go.uab.edu/cardiorenal

CRPM

10th Anniversary Celebration

Cardio Renal Physiology and Medicine

CARDIO-RENAL PHYSIOLOGY & MEDICINE

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

CARDIO-RENAL PHYSIOLOGY & MEDICINE

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

10th Anniversary Celebration

CRPM

Cardio Renal Physiology and Medicine

8: 30 A.M.	**Welcome and Overview** **David M. Pollock, PhD** *Co-Director, Section of Cardio-Renal Physiology & Medicine* **Anupam Agarwal, MD** *Senior Vice President for Medicine and Dean, Heersink School of Medicine* **Seth Landefeld, MD** *Department of Medicine Chair, Heersink School of Medicine* **Orlando Gutierrez, MD** *Director, Division of Nephrology*
9:00 A.M.	***One gene, two phenotypes, and their relevance at 30 nanometers*** **Friedrich C. Luft, MD** *Charité Senior Professor Experimental and Clinical Research Center* *MDC/Charité, Berlin, Germany* Moderator: David M. Pollock, PhD
10:00 A.M.	***Circadian clock crosstalk in cardiorenal physiology*** **Michelle L. Gumz, PhD** *Professor, Department of Physiology and Aging University of Florida* Moderator: Paramita Pati, PhD
10:40 A.M.	**Break**
11:40 A.M.	***Obesity and hypertension: What's the connection?*** **Greg Fink, PhD** *Professor, Pharmacology & Toxicology Michigan State University* Moderator: Bryan Becker, PhD

CARDIO-RENAL PHYSIOLOGY & MEDICINE

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

10th Anniversary Celebration

CRPM

Cardio Renal Physiology and Medicine

11:00 A.M.	***The Aquaporin-2 Story*** **Mark Knepper, MD** *Director, Epithelial Systems Biology Laboratory* *National Heart Lung and Blood Institute* Moderator: Kelly Hyndman, PhD
12: 30 P.M.	**Lunch**
1:30 P.M.	**CRPM Pipeline Programs** **Jennifer S. Pollock, PhD** *Co-Director, Section of Cardio-Renal Physiology & Medicine*
1:45 P.M.	***The power of Physiology as a platform for translational research*** **Patricia E. Molina, MD, PhD** *Richard Ashman, PhD Professor & Chair of Physiology* *Director Alcohol and Drug Abuse Center of Excellence* *LSU Health Sciences Center* Moderator: Jennifer S. Pollock, PhD
2:30 P.M.	**CRPM Trainee Data Diuresis** **Carmen De Miguel, PhD., MS, Lisa Curtis, PhD**
3:30 P.M.	***High-throughput cellular genetics to link endothelial cells to cardiorenal disease*** **Rajat M. Gupta, MD** *Assistant Professor of Medicine, Harvard Medical School* *Medical and Population Genetics Group, Broad Institute* Moderator: Keri Kemp, PhD
4:15 P.M.	**Posters and Networking Reception**
6:30 P.M.	**Dinner - Drs. Pollock Home (Reservation Required)**

Letter from the directors

David Pollock, Ph.D. **Jennifer Pollock, Ph.D.**

Dear Colleagues and Friends,

We are excited to celebrate the 10th Anniversary of the Section of Cardio-Renal Physiology & Medicine (CRPM) at the University of Alabama at Birmingham (UAB). We are humbled by the profound impact our work is having on the lives of individuals at UAB and beyond. We hope that you will enjoy this celebration with us and look forward to continued success in our efforts to contribute to better health for all.

The impact of the CRPM could never have been accomplished without the dedication and engagement of our students, fellows, and collaborating faculty. Importantly, the pipeline for trainees and early career faculty extends from undergraduate students to early career faculty transitioning to independent investigator status. We are especially proud of our faculty who have transitioned from trainees to become world-renowned experts and leaders in Cardio-Renal Physiology & Medicine at UAB and other institutions across the US.

