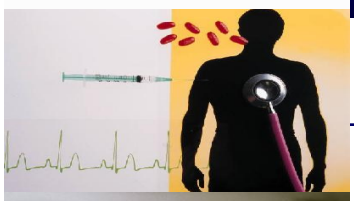

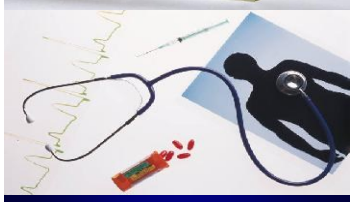

T.H.R.C.E.

TULANE HYPERTENSION AND RENAL CENTER OF EXCELLENCE

Winter 2017 ***Volume 16, Issue 3***

March 8, 2018 is World Kidney Day! A joint initiative of the International Society of Nephrology (ISN) and the International Federation of Kidney Foundations (IFKF), World Kidney Day (WKD) began in 2006 as a global health awareness campaign that focuses on the importance of kidneys and the mechanisms that reduce kidney disease. WKD has been celebrated ever since, every second Thursday of March, in more than 100 countries on 6 continents. Each year, the campaign focuses on a theme. The 2018 theme, "**Kidneys & Women's Health. Include, Value, Empower**," focuses on the fact that Chronic kidney disease (CKD) affects almost 195 million women worldwide and is currently the 8th leading cause of death in women, with close to 600,000 deaths each year. CKD is a worldwide public health problem with adverse outcomes of kidney failure and premature death. *(Details on WKD can be accessed at: www.worldkidneyday.org)*

In honor of WKD, THRCE has scheduled two special events on March 8th 2018:

- From 9am until 3pm, THRCE, the Department of Physiology, the Department of Medicine (Section of Nephrology), and the National Kidney Foundation of Louisiana, will conduct a "**Tulane WKD Health Screening Fair**" in the Lobby of Tulane University Hospital and Clinics. This free program is designed to screen people at risk for CKD and promote CKD awareness among the public. Participants will be screened for blood pressure & the risk for developing kidney disease.

- At 4pm, a Special WKD THRCE Seminar will be held in Room# 4700 in Tulane University, the School of Medicine. The seminar titled, "Dietary Salt Intake and Hypertension: Role of the Endothelium and Kidney," will be presented by the distinguished **Dr. Paul W. Sanders**, Professor of Medicine at the University of Alabama in Birmingham, Alabama.

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THRCE PARTICIPATES IN THE AHA 2017 HEART WALK

THRCE member participated in the 2017 Heart Walk sponsored by the American Heart Association on Saturday, November 11th. 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 Heart Walk was held at Champions Square in New Orleans and included numerous fun-filled health and wellness activities, free food and entertainment. Team Coaches for Tulane University were Nina Majid (THRCE & Physiology Team), Gayle Evans (Medicine Team), Dr. Prasad Katakam (Pharmacology Team), Gari Sampey (Psychiatry & Behavioral Sciences Team), and Dr. Robert Hende (Tulane Heart & Vascular Institute Team). Team coaches coordinated fundraisers and recruited members who helped raise funds and participated as walkers. Some of the participants in the Heart Walk were Emanuel Gerard, Charlene Esteves, Juan Viles-Gonzalez, Dewan Majid, Ben Ogola, Eric Simon, Dionne Richard, Kellie Tonglet, Treasure Schwab, Kyle Godfrey, Liu Hongbing, Gabriel Navar, Sarah Lindsey, Ryo Sato, Akemi Sato, Prerna Kumar, and Debbie Olavarrieta. TSOM team coaches and members helped raise over $2,415 for the AHA fundraising campaign. Overall, the AHA Heart Walk, with the fundraising support from Tulane and other companies in New Orleans, raised over $348,819; this fund will be used to accomplish the AHA mission of building healthier lives free from cardiovascular diseases and stroke.

2017 Heart Walk: Some of the participant walkers

GRANTS, HONORS & RECOGNITION AWARDED TO THRCE AFFILIATED INVESTIGATORS

L. Gabriel Navar, PhD:

- Invited as a Visiting Professor to lecture at the BLDE University and Medical School in Bijapur, India.
- Attended the annual retreat of the Association of Chairs of Departments of Physiology (ACDP) from November 30 till December 3. Discussions include consideration of the relationship between ACDP and the AAMC CFAS group, assessing support for science funding by the new congress and other legislative updates and ways for departments to generate more revenue including on-line courses, core lab facilities, technology transfer and MS programs.
- Selected as the recipient of the 2018 Southern Section of Clinical Investigation (SSCI) Mentor of the Year Award.
- Appointed to Membership in APS Founders Circle, 2017.
- Served on the APS Distinguished Physiologists Committee.

Kailash Pandey, PhD:

- Participated in the APS Physiological Bioenergetics Conference held in San Diego, CA, in August 2017.

Minolfa C. Prieto, MD, PhD:

- Appointed Regular Member, Hypertension & Hemodynamic Study Section, NIH from 2017-2023.
- Appointed Member of the Leadership Committee of the American Heart Association Kidney Council for Cardiovascular Disease.

Zubaida Saifudeen, PhD:

- Participated in a community outreach program called Bard Works Day, Annual Career Day at Bard Early College New Orleans: Illustrate, Ignite and Inspire!
- Spoke with high school students on careers in research and medicine.

T. Cooper Woods, PhD:

- Promoted to Associate Professor with tenure effective November 1.

Continued...

- Received a collaborative project (CRISP) Clinical Research & Innovative Support Program from Ochsner. The title of the project is "Mapping serum biomarkers of carotid plaque rupture to intra-plaque changes: Novel predictors of stroke."

