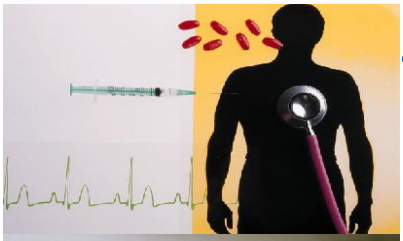
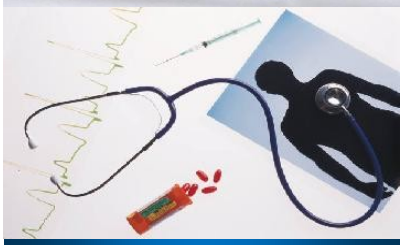




T.H.R.C.E.

TULANE HYPERTENSION AND RENAL CENTER OF EXCELLENCE

Spring 2014 *Volume 13, Issue 1*

In This Issue

Grants & Research Support Awarded to THRCE Affiliated Investigators

Dr. Jing Chen received a NIH-ROI grant to support her research. Dr. Chen was a junior faculty investigator during COBRE phase II. She received three years of research support for her study titled, "Urinary Angiotensinogen Excretion and Salt-Sensitivity of Blood Pressure." The picture on the left shows Drs. Navar and Chen celebrating the news at an award announcement event held on March 2014.

Dr. L. Gabriel Navar received a 2-year grant (CRLX030AUSNC08T) from Novartis to study, "Effects of Serelaxin on renal microcirculation under control and high angiotensin conditions," and an AHA grant for a Health Sciences Fellowship for two years that supports three medical students to have summer research experiences.

Dr. Andrea Zsombok was awarded a 5-year, NIH/R01 grant for her study, "TRPV1-dependent autonomic control in diabetes." She was also appointed to the Editorial Board of the Scientific Reports journal.

Dr. Jiang He was awarded a 5-year grant from NIH/NHLBI, to study the effectiveness of a comprehensive intervention program to improve hypertension prevention and control among uninsured patients and their families in Argentina.

Dr. Minolfa Prieto received a $25,000 Faculty Research Pilot Program Award from Tulane School of Medicine.

Dr. T. Cooper Woods was awarded a 2014 UQ-Ochsner Seed Fund for collaborative research (PI: H Bazan) and the SVS Foundation Clinical Research Seed Grant (PI: H Bazan).

Honors & Recognition Awarded to THRCE Affiliated Investigators

Dr. L. Gabriel Navar presented the Robert M. Hearin Distinguished Lecture to the Department of Pharmacology at the University of Mississippi Medical Center of March 17. The title of his lecture was "Intrarenal Renin-Angiotensin System in Hypertension." He also served on the external advisory committee for the Program Project grant at New York Medical College, and participated in the Bioinnovation IGERT Advisory Board Meeting.

A paper entitled, "Circulating Adipocytokines and Chronic Kidney Disease," by **Dr. Jing Chen and others** was highlighted in the October 9, 2013 issue of the American Society of Nephrology (ASN) online bulletin.

Dr. Dewan S. A. Majid was an invited Symposium speaker on Tumor Necrosis Factor (TNF) at the Experimental Biology Meeting held in April at San Diego, CA and presented "Effects of TNF on Renal Hemodynamics and Sodium Excretion." He is also invited as Symposium speaker at the upcoming South Asian Association of Physiology (SAAP) Conference to be held in Dhaka, Bangladesh in December, 2014.

Dr. Patrice Delafontaine was selected as the Interim Chair for the Department of Medicine.

Dr. Andrei Derbenev received the New Investigator Award from the APS Central Nervous System Section at the Experimental Biology Meeting 2014 on April 26-30, San Diego, CA.

Dr. Kenneth D. Mitchell published a paper on the Debakey Program in Medical Science Educator Journal and was a Grant Reviewer for the AHA Greater Southeast Affiliate, CardioRenal 3 Committee in April 2014.

Dr. Minolfa C. Prieto was invited speaker and Co-Chair at a symposium in San Diego, CA. The Symposium, "Physiological Genomics and Kidney and Hypertension Symposium" was held at the Experimental Biology Meeting and the title of her talk was, "Deletion of prorenin receptor (PRR) in the collecting duct attenuates hypertension during chronic Ang-II infusion."

Dr. Ihor Yosypiv was selected as the chairman for the Department of Pediatrics Research Committee.

Dr. Sergiy Sukhanov received the SFMR/SSCI Jr. Faculty Research Award at the Southern Section meeting of the Southern Society for clinical investigators held in New Orleans.

News

Continued...

Awards presented to Graduate Students & Post-doctoral fellows:

- ***2014 AFMR Southern Society for clinical investigators (SSCI) Southern Regional Meeting, New Orleans:***
  - ◊ **Dr. Umadevi Subramanian** (mentor, Dr. Pandey) received an SFMR/SSCI Trainee Research Award.
  - ◊ **Dr. Weijan Shao** (mentor, Dr. Navar) received an SFMR/SSCI Trainee Research Award.
  - ◊ **Camille Bourgeois** (mentor, Dr. Prieto): Awarded the SSCI Young Investigator Award (3rd place) for her abstract, "Novel Protective Effect of Histone Deacelytase 9 as a Repressor of Angiotensinogen Expression in Female Rat Kidneys."
  - ◊ **Tolga Caner** (mentor, Dr. Nakhoul) was awarded a "SAFMR/SSCI Student Research Travel Award" and his abstract, "DIDS inhibits ammonia transport by Rh glycoproteins," was selected for oral presentation.
  - ◊ **Ryan Walker** (mentor, Dr. Hering Smith) was selected to orally present his abstract, "Regulation of Novel Calcium-Sensitive Dicarboxylate Transport Process."
  - ◊ **David A. Thompson** (mentor, Dr. Mitchell) was awarded a "SAFMR/SSCI Student Research Travel Award."
- ***2014 Experimental Biology (EB) Meeting, San Diego, CA.***
  - ◊ **Tolga Caner** was a finalist for the Gunn Award for Excellence in Research for a graduate student held at the 2014 EB meeting. He was presented the award at the "Cell and Molecular Physiology" Section of APS.
  - ◊ **David Thompson** received a Travel Award to attend and participate at the 2014 EB Meeting held in San Diego, CA.
  - ◊ **Hong Gao** (mentor, Dr. Derbenev) received a Travel Award to attend and participate at the 2014 EB Meeting.
- ***Ivy Day Awards for the Class of 2014:***
  - ◊ **Catherine Howard** received the Hymen S. Mayerson Award from the Department of Physiology
  - ◊ **Laleh Bahrami, James O'Hare, and Carolyn Campbell** all received the Nicholas R. Diluzio Award from the Department of Physiology.

