

Tulane Hypertension and Renal Center of Excellence

Volume 20, Issue 1

A Message from Our Director



As the Director of The Tulane Hypertension and Renal Center of Excellence (THRCE), it is my pleasure to present this Summer 2021 Newsletter to you, which highlights THRCE's ongoing research, education, and training programs in the hypertension and kidney research during the first half of the year of 2021. Although the challenges of COVID-19 pandemic continue unabated, our faculty members, postdoctoral fellows, and graduate students press forward to carry out their research activities with dedication, perseverance, and

professionalism. I would like to emphasize a few highlights as an introduction to the newsletter. First, the Department of Medicine at Tulane University School of Medicine has recently recruited Dr. Robert Hoover, M.D., from Emory University School of Medicine to be the new Nephrology and Hypertension Section Chief. As an outstanding physician scientist and expert in studying kidney distal tubular transport and salt-sensitive hypertension, Dr. Hoover brings new expertise to the THRCE and Tulane University's hypertension and kidney research programs. Second, to help educate, promote, and improve the THRCE's hypertension and kidney research, we continued to invite internationally and nationally well-recognized scientists to give Zoom seminars at THRCE's Frontiers in Hypertension and Kidney Research Seminar Series. These speakers included, but not limited to, Bruce A. Molitoris, M.D., of Indiana University School of Medicine and an expert in intravital multiphoton kidney imaging; Jan Danser, Ph.D., of Rotterdam, The Netherlands, an expert in cardiovascular and kidney tissue renin-angiotensin system; John C. He, M.D., the Nephrology Division Chief of the Icahn School of Medicine at Mount Sinai in New York and an expert in single cell analysis for diabetic kidney diseases; Jennifer C. Sullivan, Ph.D., of Augusta University and an expert in sex differences in hypertension and kidney research; Hong S. Lu, M.D., Ph.D., of the University of Kentucky and an expert in liver angiotensinogen and angiotensin II-induced atherosclerosis; Hua Linda Cai, M.D., Ph.D., of the David Geffen School of Medicine at UCLA and an expert in angiotensin II-induced cardiovascular diseases; and Dr. Pedro A. Jose of George Washington University School of Medicine and an expert in renal dopamine system and hypertension research. Third, our faculty members and postdoctoral fellows continued to write and submit grant proposals to American Heart Association and National Institute of Health to seek research funding. Fourth, our faculty members and postdoctoral fellows have actively participated in national and international research conferences and published their research in high impact journals. Finally, the Tulane University School of Medicine has continued to invest in acquiring new equipment, resources, core facilities to support THRCE's hypertension and kidney research programs. Specifically, we have generated many new lines of global,



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Honors to THRCE Investigators

L. Gabriel Navar, PhD:

- Receives the status of Fellow of the International Society of Hypertension. He was one of the awardees that joined the initial cohort of International Society of Hypertension Fellows as recognition for their scientific excellence.
- Review Editor on the Editorial Board of Renal and Epithelial Physiology (specialty section of Frontiers in Physiology).

Jia L. Zhuo, MD, PhD:

- Session Chair and Moderator: of the Recent Advances in Ion Transporters and Water Channels in Fluid Balance and Blood Pressure Regulation Session sponsored by APS Water and Electrolyte Homeostasis Section at the 2021 EB meeting.
- Guest Editor on the "Renin-Angiotensin-Aldosterone System in Pathologies" to be published in the Special Issue of the International Journal of Molecular Sciences.
- Nominated for membership to the Sigma Xi, the Scientific Research Honor Society.

Kathleen Hering-Smith, MS, PhD: Session Chair of the Carl W. Gottschalk Distinguished Lectureship sponsored by APS Renal Section at the 2021 EB Meeting.

Eric Lazartigues, PhD: Session Chair and Moderator of the Exosomes in the Central Nervous System: Bursting the Bubble Session sponsored by APS Neural Control and Autonomic Regulation Section at the 2021 EB meeting.

Andrea Zsombok, PhD: Session Co-Chair of the Autonomic Circuits Underlying Metabolic and Cardiovascular Homeostasis Session sponsored by APS Neural Control and Autonomic Regulation Section of at 2021 EB meeting.

cell- and tissue-specific genetically modified mouse models to the THRCE's mutant mouse phenotype core, a high-resolution Nikon confocal microscopic imaging system, and an AGILENT TECHNOLOGIES Seahorse XFe24 Analyzer to enhance our research capacity. I would like to thank all members of the THRCE for their dedication and persevere to their research work and our expert seminar speakers to share their exciting hypertension and kidney research with us. On behalf of the THRCE, I sincerely wish everyone a safe, healthy, and successful 2021 during this challenging time due to the COVID-19 pandemic.

Sincerely,

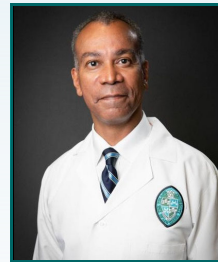


Zhuo, Jia, M.D, Ph.D.

Director, Tulane Hypertension & Renal Center of Excellence

Professor, Department of Physiology & Medicine

Dr. Robert Hoover appointed section chief of Nephrology and Hypertension at Tulane



Robert S. Hoover, MD, was recently appointed section chief of Nephrology and Hypertension in the Deming Department of Medicine at Tulane University School of Medicine in July 2021, with the focus on improving patient care and enhancing the section's training and research in hypertension and kidney diseases. Before joining Tulane, Dr. Hoover was an Associate Professor of Medicine in the Division of Renal Medicine at Emory University School of Medicine in Atlanta. Dr. Hoover, a California native, received his bachelor's degree in chemistry magna cum laude from Howard University in 1987 and his MD degree from UCLA in 1991. He undertook his internal medicine residency at Emory University and nephrology fellowships at Brigham & Women's Hospital/Harvard Medical School and Vanderbilt, respectively. Dr. Hoover was an Associate Editor of American Journal of Physiology Renal Physiology during last 2 terms, and currently is the Chair of the American Heart Association (AHA) Council on Hypertension SCILL Committee, a member of the AHA National SCILL committee, and the AHA Council on the Kidney in Cardiovascular Disease (KCV) Nominating Committee. He is also a member of the American Society of Nephrology (ASN) Workforce and Training Committee. Dr. Hoover specializes in studying kidney distal nephron transport and hypertension, and his research is continuously supported by National Institute of Diabetes and Digestive and Kidney Diseases. He will bring his expertise and leadership to the THRCE and Tulane University's basic science and translational hypertension and kidney research programs.

