



THRCE.

TULANE HYPERTENSION AND RENAL CENTER OF EXCELLENCE

Fall & Winter 2016

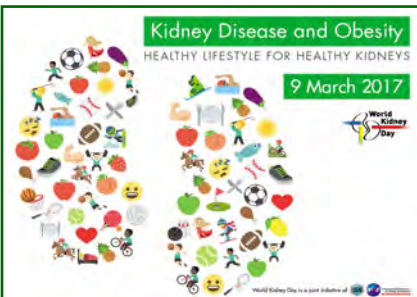
Volume 15, Issue 2 & 3

COBRE AWARDS THREE PILOT PROJECT GRANTS

Each year, the COBRE provides three pilot projects grants of \$45,000 to support scientific research related to hypertension. These pilot project awards provide one year of research support for novel, innovative projects that address important and significant issues related to the broad area encompassed by hypertension, renal and cardiovascular research. Applications are subjected to a rigorous internal and external review process to ensure that funds are provided only to highly meritorious projects that are likely to lead to extramural research support and will stimulate multidisciplinary collaborative interactions. The 2016-2017 COBRE Pilot Project award recipients are Drs. Majid, Pandey and Hering-Smith.

- **Pilot Project 1:** *TNF- α receptors in intrarenal angiotensinogen regulation during high salt intake.*
PI: Dewan S. A. Majid, MBBS, PhD, Department of Physiology.
- **Pilot Project 2:** *Genetic Basis of Inflammation and Cardiovascular Dysfunction.*
PI: Kailash, N. Pandey, PhD, Department of Physiology.
- **Pilot Project 3:** *Novel Mechanism of Diabetic Ketoacidosis*
PI: Kathleen S. Hering-Smith, PhD, Department of Medicine.

MARCH 9, 2017 IS WORLD KIDNEY DAY!



Kidney disease is more likely to develop in obese people including in those with diabetes and hypertension, so the 2017 World Kidney Day (WKD) focus is on the relationship between obesity and kidney disease. Obesity increases the risk of death and contributes to many other diseases such as heart disease, diabetes, hypertension, high cholesterol, obstructive sleep apnea, fatty liver, gall bladder disease, osteoarthritis, various cancers, mental disorders, and poor quality of life. Evidence indicates that obesity is a risk factor for the development of chronic kidney disease (CKD) and end-stage renal disease (ESRD). Reducing obesity may reverse or slow CKD progression. WKD is a joint initiative of the International Society of Nephrology (ISN) and the International Federation of Kidney Foundations (IFKF). Please access: www.worldkidneyday.org for more details.

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THRCE CO-SPONSORS 2016 MAYERSON DiLUZIO LECTURE



Joey Granger, Ph.D.

Joey Granger, PhD was awarded the 2016 Mayerson-DiLuzio Lectureship at Tulane University. He presented, "Potential Therapeutic Targets for the Treatment of Preeclampsia." on March 4, 2016. The Lectureship was established to honor the memory of Drs. Hyman S. Mayerson and Nicholas R. Di Luzio, who presided as Chairmen of the Tulane Physiology Department.

Dr. Granger is the Billy S. Guyton Distinguished Professor, Professor of Physiology and Medicine, Director of the Cardiovascular-Renal Research Center, and Dean of the School of Graduate Studies in the Health Sciences at the University of Mississippi Medical Center in Jackson, MS. He earned his doctorate from Arthur C. Guyton's Physiology Department at the University of Mississippi Medical Center, completed his postdoctoral training at the Mayo Clinic and Foundation, and has served as a faculty member at Mayo, as well as Eastern Virginia Medical School before returning to the University of Mississippi School of Medicine in 1990. In 1996, he became the Associate Director of the Center for Excellence in Cardiovascular-Renal Research. He was named the Billy S. Guyton Distinguished Professor in the Department of Physiology and Biophysics in 2004 and appointed Dean of the School of Graduate Studies in the Health Sciences in 2007.

Dr. Granger's research has focused on the role of the kidneys in the pathogenesis of hypertension. His early research examined the importance of atrial natriuretic peptide (ANP) in long-term control of sodium balance and arterial pressure. He demonstrated that ANP had potent actions on the renin-angiotensin system and that chronic physiological elevations in plasma ANP produced long-term improvement in renal pressure natriuresis and reductions in arterial pressure. His later work investigated the role of the renal endothelin and nitric oxide systems in various models of salt-sensitive hypertension.

Dr. Granger has been a member of Council on Hypertension for over 30 years and has served on the Council's Leadership Committee for the last 12 years. He has served on numerous Council's committees including as Chair of the Harry Goldblatt Award Selection Committee, Chair of Hypertension Summer School Organizing Committee, Chair of Awards Committee, Vice Chair Trainee Advisory Committee. He also served as a member of the Council's Professional Education Committee, Liaison Member for Basic Science Council, Publications Committee, and Council's Strategic Planning Committee.

Continued...

Dr. Granger also served as President of the American Physiology Society in 2012 and currently serves on Leadership committee of the Inter-American Society of Hypertension. He also served on scientific study sections for the American Heart Association, National Institutes of Health, NASA, and the Veterans Administration. He recently served as chair of the Hypertension and Microcirculation NIH study section. He also served on the National Board Medical Exam Physiology Test Development Committee. He has authored or co-authored over 250 peer-reviewed publications, many of them in the Hypertension journal. Dr. Granger is currently an Associate Editor for Hypertension and serves as Co-Editor with his brother, Neil Granger, on the eBook series entitled Integrative Systems Physiology. He served as the Editor of the Council for High Blood Pressure Newsletter and an Associate Editor for News in Physiological Sciences and American Journal of Physiology: Regulatory and Integrative Physiology. He is serving or has served as a member of Editorial Boards of American Journal of Hypertension, American Journal of Physiology: Renal Physiology, American Journal of Physiology: Regulatory and Integrative Physiology, Journal of CardioMetabolic Syndrome and the Journal of the American Society of Hypertension.

Dr. Granger has received several awards including the 2010 American Heart Association Distinguished Scientist Award, American Physiological Society 2008 E.H. Starling Distinguished Lecture Award, American Physiological Society 2008 Bodil M. Schmidt-Nielsen Distinguished Mentor and Scientist Award, Dahl Memorial Lecture of the American Heart Association, American Society of Hypertension Young Scholar Award, the International Society of Hypertension Demuth Research Award, Inter-American Society of Hypertension Young Investigator Award, the Regulatory and Integrative Physiology Young Investigator Award of the American Physiological Society Water and Electrolyte Section, the Harold Lamport Award of the Cardiovascular Section of the American Physiological Society, the Henry Pickering Bowditch Lecture of the American Physiological Society, and the Established Investigator Award of the American Heart Association.

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HONORS & RECOGNITION AWARDED TO THREE AFFILIATED INVESTIGATORS

Andrei Derbenev, PhD:

- Promoted to Associate Professor with tenure.
- Executive Board Member of the Tulane Brain Institute.

Samir El-Dahr, MD:

- Appointed on the Board of Directors of the Association of North American Medical School Pediatric Departments Chairs (AMSPDC).

L. Lee Hamm, MD:

- Was an abstract grader at the 2016 Council on Hypertension Scientific Sessions

Sarah Lindsey, PhD:

- Moderator at the Oral Session, "Vascular Biology and Dysfunction" at the 2016 Council on Hypertension Scientific Sessions.