From investigating the molecular mechanisms underlying cardiovascular and renal diseases to developing novel therapies and interventions, our faculty, students, fellows, and staff are dedicated to advancing the field and improving outcomes for patients. Much of our success during the past 10 years has been supported by access to state-of-the-art facilities and resources and collaboration opportunities with leading experts across disciplines. We remain steadfast in our commitment to advancing scientific knowledge, supporting the biomedical community, and training the next generation of researchers in the cardiovascular and kidney fields.

We came here for the tremendous opportunities to expand our research, participate in the training of future investigators, and serve in ways that will advance research in a translational and cross-disciplinary way that we believe has had a significant impact on research not only at UAB but in the broader biomedical research community.

Whether you are a prospective student, researcher, or clinician, **we welcome you to join us** in our mission to advance the science and practice of cardiovascular and kidney health.

Looking forward to welcoming you to the CRPM 10th Anniversary,

David and Jennifer

CRPM Core Faculty

Jennifer Pollock, PhD
Endowed Professor of Nephrology

David Pollock, PhD
James Schafer Endowed Professor

Ed Inscho, PhD
Professor, Division of Nephrology

Subhashini Bolisetty, PhD
Associate Professor, Division of Nephrology

Kelly Hyndman, PhD
Associate Professor, Division of Nephrology

Michael Seifert, MD
Professor, Department of Pediatrics

Takamitu Saigusa, MD
Associate Professor of Nephrology

Carmen De Miguel, PhD
Assistant Professor, Division of Nephrology

Bryan Becker, PhD
Assistant Professor, Division of Nephrology

Malgorzata Kasztan, PhD
Assistant Professor, Department of Pediatrics

Paramita Pati, PhD
Instructor, Division of Nephrology

CRPM Affiliated Faculty

Paul Sanders, MD
Professor, Division of Nephrology

Sonia Fargue, MD, PhD
Assistant Professor, Department of Urology

John Knight, PhD
Professor, Department of Urology

Lisa Curtis, PhD
Associate Professor, Division of Nephrology

James Odum, MD
Assistant Professor, Department of Pediatrics

Jeffrey Lebensburger, DO
Professor, Department of Pediatrics

CRPM Emeritus

Dr. P. Darwin Bell - Emeritus Professor

IMPACT ON TRAINING

The Cardio-Renal Physiology and Medicine Section, with the insight and leadership from Dr. Anupam Agarwal and now Dr. Orlando Gutierrez, provides a vibrant training environment for all career stages. The implementation of the various training programs has built a culture of community for Cardio-Renal researchers and clinicians at UAB. Notably, several of our training programs are supported with extramural NIDDK funding (see graphic below). These activities have sustained success over the past 10 years and are the foundation of the CRPM's Impact on training.

We developed and continue to offer two graduate courses in kidney physiology, directed each by Dr. Kelly Hyndman and Dr. Subhashini Bolisetty. A CardioRenal journal club includes CRPM Section faculty as facilitators and lecturers, under the leadership of Dr. John Knight. These courses and journal club have included scholars in and outside CRPM. We also initiated a program for predoctoral students and postdoctoral fellows to gain skills in grant peer reviewing with the Scientific Mentoring And Research Training or SMART program with early career and established faculty members facilitating this endeavor. Dr. Bryan Becker currently facilitates the SMART program, with Drs. Josh Speed and Carmen De Miguel as former leaders.

CardioRenal and affiliated faculty, students, and fellows across our UAB community are the backbone of sustaining our summer research programs. Kidney, Urology, and Hematology Undergraduate Research Experience (KUH KURE) has served as a leader in summer kidney research experiences for the past 8 years (6 years with NIH funding). The culture of training within CRPM and the kidney community at UAB has allowed this program to thrive and successfully train over 120 undergraduates in kidney research. PRedOctoral PhD and MD research training in Teams (PROmoTE) is in its 6th year as an NIH-funded program bringing together pre-matriculating PhD and MD researchers for a summer team science translational research experience under the mentorship of PhD and MD Faculty. The PROmoTE Program has trained 34 pre-matriculating and post-baccalaureate scholars with alumni of the program continuing into kidney research, starting a nephrology interest group in medical school, and on the trajectory to become the future MD and PhD kidney focused investigators.

