Greetings from the WHRC!

Summer is upon us and so are the busy days ahead. Many of us have MSRP or SURE students in the labs for the summer to participate in research projects.

We are still awaiting word on our T32 proposal, entitled “Multidisciplinary Training in Sex and Gender Differences”. It was reviewed on June 20, 2013, and we should have the reviews soon. With the low funding levels of NIH right now, we are anticipating having to resubmit, providing the reviews are addressable.

We are arranging outside speakers for the seminar series for this Fall. We will send out more information when we firm up dates so you can mark your calendars.

Enjoy the summer!

Janie

From the Director

Jane F. Reckelhoff

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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. Merry Lindsey, PhD, Professor of Physiology is the Director of the Jackson Center for Heart Research. Dr. Lindsey is a graduate of Baylor College of Medicine in Houston, TX, where she received a PhD in cardiovascular sciences. She completed her fellowship training at Brigham and Women’s Hospital and Harvard Medical School and has served on the faculty at the Medical University of South Carolina and the University of Texas Health Science Center at San Antonio before arriving in Jackson in January.

Dr. Lindsey is a fellow of the American Physiological Society and the American Heart Association. The coauthor of more than 95 articles in peer reviewed journals and eight book chapters, she is principal investigator or co-investigator of four ongoing research projects, three of which are funded by the National Institutes of Health. She is the director of the San Antonio Cardiovascular Proteomics Center, which is one of seven proteomics centers funded by the National Heart, Lung, and Blood Institute. She has served as a journal reviewer or editor for over 100 journals and has reviewed grants for over 10 funding agencies, including the National Institutes of Health, the American Heart Association, and numerous international agencies. Dr. Lindsey came to UMMC to promote translational heart research, focused on studies that span from bench to bedside.

The focus of her research team is cardiac extracellular matrix biology, particularly changes to the matrix that are the cause or effect of pathophysiological processes. These changes include cell-matrix interactions, which both affect and react to processes involved in tissue repair. Her research team primarily uses a model of myocardial infarction (MI; heart attack) to measure the physiological biochemical, cell biological, and proteomic responses to cardiac injury. The major projects currently underway include examination of the role of macrophage-derived matrix metalloproteinases (MMPs) in cardiac remodeling post-MI; the role of the cardiac fibroblast in the remodeling process, and the influence of aging on LV remodeling. A key component of all the projects is the similarities and differences in response between the sexes.
Dr. Michelle Y. Owens, MD, Associate Professor and Vice Chair of OBGYN, was recently elected by the American College of Obstetricians and Gynecologists (ACOG) as its Young Physician-at-Large. Dr. Owens, who also serves as the Assistant Fellowship Director of Maternal-Fetal Medicine and Medical Director of the Winfred L. Wiser Hospital for Women and Infants, assumed the office May 9. The ACOG is a nonprofit membership organization that advocates for quality healthcare care for women and continuing education of its members. It promotes patient education and raises awareness of changing issues facing women's health care.

Dr. Gene Bidwell, Ph.D., Assistant Professor in the Department of Neurology and collaborators Dr. Eric George, Dr. Joey Granger, and Dr. Barbara T. Alexander recently received funding from an American Heart Association Scientist Development Grant to explore the efficacy and safety of two of their novel therapeutic agents for treatment of preeclampsia. Dr. Bidwell’s research interests include targeting drug delivery, therapeutic peptides, and protein-based therapeutics. His background and training included the development of stimulus-responsive drug carriers for targeting drugs to solid tumors. He utilizes a thermally responsive carrier to target therapeutic peptides and small molecule chemotherapeutics to tumor sites using focused heating. His current research interests include engineering protein carriers for delivery of peptide and protein–based therapeutics in several disease models, including preeclampsia, neurodegenerative disorders, and ocular diseases.

