L. GABRIEL NAVAR RECIPIENT OF WALTER B. CANNON AWARD

L. Gabriel Navar, Ph.D., Professor and Chairman of the Department of Physiology, and Co-Director of the Renal and Hypertension Center at Tulane Health Science Center, School of Medicine, received the American Physiological Society’s (APS) Top Honor, the Walter B. Cannon Award on April 21st, at the 2012 Experimental Biology Meeting in San Diego, CA. The Walter B Cannon award is the Society’s pre-eminent lecture award designed to recognize an outstanding scientist for his or her contributions to the field of Physiology. Dr. Navar, the 30th recipient of the award, presented the lecture, “The Wisdom of the Body Revisited: A Tribute to Walter B. Cannon and His Concept of Homeostasis as applied to Pathophysiology or Hypertension,” which pays tribute to Dr. Cannon’s groundbreaking book, The Wisdom of the Body, first published in 1932.

Walter B. Cannon Award is named after a renowned physiologist who is recognized for his development of the concept of the emergency function of the sympathetic nervous system. This led to the development of the key physiological concept of homeostasis. Dr. Cannon was affiliated with the APS for nearly 40 years, including two terms as president (1914-916). He is commemorated each year with the Walter B. Cannon Memorial Lecture, a plenary lecture given at the Society’s annual meeting.

Dr. Navar’s selection for the award acknowledges his significant contributions to the study of renal physiology and its relationship to hypertension. His early work focused on understanding basic interactions between the kidney blood flow and the regulation of salt and water
balance and the interactions between blood pressure and the excretion of salt and water. Over time, he and others came to understand that the excretion of salt and water are very important in the regulating blood pressure and that blood pressure was equally as important in regulating the body’s salt and water balance.

They also came to understand that the single most important hormonal system involved in regulating salt balance in the body was the renin-angiotensin system (RAS). Ultimately they discovered that this system affects salt excretion and that RAS plays a key role in regulating blood pressure and causing high blood pressure (hypertension). He and others have now focused their efforts on understanding why and how this system becomes disrupted in a way that leads to hypertension.

These findings have been important in helping physicians, researchers, and others find ways to address the skyrocketing problem of hypertension which affects one in three American adults and can lead to heart disease and stroke, the first and third leading causes of death in the United States. For 2010, the estimated costs associated with the disorder in the U.S. was $93.5 billion.

Dr. Navar received his PhD from the University of Mississippi under the mentorship of the famed physiologist, Arthur C. Guyton. He later held appointments at the University of Mississippi School of Medicine and at the University of Alabama at Birmingham. He joined Tulane in 1988, where he has built a successful research program which has contributed significantly to fundamental research in the areas of renal hemodynamics and hypertension. Dr. Navar is a former President of the APS and the former Associate Editor of the American Journal of Physiology: Renal Physiology, and has been active on many of the Society’s committees. In 2006 he received the APS’s Distinguished Mentor and Scientist award from the “Women in Physiology” Committee in recognition of his dedication and commitment to training young physiologists.
TULANE COBRE
EXTERNAL ADVISORY COMMITTEE MEETING

From March 7th to 9th, 2012, the Tulane COBRE External Advisory Committee (EAC) met to review progress of COBRE sponsored research at the Tulane Hypertension and Renal Center of Excellence. EAC Committee members who attended the meeting were:

- Michael Klag, MD, MPH., FACP, Dean, Bloomberg School of Public Health, The John Hopkins University, School of Medicine, Baltimore, Maryland.
- R. Ariel Gomez, MD, Harrison Distinguished Professor of Pediatrics & Biology, at the University of Virginia School of Medicine, Charlottesville, VA.
- Mohan K. Raizada, PhD, Distinguished Professor, Department of Physiology and Functional Genomics at the University of Florida, Gainesville, FL.
- Norman Rosenblum, MD, Professor of Pediatrics & Physiology and Associate Dean of the Physician Scientist Training program, at the University of Toronto, in Ontario, Canada.
Unable to attend were EAC members Dr. Thomas Coffman, Professor & Division Chief of Medicine and Nephrology at Duke University, and Dr. Orson Moe, Professor Internal Medicine in Nephrology, University of Texas Southwestern Medical School.

The EAC site visit proved very productive, producing many helpful suggestions for the junior faculty investigators who presented their project updates to the EAC members. Throughout the year, the EAC members have provided their valuable services in reviewing the research plans of each new junior faculty investigators.

The following are pictures taken at the EAC formal dinner held March 8, 2012.
Dr. Arpan Maiti, a Research Associate from the University of Kalyani, West Bengal, India, joined Tulane University as a Fulbright Scholar in the Department of Physiology, under the mentorship of Professor, Dr. Dewan. S. A. Majid. Dr. Maiti received the Fulbright Award for the academic session 2011-2012 on March, 2011 in the Fulbright Post-Doctoral Research category. The Fulbright Program is the flagship international educational exchange program sponsored by the U.S. Government. As this award is also partly funded by the Government of India, it is also known as Fulbright-Nehru Post-Doctoral Research Fellowship. Although the term of this award is one year, there is scope for extension, subject to approval by the Fulbright Commission of India and USA Government.

The Fulbright Program was established by the U.S. Congress in 1946 under legislation by Senator J. William Fulbright of Arkansas and is designed to increase mutual understanding between the people of the United States and the people of other countries. Out of thousands of applicants, the program selects top graduate students, young professionals and artists from abroad to conduct research and study in the United States.

