

THRCE.

TULANE HYPERTENSION AND RENAL CENTER OF EXCELLENCE

Winter 2016

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— KIDNEY —
DISEASE
& CHILDREN

**ACT EARLY
TO PREVENT IT!**

World Kidney Day (WKD) is a global health awareness 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 worldwide. WKD began in 2006 and has been celebrated every year since then in more than 100 countries on 6 continents. 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. 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.

Every year, the campaign focuses on a theme. The focus on the 2016 WKD is “Kidney Disease & Children: Act Early to Prevent It.” 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://www.worldkidneyday.org/>

In honor of the World Kidney Day, THRCE and the Department of Medicine will conduct a health screening event at the Lobby of the Tulane Hospital, the Reilly Pavilion, from 9am till 3pm. The goal is to screen participants during the 6 hour period for blood pressure and the risk for developing kidney disease. If anyone is interested in volunteering their time and services for a couple of hours towards the health screening event, please contact Nina Majid at htnctr@tulane.edu.

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HONORS & RECOGNITION AWARDED TO THREE AFFILIATED INVESTIGATORS

L. Gabriel Navar, PhD

- Drs. Navar and Mitchell were awarded AHA GSA Summer 2016 Health Sciences Fellowship Award which will provide 2 more years of support for medical students to participate in summer research activities.
- In December 18, 2015, Drs. Navar, Woods and Sato were awarded a 1-year Janssen Pharmaceutical Company research grant entitled, "Role of Kidney Production of Angiotensinogen in the Reduction of Blood Pressure by SGLT2 Inhibition under Diabetic and Non-diabetic Conditions."
- Participated at the 2015 AHA Heart Walk held on November 7, 2015.
- Served as a co-chair for the Cardiovascular Research Session at the Southeast Regional IDeA Meeting held at Biloxi, Mississippi in November 2015.
- Moderator for the Poster Session, "Chronic Kidney and Renal Session" at the 2015 Council on Hypertension Scientific Sessions held at Washington, DC.
- Workshop participant at the meeting of the Association of Chairs for Departments of Physiology "Chair Burnout: Identification, coping and prevention" held at St. Thomas, US Virgin Islands in December 4, 2015.
- Named to the inaugural class of Fellows of the American Physiological Society.

M-Altaf Khan, PhD

- Was promoted to Assistant Professor in the research track in the Department of Medicine, Section of Nephrology & Hypertension.

Sarah Lindsey, PhD:

- Awarded AHA Grant-In-Aid for her research, "Environmental Estrogens in Female Cardiovascular Health."
- Postdoctoral student, Margaret Zimmerman, PhD, received Postdoctoral Fellowship award for her study, "Renoprotective Effects of the G Protein-Coupled Estrogen Receptor."
- Participated in an education program at the Morris Jeff Community School and educated 7th grade students about the circulatory system.
- Appointed Adjunct Assistant Professor in Physiology.

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

Hongbing Liu, PhD:

- Will present abstract at Southern Society of Pediatric Research and selected as a recipient of the 2016 SSPR Young Faculty Award.

Kayoko Miyada, PhD:

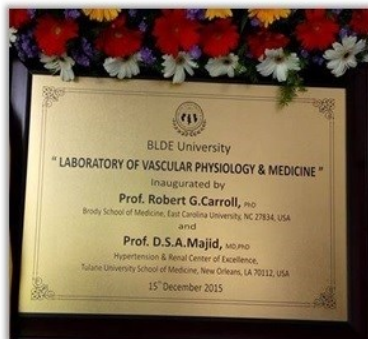
- Recipient of the 2015 Tinsley Harrison Award for her article entitled, "Renoprotective effects of direct renin inhibition in glomerulonephritis" which was published in October 2014 issue of the American Journal of the Medical Sciences, (AJMS). This award is given by the Editors for the best original manuscript published in the AJMS between October 2014 and September 2015.

Dewan S. A. Majid, MD, PhD:

- On September 16th, Chaired the Oral Session titled, 'Salt & Hypertension II' held at the 2015 AHA/ASA Council on Hypertension Scientific Sessions meeting held in Washington DC.
- On December 15th, officially inaugurated the "Laboratory of Vascular Physiology & Medicine" at the B.M. Patil Medical College at BLDE University, in Bijapur, Karnataka, India. Along with presenting invited lectures, participated in the "International CME 2015" program titled, "Challenges in Medical Teaching and Research: Global Perspective," organized by the Departments of Medical Education and Physiology



Dr. Dewan Majid was invited, along with Dr. Robert Carroll, to inaugurate the opening of the "Laboratory of Vascular Physiology & Medicine" at BLDE University in India. In addition, they each had a tree planted outside the new facility in their name.



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

Nazih L. Nakhoul, PhD:

- Selected to serve on the Tulane IBC committee Board.

Virginia Reverte Ribo, PhD:

- Postdoctoral Fellow, Dr. Reverte-Ribo (mentor: Dr. Prieto) received the John F. Perkins, Jr. Memorial Award for International Physiologists from APS which includes a cash award of \$5,000.

Zubaida Saifudeen, PhD:

- Awarded NIH-NIDDK R56 grant for her project, "Energy metabolism regulation of nephrogenesis."
- Appointed as Adjunct Associate Professor in the Department of Physiology.