Hongbing Liu, PhD:

- Received a Young Investigator Travel award of \$1,200 to assist in the travel expenses to attend the NISBRE meeting held in June, 2016 at the 6th Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE).
- Appointed as committee member and Faculty co-Chair of "Tulane University's Building Bridges Faculty and Staff Alliance for Underrepresented Faculty, Staff, and Students"

Kenneth D. Mitchell, PhD:

- Nominated for the T1 Best Professor of the Year Award and the T1 Best PBL Facilitator Award.
- Received the T1 Best Facilitator Award from the Owl Club.

Dewan S. A. Majid, MD, PhD:

- Elected to serve on the University Senate for the 2016-2017 term.
- Awarded a COBRE Phase III Pilot Project Award.

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Honors & Recognition Awarded to THRCE Affiliated Investigators, continued...

Walter Lee Murfee, PhD:

- Awarded a 4 year NIH/NIA RO1 for his project, "Angiogenesis Model for Aging Research". Dr. Murfee was a former Junior Faculty Investigator of the COBRE on Hypertension & Renal Biology.
- Recognized at the Synergy event for receiving his first R01 grant from NIH.

L. Gabriel Navar, PhD:

- Awarded Year-5 of the NIH/NIGMS CoBRE III Grant (5P30GM103337) for the period 08/01/2016- 07/31/2017.
- Chaired poster Session titled, "Salt and Hypertension" 2016 Council on Hypertension Scientific Sessions
- Awarded, with Dr. Sato, a COBRE supplement grant of \$349,716 DC to update COBRE Core Facilities.
- Awarded with co-investigators, Drs. Sato & Woods, a Janssen IIS grant titled, "Role of Kidney Production of Angiotensinogen in the Reduction of Blood Pressure by SGLT2 Inhibition under Diabetic and Non-diabetic Conditions."

Kailash N. Pandey, PhD:

- Awarded the Carol Lavin Bernick Faculty Grant award of the amount of \$13,000, by the Tulane Bridge Funding Committee.
- Awarded a COBRE Phase III Pilot Project Award.

Minolfa C. Prieto, MD, PhD:

- Elected to serve on the Personnel and Honors Committee for the Tulane School of Medicine during the 2016-2019 term.
- Received the 2016 Young Investigator award from the American Physiological Society during the Experimental Biology Meeting held in San Diego, CA in April 2-6, 2016.
- Moderator at the Oral Session, "Renin Angiotensin System" at the 2016 Council on Hypertension Scientific Sessions.

Ryosuke Sato, PhD:

- Recognized at the Synergy event for receiving his first R01 grant from NIH.
- Awarded as co-investigator a COBRE supplement grant; PI: Dr. Navar.
- Co-Investigator on a 2-year Janssen IIS grant awarded in November 2016.

Continued...

Honors & Recognition Awarded to THRCE Affiliated Investigators, continued...

Zubaida Saifudeen, PhD:

- Elected to serve on the BMS Steering Committee
- Elected to serve on the Faculty Advisory Committee for the 2016-2017 term.

T. Cooper Woods, PhD :

- Received an RO1 Grant from NIH-NHLBI for his project titled, "Role of VSMC-Derived Exosomes in the Cardiovascular Complications of Diabetes."
- Received patent, "Use of miR-221 and 222 lowering agents to prevent Cardiovascular Disease in Diabetic Subjects," in September 2016.
- Elected to serve on the Faculty Advisory Committee for the 2016-2017 term.
- Appointed to the Tulane Uptown and Downtown Campuses Institutional Animal Care and Use Committee (IACUC) effective August 1, 2016.
- Received the 2016 Diabetes Research Leadership Award from the American Diabetes Association.
- Appointed as tenure track faculty member of Department of Physiology.
- Selected as a finalist for the 2016 Diabetes Research Leadership Award. The award is sponsored by Mr. Joe Canizaro to recognize those researchers in our community committed and driven to finding a cure for diabetes.
- Appointed to the VA Office of Research & Development's Cardiology-B (CARB; vascular disease) study section.
- Nominated for the T1 Best Professor of the Year Award and the T1 Best PBL Facilitator Award.
- Spinoff company from his laboratory, Carre BioDiagnostics, LLC, won \$25,000 at the 5th Annual BioChallenge Pitch Competition.
- Recognized at the Synergy event for receiving his first R01 grant from NIH.
- Co-Investigator on a 2-year Janssen IIS grant awarded in November 2016.

Andrea Zsombok, PhD:

- Selected as member of the APS Science Policy committee and editorial member of the Journal of Diabetes and Its Complications until Dec 31, 2018.
- Elected Tulane General Medical Faculty Vice Chair for the 2016-2017 term.
- Regular member of Neuroendocrinology, Neuroimmunology, Rhythm and Sleep NIH Study Section from July 1, 2016 to June 30, 2022.
- Executive Board Member of the Tulane Brain Institute.

Continued...

Honors & Recognition Awarded to THRCE Affiliated Investigators, continued...

Graduate & Post-doctoral fellows:

- Aaron Brug, medical student, in Dr. Woods' laboratory received an American Heart Association 2016 Student Scholarship in Cardiovascular Disease and Stroke.
- Dr. Lucienna Lara Morcillo, Federal University of Rio de Janeiro, received an APS Research Career Enhancement award and will be working in the laboratory of Dr. Prieto as a visiting professor in August. Dr. Morcillo will be training in telemetry.
- Sierra Butcher received the Campbell Award in Endocrinology and Metabolism from the American Physiological Society, Dr. Zsombok, mentor.
- Tulane Summer Undergraduate Research Program in Neuroscience: Ryan Parmoon, undergraduate neuroscience student, received a fellowship for summer to work with Dr. Derbenev.

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2016 Summer Students welcomed to THRCE

Each year meritorious Medical and Undergraduate Research Students are selected to work with faculty researchers affiliated with the Tulane Hypertension & Renal Center of Excellence for 8 to 10 weeks during the summer. Each student receives a stipend, are exposed to the valuable nature of a career path in research, and have the opportunity to attend the various THRCE events and Seminars. The following students were selected for the 2015 Summer Research Program:

MEDICAL STUDENTS:

Sponsor: AHA Summer Fellowship Program

- **Aaron Brug**
Mentor: Dr. T. Cooper Woods
- **Nashira Howe**
Mentor: Dr. Zubaida Saifudeen
- **Catherine McNulty**
Mentor: Mentor: Dr. David W. Busija
- **Krishna Pandya**
Mentor: Dr. Kailash N. Pandey

Sponsor: Bourgeois Medical Research Endowment

- **Andrew Curnow**
Mentor: Dr. Minolfa Prieto
- **Joseph M. Garagliano**
Mentor: Dr. Ryosuke Sato
- **Leah Ott**
Mentor: Dr. Kenneth D. Mitchell

Sponsor: NIH ROI 554308

- **Kayla Hudson**
Mentor: Dr. T. Cooper Woods, PI

UNDERGRADUATE STUDENTS:

- **Lauren Nguyen**
Mentor: Dr. Hongju Wu
- **Anadil Zakaria**
Mentor: Dr. Hongju Wu
- **Ryan Parmoon**
Mentor: Drs. A. Derbenev & A. Zsombok

- **Megan Drewett**
Mentor: Dr. Minolfa Prieto
- **Aline Leal Cortes**
Mentor: Dr. Minolfa Prieto
- **Christopher Wong**
Mentor: Dr. Minolfa Prieto
- **Emma Lewis**
Mentor: Drs. Abdalnour-Nakhoul & N. Nakhoul

VISITING SCIENTIST:

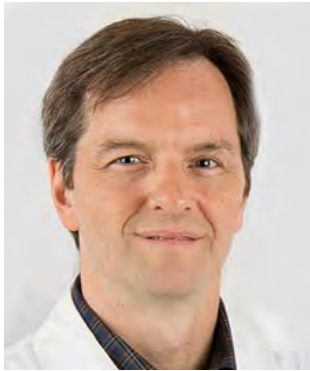
Mentor: Dr. Navar

- **Alberto Parra**
Mentor: Dr. Navar

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THRCE SPONSORED LOCAL, NATIONAL & INTERNATIONAL SPEAKERS

THRCE sponsors bi-weekly seminars by scheduling nationally and internationally recognized investigators and clinicians in the field of hypertension research, treatment and education. From May through December, 2016, the center hosted the following speakers to present THRCE seminars; summaries were provided by the speakers.