Dr. Maiti research titled, “Peroxynitrite and Angiotensin-III interactions in the kidney,” elucidates whether Angiotensin-III is equipotent to Angiotensin-II in the Renin-Angiotensin System at identical plasma concentrations in regard to interaction with peroxynitrite (ONOO⁻) in kidney, inducing alterations in renal hemodynamics and excretory responses, in addition to renotoxic action leading to cell death by affecting Na+K+ATPase and mitochondrial functions. As major renal therapeutical agents are not fully effective in combating the renotoxic effects of ONOO⁻, this study will help to develop new therapeutic strategies in renal diseases focusing on Angiotensin-III and ONOO⁻ interactions in the kidney.

Dr. Maiti said he selected Tulane because of its impressive research record. He expresses gratitude to Dr. Majid for supporting his application for the award and providing him the opportunity to come to Tulane University for this post-doctoral training. He also thanks Dr. Navar, Chair of the Department of Physiology, the faculty, post-doctoral fellows, research assistants, and office staff for helping him to adjust to his new place of residence and make his stay in Tulane a memorable experience he will forever treasure.
ACHIEVEMENTS & SUCCESSES BY COBRE/THRCE AFFILIATED INVESTIGATORS

Between January and April, 2012, faculty, postdocs, and students supported by COBRE and affiliated with THRCE were recognized for various awards both national and international. The following three pages are dedicated to their achievements.

Several individuals received awards for their abstracts that were submitted for presentation at the Southern Section-American Federation for Medical Research (SAFMR) and the Southern Society for Clinical Investigation (SSCI) held in New Orleans at the Hotel InterContinental on February, 2012.

◊ The following received Postdoctoral Fellow Awards:
  ◆ Dr. Alexis Gonzalez (mentors Drs. LG Navar & MC Prieto) and
  ◆ Dr. Purnima Singh (mentor Dr. DSA Majid).

◊ The following students received SAFMR/SSCI Outstanding Student Research Awards:
  ◆ Catherine G. Howard (mentor Dr. KD Mitchell),
  ◆ Liu Liu (mentor Dr. MC Prieto),
  ◆ Amy E. Collins (mentor Dr. KD Mitchell),
  ◆ Laleh Bahrami (mentor Dr. DSA Majid), and
  ◆ Min-Young Kwak (mentor Dr. KD Mitchell).

Some SAFMR/SSCI winners pictured, from left to right, Dr. Alexis Gonzalez, Dr. Purnima Singh, Mr. Liu Liu & Miss. Laleh Barhami.
Ming Yang (Mentor: Dr. W. Lee Murfee) was awarded the Microcirculatory Society's “Benjamin W. Zweifach” Graduate Student Travel Award and the American Association of Anatomists (AAA) Travel Award at the 2012 Experimental Biology.

Dr. Shaowei Chen (mentor: Dr. Samir El-Dahr) was selected for the “Society for Pediatric Research (SPR) Basic Science Fellow Award.” The award was presented at the 2012 PAS (Pediatric Academic Societies) Annual Meeting held in Boston, MA, on April 29th, 2012.

Dr. Hua Peng (mentor: Dr. Yumei Feng) and Min-Young Kwak (mentor: Dr. Kenneth D. Mitchell) were awarded 2012 Caroline tum Suden/Francis A. Hellebrandt Professional Opportunity Awards at Experimental Biology 2012 meeting in San Diego, California. This year the Women in Physiology Committee received 127 excellent applications from which only 36 were selected for the award.

Dr. Wencheng Li (mentor: Dr. Yumei Feng) was selected as a 2012 Cardiovascular Section Research Recognition Award recipient by the American Physiology Society. This year, only 9 applicants of 122 were selected. He was also selected as an oral presentation winner and won the Trainee Research Recognition Award from Physiological Genomics Group.

Undergraduate Student, Christie Kimball, (mentor: Dr. Yumei Feng) received 2012 APS Undergraduate Summer Research Fellowship. Each student receives a $4,000 stipend to cover living expenses during the 10-week fellowship and will also receive an additional $1,300 in travel funds to present their research at the Experimental Biology 2013 meeting in Boston, MA which is expected to attract nearly 14,000 scientists.

Undergraduate Students, Imran J. Anwar (mentor Dr. Andrei V. Derbenev) and Michael Cox (mentor Dr. Norman Kreisman) were accepted into Tulane’s Neuroscience Summer Research Program. Both will receive a stipend of $2,500 to conduct research for a minimum of eight weeks.
Catherine G. Howard, MD/PhD Student (mentor, Dr. Kenneth D. Mitchell), was selected by ISH as the New Investigator of the Month for February 2012. The ISH New Investigators Network (ISHNIN) was established to serve as a platform for interaction between students and new investigators and allow new avenues for communication, collaboration and education. Those joining the Network will be provided with ISH sponsored mentorship opportunities, information on national and international hypertension symposia, and opportunities for financial support exclusive to Network members. All hypertension research trainees are welcome, including those that are not yet ISH members or Research Fellows.

Catherine Howard was also selected to serve as a student member on the Tulane School of Medicine’s Admissions Committee, and for the next two years, will form part of the team of faculty and students who shape the future of Tulane Medical School.

Miss. Howard also completed her PhD program on May 3, 2012.

Dr. Mingguo Feng, a research scientist and faculty affiliated with THRCE, received the 2012 American Physiological Society Renal Section Research Recognition Award at the APS Renal Awards Banquet held at 2012 EB meeting in San Diego, California. The annual faculty award is awarded to an outstanding investigator engaged in the research field of renal physiology.
**COBRE Investigators Featured on the Front Covers of Top Scientific Journals**

**Dr. Ihor V. Yosypiv:**

A manuscript "Ontogeny of angiotensin-converting enzyme 2," by Drs. Yosypiv and Renfang Song and technician, Mr. Graeme Preston, is featured on the cover of January 2012 issue of Pediatric Research. In the manuscript, using model organisms, the authors describe the expression and discuss the roles of ACE2 in morphogenesis of key organ systems such as CNS, cardiovascular, pulmonary and renal.