Ryosuke Sato, PhD:

- Received Notice of Award from NIH/NIDDKD for a 5 years R01 grant titled: "Histone deacetylase 9 is an epigenetic suppressor of intrarenal angiotensinogen, serving as a key mechanism in angiotensinogen augmentation in hypertension." The project period is December 2015 to November 2020.

T. Cooper Woods, PhD:

- From November 1st, was officially transferred from the Heart and Vascular Institute in the Department of Medicine to the Department of Physiology as a tenure track Assistant Professor.

Andrea Zsombok, PhD:

- Received a Tulane CELT Award for her project with undergraduate student, Samantha Sagaser.
- Participated as a panel discussion leader along with Dr. Jazwinski for the Faculty Career Development Club, NIH Bio-sketch discussion on November 2, 2015.

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THRCE PARTICIPATES IN THE AHA 2015 HEART WALK

Representatives of THRCE participated in the 2015 Heart Walk sponsored by the American Heart Association on Saturday, November 7nd. The Heart Walk is an annual event to raise money for the American Heart Association. The funds raised is used for critical research and education on cardiovascular diseases. The event was scheduled to be held at LaSalle Park but due to rain the decision was made to move the venue to Clearview Mall in Metairie. Along with the non-competitive walk, the event includes numerous fun-filled health and wellness activities, free food and entertainment. Nina Majid, Michelle Frederick, and Gayle Evans were the Team Captains for Tulane School of Medicine (TSOM). Team captains were responsible for coordinating and recruiting team leaders throughout the medical school. TSOM-departmental team leaders were Nina Majid (Physiology & THRCE), Dr. Prasad Katakam (Pharmacology), Rachel Cruthirds (Clinical Translational Unit), Gayle Evans (Medicine), Ms. Suzy Mason (TSOM-Heart & Vascular Institute), Ms. Michelle Frederick (Endocrinology), Barbara Valo (Matas Library), Maria Arabie (Neurology). The team leaders were responsible for recruiting members who helped them raise funds and participated as walkers at the Heart walk. Raffles and bake sales were some of the fund-raising activities organized by the teams. TSOM team leaders, along with their members, helped raise over \$3,000 for the AHA fundraising campaign. Overall, the AHA Heart Walk, with the fundraising support from Tulane and other companies in New Orleans, raised over \$502,000; this fund will be used to accomplish the AHA mission of building healthier lives free from cardiovascular diseases and stroke.



2015 Heart Walk: Some of the participant walkers

SCIENCE IN NEWS: SUBSTANTIAL BENEFIT FOR MORE INTENSIVE MANAGEMENT OF SYSTOLIC BLOOD PRESSURE

In September 2015, the National Heart Lung and Blood Institute (NHLBI) announced that a landmark study on blood pressure management will be stopped early because the data shows definite and substantial benefit for more intensive treatment. The NHLBI announced blood pressure intervention was ended early so that the results could be disseminated quickly. A paper will be published in the next few months.

The Systolic Blood Pressure Intervention Trial (SPRINT) studied people over age 50 who had high blood pressure and at least one other risk factor for heart disease. The results show that using medicines to reduce systolic blood pressure to 120 mm Hg reduced rates of heart attack, heart failure and stroke by nearly one-third and death by nearly one-quarter compared to reducing blood pressure to less than 140 mm Hg. The American College of Cardiology/American Heart Association Taskforce on Practice Guidelines has already begun the review process, in partnership with the National Heart, Lung, and Blood Institute, to update national blood pressure guidelines for clinicians to follow as the national standard for hypertension prevention and treatment. The SPRINT findings will factor in to decision-making for the updated guidance.

More information on this ground-breaking clinical trial will be forthcoming once the data on the NIH's SPRINT trial is published.

UPCOMING MEETINGS:

- Southern Regional Meeting of SSCI/ AFMR/SSPR Societies
~ New Orleans, LA, February 18-20, 2016.
- The Experimental Biology Meeting
~ San Diego, CA, April 2-6, 2016.
- Tulane University 27th Annual Health Sciences Research Days
~ New Orleans, LA, April 6-7, 2016.
- 6th Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE) Conference
~ Washington, DC, June 26-29, 2016.

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THRCE SPONSORED LOCAL, NATIONAL & INTERNATIONAL SPEAKERS

THRCE regularly sponsors bi-weekly seminars by scheduling local, national, and internationally recognized investigators and clinicians in the field of hypertension and kidney research, treatment and education. From September through December, 2015, the center hosted the following speakers to present THRCE seminars:



- **Kathleen Hering-Smith, MS, PhD**
*Associate Professor,
Department of Medicine & Department of Physiology,
Director, Tulane Freezer Farm,
Tulane University School of Medicine, New Orleans, LA.*

On September 10th, 2015, Dr. Hering-Smith presented "Signaling from the Cycle: Pleiotropic Effects of Citrate Transporter."

