



# THRCE.

TULANE HYPERTENSION AND RENAL CENTER OF EXCELLENCE

Summer 2015

Volume 14, Issue 2

## COBRE AWARDS THREE PILOT PROJECT GRANTS

Each year, the COBRE provides three pilot projects grants of \$45,000 to support scientific research related to hypertension. These pilot project awards provide one year of research support for novel, innovative projects that address important and significant issues related to the broad area encompassed by hypertension, renal and cardiovascular research. Applications are subjected to a rigorous internal and external review process to ensure that funds are provided only to highly meritorious projects that are likely to lead to extramural research support and will stimulate multidisciplinary collaborative interactions. The 2015-2016 COBRE Pilot Project award recipients are Drs. Majid, Liu and Khan.

- **Pilot Project 1:** *Roles of TNF- $\alpha$  receptors in high salt induced exaggerated hypertensive and renal injury responses to Angiotensin II.*  
**PI: Dewan S. A. Majid, MBBS, PhD,** Department of Physiology.
- **Pilot Project 2:** *Histone Deacetylases 1 and 2 in Kidney Development.*  
**PI: Hongbing Liu, PhD,** Division of Pediatrics Nephrology, Department of Pediatrics, and Department of Biochemistry.
- **Pilot Project 3:** *Roles of TLRs and ROS in contrast-induced nephropathy and new therapeutic strategies.*  
**PI: M-Altat Khan, PhD,** Section of Nephrology & Hypertension, Department of Medicine.

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### UPCOMING MEETINGS:

- The American Society of Nephrology – Kidney Week ~ San Diego, CA, November 3- 8, 2015.
- 3<sup>rd</sup> Biennial Southeast Regional IDeA Meeting ~ Biloxi, Mississippi, November 11-13, 2015.
- Southern Regional Meeting 2016 ~ New Orleans, February 18-20, 2016.
- The Experimental Biology Meeting ~ San Diego, CA, April 2-6, 2016.

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## THREE CO-SPONSORS 2015 MAYERSON DI LUZIO LECTURE



*Dr. Navar with Dr. Boron*

The Tulane Hypertension & Renal Center of Excellence and the Department of Physiology at Tulane co-sponsored the 2015 Mayerson-Di Luzio Lectureship that was presented by Walter F. Boron, MD,PhD. The Lectureship was established to honor the memory of Drs. Hyman S. Mayerson and Nicholas R. Di Luzio, who presided as Chairmen of the Tulane Physiology Department.

Dr. Walter F. Boron received his MD and PhD degrees from Washington University in St. Louis, Missouri, then completed his postdoctoral training in the Department of Physiology at Yale University under the direction of Dr. Emile Boulpaep. He was appointed to the Yale faculty in 1980. He quickly rose

through the ranks, and was appointed Chair of the Department of Cellular and Molecular Physiology in 1989. In 2007, he relocated as Chair of the Department of Physiology and Biophysics at Case Western Reserve University in Cleveland, Ohio, where he also serves as the David N. and Inez Myers/Antonio Scarpa Professor.

During his postdoctoral years, Dr. Boron, together with Dr. Boulpaep, discovered the electrogenic Na/HCO<sub>3</sub> cotransporter, which plays a central role in HCO<sub>3</sub><sup>-</sup> reabsorption in the renal proximal tubule. Dr. Boron's research now focuses on three major research areas: pHi (Intracellular pH) homeostasis, CO<sub>2</sub>/HCO<sub>3</sub><sup>-</sup> sensing, and gas channels—which have evolved from his longstanding interest in pHi homeostasis. This subject is important because virtually every biological process—including cell division; metabolism; and action of channels, transporters, and structural proteins—depends on pHi.

Dr. Boron is an active member of several societies, including the American Physiological Society (APS), the American Society of Nephrology (ASN), Physiological Society, Society of Neuroscience, Biophysical Society, and the International Union of Physiological Societies (IUPS), where he has served as a member of the National Organizing Committee, Chair of the Programming Committee, and Secretary-General. He is a former President of the APS. He has held several editorial positions and has published over 250 peer-reviewed manuscripts, book chapters, editorials and review articles. Additionally, Dr. Boron is co-editor, of the text book, *Medical Physiology*. He has also received several awards including the Robert F. Pitts Award from IUPS, Homer Smith Award from ASN, and the Sharpey-Schafer Award from the Physiological Society. Most recently, Dr. Boron was elected to the Institute of Medicine of the National Academies, which is one of the most prestigious societies for health and medicine in the United States.

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## HONORS & RECOGNITION AWARDED TO THREE AFFILIATED INVESTIGATORS

### **Andrei Derbenev, PhD:**

- Promoted to Associate Professor effective July 1, 2015.
- Received Notice of Award from NIHLBI for a R01 grant titled: "Sympathetic control and hypertension via brainstem cannabinoid signaling."
- Received a Neuroscience Bridge Award.

