March 8, 2018 was World Kidney Day (WKD). To commemorate 2018 WKD, THRCE set up a Tulane Kidney Health Screening Fair in collaboration with the National Kidney Foundation of Louisiana and the Departments of Physiology and Medicine, Section of Nephrology. The event was open to the public and participants were screened for blood pressure & the risk for developing kidney disease. Volunteers were Tulane Medical students who took blood pressure & BMI Measurements, and provided information of the various kidney diseases and health risks. In addition, THRCE hosted a special WKD Seminar by Dr. Paul W. Sanders, Professor of Medicine, Division of Nephrology, at the University of Alabama at Birmingham, Alabama. WKD is an international health awareness campaign that focuses on the importance of kidneys and on reducing chronic kidney disease and its associated health problems.
2018 Mayerson DiLuzio Lecture

The 2018 Mayerson-DiLuzio Lectureship was awarded to R. Ariel Gomez, MD, who presented, “Plasticity and Fate of Renin cells in Homeostasis and Disease” on March 5, 2018. Dr. Gomez is the Harrison Distinguished Professor at the University of Virginia, School of Medicine, in Charlottesville, Virginia. He is also the Professor of Pediatrics and Biology, the Founding Director of the Child Health Research Center, and the Director of the NIDDK Center of Excellence in Pediatric Nephrology at University of Virginia.

Dr. Gomez received his medical degree at the University of Buenos Aires School of Medicine in Argentina in 1975. After completing his residency in Pediatrics at the Hospital de Ninos “Ricardo Gutierrez”, Buenos Aires, Argentina, he served as Chief Resident at the same hospital followed by fellowships in Pediatric Nephrology, at the University of Iowa (1980-1983), under the mentorship of Jean Robillard, then at the University of California, San Francisco, (1983-1984), under the mentorship of Malcom Holliday and Donald Potter.

Dr. Gomez joined the University of Virginia School of Medicine in 1984 as an Assistant Professor in the Department of Pediatrics and established an independent research program that has been continuously supported by NIH funding since 1988. From 1997-2000, Dr. Gomez served as Genentech Professor and Associate Chair for Research for the Department of Pediatrics. In 2001 he became Interim Vice President for Research and Public Service and then, in 2003, Vice President for Research and Graduate Studies. He returned to full time research in 2008 as the Harrison Distinguished Professor of Pediatrics and holds a courtesy appointment in the Department of Biology at the School of Arts and Sciences.

The Mayerson-DiLuzio Lectureship was established in 1990 to honor the memories of Drs. Hyman S. Mayerson and Nicholas R. Di Luzio, who presided as Chairmen of the Tulane Physiology Department.
Tulane Professor, Dr. Dewan Majid chaired the 38th Annual Convention of the Bangladesh Medical Association of North America (BMANA) held July 26-29 at the Sheraton Hotel in New Orleans. BMANA is a nonprofit, nonpolitical, educational and charitable organization of medical professionals of Bangladeshi descent. BMANA was created in Michigan in 1981. Since then, 18 chapters of BMANA have been established across the United States. In addition to educational, cultural and charitable events organized by individual chapters, BMANA sponsors a national convention in a variety of North American cities. The conventions feature a unique blend of educational, cultural, social and humanitarian activities. This year’s convention was held in New Orleans.

Upholding BMANA’s 2018 theme, “Comprehensive Primary Care Directive in Disease Management,” the 38th annual Convention provided an innovative and comprehensive overview of the latest developments in the field of Medicine through enriched CME sessions as well as non-CME seminar programs driven by a pool of experts in various fields of specialty. Many distinguished physicians from within and outside BMANA membership participated as expert faculty in both CME as well as non-CME sessions. Apart from these lecture-oriented sessions, a topic-oriented poster session was featured with scientific materials presented by members of BMANA. The convention’s academic activities were designed to encourage and nourish the scientific endeavor among the members of BMANA.

Besides focusing on the scientific endeavors and academic program, the convention featured scientific poster sessions, non-scientific health awareness sessions (e.g. skincare, obesity, etc), Mina Bazaars, Book-fairs, Young physician symposium, City-tours, Evening shows & entertainments, and many more activities. One of the highlight of this convention was a memorable Gala Dinner event held on July 28 that included speeches by attending dignitaries, an awards ceremony and a cultural function. The awards ceremony recognized the extraordinary personnel who significantly contributed to management of patients’ care and health sectors in the United States and Bangladesh.
Co-Directors of THRCE, Dr. Lee Hamm and Dr. Gabriel Navar were among the attending dignitaries at the convention. Vice President and Dean of TUSOM, Dr. Lee Hamm participated as the Keynote Speaker. Chairman of the Department of Physiology, Dr. Gabriel Navar was recognized as the Special Guest of Honor. THRCE affiliates, Dr. Paul Whelton and Dr. Vecihi Batuman, participated as speakers at the convention’s CME sessions. Dr. Bernard Jaffe (Tulane Emeritus Professor of Surgery) was honored for his special contribution and services to Bangladesh. Since 2011, Dr. Jaffe has organized the Tulane Sponsored, “First Responder” Training Program that is held every year in Chittagong Medical College in Bangladesh.
Dr. Hamm recognized as Special Guest of Honor at BMANA Convention

Dr. Navar recognized as Special Guest of Honor at the BMANA Convention

Dr. Vecihi Batuman presenting a CME Session
INTERNATIONAL RESEARCH COLLABORATION

Six faculty members from the Chulabhorn International College of Medicine (CICM) of Thammasat University in Thailand visited the Department of Physiology and the Hypertension and Renal Center of Excellence between June 13th and 14th. The visitors included Dean, Dr. Kammal Kumar Pawa, Vice Dean, Dr. Peerapong Kitipawong, Vice Dean, Dr. Adis Tasanarong, Vice Dean, Dr. Thongchai Suntharapa, Assistant Dean, Dr. Dhave Setabutr, and Chair of Cardiovascular Technology, Mr. Anon Jantanukul.

