostasis during a fast. Conversely, in diabetic mice, hepatic CoA levels are abnormally high and unresponsive to changes in the nutritional state.
Not much is known about CoA degradation. The goal of our research is to establish the importance of two recently discovered CoA-degrading enzymes, Nudt7 and Nudt19, in the regulation of CoA levels and glucose homeostasis. In particular, we are interested in studying these enzymes in the context of diabetes and other metabolic diseases using a combination of biochemistry, animal studies and metabolomics

Dr. Bingyun Li
Associate Professor, Department of Orthopedics
Participant, WVNano Initiative
Director, Biomaterials, Bioengineering, and Nanotechnology Laboratory
School of Medicine
West Virginia University, Morgantown, WV 26506-9196
Email: bili@hsc.wvu.edu
Phone: 304-293-1075 (O)
Website: http://www.hsc.wvu.edu/som/ortho/nanomedica-group/

Nanomedicine

Nanomedicine is the medical application of nanotechnology. Participants in the INBRE program will help develop nanotechnology-based approaches to prevent implant-associated infections or to treat cancer. Two projects are available in the nanomedicine area: (i) Project #1: Antimicrobial peptide nanoparticles targeting intracellular pathogens. Antimicrobial peptide nanoparticles have been synthesized and conjugated with ligands. Participant will determine the targeting capacity of the nanoparticles and the internalization of nanoparticles inside human cells (e.g. osteoblasts). The participant will be trained to prepare experimental protocols, conduct cell culture and flow cytometry studies, characterize nanoparticles, etc. (ii) Project #2: Cellular toxicity of drug-carrying nanoparticles. Participant will synthesize and characterize nanoparticles and determine the cellular toxicity of the nanoparticles by incubating nanoparticles with a variety of cells. The participant will gain familiarity with nanoparticle synthesis, surface modification, cell culture, cell viability testing, etc. In both projects, participants will work with graduate students, post-doctoral fellows and faculty researchers in the lab. Potential participants are strongly encouraged to visit our research website at http://www.hsc.wvu.edu/som/ortho/nanomedica-group/.

Dr. Paul R. Lockman
Professor and Chair of
Basic Pharmaceutical Sciences
Robert C. Byrd Health Sciences Center of West Virginia University
Email: prlockman@hsc.wvu.edu
Phone: 304-293-0944

Significance and Translational Relevance

Brain metastases pose a life threatening problem for women with advanced metastatic breast cancer. Of women who have been diagnosed with disseminated breastcancer, ~10-16% will develop symptomatic brain metastases and at least 20-30% will have micrometastatic lesions present at autopsy. Once lesions are established in the central nervous system, only one in five women survive one year. We have recently shown that chemotherapeutics do not reach effective concentrations in ~90% of CNS metastases. Therefore, our lab is working on ways to prevent the formation of metastases in brain.

Project Information

Our lab uses cutting edge microscopy to identify single breast cancer cells that can invade into brain tissue. Once the cells are found we have techniques that can remove the individual cancer cell. Once the cell is collected the goal of the project is to identify if there is a DNA signature that allows the cancer cell to get into brain (>99% of breast cancer cells do not enter into brain tissue). Once that signature is identified it is hoped we will find a molecular target that can be blocked by a drug, which should reduce penetration of the cancer cells into brain. It is hoped this project will be a first step in the prevention of brain metastases of breast cancer.

Skills and or Experiences the student will be exposed to

1. Cell culture of human and mouse cells
2. Fluorescent microscopy –to potentially include multi-photon imaging
3. Bioluminesence imaging of cancer cells in living animals.
4. Laser micro-dissection of cells in tissue
5. RNA amplification
6. Microarray data

Dr. Yon Rojanasakul
Professor of Pharmaceutical Sciences and Mary Babb Randolph Cancer Center
Robert C. Byrd Health Sciences Center of West Virginia University
Email: yrojan@hsc.wvu.edu
Phone: (304) 293-1476
http://pharmacy.hsc.wvu.edu/departments/department-of-pharmaceutical-sciences/faculty-and-staff/?UserID=33529

Cancer Cell Biology and Nanotechnology

Major research interest is in the area of cancer development and chemotherapy. Our laboratory is particularly interested in the carcinogenic effects of engineered nanomaterials and environmental agents. We also investigate drug resistance mechanisms and new therapeutic strategies for cancer treatment. The student will learn research techniques for 1) growing and manipulating cells in culture, 2) assessing cellular responses to carcinogenic and anticancer agents, 3) identifying biomarkers and drug targets for lung cancer using various molecular biology techniques.

