

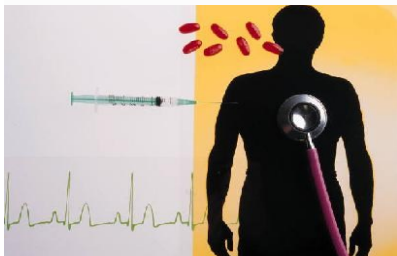


# THRCE

TULANE HYPERTENSION AND RENAL CENTER OF EXCELLENCE

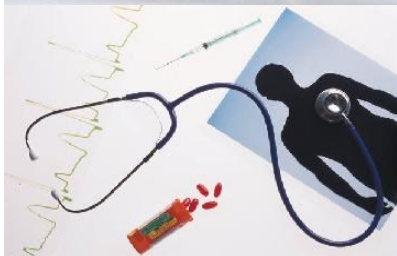
Spring 2015

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## 2015 WKD

To commemorate 2015 WKD, THRCE hosted a special WKD seminar by the renowned Dr. David G. Harrison, Professor of Medicine & Pharmacology at Vanderbilt University on March 12<sup>th</sup>, 2015. The title of the talk was, "Inflammation, Immunity and Hypertension." Dr. Harrison visited Tulane on March 11 & 12 and was invited by Dr. Navar to present the special WKD THRCE seminar and to be an Ad Hoc Committee member for the COBRE.



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## Grants, Honors & Recognition Awarded to THRCE Affiliated Investigators

The Department of Physiology was awarded the 2015 Owl Club's Outstanding Department Award. **Dr. Gabriel Navar**, Chairman, received the award on May 8, 2015.

**Dr. Norman Kreisman**, Director of the Medical Physiology Course accepted the 2015 Owl Club's T1 Course of the Year Award on May 8, 2015.

**Dr. Dewan SA Majid** was awarded an EB 2015 Travel Award at the 2015 American Physiological Society (APS) Experimental Biology (EB) meeting held in Boston, MA. The award was sponsored by the Brazilian Society of Physiology and Sociedad Chilena de Ciencias. Dr. Majid was invited to speak at the Symposium: Salt-sensitive Hypertension: The Brain or the Kidney to Blame.

**Dr. Jing Chen**, former COBRE Junior faculty Investigator and currently the Co-Director of the COBRE Clinical Core facility, received the Chairman's Award for Excellence in Research.

**Dr. Kailash N. Pandey** and **Dr. Andrei Derbenev** were both awarded the Bridge Fund Grants by Tulane University, Office of Research.

**Dr. Zsombok** was featured in the NewWave, News from Tulane University as a rising star in research who is "Unraveling the link between diabetes and the brain."

The paper by **Dr. Zubaida Saifudeen** and colleagues, "Preserving progenitor pools in the kidney: a balancing act" was featured on the "In this Issue" page of Vol. 142, Issue 7 of *Development*. "In this Issue" page features 4 or 5 papers from each issue. The aim of the feature is to highlight and explain the findings of each selected paper, and to make them accessible to all readers within the developmental biology community.

4/8/2015 Preserving progenitor pools in the kidney: a balancing act

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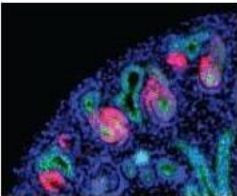
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**IN THIS ISSUE**

**Preserving progenitor pools in the kidney: a balancing act**

The nephrons are the filtration units of the kidney that excrete toxins, balance salt and water content in the blood and regulate blood pressure. Their number is determined during kidney development by the size of the nephron progenitor cell (NPC) pool, which exhausts in early postnatal life in mouse. Understanding the mechanisms that regulate the balance between NPC self-renewal and differentiation is a crucial endeavour. In this issue, two papers provide insights into the molecular cues controlling NPC self-renewal.



On p. 1228, Zubaida Saifudeen and colleagues report that the specific deletion of *p53* in mouse NPCs leads to hypoplastic kidneys, reduced nephron number and elevated blood pressure. *p53* is classically associated with restraining proliferation, but the observed phenotype suggests a positive role for *p53* in progenitor renewal: in mutants, NPC proliferation is reduced while senescence, apoptosis and the levels of known regulators of NPC survival remain unchanged. Furthermore, using functional genomics, the authors find that *p53* regulates factors involved in cell-matrix interactions and metabolism. They then show that mutants display aberrant ATP and reactive oxygen species levels in NPCs. Altogether, these results uncover an unexpected contribution of *p53* to NPC self-renewal capacity, energy metabolism and niche architecture.

## Continued...

### Dr. Alexis Gonzalez:

- Awarded the 2015 SSCI/AFMR Junior Faculty Travel Research Award for his study, "Angiotensin-II stimulates renin synthesis via calcium-dependent protein kinase C, cyclic AMP accumulation, and adenylate cyclase 6 activity in mouse renal collecting duct cells."
- As a former Postdoctoral Fellow at the Department of Physiology, visited Tulane on February 23<sup>rd</sup> and presented the Physiology Seminar, "Renin, (Pro)renin Receptor and Cyclooxygenase-2: A dynamic trio in the renal medulla for blood pressure regulation?"

### Dr. Cooper Woods:

- Received a LACaTS research grant for his study, "Plaque destabilization via shear stress and strain induced changes in NCRNA."
- Awarded the 2015 Owl Club's T1 Best Facilitator Award at the 2015 Ivy Day on May 8<sup>th</sup>.

### Awards presented to Graduate Students & Post-doctoral fellows:

- **Michael Cypress** (Mentor: Dr. Ryosuke Sato), received notification from the NIH/NIDDKD that he will be awarded the Predoctoral Fellowship Award.
- **Ryan Walker** (Mentor: Dr. K Hering-Smith) was awarded the Meritorious Research Travel Award from the Epithelial Transport Group during the APS at the 2015 EB meeting held in Boston, MA.

### 2015 SSCI/AFMR Meeting, New Orleans:

- **2015 SSPR/APA Trainee Travel Award Recipients:**
  - ◇ **Rengfang Song** ~ Mentor: Yosypiv IV
- **2015 SAFMR/SSCI Student Research Award Recipients:**
  - ◇ **Rupert Barshop** ~ Mentor: Dr. GS Berenson
  - ◇ **Tian Hu** ~ Mentor: Dr, LA Bazzano
  - ◇ **Ryan O'Leary** ~ Mentor: Dr. R Sato
  - ◇ **Badal Thakkar** ~ Mentor: Dr. GS Berenson
  - ◇ **Ryan Walker** ~ Mentor: Dr. K Hering-Smith
- **2015 SSPR Basic Science Young Investigator Award Finalist:**
  - ◇ **Jenny Ngo** ~ Mentor: Dr. Z Saifudeen
- **2015 SAFMR/SSCI Trainee Research Award Recipients:**
  - ◇ **Camilo Fernanez-Alonso** ~ Mentor: Berenson GS
  - ◇ **Venkateswara Reddy Gogulamadi** ~ Mentor: Dr. KN Pandey
  - ◇ **Indra Mani** ~ Mentor: Dr. KN Pandey
- **2015 SAFMR/SSCI Junior Faculty Research Travel Award Recipients:**
  - ◇ **Alex Gonzalez** ~ Mentor: Dr. MC Prieto.