Dewan S. A. Majid, MD, PhD:

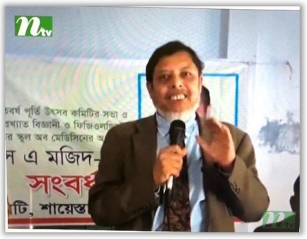
- Selected in November 2017 as the Chairman of the "Welcoming Committee" of the 2018 National Convention of Bangladesh Medical Association in North America (BMANA). BMANA is a professional organization consisting of Physicians of Bangladesh origin in North America (USA & Canada). The Convention will be held in Sheraton Hotel, New Orleans, from July 26-29, 2018.
- December 2nd till 17th attended the BLDE University at Bijapur, Karnataka, India as an invited "Visiting Professor of Medicine." Activities included the following:
  - ◊ Visiting all the Basic and Clinical Sciences departments of BM Patil Medical College, School of Nursing, and School of Pharmacy and discussed with both students and faculties the process as how to achieve and improve academic research in medical education curriculum of BLDE University.
  - ◊ Gave a series of lectures and seminar talks to Medical students, Post-graduate Students, MD Students. PhD students, and Faculties and Research Scientists.
  - ◊ External Advisor on the Thesis PhD Project of Dr. Gouer Banu, "L-NAME and sub chronic hypoxia induce alteration of vascular and renal pathophysiology in rats treated with Calcium channel blocker (cilnidipine)."
  - ◊ External Examiner for grand viva voce examination of PhD candidate, Ms. Vandali Jyoti, of the Department of Physiology at BLDE University. The title of her thesis was, "Effect of Chronic Stress on lactogenesis in humans!"
  - ◊ Assessed and reviewed the progress of the following Tulane-BLDE Joint Collaborative research:
    - ∗ Project 1: "Relationship of Urinary AGT to Central Hemodynamics and the response to antihypertensive therapy."
    - ∗ Project 2: "Renal and Cardiac functional changes in Cerebrovascular ischemic experimental model on hypoxic rats."
- On December 23, Dr. Majid visited Dhaka Medical College, Dhaka, Bangladesh and was a key participant at the Joint-discussion meeting with Physiology Faculties, Post-graduate students and graduate students of Dhaka Medical College, Sir-Salimullah Medical College and Bangabondhu Sheikh Mujib Medical University, in Dhaka, Bangladesh. Discussion Topic: "Development of Physiology teaching methodology in present medical curriculum."

Continued...

- Visited Alma mater, Sylhet Osmani Medical College, in Sylhet, Bangladesh on December 27 and was a key participant at the Joint-discussion meeting with faculties of the medical college. Discussion topic: "How to improve and give emphasis on academic research on medical curriculum in Bangladesh?"
- On December 30, received 'Memorandum of Honor' as distinguished alumni from Shaistaganj High School, Habiganj, Bangladesh

Dr. Dewan Majid Honored during his High School's Centennial Celebration as 'Most Distinguished Alumni'

A special ceremony was organized by the Centennial Celebration Committee of Shaistaganj High School in Habiganj, Bangladesh.



Joint Collaborations: & Group events:

- Drs. Navar, Sato and Woods, received additional funding through March 2018 for the Janssen project titled "Role of Kidney Production of Angiotensinogen in the reduction of Blood Pressure by SGLT2 inhibition under Diabetic and Non-diabetic conditions."
- Drs. Derbenev and Zsombok were awarded a sub-award from NIH SPARC, a collaborative grant with Pennington Biomedical Research Center, titled "Genetically-based neuro-modulation of adipose tissue functions." The project goal is to provide high resolution data at the level of the single cell.
- Drs. Mitchell and Krousel-Wood were awarded a planning grant and selected to submit a full application for the Burroughs Wellcome Fund 2018 Physician Scientist Institutional Program. If funded, the grant will support students, residents and junior faculty.
- A paper by Drs. Saifudeen, Sato and others titled, "Regulation of Nephron Progenitor Cell Self-Renewal by Intermediary Metabolism" was accepted and highlighted by the Journal of the American Society of Nephrology.

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- Drs. Gabriel Navar, Prerna Kumar, Ryo Sato, Dewan Majid, Prasad Katakam, Sarah Lindsey, and Hongbing Liu, along with Tulane staff, Nina Majid, Debbie Olavarrieta and Akemi Sato, participated at the New Orleans Heart Walk held on November 11, in Champion Square, New Orleans.

A candid shot of some of the 2017 AHA walk participants

Some participants discovered they were recorded on the Fox news!

SCIENCE IN NEWS: THE DEBATE ON DAILY SODIUM INTAKE

An article on sodium intake that was published in AARP on October 2017 quotes Dr. Gabriel Navar (https://www.aarp.org/health/healthy-living/info-2017/daily-sodium-intake-blood-pressure.html)

For years the standard advice was to cut back on salt. "The food supply is loaded with salt, which we know raises blood pressure," says Lawrence Appel, MD, a professor of medicine at Johns Hopkins University and spokesman for the American Heart Association, who advises almost everyone is to cut back on their salt intake. There has been a greater emphasis on that advice as people age when the body's ability to excrete salt declines.

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However, that long-accepted advice has recently come under fire. "The current recommendations are too extreme," insists Suzanne Oparil, M.D.,a hypertension expert at the University of Alabama at Birmingham School of Medicine. "There is zero evidence that cutting salt to very low levels like 1,500 milligrams is beneficial." Three studies have shown little or no indication that people are eating an unhealthy amount of sodium. One of those, a 2014 Danish study, set optimum sodium levels at between 2,645 and 4,945 milligrams.

