Tulane Hypertension and Renal Center of Excellence

Volume 19, Issue 2

Tulane University
SCHOOL OF MEDICINE

A Message from Our Director

Dear Colleagues,

The 2nd half of 2020 continued to impose tremendous challenges to the research activities at the Tulane Hypertension and Renal Center of Excellence (THRCE) due to the COVID-19 pandemic. Like all research institutions elsewhere, the lockdown and social distancing policy to mitigate the impact of the COVID-19 pandemic forced our THRCE faculty members and research scientists to carry out their work intermittently in the virtual setting. Despite these challenges, this Fall 2020 newsletter highlights our center's news, activities, the THRCE "Frontiers in Hypertension and Kidney Research" Zoom Seminar Series, awards, conference presentations, and publications from our members, postdocs, and students during the 2nd half of 2020. I would like to thank all members of the THRCE for their dedication and perseverance to their research work, and all our invited expert seminar speakers from around the country for sharing their exciting hypertension and kidney research with us. On behalf of the THRCE, I also sincerely wish everyone a safe, healthy, and successful 2021 during this challenging time due to the COVID-19 pandemic.

Virtual 2020 AHA Heart Walk

THRCE, along with the Department of Physiology, participated as one of 4 teams under the Tulane School of Medicine in the 2020 American Heart Association (AHA) Heart Walk. The money raised was reinvested back into our local community to fund research and other public education programs.

Due to the pandemic, unlike previous years where AHA heart Walk participants gathered at an outdoor location, the 2020 New Orleans Heart Walk was arranged as a virtual event. Participants met digitally at a designated date and time, which was scheduled at 9am on November 14th 2020, hence allowing AHA Heart Walk participants an opportunity to join the good cause and engage with other AHA walkers in a virtual setting.

The Heart Walk has always brought communities together to move more and unite around a common cause close to their heart. Although the virtual 2020 AHA Heart Walk was different from the past, it was still a large celebratory event but with the audience participating in a whole new way.

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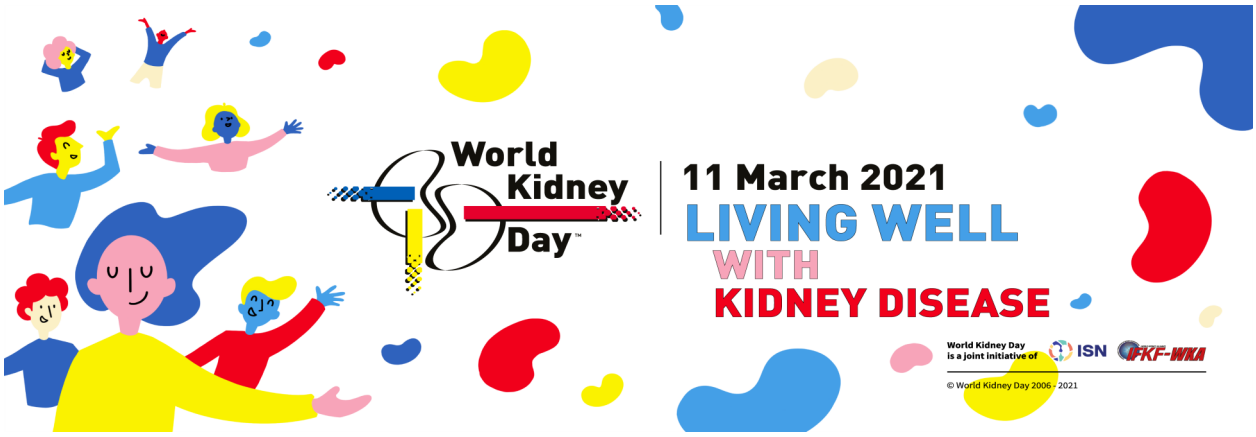


March 11th 2021 is World Kidney Day (WKD). WKD is an international health awareness campaign that focuses on the importance of the kidneys and on reducing chronic kidney disease and its associated health problems.

In previous years, THRCE would organize a Tulane Kidney Health Screening Fair to commemorate the special event. The Health Fair was organized in collaboration with the National Kidney Foundation of Louisiana and the Departments of Physiology and Medicine. This year, the pandemic forced the center to cancel the Health Fair and instead arrange a virtual Zoom WKD Special Seminar. The speaker of 2021 Special WKD THRCE Seminar will be **John Cijiang He, MD, PhD**, Professor and "Irene and Dr. Arthur Fishberg" Endowed Chair of Nephrology at the Icahn School of Medicine, at Mount Sinai in New York, NY. The Zoom meeting will be held on March 11th at 12 noon US Central time.