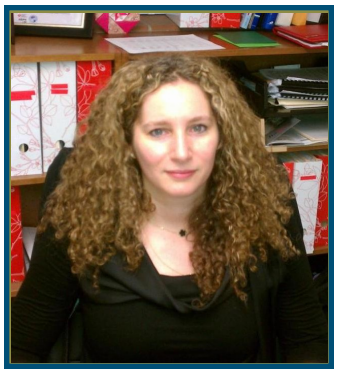
New Numbers for healthy blood pressure

For years the American Medical Association (AMA) had set the guidelines for healthy blood pressure to be 120 over 80. In December 2013, a report in the Journal of the American Medical Association reset the guidelines to a level around 140 over 90. The change is controversial with some doctors questioning the possible impact of the change to population health. You may access further details regarding the changes at:

- **http://jama.jamanetwork.com/article.aspx?articleid=1791497**
- **http://www.theneworleansadvocate.com/features/9045728-171/ama-wants-you-to-remember**

THRCE sponsor
Local, National & International Speakers

THRCE regularly sponsors bi-weekly seminars by scheduling nationally and internationally recognized investigators and clinicians in the field of hypertension research, treatment and education. From January through April, 2014, the following speakers presented THRCE seminars:



- **Andrea Zsombok, PhD**
  Assistant Professor,
  Department of Physiology,
  Tulane School of Medicine,
  New Orleans, LA.

On February 13, 2014, **Dr. Andrea Zsombok** presented "**The effect of olanzapine on brainstem neurons.**" Olanzapine, an atypical antipsychotic, alleviates symptoms of schizophrenia while producing fewer side effects compared with first generation antipsychotics. However, chronic usage remains problematic due to the propensity of olanzapine to induce weight gain and metabolic disturbances. Moreover, the cellular mechanisms underlying the weight gain and metabolic side effects are poorly understood. The central nervous system exerts both hormonal and neural control over whole body homeostasis. Neurons in the dorsal motor nucleus of the vagus (DMV) play a critical role in the regulation of autonomic functions including glucose homeostasis and Dr. Zsombok hypothesized that olanzapine disrupts neurotransmission in the DMV, and thus contribute to the dysregulation of metabolism. During the talk. Dr. Zsombok summarized their preliminary findings focusing on the effect of olanzapine on neuronal activity in the DMV.

Special THRCE Seminar in honor of World Kidney Day

- **Samir El-Dahr, MD**
  Jane B. Aron Professor of Pediatrics
  Chair, Department of Pediatrics
  Section Chief, Pediatric Nephrology
  Tulane School of Medicine,
  New Orleans, LA.

Dr. Samir El-Dahr, presented, "**Nephron Progenitors and Blood Pressure: less of one, more the other,**" on March 13, 2014. This presentation was highlighted as a Special THRCE Seminar in honor of World Kidney Day. Congenital Abnormalities of the Kidney and Urinary Tract account for a majority of children with end-stage-renal disease requiring dialysis and renal transplantation. Renewal, survival and differentiation of nephron progenitors determines the final number of nephrons, the filtering units of the kidney. Congenital reduction of nephron number, a condition called renal hypoplasia, is associated with adult hypertension and chronic kidney disease. Dr. El-Dahr's laboratory is interested in the basic mechanisms which control the survival and differentiation of nephron progenitors, a group of committed but undifferentiated "stem-like" cells located in the periphery of the embryonic kidney in confined crescent-like areas, called the nephron niche. They find that the survival and differentiation of nephron progenitors is dependent on cell-autonomous chromatin-based mechanisms mediated by histone deacetylases and histone methyltransferases. Moreover, tight regulation of the transcription factor, p53, by its negative regulator, Mdm2, plays a key in the proliferation and survival of nephron progenitors. Using the mouse kidney as their model system, they apply state-of-the-art genetic, epigenetic, biochemical and functional assays to decipher gene function during nephrogenesis. The long-term goal of Dr. El-Dahr's research is to identify novel therapies that can be applied to the study of nephron regeneration strategies in congenital and acquired renal disease.

Joint Seminar Co-Sponsored by the Department of Physiology

- **Jia L. Zhuo, MD, PhD**
  Professor, Department of Pharmacology and Toxicology
  Division of Nephrology,
  Department of Internal Medicine
  Cardiovascular-Renal Research Center
  The University of Mississippi Medical Center, Jackson, MS.

On Monday, March 17, 2014, **Dr. Jia Zhuo** presented a talk jointly sponsored by the Department of Physiology and THRCE. The talk he gave was titled, "**Current insights and new perspectives on the roles of paracrine and intracrine angiotensin II in the proximal tubule of the kidney.**" The renin-angiotensin system (RAS) is well recognized as one of the most important regulators of arterial blood pressure, cardiovascular and kidney function. New frontiers have recently emerged in the RAS research well beyond its classic paradigm as a potent vasoconstrictor, an aldosterone stimulator, or a sodium-retaining hormone. The RAS functions not only as a circulating or endocrine system, but also as local paracrine and intracrine systems in tissues. In addition to renin and angiotensin I-converting enzyme (ACE), two new members of the RAS have been uncovered, which include the renin/(Pro) renin receptor (PRR) and angiotensin-converting enzyme 2 (ACE2). Recent studies suggest that prorenin may act on the PRR independent of the classical ACE/ angiotensin II (ANG II/)AT1 receptor axis, whereas ACE2 may degrade ANG II to generate ANG (1-7), which activates the Mas receptor. There is also increasing evidence that ANG II may exert long-term genomic effects by activating its intracellular/nuclear receptors. Furthermore, there is currently a debate on the relative contribution of circulating versus local RAS to the physiological regulation of blood pressure and the development of hypertension. The objectives of this presentation was to briefly review and discuss the novel roles of the local RAS in the kidney, based on recent studies using novel transgenic mice that either overexpress or are deficient of one key enzyme, ANG peptide, or receptor of the RAS. This information may help us better understand how ANG II acts, both independently or through interactions with other members of the system, to regulate the kidney function and blood pressure in health and disease.

Continued...

- **Mark C. Chappell, PhD**
  Professor, Department of Physiology and Pharmacology,
  Director, US-Brazil Science Without Borders Program,
  Wake Forest School of Medicine,
  Winston-Salem, NC. .