Dr. Peter Stoilov
Assistant professor
WVU, Department of Biochemistry
HSN Room 3080I
Morgantown, WV 26506 24
Email: pstoilov@hsc.wvu.edu
Phone: 304-293-6334
http://www.hsc.wvu.edu/som/BMP/Faculty/Stoilov.aspx

Targeting alternative splicing in cancer therapy.

Alternative pre-mRNA splicing is the major mechanism responsible for the creation of hundreds of thousands proteins from the approximately 23,000 genes in the human genome. Misregulation of pre-mRNA splicing is frequently involved in human pathology and is likely to be a significant part of the molecular mechanisms of carcinogenesis. On a global scale, tumors of different origin share common splicing patterns that are distinct from those of the tissues of origin. Similarly, a global shift in splicing accompanies the epithelial to mesenchymal transition (EMT), a process characterized by loss of cell adhesion contacts and increased mobility, both of which are critical components of metastasis. Such tumor and cell lineage specific reprogramming of pre-mRNA splicing, and the resulting cancer specific protein isoforms provide a unique opportunity to selectively target the malignant cells in therapy.
The research in the lab is focused on investigating the roles cancer specific protein isoforms play in the development of malignancy and discovering drugs that target cancer specific alternative splicing. There are two projects that are available for students joining the lab:
Project 1. Roles of alternative protein isoforms in carcinogenesis. We have identified several exons that show EMT and cancer specific splicing patterns and there is an effort under way to expand this exons set. This projects aims to determine how protein variants created through the alternative splicing of these

exons contribute to tumor formation. Students will learn tissue culture, cloning, mammalian expression using transient transfection and retroviral vectors, RNAi, RT-PCR and western blotting.
Project 2. Screening for drugs that target cancer specific alternative splicing. We have created a unique two color fluorescent reporter designed to detect changes in alternative splicing. This project will incorporate the splicing reporter into an assay that will allow us to rapidly screen large collections of chemical compounds (100,000 or more structures) for drugs that correct the cancer specific alternative splicing of the PKM2 transcript. Students involved in this project will learn tissue culture, mammalian expression, fluorescent techniques for measuring protein expression, flow sorting, RT-PCR, experiment automation and data analysis.

Mentors at Marshall University

Mentor	Description of Research	Page #
Dr. Beverly Delidow	Inhibitors of Wnt/ß-catenin signaling alter tumor behavior in melanoma.	11
Dr. Philippe Georgel	Effects of chromatin on nuclear function; Effects of diet on breast and prostate cancers	11
Dr. Isabel Larre	Role of the receptor Na/K-ATPase/Src complex in the regulation of Tight Junctions and apical polari	12
Dr. Jiang Liu	Salt retention/salt-sensitive hypertension and heart/kidney function and remodeling	13
Dr. Shekher Mohan	The role of opioids in hemin-induced toxicity Plasticity: drug abuse preceding stroke Obesity and glial cell function	14
Dr. Sandrine Pierre	Cardioprotection by Cardiac Glycoside	14
Dr. Gary Rankin	Kidney toxicology; Metabolism of methadone	15
Dr. Nalini Santanam	Adipose tissue biology in obesity; Pain in Endometriosis; Diet, exercise, and obesity	16
Dr. Vincent Sollars	What are the processes that enable a normal cell to start misbehaving and become cancerous?	17
Dr. Monica Valentovic	Reducing cancer chemotherapy side effects Liver damage in acetaminophen overdose; Mechanisms to reduce diabetic renal complication	17
Dr. Hongwei Yu	Bacterial biofilms, lung infections and gut microbiota	18

Mentors at Marshall University

Dr. Beverly Delidow
Dr. Philippe Georgel
Dr. Isabel Larre
Dr. Jiang Liu
Dr. Shekher Mohan
Dr. Sandrine Pierre
Dr. Gary Rankin
Dr. Nalini Santanam
Dr. Vincent Sollars
Dr. Monica Valentovic
Dr. Hongwei Yu