Ihor V. Yosypiv, MD, graduated from the Tulane COBRE in Hypertension and Renal Biology (P20 RR017659) as Junior Faculty investigator and is currently Associate Professor of Pediatric at Tulane University, School of Medicine.

**Dr. Kenneth D. Mitchell:**

A color figure from a manuscript by Drs. Mitchell and Miguel L. Graciano was displayed on the cover of the January-March 2012 edition of the American Journal of Physiology Renal Physiology. The figure is from the manuscript titled, “Imatinib ameliorates renal morphological changes in CYP1A1-REN2 transgenic rats with inducible ANG II-dependent malignant hypertension.”

Kenneth D. Mitchell, PhD, is a senior mentor to investigators supported by the Tulane COBRE in Hypertension and Renal Biology and Associate Professor of Physiology at Tulane University, School of Medicine.
THRCE SPONSOR
LOCAL, NATIONAL & INTERNATIONAL SPEAKERS

THRCE regularly sponsors bi-weekly seminars by scheduling nationally and internationally recognized investigators and clinicians in the fields of hypertension research, treatment and education. The following are some of the topics that were presented at those seminars during January through April, 2012.

- **SONG HONG, PhD**,
  Assistant Professor
  Louisiana State University Health Sciences Center
  Neuroscience Center of Excellence
  New Orleans, LA.

Dr. Song Hong presented “Lipid Mediators in Renal Injury and Mechanistic Insights” at the THRCE Seminar Series on January 5, 2012. Acute kidney injury remains an important medical problem. Omega-3 fatty acid docosahexaenoic acid is converted to potent resolvins (Rv) and protectin D1 (PD1), two newly identified families of natural mediators of resolution of inflammation. The first part of this presentation reported that administration of RvDs or PD1 to mice reduced functional and morphological kidney injury caused by ischemia/reperfusion. RvD1 or PD1 reduced the injury-caused elevation of serum creatinine at 24 and 48 post-injury. Interstitial fibrosis after ischemia/reperfusion was reduced in mice treated with RvDs. These lipid mediators reduced leukocyte infiltration and blocked macrophage activation. Thus, Rv and protectins, a previously unrecognized endogenous anti-inflammatory response, may play an important role in protection against and resolution of acute kidney injury. The second part reported the enhancement of renotrophic functions of mesenchymal stem cells (MSCs, from bone marrow) by a new lipid mediator, 14S,21R-dihydroxy-docosahexaenoic acid (14S,21R-diHDHA). As MSCs migrate to injured kidneys and non-injured organs, where they survive and function in blood-rich tissue, lipid mediators generated by leukocytes modulate MSC viability and renal protective or renotropic functions. 14S,21R-diHDHA) was produced under inflammatory conditions by blood leukocytes, not by MSCs or renal glomerular endothelial and tubular epithelial cells. 14S,21R-diHDHA pretreatment enhanced amelioration of renal I/R injury mediated by intravenously-infused MSCs, as demonstrated by the reduction of I/R-induced elevation of serum creatinine levels, renal tubular cell death, and leukocyte infiltration. Effects of 14S,21R-diHDHA on MSC renotropic functions were mediated, at least in part, by inhibiting grafted MSC apoptosis and promoting MSC paracrine/endocrine functions, including upregulating hepatocyte growth factor and...
insulin growth factor-1 secretion, which involves activation of the Phosphoinositide-3-kinase pathway. Our findings thus provide a new strategy and Mechanistic Insights for the treatment of acute kidney injury.

**ON FEBRUARY 9, TWO SPEAKERS PRESENTED THE THRCE SEMINAR**

**JEFF M. SANDS, MD**  
Juha P. Kokko Professor of Medicine & Physiology,  
Director, Renal Division;  
Executive Vice-Chair, Department of Medicine  
Emory University,  
School of Medicine, Atlanta, GA.

**HUI CAI, MD**  
Assistant Professor of Medicine & Physiology,  
Renal Division  
Emory University  
School of Medicine,  
Atlanta, GA.