Dr. Mark Chappell presented "Angiotensin-(1-7) Calms AGE-RAGE in Diabetic Renal Injury" on March 27th, 2014. Diabetic injury to the kidney is a major concern in the United States and constitutes a growing burden to the health care system. Elucidation of the mechanisms of renal injury is important to advance effective therapies that combat the progression of diabetic disease and compromised renal function. Angiotensin-(1-7) (Ang 7) is an alternative product of the renin-angiotensin-aldosterone system (RAAS), a key endocrine system in the kidney that is a therapeutic target to attenuate diabetic injury. Ang 7 and its receptor Mas are widely expressed in various tissues including the brain, heart and the kidney. Although most studies reveal beneficial effects of Ang 7 that include the lowering of blood pressure, reduced cell growth, anti-inflammation and reduced fibrosis, there are various reports that Ang 7 may exacerbate tissue injury particularly within the kidney and stimulate cellular pathways similar or identical to Ang II. Dr. Chappell's study addressed the cellular effects of Ang 7 in response to chronic exposure of advanced glycation end products (AGE) in the NRK-52E renal tubule cell line. AGE exposure in the NRK-52E cells was associated with a significant reduction in the cellular levels of Ang 7 that may reflect the enhanced metabolism of the peptide rather the decreased formation from Ang I. Chronic treatment with Ang 7 abolished the AGE-induced cellular hypertrophy; however, the addition of the RAAS inhibitors lisinopril (ACE), losartan (AT1 receptor) or aliskerin (renin), failed to reduce the hypertrophic response. AGE induced an epithelial to mesenchymal (EM) phenotype in the NRK-52E cells that was abolished by Ang 7. The inhibition of AGE-dependent EM transition by Ang 7 was blocked by the selective AT7 receptor antagonist D-Ala7-Ang 7 (DALA). AGE exposure resulted in a 3-fold increase in the cytokine TGF-β that likely constitutes a key factor in the development of cellular hypertrophy and the EM phenotype. Indeed, the TGF-β receptor kinase inhibitor SB525334 abolished AGE-induced EM transition and the chronic activation of the MAP kinase ERK1/2. Although Ang 7 failed to inhibit AGE-induced release of TGF-β, the peptide blocked both AGE and TGF-β activation of ERK1/2. Pretreatment with the DALA antagonist again blocked the inhibitory effects of Ang 7 on ERK1/2 activation. Dr. Chappell conclude from the current studies that chronic AGE exposure reduced expression of the Ang 7 axis of the RAAS and this cellular deficit of Ang 7 may contribute to the deleterious actions of the AGE-RAGE pathway through activation of TGF-β/ERK1/2. Supplementation of Ang-(1-7) to existing monotherapies that block the RAAS may provide a more effective approach to attenuate diabetic renal injury.

Continued...

- **David W. Busija, MD, PhD**
  Regents Professor & Chairman,
  Department of Pharmacology,
  Tulane University School of Medicine,
  New Orleans, LA.

On April 10 **Dr. David Busija** presented a seminar titled "**Mitochondrial mechanisms during health and disease in the cerebral vasculature.**" Mitochondria are double membrane organelles within cells which generate chemical energy in the form of ATP. The ATP is distributed within cells and promotes the varied activities of the various cell types comprising the neurovascular unit (endothelium, vascular smooth muscle [VSM], astroglia, perivascular neurons, parenchymal neurons, pericytes, and microglia). Although traditionally understood as energy producers only and relegated to that role, it is now appreciated that mitochondria are involved in diverse adaptive activities such as promotion of basal cellular functions, cellular protection, and regulation of vascular tone. Mitochondrial initiated events protect the neurovascular unit against lethal stresses via a process called preconditioning which independently promotes changes in cerebrovascular tone via shared signaling pathways. Activation of the adenosine triphosphate (ATP)-dependent potassium channels on the inner mitochondrial membrane (mitoKATP channels) is a specific and dependable way to induce protection of neurons, astroglia, and cerebral vascular endothelium. Mitochondrial depolarization, via the opening of mitoKATP channels, leads to activation of protein kinases and transient increases in cytosolic calcium (Ca2+) levels that activate final mechanisms that protect the neurovascular unit against lethal stress. Release of reactive oxygen species (ROS) from mitochondria has similar protective effects.

Signaling elements of the preconditioning pathways are also involved in the regulation of vascular tone. Activation of mitoKATP channels in cerebral arteries causes vasodilation, with cell-specific contributions from endothelium, vascular smooth muscle (VSM), and nerves. Pre-existing chronic conditions such as insulin resistance and/or diabetes prevent preconditioning and impair relaxation to mitochondrial centered responses in cerebral arteries. Surprisingly, mitochondrial activation after anoxic or ischemic stress appears to protect cerebral vascular endothelium and promotes the restoration of blood flow; therefore, mitochondria may represent an important, but underutilized target in attenuating vascular dysfunction and brain injury in stroke patients.

Recent Publications

Publications

Blackstock CD, Higashi Y, Sukhanov S, Shai SY, Stefanovic B, Tabony AM, Yoshida T, Delafontaine P. Insulin-like growth factor-1 increases synthesis of collagen type I via induction of the mRNA-binding protein LARP6 expression and binding to the 5' stem-loop of COL1a1 and COL1a2 mRNA. *J Biol Chem*. 2014 Mar 14;289(11):7264-74. PMID: 24469459/ PMCID: PMC3953245.

El-Dahr SS, Hilliard S, Aboudehen K, Saifudeen Z. The Mdm2-p53 pathway: multiple roles in kidney development. *Pediatr. Nephrol*. 2014 Apr;29(4):621-7. PMID: 24077661/ PMCID: PMC3969418.

Gao H, Derbenev AV. Synaptic and extrasynaptic transmission of kidney-related neurons in the rostral ventrolateral medulla. *J Neurophysiol*. 2013 Dec;110(11):2637-47. PMID: 24027107/ PMCID: PMC3882766.

Hering-Smith KS1, Mao W, Schiro FR, Coleman-Barnett J, Pajor AM, Hamm LL. Localization of the calcium-regulated citrate transport process in proximal tubule cells. *Urolithiasis.* 2014 Mar 21. PMID: 24652587.

Hilliard SA, Yao X, El-Dahr SS. Mdm2 is required for maintenance of the nephrogenic niche. *Dev Biol.* 2014 Mar 1;387(1):1-14. PMID: 24440154/ PMCID: PMC3951515.

McLaughlin N, Wang F, Saifudeen Z, El-Dahr SS. In situ histone landscape of nephrogenesis. *Epigenetics.* 2014 Feb 1;9(2):222-35. PMID: 24169366/ PMCID: PMC3962532.