Summary: Calcium nephrolithiasis remains a frequent and serious cause of morbidity and health care costs. As well known, urinary citrate is the most important inhibitor of calcium stones because citrate, a tricarboxylate, keeps calcium soluble in the urine. But the regulation of citrate transport in the kidney has received inadequate investigation and remains poorly understood at the cell and molecular level. Urinary citrate excretion is primarily determined by its fractional reabsorption in the proximal tubule. The dicarboxylate transporter (NaDC1) cloned by Pajor has been considered the main mechanism of apical reabsorption of filtered citrate. However, our recently published studies demonstrate an additional novel mechanism which may explain the increase in citrate excretion with increases in urinary calcium found in vivo. This calcium sensitive, novel process and other transporters may contribute substantially to changes in urine citrate and other Krebs' cycle intermediates. By comparing NaDC1 knockout mice and heterozygote wild type mice, we can determine the role of NaDC1 and by inference the role of the other transporters.

The predominant urinary organic anion is citrate, a Krebs cycle intermediate that is also the most important inhibitor of calcium kidney stones. However, recent exciting studies have shown a critical importance of other urinary Krebs cycle intermediates in regulating other renal functions. This presentation addressed the regulation and importance of these Krebs cycle intermediates in distal nephron regulation.

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• **Volker H. Haase, MD**

*Professor of Medicine, Professor of Cancer Biology,
Professor of Molecular Physiology and Biophysics,
Krick-Brooks Chair in Nephrology,
Division of Nephrology and Hypertension,
Vanderbilt University Medical Center, Nashville, TN.*

Dr. Haase presented a seminar jointly sponsored by THRCE & the Department of Pediatrics. His talk, titled, “Oxygen sensing in the kidney: insights from genetic models and clinical translation” was presented on September 17th 2015.

Summary: A long-term goal of Professor Haase’s research is to understand the pathogenesis of renal anemia and to develop new and safe therapies for its treatment. Anemia is a classic manifestation of advanced chronic kidney disease (CKD) and results from the diminished ability of the diseased kidney to produce adequate amounts of erythropoietin (EPO), the glycoprotein hormone that is essential for red blood production. Renal peritubular interstitial fibroblast-like cells play a key role in adult erythropoiesis, as they are the main cellular source of EPO. Prolyl-4-hydroxylase domain (PHD) dioxygenases PHD1, PHD2 and PHD3 function as the oxygen-sensors that control EPO synthesis by regulating hypoxia-inducible factor (HIF)-2 activity. Despite their critical role in erythropoiesis, renal EPO-producing cells (REPC) are poorly characterized and the role of the PHD/HIF-2 axis in the regulation of REPC plasticity is unclear.

Professor Haase’s group has used Cre/loxP-recombination to target the PHD/HIF-2/EPO axis in FOXD1 stroma-derived renal interstitial cells and has examined the role of individual PHDs in the regulation of REPC pool size and renal EPO output.

Professor Haase shared recent unpublished findings from his group, which demonstrate that a) renal EPO production is completely contained within the FOXD1 stroma-derived cell population and that virtually all FOXD1-derived interstitial cells in renal cortex and outer medulla have EPO-producing potential, b) that PHD2 is the main regulator of HIF-2 activity and EPO synthesis in a subpopulation of renal interstitial cells and c) that PHD3 controls the conversion of a separate subset of renal interstitial cells to REPC. These findings have direct translational implications for the development and clinical evaluation of therapeutic agents that target the HIF oxygen-sensing pathway for the treatment of anemia.



- **Prerna Kumar, PhD**
Instructor,
Department of Physiology,
Tulane University School of Medicine, New Orleans, LA.

Dr. Kumar presented, “Retinoic Acid-mediated Guanylyl Cyclase/ Natriuretic Peptide Receptor A gene Regulation,” at the September 24th THRCE Seminar.

Summary: Natriuretic peptides (NPs) and their receptors have physiological and pathophysiological importance including cardiovascular and renal aspects in normal and disease conditions. Cardiac hormones atrial and brain NPs bind to their receptor-A (NPRA) which produces the intracellular second messenger cGMP in response to hormone binding to mediate their biological functions. Gene-targeting studies have shown that disruption of *Npr1* gene leads to renal insufficiency, cardiac hypertrophy, and fibrosis in *Npr1* null mutant mice. However, there is limited understanding of how *Npr1* gene is regulated at the transcription level. Utilizing molecular biology techniques and cell culture system our results show that *Npr1* gene transcription and expression is regulated by retinoic acid and its receptors involving transcription factors Ets-1 and Sp1. Our in-vivo findings demonstrate that epigenetic upregulation of *Npr1* gene transcription by retinoic acid and histone deacetylase inhibitor, sodium butyrate leads to attenuation of renal fibrotic markers and systolic blood pressure in mice with reduced *Npr1* gene copy number, which will have important implications in prevention of hypertension-related renal pathophysiological conditions.



- **Hong Lu, MD, PhD**
Associate Professor,
Internal Medicine - Cardiology,
CVRC - Core Faculty, Cardiovascular Research Center,
University of Kentucky, College of Medicine,
Lexington, KY.

Dr. Lu presented “Angiotensinogen Has Unique Functions Independent of its Role in Generating Angiotensin II,” at the October 8th, 2015 THRCE Seminar.

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Summary: Angiotensinogen (AGT) is the substrate for generating angiotensin peptides in the renin angiotensin system. AGT plays critical roles in blood pressure regulation, kidney development, and many cardiovascular related conditions through its contribution to angiotensin II production, which requires the release of 10 amino acids from the N-terminus of AGT. The fate of the rest part of AGT, des(AngI)AGT, has not been defined. Using both genetic and pharmacological methods, we have found that AGT contributes to obesity and fatty liver due to the presence of des(AngI)AGT. This finding provides insights into understanding new biological features of AGT.