Why is one set of medical experts so certain about declaring salt guilty while another set is passionately defending it? One reason is that salt affects people differently. "It's not how much salt you consume, but whether your kidneys can process the sodium it contains," says **L. Gabriel Navar, chair of the Department of Physiology and director of the Center for Biomedical Research Excellence in Hypertension and Renal Biology at Tulane University Medical Center in New Orleans**." Operating efficiently, the kidneys can get rid of a huge amount of sodium, up to 5,000 milligrams/day or more."

But not everyone can handle excess salt. About half of the population is salt sensitive: In this group, blood pressure will rise about 10 points with high salt diet. Unfortunately, scientists have yet to develop an easy-to-administer test for salt sensitivity and dramatically reducing sodium may pose its own risks. Researchers at McMaster University in Hamilton, Ontario, found that both too much sodium (7,000 milligrams/day) and too little (under 3,000 milligrams) were linked to an increased risk of cardiovascular disease. While sodium can raise blood pressure, electrolytes such as potassium keep it from climbing. "Potassium helps the kidneys get rid of salt," Dr. Navar explains, "so it's equally important to make sure you're getting enough." Bananas, sweet potatoes, canned tuna, orange juice, tomato sauce, yogurt and milk are all good sources of potassium.

While experts debate sodium levels, most agree on this: Your kitchen salt shaker isn't the culprit. Roughly 75 percent of the sodium we consume comes in processed or restaurant food. One way to control salt intake is to prepare meals yourself.If you have hypertension or prehypertension (that includes roughly one-third of Americans), then you should reduce your sodium intake. But don't try to count every milligram. Instead of worrying about the numbers, cut back on foods that are laden with salt, such as cold cuts and cured meats, pastas, pizza, baked goods, bread and soups.

THRCE SPONSOR
LOCAL, NATIONAL & INTERNATIONAL SPEAKERS

THRCE sponsors bi-weekly seminars by scheduling local as well as nationally and internationally recognized investigators and clinicians in the field of hypertension research, treatment and education. Speakers who present at the THRCE Seminar Series are asked to provide a brief summary of their talk that we can share with our newsletter audience. From September through December, 2017, the following speakers presented THRCE seminars.

- **EFRAIN REISIN, MD, FASN, FASH;FACP**
  Victor Chaltiel Professor of Medicine and
  Chief Section of Nephrology and Hypertension.
  Louisiana State University Health Sciences Center
  New Orleans, LA.

On September 7, 2017, Dr. Efrain Reisin presented "The Heart and the Kidney. A Forty Year Retrospect."

SUMMARY OF PRESENTATION:

There is an increasing global prevalence of the Metabolic Syndrome and Obesity. Both conditions are associated with higher prevalence of hypertension, cardiovascular and renal disease. The potential underlying mechanisms by which obesity and the metabolic syndrome promote hypertension include changes in cardiovascular and renal physiology induced by leptin, the sympathetic nervous system, insulin resistance, free fatty acid, natriuretic peptide and pro inflammatory cytokines. Weight reduction induced by hypocaloric diet or bariatric surgery has been effective in decreasing hypertension and improving cardiovascular and renal risks. The optimal pharmacological antihypertensive regimen for obese hypertensive subjects has not been defined.

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- **SARAH LINDSEY, PHD**
  Assistant Professor, Department of Pharmacology,
  Assistant Director, Mouse Phenotype Core Facility,
  Tulane University School of Medicine,
  New Orleans, LA.

Dr. Lindsey presented, "Estrogen Receptor Signaling in Arterial Stiffness" on September 21, 2017.

SUMMARY OF PRESENTATION:

Menopause increases arterial stiffness which accelerates end organ damage, increases cardiac afterload, and promotes heart failure with preserved ejection fraction, a disease twice as common in women than men. New drugs are needed to protect aging women from cardiovascular disease, and we propose that the Gprotein-coupled estrogen receptor (GPER) is a promising therapeutic target. Our preliminary data indicate a crucial role for this receptor in vascular health: GPER activation attenuates salt-induced vascular remodeling while GPER deletion increases pulse pressure, an in vivo indicator of arterial stiffness. The mechanism for this protection is through attenuation of oxidative stress and extracellular matrix deposition. In addition, we find that aging decreases vascular GPER expression which may decrease the effectiveness of currently available hormone therapies. Taken together, we hypothesize that vascular GPER protects from arterial stiffness, and targeting this receptor will decrease cardiovascular risk in aging women.

Our ongoing studies use a combination of in vivo, ex vivo, and in vitro approaches to assess this hypothesis in multiple ways. High-frequency ultrasound allows in vivo measurement of pulse wave velocity, the gold standard for assessing vascular stiffness. As opposed to traditional uniaxial pressure myography, biaxial mechanical phenotyping performed in collaboration with a biomedical engineer will allow the use of computational models to delineate the contributing factors for arterial stiffness. Measurements of oxidative stress will be obtained using electron spin resonance spectroscopy, a direct and sensitive approach for quantifying free radicals in biological samples. Moreover, an inducible, cell-specific GPER knockout mouse model will allow us to specifically assess the impact of decreased vascular GPER expression during adulthood on the response to nonselective estrogen therapy.

Continued...

- **KENNETH D. MITCHELL, PHD**
  Professor, Department of Physiology,
  Director, Medical Education,
  Director, DeBakey Scholars Program,
  Assistant Director, Animal Transgenic Core Facility,
  Tulane University School of Medicine, New Orleans, LA.

On October 5, 2017, Dr. Kenneth D. Mitchell, Senior COBRE Mentor, presented a seminar entitled "ANG II-Dependent Hypertension: An Unexpected Journey."