**JEFF M. SANDS, MD:**  
Dr. Jeff M. Sands presented, “Regulation of Renal Urea Transport,” at the THRCE Seminar Series on February 9, 2012. Urea and urea transporters play critical roles in the production of concentrated urine. Two urea transporters are expressed in the inner medullary collecting duct (IMCD): UT-A1 in the apical plasma membrane and UT-A3 in the basolateral plasma membrane. Mice with genetic knock-out of these two urea transporters are unable to concentrate their urine. Both vasopressin (ADH) and hypertonicity increase urea permeability in rat terminal IMCDs. Each agonist independently increases urea permeability, and the two together have a synergistic effect to increase urea permeability. Both vasopressin and hypertonicity increase UT-A1 phosphorylation and apical plasma membrane accumulation. Vasopressin activates protein kinase A and phosphorylates UT-A1 at serines 486 and 499. Hypertonicity stimulates urea permeability through protein kinase C (PKC) and intracellular calcium. We tested whether hypertonic stimulation of urea permeability results from a PKC mediated phosphorylation of UT-A1 in freshly isolated suspensions of rat IMCDs. Hypertonicity did stimulate UT-A1 phosphorylation, and this increase was blocked by pre-incubation with a PKC inhibitor. Next, IMCDs were biotinylated to assess plasma membrane UT-A1. Hypertonicity increased biotinylated UT-A1, and this increase was also blocked by pre-incubation with a PKC inhibitor. Since PKCα is a calcium-dependent PKC isoform, we tested whether it may be the PKC isoform mediating hypertonicity’s stimulation of urea transport. We measured urine osmolality in PKCα knock-out mice and found that they have a urine concentrating defect. Next, we showed that hypertonicity increased phospho-PKCα in rat IMCDs. Hypertonicity significantly increased UT-A1 phosphorylation and urea permeability in wild type mice but not in PKCα knock-out mice. Thus, both vasopressin and hypertonicity increase urea permeability through increases in UT-A1 phosphorylation and apical plasma membrane accumulation, but they do so through different signaling pathways in the IMCD.
Also on February 9, Dr. Hui Cai presented a seminar titled, “WNK4 inhibits NCC through a MAPK-ERK 1/2 signaling pathway.” Dr. Cai’s laboratory has long been interested in renal ion channel and transporter regulation by WNK kinase and its relationship to hypertension. WNK kinase is a novel serine/threonine kinase. Mutations in WNK1 and WNK4 of this kinase family result in pseudohypoaldosteronism type II (PHA II), also referred to as Gordon syndrome, or familial hyperkalemia and hypertension. PHA II is also known as one of the monogenic hypertensions. The clinical features of PHA II include hypertension, hyperkalemia and metabolic acidosis with normal renal function. Studies over the last decade demonstrate that WNK kinase represents a novel signaling pathway that plays an important role in the regulation of sodium and potassium homeostasis. Further exploration of the mechanism underlying WNK’s modulation of sodium and potassium function would provide novel insights into the pathogenesis of essential hypertension. Dr. Cai and his research associates, Drs. Xiuyan Feng, M.D., Ph.D. and Bo Zhou, Ph.D., have recently found that WNK4 modulates the function of sodium chloride contrasporter (NCC) through a MAPK-ERK 1/2 signaling pathway. In this talk, Dr. Cai presented their work on this novel WNK-mediated ERK 1/2 signaling pathway involving regulation of NCC. WNK4 was shown to phosphorylate SPAK/OSR1 kinase to activate NCC function, indicating a stimulatory signaling pathway involving NCC regulation. However, data from Dr. Cai’s lab as well as data from other laboratories have previously reported that WNK4 inhibited NCC function and protein expression which suggests an inhibitory regulatory pathway. Dr. Cai and his research associates found that WNK4 enhanced ERK 1/2 phosphorylation and knock-down WNK4 expression decreased ERK 1/2 phosphorylation in the mouse distal convoluted tubule (mDCT) cell lines. Knock-down WNK4 expression also increased total and surface NCC protein expression. Knock-down ERK 1/2 expression also increased NCC protein expression. In addition, Dr. Cai’s group found that dietary salt changes alter WNK4 and NCC expressions. High dietary salt intake increased WNK4 expression and reduced NCC protein abundance while enhancing ERK 1/2 phosphorylation, whereas low dietary salt intake decreased WNK4 expression and increased NCC protein abundance while reducing ERK 1/2 phosphorylation in rat. Aldosterone infusion in rat also increased NCC protein abundance and reduced WNK4 expression while reducing ERK 1/2 phosphorylation. These data strongly suggest that WNK4 inhibits NCC through a MAPK-ERK 1/2 signaling pathway, an inhibitory pathway involving NCC regulation that provide a novel mechanism how WNK4 regulates NCC. These data have been recently published in American Journal of Physiology; Renal Physiology and Pflugers Archiv-European Journal of Physiology.
Dr. Wei Chen presented, “The Area under the Curve - A Measure of Long-term Risk Burden in Cardiovascular Epidemiologic Research: The Bogalusa Heart Study” at the THRCE Seminar Series on February 16, 2012. Cardiovascular disease risk variables change with age, like body weight, blood pressure, lipid variables, glucose, etc. The total variation of longitudinal data can be partitioned at least into two components, among- and within-person variation. Longitudinal changes of cardiovascular risk variables in the same person are determined by the within-person variation over time. Among the longitudinal analysis models and approaches, the area under the curve (AUC) of serially repeated measurements over time represents a useful and flexible method for analysis of cardiovascular disease risk variables. Calculation of the AUC values for each individual includes three steps: construction of a growth curve, integration of the curve parameters and being divided by the number of follow-up years. The data presented are all from the Bogalusa Heart Study, a long-term biracial (black-white) community-based epidemiological study of the early natural history of cardiovascular disease beginning in childhood since 1973. The application of the AUC method to the longitudinal database of the Bogalusa Heart Study includes cardiovascular disease genetic analysis, aging study, variability analysis and birth weight analysis. The AUC method has advantages over other longitudinal analysis models: 1) the AUC value can be used as either a dependent or an independent variable to measure a long-term risk burden, 2) it measures a combination of linear and nonlinear trends, 3) multiple long-term measures can be derived, and 4) it has a greater power. On the other hand, this method also has limitations: 1) it requires a sufficient number of measurements, and 2) sometimes it has model fitting problems.
Dr Batuman presented, “Inflammatory pathways in acute kidney injury and the renoprotective role of PACAP38,” at the THRCE seminar series on March 1\textsuperscript{st} 2012. Dr Batuman’s research focuses on the cellular and molecular mechanisms of acute kidney injury in various experimental models including ischemia/reperfusion injury, and nephrotoxic injury caused by such agents as cisplatin, cyclosporine, contrast dye, etc., as well as kidney injury associated with myeloma light chains. Dr Batuman’s laboratory has been studying the role of immune pathways involved in repair processes that maybe a daptive and lead to regeneration and recovery or maladaptive that can further aggravate injury leading to chronic kidney disease. Alterations in both innate immunity involving the role of toll-like receptors and adaptive (acquired) immunity in the pathogenesis of acute kidney injury are explored. Together with his team of collaborators, Dr Batuman has been investigating the therapeutic effects of pituitary adenylate cyclase activating polypeptide (PACAP)38, and its role in modulating the immune responses to help protect kidney cells from injury and promote regenerative processes. In his seminar Dr Batuman presented experimental findings on alterations in particularly innate immune responses and the role of inflammation mediated by proinflammatory cytokines that aggravate or exaggerate renal injury in kidney cell cultures and mice. In these studies, PACAP38 administered prior to injury, and in some cases, even after the injury helped to ameliorate injury and recovery from injury. Dr Batuman presented experimental evidence demonstrating PACAP38 as a potentially novel kidney-protecting drug that may have a wide range of use in various types of acute and chronic kidney disease.
On March 8, 2012, Dr. Norman Rosenblum presented a seminar on the varied and critical functions of Hedgehog-GLI signaling in the normal and malformed kidney. Human kidney malformation (a group of disorders termed CAKUT) is the major cause of childhood kidney failure. Yet, the underlying molecular mechanisms are largely undefined and no specific treatments are available. Dr. Rosenblum's lab showed that complete deficiency of Sonic Hedgehog results in bilateral absence of kidney tissue or a single malformed kidney. Remarkably, these malformations are dependent on the formation of GLI3 repressor (GLI3R), a short transcriptional repressor, generated from GLI3, a Hedgehog transcriptional effector. Members of the Rosenblum lab are now investigating how GLI3R controls the formation of the ureteric bud, the outgrowth of which instigates kidney formation by the metanephric blastema. The Rosenblum Lab has elucidated specific functions for Hedgehog-GLI signaling during stages of kidney development when the cortex and medulla become distinct regions. The cortex, which is uniquely constituted by glomeruli, is dependent on the presence of GLI3R; indeed, nephrogenesis requires GLI3R expression in distal ureteric branches. In contrast, GLI3R is deleterious to the functions of pacemaker cells in the renal pelvis and upper ureter. Abnormal pacemaker function gives rise to non obstructive hydronephrosis, a common pediatric condition. In work, as yet unpublished, the Rosenblum Lab is determining the relation between Hedgehog signaling and primary cilia in the kidney in vivo. Results demonstrate that primary cilia act within ureteric and mesenchyme cells control nephron number via distinct cell-specific mechanisms. Together, Dr. Rosenblum's work is providing novel and important insights into control of normal developmental mechanisms in the kidney and the generation of kidney-urinary tract malformation.
On March 15, Dr. Rafael Rubio Garcia presented a talk titled, “Does the Coronary Endothelium behave as a Functional Diffusion Barrier to Diverse Intravascular Hormones?” More than 30 years of research have shown that the endothelium is a heterogeneous and complex regulatory cell that is target of important pathologies. The endothelial cell is a multifunctional and multi-signaling entity involved in different processes such as selective regulation of: hormone-dependent and/or flow-dependent diverse parenchymal functions and metabolisms, also blood coagulation, thrombosis and tissue inflammation. The endothelium is not an inert physical diffusional barrier, but a selective interface in the transfer of diverse solutes and even cells across it. It is increasingly clear that in endothelial cells these complex processes are initiated, even restricted to the luminal cell membrane. The luminal endothelial membrane is either the site of reception of diverse stimuli or/and the site of initial signaling that regulates these processes. The time is ripe to define what are the basic findings that are here to stay and the solid foundations for future work.