One of the current areas of focus in Dr. Bidwell’s lab is drug delivery during pregnancy. He is developing carriers that can be fused to therapeutic agents, including peptides and proteins, that prevent them from crossing the placenta and reaching the baby. The goal is to develop a means to treat disorders of pregnancy such as preeclampsia without risking harm to the developing fetus from drug exposure.
Highlights from the WHRC

Kudos

The Department of Medicine’s 2013 Research Day recently hosted its oral and poster presentations by participants in UMMC’s Medical Student Research Program (MRSP). The Purpose of the MRSP is to promote interest in research and to foster the development of students into Academic Clinicians. Awardees from Research Day 2013 included a number of medical students working in laboratories of WHRC investigators.

Christian Barnes, M4, mentored by Dr. Ken Liechty, previously in the Department of Pediatric Surgery, was the 1st place winner for his oral presentation entitled “Improved Biomechanical Properties of Diabetic Skin Following Overexpression of Stromal-Derived Growth Factor 1 a (SDF-1a).”

Thomas P. Royals, M4, mentored by Dr. Barbara T. Alexander in the Department of Physiology and Biophysics was the 3rd Place winner in the Oral Presentation category for his talk entitled “The Effect of Intrauterine Growth Restriction on Bone Remodeling Biomarkers and Femur Biomechanics.” Pictured L to R: Thomas Royals and Dr. Alexander.

Hurtis Tullos, M3, mentored by Dr. Richard Roman in the Department of Pharmacology and Toxicology received 3rd Place in the Poster Competition for his poster entitled, “Cerebral Autoregulation: The Genetic Basis of The Myogenic Response.” Hurtis Tullos is pictured on the left.
Kudos

Ashlyn C. Harmon, a PhD student in the laboratory of Dr. Michael Garrett in the Department of Pharmacology and Toxicology was awarded Best Presentation by a Pre-doctoral Trainee for her talk entitled “Identifying generic variants causative of increased kidney disease in the S.SHR(11) congenic model” at the Gulf Coast Physiological Society (GCPS) Meeting held in May 2013. in Mobile, AL. The GCPS was founded in 1999 as a professional association of physiologists in Louisiana, Mississippi, and Alabama. It was established to foster collaborative interactions related to research and education.

Dr. Michael Ryan, PhD, Associate Professor of Physiology and Biophysics and Dr. Kimberly Simpson, PhD, Associate Professor of Neurobiology and Anatomical Sciences are recent inductees into the Nelson Order. The Nelson order recognizes outstanding educators among the UMMC faculty. Faculty are nominated by their respective dean on the basis of teaching performance following review procedures unique to each school. Nelson Order members receive a purple stole to be worn with faculty regalia at commencement where they are publically recognized. Dr. Ryan was recognized by the School of Dentistry; Dr. Simpson was recognized by the School of Medicine.

Dr. Simpson was also awarded the first Regions Bank TEACH Prize and plaque during The Nelson Order 2013 induction May 1. The TEACH Prize, which includes a $10,000 cash reward, recognizes a faculty member who most exemplifies the values of student engagement, intellectual challenge and dedication to the craft of education that drive UMMC’s educational mission.
Kudos

Dr. Joy Intapad, PhD, an Instructor and post-doctoral fellow in the laboratory of Dr. Barbara T. Alexander in the Department of Physiology and Biophysics and Dr. Denise Cornelius, PhD, a post-doctoral fellow in the laboratory of Dr. Babbette LaMarca in the Department of Pharmacology and Toxicology were recipients of 2013 Research with Distinction Certificates for Post-Doctoral Trainees presented by the Water & Electrolyte Homeostasis Section of the American Physiological Society at the annual Experimental Biology meeting held in April.

Keisa Mathis, PhD, an Instructor and post-doctoral fellow in the laboratory of Dr. Michael Ryan in the Department of Physiology and Biophysics was a Recipient of the Juan Carlos Romero and Water & Electrolyte Homeostasis (WEH) Section Postdoctoral Research Recognition Award. The awardee was selected from 3 finalists and selection was based on their oral presentations presented at the Experimental Biology meeting held in Boston in April 2013. Shown with Dr. Mathis is Dr. Jane Reckelhoff, past Chair of the WEH Section of the American Physiological Society.

