A Message from Our Director

It is my pleasure to bring to you the latest news and updates on Tulane Hypertension and Renal Center of Excellence (THRCE)’s hypertension and kidney research, teaching, and training activities, and share with you some highlights on our faculty members and trainees’ accomplishments in this newsletter. This newsletter also marks the 2nd anniversary of the COVID-19 pandemic outbreak and my appointment as the new director of THRCE at Tulane University School of Medicine. The last 2 years have imposed tremendous challenges to every one of our faculty members, postdoctoral fellows, and graduate students in carrying out their research and training activities. However, most of our members have been able to meet these challenges with perseverance and professionalism. We are hopeful that this pandemic is finally over, and we are returning to a normal pre-pandemic work and life. During the 1st half of 2022, THRCE continued to run a robust Frontiers in Hypertension and Kidney Research Seminar Series by inviting many nationally well-recognized and accomplished scientists to give zoom seminars. I especially thank our invited seminar speakers, including Drs. Zhongjie Sun (The University of Tennessee Health Sciences Center), Yumei Feng Earley (The University of Nevada), Tony Y. Hu (Tulane Center for Cellular and Molecular Diagnosis), Steven D. Crowley (Duke University School of Medicine), Manoocher Soleimani (The University of New Mexico School of Medicine), Ruisheng Liu (The University of South Florida), and Daniel Batlle (Northwestern University Feinberg School of Medicine) for spending their valuable time to share with us their most recent frontier hypertension and kidney research. The Frontiers in Hypertension and Kidney Research Seminar Series continues to play a key role in promoting and improving the THRCE’s research and training programs. Second, one of most important achievements from our faculty members in this newsletter includes that Dr. Andrea Zsombok has been awarded a new 5-year project grant as a key project in a new Tulane Brain Institute Program Project Grant. Furthermore, Dr. Dewan Majid was awarded Fellowship status of the American Physiological Society (FAPS), Drs. L. Gabriel Navar, Dewan Majid, Xiao Li, and myself were appointed Associate Editors in the Journal Frontiers in Physiology Renal Physiology. I, along with Dr. Ryosuke Sato also serve as Guest Editors in a special issue on "Renin-Angiotensin-Aldosterone System in Metabolism and Disease" in International Journal of Molecular Sciences (IJMS), respectively. Finally, THRCE’s faculty members, postdoctoral fellows and graduate students remained very active in presenting their new research results at many local, national and international meetings. Once again, I would like to thank all members of the THRCE for their dedication and perseverance to their research work, and sincerely wish everyone a safe, healthy, and successful 2022.

Sincerely, Jia ‘Joe’ Zhuo, MD, PhD
Honors to THRCE Investigators

Kathleen Hering-Smith, PhD:
- Chaired the following three sessions at the 2022 Experimental Biology Meeting. On April 3, 2022: Carl W. Gottschalk Distinguished Lectureship and The Renal Poster & Professors. April 4, 2022: The Renal Section Business Meeting.

Prerna Kumar, PhD:
- Awarded SAFMR/SSCI Junior Faculty Research Travel Award at the 2022 Southern Regional Meeting held in February 2022.
- Promoted to Assistant Professor effective July 1, 2022.

Dewan S. A. Majid, MD, PhD:
- Inducted as ‘Fellow of the American Physiological Society’ (FAPS).
- Appointed Associate Editor of Frontiers in Physiology, Board of Renal Physiology and Pathophysiology (specialty section of Frontiers in Physiology).
- Topic Editor: Frontiers in Physiology, Theme topic: ‘Physiological and pathophysiological roles of TNF-α in the kidney.
- Abstract Reviewer: 2022 AHA Hypertension Council meeting.
- Co-Guide for PhD Thesis (External): Candidate’s name: Gouher Banu Shaikh, MD. Associate Professor, Department of Physiology, BLDE (Deemed to be University) Shri B.M. Patil Medical College, Hospital & Research Centre, Vijayapura – 586 103, India.