The CICM was established with the purpose of playing a key role in ASEAN community (a regional organization comprised of ten Southeast Asian Countries) to provide next generation medical and biomedical science professionals with a standardized international institution. Part of the visit was to finalize a Memorandum of Understanding (MOU) between the Chulabhorn International College of Medicine and Tulane University School of Medicine (TUSOM) that was signed by Dr. Hamm and Dr. Pawa on June 13th. In addition, Dr. Tasanarong presented the HRCE seminar on June 14. The visit and MOU were facilitated by Dr. Supaporn (Tom) Kulthinee. Dr. Kulthinee is currently postdoctoral fellow under the direction of Dr. Navar. After completion of her postdoctoral fellowship, she will return to serve as a faculty position at the CICM. The MOU is intended to explore and promote collaborative research activities between faculties in the Department of Physiology at the THRCE, and the CICM. Collaborative research projects that have begun as an outcome of the agreement are primarily focused on the renal and neural mechanisms of hypertension, diabetes mellitus and the associated cardiovascular and renal disorders. The scientific networking both interinstitutional and individually will be used as a powerful tool to promote learning and professional growth in academics.
Dr. Navar and the faculty from CICM

GRADUATE STUDENT RECRUITMENT OPPORTUNITY AT THE 2018 EB MEETING

Dr. Navar and various faculty participated in the Graduate Student Recruitment Opportunity at the 2018 Experimental Biology meeting that was held in San Diego, CA from April 21-25, 2018.
GRANTS, HONORS & RECOGNITION AWARDED TO THRCE AFFILIATED INVESTIGATORS

L. Gabriel Navar, PhD:
- Attended the annual retreat of the Association of Chairs of Departments of Physiology (ACDP) November 30 – December 3. Discussions included consideration of the relationship between ACDP and the AAMC CFAS group, assessing support for science funding by the new congress and other legislative updates, creative ways for departments to generate more revenue including on-line courses, core lab facilities, technology transfer and MS programs.
- Recognized as outstanding mentor in an article that was published in the April 2018 issue of the Newsletter, INSIDE TULANE MED.
- Honored with the 2018 Mentor of the Year Award from the Southern Society for Clinical Investigation (SSCI) for his more than 30 years of guidance to students and junior faculty. The award was presented at the Plenary meeting on Friday, February 23, 2018 at the InterContinental New Orleans.
- Awarded a grant from the Carol Lavin Bernick Faculty Grant Program.

Kathleen Hering-Smith PhD:
- Elected to be Councilor of the SSCI.

Norman Kreaisman, PhD:
- Presented a Case-Based Learning seminar on March 7, 2018 to the Tulane University, Structural & Cellular Biology Department.
- Recipient of the “T2 Best Integrated Module” and “T2 Course of the Year” Awards at the Owl Club Awards Ceremony.

Prerna Kumar, PhD:
- Participated as judge at various occasions: At the Greater New Orleans Science and Engineering Fair Senior Division, at the Tulane University Health Sciences Research Days on February 19, and the Tulane University Lavin-Bernick Center on February 28.

Jean-Pyo Lee, PhD:
- Received Bridge Funding from the Tulane School of Medicine Bridge Program.
- Participated in the International Stroke Conference (ISC) in Los Angeles, CA, January 24-25 as moderator and presenter. She moderated two oral abstract sessions one, on January 24th titled “Clinical Rehabilitation and Recovery” and another on January 25th titled “Vascular Cognitive Impairment.”
Continued...

- Served as an abstract reviewer for Council on Arteriosclerosis, Thrombosis and Vascular Biology (ATVB) Meeting held in May 2018 in San Francisco, CA.
- Paper titled, “Neural Stem Therapy for Sub-acute and Chronic Ischemic Stroke” was accepted for publication in Stem Cell Research and Therapy.
- Participated in American Heart Association (AHA) Grant Peer Review Study Section (Vascular Endothelial Biology Basic).

**Dewan S. A. Majid, MD. PhD:**
- On January 5, 2018, received two “Memorandum of Honor” as a distinguished citizen of Bangladesh. One from the ‘Habiganj District Civic Association” in Habiganj, Bangladesh and the other from the “Shaistaganj Press Club” in Shaistaganj, Bangladesh.

**Kenneth D. Mitchell, PhD:**
- Nominated for Owl Club’s “Best T1 PBL Facilitator” award and the “Best T1 Module award.

**Kailash Pandey, PhD:**
- Awarded a grant from the Carol Lavin Bernick Faculty Grant Program.
- Participated in the AHA Vascular Discovery: From Genes to Medicine conference that was held in San Francisco, CA from May 10-12, 2018.