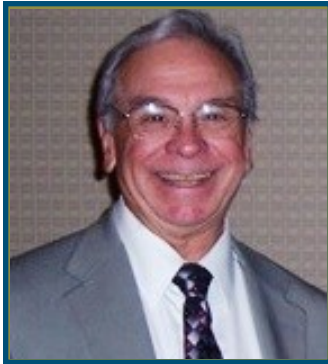
Ryan O'Leary at the 2015 SAFMR/SSCI

### 2015 Ivy Day, Tulane University School of Medicine, New Orleans:

- ◇ **Jennifer A. Wall**, Debakey Scholar, Mentor: Dr. KD Mitchell, was the recipient of the Hyman S. Mayerson Award
- ◇ **Christina I. Luffman**, Mentor: Dr. MC Prieto, was the recipient of the Nicholas R. DiLuzio Award.

## 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, 2015, the following speakers presented THRCE seminars:



- **L. Gabriel Navar, PhD**  
*Chair, Department of Physiology,*  
*Co-Director of THRCE,*  
*Director, Center of Biomedical Research*  
*Excellence in Hypertension & Renal Biology,*  
*Tulane University, School of Medicine, New Orleans, LA.*

On January 15<sup>th</sup> 2015 Dr. Gabriel Navar presented, “Translational Studies on Activation of the Intrarenal Renin-Angiotensin System in Type-1 Diabetes.”

Summary: Although previous studies indicate that the intrarenal renin-angiotensin system (RAS) is activated in Type-1 diabetes, there is very little direct evidence demonstrating that intrarenal angiotensin II is actually elevated in experimental animal models and human subjects. Studies in hypertension models have shown that the intrarenal activity of the renin-angiotensin system is reflected by the urinary angiotensinogen (uAGT) excretion rate, which is noninvasive and can be simply performed in human subjects. To evaluate the status of the renin-angiotensin system in diabetes, studies were performed measuring the uAGT in young patients with short duration diabetes mellitus (DM) and its relationships with Hb A1c and urinary isoprostanes. Blood and urine samples were collected from 80 young (15±1 years) patients with short duration Type-1 DM treated only with insulin and 40 control subjects. Serum glucose levels were 85±4 mg/dl in control subjects and 192±11 mg/dl in DM patients. Urinary Alb/Cre and uPro/Cre ratios were not significantly different in DM patients compared to control (8.6±.9 vs 9.7±.6 and 51±8 vs 62±14 mg/g). However, the uAGT/Cre ratios were significantly elevated in the DM patients (6.8±.8 vs 16.5±1.5). Correlation analysis demonstrated highly significant relationships (P<.0001) between uAGT/Cre and HbA1C (R=.44) and urinary 8-isoprostanes (R=.52) in the DM patients. These results indicate that,

## Continued...

even in young non-albuminuric patients with relatively short duration of DM, uAGT excretion rates are increased suggesting early activation of the intrarenal renin-angiotensin system, and are correlated with HbA1C and urinary isoprostane levels. Accordingly, uAGT levels may serve as an early marker of renal renin-angiotensin status potentially useful in monitoring clinical response to diabetes therapy.

*This study was supported by grants from NIH/NIDDK (R21DK094006) and NIH/NIGMS IDeA Program (COBRE, P30GM103337)  
Co-Authors include: Akemi Katsurada, Vivian A. Fonseca, Minolfa C. Prieto, Stuart Chalew, Ryosuke Sato, Hiroyuki Kobori.*



- **Patrick Burgess, MD**  
*Chief Medical Officer,  
MD Scientific LLC.,  
Charlotte, NC.*

Dr. Patrick Burgess presented, “New Findings from BOSS (Bicarbonate or Saline study)... A Reduced death related to bicarbonate administration prior to coronary contrast,” on January 29<sup>th</sup> 2015.

Summary: The BOSS trial was a phase 3 trial for the FDA comparing sodium bicarbonate with high dose saline pre- and post-contrast exposure to evaluate the effect on chronic kidney injury and death in subjects with advanced chronic kidney disease followed for 6 months after iodinated contrast exposure. The purpose of the trial was to establish a “new indication” for the use of isotonic sodium bicarbonate solution for the prevention of kidney injury. The findings of this trial revealed:

- ♦ A small difference in the degree of chronic kidney injury as measured by a sustained loss of eGFR or dialysis between the two cohort over 6 months,
- ♦ An incidence of acute kidney injury and dialysis that was substantially lower in both study cohorts compared to the predicted incidence of kidney injury and dialysis using published risk scoring methods (a post hoc finding),
- ♦ A surprising post-hoc finding of a highly significant death benefit in subjects undergoing coronary angiography, 67% reduction in death, p=0.018,
- ♦ A post-hoc finding of a 80% reduction in death at 6 months for those subjects undergoing coronary angioplasty.

A meta-analysis of bicarbonate vs saline studies published since the first

## Continued...

bicarbonate-CIN paper in 2004 reveals that bicarbonate appears to have benefit compared to saline although a high degree of heterogeneity is reported. The reduction in acute kidney injury also appears to be dose related, if the meta-analysis is performed based on administered dose. Studies that administered less than 1 mEq of sodium bicarbonate per kg showed no benefit for the prevention of acute kidney injury compared to saline.

A meta-analysis of reported mortality in these bicarbonate trials that reported only coronary angiography reveals a 50% reduction in death at one year in the bicarbonate treated subjects,  $p=0.003$  with no heterogeneity.

A single center study from Italy, using the previous year's data as control, reported a 60% reduction for in-hospital death ( $p=0.05$ ). The subjects of this study were all urgent angioplasty cases with no kidney function criteria for study inclusion... all subjects had a mean eGFR of 75.

Are the post-hoc findings of the BOSS trial lead generating or simply a finding of chance? That is the question and that will be the point of my discussion after review of the data that is summarized above.



- **Bysani Chandrasekar, DVM, PhD**  
*Professor, Heart & Vascular Institute*  
*Tulane University School of Medicine, New Orleans, LA.*

On February 12<sup>th</sup> 2015 Dr. Bysani Chandrasekar presented, "RECK and cardiovascular diseases."

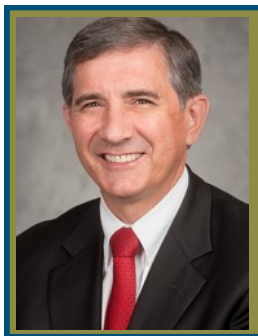
Summary: Hypertensive heart disease (HHD), a leading cause of heart failure (HF), is characterized by progressive cardiac hypertrophy, fibrosis, and dysfunction. Changes that include cytokine induction, growth factor expression, MMP activation, and extracellular matrix degradation and deposition contribute to cardiac hypertrophy and fibrosis (adverse cardiac remodeling), and promote transition from compensated hypertrophy to HF. Therefore, therapies that target hypertrophic and fibrotic mechanisms may effectively delay the natural progression of HHD.