L. Gabriel Navar, PhD:
- Featured in the Tulanian Winter 2022 Edition along with other winners who are Research Hall of Fame Award recipients, better known as lifetime achievement honorees.
- Appointed Associate Editor of Frontiers in Physiology, Renal Physiology, and Pathophysiology.
- Nominated for the “Owl Club’s” Best Elective/Online Course Award for the Medical Spanish Course.
- Invited to join the Editorial Board for Exploration of Medicine, 2022.

Kailash Pandey, PhD:
- Appointed as Co-Editor of Frontiers in Molecular Neuroscience-Special Topic: Multi-Limbed Membrane Guanylate Cyclase Cellular Signaling Pathway.

Minolfa Prieto, MD, PhD:
- Awarded NIH, NHLBI Grant as Chair of the 2022 Angiotensin Gordon Research Conferences (GRC)/Gordon Research Seminars (GRS) Meeting to be held in Ventura, California between November 13 and 18, 2022.
- Appointed as a member of the TUSOM Strategies for Tomorrow Committee and of the Equity, Diversity, and Inclusion (EDI) Council
- Appointed co-investigator in the Cardiometabolic Core (Core B) for the project entitled, “Estrogens, Cardiometabolic Health, and the Aging Brain.” She will provide expertise to the management of experimental hypertension animal models, specifically for the chronic angiotensin II-infused female rat model.

Nazih L. Nakhoul, PhD:
- Selected to be a member of the Editorial Board of Membrane Physiology and Membrane Biophysics (specialty section of Frontiers in Physiology, Frontiers in Physics and Frontiers in Cell and Developmental Biology.
January 20th, 2022, Zhongjie Sun, MD, PhD, Professor and Thomas A. Gerwin Chair of Excellence in Physiology at the University of Tennessee, presented, “Epigenetic regulation of kidney function and blood pressure by KDM6A” at the THRCE Frontiers in Hypertension and Kidney Research Seminar

Summary of presentation:
Epigenetic modification of histone alters gene transcriptional states and regulates various biological processes including development, cell differentiation, disease progression, and aging. In this seminar, Dr. Sun discussed the potential role of lysine (K)-specific demethylase 6A (KDM6A) in the regulation of normal kidney function and blood pressure. His seminar covered the underlying mechanisms that KDM6A regulates Na transporters, Na excretion, and salt sensitivity of blood pressure. Dr. Sun further discussed how upregulation of histone 3 lysine (K)-27 trimethylation (H3K27me3) impairs kidney function and promotes salt-sensitive hypertension in aging.
Yumei Feng Earley, MD, PhD presented, “The Brain Prorenin-Angiotensin System in the Regulation of Blood Pressure and Glucose Metabolism” on February 3rd, 2022, at the THRCE Frontiers in Hypertension and Kidney Research Seminar. Dr. Feng is Professor of Pharmacology, Physiology & Cell Biology, at the University of Nevada, School of Medicine.

**Summary of presentation:**
Approximately one in every three adults in the United States has hypertension. Elevated BP is projected to cost $100 billion in medical services, medications, and missed days of work annually in the US, making it one of the largest expenses in our nation’s healthcare budget. Hypertension is also the most important risk factor for other cardiovascular diseases, including stroke, myocardial infarction, congestive heart failure and chronic kidney diseases, and remains the number one cause of morbidity and mortality in the US. The long-term goal of Dr. Feng Earley’s research program is to advance our understanding of the neural mechanisms that regulate blood pressure (BP) and cardiovascular function.

Dr. Earley is fascinated by the complex neural circuits that play a pivotal role in neural autonomic and endocrine regulation of the cardiovascular system. Her laboratory has discovered a novel pathway for brain angiotensin II formation mediated by the (pro)renin receptor and identified the functional importance and mechanisms of action of the (pro)renin receptor in blood pressure regulation, hypertension and high-fat-diet–induced metabolic disorders. In this seminar, Dr. Earley will share with the on-going study from her laboratory on the brain prorenin-angiotensin system in the blood pressure and metabolic regulations.