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 July 2020 through December 2020, the following speakers presented THRCE Sponsored Seminars.

Current and past THRCE Seminars along with cloud recordings of Zoom Seminars can be accessed at our THRCE website: ***https://medicine.tulane.edu/tulane-hypertension-renal-center-excellence/seminar-series.***

Frontiers in Hypertension and Kidney Research Seminar

On July 9, 2020 **Eman Gohar, PhD** presented her research findings at a Frontiers in Hypertension and Kidney Research Seminar. Dr. Gohar is an Instructor in the Department of Medicine at The University of Alabama at Birmingham, Alabama. The title of her presentation was, "**G protein-coupled Estrogen Receptors in the Kidney.**"

SUMMARY OF PRESENTATION:

The novel G protein-coupled estrogen receptor (GPER) is a membrane-associated receptor that mediates rapid estrogenic signaling. GPER is ubiquitously expressed in multiple organ systems, including the cardiovascular and kidney systems. Recent evidence from our group highlights GPER as a novel female-specific pro-natriuretic factor. Endothelin receptors A and B cooperate to mediate GPER-induced natriuresis. In addition, Dr. Gohar's recent data suggests that GPER activation protects against salt-induced renal injury by preserving proximal tubule brush border integrity. Overall, emerging evidence indicates a crucial role for GPER in the maintenance of cardiovascular and kidney health in females.

Frontiers in Hypertension and Kidney Research Seminar continued ...

Barbara Alexander, PhD, presented, "**Low Birth Weight and Increased Cardiovascular Risk**" on July 23, 2020. Dr. Alexander is Professor of Physiology & Biophysics and Director of the Analytical and Assay Laboratory in the University of Mississippi Medical Center in Jackson, Mississippi.

SUMMARY OF PRESENTATION:

Essential hypertension is a complex condition of unknown pathogeneses. Recent advances in the field of developmental origins of increased blood pressure and cardiovascular (CV) risk add another layer of complexity. Complications during pregnancy that impair fetal growth and contribute to the developmental origins of increased blood pressure and CV risk in the offspring are varied and include preeclampsia, diabetes, maternal obesity, parental smoking, maternal stress, alcohol consumption, or age and poor perinatal care. Placental ischemia, the initiating event in preeclampsia is the leading cause of intrauterine growth restriction (IUGR) in the Western world. Low birth weight (LBW) serves as a crude proxy for IUGR and 8.1% of all births in the US are LBW. A greater prevalence of LBW is localized in the Southern US, a region also compromised by elevated risk for hypertension and CV disease. Currently there are no effective drug treatments to prevent or treat preeclampsia. The only treatment option involves early delivery. Yet, birth before 37 weeks resulting in preterm delivery is also associated with increased blood pressure in the offspring. Thus, there is a critical need to develop therapeutic interventions for preeclampsia that not only improve maternal health but also mitigate IUGR and increased blood pressure in the offspring. It is well established that birth weight is inversely related to blood pressure. Although this relationship is observed in both LBW men and women, CV risk is greater in LBW men in young adulthood compared to age-matched LBW women. However, the prevalence of hypertension is almost 2- fold greater in LBW women compared to age-matched normal birth weight women by age 60. LBW is also an independent predictor of CV disease after menopause suggesting CV risk is amplified in LBW women with aging. Yet, how LBW amplifies CV risk in LBW women is not known. Numerous studies indicate that blood pressure is increased in offspring born to women with preeclampsia. Thus, Dr. Alexander's laboratory uses a clinically relevant and well-established model of preeclampsia that results in IUGR and increased blood pressure in the offspring to explore the mechanisms that program IUGR during preeclampsia, whether maternal interventions that improve maternal health also alleviate impaired fetal growth and increased CV risk in the offspring, and how sex and age alter increased CV that has its origins in early life.

Chih-Hong Wang, PhD, presented "**Inhibition of the renin-angiotensin system improves leptin and insulin sensitivity**" on August 6th 2020. At the time of his presentation, Dr. Wang, was Research Investigator at the Department of Internal Medicine in the University of Michigan Medical School. On September 1st 2020, Dr. Wang joined Tulane University School of Medicine as Assistant Professor at the Department of Physiology and the Tulane Hypertension and the Renal Centre of Excellence.

Honors to THRCE Investigators

Dr. Navar received a CLB (Carol Lavin Bernick) Faculty Grant for a research project with medical student, **Emily Pemberton**, titled, "Sex Differences in the Development of Hypertension and Renal Injury in Unilateral Renal Artery Stenosis."

Dr. Hering-Smith elected as Chair of the APS Renal Section and is now on the APS Steering Advisory Committee.