On March 29, Dr. Gregory Fink presented a talk titled, “Targeted Sympathetic Ablation for the Treatment of Hypertension.” The presentation focused on a very new approach now being tested clinically around the world for the management of drug-resistant hypertension. Drug resistant hypertension is defined as persistently elevated arterial blood pressure in a patient who adheres to maximum tolerated doses of 3 antihypertensive drugs including a diuretic. The new approach for lowering blood pressure in such patients is
called catheter-based renal nerve ablation, i.e. inserting a catheter in both renal arteries and applying radiofrequency energy to destroy the nerve fibers that enter (sympathetic nerves) and leave (sensory nerves) the kidney along the renal arteries (renal denervation), without injuring the artery itself. Early clinical results have shown that the procedure is safe and brings about an impressive reduction in blood pressure that lasts for at least two years. The question addressed by Dr. Fink’s presentation was: Can we use experimental animal models of hypertension to study how this procedure works to lower blood pressure, and predict which patients would be most likely to have a successful outcome? Dr. Fink reviewed the history of renal denervation studies in animals, and showed recent data from his laboratory on the effects of renal denervation in several different common rat models of hypertension. The results suggest that a specific strain of rat – the spontaneously hypertensive rat, or SHR – may be the best experimental model to use to understand how the clinical procedure works. Dr. Fink also provided historical clinical data, and recent experimental results, suggesting that removing sympathetic nerves to other organs in the body (e.g. the intestines) also may be an effective strategy for treating hypertension.

Dr. Lee Murfee presented a THRCE seminar on April 12, 2012. Hypertension is associated with an increase of microvascular resistance, in part, due to structural rarefaction caused by the loss of blood microvessels. Given that the development of elevated blood pressure is accompanied, and in some cases preceded by, a loss of microvessels, therapies aimed at reversing microvascular rarefaction could represent candidate treatments of hypertension. Rationale for this type of therapy requires better understanding the causes and effects of microvascular network patterns during hypertension. The focus of this presentation was on new answers to two questions:

1) Are adult hypertensive microvascular networks able to undergo angiogenesis (blood vessel growth)?
2) Do microvascular network pattern alterations during hypertension cause increased resistance?
Consistent with hypertension associated rarefaction, un-stimulated mesenteric networks from adult spontaneously hypertensive rats (SHRs) display decreased vascular area and length density compared to normotensive controls. However, SHR networks are able to undergo angiogenesis and differences in angiogenic metrics compared to normotensive networks depend on specific time points during the time course of network growth. These findings offer an explanation for contrasting results from the literature regarding whether angiogenesis is impaired in the SHR. In addition to rarefaction, un-stimulated adult SHR mesenteric networks display an increase in arteriole-venous (A/V) connections. The connections serve to offset the effects of vessel loss on local network resistance. Using real geometry measurements from intact microvascular networks and a computational model, SHR network resistance can be shown not to be elevated compared to normotensive levels. The results highlighted by this presentation provide new perspectives for future studies aimed at understanding the role of microvascular network patterns in hypertension.