More recent endeavors that have expanded our training impact include:

- Kidney Club, an outreach program that Dr. Carmen De Miguel leads focuses on high school students in the Birmingham City schools.
- ·UAB Kidney Disease Screening Awareness Program or KDSAP. This program is coordinated by UAB undergraduate students with Dr. Taka Saigusa working as the faculty advisor.
- Student Interest in Nephrology Group or SING. This program is coordinated by Heersink School of Medicine students with Dr. Navya Eleti serving as the faculty advisor. Many SING students work with Nephrology faculty on short-term research or writing projects.
- GAp year INternship or GAIN. This program is coordinated by Rena Becker to facilitate one-year internships with recent post-baccalaureate students to work in Nephrology faculty laboratories. Currently, 16 gap years are active in the gap year community with 9 mentored by CRPM faculty.
- KURE-Mentoring Academy – a new initiative, funded through a grant supplement, to support the training of near peer mentors engaging the summer research programs, currently 36 near peer mentors have been trained through this initiative in anticipation of more to join the March training.

IMPACT ON TRAINING

Current Pre and Postdoctoral Scholars

10 Years of Training Success Across the Pipeline

Kidney Club
High School Science Engagement

KDSAP
*Student-led Organization

KURE
Undergraduate Research Experience

GAIN
Gap Year Internship

PROmoTE
Entering MD and PhD Trainee Summer Research Experience

Deep South KUH PRIME

SMART
SCIENTIFIC MENTORING AND REVIEW TRAINING

IMPACT ON TRAINING

TRAINEE GRANTS RECEIVED

PREDOCTORAL

- 4 — NIH F AWARDS
- 5 — AHA
- 9 — T32/TL1

POSTDOCTORAL

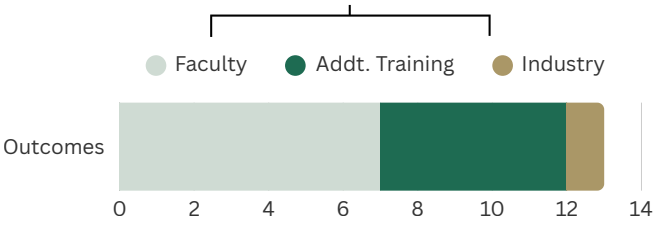
- 5 — NIH F & K AWARDS
- 8 — AHA, ASN, & APS
- 12 — T32/TL1

20 PhD Scholars

Current

Former

21 Postdoctorate



Mentoring

16 UAB Mentoring Awards

59 Near Peer Mentors in Summer Programs

75+ Undergraduates Mentored

37 Near Peer Mentors trained in KURE Mentoring Academy

Development & Training

2 NIH R25 DK Training Grants

- *PI: Dr. Jennifer Pollock*

Predoctoral NIH DK T32

- *PI: Dr. Jennifer Pollock*

Deep South KUH PRIME U2C/TL1

- *Includes CRPM Faculty: Drs. David Pollock, Jennifer Pollock, Kelly Hyndman, and Jeff Lebensburger*