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.
Highlights from the WHRC

Kudos

Dr. James Martin, MD, Professor of OB-GYN, was recently inducted by the Royal College of Obstetricians and Gynaecologists as an honorary fellow ad eundem on June 24th at its annual meeting held in Liverpool England. Ten fellows are inducted every year from around the world and recognize persons who are not members of the College but who have contributed to the advancement of the science or practice of obstetrics and gynecology. Dr. Martin was also honored on April 19th by the University of North Carolina School of Medicine with one of its three Distinguished Medical Alumnus Awards for this year. This award honors alumni who have significantly enhanced the reputation and prestige of the School of Medicine.

In the News

Dr. Jane Reckelhoff, PhD, Billy S. Guyton Distinguished Professor, Professor of Physiology & Biophysics, and Director of the Women’s Health Research Center, was accepted into the year-long Executive Leadership in Academic Medicine (ELAM) Program at Drexel University’s College of Medicine. One of 54 women in this year’s program, Dr. Reckelhoff started online assignments and community building activities in May. Fellows begin the first of three weeklong, in-residence sessions when they meet for the first time in Pennsylvania in September. Fellows also complete an Institutional Action Project, designed to address a strategic institutional priority. Projects not only help participants understand challenges facing academic health centers and the skills a leader must possess to address these challenges, but also often result in changes at their institutions. More than 800 program alumnae worldwide serve in leadership positions, including dept. chairs, research center directors, deans and college presidents, as well as chief executives in health-care & accrediting organizations.
The Women’s Interagency HIV Study (WIHS, https://statepiaps.jhsph.edu/wihs/), funded principally by NIAID and in part by 3 other NIH institutes has now come to the South! WIHS is a long-standing interval cohort study since 1992, involving thousands of HIV-positive and HIV-negative women across the United States. To date, WIHS has enrolled and followed women only in Northern and Western areas of the country, but 2013 marked the addition of 4 Southern sites: a shared cohort between UMMC and UAB, one at Emory, one at the University of Miami, and one at UNC. Women will be followed at bi-annual study visits where data on multiple physical, biological and psychosocial variables will be gathered. Data are available for analysis from the past 20 years, and more than 500 publications have been published using these data. An exciting new addition is the information gained from Southern cohorts, where the HIV epidemic is increasing at a much faster rate than other parts of the country, especially amongst black females. It is anticipated that discoveries gained from this population will greatly enrich our knowledge about HIV, the longitudinal effects it has on women living with HIV, and how the Southern experiences may be different from other areas. The whole UAB-MS cohort is headed by Michael Saag, MD at the Center for AIDS Research at UAB, while the local UMMC PI is Dr. Deborah Konkle-Parker, PhD, FNP, Associate Professor in the Dept. of Medicine/ Division of Infectious Diseases. The research team expects important science to be generated to improve lives of women living with HIV, and to expand knowledge related to HIV prevention and treatment. Science that is a high priority includes Hepatitis C, renal effects of HIV, cardiovascular issues and menopause, HPV, microbiome of the female genital tract, immunology, access to care, stigma, and multiple other investigations of interest to WIHS and local scientists. For more information, contact Deborah Konkle–Parker, (dkparker@umc.edu).
Zhu H, Bhaijee F, Ishaq N, Pepper DJ, Backus K, Brown AS, Zhou X, Miele L. Correlation of Notch1, pAKT and nuclear NF-κB expression in triple negative breast cancer. *Am J Cancer Res. 2013;3:230-239.* Triple-negative breast cancers (TNBC) account for approximately 15% of all breast cancers. Gene expression profiling reveals elevated Notch1 mRNA expression in TNBC. Notch ligands, Jagged1 and Jagged2, are correlated with poor prognosis in TNBC. Inhibition of cell growth, migration, invasion, and induction of apoptosis caused by Notch1 or Jagged1 inhibition may be attributed in part to inactivation of the AKT signaling pathway. In addition, Notch1 activates NF-κB and AKT can mediate NF-κB activation. This study evaluated Notch1 protein expression and correlated it with expression of pAKT and nuclear NF-κB p65 (RelA) in TNBC. Results from this study suggest that cross-talk between Notch1, AKT and NF-κB identified in preclinical models may operate in a significant fraction of human TNBC, and that combination therapy with agents targeting these pathways warrants further investigation.