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Reversion-inducing cysteine-rich protein with Kazal motifs (RECK) is a unique membrane-anchored protein that inhibits multiple mediators considered responsible for hypertrophy and fibrosis in the heart. Recently we reported that elevated angiotensin II (ANG II) suppresses RECK in mouse hearts and isolated cardiac fibroblasts. Similar results are obtained in endothelial cells and smooth muscle cells. In contrast, ANG II induces activation of MMPs 2, 7, 9 and 14 in the heart. These results suggest that loss of RECK might contribute causally to HHD development and progression. Therefore, sustaining RECK expression in the heart may inhibit chronic ANG II-induced adverse cardiac remodeling and dysfunction by suppressing the spatiotemporal expression of multiple pro-hypertrophic and pro-fibrotic pathways. To address our hypothesis, we are investigating whether RECK overexpression in an inducible cardiomyocyte-specific manner inhibits ANG II-induced myocardial hypertrophy, fibrosis and dysfunction. Since pharmacological agents that induce RECK expression are unavailable, we are investigating the efficacy of AAV9-mediated RECK overexpression in the heart on inhibition of ANG II-induced adverse cardiac remodeling and dysfunction. Using isolated cardiac cells, we will identify the molecular mechanisms involved in ANG II-induced RECK suppression and determine how RECK overexpression blunts ANG II-, mechanical stretch-, and CT-1-induced cardiomyocyte growth/death in vitro. Our goal is to (i) identify RECK as a critical anti-hypertrophic and anti-fibrotic factor, and (ii) demonstrate that its induction in the heart offers a novel therapeutic approach to blunt progression of adverse structural remodeling in HHD.

### 2015 MAYERSON-DILUZIO LECTURE

Jointly Sponsored by THRCE & the Department of Physiology



- **Walter F. Boron, MD, PhD**

*David N. & Inez Myers/Antonio Scarpa Professor & Chairman,  
Department of Physiology & Biophysics,  
Case Western Reserve University,  
School of Medicine, Cleveland, OH.*

On Monday, March 9<sup>th</sup> 2015 Dr. Walter Boron presented “Role of gas channels in the permeability of red blood cells to CO<sub>2</sub> and O<sub>2</sub>.”

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Summary: The traditional view (stemming the pioneering work of Mitchell, Graham, Wroblewski, and Overton beginning nearly two centuries ago) has been that all gases cross all membranes simply by dissolving in the membrane lipid. Two observations from our group are changing that perception. First, Waisbren et al (Nature, 1994) discovered the first membranes with negligible CO<sub>2</sub> permeability. Second, Nakhoul (Am J Physiol, 1998) demonstrated the first gas channel – which is in fact the water channel aquaporin 1 (AQP1) – by finding that the heterologous expression of human AQP1 in *Xenopus* oocytes accelerates the fall of intracellular pH (pHi) elicited by exposing the cell to CO<sub>2</sub>. We have now introduced a new approach for assessing the movements of gases that affect pH: we use a microelectrode to monitor the pH on the surface of an oocyte (pHS). The influx of CO<sub>2</sub> (which causes a sustained fall in pHi) causes a transient rise in pHS, the magnitude of which is proportional to CO<sub>2</sub> influx. Similarly, the influx of the weak base NH<sub>3</sub> causes a transient fall in pHS. We used this approach to study the CO<sub>2</sub>-vs-NH<sub>3</sub> selectivity of several AQPs as well as members of the Rh family. We find that each channel has a characteristic selectivity for CO<sub>2</sub> vs NH<sub>3</sub> – the first example of gas selectivity. Studies with inhibitor and point mutations suggest that CO<sub>2</sub> moves-predominantly or exclusively, depending up on the channel – through the central pore that is at the middle of AQP1 and AQP5 tetramers or Rh trimers.

In terms of physiological significance, renal proximal tubules reabsorb ~80% of all filtered HCO<sub>3</sub><sup>-</sup> by moving CO<sub>2</sub> across the apical membrane and then HCO<sub>3</sub><sup>-</sup> across the basolateral membrane. Apical AQP1 appears to be responsible for ~60% of the CO<sub>2</sub> uptake from lumen to cell. Moreover, we and others have shown that AQP1 and the Rh complex together account for ~90% of all CO<sub>2</sub> permeability in RBCs. Our most recent work indicates that the majority of O<sub>2</sub> transport across RBC membranes occurs through channels, with AQP1 and the Rh1 complex accounting for ~30% of the total. Thus, at least in certain cells that perform gas transport at high rates, gas channels appear to play important physiological roles. Looking to the future, it is easy to imagine how one might exploit channels to modulate gas transport both in health and disease. For example, one might create channels permeable to a single gas or develop drugs to block specific channels.



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**Special THRCE Seminar in honor of World Kidney Day (WKD)  
Jointly Sponsored by THRCE & the Department of Physiology**



- **David G. Harrison, MD**  
*Betty and Jack Bailey Professor of  
Medicine and Pharmacology,  
Director of Clinical Pharmacology,  
Vanderbilt University, Nashville, TN.*

March 12<sup>th</sup> 2015 was WKD. To commemorate 2015 WKD, THRCE and the Department of Physiology co-hosted a special seminar by the renowned Dr. David Harrison. The title of the talk was, "Inflammation, Immunity and Hypertension."

Summary: For more than 50 years, it has been recognized that immunity contributes to hypertension. Recent data from our laboratory and others have defined an important role of T cells and various T cell-derived cytokines in several models of experimental hypertension. These studies have shown that stimuli like angiotensin II, DOCA-salt and excessive catecholamines activate effector T cells that infiltrate the kidney and perivascular regions of both large arteries and arterioles. There is also accumulation of monocyte/macrophages in these regions. Cytokines released from these cells, including IL-17, IFN-g, TNF $\alpha$  and IL-6 promote both renal and vascular dysfunction and damage, leading to enhanced sodium retention and increased systemic vascular resistance. The renal effects of these cytokines remain to be fully defined, but include increased sodium reabsorption, glomerular damage and interstitial fibrosis. Very recent experiments have defined a link between oxidative stress and immune activation in hypertension. These have shown that hypertension is associated with formation of reactive oxygen species in dendritic cells that lead to formation of gamma ketoaldehydes, or isoketals. These rapidly adduct to protein lysines and are presented by dendritic cells as neoantigens that activate T cells and promote hypertension. Thus, cells of both the innate and adaptive immune system contribute to end-organ damage and dysfunction in hypertension. Therapeutic interventions to reduce activation of these cells may prove beneficial in reducing end-organ damage and preventing consequences of hypertension including myocardial infarction, heart failure, renal failure and stroke.

News



- **Nazih L Nakhoul, PhD**  
*Associate Professor,  
Departments of Medicine & Physiology,  
Tulane University School of Medicine, New Orleans, LA.*

On April 9<sup>th</sup> 2015 Dr. Nazih Nakhoul presented, "Rh Glycoproteins: Gas channels or the missing ammonium transporters?"

Summary: In mammals, acid-base homeostasis is critically dependent on renal production of  $\text{NH}_3/\text{NH}_4^+$  & excretion of  $\text{NH}_4^+$  in the urine. Renal ammoniogenesis and  $\text{NH}_4^+$  transport are highly regulated and  $\text{NH}_4^+$  excretion increases several folds during chronic acidosis. Whereas  $\text{NH}_3$  was previously assumed to mainly diffuse through the cell membrane,  $\text{NH}_4^+$  has to be transported by membrane transporters or channels. The apical membrane of collecting duct cells is one site where rate-limiting rapid  $\text{NH}_3$  diffusion has to occur. The basolateral membrane, on the other hand, is the site where  $\text{NH}_4^+$  transport occurs presumably by one or more membrane transporters. No specific  $\text{NH}_3/\text{NH}_4^+$  transporters are yet identified in the collecting duct.

The Rh glycoproteins belong to the SLC42 mammalian solute transporter family. Three members of this family are identified and cloned. RhAG is one component of the "Rh complex" in the red blood cell that is mostly known for its immunogenic characteristics. The other 2 members are Rhbg and Rhcg which are expressed in several tissues including kidney, liver and skin. In the kidney collecting duct Rhbg is expressed at the basolateral membrane of alpha intercalated cells whereas Rhcg is expressed at the apical membrane. Although thought to be involved in  $\text{NH}_3/\text{NH}_4^+$  transport the function of Rh proteins is not yet clear.