Miyata K, Satou R, Shao W, Prieto MC, Urushihara M, Kobori H, Navar LG. ROCK/NF-κB axis-dependent augmentation of angiotensinogen by angiotensin II in primary-cultured preglomerular vascular smooth muscle cells. *Am J Physiol Renal Physiol*. 2014 Mar 15;306 (6):F608-18. PMID: 24431199/ PMCID: PMC3949040 .

Navar LG. Intrarenal renin-angiotensin system in regulation of glomerular function. *Curr Opin Nephrol Hypertens*. 2014 Jan;23(1):38-45. PMID: 24275770/ PMCID: PMC3982859.

Parsa A, Kao WH, Xie D, Astor BC, Li M, Hsu CY, Feldman HI, Parekh RS, Kusek JW, Greene TH, Fink JC, Anderson AH, Choi MJ, Wright JT Jr, Lash JP, Freedman BI, Ojo A, Winkler CA, Raj DS, Kopp JB, He J, Jensvold NG, Tao K, Lipkowitz MS, Appel LJ; AASK Study Investigators; CRIC Study Investigators. APOL1 risk variants, race, and progression of chronic kidney disease. *N Engl J Med*. 2013 Dec 5;369(23):2183-96 PMID: 24206458/ PMCID: PMC3969022

Scialla JJ, Xie H, Rahman M, Anderson AH, Isakova T, Ojo A, Zhang X, Nessel L, Hamano T, Grunwald JE, Raj DS, Yang W, He J, Lash JP, Go AS, Kusek JW, Feldman H, Wolf M; Chronic Renal Insufficiency Cohort (CRIC) Study Investigators. Fibroblast growth factor-23 and cardiovascular events in CKD. *J Am Soc Nephrol*. 2014 Feb;25(2):349-60. PubMed PMID: 24158986; PMCID: PMC3904568.

Shah N, Chainani V, Delafontaine P, Abdo A, Lafferty J, Abi Rafeh N. Mammographically detectable breast arterial calcification and atherosclerosis. *Cardiol Rev.* 2014 Mar-Apr;22(2):69-78. PMID: 23584424.

Publications

Continued...

Siddesha JM, Valente AJ, Sakamuri SS, Gardner JD, Delafontaine P, Noda M, Chandrasekar B. Acetylsalicylic acid inhibits IL-18-induced cardiac fibroblast migration through the induction of RECK. *J Cell Physiol*. 2014 Jul;229(7):845-55. PMID: 24265116/ PMCID: PMC3951845.

Siddesha JM, Valente AJ, Yoshida T, Sakamuri SS, Delafontaine P, Iba H, Noda M, Chandrasekar B. Docosahexaenoic acid reverses angiotensin II-induced RECK suppression and cardiac fibroblast migration. *Cell Signal*. 2014 May;26(5):933-41. PMID: 24447911/ PMCID: PMC3951845

Singh P, Castillo A, Majid DS. Decrease in IL-10 and increase in TNF-α levels in renal tissues during systemic inhibition of nitric oxide in anesthetized mice. *Physiol Rep*. 2014 Feb 10;2(2):e00228. doi: 10.1002/phy2.228. PMID: 24744897/ PMCID: PMC3966239

Wencheng Li, Hua Peng, Eamonn P. Mehaffey, Christie D. Kimball, Justin L. Grobe, Jeanette M.G.van Gool, A.H. Jan Danser, Atsuhiro Ichihara, and Yumei Feng. Neuron-specific (pro)renin receptor knockout prevents the development of salt-sensitive hypertension. *Hypertension* 2014 Feb; 63(2): 316-23. PMID: 24246383/PMCID: PMC3947277.

Xing SS, Shen CC, Godard MP, Wang JJ, Yue YY, Yang ST, Zhao Q, Zhang SB, Wang TX, Yang XL,Delafontaine P, He Y, Song YH. Bortezomib inhibits C2C12 growth by inducing cell cycle arrest and apoptosis. *Biochem Biophys Res Commun*. 2014 Mar 7;445(2):375-80. PMID: 24525132/ PMCID: PMC3971480.

Yang W, Xie D, Anderson AH, Joffe MM, Greene T, Teal V, Hsu CY, Fink JC, He J, Lash JP, Ojo A, Rahman M, Nessel L, Kusek JW, Feldman HI; CRIC Study Investigators. Association of kidney disease outcomes with risk factors for CKD: findings from the Chronic Renal Insufficiency Cohort (CRIC) study. *Am J Kidney Dis*. 2014 Feb;63(2):236-43. PMID: 24182662; PMCID: PMC3946885.

Yoshida T, Galvez S, Tiwari S, Rezk BM, Semprun-Prieto L, Higashi Y, Sukhanov S, Yablonka-Reuveni Z, Delafontaine P. Angiotensin II inhibits satellite cell proliferation and prevents skeletal muscle regeneration. *J Biol Chem*. 2013 Aug 16;288(33):23823-32. PMID: 23831688/ PMCID: PMC3745329.

Yoshida T, Tabony AM, Galvez S, Mitch WE, Higashi Y, Sukhanov S, Delafontaine P. Molecular mechanisms and signaling pathways of angiotensin II-induced muscle wasting: potential therapeutic targets for cardiac cachexia. *Int J Biochem Cell Biol*. 2013 Oct;45(10):2322 -32. PMID: 23769949/ PMCID: PMC3759646.

Yosypiv IV. Renin-angiotensin system in ureteric bud branching morphogenesis: implications for kidney disease. *Pediatr Nephrol*. 2014 Apr;29(4):609-20. PMID: 24061643.

Zhao Z, Wang H, Jessup JA, Lindsey SH, Chappell MC, Groban L. Role of estrogen in diastolic dysfunction. *Am J Physiol Heart Circ Physiol*. 2014 Mar 1;306(5):H628-40. PMID: 24414072/ PMCID: PMC3949059.

Presentations

From January through April 2014 investigators and physicians affiliated with T.H.R.C.E. participated in many regional, national, & international meetings. Please note: Also listed are meetings attended before January 2014 but were not included in the previous Newsletter edition.