Dr. Hongbing Liu was elected President & Board Member, New Orleans Chinese Association and the Director of the Academy of Chinese Studies in New Orleans.

Postdoctoral Fellows, Gradate & Medical Students:

Ana Paula Leite, PhD (Mentor: Dr. Zhuo): Invited to participate on the 2021 Southern Regional Meetings' Young Investigators' Virtual Forum on February 24, 2021 to present, "Proximal Tubule -Specific deletion of Mitochondrial Protein Sirtuin-3 in the kidney attenuates angiotensin II-induced hypertension and augments natriuretic responses in female mice."

Emily Pemberton (Mentor: Dr. Navar), received an ASPIRE grants from the Biomedical Sciences Department, which provided funding for her summer research project. She will present her work at the Southern Regional Meeting of the SSCI/AFMR and in the Tulane Health Sciences Research Day. She was also selected to receive the Warren R. Bourgeois III and Usha Ramadhyani Student Research Award.

SUMMARY OF PRESENTATION:

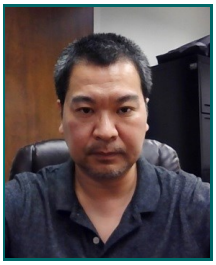
"Obesity is a central metabolic syndrome, which is often associated with leptin resistance and leads to insulin resistance. However, how to improve leptin sensitivity and ameliorate metabolic syndrome is still unclear. Inhibition of the renin angiotensin system (RAS) by angiotensin receptor blocker (ARB) or angiotensin converting enzyme inhibitors (ACEI) decreases blood pressure, and improves insulin sensitivity. We have demonstrated that mice lacking renin (*Ren1c*) have low blood pressure, and are lean and insulin sensitive without changes in food intake and physical activity, but its mechanism is not fully understood. Interestingly, we found that decreased tissue expression of suppressor of cytokine signaling 3 (SOCS3), a molecule that contributes to leptin resistance, were significantly decreased in *Ren1c-/-* mice. Therefore, the aim of the present study is to investigate whether inhibition of RAS improves leptin and insulin sensitivity. After exogenous leptin administration (100µg/kg/day), the phosphor-STAT3 levels were significantly increased, while AMPK activity levels were decreased in the hypothalamus of *Ren1c-/-* mice. These data suggest that *Ren1c-/-* mice had more leptin sensitive than WT mice. However, it could be simply due to lower plasma leptin levels in *Ren1c-/-* mice. To test this possibility we generated mice lacking both renin and leptin (R*en1c-/-;ob/ob*) and found that *Ren1c-/-;ob/ob* mice had 10% lower body weight than *ob/ob* mice due to decreased body fat. Loss of fat mass is associated with decreased triglyceride storage and increased fecal fat excretion in *Ren1c-/-;ob/ob* mice. To test leptin sensitivity, exogenous leptin treatment resulted in improved leptin sensitivity through decreased SOCS3, and increased phospho-STAT3 in *Ren1c-/-;ob/ob* mice. These data are consistent with increased POMC and decreased NPY expressions in the hypothalamus and further reduced food intake and increased energy expenditure in *Ren1c-/-;ob/ob* mice. Most importantly, leptin sensitivity also improved glucose tolerance and insulin tolerance in *Ren1c-/-;ob/ob* mice. These results were recapitulated by using a type 1 Ang II receptor blocker losartan. Therefore, this study demonstrated that inhibition of RAS improves leptin and insulin sensitivity, and may be useful in treating human obesity and diabetes."

Dewan S.A. Majid, MD, PhD, presented, "**Protective role for TNF receptor type-1 in the renal responses to high salt intake**" on August 20, 2020. Dr. Majid is a Professor of Physiology and Director of the THRCE Phenotyping Core at Tulane University School of Medicine.

SUMMARY OF PRESENTATION:

"Salt-sensitive hypertension (SSH) and its' co-morbidity/mortality pose a major health problems on US population. To this great challenge, the proper management of this clinical condition remains nebulous, mainly because it has not been established why chronic high salt (HS) intake raises blood pressure (BP) in some individuals (salt-sensitive) but not in others (salt-resistant) despite many efforts to resolve this through many clinical/epidemiological/experimental studies. As the level of tumor necrosis factor- alpha (TNFα; pro-inflammatory cytokine) is elevated during chronic HS intake, the current investigative efforts in my laboratory is focused to elucidate its causal relationship with the development of SSH. Chronic HS intake induces an immune response activating the mononuclear phagocyte system (MPS) to release TNFα that appears in the circulation in its soluble form (sTNFα). Circulating sTNFα induces natriuresis by activating its receptor type 1 (TNFR1) in the renal tubules indicating a physiological protective function for the TNFα-TNFR1 axis during HS intake. However, this protective function seems to be compromised in nitric oxide (NO) deficient conditions as it is observed that the HS induced increase in renal tissue TNFR1 expression is attenuated in mice chronically treated with a NO synthase inhibitor or in eNOS knockout (KO) mice. Activated MPS cells also release abundant NO along with TNFα. Thus, when NO level decreases, TNFα induces variable salt excretion responses that can be responsible for BP heterogeneity in humans. Renal angiotensinogen (AGT) production induced by chronic angiotensin II (AngII) treatment is increased in TNFR1KO mice indicating a protective role for TNFR1 in suppressing AGT formation. Observation of diurnal