2021 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. Due to the pandemic, the 2020 AHA heart Walk was arranged as a virtual event where participants met digitally, hence providing participants with an opportunity to engage with other AHA walkers in a virtual setting. Until further notice, the 2021 AHA Heart Walk is being organized as an outdoor event that will be held at Lasalle Park in Metairie on Saturday, November 13, 2021. Funds raised in the walk are matched by the AHA's national office and reinvested into the community by funding research, prevention, and treatment of cardiovascular diseases and stroke. Tulane investigators have been the recipients of numerous AHA grants and by the participation of THRCE in AHA Heart walks, we hope to help AHA continue to fund future investigators.

Frontiers in Hypertension and Kidney Research Seminar



January 7th, 2021, **Bruce A. Molitoris, MD**, Distinguished Professor of Nephrology at Indiana University School of Medicine presented, **“Rapid Endothelial clearance of carbamylated albumin: potential for inflammation?”** at the THRCE Frontiers in Hypertension and Kidney Research Seminar.

SUMMARY OF PRESENTATION:

Chronic kidney disease results in high serum urea concentrations leading to excessive protein carbamylation, primarily albumin due to its concentration and long half-life. This is known to be associated with increased cardiovascular disease and mortality. In Dr. Molitoris's study, carbamylation of albumin markedly increased vascular clearance of carbamylated albumin and altered the distribution in both the kidney and liver at 16hrs post intravenous injection. Carbamylation of albumin had no effect on glomerular filtration or proximal tubule uptake. By evaluating the time course of carbamylation and associated charge, size, shape and binding parameters in combination with in-silico analysis and mass spectrometry, the critical binding interaction impacting carbamylated albumin's reduced FcRn binding was identified as K524. These data indicate urea mediated time-dependent carbamylation of albumin lysine K524 resulted in reduced binding to FcRn that contributed to altered albumin transport leading to increased vascular clearance and increased liver and endothelial tissue accumulation.



Peter M. Abadir, MD, Associate Professor of Medicine at John Hopkins University, School of Medicine, presented **“The Biology of Frail Angiotensin System Translated: Worn-out Mitochondria to Poor Wound Healing”** on January 21, 2021.

Researchers in the field of cardiovascular, hypertension, kidney, and associated diseases are invited to present a THRCE Seminar. Speakers who present are asked to provide a brief summary of their talk that we share with our newsletter audience.

From January 2021 through June 2021, the following speakers presented THRCE Sponsored Seminars.

Honors to THRCE Investigators, Cont...

Chih-Hong Wang, PhD and **T. Cooper Woods, PhD** was awarded \$25,000 from the School of Medicine Pilot Program Funding.

Minolfa C. Prieto, MD, PhD is the Chair of the 2022 Gordon Research Conference (GRC) on Angiotensin that will be held from February 27-March 4, at the Ventura Beach Marriott in Ventura-USA

Dr. T. Cooper Woods served on two NIH study sections during the June and July 2021.

Dr. Zsombok participated in NIH NNRS study section in June 2021.

Postdoctoral Fellows, Graduate & Medical Students:

Ana Paula Leite, PhD (Mentor: Dr. Zhuo): Selected as one of the recipients of the 2021 Research Recognition Award of the APS Renal Section.

Owen Richfield, PhD (Mentor: Dr. Navar): Awarded 1st place award for Renal Research from the Renal Section of APS during the 2021 Experimental Biology meeting.

Medical student, **Sarah M. Nwia, MS** (Mentor: Dr. Zhuo): Awarded the Warren R. Bourgeois III and Usha Ramadhyani Student Research Award to support her summer research.

Frontiers in Hypertension and Kidney Research Seminar continued ...

SUMMARY OF PRESENTATION:

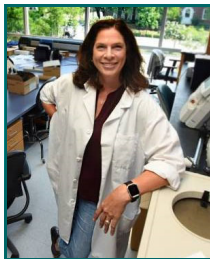
After Dr. Peter Abadir's presentation, participants were able to identify specific biological pathways that impact the development of frailty and understood how dysregulation in the renin-angiotensin system (RAS) impacts the pathologies that slow wound healing in frail, older adults, and how topical angiotensin receptor blockers may improve wound healing.



A.H.J. (Jan) Danser, PhD, Professor of Pharmacology at the Department of Internal Medicine in Erasmus Medical Center, Wytemaweg in Rotterdam, Netherlands, presented **"Angiotensinogen siRNA as a new tool to combat hypertension and renal disease. Lessons from animal studies,"** on February 18th 2021.

SUMMARY OF PRESENTATION:

Coexistence of hypertension and chronic kidney disease synergistically aggravates the risk of cardiovascular and renal morbidity and mortality. These high-risk, multi-morbid patient populations benefit less from currently available antihypertensive treatment, including blockers of the renin-angiotensin aldosterone system (RAAS), either due to non-adherence or to the upregulation of counterregulatory mechanisms like a rise in renin. An exciting novel approach to block the RAAS is angiotensinogen suppression by making use of liver-targeted angiotensinogen small interfering (si)RNA. This approach has the advantage of requiring only a few injections per year, thus potentially annihilating the problem of non-adherence. Moreover, deleting angiotensinogen implies that upregulating renin would not restore angiotensin II, i.e., the potential for counterregulation is limited. The talk critically discussed angiotensinogen suppression, focusing on data obtained with angiotensinogen siRNA in hypertensive rats with normal or low RAAS activity (spontaneously hypertensive rats and DOCA-salt rats, respectively) and in rats with chronic kidney disease (5/6th nephrectomy model). Finally, it addressed rescue mechanisms in emergency situations: i.e., what to do if the RAAS is urgently needed after angiotensinogen has been suppressed. Taken together, the presentation provided a complete insight into angiotensinogen siRNA as a new treatment tool, which is already being evaluated in patients.