Special THRCE Seminar

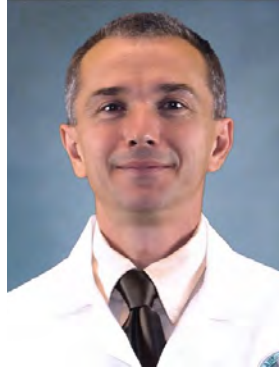
Co-Sponsored by the Department of Pediatrics

- **Maxime Bouchard, PhD**

*Associate Professor, Department of Biochemistry,
Rosalind & Morris Goodman Cancer Research Center,
McGill University, Montréal, Québec, Canada.*

On Wednesday, May 11th, 2016, Dr. Maxime Bouchard presented “Apoptotic control of urinary tract morphogenesis.”

Summary: Programmed cell death is essential for normal tissue morphogenesis and its failure is associated with developmental defects and cancer progression later in life. In the urogenital system, Dr. Bouchard’s group previously reported that ureter maturation, the process by which the ureter is inserted in the bladder wall during embryonic development, requires the precise removal of intervening tissue by apoptotic cell death. They further identified LAR-family tyrosine phosphatases (LAR-RPTPs) as necessary for this process. Accordingly, LAR-RPTP mutant animals harbour reduced apoptosis and vesicoureteral junction obstruction (VUJO). More recently Dr. Bouchard’s group identified the molecular pathway regulated by LAR-RPTPs in this process. They find that the LAR-family phosphatases repress the cellular inhibitor of apoptosis protein-1 (cIAP1), which acts as a negative regulator of caspase 3. Accordingly, the cIAP1 is crucial for ureter maturation as its inactivation leads to ureter mispositioning and vesicoureteral reflux (VUR) as a consequence of excessive apoptotic cell death. Hence, an important conclusion from this work is that apoptotic cell death need to be finely controlled during urinary tract morphogenesis, as either a reduction or an excess of apoptosis lead to urinary tract disease state. In this respect, VUJO and VUR are closely related defects in regard to apoptotic control of urinary tract morphogenesis.



- **Ihor V. Yosypiv, MD**
*Associate Professor,
Department of Pediatrics,
Chief, Division of Pediatric Nephrology,
Tulane University School of Medicine, New Orleans, LA.*

On May 19th, 2015, Dr. Yosypiv presented “Translational studies on the role of the renin-angiotensin system in congenital anomalies of the kidney and urinary tract (CAKUT).”

Summary: Congenital Anomalies of the Kidney and Urinary Tract (CAKUT), including renal hypodysplasia (RHD), account for a majority of children with end-stage-renal disease requiring dialysis and renal transplantation. Congenital reduction of nephron number, a condition called RHD, is associated with subsequent hypertension and chronic kidney disease in humans. Dr. Yosypiv’s laboratory is interested in the basic mechanisms which control UB branching morphogenesis and nephrogenesis, and the role of the renin-angiotensin system (RAS) gene mutations in human CAKUT. We examined cytogenomic aberrations and performed Sanger sequencing of key RAS genes in children with multicystic dysplastic kidney (MCDK) and performed Sanger sequencing of key RAS genes in children with other forms of CAKUT. We identified novel associations of mutations in the genes encoding renin, AGT, ACE or AT1R with isolated MCDK, and of the prorenin receptor (PRR) mutations with other forms of CAKUT in children in the United States. These findings highlight the crucial role of the RAS in the pathogenesis of MCDK and CAKUT in children and may help develop novel therapies that can be applied to the study of nephron regeneration strategies in CAKUT.



- **Walter Lee Murfee, PhD**
*Associate Professor,
Department of Biomedical Engineering,
Adjunct Associate Professor of Physiology,
Tulane University School of Engineering,
New Orleans, LA.*

Dr. Murfee presented, “Applications of Computational and Experimental Approaches for Investigating Microvascular Structure and Remodeling” on June 2nd 2016.

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Summary: Quantitative approaches for studying the microcirculation include computational methods and integrative experimental models. This presentation will provide examples of applying both approaches. The first objective will be to highlight the use of a computational method for gaining new insight the suction pressure required for fluid flow through initial lymphatic networks. The second objective will be to introduce the rat mesentery culture model as a new experimental tool for cell dynamics studies during angiogenesis and lymphangiogenesis in intact microvascular networks. Overall, our results will emphasize the value of applying integrative approaches for advancing our understanding of microvascular structure and growth dynamics in an adult tissue.



- **Hongbing Liu, PhD**

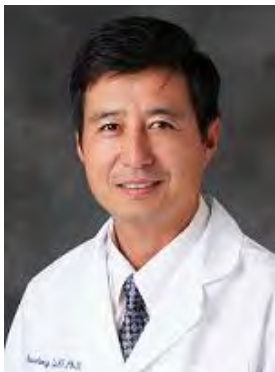
*Assistant Professor,
Division of Pediatrics Nephrology,
Department of Pediatrics & Department of Biochemistry,
Tulane University School of Medicine, New Orleans, LA.*

Dr. Liu presented, "Histone deacetylases 1 and 2 balance nephron progenitor renewal and differentiation during Kidney organogenesis" at the June 16th THRCE Seminar.

Summary: Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) are a major cause of morbidity in children, constituting approximately 20~30% of all anomalies identified in the prenatal period. CAKUT plays a causative role in 30~50% of cases of end stage renal disease (ESRD) in children, and predisposes to the development of hypertension and other renal-cardiovascular diseases in patients that survive to adolescence and adulthood. The long-term goal of our study is to uncover the epigenetic mechanisms accounting for CAKUT. We investigate the functions of class I histone deacetylases (HDACs), HDAC1 and HDAC2, in nephron progenitor cells (NPCs). Our data revealed that concurrent deletion of both HDAC1 and 2 resulted in early postnatal lethality. At birth, NPCHdac1/ 2-/- mice exhibit bilateral renal hypoplasia, including small kidney size, decreased number of nephrons and formation of multiple cysts. Double deletion of Hdac 1 and Hdac2 in the NPC depletes the cap mesenchyme and blocks nephron formation at the renal vesicle stage, due to defective cell proliferation and repression of the Notch/Lhx1 pathways. We also found that NPCHdac1,2-/- kidneys ectopic expression of Wnt4 which indicates that HDAC1/2

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prevents premature differentiation of CM cells through inhibition of Wnt/ β -catenin target genes, including Wnt4. Our study shows that Histone Deacetylases 1 and 2 are required for gene expression and the balance of self-renewal and differentiation of renal progenitor cells.



- **Ruisheng Liu, MD, PhD**

*Professor, Department of Molecular Pharmacology & Physiology
University of South Florida,
Tampa, FL*

Dr. Ruisheng Liu presented “Novel Mechanism and Therapeutic Target for Salt-Sensitive Hypertension,” at the July 14th 2016 THRCE Seminar.