**Kathryn Sandberg, PhD**

*Director, Center for the Study of Sex Differences in Health, Aging, and Disease*

*Professor, Nephrology & Hypertension, Department of Medicine*

*PhD Program Director, Physiology & Biophysics*

*Department of Biomedical Engineering, Georgetown University, Washington, DC.*

Kathryn Sandberg PhD, Director of Center for the Study of Sex Differences in Health, Aging, and Disease, visited Tulane and presented a talk hosted jointly by THRCE & the BIRCWH program. The talk, “T cell modulation of hypertension: SeXX matters!” was presented on April 11, 2012.
Recent Publications (includes those omitted from previous newsletters)


**Book Publication**

From January through April, 2012, investigators and physicians affiliated with T.H.R.C.E. participated in the following regional, national, and international meetings.

Southern Regional Meeting, Feb. 9-11, New Orleans, LA

- **Bahrami L, Singh P, Castillo A, Majid DS.** TNF-α Receptor Type 2, but not Type 1, is involved in the Renal Tissue Injury Response to Chronic Angiotensin II Administration in Mice. (SAFMR/SSCI Student Research Award Winner). Abstract 417.

- **Benjamin JS, Williams S, Albert B, Yosipiv IV.** Renal Hypouricemia in a child with Crohn’s Disease. Abstract 263.


- **Chen S, Rosenberg S, Yao X, El-Dahr SS.** Mice Lacking Histone Deacetylases 1 and 2 in the Ureteric Epithelium Exhibit Renal Cystic Hypoplasia. (SSPR/APA Trainee Travel Award Winner). Abstract 153.

- **Chong E, El-Dahr S, Yosipiv I.** A Newborn with Bilateral Multicystic Kidney Dysplasia and Cerebellar Hypoplasia. Abstract 266.


- **Gonzalez AA, Luffman C, Green T, Vio C, Prieto MC.** Activation of the (Pro)Renin Receptor contributes to the Angiotensin II Mediated Increase in Cyclooxygenase-2

- **Howard CG, Mitchel KD.** Chronic Direct Renin Inhibition Improves Renal Hemodynamics in Cyp1A1-REN2 Transgenic Rats with Angiotensin II-

- **Hilliard SA, El-Dahr SS.** The Proto-Oncogene, MDM2, is required for maintenance of the CAP Mesenchyme. (SSPR/APA Trainee Travel Award Winner). Abstract 412.


- **Gonzalez AA, Luffman C, Green T, Vio C, Prieto MC.** Activation of the (Pro) Renin Receptor contributes to the Angiotensin II mediated increase in Cyclooxygenase-2 Expression in the Rat Renal Inner Medulla. (SAFMR/SSCI Trainee Research Award Winner). Abstract 413.


- **Mabry C, Kleinpeter MA, Engel L, Glancy DL.** Abnormal ECGS in a woman with Human Immunodeficiency Virus and Medication-Induced Fanconi Syndrome. Abstract 195.


- **Singh P, Castillo A, Islam MT, Majid DS.** Systemic Inhibition of Nitric Oxide Synthase Reduces Plasma Levels of Anti-Inflammatory Interleukins in
Continued...

Anesthetized mice. (SAFMR/SSCI Trainee Research Award Winner). Abstract 528.

- **Song R, Preston G, Yosypiv I.** Endogenous Angiotensin (ANG) II Promotes Papillogenesis during Late Metanephric Development. (SSPR/APA Trainee Travel Award Winner). Abstract 290.


2012 Experimental Biology Meeting, April 21-25, San Diego, CA.

- **Choi S, Kassan M, Umezawa K, Islam MT, Matrougui K.** Nuclear Factor kappa B (NFkB) Inhibition Improves Vascular Function in Type 2 Diabetic Mice. FASEB J March 29, 2012 26:1057.16


- **Collins AE, Howard CG, Mitchell KD.** Salt-deficient diet does not attenuate the development of slowly progressive ANG II-dependent hypertension in Cyp1a1-Ren2 transgenic rats. FASEB J March 29, 2012 26:688.1

- **Feng M, Navar LG.** Nebivolol induced vasodilation of renal afferent arterioles involves [beta]3 adrenergic receptor activation. FASEB J March 29, 2012 26:690.15

- **Galan M, Kassan M, Alkhafaf Q, Islam MT, Matrougui K.** ER stress induction increases NADPH oxidase and reduces eNOS activity in endothelial cells. FASEB J March 29, 2012 26:863.11
Gonzalez AA, Rajo M, Kassan M, Matrougui K, Prieto MC. Downregulation of the (pro)renin receptor by insulin is potentiated by high glucose in mouse renal collecting duct cells. FASEB J March 29, 2012 26:1068.11


Li W, Peng H, Ichihara A, Feng Y. (Pro)Renin receptor deletion prevents the development of DOCA-salt hypertension in neuron-specific (Pro)Renin receptor knockout mice. FASEB J March 29, 2012 26:874.4