To study function of Rh proteins, we measured  $\text{NH}_3/\text{NH}_4^+$  transport by Rhbg and Rhcg expressed in *Xenopus* oocytes and compared it to  $\text{H}_2\text{O}$  injected oocytes. To assess transport we used ion-selective microelectrodes to measure ammonium- and methyl ammonium-induced intracellular pH ( $\text{pH}_i$ ), extracellular surface pH ( $\text{pH}_s$ ) and transmembrane current ( $I_m$ ) changes. In oocytes expressing Rhbg, 5mM  $\text{NH}_4\text{Cl}$  ( $\text{NH}_3/\text{NH}_4^+$ ) caused a decrease in  $\text{pH}_i$ , depolarization of the cell, decrease in  $\text{pH}_s$  and an inward current. On the other hand, 5 mM methyl ammonium hydrochloride

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(MA/MA<sup>+</sup>) caused an increase (not a decrease) in pHi, a decrease in pHs, depolarization of the cell and an inward current. In H<sub>2</sub>O-injected oocytes the changes were much smaller: 5 mM NH<sub>3</sub>/NH<sub>4</sub><sup>+</sup> caused a small and slow decrease in pHi, a small inward current, depolarized the cell and decreased pHs slightly. In H<sub>2</sub>O-injected oocytes MA/MA<sup>+</sup> did not elicit any change in pHi, pHs, V<sub>m</sub> or I<sub>m</sub>. Oocytes expressing Rhcg behaved similarly to H<sub>2</sub>O-injected oocytes except that NH<sub>3</sub>/NH<sub>4</sub><sup>+</sup> induced a significant sustained decrease in pHs. These data indicate that: 1) Rhbg transports NH<sub>4</sub><sup>+</sup> in an electrogenic manner; 2) Rhbg also transports NH<sub>3</sub>; 3) Rhcg is predominantly an NH<sub>3</sub> transporter. As such Rhbg and Rhcg can act in tandem to transport NH<sub>4</sub><sup>+</sup> at the basolateral membrane and NH<sub>3</sub> at the apical membrane of the renal collecting duct. It is a unique property that Rh proteins are able to transport both a gas (NH<sub>3</sub>) and an ion (NH<sub>4</sub><sup>+</sup>).



- **Kafait U. Malik, PhD**  
*Professor, Department of Pharmacology,  
 College of Medicine,  
 University of Tennessee, Health Science Center,  
 Memphis, TN.*

On April 23<sup>rd</sup> 2015 Dr. Kafait Malik presented, "Contribution of Cytochrome P450 1B1 to sex differences in the development of hypertension and its pathogenesis."

Summary: Hypertension is a major cause of cardiovascular disease, and studies in several animal models of hypertension, and epidemiological and clinical studies, have demonstrated a sexual dimorphism in the development of hypertension and cardiovascular disease. Men have a higher risk of developing hypertension than do premenopausal women of the same age. These sex differences in blood pressure (BP) control have been attributed to sex chromosomes and gonadal hormones. For example, angiotensin II (Ang II) a circulating and locally generated bioactive peptide increases BP to a greater degree in males than in females, and castration protects males, whereas ovariectomy prevents protection in female mice against Ang II-induced hypertension. However, the mechanism of opposite role of male and female sex hormones in humans and experimental models of hypertension is not known.

## Continued...

Our studies have shown that cytochrome P450 (CYP) 1B1 enzyme, which is highly expressed in extra-hepatic tissues including cardiovascular-renal system and can metabolize fatty acids, sex steroids and carcinogens, and generates oxidative stress contributes, to the development of Ang II and other models of experimental hypertension and associated pathogenesis and end organ damage in male rats and mice. Now, we have found that Ang II infusion increases plasma levels of CYP1B1-generated testosterone metabolite 6 $\beta$ -hydroxytestosterone (6 $\beta$ -OHT), in wild type (*Cyp1b1*<sup>+/+</sup>) but not CYP1B1 gene disrupted (*Cyp1b1*<sup>-/-</sup>) male mice. Moreover, Ang II-induced increase in systolic blood pressure and associated cardiac hypertrophy and fibrosis, renal dysfunction, increased oxidative stress and end organ damage that were minimized in male *Cyp1b1*<sup>-/-</sup> or castrated *Cyp1b1*<sup>+/+</sup> mice, were restored by treatment with 6 $\beta$ -OH. These data suggest that the testosterone metabolite, 6 $\beta$ -OH, contributes to Ang II-induced hypertension and associated cardiac pathogenesis in male mice. Moreover, cytochrome P450 1B1 could serve as a novel target for developing agents for treating renin-angiotensin and testosterone-dependent hypertension and associated pathogenesis in males.

CYP1B1 has a high affinity for estrogen, and estrogen and its metabolites exert both pro- and anti- proliferative effects. Therefore, we investigated the contribution of CYP1B1, estrogen, and its metabolites in the development of Ang II-induced hypertension in female *Cyp1b1*<sup>+/+</sup> and *Cyp1b1*<sup>-/-</sup> mice. Interestingly, in contrast to male mice, Ang II infusion increased systolic blood pressure to a greater degree in *Cyp1b1*<sup>-/-</sup> than in *Cyp1b1*<sup>+/+</sup> mice, and also in *Cyp1b1*<sup>+/+</sup> female mice treated with CYP1B1 inhibitor, 2,4,3 $\epsilon$ 5 $\epsilon$ -tetramethoxystilbene (TMS, 300  $\mu$ g/kg, every 3<sup>rd</sup> day, i.p.), for 2 weeks or in ovariectomized mice. Also Ang II produced cardiac fibrosis, renal dysfunction, oxidative stress and end organ damage in *Cyp1b1*<sup>-/-</sup> but not *Cyp1b1*<sup>+/+</sup> female mice, that were minimized by estradiol metabolite and 2-methoxy estradiol (2MeE) generated by catechol-O-methyltransferase from 2-hydroxyestradiol, the CYP1B1 generated estradiol metabolite. These data suggest that CYP1B1 derived estradiol metabolites 2-MeE2 could be effective in treating hypertension and associated cardiovascular pathophysiology in women with reduced estrogen or increased testosterone levels (polycystic ovary syndrome). Moreover, agents that inhibit CYP1B1 activity could be detrimental to the cardiovascular system, and could cause hypertension and associated pathogenesis in females.

## Recent Publications: From January through April 2015

# Publications

**Adli M, Parlak M, Li Y, El-Dahr S.** Epigenetic States of Nephron Progenitors and Epithelial Differentiation. *J Cell Biochem.* 2015 Jan 5. doi: 10.1002/jcb.25048. [Epub ahead of print] PMID: 25560433.

**Anderson AH, Yang W, Townsend RR, Pan Q, Chertow GM, Kusek JW, Charleston J, He J, Kallem R, Lash JP, Miller ER 3rd, Rahman M, Steigerwalt S, Weir M, Wright JT Jr, Feldman HI; Chronic Renal Insufficiency Cohort Study Investigators.** Time-updated systolic blood pressure and the progression of chronic kidney disease: a cohort study. *Ann Intern Med.* 2015 Feb 17;162(4):258-65. doi: 10.7326/M14-0488. PMID: 25686166, PMCID: PMC4404622

**Chen S, Yao X, Li Y, Saifudeen Z, Bachvarov D, El-Dahr SS.** Histone deacetylase 1 and 2 regulate Wnt and p53 pathways in the ureteric bud epithelium. *Development.* 2015 Mar 15;142(6):1180-92. doi: 10.1242/dev.113506. PMID: 25758227, PMCID: PMC4360175.