Jennifer C. Sullivan, PhD, Interim Dean of the Graduate School and Professor of Physiology at the Medical College of Georgia, Augusta University, presented a THRCE talk on March 4th titled, **"Do T Cells Underlie Sex Differences in Blood Pressure Control?"**

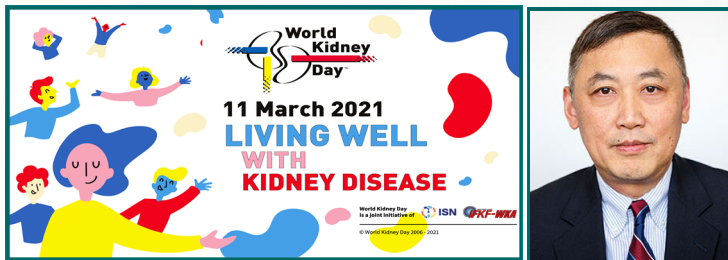
SUMMARY OF PRESENTATION:

Hypertension affects ~46% of U.S. adults and is the most common independent risk factor for cardiovascular disease (CVD), the leading cause of premature death globally. In ~85% of cases, the cause of hypertension is unknown and despite the impact of hypertension on overall morbidity and mortality, efforts to control BP remain

Frontiers in Hypertension and Kidney Research Seminar continued ...

relatively poor, with only ~50% of patients treated for hypertension attain adequate BP control. Although both sexes develop hypertension, young women are protected from hypertension relative to age-matched men. Greater understanding of the mechanisms underlying increases in blood pressure in both sexes are needed to improve treatment options for both men and women and lessen the overall burden of CVD.

It is well accepted that hypertension is a state of low-grade inflammation and T cells contribute to the development and maintenance of hypertension in both sexes. While pro-inflammatory effector T cells are necessary for the development and maintenance of hypertension, anti-inflammatory T regulatory cells limit increases in blood pressure. There are numerous reports of sex differences in T regulatory cells, with females having greater T regulatory cells relative to males. Dr. Sullivan's seminar provided information regarding the impact of biological sex on the T cell profile in key organs that control blood pressure, examined the role of T cells in the control of blood pressure, and began to explore the mechanisms by which females maintain more T regulatory cells vs. males.



March 11th 2021 was **World Kidney Day** (WKD). To commemorate WKD, THRC hosted a special seminar by John **Cijiang He, MD, PhD**. Dr. He is the "Irene & Dr. Arthur Fishberg" Endowed Chair of Nephrology, and Professor of Medicine & Pharmacological Sciences at the Icahn School of Medicine at Mount Sinai, New

York. The title of the Special 2021 WKD THRC Seminar was, "**Single cell analysis for diabetic kidney disease.**"

SUMMARY OF PRESENTATION:

Diabetic kidney disease (DKD) is the most common kidney disease. Regardless of the current treatments, many patients progress to kidney failure. Therefore, it is critical to better understand the mechanisms mediating the progression of DKD. Single cell RNA-sequence is a technology which could help to profile gene expression at the single cell level. Using this technique, Dr. He and his research team were able to identify genes and pathways altered in DKD for each kidney cell types. Studies such as Dr. He's will eventually help in the discovery of potential new therapies for DKD.



Hong S. Lu, MD, PhD, presented, "**Angiotensinogen links liver and kidney to atherosclerosis,**" on March 18th 2021. Dr. Lu is Professor of Internal Medicine & Physiology at the University of Kentucky College of Medicine in Lexington, Kentucky.

Frontiers in Hypertension and Kidney Research Seminar continued ...

SUMMARY OF PRESENTATION:

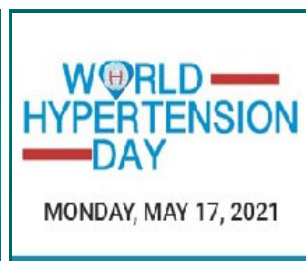
The renin-angiotensin system plays a critical role in the development of atherosclerosis, a major cause of mortality and morbidity in the United States. Mechanisms by which the renin-angiotensin system contributes to atherosclerosis have been focusing on effects of angiotensin II (Ang-II) production and its action through Ang-II type 1 receptors within atherosclerotic lesions. Angiotensinogen (AGT) is the substrate of all angiotensin peptides. AGT derived from hepatocytes is filtered through glomeruli and retained by megalin, a member of LDL receptor superfamily, in proximal tubule cells of kidney. Depletion of AGT in hepatocytes reduces hypercholesterolemia-induced atherosclerosis, diminishes AGT in proximal convoluted tubules, and reduces renal Ang-II concentrations in mice. Dr. Lu's research supports that hepatocyte-derived AGT contributes to atherosclerosis that is associated with kidney, but not plasma, Ang-II production.



Hua Linda Cai, MD, PhD, Professor of Anesthesiology & Medicine and Director of Translational Research at the David Geffen School of Medicine at UCLA, presented on April 15th, “**Novel molecular mechanisms and therapeutics of cardiovascular, respiratory and metabolic diseases**” at the THRCE Frontiers in Hypertension and Kidney Research Seminar.

SUMMARY OF PRESENTATION:

In this seminar Dr. Cai discussed novel molecular mechanisms underlying development of major cardiovascular, respiratory and metabolic diseases including hypertension, aortic aneurysms, diabetic vascular diseases, ischemia reperfusion injury of the heart/myocardial infarction, pulmonary hypertension, e-Cigarettes injuries and COVID-19. Novel therapeutics derived from these novel insights of disease mechanisms were addressed. The contents mostly focused on roles of NADPH oxidase (NOX) activation and its downstream oxidase effectors such as uncoupled eNOS and dysfunctional mitochondria. Specific and selective roles of NOX isoforms in various disease states were also discussed.



World Hypertension Day (WHD) fell on Monday, May 17, 2021. As the primary focus of Tulane Hypertension and Renal Center of Excellence (THRCE) is Hypertension and its related diseases, WHD has a special significance with THRCE. To commemorate WHD, THRCE hosted a special WHD Seminar on May 17 presented by **Pedro A. Jose, MD, PhD**. Dr. Jose is Professor of Medicine, Pharmacology, & Physiology at George

Washington University, the School of Medicine & Health Sciences in Washington D.C.. The title of the Special THRCE WHD Seminar was “**Renal dopamine and salt sensitivity of blood pressure.**”

SUMMARY OF PRESENTATION:

Salt sensitivity of blood pressure, whether in hypertensive or normotensive subjects, is associated with increased cardiovascular risk and overall mortality. Salt sensitivity can be treated by reducing salt (NaCl) consumption. However, decreasing salt intake in some may actually increase cardiovascular risk, including an increase in blood

pressure, a state of inverse salt sensitivity. Several genes are associated with salt sensitivity and inverse salt sensitivity. Some of these genes encode proteins expressed in the kidney that are needed to excrete a sodium load, for example, dopamine receptors and their regulators, G protein-coupled receptor kinase 4 (GRK4). Dr. Jose's presentation examined research in this field that has provided several translational opportunities, ranging from diagnostic tests to gene therapy, such as: 1) a test in renal proximal tubule cells isolated from the urine of humans that may determine salt sensitivity by analyzing the recruitment of dopamine D1 receptors to the plasma membrane; 2) the presence of common variations of the GRK4 gene that are not only associated with hypertension but may also predict the response to antihypertensive therapy; 3) genetic testing for gene variations of the dopamine D2 receptor that may be associated with hypertension and inverse salt sensitivity and may increase the susceptibility to chronic kidney disease because of loss of the anti-oxidant and anti-inflammatory effects of the renal dopamine D2 receptor, and 4) in-vivo renal-selective amelioration of renal tubular genetic defects by a gene transfer approach, using AAV vectors introduced to the kidney by retrograde ureteral infusion.