American Heart Association Scientific Session, Dallas, TX; Nov. 16-20, 2013

- **Higashi y, Shai S, Sukhanov S, Kim C, Snarski P, Delafontaine P**. Insulin-like growth factor 1 regulates lipid accumulation in macrophages – a potential mechanism for insulin-like growth factor 1 mediated atheroprotection. Abstract Poster Session APS.727.01.
- **Lightell DJ Jr, Woods TC**. Accelerated Neointimal Hyperplasia in a Diabetic Mouse Model via Elevated microRNA-221/222.
- **Sukhanov S, Vaughn C Snarkski P, Kim C, Delafontaine P.** Macrophage 12/15-lipoxygenase Mediates Insulin-like Growth Factor I (IGF-1)-induced Suppression of Foam Cells: Potential Mechanism Responsible for IGF-1-induced Atheroprotection. Abstract Poster Session 8799/ATVB19, BASC.03.
- **Yoshda T, Yablonka-Reuveni Z, Delafontaine P**. Angiotensin II Type 2 Receptor Regulates Skeletal Myoblast Differentiation: Implications for Treatment of Cachexia and Skeletal Muscle Wasting. Abstract Poster Session APS.712.01. Session: Growth Factors, Cytokines, Signal Transduction
- **Sukhanov S, Yoshda T, Higashi Y, Shai S, Kim C, Delafontaine P**. GAPDH Interaction With APE1 Endonuclease Protects Smooth Muscle Cells Against Cell Death: Potential Role of These Enzymes in Prevention of Atherosclerotic Plaque Destabilization. 15038/7081, Abstract Poster Session APS.711.01. Session: Redox Signaling and Oxidative Stress.

The Gerontological Society Annual Scientific Meeting, NO, LA, Nov. 20-24, 2013.

- **Patrice Delafontaine**. Aging, Atherosclerosis, and IGF-1. Abstract ID: 1702828.

American Society for Cell Biology Annual Meeting, NO, LA; Dec. 14-18, 2013

- **Bourgeois CT, Satou R, Prieto M.** Histone deacetylase 9 is a repressor of angiotensinogen expression in renal proximal tubular cells.
- **Bourgeois CT, Satou R**. Inhibition of histone deacetylases suppresses angiotensinogen expression via suppressor of cytokine signaling 1 augmentation in renal proximal tubular cells.

Continued...

- **Mani I, Garg R, Pandey KN.** Immunofluorescence visualization of the internalization and intracellular trafficking of Guanylyl Cyclase/Natriuretic Peptide Receptor-A in sub-cellular compartments.
- **Penrose HM, Satou R, Navar LG**. Signal transducer and activator of transcription 1 regulates interferon-γ-induced angiotensinogen and monocyte chemoattractant protein-1 expression in a bidirectional manner in primary rat mesangial cells.

Southern Regional Meeting, NO, LA; Feb. 20-22, 2014

- **Blackstock C, Higashi y, Sukhanov S, Delafontaine P.** Insulin-like growth factor-1 increases collagen type 1 synthesis via inducing expression of the MRNA binding protein LARP6 and its binding to the 5'stem-Loop of Col1A1 and COL1A2 MRNA. J Invest Med 62:449, 2014. Poster.
- **Bourgeois c, Rui P, Sato R, Prieto MC**. Novel protective effect of histone deacetylase 9 as a repressor of angiotensinogen expression in the female rat kidney. J Invest Med 62:546/510, 2014. Poster.
- **Caner T, Abdulnour-Nakhoul S, Brown K, Hamm LL and Nakhoul NL.** DIDS inhibits ammonia transport by mammalian RH glycoproteins. J Invest Med 62:579, 2014. Poster.
- **Doose M, Yosypiv IV**. Midaortic syndrome in pediatric patient with known renovascular hypertension
- **Bhatt A, Feng Y, Kumar P**. Hydrocortisone pre-treatment reduces hypoxic ischemic brain injury in neonatal rats. J Invest Med 62:539, 2014. Poster.
- **Galvez S, Yoshida T, Sukhanov S, Delafontaine P**. Angiotensin II suppresses muscle regeneration in the murine model of muscular dystrophy. J Invest Med 62:550, 2014. Poster.
- **Higashi y, Shai S, Sukhanov S, Kim C, Snarski P, Delafontaine P**. Insulin-like growth factor 1 regulates lipid accumulation in macrophages – a potential mechanism for insulin-like growth factor 1 mediated atheroprotection. J Invest Med 62: 523, 2014. Poster.
- **Huntwork MP, Howell MP, May J, Yosypiv IV, Singleton T**. Foamy urine and sickled cells. Does not acknowledge COBRE. J Invest Med 62:481, 2014. Poster.
- **Miyata K, Sato R, Navar L.** Endotherial cells contribute to angiotensinogen augmentation in vascular smooth muscle cells of afferent arterioles. J Invest Med 62:579, 2014.
- **Monlezun D, Chen T, Ramalingam A, Song R, Janssen A, Preston G, Yosypiv IV.** Cytogenomic aberrations are common defects in patients with isolated Multicystic Dysplastic Kidney. J Invest Med 62: 423, 2014. Poster.

Presentations

Continued...

- **Riedl L, Song R, Yosypiv IV.** Lack of the Prorenin Receptor (PRR) in the Ureteric Bud (UB) Disrupts Developmental Programming of Nephrogenesis. J Invest Med 62:579, 2014. Oral.
- **Sato R, Miyata K, Navar L**. Macrophages contribute to angiotensin II mediated angiotensinogen stimlation in renal proximal tubular cells. J Invest Med 62:545, 2014.
- **Shao W, Bivona BJ, Kobori H, Navar L.** Increased Rho-kinase activity in renal afferent arterioles of angiotensin II infused hypertensive rats. J Invest Med 62:409, 2014.
- **Singh P, Stephenson R, Majid DSA.** Changes in plasma and renal tissue levels of inflammatory cytokines during chronic high salt intake in wildtype and eNOS knockout mice.
- **Song R, Riedl L, Yosypiv IV.** Dot1/H3K79 pathway mediates defective ureteric bud (UB) branching leading to renal hypodysplasia (RHD) in prorenin receptor (PRR) PRRUB-/- mice. J Invest Med 62:545, 2014. Oral.
- **Sukhanov S, Snarkski P, Shai S, Higashi Y, Delafontaine P**. IGF-1 reduces monocytes recruitment into the atherosclerotic plaque and suppresses chemokines: Potential mechanism mediting IGF-1-induced atheroprotection. J Invest Med 62:549, 2014. Poster.
- **Tabony AM, Delafontaine P**. Protein phosphate 2C-Alpha knockdown reduses angiotensin II-mediated skeletal muscle wasting via restoration of mitochondrial recycling and function. J Invest Med 62:556, 2014.
- Thompson DA, Seth DM, Davis PD, Mitchell KD. PDGF receptor antagonism prevents the increase in kidney angiotensin II levels in CYP1A1-REN2 transgenc rats with angiotensin II-dependent malignant hypertension. J Invest Med 62:578, 2014. Poster.
- **Walker R, Coleman-Barnett JA, Hamm LL, Hering-Smith K.** Regulation of novel calcium-sensitive dicarboxylate transport process. J Invest Med 62:547, 2014. Poster.
- **Yoshda T, Delafontaine P**. Angiotensin II type 2 receptor regulates skeletal muscle stem cell differentiation: implications for treatment of cachexia and skeletal muscle wasting. J Invest Med 62:548, 2014. Poster.
- **Zhang S, Coleman-Barnett JA, Sato R, Hamm LL, Hering-Smith KS.** Proximal tubule transport systems for citrate: Cell culture heterogeneity. J Invest Med 62:580, 2014. Poster.