- Glenn M. Toney, PhD, FAHA
*Ashbel Smith Professor,
Department of Physiology,
University of Texas Health Science Center,
San Antonio, TX.*

On Monday, Oct. 12th, 2015, Dr. Toney presented “What the Brain Knows about Blood Pressure: Emerging Concepts.” The seminar was jointly sponsored by THRCE & the Department of Physiology.

Summary: Beginning with the first recordings of the action potential traffic in mammalian sympathetic nerves (ca. 1932), two dominant bursting patterns were identified – a respiratory rhythmic bursting pattern and a cardiac rhythmic bursting pattern. It was subsequently determined that these patterns arise from a brainstem delimited cardio-respiratory neural network. From the mid-1970’s, studies have provided compelling evidence that sympathetic nerve activity becomes exaggerated in many different cardiovascular and metabolic diseases, including hypertension and heart failure as well as obesity and diabetes. Further evidence demonstrates that this disease-related exaggerated sympathetic activity is generated largely by activity of neurons in higher brain regions, namely the forebrain and hypothalamus. Dr. Toney presented studies aimed at determining how forebrain and hypothalamus-driven sympathetic activation interfaces with brainstem-driven cardio-respiratory bursting patterns. The working hypothesis presented was that sympathetic activity sourced from higher brain regions will enhance one or both of the dominant cardio-respiratory activity patterns by modulating activity within the

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brainstem network. In doing so, the activity of neurons in the forebrain and hypothalamus would be integrated into the brainstem-driven cardiac and respiratory bursting patterns, effectively amplifying these patterns. Dr. Toney presented data suggesting that this may not be the case. Instead, evidence was presented showing that exaggerated sympathetic activity resulting from acute, sub-acute and chronic activation of the forebrain-hypothalamic circuitry by sodium and angiotensin II stimulates a non-respiratory and non-cardiac rhythmic component of sympathetic activity that is normally quiescent. The notion that bursts of sympathetic activity that are not rhythmic with either the cardiac or respiratory cycle could be a previously unrecognized contributor to heightened blood pressure and may contribute to functional deterioration of end organs in cardiovascular and metabolic diseases was emphasized.



- **Robert H. Eckel, MD**

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

Dr. Eckel presented a special Seminar jointly sponsored by THRCE the Provost Faculty Networking Seminar & the Diabetes Research Program. His talk, "What's a Lipoprotein Processing Enzyme Doing in the Brain?" was presented on October 15, 2015.

Summary: Lipoprotein lipase (LPL) is an important enzyme that breaks down triglycerides (fats) absorbed after and produced by the liver. LPL is present in many tissues including heart, muscle and adipose tissue but is also found in the brain. My laboratory has produced a mouse by genetic engineering that does not make LPL in neurons in the brain. These mice eat more, become sedentary and get fat. As they age, two interesting things happen: 1. they have better glucose tolerance despite being obese; and 2. they have abnormal behavior, anxiety and reduced learning and memory. Working with Dr. Zsombok at Tulane we have some evidence that in a specific brain region that controls glucose metabolism the absence of LPL produces signals that make the mice have better rather than worse glucose tolerance. Overall, LPL appears important in the brain by delivering fat that controls a number of processes related to weight, glucose tolerance and behavior.



- **Lydia Bazzano, MD, PhD**

*Lynda B. and H. Leighton Steward Professor in Nutrition,
Director, Center for Lifespan Epidemiology Research
Associate Professor of Epidemiology
Clinical Assistant Professor of Medicine, Dept. of Epidemiology,
Tulane University School of Public Health & Tropical Medicine,
New Orleans, LA.*

On November 5th, 2015 Dr. Bazzano presented, “Postural Hand Tremor & Hypertension in Adults.”

Summary: Postural hand tremor and blood pressure are both increased by adrenergic stimulation and reduced by beta blockade, indicating that they may share a common underlying pathophysiology. We prospectively examined the relationship between postural hand tremor and incident hypertension in a community-based cohort of 715 (184 black, 531 white) adults without hypertension and not using medications to control tremor (e.g. β -blockers). At baseline, tremor was measured with participants holding a laser pointer aimed at a sheet of Polaroid film 8 feet away with arm outstretched for eight seconds in a darkened room. Tremor was characterized by the width of the circular diameter encompassing all exposures and enumeration of exposure dots in the same area. Incident hypertension was defined as new elevation of blood pressure (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg, based on an average of six readings over two visits), or antihypertensive medication use. During a median follow-up of 6.4 years, 198 (69 black and 129 white) participants developed hypertension. Tremor measurements (by quartile) were positively associated with incident hypertension after adjustment for demographics, lifestyle and metabolic risk factors at baseline. There was significant interaction by race ($p=0.01$). Among whites, tremor was positively associated with incident hypertension (HR highest vs. lowest quartile: 2.35 [95%CI: 1.35-4.09], P-trend: 0.007 dot method; and 3.02 [1.69-5.38], P-trend: 0.002 circular method). Among blacks, tremor was not associated with hypertension risk. In this community-based cohort, postural hand tremor was strongly associated with the risk of incident hypertension among whites, and merits further study as a potential indicator of risk for hypertension.