Summary: Tubuloglomerular feedback (TGF) response operates at the level of juxtaglomerular apparatus (JGA) in each nephron, causing single nephron GFR (SNGFR) to be inversely dependent on the tubular flow to the macula densa. Increases in NaCl delivery to the macula densa initiate a TGF response that constricts the afferent arteriole (Af-Art) and decreases SNGFR. This negative feedback loop prevents acute fluctuations in Af-Art pressure from altering SNGFR and stabilizes NaCl delivery to the distal nephron.

We recently reported that the macula densa expresses α , β , and γ splice variants of NOS1, and that expression of NOS1 β increases in animals fed a high salt diet. Therefore, NOS1 β may be a salt-sensitive isoform in the macula densa that modulates TGF response, promotes sodium excretion and protects against the development of salt-sensitive hypertension. To test this hypothesis, we developed a tissue-specific knockout strain, in which all the NOS1 splice variants were deleted from the macula densa. We found that the expressions of NOS1 β mRNA and protein were 30 and 5 folds higher respectively than that of NOS1 α in the renal cortex of C57BL/6 mice. We then compared the NO generation by the macula densa in isolated perfused juxtaglomerular apparatus in WT and a NOS1 α KO strain in the same genetic background. We found that the production of NO was similar in these strains, indicating that NOS1 β rather than NOS1 α , is responsible for most of the NO generated by the macula densa. To study the physiological

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significance of the NOS1 β in the macula densa, we bred NKCC2 Cre mice with NOS1 floxed mice to produce macula densa specific NOS1 knockout (MD-NOS1KO) mice and littermates of NOS1 flox/flox or C57BL/6 WT mice as controls. The TGF response was significantly enhanced in MD-NOS1KO mice, both in vitro and in vivo. GFR, urine flow and Na⁺ excretion were significantly lower in the MD-NOS1KO than in control mice following acute volume expansion. Mean arterial pressure (MAP) increased by 9.8 \pm 1.1 mmHg in MD-NOS1KO mice vs 3.3 \pm 0.7 mmHg in NOS1 flox/flox mice (p <0.05) fed a high salt diet. Moreover, MAP increased by 61.6 \pm 3.7 mmHg in the KO mice vs 32.0 \pm 1.7 mmHg in WT mice in response to infusion of Ang II plus a high salt diet.

The results indicate that NOS1 β is a primary isoform of NOS1 expressed in the macula densa and that deletion of NOS1 β from the macula densa enhances TGF response, blunts the natriuretic response to acute volume expansion and promotes the development of salt-sensitive hypertension. These findings provide a novel mechanism for salt sensitivity of blood pressure and demonstrate the significance of TGF response in long-term control of sodium excretion and blood pressure.



- **Minolfa C. Prieto, MD, PhD**

Associate Professor,

Department of Physiology,

Tulane University School of Medicine, New Orleans, LA.

On July 28th, 2016, Dr. Minolfa Prieto presented “Clinical Implications of the Prorenin Receptor in Diabetes Mellitus.”

Summary: Patients with obesity and diabetes mellitus (DM) are at higher risk for hypertension (HTN) and severe CV consequences; however, the mechanisms involved remain unclear. The prorenin receptor (PRR) is a new component of the RAS expressed in brain, lung, placenta, kidney, and fat. The PRR has two molecular forms: a cell membrane-bound form and a soluble (sPRR) form. sPRR binding to prorenin or renin activates prorenin, enhances activity of renin resulting in RAS activation by promoting Ang I formation. Diabetic patients exhibit high

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circulating levels of prorenin which are associated with microvascular complications. We quantified sPRR levels in plasma from 201 patients (mean age, 41 ± 13 years; 39% men), including 107 controls (Ct; BMI < 30), 66 obese (Ob; BMI ≥ 30) and 28 obese with T2D (Ob+T2D) patients. We used waist to hip ratio (WHR) as a measure of abdominal adiposity. Plasma sPRR levels measured by ELISA were significantly higher in Ob+T2D patients ($21,481.7 \pm 1,600.5$ pg/mL) compared to Ct ($16,488.4 \pm 417.9$ pg/mL) and Ob ($16,598.5 \pm 538.7$ pg/mL; $P < .0001$). Urine Albumin/Cr ratio showed a similar trend (Ob: 31.0 ± 4 , Ob+T2D: 53.1 ± 8 vs. Ct: 24.9 ± 2 mg/g uCr; $P < 0.0001$). Simple regression analysis indicated plasma sPRR levels negatively correlated with WHR in the Ob+T2D ($r = -0.4062$, $P = 0.0395$) but not with Ct or Ob patients. Control lean men patients exhibited significantly higher plasma sPRR levels compared to women ($18,066.6 \pm 795.5$ vs. $15,391.7 \pm 389.1$ pg/mL; $P < 0.01$). Interestingly, the plasma sPRR differences among groups of same sex were greater in Ob+T2D women compared to Ct ($20,972.3 \pm 1,659.8$ pg/mL vs. $15,391.7 \pm 389.1$ pg/mL; $P < 0.0001$) and Ob ($15,794.4 \pm 649.5$ pg/mL; $P < 0.0001$) patients, but did not differ among men groups. The interaction between sex and group was significant ($p = 0.036$) suggesting that the increase of plasma sPRR levels in T2D patients is greater in women than men. Multiple regression analysis, adjusted by age, WHR, and groups indicated a significant association between plasma sPRR levels and T2D status in women ($P < .0001$) but not men. Our data indicate that plasma sPRR levels are associated with T2D in women but not in men, and that this effect is independent of obesity. Understanding the obesity-hypertension link during DM is crucial to developing new therapeutic targets to tailor the control of complications in T2DM in men and women.



- **Samir El-Dahr, MD**

*Jane B. Aron Professor of Pediatrics,
Chair, Dept. of Pediatrics,
Tulane University School of Medicine,
New Orleans, LA.*

On August 11, Dr. Samir El-Dahr presented the THRCE seminar titled "Synthetic Nephron Progenitors for Chronic Kidney Disease."

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Summary: Low nephron endowment causes hypertension, chronic kidney disease, and end-stage renal disease requiring renal replacement therapy in children and adults. The premise of multi-potent progenitor cell-based replacement therapy for individuals with low nephron endowment critically depends on scientific and technical advances that foster efficient propagation of native or pluripotent cell-derived nephron progenitor cells (NPC). Genetic and functional analyses in mice indicate that NPC residing in the cap mesenchyme “age” during maturation, i.e., while Young E13 NPC stay in the niche and engage in self-renewal, Old P0-P2 NPC have a shorter life span because they exit the niche at a higher rate and differentiate into nascent nephrons. The biological basis of NPC aging is not well understood. Changes in the niche microenvironment are not sufficient to explain Old NPC’s greater propensity to differentiate since P2-NPC cannot sustain their progenitor state even in optimal growth factor media. Utilizing genome-wide mapping of open (accessible) chromatin [ATAC-seq], we identified intrinsic age-associated chromatin state transitions in Young and Old NPC. This exciting finding prompted us to hypothesize that Old NPC are epigenetically “primed” for differentiation, which contributes to their limited life span. We subsequently utilized an integrative systems biology approach to delineate the active enhancer landscape and transcriptional regulatory network of the Young and Old NPC. We constructed a comprehensive map of the age-dependent chromatin state transitions in freshly isolated Young (E13) and Old (P0-P2) NPC, and integrated this knowledge with enhancer histone signatures, transcriptional profiles, and transcription factor occupancy. We are currently examining whether *ex vivo* expansion triggers remodeling of the chromatin landscape by comparing the epigenomic profiles of native and expanded Young and Old NPC. Our lab also demonstrated that the Polycomb Repressive Complex 2 (PRC2) restrains remodeling of differentiation gene enhancers in the Young NPC. Using gene targeting and epigenome profiling, we demonstrated the critical role of PRC2 in controlling access to enhancers of *Cdkn2a/p16* and *Wnt4* and we are applying CRISPR-dCas9-targeted epigenome editing to re-write the histone signature of developmental enhancers and rejuvenate the PRC2-mutant NPC. Knowledge of the enhancer landscape of nephron progenitors during maturation can potentially open the way to development of targeted epigenetic therapy to maintain the stemness or rejuvenate the aging NPC, and to refine existing NPC propagation protocols.