**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. Epub 2013 May 6. PMID: 23434616.

**Cuevas CA, Gonzalez AA, Inestrosa NC, Vio CP, Prieto MC.** Angiotensin II increases fibronectin and collagen I through the  $\beta$ -catenin-dependent signaling in mouse collecting duct cells. *Am J Physiol Renal Physiol.* 2015 Feb 15;308(4):F358-65. doi: 10.1152/ajprenal.00429.2014. Epub 2014 Nov 19. PMID: 25411386. PMCID: PMC432949.

**Feng W, Chumley P, Prieto MC, Miyada K, Seth DM, Fatima H, Hua P, Rezonzew G, Sanders PW, Jaimes EA.** Transcription factor avian erythroblastosis virus e26 oncogen homolog-1 is a novel mediator of renal injury in salt-sensitive hypertension. *Hypertension.* 2015 Apr;65(4):813-20. doi: 10.1161/HYPERTENSIONAHA.114.04533. Epub 2015 Jan 26. PMID: 25624342.

**Giani JF, Janjulia T, Kamat N, Seth DM, Blackwell WL, Shah KH, Shen XZ, Fuchs S, Delpire E, Toblli JE, Bernstein KE, McDonough AA, Gonzalez-Villalobos RA.** Renal angiotensin-converting enzyme is essential for the hypertension induced by nitric oxide synthesis inhibition. *J Am Soc Nephrol.* 2014 Dec;25(12):2752-63. doi: 10.1681/ASN.2013091030. Epub 2014 Jul 10. PMID: 25012170/ PMCID: PMC4243348.

**Gonzalez AA, Prieto MC.** Renin and the (pro)renin receptor in the renal collecting duct: Role in the pathogenesis of hypertension. *Clin Exp Pharmacol Physiol.* 2015 Jan;42(1):14-21. PMID: 25371190.

**Gonzalez AA, Prieto MC.** Roles of collecting duct renin and (pro)renin receptor in hypertension: mini review. *Ther Adv Cardiovasc Dis.* 2015 Mar 16. pii: 1753944715574817. PMID: 25780059.

**Gonzalez AA, Womack JP, Liu L, Seth DM, Prieto MC.** Angiotensin II increases the expression of (pro)renin receptor during low-salt conditions. *Am J Med Sci.* 2014 Nov;348(5):416-22. PMID: 25250989.

**Kassan M, Choi SK, Galán M, Trebak M, Belmadani S, Matrougui K.** Nuclear factor kappa B inhibition improves conductance artery function in type 2 diabetic mice. *Diabetes Metab Res Rev.* 2015 Jan;31(1):39-49. doi: 10.1002/dmrr.2542. PMID: 24652705.

## Recent Publications: From January through April 2015

**Li W, Sullivan MN, Zhang S, Worker CJ, Xiong Z, Speth RC, Feng Y.** Intracerebroventricular infusion of the (Pro)renin receptor antagonist PRO20 attenuates deoxycorticosterone acetate-salt-induced hypertension. *Hypertension*. 2015 Feb;65(2):352-61. PMID: 25421983.

**Li Y, Liu J, Li W, Brown A, Baddoo M, Li M, Carroll T, Oxburgh L, Feng Y, Saifudeen Z.** p53 enables metabolic fitness and self-renewal of nephron progenitor cells. *Development*. 2015 Apr 1;142(7):1228-41. doi: 10.1242/dev.111617. PMID: 25804735, PMCID: PMC4378244.

**Majid DS, Prieto MC, Navar LG.** Salt-Sensitive Hypertension: Perspectives on Intrarenal Mechanisms. *Curr Hypertens Rev*. 2015 May 30. [Epub ahead of print]. PMID: 26028244.

**Satou R, Shao W, Navar LG.** Role of stimulated intrarenal angiotensinogen in hypertension. *Ther Adv Cardiovasc Dis*. 2015 May 18. pii: 1753944715585512. [Epub ahead of print] Review. PMID: 25987608.

**Sukhanov S, Snarski P, Vaughn C, Lobelle-Rich P, Kim C, Higashi Y, Shai SY, Delafontaine P.** Insulin-like growth factor I reduces lipid oxidation and foam cell formation via downregulation of 12/ 15-lipoxygenase. *Atherosclerosis*. 2015 Feb;238(2):313-20. PMID: 25549319/ PMCID: PMC4298481.

**Wilson FP, Xie D, Anderson AH, Leonard MB, Reese PP, Delafontaine P, Horwitz E, Kallem R, Navaneethan S, Ojo A, Porter AC, Sondheimer JH, Sweeney HL, Townsend RR, Feldman HI; CRIC Study Investigators.** Urinary creatinine excretion, bioelectrical impedance analysis, and clinical outcomes in patients with CKD: the CRIC study. *Clin J Am Soc Nephrol*. 2014 Dec 5;9(12):2095-103. PMID: 25381342/ PMCID: PMC4255402.



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

***18<sup>th</sup> Meeting of the Southeast Ultrafast Conference, Tallahassee, FL, January 15-16, 2015***

- **Trimmer E, Alexander B, Barnes H, Mostany R.** Dendritic spine dynamics in the barrel cortex across the estrous cycle in female mice.
- **Voglewede R, Allen M, Mostany R.** Dendritic spine turnover within the mouse primary somatosensory barrel cortex following sensory manipulation.

***12<sup>th</sup> Annual Advanced Imaging Methods Workshop, Berkeley, CA, February 4-6, 2015***

- **Voglewede R, Allen M, Mostany R.** Dendritic spine turnover within the mouse primary somatosensory barrel cortex following sensory manipulation.

***Southern Regional Meeting, NO, LA; Feb. 26-28, 2015***

- **Barshop RP, Fernandez-Alonso C, Chen W, Srinivasan SR, Berenson GS.** Measures of obesity and oxidative stress: The Bogalusa Heart Study. Abstract 4, P. 11/281.
- **Baskind H, Morava-Koziecz E, Andersson H, Yosypiv IV.** Pediatric patient with severe hypertension and multiorgan vascular aneurysms. Abstract 544, P. 51/321.
- **Cantu MS, Kidd L, Singh D, Yosypiv IV.** Acute kidney injury and hypertensive emergency in a patient with class V lupus nephritis. Abstract 20, P. 14/284.
- **Delafontaine P.** Mechanisms of cachexia in chronic disease states. Symposium Talk.
- **Fernandez-Alonso C, Barshop RP, Sun D, Li S, Chen W, Berenson GS.** Inflammation and arterial compliance: A paradox? The Bogalusa Heart Study. (SAFMR/SSCI Trainee Research Travel Award Winner) (SSCI), Abstract 364, P. 38/308.
- **Gogulamudi V, Subramanian U, Pandey KN.** Effect of rapamycin on the expression of T Regulatory cells in guanylyl cyclase/natriuretic peptide receptor-A gene-knockout mice. (SAFMR/SSCI Trainee Research Travel Award Winner) Abstract 442, P. 43/313.
- **Gonzalez AA, Liu L, Bourgeois CR, Ibaceta C, Prieto MC.** Angiotensin II stimulates renin synthesis via calcium-dependent protein kinase C, cyclic AMP accumulation & Adenylate cyclase 6 activity in mouse renal collecting duct cells. (SAFMR/SSCI Junior Faculty Research Travel Award Winner), Abstract 441, P. 43/313.