Maiti AK, Islam MT, Majid DSA. Enhancement of cellular Na+K+ATPase activity in the mouse renal tissue in-vitro with low concentration of peroxynitrite. FASEB J March 29, 2012 26:885.4
• O'Hare JD, Miyata K, Fourrier TL, Krantz AM, Derbenev AV, Zsombok A. Central TRPV1 signaling regulates systemic blood glucose levels and hepatic PEPCK protein expression. FASEB J March 29, 2012 26:701.5

• Peng H, Li W, Seth D, Navar LG, Feng Y. (Pro)renin receptor over-expression induces angiotensin II-independent NADPH oxidase activation through PI3K - ERK signaling in Neuronal cells. FASEB J March 29, 2012 26:893.4


• Singh P, Bahrami L, Castillo A, Majid DSA. Involvement of TNF- (alpha) receptor type 2, but not the type 1, in angiotensin II induced renal tissue injury in mice. FASEB J March 29, 2012 26:868.20


• Stapor PC, Ahsan T, Murfee WL. NG2 Inhibition Decreases Endothelial Cell Sprouting Along Venules: A Novel In Situ Angiogenesis Assay To Investigate Multicellular Interactions. Oral Presentation.

• Yang, Ming, Murfee WL. The Effect of Network Pattern Alterations On Microvascular Resistance In Hypertension. Oral Presentation.

Health Sciences Research Days, April 2012, Tulane University, New Orleans, LA

• Anwar IJ, Derbenev AV. Thermosensitive Synaptic Transmission in the Brainstem.

• Cao T, Li W, Feng Y. Brain (Pro)Renin Receptor Knockdown Modulates the body fluid Homeostasis during Angiotensin II-Dependent Hypertension.

• Collins A, Howard CG, Mitchel KD. Blood Pressure and Renal Hemodynamics in Hypertensive Cyp1A1-REN2 Transgenic Rats fed a Sodium-Deficient Diet.
Collins A, Howard CG, Mitchel KD. Salt-Deficient Diet does not Attenuate the Development of Slowly Progressive Ang II-Dependent Hypertension in Cyp1A1-REN2 Transgenic Rats.


Howard CG, Mitchel KD. Chronic Direct Renin Inhibition Improves Renal Hemodynamics in Cyp1A1-REN2 Transgenic Rats with Angiotensin II-Dependent Malignant Hypertension.


Krantz AM, Fourrier TF, Zsombok A. A Subpopulation of Kidney-Related Neurons in the Paraventricular Nucleus of the Hypothalamus Expresses TRPV1 and IRS2.


Li W, Peng H, Ichihara A, Feng Y. (Pro)Renin receptor deletion prevents the development of DOCA-salt hypertension in neuron-specific (Pro)Renin receptor knockout mice.


Maiti AK, Islam MT, Majid DSA. Enhancement of cellular Na+K+ATPase activity in the mouse renal tissue in-vitro with low concentration of peroxynitrite.
• O'Hare JD, Miyata K, Fourrier TL, Krantz AM, Derbenev AV, Zsombok A. Central TRPV1 signaling regulates systemic blood glucose levels and hepatic PEPCK protein expression.

• Peng H, Li W, Seth D, Navar LG, Feng Y. (Pro)renin receptor over-expression induces angiotensin II-independent NADPH oxidase activation through PI3K - ERK signaling in Neuronal cells.


• Rands VF, Seth D, Prieto MC. Salt-Sensitive Hypertension Displays Sex Difference during ANG II-Dependent Hypertension in Sprague Dawley Rats.


• Yang M, Murfee WL. The Effects of Network Pattern Alterations on Microvascular Resistance in Hypertension.

• Zsombok A, Miyata K, Hebert KD, Luffman C, Prieto MC. Short term High Dietary Salt Treatment Increases TRPV1 Protein Expression in the Rat Hypothalamus in a Sex-Dependent manner.

2012 PAS (Pediatric Academic Societies) Annual Meeting, April 29, Boston, MA

• Chen S, Yao X, El-Dahr SS. HDAC1 and HDAC2 are critical in renewal and differentiation of nephron progenitor cells. Oral presentation. Winner of the Basic Science Fellow Award.
**THRCE Seminars**

**January 5, 2012**

**Song Hong, PhD**  
Assistant Professor,  
Louisiana State Univ. Health Sci. Ctr.,  
Neuroscience Ctr. of Excellence, New Orleans, LA.  
"Lipid Mediators in Renal Injury and Mechanistic Insights."

**January 19, 2012**

**M.A. "Tonette" Krousel-Wood, MD**  
Associate Dean / Associate Provost for Health Sciences,  
Professor of Clinical Epidemiology,  
Department of Epidemiology,  
Tulane University School of Public Health & Tropical Medicine,  
New Orleans, LA.  
"The role of adherence in achieving treatment goals in hypertensive patients."

**February 2, 2012**

No Meeting  
Meeting Rescheduled To February 9, 2012.

**February 9, 2012 **

Special THRCE Seminar - 2 Speakers.  

**Jeff M. Sands, MD**  
Juha P. Kokko Professor of Medicine and Physiology,  
Director, Renal Division;  
Executive Vice-Chair, Department of Medicine,  
Emory University School of Medicine, Atlanta, GA.  
"Regulation of Urea Transport in the IMCD."

**Hui Cai, MD**  
Assistant Professor, Department of Medicine & Physiology, Renal Division;  
Emory University School of Medicine, Atlanta, GA.  
"WNK4 Inhibits NCC through a MAPK/ERK1/2 Signaling Pathway."

**February 16, 2012**

**Wei Chen, MD, PhD**  
Research Professor, Center for Cardiovascular Health,  
Department of Epidemiology,  
School of Public Health & Tropical Medicine,  
Tulane University, New Orleans, LA  
"The Area under the Curve (AUC) - A Measure of Long-term Risk Burden in Cardiovascular Epidemiologic Research: The Bogalusa Heart Study."