Jing Wu, PhD, Instructor in the Department of Physiology at Medical College of Wisconsin, presented, “**PPAR γ Downstream Pathways in Salt Sensitive Hypertension: Renal Hemodynamic and Immune Mechanisms,**” at the May 27th THRCE Frontiers in Hypertension and Kidney Research Seminar.

SUMMARY OF PRESENTATION:

Individuals with type II diabetes (T2DM) and metabolic syndrome (MS) display decreased activity of peroxisome proliferator activated receptor gamma (PPAR γ) and often develop salt-sensitive hypertension. PPAR γ activation by thiazolidinediones (TZDs) lowers blood pressure in T2DM and MS. Moreover, PPAR γ impairment caused by dominant negative mutations (e.g. P467L) that block PPAR γ activation by ligands cause severe early onset HT in humans, while selective expression of these mutations in vascular smooth muscle (VSM) recapitulates human HT in mice (S-P467L), suggesting impairment of vascular PPAR γ is causal.

Using S-P467L mice as a model of vascular PPAR γ impairment, Dr. Wu and his study team have discovered a previously unidentified role of smooth muscle PPAR γ in regulating renal vascular function, renal sodium/water retention, and salt sensitivity (Wu, J et al. Cardiovascular Research 2021. PMID: 32428209). The blunted renal perfusion in high salt-fed S-P467L mice is associated with decreased intrarenal nitric oxide (NO) bioavailability but not renal oxidative stress and the increased sodium retention was mediated by a lack of salt-induced suppression of NKCC2. They have further demonstrated that the detrimental effects of PPAR γ impairment in VSM are mediated, at least in part, by enhanced PGE2/E-Prostanoid Receptor 3 (EP3) signaling in both systemic and renal blood vessels, causing increased renal vascular resistance and blunted renal blood flow during excess salt loading (Wu, J et al. Hypertension 2021. PMID: 33641369). Pharmacological inhibition of EP3 improves vasodilation in renal vessels and attenuates salt-sensitive hypertension during PPAR γ impairment.

Frontiers in Hypertension and Kidney Research Seminar continued ...

The anti-inflammatory effects of PPAR γ are well-documented. Dr. Wu's previous publication shows that in vascular smooth muscle cells PPAR γ facilitates nuclear export NF-kB p65 subunit and inhibits TNF-alpha/NF-kB-induced chemoattractant signals (MCP-1, VCAM-1) (PMID: 28507170). Chronic high salt alone is sufficient to induce vascular infiltration of macrophages and activated macrophages are a major source of TNF-alpha. Thus, vascular PPAR γ interference creates a pro-inflammatory local environment that attracts additional immune cells, which in turn causes vascular inflammation, arterial stiffening and kidney damage during salt-sensitive hypertension.



On June 24, 2021, **QingQing Wei, PhD**, presented, “**Cell death and non-coding RNA Regulation in kidney Injury**” Dr. Wei is Assistant professor of Cellular Biology & Anatomy at the Medical College of Georgia, Augusta University.

SUMMARY OF PRESENTATION:

Acute kidney injury (AKI) and chronic kidney disease (CKD) are two of the major renal diseases clinically. AKI is characterized by renal tubular cell death and abrupt renal function loss, which is associated with high clinical mortality. CKD is featured by renal tubular repair and fibrosis development and affect a large population of patients. Emerging evidence implicates that non-coding RNAs are critical regulators and novel therapeutic targets in both AKI and CKD conditions.

In AKI, Dr. Wei and her research team's early studies indicated that mitochondria-mediated apoptosis is crucial in renal tubular cell death and mitochondrial fragmentation is an early event to promote renal apoptosis. By examining the differentially expressed microRNAs in ischemic AKI mouse model, they found that microRNA-668 (mir-668) can significantly protect kidney from ischemic injury through the inhibition of renal apoptosis. Mir-668 is transcriptionally up-regulated by HIF-1a. In renal cells, it can suppress mitochondrial fragmentation and apoptosis. Further examination of mir-668 targets indicated that it can protect mitochondria by targeting MTP18. Meanwhile, they also identified that long non-coding RNA GSTM3P1 showed high affinity to mir-668. The analysis of GSTM3P1 and its rodent homologue gstm2-ps1 revealed that GSTM3P1/gstm2-ps1 is up-regulated in early stage of ischemic AKI to induce injury. The potential underlying mechanisms may involve the inhibition of mir-668 and its parent gene GSTM3.

In CKD, Dr. Wei and her research team finds that a miRNA gene (mir-219-2) is hypermethylated in multiple rodent models and its expression is suppressed both in vitro and in vivo. The further functional analysis indicates that mir-219 is a pro-fibrotic microRNA and anti-mir-219 oligo treatment results in fibronectin inhibition in unilateral ureteral obstruction induced CKD. Now Dr. Wei and her research team are trying to understand the downstream targets of mir-219 by systematically analyzing the mRNAs binding to mir-219 in RNA-induced silencing complex.

Abstracts & Presentations

SOUTHERN REGIONAL/AFMR VIRTUAL MEETING, FEB. 25-27, 2021

Leite APO, Li XC, Zhuo JL. Proximal tubule-specific deletion of mitochondrial protein sirtuin 3 in the kidney attenuates angiotensin II-induced hypertension and augments natriuretic responses in female mice. Oral Presentation

Majid DSA, Osuji C, Talwar S, Abdel-Mageed AB, Castillo A. Tumor necrosis factor-alpha receptor type-1 protein level decreases in renal cortical but not in medullary tissue during high salt intake in nitric oxide deficient mice. Abstract A105. J Invest Med; 69:459. ORAL presentation.