Near Peer Mentoring Training Academy

Weekly Cardio Renal Journal Club

- *Led by Dr. John Knight*

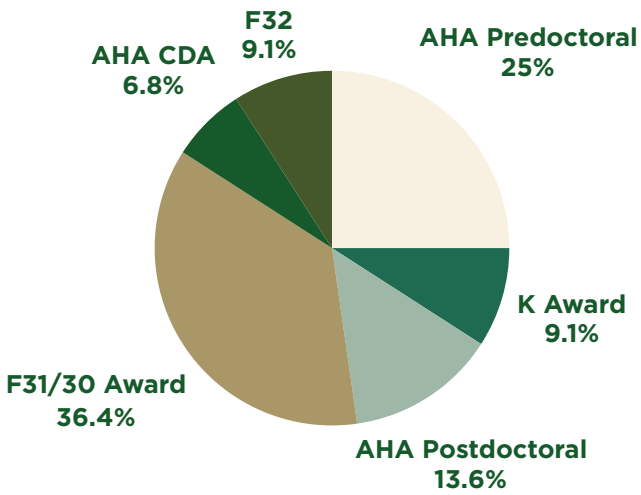
2 New Renal focused GBS courses

- *Led by Drs. Kelly Hyndman and Subhashini Bolisetty*

Monthly PIP/WIP Training for Pre and Postdoctoral scholars

SMART Reviews

44 Completed SMART Reviews



IMPACT ON SERVICE

Academic service in research embodies the ethos of collaboration, mentorship, and knowledge dissemination within the academic community. In terms of CRPM faculty, this is in our basic DNA. It is a part of being a complete scientist. We are a community of “doers” as we often like to say.

Our service is a key component of why we do what we do as faculty in biomedical science. It extends beyond individual pursuits of scholarly inquiry to encompass activities that contribute to the advancement of one's field and the academic community as a whole. For our faculty, this service has taken many forms, including peer review of research papers, serving on editorial boards, organizing conferences or seminars, participating in academic societies, and mentoring junior researchers.

Engaging in academic service fosters a sense of responsibility and reciprocity among researchers, as they contribute their time, expertise, and insights to support the integrity and quality of scholarly work. Ultimately, academic service plays a vital role in maintaining the robustness and vitality of the research ecosystem, facilitating the exchange of ideas, fostering interdisciplinary collaborations, and promoting the dissemination of knowledge to broader audiences.

Perhaps one of our greatest assets in CRPM is our culture. A culture of excellence, but also of giving back so that we gain more than we give. We have often heard that “culture trumps strategy every time” and nothing could be more true about the CRPM.

106 **EXTRAMURAL STUDY SECTIONS INCLUDING:**

10	57	103	16
Study Session Chair Positions	Editorial Boards	Campus Committees	Editor and Guest Editor Positions

American Physiological Society Presidents **2**

IMPACT ON RESEARCH

The CardioRenal Physiology & Medicine (CRPM) Section traces its roots back to a serendipitous conversation between Nephrology Division Director Anupam Agarwal and Drs. David and Jennifer Pollock. This led to its establishment in 2014 as a basic and translational research program with support from Seth Landefeld and the School of Medicine. Initially comprising three senior faculty and one junior faculty member, the CRPM has since expanded to eleven NIH-funded labs, incorporating Assistant and Associate Professors over the years.

Despite facing the ever-increasing challenge typical of academic research funding, the CRPM has achieved significant milestones, securing multi-investigator grants and facilitating the transition of senior fellows into tenure-track positions. Its impact is evident in the numerous awards and grants received, including NIH P01 awards, R01s, K-awards, an AHA Strategically Focused Network Grant, and training grants from various organizations. Notably, its presence within a clinical department addresses critical research gaps in kidney physiology and vascular biology at UAB.

Since 2014, CRPM faculty and trainees have garnered numerous honors for their research efforts, including Pittman Scholars, Endowed Professorships, and Max Cooper Awardees. Its research endeavors have attracted substantial funding, totaling over $50 million from NIH, AHA, other organizations, and industry sources.

The CRPM's research scope has widened to encompass diverse cardiorenal issues, including sickle cell nephropathy, water and electrolyte disorders, and the role of the autonomic nervous system in renal function control. Collaboration among its investigators is a cornerstone, facilitated by regular forums that promote idea-sharing and feedback. This collaborative spirit fosters a conducive environment for scientific breakthroughs, evident in impactful publications across prestigious journals.

In essence, the CRPM's decade-long journey underscores its commitment to advancing understanding in kidney disease, hypertension, obesity, and diabetes. Looking ahead, the collaborative ethos and research excellence within the CRPM position it to continue making significant contributions to the field for years to come.