**Minolfa Prieto, PhD:**
- Attended the Gordon Research Conference on Angiotensin held in Ventura, CA from February 19-23, 2018.
- Elected Co-Chair of the 2020 Gordon Research Conference on Angiotensin, which will be held in Lucca, Tuscany, Italy.
- Received an award from NIH-NCATS Multidisciplinary Network Pilot Program grant of the CCTS-UAB. The title of the project is “Impact of Plasma Soluble Prorenin Receptor in Type 2 Diabetic Patients.”
- Participated in NIHHLBI study section from June 14-15, 2018 in Washington, DC.

**Zubaida Saifudeen, PhD:**
- Awarded an NIH R01 grant titled, “Intermediary Metabolism Control of Nephron Progenitor Lifespan.”

**Weijian Shao, PhD:**
- Received the outstanding staff member award during the December 2017 Annual Department of Physiology Holiday event.

**Cooper Woods, PhD:**
- Nominated for Owl Club Award, “Best T1 Professor”, won “Best T1 PBL Facilitator” award, and was recognized for the Excellence in Teaching award.
- Received the coveted Owl Club’s “Excellence in Teaching” award by receiving the highest score for a faculty liked by their students.
Continued...

- Participated in a VA Cardiology-B study section on June 6, 2018 in Washington, DC.

Andrea Zsombok, PhD:
- Participated in a NIH Study Section held in New Orleans from February 1-2.

STUDENTS, POST-DOCTORAL FELLOWS, & RESEARCH SCIENTISTS II:

**Research Scientist II:**
- The poster by **Hong Gao** (Mentor: Andrei Derbenev) presented at the Tulane University 29th Annual Health Sciences Research Days event that was held in February 2018 was selected for the Research in Neuroscience Award Sponsored by the Tulane Brain Institute. Her study was titled, “Emerging Mechanism of Glycine in control of Baroreflex.”

**Post-doctoral fellows:**
- **Supaporn Kulthinee** (Tom) and **Bruna Visniauskas** received APS 2018 Caroline Tum Suden/Frances Hellebrandt Professional Opportunity Awards to participate in the 2018 Experimental Biology Meeting.
- **Dr. Bruna Visniauskas** (mentor, Dr. Prieto) was selected as an oral presenter at the Renal Section Young Investigator Award Symposium, which will be held during the EB Meeting, on Sunday, April 22, 2018, 8:30-10:00AM in San Diego, CA.
- **Dr. Bruna Visniauskas** attended the Gordon Research Conference on Angiotensin in Ventura, CA from February 19-23, 2018.

**Graduate & Medical Students:**
- **Camille R. T. Bourgeois** (Mentor: Dr. Dr. Prieto) received the Hymen Mayerson award at the Ivy Day Awards Ceremony.
- **Joseph M. Garagliano** (Mentor: Dr. Sato) received:
  - The Nicholas Di Luzio award at the Ivy Day Awards Ceremony.
  - Excellence in Research and Presentation by a 4th Year DeBakey Scholar for his study, “Advanced Glycation end products stimulate angiotensinogen expression in renal proximal tubule cells”. The award was sponsored by the Dean of the School of Medicine and the poster was presented at the Tulane University 29th Annual Health Sciences Research Days event that was held in February 2018.
- **Michael Cypress** (Mentor: Drs. L. Gabriel Navar and Ryo Sato), graduated with a PhD in Physiology in May 2018.
- **Eamonn P. Mehaffey** (Mentor: Dr. Majid) received the Nicholas Di Luzio awards at the Ivy Day Awards Ceremony.
- Graduate Students **Justine Greco and Hunter Douglas**, were recognized with the “Honors in Physiology” Award for their outstanding academic achievement.
- **Stacy Yanofsky** (Mentor: Dr. Sato) and **Jennifer Hong** (Mentor: Dr. Prieto) were recipients of the Warren R. Bourgeois, III, MD and Usha Ramadhyani Bourgeois, MD Student Research Endowed Fund to support their summer research.
2018 SUMMER RESEARCH STUDENTS

Each year meritorious Medical and Undergraduate Research Students are selected to work with faculty who are affiliated with the THRCE. While some students begin and complete their research during their summer break, others continue their research beyond the summer, making time in between their academic studies. Some students receive a stipend while others are volunteers, but all students are exposed to the valuable nature of a career path in research, and have the opportunity to attend the various THRCE events and Seminars. The following students were selected for the 2018 Research Program:

MEDICAL STUDENTS:

DeBakey Scholar

• Kenny Vongbunyong
  Mentor: Dr. T. Cooper Woods

Tulane Medical Student Volunteers

• Thaidan Pham
  Mentor: Dr. T. Cooper Woods
• Christin Tee
  Mentor: Dr. Minolfia C. Prieto
• Cassidy Werner
  Mentor: Dr. A. Zsombok
• David P Le
  Mentor: Dr. Jean-Pyo Lee
• Arindra Jayasekara
  Mentor: Dr. Jean-Pyo Lee

