Greetings WHRC members!

I can’t believe 2013 is almost over! We have had a busy year in the WHRC. We submitted a T32 Training grant entitled: “Multidisciplinary Training in the Study of Sex and Gender Differences” that was not funded, but the comments were addressable. We will reapply next year. We obtained several new graduate students and postdoctoral fellows interested in the study of women health and/or sex and gender differences. The Center has had a great publication record over the past year, and even with NIH funding being low, several of our investigators obtained new funding. A number of grants have also been submitted and will be reviewed in the new year. We have had several interesting speakers over the past year, and in January we will host Majorie Jenkins from Texas Tech University, a leader in changing medical school curriculum to include sex & gender differences. She was part of a coalition who met with USMLE questions writers regarding the inclusion of questions related to sex and gender differences on the STEP exams for medical students.

As the year nears a close, I would like to thank all of you for your support of the WHRC over the past year. We hope to be able to provide more seminar speakers from both here on campus and from outside in the coming year. Janie

**Our Mission:** Women have health care issues that are different from men. Recent research indicates that there are sex differences in the incidence, outcome, and physiological and pathophysiological mechanisms responsible for various diseases. Mississippi has the dubious honor of having one of the highest incidence rates of cardiovascular disease, obesity, diabetes, hypertension, end-stage renal disease, high risk pregnancy, pre-eclampsia (pregnancy induced hypertension), infant mortality and poor child health outcomes in the United States. The Women’s Health Research Center (WHRC) was established in 2009 at the University of Mississippi Medical Center (UMMC) to accomplish the major goal of fostering excellence in basic and clinical research in issues that affect women’s health across their lifespan.
Dr. Elise Gomez-Sanchez, DVM, PhD, trained as a veterinarian, earned a PhD in Physiology and Pharmacology and did a Post-Doctoral Fellowship in Pharmacology at UT-Southwestern in Dallas. She has been a research scientist for the VA with a primary appointment in the Department of Medicine in the affiliated Medical School funded by Merit Review, NIH and American Heart Association grants from April 1984 to the present. She has been a peer reviewer for several study section of the NIH, American Heart Association and the VA Merit Review system and member of the editorial boards of several peer-reviewed journals.

Her most recent work addresses the biology of the mineralocorticoid receptor with a primary focus on the regulation and activity of the mineralocorticoid receptor in the brain, as well as mechanisms for ligand specificity including metabolism and synthesis of corticosteroids in the brain. Her lab was the first to demonstrate that infusion of aldosterone in minute quantities into the lateral ventricle induced hypertension and that central infusion of a mineralocorticoid receptor antagonist at a dose that was ineffective systemically, blocked the hypertension, induced by systemic aldosterone excess, as well as in salt-sensitive hypertension models in which aldosterone is low, despite a clinical syndrome similar to mineralocorticoid excess. This led to studies of pre-ligand specificity for the mineralocorticoid receptor and studies of 11b-steroid dehydrogenases, as well as the regulation and role of extra-adrenal synthesis of corticosteroids. She is also investigating the role of local and brain mineralocorticoid receptors in the control of inflammation that underlies sympathetic nervous system activation and much of the cardiovascular and renal damage produced by a high sodium intake. Her 110 peer reviewed publications and 4 chapters represent this work.

In collaboration with Celso Gomez-Sanchez, the laboratory has developed and freely disseminates to other investigators tools for such studies including poly- and monoclonal antibodies, cell models, specific plasmids, and viral vectors. Her associations with the Departments of Neurobiology & Anatomical Sciences and Psychiatry, as well as the interdepartmental graduate Program in Neurosciences, has provided the ability to map adrenal steroid receptors within neurons in different parts of the brain and demonstrate the effects of osmotic and psychological stress on subcellular localization and function. She retains active veterinary licenses and an avid interest in infectious diseases and zoonoses, and regularly participates in the Division of Infectious Disease seminar series and ER consultations to identify venomous animals and plants.
HIGHLIGHTS from the WHRC

Kudos

The Annual Graduate Student Research Day event spotlights the research activities of students within the School of Graduate Studies in the Health Sciences. This year's event featured poster presentations by UMMC graduate students and post-doctoral fellows. Recipients of Research Recognition Awards from the 2013 Research Day sponsored by the School of Graduate Studies in the Health Sciences Alumni Chapter held on October 25th included a number of trainee members of the WHRC:

Maryam Syed, a graduate student in the laboratory of Dr. Damien Romero in the Department of Biochemistry, Tiffany Slaughter White, a graduate student in the laboratory of Dr. Jan Williams in the Department of Pharmacology and Toxicology, Ellen Gillis, a graduate student in the laboratory of Dr. Jennifer Sasser in the Department of Pharmacology and Toxicology, John Henry Dasinger, a graduate student in the laboratory of Dr. Barbara T. Alexander in the Department of Physiology and Biophysics, and Dr. Kristine Y. DeLeon-Pennell, a post-doctoral fellow in the laboratory of Dr. Merry Lindsey in the Department of Physiology and Biophysics. Pictured L to R are Maryam Syed, Tiffany Slaughter White, Ellen Gillis, John Henry Dasinger, and Dr. Kristine Y. DeLeon-Pennell.

WHRC Seminar

Dr. Marjorie Jenkins, M.D, Associate Dean for Women in Health and Science will present the next WHRC seminar on January 13th, 4 pm; Room 6a. Her presentation will include national initiatives in Sex and Gender-Based Medicine (SGBM) and national survey data regarding medical schools’ approach to both women’s health and sex and gender medicine.
**HIGHLIGHTS from the WHRC**

**Kudos**

**Dr. Nicole Lee, MD, MPH**, was recently elected as the 2013-2014 American Medical Association Resident & Fellow Section Vice-Speaker. As part of her responsibilities, she served as the co-coordinator of the 11th annual Resident & Fellow Section National Research Symposium. The symposium, which took place on Friday November 15th as part of the AMA National Interim Meeting in National Harbor, MD, included hundreds of poster presentations and about 30 presentations as part of the oral competition. Dr. Lee is a first year Maternal Fetal Medicine Fellow and she is also concurrently earning a Masters of Science in the Biomedical Sciences. She is performing her research in the laboratory of Dr. Richard Roman and Dr. Babbette LaMarca in the Department of Pharmacology and Toxicology.

**Dr. Lisandra de Castro Bras, PhD**, a post-doctoral fellow in the laboratory of Dr. Merry Lindsey in the Department of Physiology received a Basic Cardiovascular Sciences [BCVS] Abstract Travel Grant to the AHA Scientific Sessions in Dallas, TX. The objective of this award is to support trainees and early career investigators. This award recognizes meritorious work by young investigators in training, encourages participation in the AHA Scientific Sessions, and provides a small stipend to help defer travel expenses to present their work at the AHA Scientific Sessions.

**Dr. Kristine DeLeon-Pennell, PhD**, a post-doctoral fellow in the laboratory of Dr. Merry Lindsey in the Department of Physiology received a 2013 Functional Genomics and Translational Biology [FGTB] Minority Travel Grant to attend the AHA Scientific Sessions in Dallas, TX. The objective of this award is to support trainees and early career investigators. This award recognizes meritorious work by young investigators in training, encourages participation in the AHA Scientific Sessions, and provides a small stipend to help defer travel expenses to present their work at the AHA Scientific Sessions.
Dr. Lisandra de Castro Bras, PhD, a post-doctoral fellow in the laboratory of Dr. Merry Lindsey in the Department of Physiology is the recipient of a Scientist Development Grant from the American Heart Association. The title of her project is, “MMP-9 Generated Collagen C-peptide Roles in Post-myocardial Infarction Remodeling.”

Dr. Keisa Mathis, PhD, an Instructor in the laboratory of Dr. Mike Ryan the Department of Physiology is also the recipient of a Scientist Development Grant from the AHA. The title of her project is “The role of the cholinergic anti-inflammatory pathway in renal function and hypertension.”

The purpose of the AHA SDG is to support highly promising beginning scientists in their progress towards independence by encouraging and adequately funding their research projects to bridge the gap between completion of their research training and preparing them for transition to independence.

Dr. Kedra Wallace, PhD, a post-doctoral fellow in the department of Obstetrics and Gynecology is the recipient of Research Career Enhancement Award from the American Physiological Society (APS) to travel to the University of Vermont to work with Dr. Marilyn Cipolla. The purpose of this award is to support short-term visits to other laboratories to acquire new specific skills and enhance the career potential of a regular APS member. The purpose of Dr. Wallace’s visit is to receive training in techniques to measure blood-brain barrier permeability in the rat.