### **Kathleen Hering-Smith, PhD:**

- Appointed to serve on the Editorial Board of the American Journal of Physiology-Renal Physiology beginning July 1, 2015.
- Selected for the APS Professional Communications Skills Workshop Advance Course.

### **Norman Kreisman, PhD:**

- As Course Director, was awarded the T1: Course of the Year Award for the 1<sup>st</sup> Year Medical Class at Tulane University, School of Medicine. The award was presented at the 2015 Owl Club Awards ceremony held on May 8, 2015.
- Nominated for Owl Club's W. Clifford Newman Student Advocacy Award.

### **Dewan S. A. Majid, MD, PhD:**

- Awarded one of three COBRE Phase III Pilot Project Awards.
- Received a travel award for International travel from the Provost's Office.

### **Kenneth D. Mitchell, PhD:**

- Nominated for Owl Club's T1: Professor of the Year Award.

### **L. Gabriel Navar, PhD:**

- Awarded Year-4 of the NIH/NIGMS CoBRE III Grant (5P30GM103337) for the period 08/01/2015 - 07/31/2016.
- As Chair of the Department of Physiology, was awarded the coveted Owl Club's 2015 Overall Outstanding Department Award.
- Named to the inaugural class of Fellows of the American Physiological Society.
- On July 27<sup>th</sup>, 2015, presented the Keynote Lecture at West Virginia INBRE meeting at Marshall University in Huntington, WV.

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Honors & Recognition Awarded to THRCE Affiliated Investigators, continued...

### **Kailash N. Pandey, PhD:**

- Awarded Pilot Bridge fund from Tulane University, SOM Research Program.
- Awarded \$52,000 COBRE-Aging Pilot Project Grant.
- Received a travel award for International travel from the Provost's Office.
- Nominated for Owl Club's Best Facilitator (PBL/TBL/JiTT) (Inaugural Award), for the 1<sup>st</sup> Year Medical Class at Tulane University School of Medicine.

### **Minolfa C. Prieto, MD, PhD:**

- Invited to serve as a member of the American Heart Association Greater Southeast Affiliate Research Committee.

### **Zubaida Saifudeen, PhD:**

- Awarded NIH-NIDDK R56 grant for her project, "p53-Regulated Metabolic Fitness in Nephron Progenitor Renewal."
- Elected Faculty Advisory Committee member for Tulane University SOM.
- Appointed to BMS steering committee.
- Appointed as Adjunct Associate Professor in the Department of Physiology.

### **T. Cooper Woods, PhD :**

- Awarded the T1: Best Facilitator (PBL/TBL/JiTT) Inaugural Award for the 1<sup>st</sup> Year Medical Class at Tulane University, School of Medicine at the 2015 Owl Club Awards ceremony held on May 8, 2015.
- Awarded Pilot Bridge Award from Tulane University, SOM Research Program.
- Nominated for Owl Club's T1: Professor of the Year Award.

### **Andrea Zsombok, PhD:**

- Promoted to Associate Professor effective July 1, 2015.
- Featured in the "New-Wave: News from Tulane University" as a rising star in research who is "Unraveling the link between diabetes and the brain."
- Appointed as Editorial board member: AJP Regulatory, Integrative and Comparative Physiology.

### **Graduate & Post-doctoral fellows:**

- Michael Cypress received a one-year Pre-Doctoral Fellowship Award from the American Heart Association.

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Honors & Recognition Awarded to THRCE Affiliated Investigators, continued...

- Mr. Cypress was also awarded NIH/NIDDKD NRSA Award, 1F31DK107185, for his project titled, "SGLT2 Mediates Glucose-Induced Angiotensinogen Synthesis in Proximal Tubule Cells."
- Medical Student, Christina I. Luffman, received the Nicholas R. DiLuzio Award at the Ivy Day Ceremony held May 15<sup>th</sup>, 2015.
- Medical Student, Jennifer A. Wall, received the Hyman S. Mayerson Award at the 2015 Ivy Day Ceremony.
- Medical student, Joseph M. Garagliano was the Recipient of the 2015 Warren R. Bourgeois, III, MD and Usha Ramadhyani, MD Student Research Endowed Fund Award.