SUMMARY OF PRESENTATION:

Dr. Mitchell explained that studies performed in his laboratory demonstrated that the renal functional and morphological changes that occur in Cyp1a1-Ren2 transgenic rats with ANG II-dependent malignant hypertension are characterized by decreased GFR and RBF, increased RVR, increased proliferating cell number in cortical tubules and cortical interstitium and increased collagen deposition in the renal interstitium. Such renal pathological changes involve activation of PDGF receptor-related kinase, and blocking this pathway ameliorates the renal morphological abnormalities observed in this model of ANG II-dependent malignant hypertension. In addition, chronic PDGF receptor antagonism with imatinib mesylate improves renal hemodynamics independent of changes in blood pressure in Cyp1a1-Ren2 rats with ANG II-dependent malignant hypertension. Collectively, the data presented indicate that elevated levels of PDGF protein and PDGF receptors contribute importantly to the renal injury, the derangements in renal hemodynamics and the increased urinary protein excretion in ANG II-dependent malignant hypertension.

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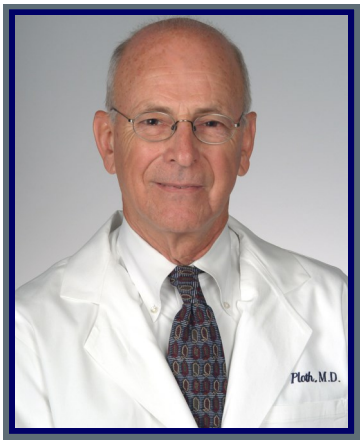

- **DAVID W. PLOTH, MD**
  Professor, Department of Physiology,
  Distinguished Professor, Endowed Chair: Williams
  Department of Medicine, Division of Nephrology,
  Medical University of South Carolina, Charleston, SC.

On October 12, 2017, Dr. Ploth presented, "Unexpected Prevalence of CKD, Diabetes, & Hypertension in Rural Tanzania."

SUMMARY OF PRESENTATION:

Non-communicable diseases (NCD) including chronic kidney disease (CKD) and the typically comorbid conditions of diabetes mellitus (DM), hypertension (HTN), and cardiovascular disease represent increasing public health challenges in low- and middle-income countries. The present studies were conducted to explore the hypothesis that there are previously underappreciated and interrelated epidemics of CKD, DM, and HTN in rural Tanzania. To explore this hypothesis we initially assessed prevalence in a probability-based sample of 740 subjects who were randomly sampled from households in a geographic area in Kisarawe District of rural Tanzania, which has a population of 21,205.

In the random household sample the prevalence of CKD stages 3 to 5 was associated with higher age ($p < 0.05$) and male gender ($p<0.05$). The prevalence of CKD stage 5 among those aged 18-26 years was surprisingly high (5.7%), which suggests a possible role for infectious agents in the pathogenesis of CKD in rural Tanzania. In the clinic-based sample we found similar results, with elevated markers for CKD, DM, and HTN. The prevalence of all stages of HTN increased with advancing age ($p < 0.05$). We observed a significant, direct relationship between increasing levels of BP and the prevalence of glycosuria(<0.05). Proteinuria was also associated with elevated BP ($p < 0.05$).

In summary we observed unexpectedly high and similar prevalence estimates for CKD, HTN and DM in a probability based sample in rural Tanzania and from observations in a walk-in community clinic. The higher than expected prevalence of these NCD's will likely contribute to rapidly accelerating rates of cardiovascular

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morbidity and mortality in these areas. Additional studies are desperately needed to expand the characterization and define the causality of the CKD, HTN and DM that we observed in this rural setting. It is imperative that as these additional studies are performed, the prevalence and incidence of these non-communicative diseases be monitored in response to prevention and treatment paradigms directed at reducing of the risk of kidney disease, DM, HTN and cardiovascular disease in order to prevent a major public health threat in Tanzania.

- **PRERNA KUMAR, PHD**
  Instructor, Department of Physiology,
  Tulane University School of Medicine,
  New Orleans, LA.

Dr. Kumar presented, "Sodium Butyrate and Retinoic acid Attenuate Renal Inflammation and Fibrosis in Npr1 Haplotype Mice" on October 19, 2017.

SUMMARY OF PRESENTATION:

Cardiac hormones atrial and brain natriuretic peptides bind to their receptor guanylyl cyclase/natriuretic peptide receptor-A (GC-A/NPRA), which plays a critical role in the regulation of blood pressure and fluid volume homeostasis. Mice lacking functional Npr1 gene (coding for GC-A/NPRA) exhibit renal insufficiency, cardiac hypertrophy and fibrosis. However, the underlying mechanisms remain largely unclear. Our findings in Npr1 haplotype mice model demonstrate that epigenetic upregulation of Npr1 gene transcription by retinoic acid and histone deacetylate inhibitor, sodium butyrate leads to attenuation of renal inflammation and fibrosis and systolic blood pressure. Moreover, retinoic acid and sodium butyrate enhance signal transducer and activator of transcription 1 acetylation in the kidneys of Npr1 haplotype mice. The acetylated STAT1 forms a complex with nuclear factor-κB p65, thereby inhibiting its DNA-binding activity and downstream proinflammatory signaling cascades. The current findings will help in developing interventional therapies and new treatment strategies for hypertension and renal dysfunction in humans.

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- **EDGAR A. JAIMES, MD**
  Chief of Renal Service, Department of Medicine,
  Memorial Sloan Kettering Cancer Center,
  Professor of Medicine, Weill Cornell Medical College,
  New York, NY.

