Hypertension In The News

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"have discovered a treatment effective in blocking the growth and shrinking the size of lung cancer tumors in mice"

Small Peptide Found to Stop Lung Cancer Tumor Growth in Mice

In new animal research investigators Drs Ann Tallant and Patricia E. Gallagher at Wake Forest University School of Medicine, discovered a treatment effective in blocking the growth and shrinking the size of lung cancer tumors in mice. This study, developing out of basic science research into the factors regulating the growth of vascular cells, was recently published in Molecular Cancer Therapeutics, a journal of the American Association for Cancer Research. Their research is the first to show that treatment with a specific peptide, angiotensin-(1-7), reduces lung tumor growth by inhibiting blood vessel formation. Treatment with angiotensin-(1-7) reduced lung tumor weight by 60%; further analysis also showed that the tumors from mice treated with the peptide had significantly fewer blood vessels compared to the tumors from the saline-treated animals. Dr Tallant and Gallagher said the treatment likely has applications beyond lung cancer – they have collected data showing it is effective on breast, colon and brain tumors, as well. The treatment also presents an attractive possibility for future human cancer therapy from a cost perspective, they said. Co-investigators on the study were graduate students David R. Soto-Pantoja and Jyotsana Menon of the School of Medicine. The first clinical trial of angiotensin-(1-7) has been completed at the School of Medicine and the results are currently being reviewed.

- Excerpt from Wake Forest News 08/26/09; Link to entire article http://www2.wfubmc.edu/News/NewsARticle.htm?ArticleID=2693

The Following have been Appointed as Affiliate Members of the Hypertension and Vascular Research Center:

Aileru Azeez
Ronny Bell
Mark Cline
Barry Freedman
David Goff
Leann Groban
David Herrington
Jay Kaplan
Lorna Moore
Michael O'Shea
Mike Robbins
David Sane
Tom Smith
Mary Sorci-Thomas
Charles Tegeler
Lisa Washburn

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Researchers Identify Key Contributor to Preeclampsia

Preeclampsia, the second leading cause of maternal death, is a disorder that occurs only during pregnancy and the postpartum period.

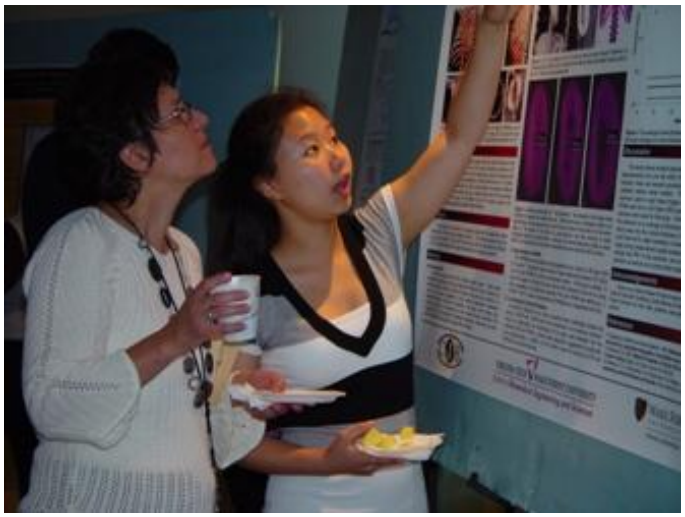
In normal pregnancy, the uterus has lower renin-angiotensin system (RAS) activity, producing less of angiotensin II, a vasoconstrictor which binds to its receptor and dilates the blood vessels. This results in lower blood pressure and allows more oxygen and nutrients to pass from the mother's uterus to the placenta and fetus. In preeclamptic women, however, the activity of the RAS is increased in the uterus, yet the mother's vessels remain dilated and the fetus' vessels constrict more than normal. The present study focused on uncovering the reason for this.

Surprisingly, the angiotensin II receptors were not detectable in the uteri of pregnant or preeclamptic women. In preeclamptic women, where uterine angiotensin II is high, the hormone does not bind to its receptors in the uterus as it should, but instead passes through to the vessels of the fetal placenta and constricts the fetus' vessels, limiting the fetus' oxygen and nutrient intake and often causing low birth weight.

This study lead by Dr. K. Bridget Brosnihan, Professor at the Hypertension Center, provides some insight into maternal factors that may augment the disease. The article was selected by Endocrine Reviews for comment and as part of the anthology of Translational Research in Endocrinology & Metabolism September, 2009.