### **2015 SSPR/APA Trainee Travel Award Recipients:**

(Annual Southern Regional Meeting of SSCI/ AFMR, New Orleans)

#### ◇ **2015 SAFMR/SSCI Student Research Award Recipients:**

- O'Leary, Ryan ~ Mentor: Dr. R Sato
- Walker, Ryan ~ Mentor: Dr. K Hering-Smith

#### **2015 SAFMR/SSCI Trainee Research Award Recipients:**

- Gogulamadi, Venkateswara Reddy ~ Mentor: Dr. KN Pandey
- Mani, Indra ~ Mentor: Dr. KN Pandey

#### **2015 SAFMR/SSCI Junior Faculty Research Travel Award Recipients:**

- Gonzalez, Alex ~ Mentor: Dr. MC Prieto

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## 2015 New Orleans Heart Walk

THRCE is participating in the New Orleans Heart Walk benefiting the American Heart Association (AHA). Cardiovascular diseases or stroke have or will somehow affect many of our friends, family members and/or co-workers. The funds raised will be used for critical research and education on cardiovascular diseases. **Please support the 2015 AHA fundraiser by:**

1. Making a secure, online, tax-deductible donation by visiting the page, <http://neworleansheartwalk.kintera.org/>.
2. **Volunteering your time and join in the walk!** The 2015 Heart Walk is happening Saturday, November 7 at LaSalle Park. It's a fun filled event and it's for a good cause.



*2014 Heart Walk: Participant walkers from the various TSOM teams*

The money raised often helps right here in the Tulane community! Tulane School of Medicine Hypertension and Renal Center of Excellence centralizes and coordinates Tulane research activities related to cardiovascular, kidney, and hypertension diseases. The center houses a

state-of-the-art Molecular, Imaging, and Analytical Core, the Animal and Gene-Targeted Core, the Mouse Phenotyping core, and the Clinical & Translational Core facilities. The center is composed of faculty from multi-disciplinary fields that are specifically dedicated to investigative efforts, patient care, and public education in the crucial areas of hypertension and kidney diseases. Funds raised by the American Heart Association have provided support to our faculty, in the THRCE. Your help raising funds for the AHA may directly come back and support research, patient care, and educational programs at Tulane.

News



### MARCH 10, 2016 IS WORLD KIDNEY DAY!

The focus on the 2016 World Kidney Day (WKD) is "*Kidney Disease & Children: Act Early to Prevent It.*" Within both higher and lower income countries there are communities that are at greater risk than others because of their socioeconomic status, ethnic origin, and/or where they live. WKD is a global health campaign that aims to raise awareness of the importance of our kidneys to our overall health, and to reduce the frequency and impact of kidney disease and its associated health problems. Taking steps to live a healthy lifestyle clearly helps to reduce risk, and early detection and treatment can slow or prevent the progression of Chronic Kidney Disease (CKD), and reduce the increased incidence of associated cardiovascular disease. WKD is a joint initiative of the International Society of Nephrology (ISN) and the International Federation of Kidney Foundations (IFKF). More information on WKD can be accessed at: <http://http://www.worldkidneyday.org/>

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## THE EFFECTS OF SALT DIET ON BLOOD PRESSURE

According to a study published in the Journal of the American Heart Association, people who regularly consume high-salt diets and people who gradually increase salt in their diet, face an increased risk of high blood pressure.



The three-year study conducted in Japan enlisted over 4,000 people with normal blood pressure. Although almost 23 percent of the participants eventually developed high blood pressure, progressively higher blood pressure was evident in participants who ate sodium-high diets or who gradually increased their sodium intake.

The amount of salt consumed by a person was estimated by analyzing the amount of salt excreted in their urine. At the end of the study, those eating the least amount of sodium were consuming 2,925 mg per day, and those eating the most sodium were consuming 5,644 mg per day. "Americans consume an average of nearly 3,500 milligrams of sodium a day, which is about 1,000 milligrams more than any public health group recommends," said Tomonori Sugiura, M.D., Ph.D., the study's lead author and an assistant professor in the department of cardio-renal medicine and hypertension at the Nagoya City University Graduate School of Medical Sciences in Nagoya, Japan. The American Heart Association recommends consuming no more than 1,500 mg of sodium per day. More than 75 percent of sodium in the U.S. diet is found in the salt added to processed food. In the United States, about nine of every 10 people consume too much sodium. The Salty Six foods – breads and rolls, cold cuts and cured meats, pizza, poultry, soup and sandwiches – are the leading sources of overall sodium in the American diet.

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The Effects of Salt Diet on Blood Pressure, continued...

“In our study, it did not matter whether their sodium levels were high at the beginning of the study or if they were low to begin with, then gradually increased over the years – both groups were at greater risk of developing high blood pressure,”

In some people, sodium increases blood pressure because it holds excess fluid in the body, creating an added burden to the heart. High blood pressure is a major risk factor for heart attack, stroke and heart failure.

Although the research focused on Japanese participants, the findings have universal implications. “Reducing sodium intake can save lives, save money and improve heart health – no matter what background or nationality a person is,” said Sugiura.