November 2nd 2017 THRCE Seminar, "Hypertension, Renal Disease and Cancer" was presented by Dr. Edgar Jaimes.

SUMMARY OF PRESENTATION:

Acute and chronic kidney disease are highly prevalent in cancer patients both as result of the cancer itself or as result of treatment either medical or surgical. The development of novel treatments for cancer, including targeted and biological therapies, have resulted in a significant increase in the rate of renal injury both acute and chronic. In this seminar we will review the different mechanisms of vascular and renal injury in the cancer patient including mechanisms due to the cancer itself as well as secondary to novel targeted therapies. We will also discuss potential areas of research that could increase our understanding of the mechanisms involved and strategies for treatment.

- **AKIRA NISHIYAMA, MD, PHD**
  Chairman & Professor,
  Department of Pharmacology,
  Kagawa University Medical School,
  Kagawa, Japan.

"(Pro)renin receptor as a therapeutic target of cancer" was presented by Dr. Nishiyama on November 3rd, 2017.

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SUMMARY OF PRESENTATION:

Recent studies have revealed that (pro)renin receptor ((P)RR) is an essential component of the Wnt receptor complex composed of Frizzled and low density lipoprotein receptor-related protein 6 (LRP6). Since constitutive activation of Wnt/β-catenin signaling pathway is prevalent without any active mutation in pancreatic ductal adenocarcinoma (PDAC), we first investigated whether (P)RR becomes a therapeutic target of PDAC. We found an aberrant expression of (P)RR in premalignant PanIN and PDAC lesions of pancreatic tissues, as well as 6 different cultured human PDAC cell lines. Inhibiting (P)RR with siRNA or monoclonal (P)RR antibodies attenuated cultured PDAC cell proliferation, which was associated with inactivation of Wnt/β-catenin signaling pathway. On the other hand, overexpression of (P)RR in human pancreatic ductal epithelial (HPDE) cells activated Wnt/β-catenin signaling pathway and induced inappropriate cell proliferation. In nude mice subjected to subcutaneous implantation of human PDAC cells, intravenous administration of (P)RR antibodies significantly inhibited tumor growth, which was associated with inhibition of Ki-67 expression and β-catenin activity. Similarly, (P)RR expression was aberrant in colon cancer and glioblastoma tissues. Furthermore, both in vitro and in vivo data showed that blockade of (P)RR significantly inhibited the progression of these cancer cells. Finally, recent studies with whole genome analyses have revealed that in addition of the activation of Wnt/β-catenin signaling pathway, (P)RR overexpression directly induces genomic instability. These data are consistent with the hypothesis that (P)RR is essentially involved in carcinogenesis and, therefore, potential therapeutic target of cancer.

- **JING CHEN, MD, MD, MMSC, MSC**
  Professor, Department of Medicine,
  Division of Nephrology & Hypertension,
  Tulane University School of Medicine,
  New Orleans, LA.

On November 16th 2017, Dr. Chen presented "Lowering Blood Pressure with Anti-inflammatory Agents: A Crazy Idea or an Evolving Paradigm?"

Continued...

SUMMARY OF PRESENTATION:

Hypertension is highly prevalent and a major cause of cardiovascular disease (CVD) and mortality worldwide. Hypertension is a complex condition, and about 90% of cases that are classified as essential hypertension have no known precise cause. Recently, increased evidence suggests that inflammation, oxidative stress, and endothelial dysfunction may play a key role in the upstream etiology of hypertension. Dr. Chen reviewed the research findings from animal and perspective cohort studies, as well as clinical trials, to illuminate the underlying pathogenesis of inflammation that leads to hypertension and its associated cardiovascular complications. She also presented their study findings that suggested specific inflammatory pathways involving interleukin-6, tumor necrosis factor alpha, and transforming growth factor beta may play a role in resistant hypertension among patients with chronic kidney disease. In addition, she presented their data that suggested that treating inflammation, oxidative stress, and endothelial dysfunction with sodium nitrite and isoquercetin might lower blood pressure. She speculated that reducing inflammation may be critical in the primary prevention of hypertension and the associated cardiovascular disease.

UPCOMING MEETINGS:

- The Experimental Biology Meeting
  ~ San Diego, California, April 21–25, 2018
- 7th Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE) Conference
  ~ Washington, District of Columbia, June 24-26, 2018.
- AHA Council on Hypertension | Council on Kidney in Cardiovascular Disease
  ~ Chicago, Illinois, September 6-9, 2018
- American Society of Nephrology (ASN) Kidney Week 2018
  ~ San Diego, California, October 23 - 28, 2018.

Publications

Recent Publications (includes those omitted from previous newsletters)