IMPACT ON RESEARCH

Awards Processed 2014 - 2024

NIH	$44,110,897	Societies & Foundations	$2,878,588
AHA	$3,546,821	Industry	$92,829

Total $50,629,135

HONORS & AWARDS

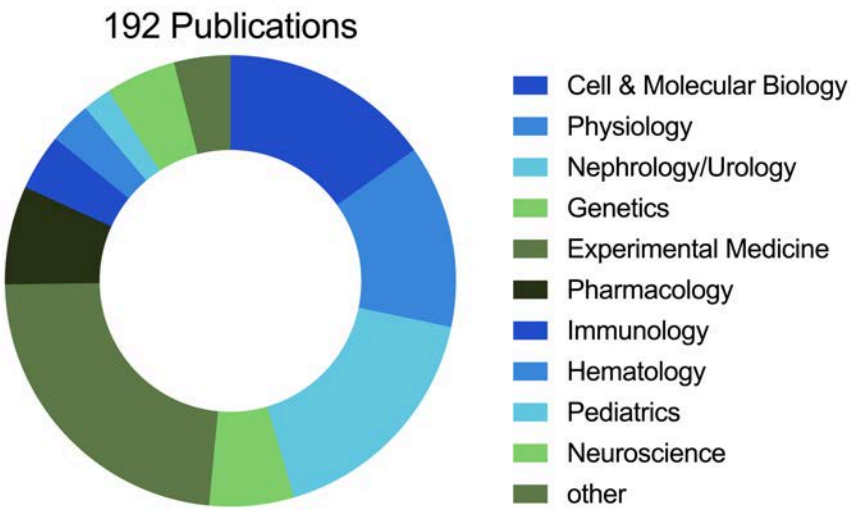
3 Pittman Scholars

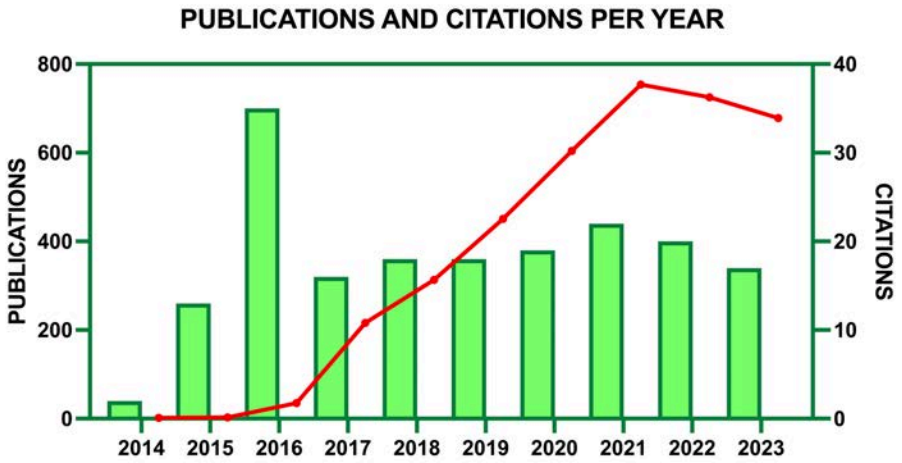
3 Endowed Professorships

2 Max Cooper Awardees

142

NATIONAL HONORS AND AWARDS





Dr. Bryan Becker

Unraveling the Role of Renal Nerves in Hypertension

In the battle against hypertension, a recent study by Assistant Professor Dr. Bryan Becker sheds light on its complex mechanisms. Hypertension, marked by high blood pressure, is a leading risk factor for cardiovascular issues, prompting urgent medical attention.

Researchers acknowledge the multifaceted nature of hypertension, with genetics and lifestyle contributing significantly. One intriguing area of exploration is the role of renal nerves in regulating sodium and water balance. These nerves modulate critical factors like glomerular filtration rate and sodium reabsorption by influencing sympathetic innervation of renal arterioles and tubules.

Central to this regulation is the renal endothelin (ET) system, particularly the activity of renal tubular ETB receptors, which promote sodium excretion in response to high salt intake. The study, conducted on rats lacking ETB receptors, aimed to understand their role in renal nerve activity during high-salt diets. Surprisingly, these rats showed elevated sympathetic nerve activity, even after salt intake, indicating the crucial role of ETB receptors in inhibiting sympathetic activity in response to physiological changes.