The study highlights the importance of maintaining a lifetime of lower-salt diet and confirms the findings of other studies that show strong associations between salt in the diet and high blood pressure. Further details on the study can be accessed at: <http://jaha.ahajournals.org/content/4/8/e001959.full>.

## THRCE Welcomes 2015 Summer Students

Each year meritorious Medical and Undergraduate Research Students are selected to work with faculty researchers affiliated with the Tulane Hypertension & Renal Center of Excellence for 8 to 10 weeks during the summer. Each student receives a stipend, are exposed to the valuable nature of a career path in research, and have the opportunity to attend the various THRCE events and Seminars. The following students were selected for the 2015 Summer Research Program:

**Sponsor: AHA Summer Fellowship Program**

- **Elizabeth Jane Kream**  
*Mentor: Dr. T. Cooper Woods*
- **Jennifer A. Marks**  
*Mentor: Dr. Kenneth D. Mitchell*
- **Eamonn Patrick Mehaffey**  
*Mentor: Dr. Dewan S. A. Majid*

**Sponsor: Cobre Core/Dr. Krane Funds**

- **Gregory T. Minutillo**  
*Mentor: Dr. L. Gabriel Navar*

**Sponsor: Bourgeois Medical Research Endowment**

- **Joesph M. Garagliano**  
*Mentor: Drs. Navar/Sato*

**Sponsor: Department of Physiology**

- **Alexander LeBental**  
*Mentor: Dr. Kenneth D. Mitchell*
- **Sullivan Smith**  
*Mentor: Dr. T. Cooper Woods*

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## THRCE SPONSORED 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 May through August, 2015, the center hosted the following speakers to present THRCE seminars:



- **Ihor V. Yosypiv, MD**  
*Associate Professor,  
Department of Pediatrics,  
Chief, Division of Pediatric Nephrology,  
Tulane University School of Medicine, New Orleans, LA.*

On May 7<sup>th</sup>, 2015, Dr. Yosypiv presented “Prorenin receptor-V-ATPase cross-talk in kidney development.”

**Summary:** Congenital Anomalies of the Kidney and Urinary Tract (CAKUT), including renal hypodysplasia (RHD), account for a majority of children with end-stage-renal disease requiring dialysis and renal transplantation. Nephron induction during kidney development is driven by reciprocal interactions between progenitor cells of the cap mesenchyme (CM) and the ureteric bud (UB). Congenital reduction of nephron number, a condition called RHD, is associated with subsequent hypertension and chronic kidney disease in humans. Dr. Yosypiv’s laboratory is interested in the basic mechanisms which control UB branching morphogenesis. The prorenin receptor (PRR) is a receptor for renin and prorenin, and an accessory subunit of the vacuolar proton pump H<sup>+</sup>-ATPase (V-ATPase). Dr. Yosypiv demonstrated that conditional deletion of the PRR in the UBs and their derivatives in mice disrupts normal kidney development, ultimately resulting in congenital RHD and urine acidification defects. V-ATPases are expressed in intracellular compartments of virtually all cell types and play important roles in protein trafficking and degradation via acidification of intracellular organelles. In the intercalated cells of the collecting duct, V-ATPase is present at the plasma membrane where it is important for urine acidification. The long-term goal of Dr. Yosypiv’s research is to identify deleterious mutations of the PRR gene in humans with CAKUT and to develop novel therapies that can be applied to the study of nephron regeneration strategies in CAKUT.

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# News



- **Walter Lee Murfee, PhD**  
*Associate Professor,  
Department of Biomedical Engineering,  
Adjunct Associate Professor of Physiology,  
Tulane University School of Engineering,  
New Orleans, LA.*

Dr. Murfee presented, "Hypertension to Aging: Advancing Our Understanding of Microvascular Growth" at the May 21<sup>st</sup> THRCE Seminar.

**Summary:** Given that microvascular network structure and growth are common denominators for multiple other pathologies, a need exists to better understand how network patterns change, the functional effects of these changes and the causes for these changes. Dr. Murfee's presentation highlighted his laboratory's most recent efforts to advance our understanding in the context of hypertension and aging. By quantifying the microvascular growth responses in networks harvested from adult, hypertensive and aged animals, Dr. Murfee offered new explanations for what has been reported to go wrong in the literature. Dr. Murfee also shared his group's recent development of a new experimental model for investigating cell dynamics in a real microvascular network scenario. The results from both the basic science and applied studies support the impact of an integrative approach.



- **Margaret Zimmerman, PhD**  
*Post-Doctoral Fellow,  
Department of Pharmacology,  
Tulane University School of Medicine, New Orleans, LA.*

Dr. Zimmerman presented, "Sex specific effects of chronic Ang II infusion on renal T cells," at the June 4<sup>th</sup> THRCE Seminar.