changes reveals that AGT level increases while sTNFα level decreases during inactive period facilitating a characteristic 'non-dipping' BP pattern in AngII induced SSH in mice. The experiments are being conducted in both in-vivo (acute and chronic studies in mice) and in-vitro cultured cell-preparations of MPS and renal tubular epithelial cells. HS induced responses is being assessed in 'normal' condition and in the conditions of NO deficiency and elevated AngII in these preparations. The hypothesis being tested in my laboratory is: 'Chronic HS intake in NO deficient state downregulates renal tubular TNFR1 activity that enhances intrarenal AGT formation, leading to sodium retention and increased BP and thus, transforms a 'salt-resistant' state to a 'salt-sensitive' state. The overall objective of these experiments is to define the interactions between NO and TNFR1 activity and to determine how HS intake induces BP heterogeneity during HS intake. In long-term, these results will be of cardinal importance in developing 'translational research projects' that will resolve the etiology of SSH."



On September 3, **Ryosuke Sato, PhD**, presented, "**Establishment of Novel Humanized Kidney Models for Medical Research: Engrafted Human Kidney Organoids to Animal Kidney**." Dr. Sato is an Assistant Professor of Physiology and Director of the THRCE Molecular Core at Tulane University School of Medicine.

SUMMARY OF PRESENTATION:

"Our research group has created human kidney organoids using iPS cells under *in vitro* setting. We characterized the kidney organoids and investigated the renin-angiotensin system in the organoids. Moreover, we have recently been trying to establish engrafted human kidney organoids under mouse renal capsules. Further grown organoids and adhesion to the host mouse kidney was observed 2 weeks after the implantation. Importantly, these engrafted organoids exhibited development of vascularization and glomerular formation. These engrafted human kidney organoids can be novel and powerful translational models to hypertension and associated kidney injury research, which will enhance the progression and knowledge of these diseases in humans. In the seminar, I shared the obtained results using these *in vitro* and *in vivo* models."

Ryuji Morizane, MD, PhD, presented, "**Kidney Organoids for Disease Modeling and Regenerative Medicine**" on September 17, 2020. Dr. Morizane is an Assistant Professor in Medicine at Harvard Medical School in Boston, Massachusetts.

SUMMARY OF PRESENTATION:

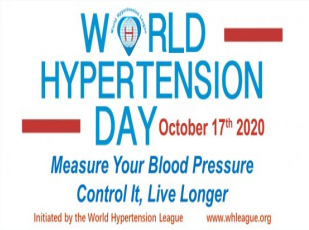
Dr. Morizane's laboratory developed an efficient, chemically defined protocol for differentiating human pluripotent stem cells into multipotent nephron progenitor cells (NPCs) that can form kidney organoids. By recapitulating metanephric kidney development *in vitro* Dr. Morizane and his investigators were able to generate SIX2+SALL1+WT1+PAX2+ NPCs with 80-90% efficiency within 8-9 days of differentiation. NPCs form kidney organoids containing epithelial nephron-like structures expressing markers of podocytes, proximal tubules, loops of Henle and distal nephrons in an organized, continuous arrangement that resembles the nephron *in vivo*. The organoids express genes reflecting many transporters seen in adult metanephric-derived kidney, enabling assessment of transporter-mediated drug nephrotoxicity. Repetitive drug-induced injury to kidney organoids causes interstitial fibroblast expansion with characteristics of myofibroblasts, indicating kidney organoids can be used to model kidney fibrosis *in vitro*. Polycystic kidney disease (PKD) patient-derived organoids exhibit cystic phenotypes. Hence the generated kidney organoids

are effective tools to study genetic disorders of the kidney as well as mechanisms of kidney injury and fibrosis. Microphysiological platforms *in vitro* facilitate kidney organoid vascularization and maturation, which may lead to the development of functional bioengineered kidneys in the future.