Tony Y. Hu, PhD, Professor and Director of the Center for Cellular and Molecular Diagnostics at Tulane University School of Medicine, presented “Written in Blood-Nanotechnology-enabled Biomarker Discovery for Disease Diagnosis” on February 17th, 2022.

**Summary of presentation:**
Dr. Hu’s research focuses on the development of nanomaterial platforms and proteomic approaches that are designed to enrich biomarker capture from microbial pathogens, or enhance biomarker signal, to improve the detection sensitivity, specificity, or quantitation of pathogen-derived soluble or extracellular vesicle (EV)-associated factors in complex biological samples. His research differs from conventional biomarker discovery and detection research for clinical microbiology in that it employs the special properties of nanomaterials to improve assay performance and reproducibility. This can have profound impact on the ability to detect and quantitate target low abundance biomarkers in complex mixtures, allowing the analysis of biomarkers that would otherwise be undetectable. Dr. Hu has made significant contributions to microbial diagnostics for critical global health initiatives, including a serum/plasma assay for all forms of tuberculosis and a mass spectrometry-based approach to differentiate closely related mycobacterium and Ebolavirus species.
A Special THRCE Seminar was hosted on March 17th, 2022 to commemorate National Kidney Month 2022. The National Kidney Month and World Kidney Day are national and global health awareness campaigns 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. The Seminar titled, “Regulators of Dendritic Cell-Mediated T Cell Activation in Salt-sensitive Hypertension,” was presented by Steven Daniel Crowley, MD, Professor of Medicine at Duke University School of Medicine.

**SUMMARY OF PRESENTATION:**

The immune response plays a critical role in the pathogenesis of hypertension, and immune cell populations can promote blood pressure elevation via actions in the kidney. Among these cell lineages, dendritic cells (DCs), the most potent antigen-presenting cells, play a central role in regulating immune response during hypertension and kidney disease. DCs become mature and express costimulatory molecules on their surface once they encounter antigen, allowing them to stimulate T cells. Activated T cells accumulate in the hypertensive kidney, release effector cytokines, promote renal oxidative stress, and promote renal salt and water retention. Individual subsets of activated T cells can secrete tumor necrosis factor-alpha, interleukin-17A, and interferon-gamma, each of which has augmented the elevation of blood pressure in hypertensive models by enhancing renal sodium transport. Fms-like tyrosine kinase 3 ligand dependent classical DCs are required to sustain the full hypertensive response, whereas the ubiquitin editor A20 in dendritic cells constrains blood pressure elevation by limiting T cell activation. This talk will address mechanisms through which DC-T cell interactions modulate levels of pro-hypertensive mediators to regulate blood pressure via actions in the kidney.

**Manoocher Soleimani, MD,** Professor of Medicine at the University of New Mexico, the School of Medicine, presented a THRCE seminar on April 14th titled, “Hypertension in Metabolic Syndrome: The Role of Fructose and Salt Absorbing Transporters in the Small Intestine.”

**SUMMARY OF PRESENTATION:**

The prevalence of obesity/metabolic syndrome in the U.S. population has increased steadily and drastically since the 1960s, based on the data from the CDC. The presence of hypertension in obesity/metabolic syndrome is associated with a significant increase in morbidity and mortality due to stroke, cardiovascular ailment and kidney disease. Despite the threat of serious conditions, the pathogenesis of hypertension in obesity/metabolic syndrome remains poorly understood. According to the AHA and CDC, Americans are consuming on average ~ 355 calories/day of sugar- mostly in the form of fructose, including the high fructose corn syrup. In addition, Americans consume ~2-3 times the recommended amount of salt. The studies in Soleimani’s laboratory showed the novel interaction between fructose and salt-absorbing transporters in the mouse small intestine. These studies further indicated that: 1)
GLUT5 is the main fructose-absorbing transporter; and 2) Fructose stimulates salt absorption in the mouse jejunum by activating the apical Cl-/HCO3- exchanger SLC26A6 (PAT1), which works in tandem with the Na+/H+ exchanger NHE3. In addition, the Preliminary Studies in the laboratories of Soleimani and his collaborators demonstrate remarkable similarities in differentially regulated genes between jejunum of fructose-fed mice and the intestinal epithelial enteroid cultures from obese individuals. Dr. Soleimani proposes that increased dietary fructose activates the fructose-and salt-absorbing transporters/pathways in the intestine and kidney; thereby, resulting in a state of salt overload and eventually leading to hypertension.