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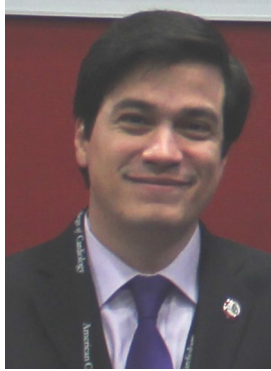
- **Hee-Won Park, PhD**

*Associate Professor of Biochemistry and Molecular Biology
Tulane Cancer Center,
Contributing Member in the Signaling & Clinical Programs,
Tulane University School of Medicine, New Orleans, LA.*

Dr. Park presented, "Structure-Based Search for Selective Inhibitors of Aldosterone Synthase," at the November 19th THRCE Seminar.

Summary: Mitochondrial cytochrome P450 11B2 (CYP11B2) catalyzes the biosynthesis of aldosterone, which is implicated in the pathogenesis of hypertension and heart failure. The nucleotide sequence of human CYP11B2 (hCYP11B2) is similar to that of human CYP11B1 (hCYP11B1), an enzyme responsible for the production of cortisol. High sequence identity between these two enzymes makes it difficult to discover the inhibitors of hCYP11B2 that do not suppress hCYP11B1 activity. Based on our recent structure of hCYP11B2 in complex with the substrate deoxycorticosterone, we have found that the H-helix region includes the most important amino acids that determine the different enzymatic activities of hCYP11B1 and hCYP11B2. This H-helix region is near the putative product exit channel of hCYP11B2, possibly affecting the conformation of the product exit channel, mainly closed when either a substrate or an intermediate are bound. We predict that the product exit channel of hCYP11B1 is more open than that of hCYP11B2, permitting the departure of the one-step reaction product (cortisol). On the other hand, the product exit channel of hCYP11B2 is mainly closed and remains closed until the three-step reaction product (aldosterone) is made. This finding suggests that the conformational property of the product exit channel of hCYP11B2 is different from that of hCYP11B1, biasing toward the retention of steroid intermediate in the active site. Here, we identified the 50 best-fit candidates by docking drug-like compounds into the active site of hCYP11B2 and will perform the following experiments to identify the selective inhibitors of hCYP11B2. (1) Spectral determinations for the candidate compounds binding at the active site of hCYP11B2, but not of hCYP11B1 (2) In vitro enzyme activity and cell-based analyses for the inhibition of aldosterone production by the candidate compounds, and (3) Crystallographic validation for the candidate compounds to bind at the active site of hCYP11B2. Together, newly discovered hCYP11B2-selective inhibitors may offer a novel therapeutic approach for both lowering blood pressure and preventing the non-genomic effects of aldosterone.

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- **Camilo Fernandez, MD, MSc, MBA, MCTS, FASH.**

Senior Investigator:

*H.L. Brighton Center for Advanced Cardiovascular Diagnostics
HeartGEN Institute, Baltimore, MD*

Research Associate:

*Tulane University-Department of Epidemiology,
Tulane University School of Public Health & Tropical Medicine,
New Orleans, LA*

Dr. Fernandez presented “Genetic Determinants of Adult Hypertension: What Phenotype Are We Actually Predicting?” at the December 17th THRCE seminar.

News

Recent Publications

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Kelly TN, Raj D, Rahman M, Kretzler M, Kallem RR, Ricardo AC, Rosas SE, Tao K, Xie D, Hamm LL, He J; CRIC Study Investigators. The role of renin-angiotensin-aldosterone system genes in the progression of chronic kidney disease: findings from the Chronic Renal Insufficiency Cohort (CRIC) study. *Nephrol Dial Transplant.* 2015 Oct;30(10):1711-8. doi: 10.1093/ndt/gfv125. PMID: 25906781.