- **Bazan HA, Lu Y, Jun B, Fang Z, Woods TC, Hong S. Circulating inflammation -resolving lipid mediators RvD1 and DHA are decreased** in patients with acutely symptomatic carotid disease. *Prostaglandins Leukot Essent Fatty Acids. 2017 Oct;125:43-47. doi: 10.1016/j.plefa.2017.08.007. PMID: 28987721*
- **Cortes AL, Gonsalez SR, Rioja LS, Oliveira SSC, Santos ALS, Prieto MC, Melo PA, Lara LS.** Protective outcomes of low-dose doxycycline on renal function of Wistar rats subjected to acute ischemia/reperfusion injury. *Biochim Biophys Acta. Epub 2017 Oct 5;1864(1):102-114. doi: 10.1016/j.bbadis.2017.10.005. PMID: 28987762, PMCID: PMC5705293.*
- **Gao H, Molinas AJR, Miyata K, Qiao X, Zsombok A.** Overactivity of Liver-Related Neurons in the Paraventricular Nucleus of the Hypothalamus: Electrophysiological Findings in db/db Mice. *J Neurosci. 2017 Nov 15;37 (46):11140-11150. doi: 10.1523/JNEUROSCI.1706-17.2017. Epub 2017 Oct 16. PMID: 29038244, PMCID: PMC5688523.*
- **Gonzalez AA, Salinas-Parra N, Leach D, Navar LG, Prieto MC**. PGE2 upregulates renin through E-prostanoid receptor 1 via PKC/cAMP/CREB pathway in M-1 cells. *Am J Physiol Renal Physiol. 2017 Oct 1;313(4):F1038-F1049. doi: 10.1152/ajprenal.00194.2017. PMID: 28701311, PMCID: PMC5668586.*
- **Gonzalez AA, Zamora L, Reyes-Martinez C, Salinas-Parra N, Roldan N, Cuevas CA, Figueroa S, Gonzalez-Vergara A, Prieto MC**. (Pro)renin receptor activation increases profibrotic markers and fibroblast-like phenotype through MAPK-dependent ROS formation in mouse renal collecting duct cells. *Clin Exp Pharmacol Physiol. 2017 Nov;44(11):1134-1144. doi: 10.1111/1440-1681.12813. PMID: 28696542, PMCID: PMC5643228.*
- **Hennrikus M, Gonzalez AA, Prieto MC**. The prorenin receptor in the cardiovascular system and beyond. Am J Physiol Heart Circ Physiol. Epub 2017 Nov 3;314(2):H139-H145. doi: 10.1152/ajpheart.00373.2017. PMID: 29101170
- **Lightell DJ Jr, Moss SC, Woods TC**. Upregulation of miR-221 and -222 in response to increased extracellular signal-regulated kinases 1/2 activity exacerbates neointimal hyperplasia in diabetes mellitus. Atherosclerosis. *Epub 2017 Dec 9. doi: 10.1016/j.atherosclerosis.2017.12.016. PMID: 29276985, PMCID: PMC5812823*
- **Majid DSA**. Peroxynitrite in the regulation of renal function: Implications in physiology and in pathophysiology of salt-sensitive hypertension. Chinese Journal of Hypertension (Invited Review article; In press)

Publications

Continued...

- **Mehaffey E, Majid DSA**. Tumor necrosis factor-α, kidney function, and hypertension. *Am J Physiol Renal Physiol. 2017 Oct 1;313(4):F1005-F1008. doi: 10.1152/ajprenal.00535.2016. PMID: 28724611, PMCID: PMC5668589*
- **Prieto MC, Reverte V, Mamenko M, Kuczeriszka M, Veiras LC, Rosales CB, McLellan M, Gentile O, Jensen VB, Ichihara A, McDonough AA, Pochynyuk OM, Gonzalez AA.** Collecting duct prorenin receptor knockout reduces renal function, increases sodium excretion, and mitigates renal responses in ANG II-induced hypertensive mice. *Am J Physiol Renal Physiol. 2017 Dec 1;313(6):F1243-F1253. doi: 10.1152/ajprenal.00152.2017. PMID: 28814438, PMCID: PMC5814641.*
- **Salinas-Parra N, Reyes-Martínez C, Prieto MC, Gonzalez AA.** Prostaglandin E2 Induces Prorenin-Dependent Activation of (Pro)renin Receptor and Upregulation of Cyclooxygenase-2 in Collecting Duct Cells. *Am J Med Sci. 2017 Sep;354(3):310-318. doi: 10.1016/j.amjms.2017.05.018. PMID: 28918839, PMCID: PMC5657580.*
- **Singh P, Castillo A, Islam MT, Majid DSA.** Evidence for Prohypertensive, Proinflammatory Effect of Interleukin-10 During Chronic High Salt Intake in the Condition of Elevated Angiotensin II Level. *Hypertension. 2017 Oct;70(4):839-845. doi: 10.1161/HYPERTENSIONAHA.117.09401. PMID: 28847894, PMCID: PMC5657538.*
- **Shao W, Rosales CB, Gonzalez C, Prieto MC, Navar LG**. Effects of serelaxin on renal microcirculation in rats under control and high-angiotensin environments. *Am J Physiol Renal Physiol. Epub 2017 Oct 4;314(1):F70-F80. doi: 10.1152/ajprenal.00201.2017.PMID: 28978531.*

Presentations

From September through December 2017, investigators and physicians affiliated with T.H.R.C.E. participated in many regional, national, & international meetings

AHA Council on Hypertension Joint Sessions; Sept. 13-16, 2017; San Francisco, CA.

- **Satou R, Woods TC, Miyata K, Cypress MW, Katsurada A, Dugas CM, Lightell, Jr D, Navar LG.** Blockade of Sodium Glucose Cotransporter 2 by Canagliflozin Suppresses High Glucose induced Angiotensinogen Augmentation in Renal Proximal Tubular Cells. #P414
- **Woods TC, Satou R, Miyata K, Katsurada A, Dugas CM, Lightell, Jr D, Navar LG.** Sodium Glucose Cotransporter 2 Inhibition by Canagliflozin Attenuates Intrarenal Angiotensinogen Augmentation in Type 2 Diabetes Mellitus. #P464

ASN Kidney Week; Oct 31 - Nov 5, 2017; New Orleans, LA.