Continued...



- **Paul K. Whelton, MB, MD, MSc.**

*Show Chwan Professor of Global Public Health,
Tulane University, School of Public Health & Tropical Medicine,
New Orleans, LA.*

Dr. Whelton presented “The Systolic Blood Pressure Intervention Trial (SPRINT): Major findings and Implications for Clinical Practice” on August 25, 2016.

Summary: High blood pressure (BP) is the leading risk factor for cardiovascular disease (CVD), accounting for about 10% of all deaths and 7% of disability-adjusted life years, worldwide. It is the only risk factor that results in more deaths than tobacco products.

Antihypertensive drug therapy lowers the risk of CVD in adults with hypertension but the optimal target for BP during treatment has been uncertain. The National Institutes of Health (NIH) supported Systolic Blood Pressure Intervention Trial (SPRINT) was designed to answer this question by randomly assigning a diverse group of 9361 non-diabetic adults ≥ 50 years, with a systolic BP 130-18Hg and at high risk for CVD, to an intensive treatment BP goal (< 120 mm Hg) or a standard treatment goal (< 140 mm Hg). The primary outcome was a composite of CVD events. The trial was stopped, after a median of only 3.26 years, because occurrence of the primary outcome was approximately 25% less common in the intensive treatment group. In addition, all-cause mortality was about 27% less common in the intensive treatment group. Similar benefits of intensive treatment were seen in all six pre-specified groups of special interest, including in seniors > 75 years old at baseline (even in the sub-group of seniors with frailty and those with the slowest gait speed). There was no difference between the two treatment groups in the primary renal disease outcome or in the overall experience for serious adverse events (SAEs). However, SAEs with electrolyte abnormalities, and acute kidney injury, hypotension and syncope, but not injurious falls, were more common in the intensive treatment group. The long-term implications on these SAEs are uncertain.

The SPRINT results provide strong evidence that more intensive antihypertensive therapy than is currently recommended in most BP guidelines is likely to

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beneficial in older non-diabetic adults with hypertension and an increased risk of CVD. About 17 million US adults (8%) would meet the SPRINT inclusion and exclusion criteria. The SPRINT results may apply to other groups at high risk for CVD who would not meet the study's inclusion and exclusion criteria. Among adults who would be excluded, approximately 33% with diabetes mellitus, 23% with a history of stroke, and 7.5% with age < 50 years, would meet the other SPRINT eligibility criteria. Generalizing the results to such persons has to be undertaken with caution but may be reasonable. Caution is also appropriate in generalizing the SPRINT results to countries where the predominant pattern of CVD is non-ischemic stroke and is essential in those at relatively low risk for CVD. Independent of the extent to which the results should be generalized, SPRINT is likely to have a major impact on the practice of medicine



- **Kailash N. Pandey, PhD**
*Professor, Department of Physiology,
Tulane University School of Medicine, New Orleans, LA.*

Dr. Dr. Pandey presented “Stimulatory and Repressive Limbs of Npr1: Regulation of Blood Pressure and Renal Injury” at the September 8th THRCE Seminar.

Summary: Cardiac hormones atrial and brain natriuretic peptides (ANP and BNP) and their cognate receptor guanylyl cyclase/natriuretic peptide receptor-A (GC-A/NPRA) produce the signal through the generation of second messenger cGMP and play critical roles in the regulation of body fluid volume and blood pressure homeostasis. Polymorphisms in genes that encode ANP (Nppa), BNP (Nppb) and NPRA (Npr1) are associated with hypertension and heart failure. Thus, gaining insights into the intricacies of Npr1 transcription and ANP-BNP/NPRA/cGMP signaling pathways is of pivotal importance for understanding both receptor biology and the disease state arising from abnormal hormone-receptor interplay at the molecular level. In particular, Npr1 is a regulable gene and its expression and the receptor signaling is modulated in both in vitro and in vivo conditions by a number of factors, including hormones, growth factors, extracellular osmolality, and select physiological and pathophysiological milieu. Our previous and ongoing works will

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highlight the two regulatory aspects of Npr1 transcription and receptor signaling by stimulatory hormones such as All-trans retinoic acid (ATRA) and inhibitory hormones such as angiotensin II (Ang II) and transforming growth factor-beta 1 (TGF- β 1). The activated hormonal regulation of Npr1 is achieved by the recruitment of positive transcription factors (TFs) and active histone marks; however, on the contrary, the inhibited regulation of Npr1 is achieved by involving the recruitments of negative TFs and repressive histone marks at the Npr1 promoter. The positive and negative regulation of Npr1 expression and receptor signaling impact and modulate blood pressure homeostasis and renal and cardiovascular functions in physiological conditions and pathophysiological disease states.

We anticipate that our research findings will provide new insights into the mechanistic aspects and the roles of the regulated Npr1 transcription and ANP-BNP/NPRA/cGMP signaling in developing new therapeutic strategies for the treatment and prevention of hypertension and cardiovascular diseases.



- **Leonard G. Meggs, MD,**
Nephrologist
Ochsner Medical Center, New Orleans, LA.

Dr. Meggs presented “p66 Controls Aging Phenotypes in Diabetic Kidneys” at the October 6th THRCE seminar.

Summary: The p66 protein controls cellular responses to oxidative stress, aging and apoptosis. Hyperglycemia constitutively activates the p66 protein in kidneys of diabetic mice. In this study, we test the hypothesis aging phenotypes (stem cell depletion, glomerulosclerosis, interstitial fibrosis and tubular atrophy), commonly associated with the broad category of chronic kidney diseases, are p66 dependent in diabetic kidneys. To evaluate the effect of constitutive p66 expression on the phenotype of tissue stem cells, Sca-1+mesenchymal stem cells (Sca-1+MSCs) were isolated from kidneys of WT and p66 KO mice. Our results show WT-MSCs plated in high glucose media, acquire the senescent phenotype by day 6, whereas p66 KO-MSCs remain in active growth phase at day 12. To test whether constitutive p66

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expression has detrimental effects in vivo, we examined kidneys from aged match Akita-diabetic mice and p66 KO-Akita diabetic mice. We were unable to identify Sca-1+MSCs in Akita kidneys, whereas small clusters of Sca-1+MSCs were observed in kidneys of p66 KO-diabetic. Akita kidneys also show advanced histologic markers of aging coupled with striking increase in urine albumin excretion. By contrast, these changes were barely detectable in kidneys of p66 KO-Akita. Together, these data establish a genetic link between constitutive p66 expression in diabetic kidneys and aging phenotype(s) that may be precursors to diabetic nephropathy or surrogate markers of an accelerated aging phenotype.



- **John K. Maesaka, MD**
*Chief Emeritus, Nephrology, Director of Research,
 Professor of Medicine SUNY,
 Stony Brook Medical Sch., Stony Brook, NY,
 Winthrop Nephrology Associates,
 Winthrop University Hospital, Mineola, NY.*

Dr. John Maesaka, delivered "Review of Natriuretic Factors in Cerebral/ Renal Salt Wasting Syndrome" at the October 20th THRCE seminar.