Nikolli I, Delafontaine P, Sukhanov S. Glyceraldehyde-3-phosphate dehydrogenase prevents deleterious effects of anti-tumor drug etoposide on vascular smooth muscle cells

Abstract 22. J Invest Med, 2021: 69 (2).

Pemberton E, Shao W, Bell AL, Navar LG. Sex Differences in hypertension and renal injury in 2-Kidney 1-Clip Goldblatt hypertensive rats: Effect of Ovariectomy.

Richfield O, Cortez R, Navar LG. Increased Glomerular Capillary wall strain precedes Glomerulopathy in the diabetic rat.

Snarski P, Sukhanov S, Yoshida T, Higashi Y, Danchuk S, Shai SY, Chandrasekar B, Delafontaine P. Macrophage specific igf-1 downregulates CXCL12 chemokine and decreases atherosclerotic burden in apoe-null mice. Abstract 61. J Invest Med, 2021: 69 (2).

TULANE ANNUAL HEALTH SCIENCES RESEARCH DAYS, APRIL 14-15, 2021

Abdullah A, Karim M, Legendre M, Friedman J, Rodrigues L, Bitonti N, Kosowski E, Drury R, Packer J, Cotton-Betteridge A, Shaheen F, Guidry C, Duchesne J, Taghavi S, Jackson-Weaver O. Succinate Drives Reactive Oxygen Species Mediate Endothelial Glycocalyx Damage in Hemorrhagic Shock and Resuscitation.

Benjamin B, Intapad Suttira I. Reduced Uterine Perfusion Pressure (RUPP) Impairs Blood Pressure (BP) Regulation and Renal Function in IUGR mouse offspring.

Bell A, Shao W, Katsurada A, Sato R, Navar LG. Sex Differences in Urinary Angiotensinogen Excretion, Renal Function, and Systolic BP in 2-Kidney, 1-Clip Hypertensive Rats.

Bradford AB, Woods TC. Loss Of Insulin-like Growth Factor 1 Receptor In Vascular Smooth Muscle Cells Promotes Increased Mirna-221 And -222 In Type 2 Diabetes.

Bundy JD, Tian L, Krousel-Wood M, Hendel RC, Whelton PK, He J. Sex Difference in the prevalence of Ideal cardiovascular health among US adults.

Cikic S, Chandra PK, Rutkai I, BaddooMC, Flemington EK, Katakam PVG, Busija DW. Sex

Differences in Gene-Expression between Brain Arteries and Cortical Microvessels in Mice revealed by RNA-Sequencing.

Cotton-Betteridge A, Packer J, Abdullah S, Bitonti N, Kosowski E, Duchesne J, Taghavi S, Jackson-Weaver O. Endothelial glycocalyx damage is induced by elevated plasma succinate.

Horton AC, Wilkinson MM, Kilanowski-Doroh IM, Ogola BO, Lindsey SH. Dihydrotestosterone Induces Arterial Stiffness in Female Mice.

Leite APO, Li XC, Hassan R, Zhang Z, Zhuo JL. The Role of Superoxide in Sex Differences in Angiotensin II-induced Hypertensive and Natriuretic Responses in Mice with Proximal Tubule-Specific Deletion of Mitochondrial Protein Sirtuin 3 in The Kidney.

Majid DSA. THRCE Mouse Phenotyping Core Facility: Research Resource

Maroney KJ, Huang Z, Mills KT, Irazola V, Poggio A, Beratarrechea A, Chen C, Gibbons L, Chen J, Rubinstein A, He J. The Multilevel mediation analysis of a multicomponent intervention on blood pressure control in low-income patients in Argentina.

Presentations listed under Abstracts & Presentations were virtually presented between January through June 2021 by THRCE affiliated investigators

Abstracts & Presentations Cont...

Ogola BO, Visniauskas B, Harris NR, Kilanowski-Doroh I, Horton A, Diaz Z, Laradji MM, Lindsey SH. Aldosterone-induced arterial stiffening and cardiac dysfunction in male and female G protein-coupled estrogen receptor null mice.

Patel NR, Prieto MC, Meadows SM. ATP6AP2 Modulates Physiological and Pathological Angiogenesis during Retina Development.

Pemberton E, Shao W, Sato A, Bell A, Brookshire T, Navar LG. Effect of Ovariectomy on sex-dependent differences in Hypertension and Renal Injury in 2-Kidney 1-Clip Hypertensive rats.

Riccio IR, Chan KJ, Yokota R, Intapad S. Sphingosine-1-phosphate Signaling Pathway is Altered in Brain Microvessel of Intrauterine Growth Restricted Mice

Richfield O, Cortez R, Navar LG. A Novel Model of Renal Autoregulation Demonstrates Dynamic Modulatory Interactions between TGF and Myogenic Mechanisms

Sato R. THRCE Molecular, Imaging, and Analytical Core Facility. Section: Research Resource

Schechter DR, Diepenbrock CM, Addison AB, Hilliard SA, El-Dahr SS. Conserved developmental enhancers of single nucleotide variants linked to chronic kidney disease

Siino A, Ngo NYN, Chen CH, Tortelote GG, El-Dahr SS, and Liu HB. Developmental Programming of Chronic Kidney Disease by Histone Deacetylases

Snarski P, Sukhanov S, Yoshida T, Higashi Y, Danchuk S, Shai SY, Chandrasekar B, Delafontaine P. Macrophage Specific Insulin-like growth factor-1 increases features of atherosclerotic plaque stability via reduction of CXCL12.

Vongbunyoung KE, Brug A, Smith S, Bazan H, Wood TC. Acute carotid plaque rupture is characterized by an anti-proliferative serum miRNA profile

Abdullah A, Karim M, Legendre M, Friedman J, Rodrigues L, Bitonti N, Kosowski E, Drury R, Packer J, Cotton-Betteridge A, Shaheen F, Guidry C, Duchesne J, Taghavi S, Jackson-Weaver O. Succinate Drives Reactive Oxygen Species Mediate Endothelial Glycocalyx Damage in Hemorrhagic Shock and Resuscitation.

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Horton AC, Wilkinson MM, Kilanowski-Doroh IM, Ogola BO, Lindsey SH. Dihydrotestosterone Induces Arterial Stiffness in Female Mice.