Sponsor: Bourgeois Medical Research Endowment

• Jennifer Hong
  Mentor: Dr. Minolfia C. Prieto
• Stacy Yanofsky
  Mentor: Dr. Ryosuke Sato

Sponsor: Pediatric Nephrology Centers of Excellence, University of Virginia

• Ilona Brumfield
  Mentor: Dr. Zubaida Saifudeen

UNDERGRADUATE STUDENTS:

Louisiana Biomedical Research Network-LSU

• Peace Ekpo
  Mentor: Dr. Dewan S. A. Majid
  Southern University of New Orleans

Sponsor: LSUHSC Summer scholarship Award

• Marco Acosta
  Mentor: Dr. Minolfia C. Prieto
  University of La, Lafayette

Sponsor: PT Summer Student

• Stephanie Crabtree
  Mentor: Dr. Minolfia C. Prieto

UPCOMING MEETINGS

• September 6-9, 2018 ~ Hypertension Council meeting, in Chicago, IL
• October 23-27, 2018 ~ American Society of Nephrology Annual Meeting in San Diego, CA.
• October 25-28, 2018 ~ American Physiology Society (APS) Intersociety Meeting on Comparative Physiology: Complexity and Integration Conference. Meeting to be held in New Orleans, LA.
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 the THRCE Seminar Series are asked to provide a brief summary of their talk that we can share with our newsletter audience. From January through August, 2018, the following speakers presented THRCE seminars:

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

Dr. Hongbing Liu was the first speaker at our THRCE Seminar Series for the year 2018. Dr. Liu presented “Intrauterine growth restriction (IUGR) and kidney development.” on January 11, 2018.

SUMMARY:

Nephron progenitor cells (NPC) are a subset of the metanephric mesenchyme cells, which continually give rise to nephrons thereby self-renewing and differentiating before the termination of nephrogenesis. HDACs are a group of epigenetic regulators that control cell fate but their role in balancing NPC renewal and differentiation is unknown. NPC-specific deletion of HDAC1 and HDAC2 genes in mice results in early postnatal lethality due to renal hypo-dysplasia and loss of NPC. HDAC1/2 interact with the NPC renewal regulators Six2, Osr1 and Sall1, and are co-bound along with Six2 on the Six2 enhancer. Although the mutant NPC differentiate into renal vesicles, HDAC1/2 mutant kidneys lack nascent nephrons or mature glomeruli, a phenocopy of Lhx1-mutants. Transcriptional profiling and network analysis identified disrupted expression of Lhx1 and its downstream
genes Dll1 and Hnf1/4 as key mediators of the renal phenotype. In addition, although HDAC1/2-deficient NPC and RV overexpress hyperacetylated p53, TP53 deletion failed to rescue the renal dysgenesis. We conclude that the epigenetic regulators, HDAC1 and HDAC2, regulate nephrogenesis via interactions with the transcriptional programs of nephron progenitors and renal vesicles.

- Benard O. Oogola, PhD
  Postdoctoral Fellow, Department of Pharmacology,
  Tulane University School of Medicine,
  New Orleans, LA.

Dr. Benard O. Ogola, presented “GPER Attenuates Angiotensin II-Induced Oxidative Stress via cAMP-Mediated Regulation of NOX4,” on February 22, 2018.

SUMMARY:
Our previous work shows that the G protein-coupled estrogen receptor (GPER) is protective in the vasculature and kidneys during Ang II-dependent hypertension, in part by inhibiting oxidative stress. In addition, we find that acute estrogenic signaling via GPER involves activation of the cAMP signaling pathway in vascular smooth muscle cells. Ang II stimulates the production of reactive oxygen species (ROS) via NADPH oxidase (NOX) complex activation. Our current findings indicate that Ang II increased oxidative stress, NADP/NADPH ratio, and NOX4 expression in rat aortic smooth muscle cells, while treatment with the GPER agonist G-1 prevented these changes through cAMP signaling. Moreover, aortas from GPER knockout mice had increased oxidative stress and NOX4 expression compared with wild type aortas.

Arterial stiffness occurs in response to aging, hypertension, and other conditions of oxidative stress and is an independent predictor of cardiovascular disease. Previous results from our lab suggest that GPER induces protection from arterial stiffness, perhaps through this antioxidant mechanism. The gold standard of measuring arterial stiffness is pulse wave velocity (PWV), measured as the pulse wave transit
time from the carotid to femoral artery. Because this method has technical limitations, we developed a method to measure local carotid PWV using ultrasound M-mode or color Doppler. The two methodologies were highly correlated, and increased carotid PWV was observed in both male and female mice with aging. Additionally, both methods correlated with ex vivo carotid thickness. Ultrasound measurements also showed a decrease in systolic function with aging, which is less prominent in female mice. Future studies will assess how genetic deletion of GPER alters vascular and cardiac function.

Taken together, our preliminary data indicate the importance of GPER in protection against Ang II-induced oxidative stress. Furthermore, treatments targeting GPER may prevent vascular dysfunction and cardiovascular risk.

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

- Paul W. Sanders, MD
  Professor, Department of Medicine,
  University of Alabama at Birmingham,
  Division of Nephrology, Department of Medicine,
  Birmingham, AL.