Summary: In the lecture, Dr. Maesaka reviewed the status of hyponatremia by covering some of the controversies and misconceptions in our approach to hyponatremia and presented a new algorithm based more on pathophysiologic applications rather than the outmoded volume approach. Hyponatremia, serum sodium < 135 mEq/L, is the most common electrolyte abnormality and is in a state of flux. Hyponatremic patients are symptomatic and should be treated but our inability to consistently determine the causes of hyponatremia has hampered the delivery of appropriate therapy. This is especially applicable to differentiating SIADH from cerebral salt wasting (CSW) or more appropriately, renal salt wasting (RSW), because of divergent therapeutic goals, to water-restrict in SIADH and administer salt and water in RSW. Differentiating SIADH from RSW is extremely difficult because of identical clinical parameters that define both syndromes and the mindset that CSW occurs rarely. It is thus insufficient to make the diagnosis of SIADH simply because it meets the defined characteristics. He reviewed the pathophysiology of SIADH and RSW, the evolution of an algorithm that is based on determinations of fractional excretion (FE) of urate and distinctive responses to

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saline infusions to differentiate SIADH from RSW. This algorithm also simplifies the diagnosis of hyponatremic patients due to Addison's disease, reset osmostat and prerenal states. It is a common perception that we cannot accurately assess the volume status of a patient by clinical criteria. The new algorithm eliminates the need to determine the volume status with the realization that too many factors affect plasma renin, aldosterone, atrial/brain natriuretic peptide or urine sodium concentration to be useful. Reports and increasing recognition of RSW occurring in patients without evidence of cerebral disease should thus elicit the need to consider RSW in a broader group of patients and to question any diagnosis of SIADH. Based on the accumulation of supporting data, he made the clinically important proposal to change CSW to RSW, to eliminate reset osmostat as type C SIADH and stress the need for a new definition of SIADH.



- **Richard N. Re, MD**
*Scientific Director,
Ochsner Clinic Foundation,
New Orleans, LA.*

Dr. Richard Re presented "Intracrine Physiology" on November 3rd, 2016.

Summary: This seminar described studies of the intracellular actions of the peptide hormone angiotensin II including actions at the cell nucleus and mitochondria. Based on this work, the speaker has coined the term intracrine to describe action by an extracellular signaling peptide/protein in either its cell of synthesis or in target cells after internalization. Surprisingly, many peptides and proteins serve as intercellular signaling factors and also act in cell interiors. These intracrine factors are varied in structure and include growth factors, cytokines, enzymes, and DNA binding proteins among others. The biology of some of these factors was reviewed. These peptides are involved in a wide variety of normal functions including growth and differentiation. The speaker's group has developed general principles of intracrine biology and physiology. The possibility that this kind of functionality is involved in progressive cardiorenal diseases such as congestive heart failure and diabetic nephropathy as well as certain other chronic disorders was considered.

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News



- **Ann Marie Navar, MD, PhD**
*Cardiologist,
Duke University, Health Center at Southpoint,
Durham, NC.*

Dr. Ann Marie Navar presented, "Using Cardiovascular Disease Risk to Guide Therapy: Reconciling our Janus-faced approach to hypertension and cholesterol" on November 10th, 2016.

Summary: Current guideline-based management paradigms for blood pressure and cholesterol are markedly different. Cholesterol guidelines largely ignore the level of cholesterol and recommend statins to highest risk groups. This approach leaves many young adults untreated, potentially exposing them to years of vascular insult from prolonged exposure to high cholesterol. It may also over-treat older adults, including those who are high risk merely by age alone. On the other hand, blood pressure management strategies focus on treating blood pressure targets and treat all adults, regardless of risk. This avoids the problem of under-treatment of young adults as seen with lipid guidelines, but leaves clinicians with two very different approaches to risk factor modification.

New trials in hypertension focusing on cardiovascular disease risk may allow for a reconciliation of approaches. For both cholesterol and hypertension, the absolute benefit of therapy depends on both the starting risk of cardiovascular disease and the degree of risk factor reduction. The SPRINT study, which achieved a large decrease in SBP in the intervention arm and included high risk adults, showed additional BP lowering beyond 140 mmHg decreased the risk of cardiovascular disease. In HOPE-3, intermediate risk adults with starting blood pressures below 143.5 mmHg did not benefit from a more modest degree drop in blood pressure (6 mmHg). Both SPRINT and HOPE-3 results are consistent with absolute risk reduction estimates from pooled analyses of clinical trials.

Cholesterol guidelines have introduced clinicians to the concept of using risk to guide statin therapy. New BP guidelines will now almost certainly incorporate CVD risk, an important step to reconciling the clinical approach to CVD prevention. Yet

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how to communicate risk with patients is unknown. Patients don't understand CVD risk, and small changes in how risk is presented to patients can affect patient willingness to engage in therapy. A risk-based paradigm presents new opportunities for researchers to evaluate effective strategies for patient engagement and shared decision making.



- **James R. Sowers, MD**

*Thomas W. and Joan F. Burns Missouri Chair in Diabetology,
Vice Chair for research, Dept. of Internal Medicine,
Professor, Dept. of Medical Pharmacology & Physiology,
Director of Center for Diabetes & Cardiovascular Research,
University of Missouri, School of Medicine, Columbia, MO.*

Dr. Sowers presented, "Cell Specific Mineralocorticoid Receptor Activation and Cardiovascular Stiffness in Obesity" at the December 1st THRCE Seminar.

Summary: Dr. Sowers presented work conducted over the past several years in which his research team had found that diets high in saturated fat and refined carbohydrates (termed western diet (WD)) cause cardiovascular (CV) insulin resistance and associated increased CV stiffness and impaired relaxation. They found that this diet has more of a negative CV impact on insulin metabolic signaling and associated stiffness in females. This is of translational relevance to the VA because of increasing numbers of female veterans and because in conditions of INS resistance such as obesity and type 2 diabetes, women display a substantially increased risk for CVD. As the lifetime risk for overweight/obesity and diabetes in women is high, associated CVD in women has become a major health problem. As people become obese and INS resistant, they manifest increasing CV stiffness, an abnormality that tracks closely with increasing CVD. INS resistance in the heart and vasculature results in decreased bioavailable nitric oxide (NO) which is associated with increased CV stiffness. Reduced bioavailable NO results in increased activity of the enzyme transglutaminase 2 (TG2), which increases collagen crosslinking and associated heart and vascular stiffness. Dr. Sowers research team have observed that females, but not males, develop INS resistance and CV stiffness after only 8 weeks of consumption of a WD. Their ongoing work in a female mouse model of INS resistance induced by a WD also demonstrates that mineralocorticoid receptor (MR) blockade improves

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heart and vascular INS resistance and stiffness. They have garnered evidence that selective knockout of the endothelial cell (EC) MR in mice abrogates the reduction in CV INS metabolic signaling and CV stiffness and impaired relaxation induced by consumption of a WD for 16 weeks. They anticipate that results from our research will yield unique insights into the mechanisms of CV disease in obese and type 2 diabetic individuals, with the goal of translating these findings into therapeutic strategies to reduce CVD, especially in overweight INS resistant and diabetic persons.



- **Paul Muntner, PhD**
*Professor and Vice Chair,
Department of Epidemiology,
University of Alabama at Birmingham,
Birmingham, AL.*

Dr. Muntner presented, “Racial Differences in Ambulatory Blood Pressure Monitoring Phenotypes: Clinical and Public Health Implications and Future Research Needs” on December 15th, 2016.