Poster Symposium

The Wake Forest University Graduate School of Arts and Sciences in conjunction with Wake Forest University School of Medicine held the Summer Research Training Programs' Poster Symposium on Friday, July 24, 2009. The federally and institutionally-funded programs represented in the symposium included the Excellence in Cardiovascular Sciences Summer Research Program (EICS), Summer Research Opportunities (SROP), and Translational Science Institute Scholars Program (TSI). A total of 42 undergraduates representing 35 colleges who participated in the programs. Along with Dr. Linda McPhail, Associate Dean of the Graduate School, Dr. Debra Diz, Professor and Interim Director of the Hypertension and Vascular Research Center, and Dr. Ann Tallant, Professor in the Hypertension and Vascular Research Center and Program Director of the Excellence in Cardiovascular Sciences Summer Research Program, there were mentors from the Department of Physics and Department of Chemistry on the Reynolda Campus as well the medical school departments of Biochemistry, Biomedical Engineering, Cancer Biology, Cardiothoracic Surgery, Hypertension and Vascular Research Center, Microbiology and Immunology, Molecular Medicine, Neurobiology and Anatomy, Obstetrics and Gynecology, Pathology-Lipid Sciences, Pathology – Tumor Biology, Physiology and Pharmacology, Public Health Sciences - Center for Public Research, Pulmonary and Critical Care, Radiation Oncology, and Regenerative Medicine .



SROP student, Hannah Kim explains her poster presentation to Dr. Jasmina Varagic.

New Hires

Manisha Nautiyal, PhD
Research Fellow
Advisor: Dr. Debra I. Diz

My research proposal seeks to evaluate the hypothesis that Ang-(1-7) regulates expression of MAP kinase phosphatase MKP-1 (negative regulator of MAPK) and protein tyrosine phosphatase 1b PTP1b (negative regulator of PI3K) in response to Ang II stimulated activation of the MAPK and PI3K pathways. Transgenic animals with altered brain RAS [(mRen2)27, ASrAOGEN and control Sprague Dawley rats] will be used to dissect out the signaling mechanism utilized by Ang-(1-7), MKP-1 and PTP1b to modulate baroreflex sensitivity and mitochondrial function. The gene and protein expression for downstream components of PI3K and MAPK pathway will be examined and immunolocalization of MKP-1 in brain with respect to angiotensin peptides will also be investigated. These studies will provide insight into the underlying mechanisms by which brain RAS components can regulate signaling pathways that are altered with aging and under various pathological conditions and will lead to new strategies that can be used to prevent and/or treat hypertension, thereby reducing the morbidity and mortality associated with cardiovascular diseases.

Matthew Satusky
Laboratory Technician III
Advisor: Dr. Bill Strawn

I am the new transgenic rat colony manager, which involves breeding different strains of rats to provide research subjects for various projects in the Hypertension Center as well as at other institutions. I have a BA in psychology from East Carolina University and am currently pursuing a BS in biochemistry from UNCG. I spent the past two years working in the animal resources department at Duke and doing parasitology research at the NC State Vet School.

Bryan Wilson
PREP Student
Advisor: Dr. Mark Chappell

Bryan's research explores intracellular mechanisms of reactive oxygen species (ROS) formation and its regulation by the renin angiotensin system (RAS). This work demonstrates the significance of an intracellular RAS in cell signaling and oxidative stress.

Recognition Awards

Dr. Sarfaraz Ahmad received his US citizenship on October 15, 2009.

Amy Arnold and Yuval Silberman were united in marriage on October 23, 2009.

Amy Arnold, graduate student, participated in the Neural Control and Autonomic Regulation section of the APS trainee advisory committee fall meeting.

Amy Arnold, Hossam Shaltout, PhD, and Aaron Trask, PhD were appointed as committee members in the Cardiovascular Division of ASPET.

Patricia DePaulis, Secretary III for Dr. Pavel Levy will be awarded for 10 years of service to the Wake Forest University School of Medicine.