## Continued...

- **Gonzales H, Sander GE.** Hypertensive crisis: The causative effects of non-steroidal anti-inflammatory drugs (NSAIDS). Abstract 448, P. 44/314.
- **Hering-Smith K, Coleman-Barnett J, Huang W, Hamm LL.** Role of NADC1 in control of urinary excretion of  $\alpha$ -ketoglutarate. Abstract 440, P. 43/313.
- **Hering-Smith K, Huang W, Coleman-Barnett J, Hamm LL.** Citrate transport in NADC1 Knockout mice. Abstract 536, P. 51/321.
- **Hu T, Bertisch S, Chen W, Harville E, Redline S, Bazzano L.** Duration of childhood obesity and relation to middle-age obstructive sleep apnea risk: The Bogalusa Heart Study. Abstract 523, P. 50/320.
- **Hu T, Stuchlik P, Yao L, Reynolds K, Whelton P, He J, Bazzano L.** Adherence to low carb and low fat diets in relation to weight loss and cardiovascular risk factor reduction. Abstract 524, P. 50/320.
- **Hu T, Bertisch S, Chen W, Harville E, Redline S, Bazzano L.** Risk if sleep apnea and subclinical cardiovascular disease in young-to-middle aged adults: The Bogalusa Heart Study. Abstract 454, P. 45/315.
- **Khan A, Teran F, Rathmell KA, Hering-Smith K, Alzoubi M, Simon EE, Batuman V.** Pathogenesis of Contrast-induced nephropathy in diabetics and exploring new therapeutics. (SAFMR/SSCI Junior Faculty Research Travel Award Winner) (SSCI). Abstract 546, P. 51/321.
- **Mani I, Pandey KN.** Visualization of internalization and intracellular trafficking of gunalyl cyclase/natriuretic peptide receptor-A with concurrent generation of CGMP. (SAFMR/SSCI Trainee Research Travel Award Winner) (SAFMR, SAFMR), Abstract 360, P. 38/308.
- **Mirani G, McNaughton J, Yosypiv IV, Schmeig JJ, Robinson J.** Persistent fevers in an 18-year old renal transplant recipient. Abstract 18, P. 14/284.
- **Ngo J, Li Y, Chen S, Yao X, Liu J, Saifudeen Z, El-Dahr S.** Deficiency of H3K79 methyltransferase DOT1L in nephron progenitor cells causes renal hypo-dysplasia. (SSPR Basic Science Young Investigator Award Finalist) Abstract 328, P. 34/304.
- **Ngo J, Li Y, Chen S, Yao X, Liu J, Saifudeen Z, El-Dahr S.** Deficiency of H3K79 methyltransferase DOT1L in nephron progenitor cells causes renal hypo-dysplasia. (SSPR Basic Science Young Investigator Award Finalist) Abstract 443, P. 43/313.
- **O'Leary R, Miyata K, Sato R.** A JAK/STAT pathway mediates activated macrophage-induced angiotensinogen augmentation in renal proximal tubular cells. (SAFMR/SSCI Student Research Travel Award Winner) Abstract 540, P. 51/321.
- **Song R, Preston G, Yosypiv IV.** RET is a direct positively regulated target of angiotensin II (ANG II) in the ureteric bud. (SSPR/APA Trainee Travel Award Winner) (SSPR). Abstract 538, P. 51/321. *Invited Talk/Oral presentation.*



*Continued...*

- **Syed SZ, Siriki R, Kidd L, Teran F, Simon EE.** Minimal change disease in systemic lulus erythematosis. Abstract 318, P. 29/299.
- **Thakkar BG, Fernandez C, Chen W, Srinivasan SR, Berenson GS.** Serum phosphorus is associated with cystatin C in whites but not in blacks: The Bogalusa Heart Study. (SAFMR/SSCI Student Research Travel Award Winner), Abstract 367, P. 38/308.
- **Walker RW, Coleman-Barnett J, Hamm LL, Hering-Smith K.** Regulation of novel calcium-sensitive dicarboxylate transport by CASR signaling. (SAFMR/SSCI Student Research Travel Award Winner) Abstract 444, P. 43/313.

*Health Sciences Research Days, Tulane, NO, LA; March 25-26, 2015*

- **Alexander B, Trimmer E, Barnes H, Mostany R.** Dendritic spine dynamics in the barrel cortex across the estrous cycle in female mice.
- **Anwar I, Zsombok A.** Olanzapine reduces neuronal activity in the dorsal motor nucleus of the vagus. C33.
- **Bourgeois C, Prieto MC.** Epigenetic factors determine sex differences in intrarenal Angiotensinogen (AGT): A novel role of histone deacetylase 9 (HDAC-9) as a repressor of intrarenal AGT to explain sex disparities in hypertension. A1
- **Cypress M, Sato R.** Upregulation of Angiotensinogen in S1 Proximal tubular cells by high glucose. A27.
- **Davidson AM, Mostany R.** Long-term, in vivo imaging of motor task-associated changes in cortical connectivity in layer v pyramidal neurons.
- **Kashyap SN, Lindsey SH.** G Protein-Coupled Estrogen Receptor Activation Attenuates Rat Aortic Smooth Muscle Cell Proliferation.
- **Enix CL, Nugent CA, Satou R, Katsurada A, Zsombok A.** Identification of TRPV1 expressing neurons in the hypothalamus.
- **Gao H, Derbenev AV.** Leptin inhibits presympathetic neurons in the rostral ventrolateral medulla. C34.
- **Jiang Y.** Leptin regulates synaptic activity of brown adipose tissue-related pre-sympathetic neurons in the paraventricular nucleus of the mice. C37.
- **Kashyap SN, Lindsey SH.** G Protein-Coupled Estrogen Receptor Activation Attenuates Rat Aortic Smooth Muscle Cell Proliferation.
- **Zimmerman MA, Kashyap SN, Trimmer EH, Daniel JM, Lindsey SH.** Midlife Ovariectomy Increases Blood Pressure in Long Evans Rats and is Attenuated by Transient or Continuous Estradiol Treatment.

## Continued...

- **Murphy B, Liu L, Kashyap S, Budish RA, Trimmer EH, Zimmerman MA, Miller K, Chappell MC, Lindsey SH.** Activation of the G protein-coupled estrogen receptor ameliorates salt-induced vascular remodeling.
- **Liu J, El-Dahr SS, Saifudeen Z.** Comparison of SORAFENIB-loaded PLGA and liposome nanoparticles in the in vitro treatment of renal cell carcinoma.
- **Majid DS, Derbenev AV.** Effects of high salt diet on renal presympathetic neuron activity. C31.
- **Mani I, Pandey KN.** The role of FQQI motif in the internalization and subcellular trafficking of Guanylyl-Cyclase/Natriuretic peptide receptor-A in cultured mouse mesangial cells. A23.
- **Murphy B, Liu L, Kashyap S, Budish RA, Trimmer EH, Zimmerman MA, Miller K, Chappell MC, Lindsey SH.** Activation of the G protein-coupled estrogen receptor ameliorates salt-induced vascular remodeling.
- **Nakhoul H.** Genomic and transcriptomic analysis of Epstein-Barr virus in lymphoid malignancies. C23.
- **Ngo J, Li Y, Chen S, Yao X, Liu J, Saifudeen Z, El-Dahr S.** Deficiency of H3K79 methyltransferase DOT1L in nephron progenitor cells causes renal hypo-dysplasia. A31
- **Song R, Yosypiv IV.** RET is a direct positively regulated target of angiotensin II (ANG II) in the ureteric bud (UB). D29.
- **Trimmer EH, Jupiter R, Kadowitz PA, Lindsey SH.** Bisphenol A works via GPER to induce detrimental cardiovascular effects.
- **Zimmerman MA, Kashyap SN, Trimmer EH, Daniel JM, Lindsey SH.** Midlife Ovariectomy Increases Blood Pressure in Long Evans Rats and is Attenuated by Transient or Continuous Estradiol Treatment.