**Summary:** The renin angiotensin system (RAS) has recently been linked to inflammation, where T cells are necessary for male experimental animals to fully develop Ang II-hypertension. Very little is known about the effect of chronic angiotensin (Ang) II on T cells in females. Helper T cells work to coordinate the immune response by stimulating

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B cells to produce antibodies, recruiting phagocytes, or activating other T cells. While there are many subtypes of helper T cells, we were interested in T helper 17 (Th17) and T regulatory cells (Tregs). Th17 cells induce a pro-inflammatory response, and Tregs suppress effector T cell activation to limit pro-inflammatory responses. Our studies show that Ang II results in female Sprague Dawley rats having greater renal counts of immuno-suppressive Tregs and cytokine IL-10, while males have more pro-inflammatory Th17 cells and cytokine IL-17, even though the Ang II-induced increases in blood pressure were comparable between the sexes. Further studies were designed to identify a molecular mechanism responsible for this sex difference in the T cell profile to Ang II infusion. While Ang II has been shown to be a pro-inflammatory T cell activator, RAS vasodilatory peptide Ang (1-7) has been shown to be anti-inflammatory. Studies in this project were designed to determine the effect of Ang (1-7) on the renal T cell profile in males and females during Ang II-hypertension, with a primary focus on Tregs and Th17. However, our results showed that inhibiting Ang (1-7) does not mediate the sex difference in Tregs and Th17 in Sprague Dawley rats during Ang II infusion. Since both Th17 cells and Tregs have been implicated in BP control, sex differences in the T cell profile could contribute to sex differences in BP, although the mechanisms responsible for the sex differences in T cells remained unknown. Albeit, it is conceivable that the sex difference in the T cell profile seen during Ang II-hypertension may be through the indirect influence of sex differences in the innate system to modulate the adaptive immune response.



- **Thomas Cooper Woods, PhD**

*Assistant Professor,*

*Department of Physiology & Tulane Heart & Vascular Institute,*

*Tulane University School of Medicine,*

*New Orleans, LA.*

Dr. Cooper Woods, presented “Use of RNA-Seq to Identify the Molecular Mechanisms of Plaque Rupture,” at the July 23<sup>rd</sup>, 2015 THRCE Seminar.

**Summary:** Our limited understanding of the mechanisms involved in plaque rupture is a critical barrier to developing methodologies for the prevention of myocardial infarction and stroke. Stable plaques are characterized by a necrotic core with an overlying fibrous cap composed of vascular smooth muscle cells (VSMCs) in a collagen rich matrix. In vulnerable plaques, the fibrous cap has thinned,

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exhibiting fewer VSMCs, decreased collagen, and increased inflammatory cells. Plaque rupture occurs when the thin fibrous cap ruptures exposing the thrombogenic components of the necrotic core and resulting in atheroembolic events. As VSMCs are the primary source for collagen in the fibrous cap, loss of VSMCs, through decreased proliferation and increased apoptosis, plays a key role in the thinning of the fibrous cap and plaque destabilization.



- **Hongbing Liu, PhD**  
*Assistant Professor,  
Department of Biochemistry and  
Department of Pediatrics,  
Tulane University School of Medicine,  
New Orleans, LA.*

On July 30<sup>th</sup>, 2015, Dr. Liu presented “Histone Deacetylases 1 and 2 in Kidney Development.”

**Summary:** Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) are a major cause of morbidity in children, constituting approximately 20~30% of all anomalies identified in the prenatal period. CAKUT plays a causative role in 30~50% of cases of end stage renal disease (ESRD) in children, and predisposes to the development of hypertension and other renal-cardiovascular diseases in patients that survive to adolescence and adulthood. The long-term goal of our study is to uncover the epigenetic mechanisms accounting for CAKUT. Here, we investigate the nephric lineage-specific functions of class I histone deacetylases (HDACs), HDAC1 and HDAC2, in kidney development. HDACs are an evolutionarily conserved group of enzymes that remove acetyl groups from histones as well as non-histone proteins. A genetic model of conditional HDAC1/2 deletion in renal progenitor cells was used for the investigation of HDAC1 and 2 function in renal progenitor cells during kidney organogenesis. Mice bearing conditional null alleles of HDAC1 and HDAC2 were crossed to Six2-CreEGFP transgenic mice to delete HDAC1 and 2 genes, specifically in nephron progenitor cells (NPC, also known as cap mesenchyme cells). Our data revealed that mice with three or less deleted alleles for HDAC 1 and 2 live until adulthood with normal growth and development, whereas concurrent deletion of both HDAC1 and 2 resulted in early postnatal lethality. At birth, NPCHDAC1, 2-/- mice exhibit bilateral renal hypoplasia,