As COVID-related restrictions were lifted, Dr. Ruisheng Liu, presented, on May 12, the center’s first “in-person-seminar” since the onset of the pandemic lockdowns. Ruisheng Liu, MD, PhD, is the Professor of Molecular Pharmacology & Physiology at the Morsani College of Medicine at University of South Florida in Tampa, Florida. He presented, “A Novel Mechanism and Therapeutic Target for Glomerular Hyperfiltration and Hypertension in Diabetes.”

**Summary of presentation:**
More than 30 million of Americans – 9.4% of the population have diabetes. An increase in GFR or glomerular hyperfiltration has been observed at early stage of about 70% of type 1 and 50% of type 2 diabetic patients and associated with an increased risk for diabetic nephropathy and worse prognosis. The rate of hypertension is more than 2-fold higher in patients with diabetes than those without the disease. Diabetic patients with hypertension exhibit an increased risk for diabetic complications, such as coronary heart disease, stroke, peripheral vascular disease, retinopathy and nephropathy. A new SGLT1-NOS1-TGF pathway has been identified that sodium-glucose cotransporter 1 (SGLT1) in the macula densa senses the increase in luminal glucose concentration, which enhances macula densa NOS1-dependent NO formation in diabetes. The macula densa NO attenuates the vasoconstrictor tubuloglomerular feedback (TGF) tone and contributes to diabetic glomerular hyperfiltration, which facilities renal excretion and maintains volume homeostasis. On the other hand, insufficient macula densa NO generation in the setting of hyperglycemia limits the increase in GFR, impairs volume- and pressure-induced natriuresis and promotes hypertension in type-1 and type-2 diabetes.

Jia Zhuo, MD, PHD, Director of Tulane Hypertension & Renal Center of Excellence and Professor of Physiology at Tulane University School of Medicine, presented, “Angiotensin II, AT1a receptor, and Na+/H+ Exchanger 3 in The Proximal Tubules: Novel Roles in Angiotensin II-induced Hypertension and Kidney Injury,” on June 9th 2022.

**Summary of presentation:**
Hypertension is well recognized to be the most important risk factor for cardiovascular diseases, stroke, and end-stage kidney diseases. A quarter of the world’s adult populations and 46% of the US adults develop hypertension and currently require antihypertensive treatments. Only 50% of hypertensive patients are responsive to current antihypertensive drugs, whereas remaining patients may continue to develop cardiovascular, stroke and kidney diseases. The mechanisms underlying the poorly controlled hypertension remain incompletely understood. Recently, we have focused our efforts to uncover additional renal mechanisms, pathways, and therapeutic targets of poorly controlled hypertension and target organ injury using
Frontiers in Hypertension and Kidney Research Seminar continued ...