Marshall University Mentor Listing According to Area of Research

Cancer Research: Delidow; Georgel; Santanam; Sollars; Valentovic
Cardiovascular Research: Mohan; Pierre; Santanam
Diabetes: Valentovic; Santanam
Hypertension: Liu
Infectious Diseases: Yu
Molecular Biology: Yu
Obesity Research: Santanam
Pain Research: Santanam
Renal Physiology: Larre
Toxicology Research: Rankin; Valentovic
Women's Health: Santanam

MENTORS
at Marshall University

Dr. Beverly Delidow
Associate Professor of Biochemistry and Molecular Biology
Joan C. Edwards School of Medicine
Marshall University
Email: delidow@marshall.edu
Phone: (304) 696-7266
http://www.marshall.edu/wpmu/bms/beverly-delidow-ph-d/

Inhibitors of Wnt/ß-catenin signaling alter tumor behavior in melanoma.
The incidence of melanoma has increased to an alarming degree in recent years. While early melanoma is both preventable and treatable, later stage invasive disease has a very poor prognosis. The Wnt signaling pathway is known to play a central role in several cancers, however comprehensive study of the role of Wnt pathway components in melanoma is lacking. We are examining the effect of blocking Wnt/ß-catenin signaling in melanoma. Our data show that inhibiting the Wnt pathway leas blocking migratory behavior of melanoma tumor cells, even in advanced lines that are resistant to other treatments. This suggests that inhibition of the Wnt pathway may be a productive route for developing new therapies. We have an active collaboration with two mathematicians to model this signaling system. The work has lead to identification of a unique signaling control node in a co-receptor protein, LRP6. The summer researcher would be invited to participate in experiments to continue examining the effect of inhibiting expression of this critical protein in melanocytes and melanoma cells by a number of means. The likely techniques would include migration and invasion assays, subcellular fractionation, western blotting, fluorescent immunocytochemistry, RNA isolation, real-time PCR, siRNA transfection and reporter gene assays.

Dr. Philippe Georgel
Marshall University
Department of Biological Sciences and Department of Biochemistry
Marshall University
Phone: 304-696-3965
Email: georgel@marshall.edu
http://mupfc.marshall.edu/~georgel

Research in my laboratory is centered on the effects of chromatin on nuclear functions, with an emphasis on transcription regulation linked to epigenetic modifications. Epigenomic research pertains to studies investigating changes in the regulation of gene expression that reflect altered states of DNA organization rather than direct changes in DNA sequence. Human DNA is packaged into repeated units of nucleoproteins (DNA plus histones) referred to as chromatin. It has long been established that both chromatin remodeling and the equilibrium between chromatin folding and unfolding act as regulating mechanisms of gene activation or repression. We recently designed a method that allows us to make physical measurements of defined chromatin fragments directly cleaved from the genome. Our results strongly suggested that the textbook dogma linking chromatin condensation with gene repression and unfolding with transcription activation was not necessarily true for all genes, and may need to be revised. My most current research projects are focused on studying the effects of diet on breast and prostate cancers. In the case of prostate cancer (PCa), we investigate the effect of Sulforaphane (SFN), a substance derived from broccoli. We are evaluating SFN effect using PCa cell lines as a model system. Initial experiments indicated that SFN can affect epigenetic modifications. We have identified a link between PCa-specific histone post-translational modifications and sulforaphane treatment. For breast cancer

(BCa), in collaboration with Dr, Hardman, we are looking at the importance of fatty acid diet (omega-3 vs. omega-6 fatty acids) on BCa incidence of mice female offspring.
We are also investigating the mechanism of action of various chromatin-associated proteins, such as MeCP2 and Sir3, on chromatin compaction and transcription regulation in various *in vitro* and *in vivo* systems.
The project that would be assigned to the selected summer student should involve prostate cancer and/or breast cancer research. It will be highly focused on epigenetic modifications (DNA methylation, chromatin structure and function, as well as microRNA) and their effect on expression of tumor suppressor genes or oncogenes.
Interns will have the opportunity to learn certain of the following techniques.
Molecular Biology: cloning and sub-cloning. Protein over-expression.
Biochemistry: Protein purification (conventional chromatography, affinity chromatography)
Southern, Northern and Western blotting.
In vitro chromatin reconstitution
Electrophoresis mobility shift assay (in agarose or acrylamide matrix).
Immuno depletion assay.
Quantitative Real Time PCR
Site-directed mutagenesis.
Chemical protein cross-linking.
HPLC and FPLC.
Biophysics: Hydrodynamic analysis (utilizing the analytical ultra-centrifuge XLA and model-E from Beckman).
Analytical agarose "Multi-gel" system or Quantitative Agarose Gel Electrophoresis (QAGE).
Cell Biology: Basic cell culture (fibroblasts, Drosophila cells and mouse primary cell culture).