Leite APO, Li XC, Hassan R, Zhang Z, Zhuo JL. The Role of Superoxide in Sex Differences in Angiotensin II-induced Hypertensive and Natriuretic Responses in Mice with Proximal Tubule-Specific Deletion of Mitochondrial Protein Sirtuin 3 in The Kidney.

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Maroney KJ, Huang Z, Mills KT, Irazola V, Poggio A, Beratarrechea A, Chen C, Gibbons L, Chen J, Rubinstein A, He J. The Multilevel mediation analysis of a multicomponent intervention on blood pressure control in low-income patients in Argentina.

Ogola BO, Visniauskas B, Harris NR, Kilanowski-Doroh I, Horton A, Diaz Z, Laradji MM, Lindsey SH. Aldosterone-induced arterial stiffening and cardiac dysfunction in male and female G protein-coupled estrogen receptor null mice.

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Pemberton E, Shao W, Sato A, Bell A, Brookshire T, Navar LG. Effect of Ovariectomy on sex-dependent differences in Hypertension and Renal Injury in 2-Kidney 1-Clip Hypertensive rats.

Abstracts & Presentations Cont...

TULANE ANNUAL HEALTH SCIENCES RESEARCH DAYS, CONT...

Riccio IR, Chan KJ, Yokota R, Intapad S. Sphingosine-1-phosphate Signaling Pathway is Altered in Brain Microvessel of Intrauterine Growth Restricted Mice

Richfield O, Cortez R, Navar LG. A Novel Model of Renal Autoregulation Demonstrates Dynamic Modulatory Interactions between TGF and Myogenic Mechanisms

Sato R. THRCE Molecular, Imaging, and Analytical Core Facility. Section: Research Resource

Schechter DR, Diepenbrock CM, Addison AB, Hilliard SA, El-Dahr SS. Conserved developmental enhancers of single nucleotide variants linked to chronic kidney disease

Siino A, Ngo NYN, Chen CH, Tortelote GG, El-Dahr SS, Liu HB. Developmental Programming of Chronic Kidney Disease by Histone Deacetylases

Snarski P, Sukhanov S, Yoshida T, Higashi Y, Danchuk S, Shai SY, Chandrasekar B, Delafontaine P. Macrophage Specific Insulin-like growth factor-1 increases features of atherosclerotic plaque stability via reduction of CXCL12.

Vongbunyong KE, Brug A, Smith S, Bazan H, Wood TC. Acute carotid plaque rupture is characterized by an anti-proliferative serum miRNA profile

JOINT MEETING OF EUROPEAN SOCIETY OF HYPERTENSION (ESH) AND INTERNATIONAL SOCIETY OF HYPERTENSION (ISH), APRIL 11-14, 2021

Leite APO, Li XC, Zhuo JL. Sex differences in angiotensin II-induced hypertension and kidney injury: role of AT1a receptors in the proximal tubules of the kidney.

Li XC, Leite AP, Zheng X, Zhao C, Chen X, Zhang L, Zhou X, Rubera I, Tauc M, Zhuo JL. Proximal tubule-specific deletion of AT1a receptors in the kidney attenuates circulating and intratubular angiotensin II-induced hypertension in mice. Oral Presentation

Li XC, Leite AP, Zheng X, Zhao C, Zhuo JL. Proximal tubule-specific deletion of AT1a receptors attenuates angiotensin II-induced hypertension by increasing glomerular filtration and pressure-natriuresis response. Oral Presentation

Majid DSA, Navar LG, Castillo A, Khan N, Shindler I. Angiotensin II induced salt-sensitive hypertension associated with inverse circadian pattern in renal generation of tumor necrosis factor -alpha and angiotensinogen in mice.

Majid DSA, Prieto MC, Castillo A, Chamberlain CM, Osuji C. Tumor necrosis factor-alpha receptor type 1 protein expression in renal cortical tissue is increased in intact but reduced in nitric oxide deficient mice during high salt intake.

Navar LG, Franco MG, Katsurada A, Dugas CM, Satou R. Enhanced Productions of Intrarenal NLRP-3 Inflammasome and Angiotensinogen in Angiotensin II-Dependent Hypertension Are Prevented by Immunosuppressant Treatment.

THE INTERNATIONAL SOCIETY OF NEPHROLOGY (ISN) WORLD CONGRESS OF NEPHROLOGY 2021 (WCN'21), APRIL 15-19, 2021.

Leite APO, Li XC, Hassan R, Zhuo JL. The role and sex differences of the mitochondrial protein Sirt3 in the proximal tubules of the kidney in the development of angiotensin II-induced hypertension.

EB MEETING, APRIL 27-30, 2021

Bradford A. Loss Of Insulin-like Growth Factor 1 Receptor In Vascular Smooth Muscle Cells Promotes Increased Mirna -221 And -222 In Type 2 Diabetes. ORAL, Abstract R4718

Braun R, Douglas H, Woods TC. Exosomes from vascular smooth muscle cells of diabetic origin promote a pro-inflammatory macrophage phenotype. ORAL, Abstract R3930

Abstracts & Presentations Cont...

EB MEETING, CONT...

Chandra P, Rutkai I, Kim H, Cिक S, Braun S, Abdel-Mageed A, Mondal D, Busija D. Latent HIV-1 Exosomes Induce Mitochondrial Hyperfusion due to Loss of Phosphorylated Dynamin-related Protein 1 in Brain Endothelium. Abstract R3920.

Chandra P, Cिक S, Baddoo M, Rutkai I, Guidry J, Flemington E, katakam P, Busija D. Multiomics Uncover Sexual Disparities in the Expression of Genes and Proteins in Rat Cerebral Microvessels. ORAL, Abstract R4023.

Hering-Smith K, Huang W, Hassan R, Li XC, Sato R, Zhuo JL, Hamm LL. Role of Proximal Tubule NHE3 in Ammonium and Krebs Cycle Metabolite Excretion. Moderator: Carl W. Gottschalk Distinguished Lectureship of the APS Renal Section. ORAL, Abstract R1878.

Kumar P, Neelamegam K, Samivel R, Xia H, Ramasamy C, Zhao H, Nguyen C, Gogulamudi V, Kapusta D, Pandey K. Regulation of Blood Pressure and Renal Fibrosis by Class I Specific HDAC Inhibitor, Mocetinostat, in Npr1 Gene-targeted Male and Female Mice. Abstract R3773.

Lazartigues E. Hypothalamic Regulation of Blood Pressure. ORAL, Abstract 70042.