Recent Publications

(Includes publication omitted from previous newsletter edition)

Bansal N, Xie D, Tao K, Chen J, Deo R, Horwitz E, Hsu CY, Kallem RK, Keane MG, Lora CM, Raj D, Soliman EZ, Strauss L, Wolf M, Go AS; CRIC Study. Atrial Fibrillation and Risk of ESRD in Adults with CKD. *Clin J Am Soc Nephrol.* 2016 Jul 7;11(7):1189-96. doi: 10.2215/CJN.10921015. PMID: 27073197; PMCID: PMC4934846.

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From May through December, 2016 investigators and physicians affiliated with T.H.R.C.E. participated in many regional, national, & international meetings.

FASEB Summer Research Conference on Renal Hemodynamics, June 19-23, 2016.

- Navar LG, Franco M, Bautista R, Cano A, Pacheco U, Santamaría J, del Valle Mondegron L, and Pérez-Mendez O. Role of Renal Purinergic Receptors P2X1, P2X4 and P2X7 in Regulation of Renal Microvasculature in Angiotensin II-induced Hypertension.

NIH, NIGMS Sixth Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE), June 26 – 28, Washington DC.

- Khan MA, Teran FJ, Hering-Smith KS, Fisher MC, Majid DSA, Navar LG, atuman V. "Pathophysiology of diabetic nephropathy in endothelial nitric oxide synthase-deficient (eNOS-/-) mice."
- Majid N. "COBRE Translational Research in Hypertension and Renal Biology."
- Liu H. "Histone Deacetylases 1 and 2 balance nephron progenitor renewal and differentiation during kidney organogenesis."
- Majid DSA. "Angiotensin II (AngII) induced intrarenal angiotensinogen (AGT) formation is augmented in TNF- α receptor type 1 (TNFR1) knockout mice."

APS Conference on Inflammation August 24-27, Westminster, Colorado.

- Majid DS. "Intrarenal angiotensinogen formation in response to chronic high salt intake and angiotensin II administration is augmented in TNF- α receptor type 1 knockout mice."

Council on Hypertension 2016 Scientific Sessions, Orlando, FL, Sept. 14–17, 2016.

- Gonsalez SR., Ferrão FM., Prieto MC, Lara LS. Renal Localization of Salt Inducible Kinase-1 and Its Regulation in Doca/salt Hypertensive Rats. Poster# P203.

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- **Gonzalez AA, Reyes-Martinez C, Zamora L, Prieto MC.** Prorenin Receptor Activation Increases Profibrotic Markers and Fibroblast Like Phenotype Through MAPK-dependent ROS Formation in Mouse Renal Collecting Duct Cells. Poster# P195.
- **He J, Chen J, Huang J, Chen J, He H, Li J, Cao J, Chen, C-S, Gu D.** Salt-sensitivity, Salt-resistance, and Incidence of Hypertension. Oral: O93.
- **Jensen DD, Feng Y.** Epigenetic Regulation of Brain (Pro)renin Receptor by Benzamil-sensitive Sodium Channel in DOCA-salt Hypertension. Oral Presentation: O74.
- **Kumar P, Periyasamy R, Gogulamudi V, Pandey KN.** Sodium Butyrate and Retinoic Acid Attenuate Renal Inflammation and Fibrosis in Npr1 Gene-targeted Haplotype Mice: Role of NF- κ B Signaling. Oral Presentation: O84.
- **Li C, Zhang Y, Chen J, Xu T, Wang D, Chen C-S, Sun Y, Peng H, He J.** Blood Pressure Trajectories in the Acute Phase And Major Clinical Outcomes Among Patients With Ischemic Stroke. Oral Presentation: O115.
- **Mukerjee S, Zsombok A, Lazartigues E.** Adam17 in the Paraventricular Nucleus Contributes to Activation of Pre-Autonomic Neurons and Maintenance of Baseline Blood Pressure. Poster# P151.
- **Pingili AK, Thirunavukkarasu S, Khan NS, Katsurada A, Majid DS, Navar GL, Malik KU.** 2-methoxyestradiol Minimizes Angiotensin Induced Hypertension and Renal Dysfunction in Ovariectomized Female and Intact Male Mice. Poster# P135.
- **Reverte V, Musial DC, Gallaty MR, Rosales CB, Parra-Vitela AJ, Prieto MC.** Increased Urinary Angiotensinogen Reflects Intrarenal Renin-angiotensin System Activation in High Fat Diet Induced-type 2diabetic Mice. Poster# P198.
- **Satou R, Franco MG, Katsurada A, Miyata K, Navar LG.** Immunosuppression Attenuates Intrarenal Angiotensinogen Augmentation in Angiotensin II Dependent Hypertension. Oral Presentation: O15
- **Satou R, Katsurada A, Miyata K, Derbenev A, Zsombok A.** Absolute Gene Quantification of Intrarenal Reninangiotensin System Components Using Droplet Digital PCR Analysis. Poster# P613.
- **Sen A, Kumar P, Lindsey SH, Katakam PV, Bloodworth M, Pandey KN.** Transforming Growth Factor β 1 Antagonizes Npr1 Expression and Vascular Signaling: Role of Transcription Factor δ EF1 Transforming Growth Factor β 1 Antagonizes Npr1 Expression and Vascular Signaling: Role of Transcription Factor δ EF1. Oral Presentation: O58.

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AHA Scientific Sessions 2016. Nov 12 - 16, 2016; NO, LA.

- **Kumar P, Periyasamy R, Gogulamudi VR, Pandey KN.** Attenuation of Renal Fibrosis and Inflammation in Npr1 Haplotype Mice by Retinoic Acid and Sodium Butyrate via Interactive Modulation of STAT1, HDACs and NF- κ B. *Circulation.* 2016;134:A12989
- **Woods TC.** Acute Carotid Plaque Rupture is Characterized by an Anti-Proliferative Serum miRNA Profile.
- **Brug AM, Smith S, Brooks AJ, Lightell DJ, Bazan HA, Woods TC.** Acute Carotid Plaque Rupture is Characterized by an Anti-Proliferative Serum miRNA Profile. *Circulation.* 2016;134:A20036.

ASN Kidney Week 2016. Nov 15 - 20, 2015; Chicago, IL.

- **Chen J, Yang W, Roy J, Zhang X, Kumbala DR, Garimella PS, Rahman M, Townsend RR, Jaar BG, Horwitz EJ, Mohanty MJ, Cedillo-Couvert EA, Sozio SM, Feldman HI, Mohler E, Hamm LL, He J.** A Predictive Model for Development of Peripheral Artery Disease among Patients with Chronic Kidney Disease. [SA-PO817]
- **El-Dahr SS, Li Y, Baddoo MC, Liu J, Saifudeen ZR, Adli M.** Epigenomic Profiles Identify Age Associated Chromatin State Transitions in Nephron Progenitors. [FR-OR035].
- **Fischer MJ, Xie D, Lamar M, Pan Q, Bazzano L, Go AS, Horwitz EJ, Tamura MK, Lustigova E, Ojo AO, Ricardo AC, Seliger SL, Taliencio JJ, Yaffe K, Lash JP.** Depressive Symptoms and Cognitive Impairment in Adults with Chronic Kidney Disease. [SA-PO942].
- **Grams M, Yang W, Rebholz C, Wang X, Porter AC, Inker L, Horwitz EJ, Sondheimer JH, Hamm LL, He J, Weir MR, Jaar BG, Shafi T, Appel LJ, Hsu C-y.** Adverse Events in Advanced Chronic Kidney Disease: The Chronic Renal Insufficiency Cohort Study. [SA-OR037]
- **Anderson AH, Roy J, Lin E, Fischer MJ, Hamm LL, Lash JP, Lustigova E, Mohler E, Ojo AO, Rahman M, Scialla JJ, Steigerwalt SP, Feldman HI.** Hospitalization Burden of Chronic Renal Insufficiency Cohort (CRIC) Study Participants. [SA-PO846]
- **Khairallah P, Isakova T, Asplin JR, Hamm LL, Dobre MA, Rahman M, Sharma K, Leonard MB, Miller ER, Jaar BG, Brecklin CS, Yang W, Feldman HI, Wolf MS, Scialla JJ.** Acid-Base and Phosphorus Homeostasis in Chronic Kidney

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Disease: Results from the Chronic Renal Insufficiency Cohort (CRIC) Study. [FR-PO433].