Isabel Larre, Ph.D.
Assistant Investigator in Residence
Marshall Institute for Interdisciplinary Research
Phone: (304) 696-3830
Email: mperez@marshall.edu

The exchange of substances between metazoans and the environment takes place across transporting epithelia that have two fundamentally differentiated features: tight junctions (TJ) and apical/basolateral polarity. The first feature, tight junctions, are the intercellular junctions primarily responsible for barrier formation, as they form paracellular diffusion barriers that regulate the flow of ions and solutes along the paracellular space. In the kidney, TJ molecular composition (claudins) determines the permeability and selectivity of different nephron segments along the renal tubule. For example, in the proximal tubule, TJ have a role in the bulk reabsorption of salt and water while in the distal nephron, TJ form cation barriers and chloride pores to facilitate sodium reabsorption and potassium as well as acid secretion. The second feature is the asymmetric distribution of protein and lipids in two domains: apical and basolateral. In the mammalian kidney, apical/basolateral polarity is essential for the uni-directional vectorial transport of ions and fluids that provides the basis for regulated reabsorptive and secretory function of the normal kidney. Thus, TJ and polarity are key to renal salt handling, and consequently the regulation of blood pressure and kidney diseases. Our laboratory is interested in understanding the regulation of TJ and apical/basolateral polarity, specifically by the Na/K-ATPase and cardiotonic steroids. Our goal is to establish both cellular and animal platforms that allow us to develop new tools drug for in vivo investigation of the role of TJ in the regulation of renal tubular structure and function. The students will be exposed to molecular, cell biology and transgenic animal techniques and approaches that are currently available to integrated renal physiology research.

Project 1: The receptor Na/K-ATPase/Src complex plays an important role in the regulation of Tight Junctions.

Rationale: It has been shown that the inhibition of Na/K-ATPasepump activity disassembles the Tight Junction. Previous work of Dr. Xie's lab has shown that Na/K-ATPase can bind to cSrc and form a receptor complex. Thus, we would like to study if Na/K-ATPase, as a receptor, regulates the development of TJ.

Method: The student will learn cell culture, Immunostaining and Western blot.

Project 2: The receptor Na/K-ATPase/Src complex plays an important role in apical polarity.

Rationale
The Na/K-ATPase must be restricted to the basolateral surfaces of renal tubule epithelial cells. Inhibiton of the Na/K-ATPase by cardiotonic steroids regulates ciliogenesis. Our interest is to study the role of the Na/K-ATPase/Src complex in this regulation.

Method: The student will learn cell culture, Immunostaining and confocal microscopy,and Western blot.

Dr. Jiang Liu
Associate Professor
Department of Pharmacology, Physiology & Toxicology
Joan C Edwards School of Medicine at Marshall University
Email: LiuJ@Marshall.edu
Phone: (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 fibro

Shekher Mohan,Ph.D.
Assistant Professor
Department of Pharmaceutical Science and Research
School of Pharmacy at Marshall University
1500 Spring Valley Drive, 234 CEB
Huntington, WV 25704
Phone: (304) 696-7371
Email: mohans@marshall.edu

The following projects are available in my laboratory:

Project 1: The role of opioids in hemin-induced toxicity: Following an intracerebral hemorrhagic stroke (ICH), components that make-up blood are released that contribute to the death of neurons and supporting cells in the brain. One such toxic component of red blood cells is hemin. Earlier work has shown that inflammatory mediators such as prostaglandins can regulate hemin-induced neurotoxicity. However, little data shows how different cells-types of brain when exposed to opioids can affect hemin-induced toxicity. Opioid abuse is a major concern here in WV and our lab aims to explore the relationship between opioid abuse and how this may affect the different cell types in the brain in relationship to stroke.

Project 2: Plasticity: drug abuse preceding stroke: Prescription drug abuse (e.g. morphine, codeine and amphetamines) amongst the younger population here is WV has increased exponentially over the last decade. However, the long-term effects of abusing these drugs on the brain remain unknown. Our lab aims to explore changes in plasticity using both cells (neurons, astrocytes & microglia) and mice following exposure to prescription drugs in relationship to stroke outcomes.