COSEHC has established an annual lectureship titled the Carlos M. Ferrario, MD, COSEHC Founders Lectureship honoring Dr. Ferrario's expertise, leadership, and his many contributions over the years since he founded COSEHC in 1992. Dr. Ferrario will present the inaugural lecture at this year's COSEHC Scientific Sessions during a luncheon held on Saturday, October 23, 2009. The title of the lecture is: *"50 years of Progress in Understanding the Renin-Angiotensin System".*

Dr. Carlos Ferrario was selected as recipient of the 2009 Novartis Award for Hypertension Research sponsored by the Council for High Blood Pressure Research and was honored at the Novartis Award Reception and Dinner on September 25th at their conference at the InterContinental Chicago O'Hare Hotel in Chicago, IL. Dr. Ferrario's research identified the mechanisms of action of angiotensin in the brain, the role of the sympathetic nervous system in cardiac hypertrophy and discovered new endocrine pathways leading to the formation of angiotensin-(1-7) and the mechanisms of action of angiotensin converting enzyme and angiotensin receptor antagonists. Dr. Ferrario is also the co-founder of the Consortium of Southeastern Hypertension Control (COSEHC). He is a sought-after speaker with a world-wide record of lectureships.

Dr. Toni Garcia-Espinosa and Dr. John Knight added to the family on April 7, 2009 with baby Sofia Knight-Garcia.

In July, 2009, JaNae Joyner-Grantham, Ph.D. was promoted to research associate with the Consortium for Southeastern Hypertension Control (COSEHC).

Mark Landrum, Laboratory Technician IV for Drs. Ann Tallant and Peg Gallagher will be awarded for 10 years of service to the Wake Forest University School of Medicine.

Sarah and Jason Lindsey added to the family on July 8, 2009 with baby Hollis Lloyd Lindsey.

LaTronya McCollum successfully defended her PhD thesis on October 16, 2009, and will be awarded her degree effective December 2009. Her mentors were Drs. Ann Tallant and Peg Gallagher. The title of the thesis was "The Role of Angiotensin-(1-7) in the Modulation of Angiotensin II-Dependent Cardiac Remodeling."

Manisha Nautiyal, PhD, has been selected as the 2009 COSEHC Warren Trust Fellow. Manisha will be recognized at the 2009 COSEHC Scientific Sessions scheduled for October 22-24, 2009. Dr. Nautiyal is working under the mentorship of Dr. Debra Diz, and her research is, "Baroreflex Regulation by Ang-(1-7) Activation of MKP-1 and PTP1b in Dorsal Medulla" Molecular Medicine and Translational Science Graduate Program"

Recognition Awards con't

Karl Pendergrass successfully defended his PhD thesis on August 24, 2009, and will be awarded his degree effective December 2009. His mentor was Dr. Mark Chappell. The title of the thesis was "Sex-Related Differences in Hypertension and Renal Injury: Role of the Renin-Angiotensin System".

Nobi Sarver, Administrative Secretary and Program Assistant for Training Programs will be awarded for 25 years of service to the Wake Forest University School of Medicine.

Nobi Sarver was promoted to Administrative Secretary.

Dr. Jasmina Varagic was promoted to Assistant Professor of Surgery.

Jessica VonCannon was promoted to Laboratory Technician IV.

Travel Awards

Kate Cook won a $200 travel award from the Molecular Medicine and Translational Science Program to attend the 5th International Tumor Microenvironment meeting October 20th – 24th in Versailles, France.

Kate Cook has been awarded an Alumni Student Travel Award for $300 for the 5th International Tumor Microenvironment meeting in Versailles, France in October.

Grant Awards

The Hypertension and Vascular Research Center at Wake Forest University School of Medicine has received renewal of a multi-million dollar grant from the National Heart, Lung and Blood Institute of the National Institutes of Health to continue the development of new approaches to treat hypertension and vascular disease. The program is its 16th year of existence at the School of Medicine.
http://www2.wfubmc.edu/News/NewsARticle.htm?ArticleID=2647

Dr. Debra Diz received an American Recovery and Reinvestment Act (ARRA) supplement award from NIGSM for the Post-baccalaureate Research Education (PREP) for development of a newsletter, Facebook page, electronic database, online applications and survey tools for better communication among current and former trainees and the program.

Dr. Maria Antonia-Garcia Espinosa received a fellowship position on the Translational Radiation Oncology (TRADONC) T32 to continue her development of translational studies using magnetic resonance imaging in spectroscopy for cardiovascular and cancer applications.

Dr. Jasmina Varagic received an American Heart Association grant entitled "Angiotensin (1-7) in salt-sensitive Hypertension."