Presentations

Continued...

Keystone Symposia – Diabetic Complications, Whistler, British Columbia Canada, March 23—28, 2014

- **Woods, Thomas C**. Loss of Insulin-like Growth Factor Receptor-1 promotes Changes in Non-coding RNA Expression that promote Intimal Thickening

Health Sciences Research Days, Tulane, NO, LA; April 2-3, 2014

- **Anwar IJ, Miyata K, Zsombok A.** Acute and subchronic effect of olanzapine on the synaptic transmission of the dorsal motor nucleus of the vagus.
- **Azimi MS, Mathur A, Mondal D, Murfee WL.** A novel ex vivo tissue culture assay for determining the effects of anti-tumor drugs on angiogenesis.
- **Budish RA, Liu L, Lindsey SH**. GPR30-induced increases in cyclic AMP involve both GαS and GαI/O subunits.
- **Caner T, Abdulnour-Nakhoul S, Brown K, Hamm LL and Nakhoul NL**. DIDS inhibits ammonia transport by mammalian RH glycoproteins.
- **D'Ambra VJL, Shai SY, Woods CT, Sukhanov S, Delafontaine P.** Smooth muscle-specific IGF-1 receptor deficiency increases atherosclerosis.
- **Gao H, Derbenev AV**. Unconventional view on gabaergic and glycinergic inhibition of RVLM neurons.
- **Hu T, Jacobs DR, Nettleton JA, Steffen L, Bertoni A, He J, Bazzano LA**. Low-carbohydrate diets and incidence, prevalence, and progression of coronary artery calcium in the multi-ethnic study of atherosclerosis (MESA).
- **Khan AM, Terran F, Rathmell K, Harrison-Bernard LM, Maderdrut JL, Simon EE, Batuman V.** Pathophysiology of contrast-induced nephropathy in elderly diabetic mice.
- **Mani I, Pandey KN.** Immunofluorescence analysis reveals the intracellular trafficking of guanylyl cyclase/natriuretic peptide receptor-a with concurrent generation of cGMP.
- **Mills KT, Chen J, Yang W, Appel LJ, Kusek J, Alper AB, Delafontaine P, Keane MG, Mohler ER, Ojo AO, Rahman M, Ricardo AC, Soliman EZ, Steigerwalt S, Townsend RR, He J.** Urinary sodium and potassium excretion and cardiovascular diseases in patients with chronic kidney disease: The chronic renal insufficiency cohort study.
- **Monlezun DJ, Chen TJ, Ramalingam A, Song R, Janssen A, Preston G, Yosypiv IV**. Cytogenomic aberrations are common defects in patients with isolated Multicystic Dysplastic Kidney.

Continued...

- **Miyata K, O'Hare JD, Fourrier TL, Krantz AM, Zsombok A**. TRPV1 in the paraventricular nucleus of the hypothalamus is involved in the regulation of glucose homeostasis. James received the award for excellence in research and presentation by a 4th year DeBakey scholar.
- **Siddesha JM, Woods TC, Yoshida T, Abdulnour-Nakhoul SM, Delafontaine P, Valente AJ, Chandrasekar B.** Reversion-inducing cysteine-rich protein with kazal motifs (RECK) plays a protective role in neointimal hyperplasia.
- **Sigmon D, Seth DM, Sato A, Davis PD, Navar LG, Mitchell KD**. Parallel changes in the urinary excretion of ANG II and angiotensinogen (AGT) and kidney ANG II levels in slowly progressive ANG II-dependent hypertension.
- **Song R, Riedl L, Yosypiv IV.** Dot1/H3K79 pathway mediates defective ureteric bud (UB) branching leading to renal hypodysplasia (RHD) in Prorenin receptor (PRR) PRRUB-/-mice.
- **Sweat RS, Chedister LO, Sloas DC, Stewart SA, Murfee WL**. The effect of aging on microvascular density and angiogenesis
- **Thomson DA, Seth DM, Davis PD, Mitchell KD.** PDGF receptor antagonism prevents the increase in kidney angiotensin II levels in angiotensin II-dependent malignant hypertension.
- **Walker RW, Coleman-Barnett JA, Hamm LL, Hering-Smith KS**. Regulation of a novel calcium-sensitive dicarboxylate transport process by calcium-sensing receptor signaling.
- **Zhang S, Huang W, Coleman-Barnett JA, Hamm LL, Hering-Smith KS.** Proximal tubule transport systems for citrate.
- **Zhao Q, He J.** Blood pressure response to the cold pressor test predicts the risk of hypertension.
- **Zhu Y, Hyun N, Zeng D, Uppal K, Tran VT, Tianwei Y, Jones D, He J, Lee ET, Howard BV, Zhao J.** Novel Metabolic Markers for the Risk of Carotid Plaque Progression in American Indians.

EB Meeting, San Diego, CA; Apr. April 26-30, 2014

- **Azimi MS, Mathur A, Mondal D. Murfee WL**. A novel ex vivo tissue culture assay for determining the effects of anti-tumor drugs on angiogenesis. FASEB J 28:676.14/A111
- **Derbenev AV, Gao H, Miyada K Zsombok A**. Synaptic plasticity of GABAergic circuitry in the RVLM during Ang II-dependent malignant hypertension. FASEB J 28:874.6/A236
- **Gao H, Derbenev AV.** Tonic GABAergic inhibition of RVLM neurons: a novel target

Continued...