- **Chen J, Bundy JD, Hamm LL, Hsu C-Y, Lash JP, Miller ER, Thomas G, Cohen DL, Raj DS, Chen H-Y, Xie D, Rao PS, Weir MR, Wright JT, Rahman M, He J.** Inflammation and Apparent Treatment Resistant Hypertension in Patients with CKD – The Results from the CRIC Study. FR-PO570, P-550.
- **Dobre MA, Townsend RR, Yang W, Anderson AH, Batuman V, JChen J, Jaar BG, Kallem RR, Rincon-Choles H, Sozio SM, Steigerwalt SP, Feldman HI, Hostetter TH, Rahman M.** Serum Bicarbonate and Pulse Wave Velocity in CKD – A Report from the CRIC Study. TH-PO452, P-216.
- **Edgington-Giordano F, Liu H, Hilliard S, Liu J, Li Y, Song R, Saifudeen ZR, El-Dahr SS.** Intrauterine Growth Restriction (IUGR) by Maternal Protein Undernutrition Disrupts the Transcriptional Networks of Energy Metabolism in Nephron Progenitors. SA-PO558, P-823.
- **El-Dahr SS, Saifudeen ZR, Liu H.** Polycomb Repressive Complex-2 (PRC2) Fine-Tunes Timing of the Final Wave of Nephrogenesis. TH-OR082 Oral, P-22.
- **Ginsberg C, Craven T, Chonchol M, Cheung AK, Sarnak MJ, Killeen AA, Raphael KL, Bhatt UY, Chen J, Chertow GM, Freedman BI, Oparil S, Wall BM, Wright CB, Shlipak M, Ix JH.** PTH, FGF23, and Effects of Intensive Blood Pressure Lowering in SPRINT Participants with CKD. FR-PO539, P– 541.
- **Gogulamudi VR, Subramanian U, Pandey KN**. Expression of T Regulatory Cells in the Kidneys of Guanylyl Cyclase/Natriuretic Peptide Receptor-A Gene-Knockout Mice. TH-PO416, P-207.
- **Harhay MN, Xie D, Hsu C-Y, Go AS, Chen J, Lash JP, Akkina S, Zhang X, Vittinghoff E, Sozio SM, Seliger SL, Dobre MA, Blumenthal JB, Deo R, Reese PP, Yaffe K, Tamura MK.** Pre-Dialysis Cognitive Impairment and Pre-Emptive

Continued...

Placement of Dialysis Access: Findings from the Chronic Renal Insufficiency Cohort Study. FR-PO774 , P-604.

- **Hsu C-Y, Hsu RK, Liu KD, Anderson AH, Chen J, Chinchilli VM, Feldman HI, Garg AX, Hamm LL, Kaufman JS, Kimmel PL, Kusek JW, Parikh CR, Ricardo AC, Rosas SE, Saab G, Sha D, Sondheimer JH, Taliercio JJ, Yang W, Go AS**. Impact of AKI on Urine Protein Excretion. FR-PO097, P-424.
- **Hsu C-y, Xie D, Zhang X, Bonventre JV, Jing Chen J, Drawz PE, Feldman HI, Go AS,4 Edward J. Horwitz EJ, Kimmel PL, Lunn MR, Mifflin TE, Ricardo AC, Waikar SS, Yang J, Liu KD**. Urine Injury Biomarker Level before and after AKI: Results from the CRIC Study and CKD Biomarker Consortium. FR-PO074, P-418.
- **Hsu RK, Hsu C-Y, McCulloch CE, Yang J, Anderson AH, Chen J, Feldman HI, He J, Liu KD, N**avaneethan SD, Porter AC, Rahman M, Tan TC, Wilson FP, Xie D, Zhang X, Go AS. Impact of AKI and Source of Serum Creatinine Measurements on Subsequent Kidney Function Decline. FR-PO098, P-425.
- **Kumar P, Nguyen C, VR, Samivel R, Pandey KN**. Mocetinostat Attenuates Renal Injury and Dysfunction via the Inhibition of HDAC in Npr1 Gene-Targeted Mutant Mouse Models. SA-PO1081, P-956.
- **Murali A, Cargill K, Mukherjee E, Saifudeen ZR, Sims-Lucas S**. HIF Regulation of Nephron Progenitor Metabolic State Mediates Cell Fate Decisions. TH-OR078 Oral, P-21.
- **Navar LG, Satou R, Miyata K, Katsurada A, Dugas CM, Lightell DJ, Woods TC.** Amelioration of Kidney Injury by Inhibition of Sodium Glucose Cotransporter 2 with Canagliflozin in Mice with Type 2 Diabetes Mellitus. TH-PO672, P-273.
- **Nazih L. Nakhoul,1 L. Lee Hamm,1 Kathleen S. Hering-Smith,1 Mohammed T. Islam,1 Solange Abdulnour-Nakhoul**. Hypercapnia Increases Urinary Ammonium Excretion and Upregulates Expression of the NH3/NH4+ Transporters Rh Glycoproteins. TH-PO1019, p-365.
- **Saraf S, Hsu JY, Chen J, Chen TK, Fischer MJ, Hamm LL, Mehta R, Sondheimer JH, Weir MR, Zhang X, Ricardo AC, Lash. JP**. Anemia Is a Risk Factor for Incident ESRD. FR-PO391, P-501.
- **Song R, Janssen AT, Kidd LR, Yosypiv IV**. Conditional Ablation of the Prorenin Receptor (PRR) in Nephron Progenitor Cells (NPCs) Results in Developmental Programming of Hypertension. Oral presentation: SA-OR050 Oral, P-85.
- **Visniauskas B, Reverte V, Rosales CB, Galeas-Pena M, Abshire CM, Lindsey S, Prieto MC.** High Fat Diet Increases Plasma Soluble Prorenin Receptor (sPRR), Ang-II, Systolic Blood Pressure (SBP), and Arterial Stiffness in Type 2 Diabetic (T2D) Male but Not in Female Mice. TH-PO694, P-278.