Request
The Consortium for Southeastern Hypertension Control (COSEHC)

The Consortium for Southeastern Hypertension Control (COSEHC) is a non-profit health organization whose mission is to empower health care professionals, patients, and the public with better knowledge, tools, and competencies through continuous quality improvement to secure vascular health for all people. COSEHC is headquartered within the Hypertension and Vascular Research Center at Wake Forest University Health Sciences.

COSEHC currently has several ongoing projects including a physician quality improvement initiative and a clinically associated research project defining a novel health paradigm called patient inertia. As a result of these projects, COSEHC has two needs in regards to student and/or volunteer assistance in completing the objectives of these projects.

Opportunity 1:
COSEHC has an immediate need for assistance with sporadic data collection and analysis as a result of its physician quality improvement initiative called ATGOAL – Aggressively Treating Global Cardiometabolic Risk Factors to Reduce Cardiovascular Events. The physician clinics participating in this project are located throughout the Southeastern United States. Thus, data collection would encompass a minimum of 8 hours per day and might require overnight travel for 2-4 nights during a given week. Primarily the data collection would be done during weekdays since clinic offices are not generally open on weekends. The individual would be paid $10 an hour for their service. All travel accommodations including mileage, hotel, and meals would be reimbursed at the COSEHC travel reimbursement policy rate. (This is the same as the Wake Forest University School of Medicine rate).

Opportunity 2:
COSEHC is seeking a 2010-2011 summer student. The student would assist with data collection, data analysis, benchmarking reports, and project documents for the physician quality improvement initiative called ATGOAL – Aggressively Treating Global Cardiometabolic Risk Factors to Reduce Cardiovascular Events. The student would accompany COSEHC staff to ATGOAL physician offices throughout the Southeast United States thus requiring local and out of state travel. Additionally, if there were breaks in the schedule for the ATGOAL initiative, the student would be trained and assist with administration and data analysis of patient inertia surveys given within the Emergency Department at Wake Forest University Baptist Hospital or local Winston Salem, NC clinics. At the end of the summer internship, the student would have ample data for abstract and poster presentation. Potential project abstracts include: 1) The comparison of baseline cardiovascular disease parameters within ATGOAL sites; 2) The effects of customized continuing medical education (CME) on cardiovascular disease parameters within ATGOAL sites; 3) The effect and comparison of patient inertia parameters on hypertension control in medical and community environments; 4) Validation of the patient inertia model; 5) Psychological Distress among Emergency Department hypertensive patients using the Brief Symptom Inventory (BSI).

Recent Publications

Journal Articles

Arnold AC, Shaltout HA, Gallagher PE, Diz DI. Leptin Impairs Cardiovagal Baroreflex Function at the Level of the Solitary Tract Nucleus. Hypertension. 2009 Nov;54(5):1001-8.

Joyner-Grantham J, Mount DL, McCorkle OD, Simmons DR, Ferrario CM, Cline DM. Patient Inertia Beliefs among Hypertensive Emergency Department Patients Reveals Hopelessness Surrounding Disease Control and a Disconnect Between Hypertension Literacy and Patient Action. [In Press (November issue), The American Journal of the Medical Sciences] 2009.

Joyner-Grantham J, Simmons DR, Moore MA, Ferrario CM. The Impact of Changing ICD Code on Hypertension-Related Mortality in the Southeastern United States from 1994-2005**.** [In Press, The Journal of Clinical Hypertension] 2009.

Park S, Bivona BJ, Kobori H, Seth DM, Chappell MC, Lazartigues E, Harrison-Bernard LM. Major role for ACE-independent intrarenal ANGII formation in type II diabetes. Am J Physiol Renal Physiol. 2009 Oct 21.

Sugulle M, Dechend R, Herse F, Weedon-Fekjaer MS, Johnsen GM, Brosnihan KB, Anton L, Luft FC, Wollert KC, Kempf T, Staff AC. Circulating and Placental Growth-Differentiation Factor 15 in Preeclampsia and in Pregnancy Complicated by Diabetes Mellitus. Hypertension. 2009 Jul;54(1):106-12.

Valdes G, Kaufmann P, Corthorn J, Erices R, Brosnihan KB, Joyner-Grantham J. Vasodilator Factors in the Systemic and Local Adaptations to Pregnancy. Reprod Biol Endocrinol. 2009 Jul 31;7:79.

Abstracts:

Ahmad S, Varagic J, Westwood B, Chappell MC, Ferrario CM. Uptake of Novel Peptide Angiotensin-(1-12) by Cardiac Myocytes. Hypertension 2009 54(4):e111.