March 8th 2018 was World Kidney Day (WKD). To commemorate WKD, THRCE hosted a special seminar by Dr. Paul W. Sanders. The title of the 2018 WKD THRCE Seminar was, “Dietary Salt Intake and Hypertension: role of the Endothelium and Kidney.”

**SUMMARY:**
Salt-resistance and salt-sensitivity refer specifically to the effect of dietary sodium chloride (salt) intake on blood pressure. Recent evidence suggests that salt-sensitivity promotes a higher mortality rate. Accumulation of salt may stimulate a vascular remodeling process that results in endothelial dysfunction, arterial stiffness, and subsequent increases in blood pressure. These vascular responses to chronic excess salt intake may be amplified in salt-sensitive individuals. Despite
remarkable advances in vascular biology, however, the pathogenesis of the complex syndrome of salt-sensitive hypertension has remained elusive. This talk will review the hemodynamic and kidney effects of increased dietary salt intake, but will focus on endothelial dysfunction, which may pose a particularly significant risk factor in the development of salt sensitivity and subsequent hypertension. Finally, there are some recent pre-clinical findings that demonstrate an interesting role for dietary potassium intake in mitigating the vascular responses to excess dietary salt.

Professor, Department of Medicine,
Dean, Emeritus, School of Medicine,
Division of Endocrinology and Metabolism
University of Virginia Health System,
Charlottesville, VA


SUMMARY:
Sodium (Na+) retention by the kidneys is considered a major mechanism by which hypertension develops, and the intrarenal renin-angiotensin system (RAS) plays an important role. The major RAS effector, angiotensin II (Ang II), acts via two major receptors, AT1R and AT2R. AT2R mediate increased sodium (Na+) excretion (natriuresis) by inhibiting Na+ reabsorption in the renal proximal tubule (RPT) and by opposing the Na+ retaining ability of Ang II via AT1R.

Compound 21 (C-21) is a highly selective non-peptide angiotensin AT2 receptor (AT2R) stimulating agent (agonist). We tested the hypothesis that chronic AT2R activation with C-21 induces natriuresis via an action at the renal proximal tubule (RPT) and lowers blood pressure (BP) in experimental angiotensin II (Ang II)-dependent hypertension.

In rats, Ang II infusion increased both sodium (Na+) retention and BP on Day 1 and BP remained elevated throughout the 7 day infusion period. Either intrarenal or systemic administration of C-21 prevented Ang II-mediated Na+ retention on Day 1,
induced continuously negative cumulative Na+ balance compared with Ang II alone, and reduced BP chronically. The effects of C-21 are likely to be mediated by action on the RPT as acute systemic C-21-induced natriuresis was additive to that induced by chlorothiazide and amiloride. At 24h of Ang II infusion, AT2R activation with C-21, both intrarenally and systemically, translocated AT2Rs from intracellular sites to the apical plasma membranes of RPT cells without altering the total cellular pool of AT2Rs and internalized/inactivated major RPT Na+ transporters Na+-H+-exchanger-3 (NHE-3) and Na+/K+ATPase (NKA). C-21 lowered BP to a similar degree whether administered before or subsequent to the establishment of Ang II-dependent hypertension.

Our previous study in normal Sprague Dawley rats and genetically engineered mice documented that acute systemic AT2R activation with C-21 induces natriuresis by translocating AT2Rs to the apical plasma membranes of RPTCs and internalizing/ inhibiting major RPTC transporters NHE-3 and NKA. The present study builds on these findings by demonstrating in an Ang II infusion model of experimental hypertension that chronic AT2R activation with C-21 prevents initial renal Na+ retention and lowers BP over a 7 day period. In addition, C-21 was an effective natriuretic and antihypertensive agent whether administered systemically or directly into the kidney in this experimental model. We also demonstrated that continuous C-21 administration, both systemically and intrarenally, induced sustained negative cumulative Na+ balance accompanied by AT2R recruitment from intracellular sites to the apical plasma membranes of RPT cells and internalization/inactivation of major RPT Na+ transporters NHE-3 and NKA. Importantly, C-21-induced natriuresis was related to inhibition of Na+ transport in the RPT as it was additive to that observed with diuretics acting at either the distal tubule or the cortical collecting duct. We further demonstrated that C-21 was equally effective in lowering BP whether administered before or after Ang II-dependent hypertension had been established.

Taken together, these results strongly support a role for AT2R agonists as natriuretic/diuretic agents that improve the pressure-natriuresis relationship and are potential candidates for the treatment of hypertension and disorders of Na+ and fluid retention in humans. Chronic AT2R activation initiates and sustains receptor translocation to RPT apical plasma membranes, internalizes/inactivates NHE-3 and NKA, prevents Na+ retention resulting in negative cumulative Na+ balance, and lowers BP in experimental Ang II-induced hypertension.
Acting uniquely at the RPT, C-21 is a promising candidate for the treatment of hypertension and Na+-retaining states in humans. These findings indicate that AT2R activation can lower BP chronically under conditions when the renin-angiotensin system is stimulated; thus, AT2Rs are predicted to be legitimate therapeutic targets for hypertension in humans. Currently no effective diuretic/natriuretic agent is available that acts in the RPT. AT2R activation, therefore, may provide a complimentary nephron-specific site for diuresis/natriuresis in humans.