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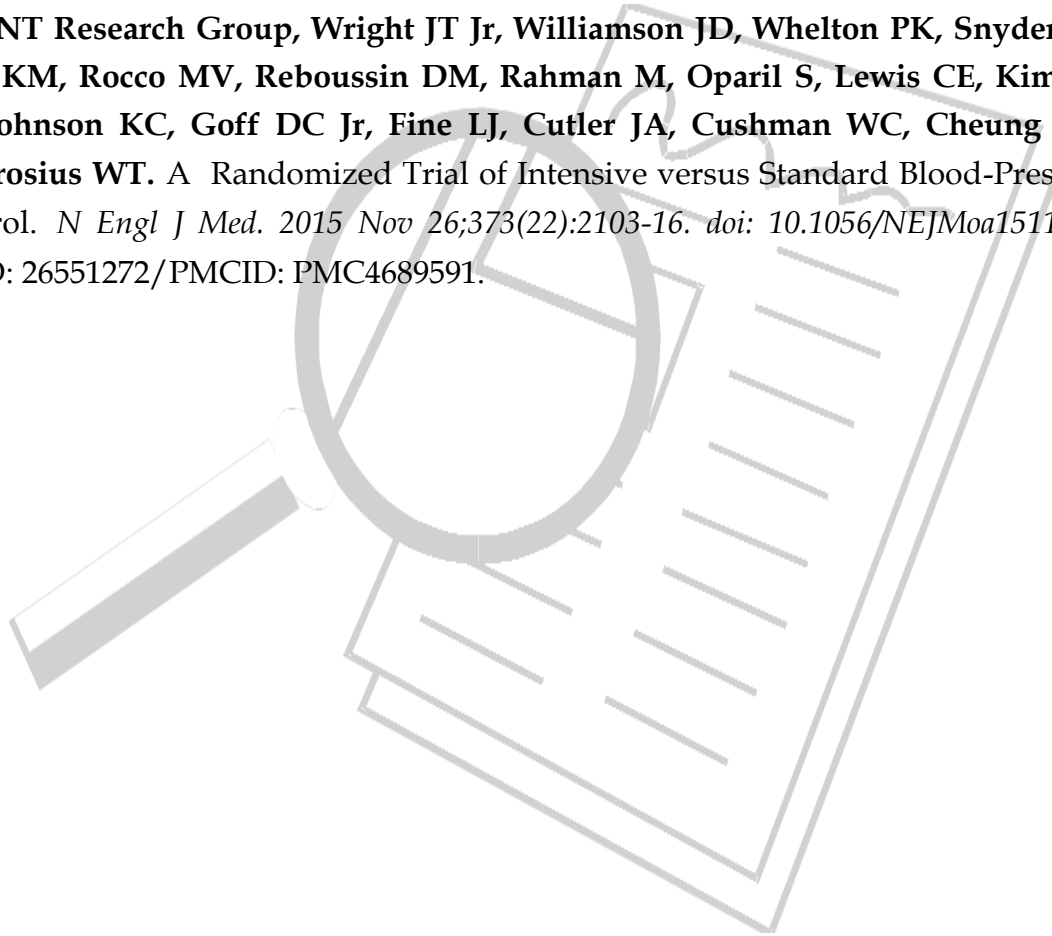
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From September through December, 2015 investigators and physicians affiliated with T.H.R.C.E. participated in regional, national, & international meetings.

Council on Hypertension 2015 Scientific Sessions, Washington, DC, Sept. 16–19, 2015

- **Gogulamudi VR, Arita DY, Bourgeois CRT, Satou R, Prieto MC.** High glucose increases prorenin receptor (PRR) at the cell plasma membrane in the collecting duct which promotes the induction of downstream fibrotic factors. P032.
- **Itani HA, Xiao L, Saleh MA, Wu J, Dale BL, Barbaro NR, Foss JD, Kirabo A, Norlander AE, Chen W, Suto R, Navar LG, Bernstein KE, Harrison DG.** The Role of Immunological Memory in Hypertension. *Hypertension* 66:A051, 2015.
- **Kumar P, Pandey KN.** Epigenetic mechanisms of sodium butyrate- and retinoic acid-dependent attenuation of renal fibrosis and inflammation in Npr1 gene-targeted mice. P047.
- **Majid, DSA, Prieto MC, Castillo A.** Tumor necrosis factor-alpha receptors (type 1 and type 2) are differentially expressed in renal tissues during chronic dietary intake of high salt and angiotensin II treatment. P247.
- **Miyata K, Weijian Shao W, Prieto M, Satou R, Katsurada A, Seth D, Mitchell KD, Navar LG.** The Combined Effects of Elevated Intrarenal Ang II and Blood Pressure Causes Greater Renal Injury in the Non-clipped Kidneys in 2K1C Rats. *Hypertension* 66:AP021, 2015.
- **Sen A, Kumar P, Pandey KN.** Transforming growth factor beta 1-mediated repression of guanylyl cyclase/natriuretic peptide receptor-A gene expression and function involving TGF-beta 1 and delta EF1 in vascular smooth muscle cells. P195.

ADA Diabetes & Endocrine Disorders for the Generalist and Specialist, New Orleans, LA, Sept. 26 2015.

- **Woods TC.** Increased Cardiovascular Risk for Patients with Diabetes.
- **Woods TC.** Diabetes Alters the Molecular Mechanisms Underlying Plaque Rupture.

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ASN Kidney Week 2015. Nov 3 - 8, 2015; San Diego, CA.

- **Song R, Preston G, Kidd L, Yosypiv IV.** Prorenin receptor regulates nephron induction during mouse kidney development. Poster at ASN, November 2015.
- **Mehta R, Cai X, Lee J, Bansal N, Scialla JJ, Sondheimer JH, Deo R, Chen J, Hamm LL, Ricardo AC, Rahman M, Navaneethan SD, Go AS, Feldman HI, Isakova T, Wolf MS.** Fibroblast Growth Factor 23 and Risk of Atrial Fibrillation in Chronic Kidney Disease: The CRIC Study. Abstract #TH-OR124
- **Chen J, Hamm LL, Kumbala DR, Chen CS, Wu KK, Kallu SG, Siriki R, Gadde S, Alper AB, Kleinpeter MA, Batuman V, Simon EE, L. Navar LG, He J.** Elevated Plasma Chymase Is Associated with Risk of Chronic Kidney Disease. Abstract #4984, Poster Board #: FR-PO553
- **Scialla JJ, Asplin JR, Dobre MA, Chang AR, Lash JP, Hsu CY, Kallem RR, Hamm LL, Feldman HI, Chen J, Appel LJ, Anderson CA, Wolf MS.** Net Acid Excretion and Progression of CKD: Results from the Chronic Renal Insufficiency Cohort Study. Abstract #FR-OR108.