- **Khan M-A, Teran FJ, Hering-Smith KS, Fisher M, Majid DS, Navar LG, Batuman V.** High Fat Diet Given with Low Doses of Streptozotocin Induces Type 2 Diabetic Nephropathy in Endothelial Nitric Oxide Synthase Knockout Mice. [PUB267].
- **Khan M-A, Batuman V.** The Role of Toll-Like Receptors in Myeloma Light Chain Toxicity on Renal Proximal Tubule Cells. [PUB023].
- **Ku E, Johansen KL, McCulloch CE, Kopple JD, Go AS, Xie D, Hamm LL, He J, Kusek JW, Navaneethan SD, Ricardo AC, Rincon-Choles H, Hsu C-y.** BMI Trajectory with Decline in Kidney Function: Results from the CRIC Study. [TH-OR061].
- **Nakhoul NL, Hamm LL, Brown K, Abdulnour-Nakhoul S.** Interaction of the Renal NH₃/NH₄⁺ Transporters Rh Glycoproteins with Cellular Proteins Involved in Acid-Base Homeostasis. [SA-PO093].
- **Orlandi PF, Fujii N, Hamm LL, Sondheimer JH, Hsu C-Y, Fischer MJ, Feldman HI.** Hematuria as a Risk Factor for the Progression of Chronic Kidney Disease. [TH-PO875].
- **Ricardo AC, Knutson K, Jinsong Chen j, Appel LJ, Bazzano L, Tamura MK, Rahman M, Steigerwalt SP, Thornton J, Weir MR, Cauter EV, Lash JP.** The Association of Sleep Duration and Quality with Chronic Kidney Disease Progression. [SA-PO788].
- **Saifudeen ZR, Liu J, Edgington-Giordano F.** PI3K Pathway Potentiates Nephron Progenitor Cell (NPC) Renewal by Promoting Glycolysis. [FR-OR037].
- **Song S, Janssen AT, Li Y, El-Dahr SS, Yosypiv IV.** Prorenin Receptor Controls Renal Branching Morphogenesis via Wnt/ β -Catenin Signaling. [FR-PO093].

THRCE investigators and physicians were invited to present at various national and international events.

Navar, L. Gabriel:

- Chaired a session on “autocoids and kidney disease” at the FASEB Summer Conference on Renal Hemodynamics and Cardiovascular Function in Health and Disease, held in Big Sky, MT from June 19-23, 2016.
- Chaired a poster session on “Salt and Hypertension,” Friday, September 16 at the Hypertension Council 2016 Scientific Sessions held in Orlando, Florida.
- Visited Winthrop University Hospital in Mineola, NY and presented Nephrology Grand Rounds on April 28. The title of his talk was “Augmentation of the intrarenal renin-angiotensin system in hypertension and diabetes.”
- Participated in the meeting of the Japanese Society of Nephrology in Sendai, Japan from September 30 till October 2. His presentation was entitled, “Intratubular renin-angiotensin system: A paradigm shift in understanding in the intrarenal renin-angiotensin-system.”

Liu, Hongbing

- “Histone Deacetylases 1 and 2 balance nephron progenitor renewal and differentiation during kidney organogenesis” on June 28 at the NIH, NIGMS Sixth Biennial National IDeA Symposium of Biomedical Research Excellence (NISBRE) held in Washington DC.

Majid, Dewan S. A.:

- Presented “Differential roles of TNF- α receptors in salt-sensitive hypertension” on August 5, 2016, at the Texas Southern University College of Pharmacy & Health Sciences in Houston, Texas.
- Attended and presented at the APS Conference on Inflammation August 24-27 in Westminster, Colorado. The title of his talk was, “Intrarenal angiotensinogen formation in response to chronic high salt intake and angiotensin II administration is augmented in TNF- α receptor type 1 knockout mice.”

Pandey, Kailash N:

- Presented a Symposium talk on September 14, titled: “Regulation of Guanylyl Cyclase/Natriuretic Peptide receptor-A Gene Transcription and Signaling: Interactive roles of histone modifications and transcription factors” at the Neuropharmacology 2016 Conference in San Antonio, TX.
- On September 16, presented “Transforming growth factor- β 1 antagonizes Npr1 expression and vascular signaling: Role of transcription factor δ EF1” at Hypertension Council 2016 in Orlando, Florida.

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- Presented a talk to the Department of Cardiovascular Diseases at Mayo Clinic in Rochester, MN on October 13, 2016. The title of his talk was “Stimulatory and Repressive Limbs of Npr1: Regulation of Blood Pressure and Cardiovascular Function.”
- Presented on November 13, “Transforming Growth Factor-Beta-Dependent Pathway Induces the Cardiac Fibrosis and Remodeling in Guanylyl Cyclase/Natriuretic Peptide Receptor-A Gene-Disrupted Mice” at the AHA scientific sessions in New Orleans.

Sato, Ryosuke

- “Immunosuppression attenuates intrarenal angiotensinogen augmentation in angiotensin II dependent hypertension” at the Hypertension Council 2016 Scientific Sessions held in Orlando, Florida.

Prieto, MC

- “From cell biology to novel physiological paradigms and the latest advances in therapeutics” at the IV International RAS Symposium event that was held in the Reboucas Convention Center, San Paulo, Brazil from July 20-21, 2016.
- “Plasma Soluble prorenin receptor levels in obese patients are associated with type 2 diabetes in women but not in men.” at the FASEB Summer Conference on Renal Hemodynamics in Big Sky, Montana.
- Participated as organizer and invited speaker in the XXIV Congress of the Brazilian Society of Hypertension and in the IV International Symposium of the RAS, held from July 21-23, 2016 in Sao Paulo-Brazil. She presented a talk on July, 21 titled, “Clinical implication of plasma soluble prorenin receptor in type 2 diabetic patients” and on July 23 she presented a talk titled, “Physiopathological connection between hypertension and diabetes.”
- Moderator for the oral session, “Renin Angiotensin System,” on September 17, 2016 at the Hypertension Council 2016 Scientific Sessions held in Orlando, Florida.
- Presented “Role of Collecting Duct Renin in the Pathogenesis of Hypertension” at the Symposium, “Feeling the Pinch of Salt: Intrarenal Renin-Angiotensin System in Hypertension” held on November 18 during the 2016 Kidney Week Meeting of the American Society of Nephrology (ASN).

Kumar, Prerna:

- “Histone Deacetylase inhibitors exhibit enhanced kidney functions in guanylylcyclase-A/Natriuretic peptide receptor-A gene-disrupted mice: Role of Epigenetic mechanisms.” at a Symposium during the EB Meeting in San Diego, CA sponsored by the APS-Physiological Genomics April 4th.

CORE Facilities & Services

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

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

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

T.H.R.C.E.

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

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The directors invite faculty members interested in participating in the activities of the T.H.R.C.E. to submit your name, phone number, fax number, and e-mail address to the Senior Administrative Program Coordinator, Nina R. Majid, by e-mail at htnctr@tulane.edu or regular mail to the address provided. Also, please forward all information (awards, publications, presentations and other news items) to this email address for inclusion in the next newsletter.

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