- Jia L. Zhuo, MD, PhD
  Professor, Department of Pharmacology & Toxicology,
  University of Mississippi Medical Center,
  Jackson, MS.

Dr. Jia L. Zhuo, presented “Roles of Proximal Tubule NHE3 in Angiotensin II-Dependent Hypertension: An Active Player or A Passive Bystander?” on April 5, 2018.

SUMMARY:
The renal mechanisms underlying angiotensin II-dependent hypertension have been extensively studied, but remain incompletely understood. Recent studies have suggested that the Na+/H+ exchanger 3 (NHE3) in the proximal tubule of the kidney plays little, if any, role in the regulation of blood pressure and angiotensin II (ANG II)-induced hypertension. To unravel the roles of NHE3 in the proximal tubule, we used global NHE3-deficient mice (Nhe3-/-), kidney-specific Nhe3-/- mice with transgenic rescue of the Nhe3 gene in small intestines (tgNhe3-/-), and proximal tubule-specific Nhe3-/- mice (PT-Nhe3-KO) to determine whether NHE3 in the proximal tubule of the kidney plays a key role in maintaining basal blood pressure homeostasis and the development of ANG II-induced hypertension. We found that under basal conditions, Nhe3-/-, tgNhe3-/-, and PT-Nhe3-KO mice had significantly lower basal systolic blood pressure and mean intra-arterial blood pressure than wildtype mice, but 24 h urinary Na+ excretion and the pressure natriuresis response were significantly increased only in PT-Nhe3-KO mice. By
contrast, Nhe3-/ - or tgNhe3-/ - mice showed significant increases in 24 h fecal Na+ excretion, whereas no difference was found in fecal Na+ excretion between wildtype and PT-Nhe3-KO mice. Infusion of ANG II (1.5 mg/kg/day, i.p.) induced severe hypertension in wildtype mice, but ANG II-induced hypertension was significantly attenuated in PT-Nhe3-KO mice. Thus our studies strongly support an important role of NHE3 in the proximal tubule of the kidney in maintaining basal blood pressure homeostasis and the development of ANG II-induced hypertension, most likely via promoting proximal tubule Na+ reabsorption.

Dr. Martha Franco Guevara, presented “ATP and activation of P2X renal receptors: A new concept in the pathophysiology of renal injury in hypertension.” on May 10, 2018.

SUMMARY:
Glomerular vasoconstriction and tubulointerstitial injury are observed before glomerular damage in models of hypertension. Increased ATP concentrations alters renal mechanisms involved in the long-term control of blood pressure, autoregulation of glomerular filtration rate and blood flow, increased tubuloglomerular feedback (TGF) responses, and decreased sodium excretion. The activation of renal purinergic receptors under an elevated interstitial ATP milieu is a fundamental pathway regulating renal hemodynamics, in particular autoregulatory responses. Elevated ATP and abnormal expression of P2X receptors has been demonstrated under a genetic background or induction of hypertension with vasoconstrictor peptides. In addition to the abnormalities of the microcirculation in the hypertensive kidney also having elevated intrarenal Angiotensin II levels (salt sensitive or Angiotensin II induced hypertension) can be prevented with the acute administration of broad purinergic P2, or specific P2Y12, P2X1 and P2X7 receptor antagonists. Furthermore, the prevention of
tubulointerstitial infiltration with immunosuppressors impairs the development of salt-sensitive hypertension, indicating that tubulointerstitial inflammation is essential for the development and maintenance of hypertension. Inflammatory cells also have abundant purinergic receptors, and their activation induces cytokine and growth factor release which in turn contributes to augment tubulointerstitial inflammation. Collectively, the evidence suggests a pathophysiological implication of activation of purinergic P2 receptors. Coexistent increases in intrarenal angiotensin II activate Ang II AT1 receptors, which interact with elevation in purinergic receptors activation in a complex manner, suggesting convergence of their post-receptor signalling processes.

- **Adis Tasanarong, MD, PhD**  
  *Professor & Nephrologist,  
  Vice Dean for Research Affairs and Innovation,  
  Chulabhorn International College of Medicine at Thammasat University,  
  Pathumthani, Thailand.*


**SUMMARY:**
Vitamin E is a term used for eight naturally occurring compounds including α (alpha), β (beta), γ (gamma) and δ (delta) derivatives of tocopherol and tocotrienol. Differences in biological activity cause discrepancies in antioxidant and anti-inflammatory properties of each tocopherol. α-Tocopherol is the most active antioxidative substance, while γ-tocopherol has higher anti-inflammatory potency than α-tocopherol. The antioxidative property of vitamin E has been demonstrated in many animal model studies; for example, in cisplatin-induced AKI and ischaemic–reperfusion injury. Some forms of vitamin E have been proposed for the prevention or treatment of several health problems, particularly arteriosclerotic heart disease and cancer, primarily due to their antioxidant and anti-inflammatory properties. It is postulated that tocopherol protects the cell membrane from lipid peroxidation and thereby acts as membrane stabilizers. In this seminar, we shown
the present study which is the first clinical trial of the antioxidant vitamin E in its forms of α- and γ-tocopherol in the prevention of CI-AKI and the results demonstrate a remarkable effect of these two compounds. Statistical analysis of the data obtained through the described prospective, double-blind, randomized and placebo-controlled trials strongly suggests that prophylactic oral administration of α- and γ-tocopherol reduces the incidence of CI-AKI compared with a placebo control when used in conjunction with 0.9% saline hydration in CKD patients undergoing coronary procedures. Interestingly, the greatest prophylactic effect of α-tocopherol was observed in the subgroups of patients with diabetes mellitus, hypertension, receiving contrast agent dosages >120 mL, patients aged 55 years or older, male gender, anaemic patients and CI-AKI risk score <10.