Arnold AC, Shaltout HA, Gallagher PE, Diz DI. Protein Phosphatase 1b Activity in the Solitary Tract Nucleus Is Necessary for Normal Baroreflex Function. Hypertension. 2009 54(4):e100.

Awumey EM, Bridges LS, Diz DI. Endothelial Nitric Oxide Synthase Knockout and Nitric Oxide Inhibition Attenuate Ca^{2+}-Induced Relaxation of Isolated Precontracted Mouse Mesenteric Arteries. Hypertension. 2009 54(4):e123.

Brosnihan KB, Dechend R, Hering L. Enhanced Expression of Human RAS mRNA in Association with Increased Ang II Suggests a Critical Role for the Maternal Placenta in Preeclampsia. Hypertension. 2009 54(4):e111.

Cohen JA, Lindsey SH, Pirro NT, Chappell MC. Urinary Angiotensinogen Associates with Estrogen and Salt Sensitivity. Hypertension. 2009 54(4):e80.

Dechend R, Hering L, Herse F, Verlohren S, Geusens N, Luft FC, Muller DN, Pijnenborg R, Brosnihan KB, Cartwright JE. Different Effects of Circulating and Local Uteroplacental Angiotensin II in Pregnancy. Hypertension. 2009 54(4):e108.

Gallagher PE, Tallant EA. Angiotensin-(1-7) Reduces MAP Kinase Activity by Upregulation of the Dual-Specificity Phosphatase DUSP1. Hypertension. 2009 54(4):e35.

Garcia-Espinosa MA, Shaltout HA, Olson J, Link K, Diz DI. In Vivo Proton Magnetic Resonance Spectroscopy Detection of Neurotransmitter/Metabolite Concentrations in Dorsomedial Medulla as a Noninvasive Predictor of Autonomic Function. Hypertension. 2009 54(4):e48.

Gilliam-Davis, S, Tommasi EN, Garcia-Espinosa MA, Chappell MC, Brosnihan KB, Diz DI. Bilateral Renal Denervation Prevents Age-Related Proteinuria Without Altering Excretion of Intrarenal Angiotensin Peptides in Sprague-Dawley Rats. Hypertension. 2009 54(4):e76.

Gwathmey TM, Pendergrass KD, Shaltout HA, Reid SD, Rose JC, Diz DI, Chappell MC. Steroid-Induced Fetal Programming Differentially Alters Nuclear Angiotensin II Receptor Expression and Function. Hypertension. 2009 54(4):e42.

Gwathmey TM, Pendergrass KD, Rose JC, Diz DI, Chappell M. Nuclear Angiotensin-(1-7) Receptors Mediate the Production of Nitric Oxide. Hypertension. 2009 54(4):e74.

Isa K, Arnold AM, Chappell MC, Diz DI. Angiotensin-Converting Enzyme Inhibition, but not AT_1 Receptor Blockade, in the Solitary Tract Nucleus Improves Baroreflex Sensitivity in Anesthetized Transgenic. Hypertensive (mRen2)27 Rats. Hypertension. 2009 54(4):e98.

Joyner-Grantham J, Simmons DR, Moore, MA, Mount DL, Cline DM, Ferrario, CM. Decreasing Cardiovascular Risk and Defining Forsyth County, NC Hypertension Inertia through a Faith- Based Cardiovascular Disease Prevention Program. National Conference to End Health Disparities. November, 2009.

Lindsey SH, Chappell MC. The GPR30 Agonist G-1 Induces Nitric Oxide-Independent Relaxation in Resistance Arteries. Hypertension. 2009 54(4):e43.

Logan EM, Johnson A, Diz DI, Aileru A. Nicotinic and AT_1 Receptors Show Enhanced Responsiveness in the Superior Cervical Ganglia of (mRen2)27 Versus Sprague-Dawley Rats. Hypertension. 2009 54(4):e85.

Mount DL, Johnson D, Rego M, Schofield K, Joyner-Grantham J. Finding a Shared Voice: Developing an African American Male Mind-Body, Healthy Living Curriculum through Community Engagement. A Preliminary Report. National Conference to End Health Disparities. November, 2009.