## Continued...

including small kidney size, decreased number of nephrons and formation of multiple cysts. Double deletion of HDAC 1 and HDAC2 in the NPC depletes the cap mesenchyme and blocks nephron formation at the renal vesicle stage, due to defective cell proliferation and repression of the HNF-Notch/Lhx1 pathways. We also found that NPCHDAC1,2-/- kidneys ectopic expression of Wnt4 which indicates that HDAC1/2 prevents premature differentiation of CM cells through inhibition of Wnt/  $\beta$ -catenin target genes, including Wnt4. Our study shows that Histone Deacetylases 1 and 2 are required for gene expression and the balance of self-renewal and differentiation of renal progenitor cells.



- **Zubaida Saifudeen, PhD**

*Associate Professor, Section of Nephrology,  
Department of Pediatrics,  
Adjunct Associate Professor of Physiology,  
Tulane Cancer Center Contributing Member: Genetics Program,  
Tulane University School of Medicine, New Orleans, LA.*

On August 13, **Dr. Saifudeen** presented a seminar titled “Metabolic Control of Nephron Progenitor Cell Renewal and Differentiation ”

**Summary:** Low nephron endowment results in hypertension and chronic kidney disease, both clinically significant diseases without a cure. Nephron progenitor cell (NPC) availability during kidney development is a major determinant of nephron number at birth. Critical questions that remain unanswered are what regulates NPC self-renewal, and how can this process be manipulated? Bioenergetic pathways have emerged as important regulators of cell fate. We hypothesized that young self-renewing NPC differ in metabolic profiles from older committed NPC. Using the Seahorse extracellular flux measurement system we show differences in metabolic profiles. Furthermore, pharmacological manipulation of metabolic pathways influences the self-renewal versus differentiation balance. Additionally, our data point to a metabolic defect as a possible contributor to the loss of self-renewal phenotype in p53-null NPC. Based on these data we conclude that maintenance of energy homeostasis in NPC is critical for a normal nephrogenesis program.

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- **Dulce Elena Casarini, PhD, FAHA.**  
*Department of Medicine, Nephrology Division,  
Oswaldo Ramos Foundation,  
Federal University of São Paulo,  
São Paulo, Brazil.*

Dr. Casarini was invited as a visiting Professor from the Federal University of São Paulo, Brazil and presented “Clinical Biomarkers” at the August 20<sup>th</sup> THRCE seminar.



- **Jing Chen, MD, MMSc, MSc.**  
*Associate Professor of Medicine,  
Department of Medicine,  
Division of Nephrology and Hypertension,  
Tulane University School of Medicine, New Orleans, LA.*

On August 27<sup>th</sup>, 2015 **Dr. Chen** presented “Biomarkers of Salt Sensitivity of Blood Pressure.”

**Summary:** About one-third of the world’s population has hypertension, which is the most important modifiable risk factor for stroke, coronary heart disease, congestive heart failure, peripheral vascular disease, and end-stage renal disease. Hypertension is also the leading preventable cause of total mortality worldwide. Salt sensitivity may play an important role in the etiology of hypertension and contribute to adverse outcomes among both hypertensive and normotensive individuals. Dr. Chen presented the current knowledge on the definition, prevalence, and evaluation of salt sensitivity of blood pressure. She presented the genetic findings in identifying salt sensitivity from the Genetic Epidemiology Network of Salt Sensitivity (GenSalt) Study and other studies, indicating that the renin-angiotensin system, sympathetic nervous system, and kallikrein-kinin system among others may play an important role in the etiology of salt sensitivity of blood pressure. She summarized potential biomarker approaches in identifying salt sensitivity. She also presented pilot study findings on the potential biomarkers in the sodium regulatory pathways in the kidneys, such as urinary angiotensinogen. The data suggest that identifying new biomarkers could help to further evaluate salt sensitivity as well as develop new pharmaceutical treatments for salt-sensitive hypertension.

## Recent Publications

(Includes publication omitted from previous newsletter edition)

**Adli M, Parlak M, Li Y, El-Dahr SS.** Epigenetic States of nephron progenitors and epithelial differentiation. *J Cell Biochem.* 2015 Jun;116(6):893-902. doi: 10.1002/jcb.25048. PMID: 25560433.

**Chi YW, Woods TC.** Clinical risk factors to predict deep venous thrombosis post-endovenous laser ablation of saphenous veins. *Phlebology.* 2014 Apr;29(3):150-3. doi: 10.1177/0268355512474254. PMID: 23434616.