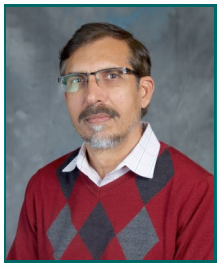
Curt D. Sigmund, PhD, presented "**Post-translational Mechanisms in Vascular Smooth Muscle Regulate Arterial Stiffness and Blood Pressure: Role of RhoBTB1/Cullin-3**" on October 1, 2020. Dr. Sigmund is the "James J. Smith & Catherine Welsch Smith" Chair and Professor at the Department of Physiology and Associate Director of the Cardiovascular Center at Medical College of Wisconsin in Milwaukee.

SUMMARY OF PRESENTATION:

"Blood vessels play an important role in the regulation of arterial blood pressure and precise blood pressure regulation requires coordination between vasodilator and vasoconstrictor signals in the endothelium and smooth muscle. Our data support the concept that PPARG acts as a sensor in endothelium to regulate redox state, and through this, bioavailability of nitric oxide, and regulates the responsiveness of the smooth muscle to nitric oxide by independently controlling a RhoA/Rho kinase (ROCK) activity that promotes constriction, and production and stability of cyclic GMP (cGMP), a critical mediator of vasodilation. We identified a novel mediator of this pathway, RhoBTB1, which protects against hypertension, vascular smooth muscle dysfunction, and arterial stiffness. Identifying the molecular targets of PPARG, such as RhoBTB1, will help lead to the design of a new class of therapeutics that regulate PPARG downstream actions more selectively."



World Hypertension Day (WHD) fell on October 17 in 2020. 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 October 15, 2020 presented by **Tahir Hussain, PhD**. Dr. Hussain is Associate Dean of Research & Graduate Programs and Joseph P. & Shirley Shipman Buckley Professor in Drug Discovery at the University of Houston in Texas. The title of the Special THRCE WHD Seminar was "**Immunomodulatory role of Angiotensin AT2 Receptor in Renoprotection**."



SUMMARY OF PRESENTATION:

"Numerous studies including ours strongly suggest that angiotensin type-2 receptor (AT_2R) activation promotes natriuresis and lowers blood pressure in various animal models, including obesity. Recent studies demonstrate an emerging role of angiotensin type 2 receptor in anti-inflammation and organ protection, particularly reno-protection. Specifically our studies show that AT_2R activation improves functional aspects of renal injury such as GFR and proteinuria in various model of renal injury such as obesity, LPS-induced and ischemia perfusion (IR). At molecular level we have found that AT_2R agonist treatment reduces proinflammatory cytokines TNFα and IL-16 and increases anti-inflammatory cytokine IL-10 in the kidney and plasma. Reduction in infiltrating immune cells such as monocytes and T cells in the kidney is observed indicating a basis of anti-inflammation and reno-protection. Furthermore, our in vitro studies in kidney cells and macrophages and in vivo studies revealed that IL-10 mediates the anti-inflammatory actions of AT_2R. AT_2R is not only protects against renal injury but it also helps repair the kidney, particularly in acute kidney injury models such as IR models."

Seminars continued

On November 12, 2020, **Robert M. Carey, MD**, presented, "**New AT2 Receptor Signaling Mechanisms in Natriuresis & Defects leading to Hypertension**." Dr. Carey is a Distinguished Professor of Medicine, Dean, Emeritus at the University of Virginia, School of Medicine at Charlottesville, VA.

SUMMARY OF PRESENTATION:

"The renin-angiotensin system (RAS) plays a critical role in the regulation of body fluid, electrolyte balance, and blood pressure (BP) both in health and disease. The RAS acts via two major receptors: Angiotensin (Ang) type-1 (AT_1R) and Ang type-2 (AT_2R). Previous studies have confirmed that, while renal AT_1Rs induce sodium (Na^+) retention, AT_2Rs increase urinary Na^+ excretion ($U_{Na}V$) at the level of the renal proximal tubule (RPT) and that, instead of angiotensin II (Ang II), des-aspartyl^1-Ang III (Ang III) is the predominant endogenous agonist for this response. In the normal kidney, AT_2Rs induce natriuresis by a bradykinin (BK)-nitric oxide (NO)-cyclic guanosine 3',5'monophosphate (cGMP)-dependent signaling cascade accompanied by AT_2R translocation to RPT apical plasma membranes and internalization/ inactivation of major RPT Na^+ transporters Na^+-H^+ exchanger-3 (NHE-3) and Na^+/K^+ATPase (NKA).