- **Chih-Hong Wang, PH.D**
  Assistant Professor,
  Department of Biological Sciences & Technology,
  National Chiao Tung University,
  Hsichu, Taiwan.

Dr. Chih-Hong Wang, presented “Inhibition of renin angiotensin system causes severe anemia due to hypothyroidism” on August 23, 2018.

**SUMMARY:**
Inhibiting the renin angiotensin system causes anemia. However, its mechanism is not fully understood. Here we provide evidence that inhibiting angiotensin II (Ang II) effects via its type 1 receptor causes tertiary hypothyroidism by directly decreasing TRH and by feedback inhibition of TRH via increased iodothyronine deiodinase Dio2 and thus T3 in the hypothalamus. Moreover, inhibiting Ang II effects via its type 1 receptor in mice causes severe normochromic, normocytic anemia with normal reticulocyte index and elevated erythropoietin, which is corrected by administration of Ang II or T3. However, Ang II did not correct anemia in wild type mice that were made hypothyroid by methimazole and sodium perchlorate. Hypothyroidism is the predominant cause of anemia induced by inhibiting RAS.


From January through August, 2018 investigators and physicians affiliated with T.H.R.C.E. participated in the following regional, national, & international meetings.

**Southern Regional Meeting, NO, LA; Feb. 22-24, 2018**

- **Dr. Navar** received the Mentor of the Year award from the SSCI meeting on February 22-24, in New Orleans.
- **Dr. Majid’s** laboratory had an oral presentation, “Protein expression of tumor necrosis factor-alpha receptor type 1 is reduced in renal cortical tissue of endothelial nitric oxide synthase knockout mice.” Other authors to the research are: DSA Majid, MC Prieto, CA Chamberlin and AA Castillo.
- **Dr. Hering-Smith** had an abstract presented orally titled, “CRISPR/CAS9-mediated knockout of sodium dicarboxylate cotransporter 1 in a proximal tubule cell line,” S Yador, J Coleman-Barnett, LL Hamm, and K Hering-Smith.

**29th Annual Health Sciences Research Days, Tulane University, NO, LA; Feb. 19-20, 2018**

- **Abshire Caleb.** (Mentor: Dr. Lindsey). GPER deletion attenuates sex differences in carotid artery phenotype.
- **Allard C.** (Mentor: Dr. Mauvais-Jarvis). Loss of nuclear estrogen receptor alpha differentially impairs insulin secretion and insulin action in male and female mice.
- **Butcher S.** (Mentor: Dr. Zsombok). Coordination of homeostatic functions by extrascapular brown adipose tissue- and pancreas-related command neurons.
- **Desmoulins L.** (Mentor: Dr. S. Lindsey). Role of hypothalamic TRPV1 expressing neurons in the regulation of energy homeostasis
- **Gao H.** (Mentor: Dr. Derbenev). Emerging mechanism of glycine in control of baroreflex.
- **Garagliano J.** (Mentor: Dr. Sato). Advanced glycation end products stimulate angiotensinogen expression in renal proximal tubule cells.
- **Kulthinee S.** (Mentor: Dr. Navar). Purinergic P2X1 Receptor in Regulating the Preglomerular Renal Microcirculation Under Elevated Angiotensin II and High Renal Perfusion Pressure Environments.
- **Kumar P.** (Mentor: Dr. Pandey). Mocetinostat attenuates renal injury and dysfunction via the inhabitation of HDAC in NPR1 gene-targeted mutant mouse models.
- **Liu H.** (Mentor: Dr. El-Dahr). Histone deacetylases 1 and 2 regulate the transcriptional programs of nephron progenitors and renal vesicles.
- **McLaughlin N.** (Mentor: Dr. El-Dahr). IL22 reduces influenza pneumonia by promoting thymic integrity and T regulatory cell maturation.
- **Molinas A.** (Mentor: Dr. Zsombok). Interaction between TRPV1-expressing neurons in the hypothalamus.
Ogola B. (Mentor: Dr. Lindsey). GPER attenuates angiotensin II-Induced oxidative stress via Camp-Mediated regulation of NOX4.

Zimmerman M. (Mentor: Dr. Lindsey). Medroxyprogesterone attenuates estradiol-induced kidney damage in midlife ovariectomized female rats.

Annual Meeting of the Wound Healing Society with the Symposium on Advanced Wound Care (SAWC), Charlotte, NC, April 25-29, 2018


Experimental Biology, San Diego, CA, April 21– 25, 2018

Sierra Butcher (Mentor, Dr. Zsombok) participated in an oral and poster presentation and received the Mead Johnson Award on Monday, April 23. The title of her presentation was “Coordination of homeostatic functions by the interscapular brown adipose tissue- and pancreas-related command neurons.”