Project 3: Obesity and glial cell function: Obesity is well known to increase the risk of cardiovascular disease. However, little is known about the obesity effects the brain and specifically, glial cells. Glial cells (e.g. microglia and astrocytes) are abundant cells types that provide key support and functionality to neurons in the brain. Our lab aims to study the role of fat on the functionality of glia cells when exposed to cardiac fat derivedfactors. The aim is to relate our finding to stroke outcomes in obese patients.

TECHNIQUES:
Techniques that will be used in the above projects are:

1. Cell culture techniques -neurons, astrocytes/microglia & endothelial cells
2. Light and immunofluorescence microscopy
3. Detection and quantification of gene expression using real-time PCR & Western blotting
4. Cell-death-live assays using UV plate readers
5. Mouse brain dissections and tissue processing for immunohistochemis

Dr. Sandrine V. Pierre
Associate Investigator & Education Coordinator
Marshall Institute for Interdisciplinary Research
Phone: (304) 696-3830
Email: pierres@marshall.edu

The Pierre lab studies specific intracellular pathways involved in the integrated response of the myocardium to ischemia-reperfusion injury and metabolic disturbances. Our goal is to develop new paradigms to therapeutically address cardiomyocyte dysfunction following myocardial infarction. 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, tail-cuff measurement of blood pressure, cardiac and vascularcatheterization). Hence, the student will be exposed to the key techniques and approaches that are currently available to integrated cardiac and vascular physiologists and pharmacologists.

Project: Cardioprotection by Cardiac Glycosides
Rationale: While cardiac glycoside is believed to increase cardiac contractility through its ability to specifically bind to and inhibit the ion pumping function of Na+/K+-ATPase, recent studies have shown that the mechanism of action of these drugs goes beyond simple modulation of ion homeostasis. 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 will lead to novel interventions for the treatment and prevention of ischemia and reperfusion injury.
Method: The student will learn the isolated Landendorff-perfused mouse heart preparation and will submit it to our standardized ischemia-reperfusion protocol in the presence or absence of different cardiac glycoside-based interventions. The student will learn how to analyze contractile function in real time, measure cardiac enzyme release and determine infarct size.

Dr. Gary O. Rankin
Professor and Chair of Pharmacology, Physiology and Toxicology
Joan C. Edwards School of Medicine
Marshall University
Email: rankin@marshall.edu
Phone: (304) 696-7319
www.marshall.edu/wpmu/bms/gary-o-rankin-ph-d/

The following projects are available in my laboratory:

Project #1: Succinimide-induced nephrotoxicity: The succinimide ring is incorporated into hundreds of chemicals used as drugs, agricultural fungicides, and industrial agents. Toxicity to the kidney (nephrotoxicity) has been associated with exposure to succinimide antiepileptic agents and some agricultural fungicides. Recent work has determined that succinimide metabolites are responsible for inducing the kidney damage, females are more sensitive than males to succinimide-induced nephrotoxicity, and the stereochemistry of the metabolites contributes to nephrotoxic potential. This project seeks to determine the exact nature of the toxic metabolites and sub-cellular renal targets of the metabolites, how metabolites gain entry into the kidney and the toxicogenomics of succinimide-induced nephrotoxicity.
Project #2: Chloroanilines are commonly used chemical intermediates in the manufacture of dyes, drugs, agricultural herbicides and fungicides and thousands of other products. Exposure to a chloroaniline can result in a number of toxicities including toxicity to the blood, liver and kidney. This project seeks to determine the chemical species (parent compound or metabolite) responsible for liver and kidney damage and the mechanism by which nephrotoxicity occurs.
Project #3: Methadone is a drug used to reduce the dependence of heroin adducts on heroin. However, some methadone users die unexpectedly when using normal doses of methadone. Preliminary studies have suggested that there may be a defect in the inactivation of methadone in the liver in these individuals who die unexpectedly. The purpose of this study is to determine if genetic polymorphisms are responsible for these deaths.
Assays and Instrumentation: Projects that will investigate nephrotoxicity will use in vitro assays that involve isolation of rat kidney cells, measurement of enzyme release from treated and control cells, and potentially, the measurement of cellular ATP levels. Toxicogenomic studies involve isolation techniques

for obtaining genetic material from treated and control rat kidneys. Additional techniques may involve Western blotting, quantifying urinary contents (protein, glucose), measuring blood urea nitrogen and glucose levels, and real time PCR techniques. Instrumentation will primarily involve the use of balances, centrifuges and UV-visible spectrophotometers. High pressure liquid chromatography and thermocycler use is also possible.