Spontaneously hypertensive rats (SHR) develop hypertension at approximately 6 weeks of age and are widely employed as a model of human hypertension. A proposed mechanism of initiation of hypertension in SHR is a primary increase in renal Na^+ reabsorption. Over time, this defect requires an increase in BP to normalize $U_{Na}V$, an adaptation that is central to the development and maintenance of hypertension. In previous studies, we have shown that both pre-hypertensive 4-week-old and hypertensive 12-week-old SHR lack natriuretic responses to renal interstitial (RI) Ang III administration, whereas Ang III induces robust natriuresis in corresponding Wistar-Kyoto control rats (WKY). The Ang III/AT2R defect in SHR does not appear to be due to accelerated Ang III metabolism. These results suggested that the Ang III/AT_2R/NHE-3 signaling pathway is a RPT-specific, natriuresis-promoting mechanism, maintaining normal body salt and fluid balance and BP, that is defective in hypertension.

Earlier this year, we reported that the defect in AT_2R-mediated natriuresis in SHR is primarily due to impaired signaling at the receptor or post-receptor level. Intrarenal infusion of highly selective non-peptide AT_2R agonist Compound 21 (C-21) in 4-week-old WKY induced a strong natriuretic response which was absent in 4-week-old pre-hypertensive SHR. This primary AT2R natriuretic defect affects virtually all known signaling pathways distal to the receptor in SHR kidneys. Importantly, natriuresis and downstream signaling, but not AT_2R recruitment, are restored in SHR with exogenous intrarenal cGMP administration. We now identify new natriuretic AT_2R signaling pathways in WKY and their corresponding defects in SHR kidneys."

On December 10, **Jia Zhuo, MD, PHD**, presented, "**How to Write R01 Grants: A Personal Experience & Perspective.**" Dr. Zhuo is the Director of the THRCE at Tulane University School of Medicine.

SUMMARY OF PRESENTATION:

Dr. Zhuo has about 30 years' success in securing extramurally sponsored research investigating the roles of circulating (endocrine), tissue (paracrine), and intratubular/intracellular angiotensin II and its receptor localization and signaling mechanisms in the hypertension and kidney research. His research has been continuously supported by grants from the National Health and Medical Research Council of Australia, American Heart Association (AHA), American Society of Nephrology (ASN), and National Institute of Health (NIH). Dr. Zhuo also served as a permanent member for NIH/Center for Scientific Review (CSR) Hypertension and Microcirculation Study Section (HM) and an Ad Hoc reviewer for numerous CSR special emphasis panels for 12 years. In this presentation, Dr. Zhuo shared his personal experience and perspectives on how to write or renew a competitive NIH R01 research proposal for funding.

Abstracts & Presentations

The following abstracts were virtually presented by THRCE affiliated investigators between July through December 2020

Hypertension Scientific Sessions 2020, September 10–13, 2020

Abdullah S, Karim MS, Legendre M, Rodriguez L, Friedman J, Taghavi S, Guidry C, Duchesne J, Jackson-Weaver O. Mitochondrial Reactive Oxygen Species Mediate Endothelial Glycocalyx Damage and Vascular Dysfunction in Hemorrhagic Shock and Resuscitation.

Bell AL, Shao WA Katsurada A, Sato R, Navar LG. Reduced Augmentation of the Intrarenal Renin-Angiotensin System (ras), Lower Systolic Blood Pressure, and Preserved Renal Function in female compared to male rats with Unilateral Renal Artery Stenosis.

Das S, Neelamegam K, Peters WN, Periyasamy R, Pandey KN. Depletion Of Cyclic-gmp Levels And The Inhibition Of Cgks Activate P21Cip1/p27Kip1 Pathways And Trigger High Blood Pressure With Renal Fibrosis And Dysfunction Aldosterone, Receptors and Signal Transduction.

Elgazzaz M, Lazartigues E. High Fat Diet Exposure Induces Epigenetic Modulation In The Brain Renin Angiotensin System. MP04 | Moderated Poster 1: Top TAC Awards: Mechanisms of Hypertension I/ Renin-Angiotensin System.

Gomes DS, Visniauskas B, Prieto MC, Lara LS. Salt-inducible Kinase (SIK): A Pharmacological Target Of Salt-sensitive Hypertension.

Hering-Smith KS, Huang W, Teran F, Sato R, Hamm L. Factors Altering Luminal Succinate Effect Blood Pressure.

Kelly TN. Blood Pressure Genetic Risk Score Predicts Blood Pressure Responses to Dietary Sodium Potassium. Oral talk, Session 5: KCVD Council Symposia: BP Genetics 2.0-Genetic Determinants, Risk Scores, and Complications.

Leite APO, Li XC, Casarini DE, Zhuo JL. Pressor, Natriuretic, and Renal responses in Angiotensin II-Induced Hypertension in male and female wild-type and proximal tubule-specific AT1A-Receptor knockout mice.