**Dobrowolski L, Kuczeriszka M, Castillo A, Majid DS, Navar LG.** Role of atrial natriuretic peptide in mediating the blood pressure-independent natriuresis elicited by systemic inhibition of nitric oxide. *Pflugers Arch.* 2015 Apr; 467(4):833-41. PMID: 24953240. PMCID: PMC4276550.

**Gonzalez AA, Liu L, Lara LS, Bourgeois CR, Ibaceta-Gonzalez C, Salinas-Parra N, Gogulamudi VR, Seth DM, Prieto MC.** PKC $\alpha$ -dependent augmentation of cAMP and CREB phosphorylation mediates the angiotensin II stimulation of renin in the collecting duct. *Am J Physiol Renal Physiol.* 2015 Aug 12;ajprenal.00155.2015. doi: 10.1152/ajprenal.00155.2015. [Epub ahead of print]. PMID: 26268270.

**Kopkan L, Husková Z, Jichová Š, Červenková L, Červenka L, Saifudeen Z, El-Dahr SS.** Conditional knockout of collecting duct bradykinin B2 receptors exacerbates angiotensin II-induced hypertension during high salt intake. *Clin Exp Hypertens.* 2015 Aug 19;1-9. [Epub ahead of print]. PMID: 26151827.

**Lee BT, Ahmed FA, Hamm LL, Teran FJ, Chen CS, Liu Y, Shah K, Rifai N, Batuman V, Simon EE, He J, Chen J.** Association of C-reactive protein, tumor necrosis factor-alpha, and interleukin-6 with chronic kidney disease. *BMC Nephrol.* 2015 May 30;16:77. PMID: 26025192. PMCID: PMC4449580.

**Majid DS, Prieto MC, Navar LG.** Salt-Sensitive Hypertension: Perspectives on Intrarenal Mechanisms. *Curr Hypertens Rev.* 2015;11(1):38-48. PMID: 26028244.

**Rebholz, C. M., J. Chen, Q. Zhao, J. C. Chen, J. Li, J. Cao, L. Gabriel Navar, L. Lee Hamm, D. Gu, J. He and Group GenSalt Collaborative Research.** Urine Angiotensinogen and Salt-Sensitivity and Potassium-Sensitivity of Blood Pressure. *J Hypertens.* 2015 Jul;33(7):1394-400. PMID: 25827430.

**Satou R, Shao W, Navar LG.** Role of stimulated intrarenal angiotensinogen in hypertension. *Ther Adv Cardiovasc Dis.* 2015 Aug;9(4):181-90. doi: 10.1177/1753944715585512. PMID: 25987608/ PMCID: PMC4624278.

***From May through August, 2015 investigators and physicians affiliated with T.H.R.C.E. participated in many regional, national, & international meetings.***

***LA CaTS External Advisory Committee Meeting, Baton Rouge, LA, May 5, 2015***

- Daniel Lightell, Jr., Hernan A. Bazan, M.D., T. Cooper Woods, Ph.D., Plaque Destabilization through Shear Stress Mediated Changes in ncRNA.

***American Diabetes Association, Boston, MA, June 5-9, 2015***

- Woods, T. Cooper. Increased Atherosclerotic Plaque Formation in Response to Exosomes Derived From VSMCs Of Diabetic Origin

***Vascular Annual Meeting, Chicago, IL, June 17-20, 2015***

- Brooks, Ashton J. Differences in carotid plaque non-coding RNAs are also observed in serum: Potential utility as a biomarker of plaque rupture..

***Society for the Study of Ingestive Behavior, Denver CO, July 7-11, 2015***

- IJ Anwar, K Miyata, CL Enix, CA Nugent, SD Sagaser, AV Derbenev, A Zsombok. TRPV1 expressing hypothalamic neurons control glucose metabolism.

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

***Navar, L. Gabriel:***

- Keynote lecture on July 27 at the Summer Research Symposium of the West Virginia IDeA Network for Biomedical Research Excellence in Marshall University. The title of his talk was "Cardiovascular health, hypertension and kidney function."
- "The role of immunological memory in hypertension" at the Council on Hypertension 2015 Scientific Sessions, held in Washington, DC, in Sept. 2015.

***Pandey, Kailash N:***

- "Targeted disruption of Npr1 gene promotes the inflammatory process and exacerbates renal remodeling in null mutant mice" at the University of Arizona, Tucson, on April 10, 2015.
- Plenary Session Lecture, "Gene-targeting of natriuretic peptide receptor-A enhances the expression of RAAS components leading to inflammatory hypertensive heart disease," at the 20<sup>th</sup> World Congress on Heart Disease, International Academy of Cardiology, held in Vancouver, BC, Canada, in July 2015. He also chaired the session on "Cellular and molecular mechanisms of cardiovascular disease, basic research II at the same meeting on July 26, 2015.