Additionally, the study revealed insights into renal nerve response, indicating desensitization but sustained elevated activity in rats lacking ETB receptors. While these findings illuminate the renal nerve-hypertension connection, unanswered questions remain, prompting ongoing investigations, including compound nerve recordings and timing experiments to align with rodents' circadian cycles. Through understanding this network's intricacies, researchers aim to identify new hypertension treatment targets.

Dr. Bryan Becker joined the Cardio-Renal Physiology and Medicine (CRPM) division in late 2015 as a postdoctoral fellow under the guidance of Dr. David Pollock. His decision to pursue postdoctoral training at the University of Alabama at Birmingham (UAB) was largely influenced by the vibrant community within the CRPM. While recognizing Dr. Pollock's mentorship as invaluable, Dr. Becker was drawn to the collaborative environment and shared research vision among fellow trainees and distinguished faculty members.

Over eight years later, Dr. Becker transitioned to a faculty position within the CRPM in 2021, reflecting his satisfaction with the choice to join the division. He continues to regard the CRPM community as its greatest strength, fostering collaborative opportunities, diverse expertise, and support for innovative research approaches.

Dr. Becker's research career focuses on unraveling the mechanisms underlying cardiovascular disease, with a specific emphasis on understanding alterations in the autonomic nervous system during hypertension and heart failure. His current research projects involve investigating the role of renal sensory nerves in the development and maintenance of hypertension, as well as exploring the circadian control of autonomic function and blood pressure using a novel circadian gene knockout rat model.

In addition to his research endeavors, Dr. Becker is deeply committed to training the next generation of biomedical researchers and medical professionals. He has mentored numerous undergraduates through summer research programs and informal laboratory settings and plays an active role in teaching within the CRPM division. Dr. Becker also directs the CRPM section's Scientific Mentoring and Review Training (SMART) program, which provides trainees with presubmission review and mock study section experience.

Currently, Dr. Becker's laboratory consists of a lab manager, undergraduate researcher, and master’s student, with plans to recruit graduate students in the near future. His research endeavors are supported by a K01 grant from the National Heart, Lung, and Blood Institute (NHLBI), focusing on elucidating the role of renal sensory nerves and altered autonomic balance in hypertension, as well as an intramural pilot grant from the Integrative Center for Aging Research.

Dr. Subhashini Bolisetty

Bolisetty Lab Unlocks the Complexity of Kidney Injury and Repair Mechanisms

The kidney, a marvel of biological engineering, orchestrates vital cellular interactions crucial for sustaining life. Recent advances in understanding kidney pathology have shed light on the complexity of progressive kidney disease and potential therapeutic interventions.

A review of current research reveals the multifaceted nature of kidney disease pathogenesis, involving intricate inflammatory and oxidative pathways. Dr. Subhashini Bolisetty and her lab have uncovered the dual role of macrophages in tissue injury and repair, highlighting their complex biology and therapeutic potential.

Traditionally seen as instigators of inflammation, macrophages exhibit nuanced functions, with subclasses contributing to either pro-inflammatory or anti-inflammatory responses. Their communication with tubular epithelium and endothelium further influences injury or resolution processes, underscoring the complexity of their biology.

Research into cytoprotective antioxidant proteins, like heme oxygenase-1 (HO-1) and ferritin heavy subunit (FtH), elucidates their role in mitigating oxidative stress and inflammation. Studies in transgenic mouse models demonstrate their influence in resolving inflammation-mediated fibrosis, offering promising therapeutic avenues.

Utilizing established models, such as the unilateral ureteral obstruction model, aids in understanding the interplay between macrophages and the kidney microenvironment in injury resolution.

Dr. Bolisetty's groundbreaking work, published in Kidney International, bridges knowledge gaps in kidney macrophage biology, providing insights into their role in injury resolution and repair. These findings not only inform therapeutic strategies for kidney diseases but also hold implications for inflammatory conditions characterized by oxidative stress and inflammation.