Southeast Regional IDeA Meeting, Biloxi, MS. Nov 12-14, 2015.

- **Liu H.** Histone Deacetylases 1 and 2 balance nephron progenitor renewal and differentiation during kidney organogenesis. *Oral Presentation.*
- **Garagliano JM, Derbenev AV, Zsombok A, Navar LG, Sato R.** Stimulating Effect of Advanced Glycation End Products on Angiotensinogen Expression in Renal Proximal Tubule Cells.
- **Gao H, Heike Muenzberg-Gruening H, Zsombok A, Derbenev AV.** Leptin Inhibits Presympathetic Neurons in the Rostral Ventrolateral Medulla.
- **Kumar P, Periyasamy R, Das S, Pandey KN.** Retinoic Acid and Sodium Butyrate Attenuate Renal Fibrosis and Inflammation in Guanylyl Cyclase-A/Natriuretic Peptide Receptor-A Gene-Targeted Mice.
- **Khan MA.** Pathophysiology of contrast-induced nephropathy and new therapeutic strategies. *Oral Presentation.*
- **Majid DSA.** Differential expression of tumor necrosis factor-alpha type 1 and type 2 receptors in the renal tissue during chronic high salt intake and angiotensin II treatment. *Oral Presentation.*
- **Majid NR.** COBRE Translational Research in Hypertension & Renal Biology

Continued...

- **Teran FJ, Huang W, Hamm LL, Hering-Smith KS.** NaDC1 Knockout: Effects on Blood Pressure and Urine pH.
- **Woods TC.** Diabetes Alters the Molecular Mechanisms Underlying Plaque Rupture.

APS Cardiovascular, Renal & Metabolic Diseases: Physiology & Gender, Annapolis, MD. Nov. 17-20, 2015.

- **Lindsey SH.** GPER and Vascular Function.
- **Navar LG, Katsurada A, Fonseca V, Prieto MC, Chalew S, Kobori H.** Augmentation of Urinary Angiotensinogen Levels in Young Men and Women with Type-1 Diabetes Mellitus.
- **Rosales CB, Arita DY, Thethi T, Fonseca V, Navar LG and Prieto MC.** Sex dimorphism in plasma soluble prorenin receptor (SPRR) levels in obese patients is associated with Type 2 diabetes mellitus in women but not in men.
- **Zimmerman MA, Hutson DD, Murphy BN, Kashyap SN, Trimmer EH, Daniel JM, Lindsey SH.** Long-term Estrogen Duration Promotes Renal Tubular Cast Formation in Aged Ovariectomized Long Evan Rats.

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

L. Gabriel Navar, PhD:

- “October 15th, 2015 – Augmentation of Intrarenal Renin-Angiotensin System in Hypertension”, presented as Visiting Professor at the ‘Cellular and Molecular Pharmacology and Physiology’ Program, held at the University of Nevada, in Reno, NV.

Dewan S. A. Majid, MD, PhD:

- October 6th, 2015 – Participated in a group discussion with the faculty and students in the Department of Physiology at Sylhet Women Medical College (SWMC) in Sylhet, Bangladesh. Topic: “How to improve Physiology curriculum activities in SWMC? – Introduction of problem based learning (PBL) sessions.”
- October 7th – “Salt sensitive hypertension: Perspectives on the renal mechanisms” at the Parkview Medical College (PMC), in Sylhet, Bangladesh.
- 20th November – “Salt-sensitive hypertension; perspectives on intrarenal mechanism” at the University of Southern Florida in Tampa, Florida.
- 23rd November – “Mechanistic inquest for salt-sensitive hypertension: where are we now?” Presented at the Physiology Seminar Series, at Tulane University.
- 8th December – “Differential roles for tumor necrosis factor-alpha receptors (type 1 and type 2) in salt sensitive hypertension.” at the Conference on ‘Neural Hormonal & Renal Interactions in Blood Pressure Control’ held in Mussoorie, Utterkhand, India.
- 12th December – Visited the ‘All Indian Institute of Medical Sciences’ (AIIMS) at Delhi, India and attended a Symposium on ‘Long term control of blood pressure’ organized by the Local Chapter of APPI (Association of Physiologists and Pharmacologists of India). Delivered a lecture titled, “Regulation of blood pressure during high salt intake; mechanistic concepts for the development of salt-sensitivity.”
- 14-18 December – Visited the B.M. Patil Medical College at BLDE University, in Bijapur, Karnataka, India:
 - ◊ Officially Inaugurated the "Laboratory of Vascular Physiology & Medicine" 15th December, 2015. Participated in a discussion meeting with Medical and Graduate students. Discussion topic: ‘Importance of Biological Research in Medical Education’.