Li XC, Leite AP, Zhang L, Zhuo JL. Proximal Tubule-specific deletion of Angiotensin II-Type 1a Receptors in the Kidney Lowers Basal Blood Pressure and Attenuates Angiotensin II-induced Hypertension by increasing Glomerular Filtration & the Pressure-natriuresis Response.

Li XC, Zhou X, Zhuo JL. Evidence For A Physiological Mitochondrial Angiotensin II-System in the Proximal Tubules of the Kidney.

Lindsey SH. Estrogen Receptor Signaling in Vascular Remodeling and Stiffness. Oral presentation - Session 3: A Focus on Women's Health.

Liu H, Koduri MM, Dragon A, Chen CH, El-Dahr SS. Histone Deacetylases 1 And 2 Regulate Six2 Function To Maintain Nephron Progenitor Cells During Nephrogenesis. Oral presentation: Abstract 9, Session AOS2 - Genetics & Genetic Models of Hypertension. Originally published 9 Sep 2020. https://doi.org/10.1161/hyp.76.suppl_1.9 l Hypertension. 2020; 76: A9

Majid DS, Castillo A. Attenuation Of Diuretic And Natriuretic Responses To Acute Saline Volume Expansion In Mice Pre-treated With Tumor Necrosis Factor-alpha (TNFα) Inhibitor, Etanercept.

Richfield O, Cortez R, Franco Ma, Navar LG. Purinergic Receptor Activation Protects Glomerular Microvasculature from Increased Mechanical Stress In Angiotensin II-induced Hypertension: A Modeling Study.

Satou R, Franco MG, Katsurada A, Dugas CM, Navar LG. Immunosuppressant Treatment Attenuates Augmentation Of Intrarenal NLRP-3 Inflammasome In Angiotensin II-dependent Hypertension.

American College of Surgeons Committee on Trauma, Region 6; Resident Paper Competition. Nov. 11, 2020

Friedman J, Abdullah S, Taghavi S, Guidry C, Duchesne J, Jackson-Weaver O. Mitochondrial reactive oxygen species cause endothelial glycocalyx shedding in a rat model of Zone 3 REBOA. Awarded First Place for Basic Science presentation.

AHA Resuscitation Science Symposium, Nov.14-16 2020

Abdullah S, Legendre M, Karim MS, Rodriguez L, Friedman J, Taghavi S, Guidry C, Duchesne J, Jackson-Weaver O. Endothelial Reactive Oxygen Species Mediate Glycocalyx Damage in Pulmonary and Intestine Vasculature in Hemorrhagic Shock in the Rat.

Invited Presentations

On October 9, 2020, Dr. Zhuo presented, "The novel roles of intratubular paracrine and intracrine angiotensin II in the kidney: new insights and future perspectives" at Saha Cardiovascular Research Center and Department of Physiology at the University of Kentucky, School of Medicine, Lexington, KY.

Dr. Zhuo presented, Intratubular intracellular and mitochondrial angiotensin II in the kidney: new insights from proof-of-concept studies," on November 6 at Department of Pharmacology at Tulane University, School of Medicine.

Dr. Navar participated in the Review of the CoBRE on "Cardiorenal and Metabolic Diseases" for the Physiology Department at the University of Mississippi Medical Center as a member of the External Advisory Board on October 29, 2020.

THRCE affiliated investigators who were invited to present and participate at various national events.

Publications

Bautista-Pérez R, Pérez-Méndez O, Cano-Martínez A, Pacheco U, Santamaría J, Rodríguez-Iturbe FRB, Navar LG, Franco M. The Role of P2X7 Purinergic Receptors in the Renal Inflammation Associated with Angiotensin II-induced Hypertension. *Int J Mol Sci. 2020 Jun 5;21(11):4041. doi: 10.3390/ijms21114041.* PMID: 32516946 PMCID: PMC7312644.

Curnow AC, Gonsalez SR, Gogulamudi VR, Visniauskas B, Simon EE, Gonzalez AA, Majid DSA, Lara LS, Prieto MC. Low Nitric Oxide Bioavailability Increases Renin Production in the Collecting Duct. *Front Physiol. 2020 Nov 17;11:559341. doi: 10.3389/fphys.2020.559341. eCollection 2020*. PMID: 33281610 PMCID: PMC7705222.

Kulthinee S, Shao W, Franco M, Navar LG. Purinergic P2X1 receptor, purinergic P2X7 receptor, and angiotensin II type 1 receptor interactions in the regulation of renal afferent arterioles in angiotensin II-dependent hypertension. *Am J Physiol Renal Physiol. 2020 Jun 1;318(6):F1400-F1408. doi: 10.1152/ajprenal.00602.2019.* PMID: 32308022 PMCID: PMC7311710.