**Conferences are held alternative Thursdays at 4:00pm in the Tulane Medical School, Pharmacology Library, Room 4700  
**Denotes the seminar date is not our normally scheduled day
<table>
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| March 1, 2012 | Vecihi Batuman, MD  
Professor of Medicine, Section of Nephrology  
Tulane University School of Medicine, New Orleans, LA  
"Inflammatory pathways in acute kidney injury and the role of PACAP-38." |
| March 8, 2012 ** | WORLD KIDNEY DAY 2012  
Special THRCE Seminar  
Norman Rosenblum, MD  
Professor of Pediatrics & Physiology,  
Associate Dean, Physician Scientist Training, Laboratory Medicine & Pathobiology,  
University of Toronto,  
Staff Nephrologist, Nephrology, The Hospital for Sick Children,  
Toronto, Ontario, Canada.  
“A GLI-ful Story: a Multifunctional Role for Hedgehog Signaling in the Embryonic Kidney.” |
| March 15, 2012 | Rafael Rubio Garcia, PhD  
Visiting Assistant Professor, Department of Physiology,  
Tulane University School of Medicine, New Orleans, LA.  
Visiting from: Dept. Physiology, Universidad Autonoma de San Luis Potosi, Mexico  
“Does the Coronary Endothelium behave as a Functional Diffusion Barrier to Diverse Intravascular Hormones?” |
| March 29, 2012 | Joint Seminar:  
THRCE & Tulane Neuroscience program  
Gregory D. Fink PhD  
Professor, Department of Pharmacology & Toxicology,  
Michigan State University,  
Michigan, MI.  
"The Role of Brain Eicosanoid in Angiotensin II-Salt Hypertension.” |
| April 12, 2012 | Walter Lee Murfee, PhD  
Assistant Professor,  
Department of Biomedical Engineering,  
Adjunct Assistant Professor, Department of Physiology,  
Tulane University, New Orleans, LA.  
“Microvascular Structure and Hypertension: New Answers to Old Questions.” |

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<td>April 26, 2012</td>
<td>No Meeting  SEMINAR CANCELLED</td>
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| May 3, 2012   | Special THRCE Seminar                                                            | Gabriel G. Haddad, MD  
Professor of Pediatrics & Neuroscience  
Chair, Department of Pediatrics, University of California, San Diego  
Physician-in-Chief and Chief Scientific Officer  
Rady Children’s Hospital-San Diego, CA | “Hypoxia susceptibility and tolerance: Using Drosophila as a genetic model.”               |
| May 10, 2012  | Special THRCE Seminar                                                            | L. Gabriel Navar, PhD  
Chair, Department of Physiology  
Director, Center of Biomedical Research  
Excellence in Hypertension & Renal Biology  
Tulane University, School of Medicine,  
New Orleans, LA. | “The Wisdom of the Body Revisited: Tribute to Walter B. Cannon & his Concept of Homeostasis as applied to Pathophysiology of Hypertension.” |
| May 24, 2012  | Bellamkonda K. Kishore, MD, PhD, MBA                                               | Research Professor of Medicine  
Principal Investigator, VA Medical Center, Nephrology Research  
VA SLC Health Care System  
Salt Lake City, UT. | “Purinergic Regulation of Renal Water and Sodium Transport.”                               |
| June 7, 2012  | No Meeting  SEMINAR CANCELLED                                                   |                                                                                              |                                                                        |
| June 14, 2012 ** | No Meeting  SEMINAR CANCELLED                                                   | Tahir Hussain, PhD  
Head and Professor,  
Department of Pharmacal Sciences, Harrison School of Pharmacy,  
Auburn University, Auburn, AL. | “Angiotensin AT2 receptor: Role in renal function and blood pressure control in obesity.” |

Conferences are held alternative Thursdays at 4:00pm in the Tulane Medical School, Pharmacology Library, Room 4700

** Denotes the seminar date is not our normally scheduled day.
Awards and Acknowledgment

L. Gabriel Navar, PhD, Chairman and Professor of Physiology presented the prestigious “Walter B Cannon Memorial Award Lecture” at the 2012 Experimental Biology meeting held in San Diego, CA. He presented, “The Wisdom of the Body Revisited: Tribute to Walter B. Cannon and His Concept of Homeostasis as Applied to Pathophysiology of Hypertension” on April 21, 2012.

Dewan S. A. Majid, MD, PhD, was elected as President of Bangladesh Medical Association of North America (BMANA), Louisiana Chapter (2012-2014).

Minolfa C. Prieto, MD, PhD, was awarded the Deep South Network for Translational Research (DSNTR) Grant Award for her research titled, “Determination of urinary renin and pro-renin in diabetic and hypertensive patients.” She was also appointed, on January 1, 2012, as member of APS Committee.

Kenneth D. Mitchell, PhD, was selected for the following position during the Spring of 2012:
- Grant Reviewer and Interim Co-Chair, AHA Greater Southeast Affiliate, Cardiorenal 1 Committee, April 2, 2012.
- Judge, Poster Session, Tulane University Health Sciences Research Days, April 2012.
- Abstract Reviewer, 66th Annual Fall Conference and Scientific Sessions of the Council for High Blood Pressure Research in Association with the Council on the Kidney in Cardiovascular Disease, 2012

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.

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.

T.H.R.C.E.

1430 Tulane Avenue, SL39
New Orleans, LA 70112

Comments are welcome:
Contact: Nina R. Majid
Senior Program Coordinator
Phone: 504-988-3703
Fax: 504-988-2675
Email: htnctr@tulane.edu
http://tulane.edu/som/thrce/