Dr. Andrei Derbenev presented a poster on Sunday, April 22, titled “Co-inhibition of neurons in the rostral ventrolateral medulla by GABA and Glycine.”

Dr. Lucie Desmoulins (Mentor, Dr. Derbenev) presented a poster on Wednesday, April 25 titled, “Role of hypothalamic TRPV1-expressing neurons in the regulation of energy homeostasis.”

Dr. Supaporn Kulthinee (Mentor, Dr. Navar) presented a poster on Monday, April 23 titled, “Interaction between angiotensin AT1 receptors and purinergic P2X receptors in regulating the preglomerular renal microcirculation under elevated angiotensin II and high renal perfusion pressure environments.” Dr. Kulthinee received a Caroline tum Suden/ Frances Helebrandt Professional Opportunity Award.

Dr. Prerna Kumar participated as an American Society for Biochemistry & Molecular Biology Undergraduate Poster Competition Judge on Saturday, April 21 at the McCormick Place Convention Center. Dr. Kumar also presented a poster on Sunday, April 22. Her abstract was titled, “Inhibition of HDAC1 and 2 Modulates the Expression and Signaling of Natriuretic Peptide Receptor A in Male and Female Gene-targeted Mutant Mice.”

Dr. Jean-Pyo Lee Co-chaired the symposium “Steroid receptor signaling in cardiovascular health and disease.”
Dr. Kailash N. Pandey’s presentation at the meeting was titled “Enhanced expression of prorenin receptor and proinflammatory cytokines in Npr1 gene disrupted mice.”

Dr. Bruna Visniauskas (Mentor: Dr. Prieto) had a poster and oral presentation on Sunday, April 22 at the Renal Section Young Investigator Award Featured Topic: Novel Roles for Renal GPCRs and Renal Effects of Hormones, Autacoids and Oxidative Stress Sessions. The title of her abstract was “Intrarenal bradykinin (BK) is decreased in mice with prorenin receptor (PRR) deficiency in the collecting duct.” Dr. Visniauskas also received the Caroline tum Suden/Frances Helebrandt Professional Opportunity Award.
THRCE investigators & physicians were invited speakers at various national & international events during January through August, 2018

L. Gabriel Navar, PhD:
- Participated in the AAMC Minority Faculty Seminar in New Orleans January 11-14. His presentation on January 13th was titled “Assembling a successful Research Team and Laboratory.”

Kathleen Hering-Smith PhD:
- “CRISPR/CAS9-mediated knockout of sodium dicarboxylate cotransporter 1 in a proximal tubule cell line,” at the SSCI Annual Meeting held in New Orleans in February 2018.

Dewan S. A. Majid, MD. PhD:
- “Problem based learning in Physiology and Medicine” was presented on January 3, 2018 in the Honor reception given by the Department of Physiology at the Women’s Medical College, in Sylhet, Bangladesh.
- “Protein expression of tumor necrosis factor-alpha receptor type 1 is reduced in renal cortical tissue of endothelial nitric oxide synthase knockout mice,” at the SSCI Annual Meeting held in New Orleans in February 2018.

Minolfa Prieto, PhD:
- “Relevance of soluble prorenin receptor in CVD” at the Vascular Biology Research Center, Medical College of Georgia on March 28 and the University of Kentucky at Lexington, Department of Pharmacology & Nutritional Sciences on Thursday April 12.
- “Bradykinin/B2R-dependent regulation of renin in the collecting duct” at the 2018 Kinin CLE Meeting held at the Western Case Reserve University, in Cleveland, OH on June 19, 2018.

Nazih L Nakhoul, PhD:
- “Properties and regulation of renal ammonia transport by Rh Glycoproteins” at Case Western University, Department of Physiology and Biophysics on January 29, 2018.

Kailash Pandey, PhD:
- Presented three invited lectures in India:
  - “Transcriptional control of Npr1 gene in the pathophysiology of hypertension” at the Department of Zoology, University of Delhi, India on April 4th.
Continued...

- “Genetic Ablation of Npr1 triggers immunogenic and renal fibrotic responses” on April 9th at the Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP, India.
- “Targeted disruption of Npr1 gene triggers renal inflammation and fibrosis with hypertension” at the Department of Biotechnology, Motilal Nehru National Institute of Technology Allahabad, UP, India on April 13th.

Cooper Woods, PhD:
- “Incubation of porcine urinary bladder matrix of endothelial cells and keratinocytes from Diabetic patients restores a non-diabetic phenotype,” at the 2018 Annual Meeting of the Wound Healing Society with the Symposium on Advanced Wound Care (SAWC), held in Charlotte, NC in April 2018.

Hongju Wu, MD:
- “The role of GLP-1 receptor in regulating glucagon secretion from pancreatic alpha cells” at the American Diabetes Association 78th Scientific Sessions held June, 2018 in Orlando, Florida.

Bruna Visniauskas, PhD:
- Post-doctoral fellow mentored by Dr. Prieto, presented at 2018 Kinin CLE Meeting held at the Western Case Reserve University, in Cleveland, OH on June 19, 2018. He presented, “Renal Kallikrein 1 activity and bradykinin levels are reduced in mice with prorenin receptor (PRR) deficiency in the collecting duct.” Dr. Visniauskas received a travel award to attend this meeting.
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.