Nalini Santanam, Ph.D., M.PH.
Professor
Department of Pharmacology, Physiology & Toxicology
Joan C Edwards School of Medicine at Marshall University
Email: santanam@marshall.edu
Phone: (304) 696-7321

The following projects are available in my laboratory:

CARDIOVASCULAR DISEASE, OBESITY and DIABETES
Project 1: Adipose (fat) tissue derived stem cell function: Adipose derived stem cells are important in tissue engineering or regenerative medicine. Our interest is to investigate genetic or epigenetic changes that occur in adipose derived stem cells during aging or obesity. We use rodent models of obesity or aging to investigate adipose stem cell function. Next generation sequencing and flow cytometry techniques will be used to investigate stem cell function.
Project 2: Diet, exercise and obesity: A long time interest of our laboratory is to study the effect of diet and exercise on cardiovascular disease, in particular "atherosclerosis" (blockage of the arteries). Our current studies will investigate if mice that express high levels of antioxidant enzymes (enzymes that decrease free radicals) are susceptible to obesity or cardiovascular disease. These mice will be fed high fat diet or put on exercise and obesity related markers will be investigated.

WOMEN'S HEALTH
Project 3: Epigenetics, Pain and Endometriosis: Endometriosis is a disease that affects 10-15% younger women. This disease is mostly accompanied by infertility and chronic pain. Endometriosis is also a risk for ovarian cancer. We have long standing interest in studying the etiology (causes) of this disease by using both animal models of endometriosis and samples from patients with endometriosis (collaboration with Department of Obstetrics & Gynecology). We are currently investigating if epigenetics plays a role in this disease.

TECHNIQUES:
The techniques that are routinely performed in our laboratory:
1. Cell culture techniques, isolation of fat cells (adipocytes) and adipose derived stem cells
2. Isolation and quantification of RNA (including miRNA) and DNA from cells or tissues
3. Detection of genes using PCR/Real time PCR
4. Detection of proteins using Western Blotting
5. Detection of reactive oxygen free radicals in cell culture system.
6. Animal studies: Studies on atherosclerosis, obesity and pain
7. Next generation sequencing for small RNA or total RNA sequencing
8. Flow cytometry

Dr. Vincent Sollars
Associate Professor of Biochemistry and Microbiology
Joan C. Edwards School of Medicine
Marshall University
Email: sollars@marshall.edu
Phone: (304) 696-7357
http://www.marshall.edu/bms/2012/08/30/vincent-e-sollars-ph-d/

The Question: "What are the processes that enable a normal cell to start misbehaving and become cancerous?" The process that cells in our bodies undergo to become cancer cells all end up producing a cell that ceases to listen and cooperate with its neighbors, which is necessary for the complex mixture of cell our bodies are. This grant will investigate a process known as "canalization", which much like a canal for water directs the flow of water, directs a cell as it matures to the necessary type of cell the body requires. Disrupting this "canalization" process can cause a cell to change and lose its direction, potentially pushing it down paths that lead to cancer.

Research Goals: The research will use both cells grown in the laboratory and animal models of human leukemia, along with advanced scientific methods to test the role of canalization in the process of maturing cells and cancer development. The research will allow students at Marshall University the opportunity to participate in cutting edge research in preparation for careers in science.

Specific Project: A cell culture model for hematopoietic stem cells is used in our laboratory. This project will involve the differentiation of these cells and the study of the effects of inhibition of canalization during this maturation of the resulting cells. Techniques involved will be flow cytometry and mammalian cell culture.