***Saifudeen, Zubaida:***

- "Metabolic regulation of nephron progenitor self-renewal" at the Southwest Regional Society for Development Biology Meeting at UT-Southwestern, Dallas, Texas on October 4th.

***Woods, Thomas C:***

- "Plaque destabilization through shear stress mediated changes in ncRNA" at the LACaTS External Advisory Committee Meeting in Baton Rouge, LA on May 5, 2015.
- "Increased cardiovascular risk for patient with diabetes" at the Diabetes and Endocrine Disorders for the Generalist and Specialist Meeting held Saturday, September 26 at Xavier University in New Orleans.

***Zsombok, Andrea:***

- "Olanzapine reduces the excitability of DMV neurons, including a subset of stomach- and liver-related neurons" at the Annual meeting of Society for the Study of Ingestive Behavior, held in Denver CO on July 8, 2015. Other authors of the study are: IJ Anwar and K Miyata.

# Calendar of Events

## ***THRCE Seminars***

October 8, 2015	<b>HONG LU, MD, PHD</b> Associate Professor, Internal Medicine - Cardiology, CVRC - Core Faculty, Cardiovascular Research Center, University of Kentucky, College of Medicine, Lexington, KY. <i>"Angiotensinogen Has Unique Functions Independent of its Role on Generating Angiotensin II."</i>
October 12, 2015 **	<b>Joint Seminar: THRCE &amp; Department of Physiology</b> <b>GLENN M. TONEY, PHD, FAHA</b> Ashbel Smith Professor, Department of Physiology, University of Texas Health Science Center, San Antonio, TX. <i>"What the Brain Knows about Blood Pressure: Emerging Concepts."</i>
October 15, 2015 **	<b>Joint Seminar:</b> <b>THRCE, Department of Physiology, &amp; Diabetes Research</b> <b>ROBERT H. ECKEL, MD</b> <i>Charles A. Boettcher Endowed Chair in Atherosclerosis</i> <i>Professor of Medicine - Division of Endocrinology, Metabolism and Diabetes, and Cardiology,</i> <i>Professor of Physiology and Biophysics</i> <i>Program Director, Adult General Clinical Research Center</i> <i>University of Colorado, Anschutz Medical Campus, School of Medicine, Aurora, CO.</i> <i>"What's a Lipoprotein Processing Enzyme Doing in the Brain?"</i>
October 22, 2015	<b>HEE-WON PARK, PHD</b> Associate Professor, Dept. of Biochemistry & Molecular Biology, Tulane Cancer Center, Contributing Member in the Signaling & Clinical Programs, Tulane University School of Medicine, New Orleans, LA. <i>Seminar Cancelled &amp; Rescheduled to November 19, 2015</i>
November 5, 2015	<b>LYDIA BAZZANO, MD, PHD</b> Lynda B. and H. Leighton Steward Professor in Nutrition, Director, Center for Lifespan Epidemiology Research, Associate Professor of Epidemiology, Clinical Assistant Professor of Medicine, Department of Epidemiology, Tulane University School of Public Health & Tropical Medicine, New Orleans, LA. <i>"Postural Hand Tremor and Hypertension in Adults."</i>
November 19, 2015	<b>HEE-WON PARK, PHD</b> Associate Professor, Dept. of Biochemistry & Molecular Biology, Tulane Cancer Center, Contributing Member in the Signaling & Clinical Programs, Tulane University School of Medicine, New Orleans, LA. <i>"Structure-Based Search for Selective Inhibitors of Aldosterone Synthase."</i>
December 3, 2015	<b>NO MEETING</b> <i>Date conflicts with Tulane Center for Aging Seminar</i> <i>Speaker: Alan Parrish, PhD; Dept. of Physiology, University of Missouri Sch. of Medicine</i> <i>Topic: "Loss of Alpha-Catenin in the Aging Kidney: Role in Acute Kidney Injury"</i>
December 17, 2015	<b>CAMILO FERNÁNDEZ A., MD, MBA</b> <i>Medical Research Specialist, CV Diseases,</i> <i>Tulane Center for Cardiovascular Health,</i> <i>The Bogalusa Heart Study,</i> <i>Tulane University School of Medicine, New Orleans, LA.</i> <b>TBA</b>

***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.***

## 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 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:** 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:** Maintains and generates new breeding pairs, performs 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/core.cfm>

### T.H.R.C.E.

*Tulane Hypertension & Renal Center of Excellence (THRCE) will appreciate any support for the continual development of the center and its CORE Facilities, the publication of the THRCE newsletters, and the support of the THRCE bi-weekly seminars series. All donations to the center and its activities are considered tax-deductible.*

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*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 Senior Administrative Program Coordinator, Nina R. Majid, by e-mail at [htnctr@tulane.edu](mailto: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.*

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