novel animal models or innovative experimental approaches. Specifically, my laboratory studied and elucidated the important roles of intratubular, intracellular and mitochondrial angiotensin II (Ang II) system in the development of Ang II-induced and 2-kidney, 1-clip (2K1C) Goldblatt hypertension. This seminar was to review and discuss recent findings from my laboratory that: a) circulating and intratubular Ang II is taken up by the proximal tubules via the (AT$_1$) AT$_{1a}$ receptor-dependent mechanism; b) intracellular administration of Ang II in proximal tubule cells, or adenovirus-mediated overexpression of an intracellular Ang II fusion protein selectively in the mitochondria of the proximal tubules induces blood pressure responses; and c) genetic deletion of AT$_1$ (AT$_{1a}$) receptors or the Na$^+$/H$^+$ exchanger 3 (NHE3) selectively in the proximal tubules decreases basal blood pressure and attenuates Ang II-induced and 2K1C Goldblatt hypertension. These studies provide a new perspective into the important roles of the intratubular, intracellular, and mitochondrial angiotensin II/AT$_1$ (AT$_{1a}$) receptor signaling in Ang II-dependent hypertensive kidney diseases.

Daniel Batlle, MD, Earle, del Greco, Levin Professor of Nephrology/Hypertension at Northwestern University, Feinberg School of Medicine in Chicago, presented on June 23rd, “ACE2, the kidney and COVID 19” at the THRCE Frontiers in Hypertension and Kidney Research Seminar.

**SUMMARY OF PRESENTATION:**
Angiotensin-converting enzyme 2 (ACE2) is a monocarboxy-peptidase that hydrolyzes Angiotensin II and other peptides. Unlike its homologue ACE, the activity of ACE2 is not affected directly by the widely prescribed ACE inhibitors. ACE2 was discovered over two decades ago and is one of the catalytically most potent enzymes known to degrade Ang II to form Ang-(1-7), a peptide that has organ-protective properties that oppose and counterbalance those of Ang II.

In addition to its role as a RAS enzyme ACE2 is the main receptor for SARS-CoV-2. This presentation will discuss potential therapeutics indications of recombinant ACE2 proteins and the important role that full length ACE2 plays as essential receptor for SARS-CoV-2 infectivity. The kidney manifestations of SARS-CoV-2 infection will likewise be discussed.

**2022 American Heart Association Heart Walk**

For the last 15 years, representatives of THRCE have participated in the annual American Heart Association (AHA) Heart Walk. The Heart Walk has always brought communities together to move more and unite around a common cause close to their heart. During the pandemic, AHA Heart Walks were organized as virtual events but the 2022 AHA Heart Walk is scheduled as an outdoor walking event for Saturday, November 19 at Lasalle Park (6000 Airline Drive, Metairie, LA 70003). The AHA heart Walk is a fund-raising event that promotes physical activity and heart healthy living in an environment that’s fun for the whole family. Every dollar raised is put back into our community to fight this deadly disease. Please join Tulane in supporting this cause by donating to the “THRCE & Physiology” team’s donation site, [http://www2.heart.org/goto/THRCE-Physiology](http://www2.heart.org/goto/THRCE-Physiology). Please also consider joining the Team “THRCE & Physiology” as a team walker.
**Abstracts & Presentations**

The following Abstracts & Presentations were presented by THRCE affiliated investigators.

**SOUTHERN REGIONAL/AFMR MEETING, FEB. 10-12, 2022**


**Kumar P, Pandya K, Nguyen CN, Pandey KN.** Vitamin D modulates histone modifications governing the natriuretic peptide receptor-A gene. (SAFMR/SSCI Junior Faculty Research Travel Award Winner) Abstract 3.


**TULANE HEALTH SCIENCES RESEARCH DAYS 2022, APRIL 20–21, 2022**


**Desmoulins LD, Molinas AJR, Derbenev AV, Zsombok A.** Hypothalamic and ventral brainstem circuits involved in the sympathetic control of the liver.

**Gao H, Desmoulins LD, Molinas AJR, Zsombok A, Derbenev AV.** Co-release of GABA and glycine in the rostral brainstem.


**Kilanowski-Doroh IM, Ogola BO, McNally AB, D’Souza SJ, Rojo MD, McLachlan JB, Machado HL, and Lindsey SH.** Ovariectomy-induced arterial stiffening is associated with downregulation of tissue resident macrophage markers.