### *EB Meeting, Boston, MA, March 28 - April 1, 2015*

- **Abdounour-Nakhoul S, Tu C-L, Que J, Islam MT, Brown K, Nakhoul NL.** Calcium sensing receptor deletion in the mouse esophagus alters the expression of cell-cell junctional proteins. P. 426, B585/998.7.
- **Ali A, Li W, Sullivan MN, Feng Y.** Neuron-specific (Pro)renin receptor deletion regulates renin-angiotensin components and contributes to the amelioration of DOCA-Salt hypertension. P. 237, B279/652.21
- **Anwar IJ, Miyata K, Zsombok A.** Olanzapine reduces neuronal activity in the dorsal motor nucleus of the vagus. P. 420, B439/985.2.
- **Azimi MS, Strong AL, Phamduy TB, Chrisey DB, Bunnell BA, Murfee WL.** Tracking human adipose-derived stem cells in an ex-vivo microvascular network model. P. 313, B37/790.2.

- **Cuevas CA, Gonzalez AA, Inestrosa NC, Vio CP, Prieto MC.** The activation of the (pro)renin receptor stimulates fibrotic factors expression independent of B-Catenin signaling pathway in collecting duct cells. P. 414, B279/971.5.
- **Derbenev AV.** Synaptic and extrasynaptic regulation of RVLM neurons: What is behind the scenes? Chaired & presented at the Symposium: Brainstem mechanisms underlying cardiorespiratory signaling: From synapsis to circuits. P. 103, S315
- **Feng Y.** CNS regulation of blood pressure via the pro-renin receptor. Invited talk, Symposium: CNS mechanisms of blood pressure regulation. P. 147, S451
- **Feng Y.** Neuron-specific (Pro)renin receptor deletion regulates renin-angiotensin components and contributes to the amelioration of DOCA-Salt hypertension. Invited talk, Symposium: Cell Signaling. P. 32, S69
- **Gao H, Muenzberg H, Derbenev AV.** Leptin Inhibits Presympathetic Neurons in the Rostral Ventrolateral Medulla. P. 332, B460/830.7.
- **Gogulamudi VR, Subramanian U, Mani I, Pandey KN.** Increased renal expression of toll-like receptor-4 in guanylyl/natriuretic peptide receptor-A gene-disrupted female mice. P. 263, A32/710.22.
- **Gonzalez AA, Cifuentes F, Ibaceta C, Zamora L, Prieto MC.** Vasopressin Type-2 receptor activation increases renin expression in mouse renal collecting duct cells through cAMP/PKA/CREB pathway. P. 324, B279/812.2.
- **Gonzalez AA.** Renin expression in kidney collecting ducts during hypertension: Is it contributing to sodium reabsorption? Invited talk, Symposium: Salt-sensitive hypertension: The brain or the kidney to blame. P. 165, S521.
- **Haney NM, Mitchell KD.** Acute blockade of PDGF receptors decreases arterial blood pressure and renal vascular resistance in Cyp1a1-Ren2 transgenic rats with angiotensin II-dependent malignant hypertension. P. 408, B156/960.1.
- **Jiang Y, Munzberg H, Derbenev AV, Zsombok A.** Leptin regulates synaptic activity of brown adipose tissue-related pre-sympathetic neurons in the paraventricular nucleus of the mice. P. 451, W280/1057.1.
- **Kashyap SN, Lindsey SH.** G Protein-Coupled Estrogen Receptor Activation Attenuates Rat Aortic Smooth Muscle Cell Proliferation. P. 411, B220/966.4
- **Kumar P, Pandey KN.** DNA methylation inhibitor regulates guanylyl cyclase/natriuretic peptide receptor-A gene expression in mesangial cells. P. 355, A82/880.25.
- **Li W, Sullivan MN, Feng Y.** Trimethylation of histone 3 lysine 4 on hypothalamic (pro)renin receptor mediates the development of DOCA-Salt hypertension. P. 419, B419/984.2
- **Lindsey SH.** Protein-Coupled Estrogen Receptor Activation Attenuates Rat Aortic

Smooth Muscle Cell Proliferation. Invited talk, Symposium: The heart of the matter: Menopause, sex steroids, and cardiovascular disease. P. 64, S175.

- **Majid DSA.** Salt sensitive hypertension: perspectives on the renal mechanisms. Invited talk, Symposium: Salt-sensitive hypertension: The brain or the kidney to blame. P. 165, S521.
- **Majid DSA, Kadowitz PJ, Castillo A.** Hypersensitive and renal injury responses in nitric oxide deficiency are unaffected by tyrosine kinase inhibition in mice. P. 408, B163/960.8.
- **Mani I, Pandey KN.** FQOI Motif in the c-terminus of guanylyl-cyclase/natriuretic peptide receptor-A mediates intracellular trafficking in mouse mesangial cells. P. 193, A409/574.24.
- **Mukerjee S, Sriramula S, Zsombok A, Lazartigues E.** Increased ADAM17 expression in ACE2 knockout mice is associated with increased excitability of paraventricular nucleus pre-sympathetic neurons. P. 420, B433/984.16.
- **Nakhoul NL, El-Dahr S, Brown K, Islam MT, Khan A, Hering-Smith K, Hamm LL, Abdounour-Nakhoul S.** A potential role of histone methyltransferase, Dot1L, in renal regulation of acid-based balance. P. 244, B456/666.29.
- **Satou R.** Activated JAK-STAT pathway by IL-6 mediates macrophage-induced angiotensinogen augmentation in renal proximal tubular cells. Invited talk, Symposium: Immune cells, the kidney and hypertension. P. 66, S180.
- **Satou R, Katsurada A, Miyata K, Kobori H, Navar LG.** Intact angiotensinogen consists of oxidized and reduced conformation in rodent plasma. P. 324, B283/812.6.
- **Satou R, O'Leary R, Miyata K, Navar LG.** Activated JAK-STAT pathway by IL-6 mediates macrophage-induced angiotensinogen augmentation in renal proximal tubular cells. P. 244, B460/667.4.
- **Sloas DC, Stewart SA, Sweat RS, Murfee WL.** Comparison of network resistances in aged versus adult microvascular networks. P. 312, B7/786.7.
- **Stewart SA, Sloas DC, Murfee WL.** Estimation of pressure drop required for lymph flow through initial collecting lymphatics. P. 228, B65/633.2.
- **Sullivan MN, Robinson JJ, Li W, Feng Y, Early S.** Endothelial cells TRPA1 channel activity delays the onset of hypertension-associated hemorrhagic stroke. P. 315, B66/795.3
- **Sweat RS, Azimi MS, Murfee WL.** Lysophosphatidic acid stimulation does not induce a lymphatic identity along blood vessels in intact microvascular networks ex-vivo. P. 227, B36/630.9.
- **Yeh AY, Satou R.** Internalized angiotensinogen is secreted to the apical side in renal proximal tubular cells. P. 408, B160/960.5.