Leite AP, Li X, Hassan R, Zhang Z, Zhuo J. The Role of Superoxide in Sex Differences in Angiotensin II-induced Hypertensive and Natriuretic Responses in Mice with Proximal Tubule-Specific Deletion of Mitochondrial Protein Sirtuin 3 in the Kidney. Abstract R2415.

Li X. Genetic Deletion of AT1a Receptors Selectively in The Proximal Tubules of The Kidney Attenuates Angiotensin II-induced Hypertensive & Glomerular Filtration Responses in Aging PT-Agr1a-/- Mice. ORAL, Abstract R2851.

Majid DSA, Osuji, C, Talwar S, Abdel-Mageed A, Castillo A. Tumor Necrosis Factor-Alpha Receptor Type-1 Protein Level Decreases in Renal Cortical But Not in Medullary Tissue During High Salt Intake in Nitric Oxide Deficient Mice. Abstract R2037. FASEB Journal, 35;S1:A235.

Mendonca N, Ling S, Bedja D, Marx R, Wu Y, Zhuo JL, Walston J, Luczak E, Anderson M, Abadir P. Dysregulation of cardiac CaMKII pathway is increased in aging and chronic inflammation. Abstract L4936.

Mohammed M, Awoal M, Lazartigues E. ACE2 Knock-out Mice Show Decreased Blood Pressure Response and Increased Anxiety-like Behavior to Acute Stress. Abstract R4431.

Neelamegam K, Ramasamy C, Pandey KN. Increased Glucose Levels in Guanylyl Cyclase/Natriuretic Peptide Receptor-A Gene-Knockout Gene-Duplication Mutant Mice. Abstract R4083.

Pemberton E, Shao W, Sato A, Bell A, Brookshire T, Navar LG. Effects of Ovariectomy on Sex-Dependent Differences in Hypertension and Renal Injury in 2-Kidney 1-Clip (2k1c) Goldblatt Hypertensive Rats. Abstract R3668.

Richfield O, Cortez R, Navar LG. A Novel Model of Renal Autoregulation Demonstrates Dynamic Modulatory Interactions between TGF and Myogenic Mechanisms. Abstract R2923.

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Snarski P, Sukhanov S, Yoshida T, Higashi Y, Danchuk S, Shai SY, Chandrasekar B, Delafontaine P. Macrophage Specific IGF-1 Overexpression Decreases Atherosclerosis, CXCL12 Chemokine, And Increases Cholesterol Efflux In ApoE Deficient Mice. Abstract R2489. FASEB Journal, 2021: 35, S1, R2489.

Sukhanov S, Higashi Y, Danchuk S, Nikolli I, Alfortish A, Goodchild T, Scarborough A, Sharp T, Schumacher J, Ivey J, Tharp D, Bowles D, Jenkins J, Garcia D, Lefer D, Delafontaine P. Insulin-like growth factor I reduces atherosclerosis in Rapacz pigs. Abstract R2068. FASEB Journal, 2021: 35, S1, R2068.

Wang C-H, Li X, Zhuo JL. Genetic Ablation of The Ren1c and Leptin Genes Improves Insulin and Leptin Sensitivity in Mice. Abstract R2986.

Zhou H, Abdulnour-Nakhoul S, Nakhoul N. The Effects of Co-Expression of Rbfg with Human CA-IV on NH3/NH4+ and CO2 Transport. Abstract R3649.

Zsombok A. Hypothalamic Preautonomic Neurons in Diabetes. ORAL, Abstract R2986.

Invited Presentation



Dewan SA Majid, MBBS, PhD, Professor of Physiology at Tulane, presented a Plenary Lecture on March 24 at the Virtual 2021 Biennial SAAP (South Asian Association of Physiologists) VII and PSI (Physiological Society of India) Conference that was held between March 24-25, 2021 at the Hamdard Institute of Medical Sciences & Research (HIMSR) in New Delhi, India. SAAP is a non-profit professional organization established by over 1200 Physiologists from SAARC (South Asian Association for Regional Cooperation)

countries that are committed to the advancement of Physiology. SAARC is an economic and political organization of eight countries in South Asia. PSI is the pioneer organization of the Physiologists of India that was established in 1934. The title of Dr. Majid's talk was, "Physiological role of cytokines during high salt intake."

Publications

Chandra PK, Cिकic S, Baddoo MC, Rutkai I, Guidry JJ, Flemington EK, Katakam PV, Busija DW. Transcriptome analysis reveals sexual disparities in gene expression in rat brain microvessels. *J Cereb Blood Flow Metab.* 2021 Mar 9;271678X21999553. doi: 10.1177/0271678X21999553. PMID: 33715494.

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Guerrero A, Visniauskas B, Cárdenas P, Figueroa SM, Vivanco J, Salinas-Parra N, Araos P, Nguyen QM, Kassan M, Amador CA, Prieto MC, Gonzalez AA. α -Ketoglutarate Upregulates Collecting Duct (Pro)renin Receptor Expression, Tubular Angiotensin II Formation, and Na⁺ Reabsorption During High Glucose Conditions. *Front Cardiovasc Med.* 2021 Jun 4;8:644797. doi: 10.3389/fcvm.2021.644797. eCollection 2021. PMID: 34179130. PMCID: PMC8220822.

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Hall JE, Navar LG, Cowley AW Jr, Summers RL, Hester RL. Thomas George Coleman, PhD (1940-2021). *Hypertension.* 2021 Jun;77(6):1800-1803. doi: 10.1161/HYPERTENSIONAHA.121.17287. PMID: 33934621.

Li XC, Leite APO, Zheng X, Zhao C, Chen X, Zhang L, Zhou X, Rubera I, Tauc M, Zhuo JL. Proximal Tubule-Specific Deletion of Angiotensin II Type 1a Receptors in the Kidney Attenuates Circulating and Intratubular Angiotensin II-Induced Hypertension in PT-Agtr1a^{-/-} Mice. *Hypertension.* 2021 Apr;77(4):1285-1298. doi: 10.1161/HYPERTENSIONAHA.120.16336. PMID: 33641366, PMCID: PMC7946728

Publications listed on the left include those published between January 2021 through June 2021 and any publications that were omitted in previous THRCE newsletters.

Publications listed on the left acknowledges either funding awards affiliated to the center, the THRCE center itself, or one of the center's CORE facilities.

Publications Cont..