- ◇ Participated in an "International CME 2015" on the theme "Challenges in Medical Teaching and Research: Global Perspective" on 15th December 2015 organized by the Departments of Medical Education and Physiology. Delivered a CME-talk in the session titled, "Mechanistic inquest for salt-sensitive hypertension; implications from bench to bedside."
- 20th December - "Salt-sensitive hypertension: Mechanistic inquests from bench to bedside" as plenary session's 'Keynote Speaker' at the FIPSPHYSICON-2015 [XXVIIth Annual Conference of The Physiological Society of India (PSI) and the VIth Congress of the Federation of Indian Physiological Societies (FIPS) conference] on 'Translational Physiology for Health Promotion' held at the University of Calcutta, in Calcutta, India.
- 21st December - "Renal mechanism of salt-sensitivity and hypertension." at the Physiology Department of University of Kalyani, in West Bengal, India.
- 26th December - "Problem based Learning (PBL) sessions as a teaching/learning strategy in Physiology" at the 'Parkview Medical College' in Sylhet, Bangladesh.
- 27th December - Visited the North-East Medical College (NEMC), Sylhet, Bangladesh and presented 2 lectures:
 - ◇ "Salt-sensitive hypertension" to the academic faculty of NEMC.
 - ◇ "Pumping action of the heart; importance of Frank-Starling relationship" to the medical students of NEMC.
- 28th December - Visited Alma-Mater, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh and presented, "High Salt Intake, Kidney Function & Hypertension."
- 29th December - "High Salt Intake & Hypertension; How these are connected" at the Sylhet Women Medical College, in Sylhet, Bangladesh.

Kailash N. Pandey, PhD:

- 1st December, 2015 - "Transcriptional regulation and function of guanylyl cyclase/natriuretic peptide receptor-A gene" at the Indian Informatics Institute of Technology, Allahabad, UP, India.
- 8th December - "Targeted disruption of natriuretic peptide receptor-A provokes proinflammatory responses with increased blood pressure, renal fibrosis, and remodeling in mutant mice" at the Neural, Hormonal and Renal Interactions in Blood Pressure Control meeting, held in Mussoorie, Uttarakhand, India.

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- 10th December - “Physiological significance of natriuretic peptide receptor-A gene transcription, expression and function” at the Delhi Pharmaceutical Sciences and Research University, in New Delhi, India.:

Zubaida Saifudeen, PhD:

- 4th October, 2015 - “Metabolic regulation of nephron progenitor self-renewal” presented at the Southwest Regional Society for Development Bio Meeting at UT-Southwestern, Dallas, Texas.

T. Cooper Woods, PhD:

- 26th September, 2015 - Presented “Increased cardiovascular risk for patient with diabetes” at the Diabetes and Endocrine Disorders for the Generalist and Specialist Meeting at Xavier University in New Orleans.

Calendar of Events

THRCE Seminars

January 14, 2016	NO MEETING <i>Date conflicts with Tulane Center for Aging Seminar</i> <i>Speaker: Amanda Jo LeBlanc, Ph.D.; Asst. Professor of Physiology, University of Louisville.</i> <i>Topic: "Reversing Coronary Microvascular Dysfunction in Aging: Role of Thrombospondin-1"</i>
January 28, 2016	DEWAN S.A. MAJID, MD, PHD, FAHA, FASN Professor, Department of Physiology, Director, Mouse Phenotype Core Facility, Tulane University, School of Medicine, New Orleans, LA. <i>"Differential roles for TNF-α receptors in salt sensitive hypertension."</i>
February 11, 2016 **	M-ALTAF KHAN, PHD, MSCR Research Assistant Professor, Department of Medicine, Section of Nephrology & Hypertension, Tulane University, School of Medicine, New Orleans, LA. <i>"Role of Inmate Immunity in the Pathophysiology of Contrast-Induced Nephropathy in Hypertensive and Diabetic Mice."</i>
February 25, 2016	Special THRCE Seminar Jointly Sponsored by: THRCE, Dept. of Endocrinology & Novo Nordisk, Inc. MATTHIAS VON HERRATH, MD Vice President & Head, Diabetes R&D Center, Novo Nordisk, Inc., Professor/Director, Center for Type 1 Diabetes Research, La Jolla Institute for Allergy & Immunology, Adjunct Professor, Dept. of Pediatrics & Medicine, University of California, San Diego, School of Medicine, La Jolla, CA. <i>"New insights into the pathology of type 1 and 2 diabetes"</i>
March 10, 2016	Special Seminar: WORLD KIDNEY DAY 2016 <i>Jointly Sponsored by THRCE & the Department of Physiology</i> HENRY A. PUNZI, MD, FCP, FASH Internist, Punzi Medical Center & Trinity Hypertension Research Institute, Carrollton, TX. <i>"Hypertension: How low should we go?"</i>
March 24, 2016	NO MEETING Good Friday Holidays
April 7, 2016	NO MEETING <i>Experimental Biology Meeting, San Diego, Ca - April 2-6 &</i> <i>Tulane Research Days, New Orleans, LA - April 6-7, 2016</i>
April 21, 2016	ANDREI V. DERBENEV, PHD Associate Professor, Department of Physiology, Tulane University, School of Medicine, New Orleans, LA. TBA
May 5, 2016	ZUBAIDA SAIFUDEEN, PHD Associate Professor, Department of Pediatrics - Division of Nephrology, Tulane Cancer Center Contributing Member: Genetics Program, Tulane University, School of Medicine, New Orleans, LA. TBA
May 19, 2016	IHOR V. YOSYPIV, MD Associate Professor, Department of Pediatrics, Chief, Division of Pediatric Nephrology, Tulane University, School of Medicine, New Orleans, LA. 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

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

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 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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