Dr. Wallace is also the recipient of a grant from the UMMC Intramural Research Support Program. The objective of this program is to strengthen the biomedical research environment at UMMC. The title of her IRSP project is, “Multi-Organ ET-1 activation and T lymphocyte infiltration in HELLP Syndrome.”
Dr. Licy Yanes, M.D., a fellow in the Division of Endocrinology at the Department of Medicine, was awarded the Endocrine Fellows Foundation Endocrine Research Grant for her project entitled “Mechanisms of Testosterone Replacement-Mediated Hypertension in Obesity-Related Hypogonadism.” Jane F. Reckelhoff, PhD, Professor of Physiology, will serve as a mentor for this grant. The Endocrine Fellows Foundation is a non-profit organization whose mission is to foster advancement of fellows in endocrinology, diabetes and metabolism through mentoring, education, research funding and career support.

Her project will determine if testosterone replacement causes an increase in the synthesis, secretion and biological activity of the vasoconstrictor agents, angiotensin II and endothelin, leading to hypertension in an animal model of hypogonadal obesity, the obese Zucker rat. Testosterone replacement use has dramatically increased in the last few years among hypogonadal men. Although testosterone replacement improves muscular strength and several metabolic parameters associated with hypogonadal states, it also increases blood pressure. Elucidating the mechanism(s) by which testosterone promotes hypertension will shed light on advancing our understanding of the complex actions of testosterone in non-reproductive organs and exploit the beneficial effects of testosterone while avoiding its undesirable cardiovascular side effects.

Dr. Norma Ojeda, MD, an Associate Professor of Pediatrics and Newborn Medicine was recently selected for membership in the Society for Pediatric Research (SPR). The SPR exists to foster the research and career development of investigators engaged in advancing the health and well-being of children and youth. The SPR bridges basic science, clinical, translational, and epidemiologic research for the advancement of the health of children worldwide. Acceptance for membership is reviewed by the SPR council which select applicants with an advanced degree (MD, PhD, DO, Pharm D, MPH, or MA/MS) and actively engaged in pediatric research.
Dr. Rodrigo Maranon, PhD, a post-doctoral fellow in the laboratory of Dr. Jane Reckelhoff in the Department of Physiology and Dr. Ana Palei, PhD, a postdoctoral fellow in the laboratory of Dr. Joey Granger are recipients of a Post-doctoral Fellowship Grant from the American Heart Association. The purpose of the AHA post-doctoral fellowship award is to help trainees initiate a career in cardiovascular research while obtaining significant results under the supervision of a mentor and provide support before they are ready for an independent stage of research.

Ellen Gillis, a graduate student in the laboratory of Dr. Jennifer Sasser in the Department of Pharmacology and Toxicology, and John Henry Dasinger, a graduate student in the laboratory of Dr. Barbara T. Alexander in the Department of Physiology were recently selected to attend the first American Physiological Society sponsored trainee workshop entitled, “Professional Integrity: Best Practices for Publishing Your Work.” This workshop will be held at Disney’s Contemporary Resort in January 2014. This is the initial pilot test of the new publication ethics modules. Course participants are graduate students in physiology, bio-engineering or biological engineering who are willing to be involved in testing and evaluating the course topics, content, assignments and evaluation tools. Only 25 students were selected and participating students will receive registration materials, subsistence and travel support. The goal of this workshop is to build graduate student skills in publication ethics and to develop an online Community of Practice (COP) designed to engage trainees and experienced scientists and engineers in ongoing discussions about scientific publishing, publication ethics, and professional standards of practice in these areas.
Physiology Understanding (PhUn) Week, a K-12 science outreach program sponsored by the American Physiological Society and Discovery U, the UMMC Graduate School pipeline and outreach program, was held Saturday, November 9, 2013 at the Mississippi Children’s Museum in concert with the Question It, Discover it Saturdays. Mike Ryan, Barbara Alexander, Jenny Sasser were the organizers of the event and participant's included 40 UMMC faculty, fellows, students and staff. The event consisted of 9 interactive stations that provided hands-on learning activities related to the structure and function of the kidneys, heart, and lungs.
Nickens MA, Long RC, Geraci SA. Cardiovascular Disease in Pregnancy: (Women's Health Series). South Med J. 2013;106(11):624-30. Cardiovascular (CV) disease is the most common cause of death during pregnancy in industrialized countries. The growing prevalence of diabetes, hypertension, obesity, hyperlipidemia, and metabolic syndrome has added to the population of pregnant women with heart disease. Physiologic changes occurring during pregnancy can stress a compromised CV system, resulting in maternal morbidity, mortality, and compromised fetal outcomes. These risks complicate affected women's decisions to become pregnant, their ability to carry a pregnancy to term, and the complexity and risk benefit of CV treatments delivered during pregnancy. Risk assessment indices assist the obstetrician, cardiologist, and primary care provider in determining the general prognosis of the patient during pregnancy and although imperfect, can aid patients in making informed decisions. Treatments must be selected that ideally benefit the health of both mother and fetus and at a minimum limit risk to the fetus during gestation.