**Leite APO, Li XC, Hassan R, Chen JX, Sato A, Dugas C, Sato R, Zhuo JL.** Angiotensin-II induced hypertension and glomerular and tubulointerstitial injury in mutant mice with kidney proximal tubule-selective deletion of mitochondrial Nad+-dependent deacetylase Sirtuin-3: Focus on Sex Differences.

**Majid DS, Zhuo JL.** CORE FACILITY POSTER: Tulane Hypertension And Renal Center of Excellence, The Mouse Phenotype Core (MPC) Facility.


**Ramasamy C, Subramanian U, Pandey KN.** Ablation of NPR1 exhibits cardiac fibrosis, hypertrophy, and congestive heart failure: Role of TGF-beta 1/SMAD Signaling Pathways.

**Sato R, Zhuo JL.** CORE FACILITY POSTER: Tulane Hypertension And Renal Center of Excellence, The Molecular, Imaging, and Analytical Core Facility.


**APS AT 2022 EB MEETING, PHILADELPHIA, APRIL 2-5, 2022**


**Bhunu B, Intapad S.** Functional & Molecular Studies of Renal Sphingosine 1 Phosphate Signaling Pathway in IUGR. Poster: E150.


Majid D, Castillo A. Increase in Salt Concentration in the Culture Media Enhances Protein Expression of Tumor Necrosis Factor-Alpha Receptor Type 1 in Cultured Renal Cortical Collecting Duct Cells But Not in Proximal Tubular Cells. Poster: E643.


**Invited Presentation**

**L. Gabriel Navar, PhD**, presented the Distinguished Lecture at the 2022 Health Sciences Research Days on April 21, 2022. The title of his lecture was “When Physiological Mechanisms Go Awry: Hypertension and Diabetes.”

**Jia Zhuo, MD, PhD** gave an invited Grand Round seminar at the Department of Pathology and Laboratory Medicine February 4, 2022. The title of his talk was “Hypertension as the key cause and therapeutic target of kidney injury: Focus on angiotensin II-induced hypertension.”

**Kathleen Hering-Smith, PhD** presented, “Networking Academia” as an APS Porter Fellow Discussion Panelist, at the APS Networking and Beyond Meeting held January 19, 2022.

**Publications**

Publications published between January through June, 2022 that acknowledges either funding awards affiliated to the center, the THRCE center itself, or one of the center’s CORE facilities.


Leite APO. Angiotensin II and NHE3 in the proximal tubules of the kidney are two key players in blood pressure control and hypertension. *EARY CAREER RESEARCHERS - ISH Hypertension News - April 2022. DOI: 10.30824/2204-


CORE Facilities & Services

Tulane Hypertension and Renal Center of Excellence (THRCE) houses 2 research core facilities developed during COBRE phases I, II, and III. These are now maintained and supported by THRCE and fees collected from the usage of some CORE facility services. The 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 Core facilities can be utilized by investigators within Tulane and other institutions for hypertension, cardiovascular and renal research. The 2 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.

◊ 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.

Other activities of the Center include the sponsorship of the biweekly THRCE meetings, and the participation in public education programs and events such as the AHA Heart Walk and National Kidney Day to increase public awareness of the dangers of hypertension and its complications.

Upcoming Meetings & Events

Hypertension 2022 Scientific Sessions
~ San Diego, California: September 7–10, 2022

ASN Kidney Week 2021
~ Orlando, Florida: November 3-6, 2022

AHA Scientific Sessions
~ Chicago, Illinois: November 5-7, 2022

20th Annual New Orleans Kidney Walk
~ The Shrine on Airline, Metairie: November 6, 2022

2022 Gordon Research Conference (GRC) on Angiotensin
~ Ventura-USA, November 13-18, 2022

2022 New Orleans Heart Walk
~ The Shrine on Airline, Metairie: November 19, 2022

2023 Southern Regional Meeting
~ Hotel Intercontinental, New Orleans: February 2-4, 2023

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