Invited Lectures

THRCE investigators & physicians were invited speakers at various national & international events during September through December, 2017

- On December 13, **Dr. L. Gabriel Navar** presented a video Lecture titled, "Regulation of Renal Hemodynamics." The lecture was prerecorded and the presentation, coordinated by Dr. Majid, was held at the BLDE University and Medical School in Vijayapura, Kamataka, India

- From December 2nd till 17th **Dr. Dewan S. A. Majid** visited the BLDE University where he toured all the Basic and Clinical Science Departments of BM Patil Medical College, the School of Nursing and the School of Pharmacy of BLDE University, and discussed with the faculties of the institutions how to achieve and improve academic research in the medical education curriculum. During his invited visit, he presented the following five seminars to the students, faculties and investigators at the institution:
  - Dec. 6 "Regulation of Blood Pressure; Physiology & Pathophysiology."
  - Dec. 8 "Tumor Necrosis Factor-, Kidney Function & Hypertension."
  - Dec. 12 "Why Physiology?"
  - Dec. 14 "Problem Based Learning in Physiology."
  - Dec. 14 "Salt-Sensitive Hypertension: Perspectives on Intrarenal Mechanisms."
- **Dr. Majid** presented "Renal Physiology; what a nephrologist should know?" on December 24 at the CME conference organized by the "Bangladesh Renal Association" at the Dhaka Club in Bangladesh.
- On November 30, **Dr. Kailash N. Pandey** presented, "Genetic and molecular determinants of natriuretic peptide receptor-A gene: Regulation of blood pressure and cardiovascular homeostasis," at the Department of Medicinal Chemistry, School of Ayurvedic Medicine, Institute of Medical Sciences, Banaras Hindu University, in Varanasi, India.
- On December 4, "Identification of significant genes responsible for regulation of blood pressure, through analysis of microarray data" was presented by **Dr. Pandey** at the Department of Applied Sciences at the Indian Institute of Information Technology, in Allahabad, India .
- **Dr. Pandey** presented, "Contribution of Npr 1 gene in the regulation of blood pressure and cardiovascular homeostasis: Role of histone modifications and transcription factors," on December 15 at the Department of Life Sciences, Amity Science, Technology & Innovation Center, Amity University, Noida-Delhi, India.
- **Dr. Zubaida Saidudeen** presented "Novel mechanisms in maintaining nephron progenitors during kidney Development" in October 2017 at the ASN Basic Science Symposium.
- **Dr. Ryosuke Sato** presented, "Inflammation regulates the intrarenal renin angiotensin system" at the ASN Basic Science Symposium in October 2017.

Calendar of Events

THRCE Seminars

January 11

HONGBING LIU, PHD
Assistant Professor, Department of Pediatrics,
Tulane University School of Medicine, New Orleans, LA.
"Intrauterine growth restriction (IUGR) and kidney development."

January 25

No Meeting
Date conflicts with medical student PBL sessions

February 8

SEMINAR CANCELLED & RESCHEDULED TO APRIL 5, 2018

February 22

BENARD O. OGOLA, PHD
Postdoctoral Fellow, Department of Pharmacology,
Tulane University School of Medicine, New Orleans, LA.
"GPER Attenuates Angiotensin II-Induced Oxidative Stress via cAMP-Mediated Regulation of NOX4."

March 8

SPECIAL THRCE SEMINAR IN HONOR OF WORLD KIDNEY DAY 2018

PAUL W. SANDERS, MD
Professor, Department of Medicine, Division of Nephrology,
University of Alabama at Birmingham, Birmingham, AL.
"Dietary Salt Intake and Hypertension: role of the Endothelium and Kidney."

March 22

ROBERT M. CAREY, MD., M.A.C.P., F.A.H.A., F.R.C.P.I.
Professor of Medicine
Dean, Emeritus, School of Medicine
Division of Endocrinology and Metabolism
University of Virginia Health System, Charlottesville, VA
"Role of AT2 receptors in cardiovascular and renal regulation."

April 5

JIA L. ZHUO, MD, PHD
Elected Fellow of AAAS, Section on Medical Sciences,
Overseas Fellow: Royal Society of Medicine, England,
Professor, Department of Pharmacology & Toxicology
Division of Nephrology, Internal Medicine,
Cardiovascular-Renal Research Center,
University of Mississippi Medical Center, Jackson, MS
"Roles of Proximal Tubule NHE3 in Angiotensin II-Dependent Hypertension: An Active Player or A Passive Bystander?"

Conferences are held alternative Thursdays at 4:00pm in the Tulane Medical School, Pharmacology Library, Room 4700
*** Denotes the seminar date is not our normally scheduled day.*

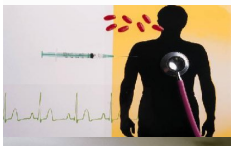
CORE FACILITIES & SERVICES

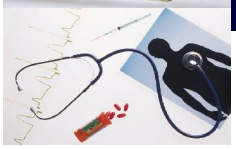
Tulane Hypertension and Renal Center of Excellence (THRCE) houses 4 research core facilities that were developed during COBRE phases I and II and are now maintained and supported by a COBRE Phase III grant awarded by the NIH/NIGMS. These core facilities are essential for the support of basic, clinical,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

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

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

T.H.R.C.E.





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

1430 Tulane Avenue, SL39
New Orleans, LA 70112

Comments are welcome:
Contact: Nina R. Majid
Phone: 504-988-3703
Fax: 504-988-2675
Email: 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 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.