for sympathetic control. FASEB J 28:1172.3/W261

- **Gao J, Smart F, Katsurada A, Navar LG, Kapusta DR**. Radiofrequency renal nerve ablation decreases blood pressure in SHR accompanied by increased urinary sodium excretion. FASEB J 28: 857.4/A57.
- **Kumar P, Periyasamy R, Das S, Pandey KN**. Retinoic acid and sodium butyrate attenuate renal fibrosis and inflammation in guanylyl cyclase-A/natriuretic peptide receptor-A gene-targeted mice. FASEB J 28:796.13/D328
- **Lindsey SH, Liu L, Chappell MC**. GPER Activation Ameliorates Vascular Remodeling in Salt-sensitive mRen2.Lewis Rats. The FASEB Journal XX, Abstract #3224
- **Majid DSA.** Effects of TNF in renal hemodynamics and sodium excretion. *Invited Lecture.*
- **Majid DS, Castillo A**. Renal responses to intra-arterial infusion of a peroxynitrite scavenging agent with or without angiotensin II in anesthetized rats. FASEB J 28:1134.4/ A729
- **Mamenko M, Zaika O, Prieto MC, Jensen BV, Doris PA, Navar GL, Pochynyuk O**. Coordinated regulation of ENaC activity in the distal nephron by aldosterone and Ang II. FASEB J 28:1088.14/A226
- **Mani I, Tripathi S, Pandey KN.** A novel cytoplasmic tail fqqi motif mediates internalization and intracellular trafficking of guanylyl-cyclase/ natriuretic peptide receptor-A. 539.4/B65
- **Murfee WL**. The effect of aging on microvascular density and angiogenesis. *Invited Lecture*.
- **Navar LG, Kobori H, Satou R, Katsurada A, Zhuo JL, Li XC.** Augmentation of kidney angiotensinogen expression and urinary angiotensinogen excretion by an intracellular angiotensin II fusion protein. FASEB J 28:1173.8/W272
- **Prieto MC, Arita DY, Bourgeois CT, Satou R.** Hyperglycemia increases prorenin receptor localization at the cell plasma membrane. FASEB J 28:1173.7/W271
- **Prieto MC.** Deletion of prorenin receptor (PRR) in the collecting duct attenuates hypertension during chronic Ang II infusion. *Invited Lecture.*
- **Satou R, Bourgeois CRT, Navar LG**. Role for histone deacetylases in regulating angiotensinogen expression mediated by the JAK-STAT pathway by suppressor of cytokine signaling in renal proximal tubular cells. FASEB J 28:1173.2/W266
- **Satou R, Miyata K, Navar LG**. Interleukin 6 derived from macrophages enhances angiotensinogen expression in renal proximal tubular cells. FASEB J 28:1173.3/ W267
- **Sigmon D, Seth DM, Sato A, Davis PD, Navar LG, Mitchell KD.** Parallel changes

Continued...

in the urinary excretion of ANG II and angiotensinogen and kidney ANG II levels in slowly progressive ANG II-dependent hypertension. FASEB J 28:1136.20/A761.

- **Subramanian U, Gogulamudi VR, Chen D, Pandey KN**. Activation of TGF-β mediated SMAD pathway induces cardiac fibrosis in mice carrying targeted disruption of guanylyl cyclase/natriuretic peptide receptor-A gene.
- **Sukhanov S, Snarkski P, Vaughn C, Kim C, Delafontaine P.** Insulin-like growth factor I (IGF-1) suppressed foam cells via downregulation of 12/15-lipoxygenase: potential mechanism responsible for IGF-1-induced atheroprotective effect. FASEB J, 28:832.14.
- **Sukhanov S, Yoshda T, Delafontaine P.** GAPDH prevents oxidant-induced apoptosis in smooth muscle cells via upregulation of APE1/Ref-1 endonuclease. FASEB J, 28:1093.1.
- **Sweat R, Chedister L, Sloas D, Stewart S, Murfee WL.** The effect of aging on microvascular density and angiogenesis. FASEB J 28:1136.20/A761
- **Sweat R, Phamduy T, Chrisey D, Murfee WL.** The effect of cancer cells on angiogenesis: engineering the cancer niche. FASEB J 28:665.4/A16
- **Thompson DA, Seth DM, Davis PD, Mitchell KD**. PDGF receptor antagonism prevents the increase in kidney ANG II levels in Cyp1a1-Ren2 transgenic rats with ANG II-dependent malignant hypertension. FASEB J 28:1136.1/A742
- **Yoshida T, Delafontaine P.** Angiotensin II type 2 receptor regulates skeletal myoblast differentiation: implications for treatment of cachexia and skeletal muscle wasting. FASEB J 28:1102.34/A436
- **Zsombok A, Jiang Y, Anwar IJ, Rezai-Zadeh K, Muenzberg-Gruening H.** Regulation of leptin receptor expressing neurons in the brainstem by TRPV1. *(Presenter: Yanyan Jiang).*

SVS Vascular Research Initiatives Conference, Toronto, ON, April 30, 2014

- **Bazan HA, Lightell DJ Jr, Woods TC.** Increased circularRNA-16 in acutely asymptomatic carotid plaques: A novel mediator of carotid plaque rupture.

Invited Lectures

THRCE investigators and physicians were invited to lecture at various national and international events.

L. G. Navar, PhD, Chairman & Professor of Physiology:

- ISN Forefronts in Nephrology Symposium, Charleston, SC. "Evolution of intrinsic intrarenal regulation: From autoregulation to multiple interacting paracrines", March 6, 2014
- ISN Forefronts in Nephrology Symposium, Charleston, SC. Moderator Session 1: "The Intrarenal Renin Angiotensin System", March 7, 2014

P. Delafontaine, PhD, Vice Chair & Professor of Medicine:

- "IGF-1 and atherosclerosis" and "Molecular mechanisms and signaling pathways of angiotensin II-induced muscle wasting" February 14, 2014, University of Nebraska, Omaha, NE
- Heart and Vascular Grand Rounds "IGF-1, Vascular Aging and Atherosclerosis" December 16, 2013 Emory University, Atlanta, GA

Invited talks at 2014 EB Meeting:

- **Dr. DSA Majid**: "Effects of TNF in renal hemodynamics and sodium excretion" at the Symposium, "Tumor necrosis factor (TNF): A two faced cytokine."
- **Dr. W.L. Murfee**: "The effect of aging on microvascular density and angiogenesis" at the Symposium, "Microcirculatory Society President's Symposium II: Rapid Fire Talks ."
- **Dr. M.C. Prieto: "**Deletion of prorenin receptor (PRR) in the collecting duct attenuates hypertension during chronic Ang II infusion" presented at the Symposium, "Physiological Genomics and Kidney & Hypertension Symposium." Also Co-Chaired at the same Symposium.

Calendar of Events

THRCE Seminars

February 13, 2014

Andrea Zsombok, PhD
Assistant Professor, Department of Physiology,
Tulane School of Medicine, New Orleans, LA.
"The effect of olanzapine on brainstem neurons."