Li XC, Zhou X, Zhuo JL. Evidence for a Physiological Mitochondrial Angiotensin II System in the Kidney Proximal Tubules: Novel Roles of Mitochondrial Ang II/AT1a/O₂⁻ and Ang II/AT2/NO Signaling. *Hypertension*. 76(1):121-132. doi: 10.1161/HYPERTENSIONAHA.119.13942. Epub 2020 Jun 1.

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Reina-Couto M, Afonso J, Carvalho J, Morgado L, Ronchi FA, de Oliveira Leite AP, Dias CC, Casarini DE, Bettencourt P, Albino-Teixeira A, Morato M, Sousa T. Interrelationship between renin-angiotensin-aldosterone system and oxidative stress in chronic heart failure patients with or without renal impairment. *Biomed Pharmacother*. 2021 Jan;133:110938. doi: 10.1016/j.biopha.2020.110938. PMID: 33171402

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Saud A, Luiz RS, Leite APO, Muller CR, Visona I, Reinecke N, Silva WH, Gloria MA, Razvickas CV, Casarini DE, Schor N. Resistance exercise training ameliorates chronic kidney disease outcomes in a 5/6 nephrectomy model. *Life Sci*. 2021 Jun 15;275:119362. doi: 10.1016/j.lfs.2021.119362. PMID: 33741414 DOI: 10.1016/j.lfs.2021.119362

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Sukhanov S, Higashi Y, Yoshida T, Mummidi S, Aroor AR, Russell JJ, Bender SB, DeMarco VG, Chandrasekar B. The SGLT2 inhibitor Empagliflozin attenuates interleukin-17A-induced human aortic smooth muscle cell proliferation and migration by targeting TRAF3IP2/ROS/NLRP3/Caspase-1-dependent IL-1 β and IL-18 secretion. *Cell Signal*. 2021 Jan;77:109825. doi: 10.1016/j.cellsig.2020.109825. PMID: 33160017 PMCID: PMC8118186.

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Zhuo JL, Soleimani M, Li XC. New Insights into the Critical Importance of Intratubular Na⁺/H⁺ Exchanger 3 and Its Potential Therapeutic Implications in Hypertension. *Review Curr Hypertens Rep*. 2021 Jun 10;23(6):34. doi: 10.1007/s11906-021-01152-7. PMID: 34110521 PMCID: PMC8314783.

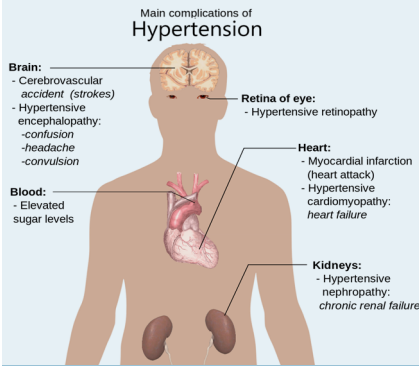
Abstract/ Publication in Press

Leite APO, Li XC, Zhuo JL. The role and sex differences of the mitochondrial protein sirtuin 3 in the proximal tubules of the kidney in the development of angiotensin II-induced hypertension. *International Society of Nephrology World Congress of Nephrology 2021*.

Leite APO, Li XC, Zhuo JL. Sex differences in Angiotensin II-induced hypertension and kidney injury: Role of AT1A receptors in the proximal tubule of the kidney. *Journal of Hypertension: April 2021 - Volume 39 - Issue - p e387*.

Your support are welcome

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



CORE Facilities & Services

Tulane Hypertension and Renal Center of Excellence (THRCE) houses 2 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 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 local and regional meetings on hypertension and public education programs to increase awareness of the dangers of hypertension and its complications.

Upcoming Meetings & Events

Hypertension 2021 Scientific Sessions
~ Virtual Meeting: Sept. 27-29, 2021

ASN Kidney Week 2021
~ Virtual Meeting: Nov 2-7, 2021

2021 New Orleans Heart Walk
~ Lasalle Park, Metairie, Nov. 13, 2021

20th Annual New Orleans Kidney Walk
~ Lafreniere Park, Metairie, Nov. 14, '21

AHA Scientific Sessions
~ Virtual Meeting: Nov. 13-15, 2021

2022 Gordon Research Conference (GRC)
on Angiotensin
~ Ventura-USA, Feb. 27-Mar. 4, 2022

Contact Address

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THRCE Frontiers in Hypertension & Kidney Research Seminar

July 8, 2021

Prasad VG Katakam, MD PhD

Associate Professor, Department of Pharmacology,
Tulane University School of Medicine, New Orleans, LA.

Talk: "Novel Effects of Nitric Oxide Synthase Inhibition on Mitochondrial Respiration."

Sept. 2, 2021

Sarah Lindsey, PhD

Associate Professor, Dr. Barbara S. Beckman Professorship in Pharmacology,
Department of Pharmacology, Tulane University School of Medicine, New Orleans, LA.

Sept. 16, 2021

Hosted Jointly by

THRCE & Kathy Newman Lecture of the Dept. of Pediatrics

Ben Fogelgren, PhD

Associate Professor, Department of Anatomy, Biochemistry, & Physiology,
John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, HI.

Talk: TBA

Sept. 30, 2021

Youhua Liu, PhD

Professor of Pathology, UPMC Endowed Chair in Tissue Biology,
University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA.

Oct. 14, 2021

Speaker: TBA/ Talk: TBA

Oct. 28, 2021

Steven Daniel Crowley, MD

Professor of Medicine, Member of the Duke Cancer Institute,
Duke University School of Medicine, Durham, NC.

Talk: TBA

Nov. 11, 2021

Speaker: TBA/ Talk: TBA

Dec. 9, 2021

Robert S. Hoover MD, FASN, FAHA

Chief of Section of Nephrology and Hypertension
Deming Department of Medicine, Tulane University School of Medicine, New Orleans, LA.

Talk: TBA

Jan. 20, 2022

Zhongjie Sun, MD, PhD, FAHA

Professor and Chair, Thomas A. Gerwin Chair of Excellence in Physiology
Co-Director, UT Methodist Cardiovascular Institute,
Department of Physiology, University of Tennessee (UT), Memphis, TN.

Talk: TBA

DURING COVID-19 RESTRICTIONS: ZOOM MEETINGS WILL REPLACE IN-PERSON MEETINGS AND ARE SCHEDULED ALTERNATIVE THURSDAYS FROM 12 NOON TILL 1 PM.