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. 2020 Jul;76(1):121-132. doi: 10.1161/HYPERTENSIONAHA.119.13942.* PMID: 32475319.

Liu H. The roles of histone deacetylases in kidney development and disease. *Clin Exp Nephrol. 2021 Jan 4.doi: 10.1007/s10157-020-01995-5.* PMID: 33398599.

Liu H, Hilliard S, Kelly E, Chen CH, Saifudeen Z, El-Dahr SS. The polycomb proteins EZH1 and EZH2 co-regulate chromatin accessibility and nephron progenitor cell lifespan in mice. *J Biol Chem. 2020 Aug 14;295(33):11542-11558. doi: 10.1074/jbc.RA120.013348.* PMID: 32554463.

Richfield O, Cortez R, Navar LG. Simulations of Glomerular Shear and Hoop Stresses in Diabetes, Hypertension, and Reduced Renal Mass using a Network Model of a Rat Glomerulus. *Physiol Rep. 2020 Sep;8(18):e14577.* PMID: 32951361 PMCID: PMC7507384. PMCID: PMC7507384.

Taghavi S., Abdullah S., Duchesne J., Pociask D., Kolls J., Jackson-Weaver O. Interleukin 22 mitigates endothelial glycocalyx shedding after lipopolysaccharide injury. **Accepted for Publication**.

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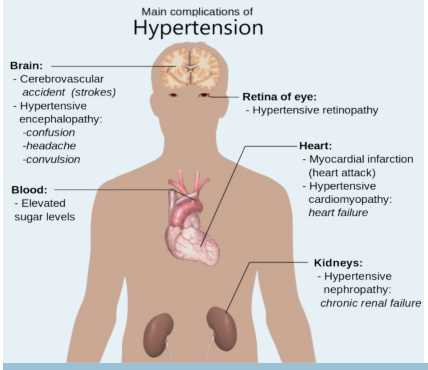
Publications listed on the left include those published between June through December, 2020 and publications that were omitted in previous THRCE newsletters.

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.

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

20th Annual SSCI Nephrology Young Investigator's Forum
~ Virtual Meeting: Feb. 24, 2021

2021 Southern Regional Meeting Jointly sponsored by Tulane University.
~ Virtual Meeting: Feb. 25 - 27, 2021

Special WKD THRCE Seminar
~ Virtual Meeting: March 11, 2021

Joint Meeting ESH – ISH 2021
~ Virtual Meeting: April 11-14, 2021

Tulane Annual Health Sciences Res. Days
~ Virtual Meeting: April 14-15, 2021

EB - Conference:
~ Virtual Meeting: April 27–30, 2021

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Tulane University

THRCE Frontiers in Hypertension & Kidney Research Seminar

Jan. 7, 2021
Bruce A. Molitoris, MD
Distinguished Professor & Professor of Medicine, Nephrology
Adjunct Professor of Anatomy, Cell Biology & Physiology
Indiana University School of Medicine, Indianapolis, IN.
"Rapid Endothelial Clearance of Carbamylated Albumin: Potential for Inflammation?"

Jan. 21, 2021
Peter M. Abadir, MD
Associate Professor of Medicine
Division of Geriatrics Medicine & Gerontology,
John Hopkins University, School of Medicine, Baltimore, MD
"The Biology of Frail Angiotensin System Translated: Worn-out Mitochondria to Poor Wound Healing."

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

March 4, 2021
Jennifer C. Sullivan, PhD, FAHA
Interim Dean of the Graduate School & Professor of Physiology,
Medical College of Georgia, Augusta University.
"Do T cells underlie sex differences in blood pressure control?"

March 11, 2021
Special WKD 2021 Seminar
John Cijiang He, MD, PhD
Professor of Medicine & Pharmacological Sciences,
"Irene and Dr. Arthur Fishberg" Endowed Chair of Nephrology,
Chief of Nephrology Division at Mount Sinai Health System,
The Icahn School of Medicine at Mount Sinai, New York, NY.
Talk: TBA

March 18, 2021
Hong S. Lu, MD, PhD
Professor, Internal Medicine & Physiology,
Cardiovascular Research Center, University of Kentucky College of Medicine, Lexington, KY.
"Angiotensinogen links liver and kidney to atherosclerosis."

May 27, 2021
Pedro A. Jose, MD, PhD
Past Chair, NIH Hypertension and Microcirculation Study Section,
Professor of Medicine, Pharmacology, & Physiology,
George Washington University, School of Medicine & Health Sciences, Washington, D.C.
"Renal dopamine and salt sensitivity of blood pressure."

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