Dr. Monica Valentovic
Professor of Pharmacology
Joan C. Edwards School of Medicine, Marshall University
Email: valentov@marshall.edu
Phone: (304) 696-7332
www.marshall.edu/wpmu/bms/monica-a-valentovic-ph-d/

Our laboratory is focused on exploring new interventions that will reduce the adverse effects of drugs. We have recently focused on examining ways to reduce the toxicities of cancer chemotherapy agents. Projects available in my lab:

Projects #1 Reducing serious cancer chemotherapy side effects. This is an ongoing project that has been funded by a federal grant from NIH. Our laboratory is evaluating new compounds that may reduce the adverse effects experienced by individuals treated with cancer chemotherapy drugs. In addition, another goal of this project is to come up with methods to improve the effectiveness of the cancer chemotherapeutic agents while lessening the side effects. This project has clear clinical relevance and is translational. An individual involved in this project will investigate cellular changes in toxicity, specifically we want to explore changes in the mitochondria as well as post-translational modifications of proteins caused by exposure to doxorubicin or cisplatin.

Projects #2 Identification of ways to reduce the liver damage of acetaminophen overdose. Acetaminophen (APAP) is a common ingredient in nonprescription pain, fever and flu remedies. APAP can cause liver damage when used in excess and is the #1 cause of drug induced liver failure. The purpose is to investigate new ways to lower the severe liver failure associated with acetaminophen overdose.

Acetaminophen is an over the counter agent for pain and fever that is very safe but when taken in excess can damage the liver and kidney. Once this damage occurs a liver transplant may be the only alternative. This project is examining how a nutraceutical, S-adenosylmethionine (SAMe) reduces acetaminophen mediated liver damage.

Project #3 Mechanisms to reduce diabetic renal complications: Diabetes mellitus afflicts 1 in 50 Americans. Diabetes is the major cause of kidney failure and why people must go on dialysis in the United States. The long-term goal is to examine what makes the diabetic more susceptible to kidney failure. These results may then be applied to develop new treatments for diabetics. Individuals (students or faculty) involved with this project will participate in examining cellular changes that may increase cellular stress in the diabetic kidney.

Dr. Hongwei David Yu
Professor of Biochemistry and Microbiology
Joan C. Edwards School of Medicine, Marshall University
Email: yuh@marshall.edu
Phone: (304) 696-7356
http://www.marshall.edu/wpmu/bms/hongwei-d-yu-ph-d/

My research interests focuses on bacterial biofilms, lung infections and gut microbiota. Three projects are ongoing in the Yu lab.
Project #1: *Pseudomonas* alginate regulation. *Pseudomonas aeruginosa* is a ubiquitous bacterium that readily forms a biofilm by producing a capsular polysaccharide called alginate. The overproduction of alginate (mucoidy) is a virulence factor that allows greater adhesion to lung epithelial cells, as well as protection from antibiotics and the host's immune system. Individuals afflicted with cystic fibrosis (CF) are particularly susceptible to *P. aeruginosa* infections. Mucoidy promotes the persistence of this bacterium in the lungs of CF. We study the molecular mechanisms responsible for conversion to mucoidy in clinical isolates. Elucidation of the alginate regulation will lead to better understand the pathogenesis, and development of therapeutics to improve the quality of life for individuals with CF.
Project #2: Modeling Lung infection. Most of bacterial lung infections initiate with the colonization of the upper respiratory tract. Aspiration of oropharyngeal secretions containing colonizing bacteria deep into the lung allows for the establishment of lower respiratory tract infections. Cystic fibrosis broncho-pneumonia is characterized by infections in the lower respiratory tract, which is otherwise a sterile environment. We are using an inhalation exposure system to deposit the airborne pathogens into distal airways of the mouse lungs, causing the development of lung infection. This model is being utilized to study the host and bacterial factors that confer increased susceptibility to lung infections by *P. aeruginosa*. The goal of this project is to better understand the etiology of bacterial lung infections using the mouse model for the development of novel therapeutics.
Project #3: Novel probiotics. Gut microbiota, a bacterial community made up of 500-1,000 different species, are important to human health. Among all the species, there is a morphologically-distinct symbiotic member known as segmented filamentous bacteria (SFB). The SFB belongs to a group of clostridia bacteria, which cannot be grown *in vitro*. However, the SFB play a vital role in the development of the immune system in mice. More specifically, SFB have been shown to attach to the apical epithelium of the small intestine to induce the interleukin-17-producing T helper (TH17) cells. TH17 cells are important for the protection against intestinal pathogens as well as in maintaining gut homeostatsis. In this project, we will examine possibilities of how to develop the SFB into a novel probiotic to prevent and control the gastrointestinal diseases in children.