Spradley FT, Palei AC, Granger JP. Obese melanocortin-4 receptor-deficient rats exhibit augmented angiogenic balance and vasorelaxation during pregnancy. Physiol Rep. 2013;1:e00081. While obesity is a major risk factor for preeclampsia, the mechanisms linking obesity and hypertension remain unclear. Hypertension in preeclampsia is associated with placental ischemia-induced release of anti-angiogenic soluble fms-like tyrosine kinase (sFlt-1) into the maternal circulation, which antagonizes vascular endothelial growth factor (VEGF) promoting endothelial dysfunction. Haploinsufficiency, defined as loss of one copy of a gene via a mutation, of the melanocortin-4 receptor (MC4R) is the most common cause of monogenetic obesity in humans. The purpose of this study was to determine the effects of genetic obesity on angiogenic balance, endothelial function, and blood pressure (BP) in pregnant MC4R+/- and MC4R+/+ rats. Results showed that BP and plasma sFlt-1 did not differ; yet, sensitivity to NO-donor induced vasorelaxation was greater in MC4R+/- rats suggesting that genetically obese pregnant animals have a greater angiogenic balance and dependency of vasorelaxation on nitric oxide signaling protecting against the development of hypertension.

Women’s health issues are underfunded and understudied. Help support women’s health research by making a tax-deductible contribution. Contact the Development Office at UMMC at 601-815-7473 for more information.
Lobert S, Graichen ME, Morris K. Coordinated regulation of β-tubulin isotypes and epithelial-to-mesenchymal transition protein ZEB1 in breast cancer cells. *Biochemistry.* 2013;52:5482-5490. The regulation of β-tubulin isotypes, the primary targets for antimitotic chemotherapeutic drugs like taxanes, has implications for drug response and drug resistance. The tumor suppressor miR-200c targets mesenchymal genes including ZEB1, an epithelial-to-mesenchymal inducer, and it reduces β-tubulin class III. A decrease in miR-200c and an increase in β-tubulin class III are associated with poor outcomes in ovarian cancer patients. Because miR-200c targets the ZEB1, we hypothesized that changes in ZEB1 parallel β-tubulin isotype changes, implicating β-tubulin isotypes in ZEB1-associated cell survival pathways. This work indicated that paclitaxel-induced reduction of ZEB1 and β-tubulin isotypes are, in part, due to increased activity of miR-200c and suggest that in aggressive breast cancers β-tubulin class III may be a biomarker for cell survival mediated through ZEB1-induced tumor progression pathways.

Cornelius DC, Hogg JP, Scott J, Wallace K, Herse F, Moseley J, Wallukat G, Dechend R, Lamarca B. Administration of Interleukin-17 Soluble Receptor C Suppresses TH17 Cells, Oxidative Stress, and Hypertension in Response to Placental Ischemia During Pregnancy. *Hypertension.* 2013;62:1068-1073. Preeclampsia, new onset hypertension with proteinuria during pregnancy, is associated with chronic inflammation and placental oxidative stress (ROS). Chronic interleukin-17 (IL-17) increases blood pressure, autoantibodies (angiotensin II type I receptor [AT1-AA]), and ROS during pregnancy. Therefore, the objective of this study was to determine whether infusion of soluble IL-17RC would decrease circulating TH17 cells, oxidative stress, and hypertension in the RUPP rat model of preeclampsia. IL-17 soluble receptor C binds the most active forms of IL-17 superfamily. Results from this study demonstrated that infusion of IL-17RC blunts TH17s, oxidative stress, AT1-AA, and hypertension in the rodent model of placental ischemia indicating that TH17 cells may play an important role in disease pathophysiology.