February 27

No Meeting
Mardi Gras Holiday

March 13 **

Special Seminar: WORLD KIDNEY DAY

Samir El-Dahr, MD
Jane B. Aron Professor of Pediatrics
Chair, Department of Pediatrics
Section Chief, Pediatric Nephrology
Tulane School of Medicine, New Orleans, LA.
"Nephron Progenitors and Blood Pressure: Less of one, more the other."

March 17 **

Joint Seminar: THRCE & Department of Physiology

Jia L. Zhuo, MD
Professor, Laboratory of Receptor and Signal Transduction
Department of Pharmacology and Toxicology
Division of Nephrology,
Department of Internal Medicine
Cardiovascular-Renal Research Center
The University of Mississippi Medical Center, Jackson, MS.
"Current insights and new perspectives on the roles of paracrine and intracrine angiotensin II in the proximal tubule of the kidney."

March 27 **

Joint Seminar: THRCE & Department of Pharmacology

Mark C. Chappell, PhD
Professor, Department of Physiology and Pharmacology,
Director, US-Brazil Science Without Borders Program,
Wake Forest School of Medicine,
Winston-Salem, NC.
"Angiotensin-(1-7) Calms AGE-RAGE in Diabetic Renal Injury."

April 10

David W. Busija, MD, PhD
Regents Professor & Chairman,
Department of Pharmacology,
Tulane University School of Medicine, New Orleans, LA.
"Mitochondrial mechanisms during health and disease in the cerebral vasculature."

April 24

David J. Lefer, PhD, FAHA
Professor, Department of Pharmacology,
Director, Cardiovascular Center of Excellence,
LSU Health Sciences Center,
New Orleans, LA.
"Hydrogen Sulfide in Cardiovascular Disease."

May 8

NO MEETING
No THRCE seminar due to scheduling conflict with the Center for Aging Seminar Series

The presentation for the Center for Aging Seminar Series is by Judy Delp (Associate Professor, Department of Physiology and Functional Genomics, University of Florida.

Calendar of Events

Continued...

May 19 **

Joint Seminar: THRCE & Department of Physiology

Alicia McDonough, PhD
Professor, Cell and Neurobiology Keck School of Medicine
University of South California, Los Angeles, CA.
"Integrated regulation of sodium transporters along the nephron by Angiotensin II and blood pressure."

May 22

Prasad V.G. Katakam, MD, PhD
Assistant Professor,
Department of Pharmacology,
Tulane School of Medicine,
New Orleans, LA.
"Uncoupling of Nitric Oxide Synthase and Insulin Resistance."

June 5

Daniel R. Kapusta, PhD
Professor of Pharmacology
PI and Director, COBRE Cardiovascular Research Program
LSU Health Sciences Center, New Orleans, LA.
"Radiofrequency ablation of the renal nerves & Management of Resistant Hypertension: Ongoing studies using the Spontaneously Hypertensive Rat."

June 19

NO MEETING
NIH, NIGMS Fifth Biennial National IDeA Symposium
Washington, DC, June 16 - 18, 2014

Monday, June 30 **

Joint Seminar:
THRCE & the Departments of Pharmacology & Physiology

Richard J. Roman, PhD
Professor and Chair,
Department of Pharmacology and Toxicology,
University of Mississippi Medical Center, Jackson, MS.
"CYP450 eicosanoids, Hypertension and Renal and Cerebral End Organ Damage."

July 3

No Meeting
Independence Day Holiday

July 17

Keith C. Ferdinand, MD
Chair, National Forum for
Heart Disease & Stroke Prevention
Professor of Clinical Medicine
Tulane University School of Medicine, New Orleans, LA.
Discussion Topic: The new blood pressure (BP) guidelines

July 31

Gary Sander, MD
Professor of Clinical Medicine
Tulane University School of Medicine
New Orleans, LA.
TBA

August 14

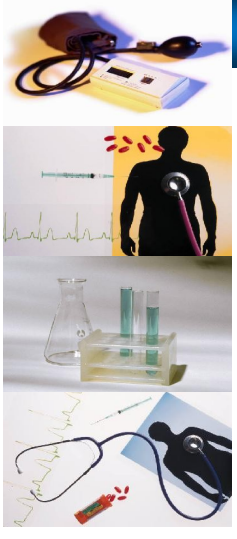
Speaker: TBA
Talk: TBA

CORE Facilities & Services

Tulane Hypertension and Renal Center of Excellence (THRCE) houses 4 research core facilities that were developed during COBRE phases I and II and are now maintained and supported by a COBRE Phase III grant awarded by the NIH/NIGMS. These core facilities are essential for the support of basic, clinical, and translational research in hypertension and renal biology and provide unique research opportunities for emerging leaders in hypertension by establishing an enriched environment in which to develop investigators in both the clinical and basic hypertension research. The resources and services provided by the Center's COBRE Core facilities can be utilized by both COBRE and other investigators within Tulane and other institutions for hypertension, cardiovascular and renal research. The 4 research Core facilities are:

- **The Molecular, Imaging, and Analytical Core**: This facility serves as the resource for instruments and equipment needed to perform advanced molecular biology, semi-quantitative immuno-histochemistry and bio-analytical experiments.
- **Animal and Gene-Targeted Core:** This facility maintains and generates new breeding pairs, does genotyping, and maintains colonies of genetically manipulated mice and rats.
- **Mouse Phenotyping Research Core (MPRC):** Contains resources to support high-tech data collection capabilities that are unique in the State of Louisiana and essential to research requiring the utilization of an array of methodologies to perform measurements of cardiovascular, blood pressure and renal function in mice.
- **Clinical and Translational Core:** Promotes and facilitates clinical and translational studies in hypertension, kidney disorders, and related cardiovascular diseases.

Other activities of the center include the sponsorship of local and regional meetings on Hypertension and public education programs to increase awareness of the dangers of hypertension. For further information regarding the Core Facilities, please access **http://tulane.edu/som/thrce/**



T.H.R.C.E.

Tulane Hypertension And Renal Center of Excellence will appreciate any support for the continual development of the center, the publication of the THRCE newsletters, and the support of the THRCE bi-weekly seminars series. Any donations to the center and its activities are considered tax-deductible.

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www.som.tulane.edu/centprog/htn/

The directors invite faculty members interested in participating in the activities of the T.H.R.C.E. to submit your name, phone number, fax number, and e-mail address to the Program Coordinator, Nina Majid by e-mail at htnctr@tulane.edu or regular mail to the address provided. Also, please forward all information (awards, publications, presentations and other news items) to this email address for inclusion in the next newsletter.