Zhang J, Dennis KA, Darling RD, Alzghoul L, Paul IA, Simpson KL, Lin RC. Neonatal citalopram exposure decreases serotonergic fiber density in the olfactory bulb of male but not female adult rats. *Front Cell Neurosci. 2013 In press.* Serotonin (5HT) is a widely distributed neuromodulator that plays an important role in regulating brain development. Manipulation of this system during early stages of neurodevelopment produces sex-specific neurobehavioral modifications that persist well into adulthood. Recent studies report altered raphe-derived 5HT transporter (SERT) immunoreactive axonal expression in several cortical target sites after brief perinatal exposure to selective 5HT reuptake inhibitors such as citalopram (CTM). Since the serotonergic raphe nuclear complex projects to the olfactory bulb (OB) and perinatal 5HT disruption has been shown to disrupt olfactory behaviors, the goal of this study was to further investigate such developmental effects in the OB of CTM exposed animals. Male and female rat pups were exposed to CTM from postnatal day 8–21. Our data revealed that the density of the SERT immunoreactive fibers decreased ~40% in the OB of CTM exposed male rats, but not female rats. At 90 days of age. Because dysfunction of the early 5HT system has been implicated in the etiology of neurodevelopmental disorders such as autism spectrum disorders (ASDs), these new findings may offer insight into the abnormal olfactory perception noted in patients with ASD.
Recent Publications

Payne TJ, Ma JZ, Crews KM, Li MD. Depressive Symptoms Among Heavy Cigarette Smokers: The Influence of Daily Rate, Gender, and Race. Nicotine Tob Res. 2013 In press. Cigarette smokers experience higher levels of depressive symptoms and are more likely to be diagnosed with depressive disorders than nonsmokers. This study examined depressive symptom expression among heavy smokers while considering the moderating roles of smoking status, gender, and race. It also investigated whether the amount of tobacco usually consumed had an impact. Smokers reporting a higher, clinically meaningful level of depressive symptoms relative to nonsmokers (27.3% of smokers vs. 12.5% of nonsmokers) scored above the clinical cutoff on the Center for Epidemiological Studies Depression (CES-D) scale (p < .001), which differed among race × gender subgroups. These findings improve our understanding of tobacco’s influence on depressive symptom expression among heavy smokers, with implications for tailoring evidence-based tobacco treatments.

Intapad S, Tull FL, Brown AD, Dasinger JH, Ojeda NB, Fahling JM, Alexander BT. Renal denervation abolishes the age-dependent increase in blood pressure in female intrauterine growth-restricted rats at 12 months of age. Hypertension. 2013; 61:828-834. Perinatal insults program sex differences in blood pressure, with males more susceptible than females. This study tested the hypothesis that age increases susceptibility to hypertension in female growth-restricted rats. Blood pressure (BP) remained similar at 6 months of age; however, a significant increase in BP was associated with a marked increase in total fat mass, visceral fat and circulating leptin, which can increase sympathetic nerve activity by 1 year of age. Bilateral renal denervation abolished hypertension in female growth-restricted rats suggesting that age-induced increases in visceral fat and circulating leptin contribute to the significant age-dependent increase in BP in female growth-restricted rats, with the renal nerves serving as an underlying mechanism.