Shaltout HA, Diz DI, Figueroa JP, Chappell MC, Rose JC. Sympathetic Nervous System Mediated Responses to Behavioral or Pharmacologic Challenges Are Exaggerated as a Result of Antenatal Betamethasone Exposure, Hypertension. 2009 54(4):e101.

Tallant EA, McCollum LT, Gallagher PE. Angiotensin-(1-7) Reduces Ang II-Induced Cardiac Hypertrophy with an Associated Increase in the Dual-Specificity Phosphatase 1 (DUSP1. Hypertension. 2009 54(4):e122.

Varagic J, Ahmad S, Brosnihan KB, Ferrario CM. Spironolactone and Angiotensin-(1-7) in Salt-Induced Cardiac Injury. Hypertension. 2009 54(4):e26.

Upcoming Events

Hypertension and Vascular Research Center Seminar Series

Monday, Nov 30th, 3 – 4, Commons 1,2,3
Monday, Jan 25th, 3 – 4, Commons 1,2,3 Lorna G. Moore, PhD, "Genomic studies of physiological adaptation to high altitude: lessons from pregnancy."

Research-In-Progress (RiP) Meetings

Wednesday, Nov 11th, 11 – 12 Jasmina Varagic, MD, PhD
Wednesday, Dec 9th, 10:45 – 12 Staff Meeting & Jonathan Cohen, DVM

Journal Club

Wednesday, Nov 4th, 11 – 12 TanYa Gwathmey, Research Fellow
Wednesday, Nov 18th, 11 – 12 Katherine Cook, Molecular Medicine and Translational Science Graduate Student
Wednesday, Dec 2nd, 11 – 12 Kyle Carver, Physiology & Pharmacology Graduate Student
Wednesday, Dec 16th, 11 – 12 Hossam Shaltout, Research Fellow

COSEHC

Dr. JaNae Joyner-Grantham will be doing a presentation entitled "Physical Health of the Whole Woman" and a blood pressure screening for Lake Norman Christian Outreach, Lake Norman, NC on November 7, 2009.

16th Annual Scientific Sessions

Sponsored by The Consortium for Southeastern Hypertension Control.

Improving Cardiovascular Outcomes Treating the Goal!

Thursday – Saturday
October 22 – 24, 2009
Marriott MeadowView Resort Convention Center
1901 MeadowView Parkway
Kingsport, Tennessee

The COSEHC employees, Jeff Atwell, Dr. JaNae Joyner, Susie Pollock, and Debbie Wirth-Simmons will be attending the meeting. Research Fellow, Dr. Manisha Nautiyal, will be honored for receiving the 2009 COSEHC Warren Trust Fellowship. Interim Director, Dr. Debra I Diz, will be presenting a workshop on Understanding the Renin-Angiotensin System with Dr. Robert Carey, University of Virginia Medical School. On Saturday at 12:30 pm Dr. Carlos M. Ferrario will be presenting the inaugural COSEHC Founders Lecture entitled "50 Years of Progress in Understanding the Renin-Angiotensin System".

Some of the program objectives are:

1. Recognize the most up-to-date evidence based standards for the treatment of hypertension, dyslipidemia, and diabetes.
2. Use evidence based tools to identify cardiometabolic risk factors.
3. Treat patients with identified risk factors early and rigorously with evidence-based interventions.

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Physiology Training Extends to Area Middle Schools

Two of our very own trainees, Drs. TanYa Gwathmey and Shea Gilliam-Davis have joined efforts with the American Physiological Society (APS) to train science educators. The APS Office of Education has developed a Teacher's forum where Science instructors from elementary through high school come to learn how to adapt aspects of physiology into their science curriculum.

In 2008, Dr. Gwathmey was awarded the APS K-12 Teaching Fellowship in which she served as Physiologist-in-Residence at the Science Teacher's Forum in Airlie, Va. During her fellowship, she developed laboratory modules to be used in science teaching manuals and also visited local middle and high schools where she and other trainees from the Hypertension Center presented lectures and laboratory demonstrations on renal-, neuro-, muscle- and cardiovascular physiology. Dr. Gwathmey also served as mentor to other trainees at the 2008 and 2009 Experimental Biology Conferences.

Dr. Gilliam-Davis served as the 2009 Physiologist-in-Residence at the Teacher's Forum and is continuing with Dr. Gwathmey to visit area schools during the annual Physiology Understanding (PhUn)Week in November.

http://www1.wfubmc.edu/School/Alumni-Affairs/Giving-Options.htm

How You Can Help