## *Continued...*

- Zimmerman MA, Kashyap SN, Trimmer EH, Daniel JM, Lindsey SH. Midlife Ovariectomy Increases Blood Pressure in Long Evans Rats and is Attenuated by Transient or Continuous Estradiol Treatment. P. 223, D119/623.7.
- Zsombok A. Central TRPV1 and regulation of glucose metabolism. Invited talk, Symposium: Hypothalamic autonomic control of metabolism. P. 105, S 319.

### *9<sup>th</sup> Organization for the Study of Sex Differences meeting, Stanford University, Palo Alto, CA, April 21-24, 2015*

- Bourgeois CRT, Satou R, Prieto MC. Epigenetic role histone deacetylase 9 (HDAC-9) as a repressor of intrarenal angiotensinogen (AGT): A novel mechanism to explain sex disparities in hypertension.

### *Society for Pediatric Research, San Diego, CA; April 24-28, 2015*

- Li Y, Ngo J, Saifudeen Z, Lopez M, El-Dahr SS. Genetic deletion of the H3K79 methyltransferase, Dot1L, from nephron stem cells causes renal hypo-dysplasia.

### *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

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

**L. Gabriel Navar, PhD:**

- Presented the THRCE Conference, “Translational Studies on Activation of the Intrarenal Renin-Angiotensin System in Type 1 Diabetes Mellitus” on January 15, 2015.

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

- Presented, “Salt sensitive hypertension: perspectives on the renal mechanisms” during the 2015 EB meeting on April 1<sup>st</sup>, 2015. The sponsor was the Brazilian Society of Physiology and Sociedad Chilena de Ciencias Fisiologicas and the symposium, “Salt-sensitive Hypertension: The Brain or the Kidney to Blame.”

**Kailash N. Pandey, PhD:**

- Presented a talk at the University of Arizona, Tucson, on April 10, 2015. The title of his talk was “Targeted disruption of Npr1 gene promotes the inflammatory process and exacerbates renal remodeling in null mutant mice.”

**Invited talks at 2015 EB Meeting:**

- Derbenev AV. Synaptic and extrasynaptic regulation of RVLM neurons: What is behind the scenes? Chaired & presented at the Symposium: Brainstem mechanisms underlying cardiorespiratory signaling: From synapsis to circuits.
- Feng Y. CNS regulation of blood pressure via the pro-renin receptor. Invited talk, Symposium: CNS mechanisms of blood pressure regulation.
- Feng Y. Neuron-specific (Pro)renin receptor deletion regulates renin-angiotensin components and contributes to the amelioration of DOCA-Salt hypertension. Invited talk, Symposium: Cell Signaling.
- Gonzalez AA. Renin expression in kidney collecting ducts during hypertension: Is it contributing to sodium reabsorption? Invited talk, Symposium: Salt-sensitive hypertension: The brain or the kidney to blame.
- Lindsey SH. Protein-Coupled Estrogen Receptor Activation Attenuates Rat Aortic Smooth Muscle Cell Proliferation. Invited talk, Symposium: The heart of the matter: menopause, sex steroids, and cardiovascular disease.
- Majid DSA. Salt sensitive hypertension: perspectives on the renal mechanisms. Invited talk, Symposium: Salt-sensitive hypertension: The brain or the kidney to blame.
- Satou R. Activated JAK-STAT pathway by IL-6 mediates macrophage-induced angiotensinogen augmentation in renal proximal tubular cells. Invited talk, Symposium: Immune cells, the kidney and hypertension.
- Zsombok A. Central TRPV1 and regulation of glucose metabolism. Invited talk, Symposium: Hypothalamic autonomic control of metabolism.

## THRCE Seminars

April 9, 2015

**NAZIH L NAKHOUL, PHD**

Associate Professor, Departments of Medicine & Physiology,  
Tulane University School of Medicine, New Orleans, LA.

*"Rh Glycoproteins: Gas channels or the missing ammonium transporters?"*

April 23

**KAFAIT U. MALIK, PHD**

Professor, Department of Pharmacology,  
College of Medicine,

University of Tennessee Health Science Center, Memphis, TN.

*"Contribution of Cytochrome P450 1B1 to sex differences in the development of hypertension and its pathogenesis."*

May 7

**IHOR V. YOSYPIV, MD**

Associate Professor, Department of Pediatrics,  
Chief, Division of Pediatric Nephrology,

Tulane University School of Medicine, New Orleans, LA.

*"Prorenin receptor-V-ATPase cross-talk in kidney development."*

May 21

**WALTER LEE MURFEE, PHD**

Assistant Professor, Department of Biomedical Engineering,  
Tulane University School of Engineering, New Orleans, LA.

*"Hypertension to Aging: Advancing Our Understanding of Microvascular Growth."*

June 4

**MARGARET ZIMMERMAN, PHD**

Post-Doctoral Fellow,

Department of Pharmacology,

Tulane University School of Medicine, New Orleans, LA.

*"Sex-Specific Effects of Chronic ANG II Infusion on Renal T-Cells."*

June 18

*Speaker: TBA*

*Talk: TBA*

July 2

**NO MEETING**

**4<sup>th</sup> of July Holidays**

July 16

**THOMAS COOPER WOODS, PHD**

Assistant Professor, Department of Physiology & Tulane Heart & Vascular Institute,  
Tulane University School of Medicine, New Orleans, LA.

*TBA*

# Calendar of Events

*Continued...*

July 30

**HONGBING LIU, PHD**

Assistant Professor, Department of Biochemistry,  
Tulane University School of Medicine, New Orleans, LA.  
*"Histone Deacetylases 1 and 2 in Kidney Development."*

August 13

**ZUBAIDA SAIFUDEEN, PHD**

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

August 27

**JING CHEN, MD, MMSC, MSC**

Associate Professor, Department of Medicine,  
Division of Nephrology and Hypertension,  
Tulane University School of Medicine, New Orleans, LA. .  
*TBA*

September 10

**KATHLEEN HERING-SMITH, MS, PHD**

Associate Professor, Department of Medicine,  
Director, Tulane Freezer Farm,  
Tulane University School of Medicine, New Orleans, LA.  
*TBA*

September 24

**PRERNA KUMAR, PHD**

Instructor, Department of Physiology,  
Tulane University School of Medicine, New Orleans, LA.  
*TBA*

October 8

*Speaker: TBA*  
*Talk: TBA*

October 15 \*\*

*Special THRCE Seminar Jointly Sponsored by  
THRCE & the Department of Neurology*

**ROBERT H. ECKEL, MD**

Charles A. Boettcher Endowed Chair in Atherosclerosis  
Professor of Medicine - Division of Endocrinology,  
Metabolism and Diabetes, and Cardiology,  
Professor of Physiology and Biophysics  
Program Director, Adult General Clinical Research Center  
University of Colorado, Anschutz Medical Campus, School of Medicine, Aurora, CO.  
*TBA*

*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

National Institute of  
General Medical Sciences



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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Comments are welcome:  
Contact: Nina R. Majid  
Phone: 504-988-3703  
Fax: 504-988-2675  
Email: [htnctr@tulane.edu](mailto:htnctr@tulane.edu)  
<http://tulane.edu/som/thrce/>

*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.*