Dr. Bolisetty is an Associate Professor in the Division of Nephrology. She received her bachelor's degree in industrial biotechnology in India and her Ph.D. at the University of Alabama at Birmingham. She received her first postdoctoral training under the guidance of Dr. James George in the department of Surgery and a second postdoctoral fellowship under the guidance of Dr. Anupam Agarwal. Dr. Bolisetty became an Assistant Professor in the Division of Nephrology in 2016 and was promoted to an Associate Professor in 2021.

Dr. Bolisetty's research program focuses on understanding the interplay between iron metabolism and inflammation in kidney disease. She has received support from various funding sources, including the NIH, AHA and PKD Foundation. She currently serves as a PI on one R01 and as a co-investigator on 4 additional R01s. She has published over 40 manuscripts, a book chapter and several review articles.

Dr. Bolisetty enjoys teaching and is involved with numerous courses for the graduate school. She is also the recipient of the UAB GBS Teaching award. She serves on the graduate thesis committee for students and serves as a mentor for graduate students and post-doctoral fellows. At UAB, she serves as the chair of the membership committee for the Asian American and Pacific Islander Faculty Association and serves as the Faculty advisor for She's the First organization. On the national front, she serves on committees for the American Physiological Society, American Society of Nephrology and American Heart Association. She also serves on the editorial board for the American Journal of Physiology Renal physiology, Canadian Journal of Physiology and Pharmacology and Frontiers in Medicine – Nephrology.

Dr. Carmen De Miguel

De Miguel and Colleagues Unlock Therapeutic Potential for Kidney Disease from the Unexpected

The intricate dance of molecular signaling pathways within the human body often reveals unexpected allies in the fight against disease. Among these allies, endothelin-1 (ET-1) emerges as a key player in the realm of renal health, exerting its influence through a network of receptors and pathways. However, recent discoveries highlight a novel contender in this arena: tauroursodeoxycholic acid (TUDCA), an endogenous bile salt with remarkable cytoprotective properties.

ET-1, a peptide with profound implications for vascular function and inflammation, operates through two G protein-coupled receptors: ETA and ETB receptors. Dysregulation of these receptors can lead to a cascade of detrimental effects, including vasoconstriction, hypertension, and renal injury. Notably, dysfunction of ETB receptors has been implicated in salt-sensitive hypertension and the associated renal damage, highlighting the potential therapeutic significance of targeting this pathway.

Enter TUDCA, a chemical chaperone with a diverse repertoire of cytoprotective actions. Originally known for its efficacy in liver diseases, TUDCA has since garnered attention for its protective effects in various organs, including the brain, heart, and now, the kidneys. Through its ability to mitigate oxidative stress, prevent mitochondrial dysfunction, and decrease cellular apoptosis, TUDCA emerges as a promising candidate for renal therapeutics.

Dr. Carmen De Miguel and her team investigated the potential of TUDCA in preventing salt-induced renal damage in a model of ETB receptor dysfunction. The results were nothing short of remarkable: TUDCA treatment effectively prevented the development of proteinuria, albuminuria, and renal tubular injury, independent of sustained blood pressure lowering. Moreover, TUDCA demonstrated anti-inflammatory properties, reducing renal cortical cell death and T cell accumulation in response to high salt intake.

The mechanisms underlying TUDCA's renoprotective effects are multifaceted. Notably, TUDCA treatment led to an upregulation of megalin expression in proximal tubules, facilitating the reabsorption of filtered proteins and reducing proteinuria. Additionally, TUDCA blunted TNF-α-dependent mechanisms contributing to salt-mediated cortical cell death, offering insights into its anti-inflammatory properties.

Importantly, the therapeutic potential of TUDCA extends beyond experimental models, holding promise for clinical applications in chronic kidney diseases exacerbated by high salt diets. Given its favorable safety profile and efficacy in diverse preclinical models, TUDCA represents a compelling avenue for further exploration in the realm of renal therapeutics.

By harnessing the cytoprotective properties of endogenous bile salts, we pave the way for novel approaches to combat renal diseases and improve patient outcomes.

Dr. De Miguel's initial breakthrough study was published in Acta Physiologica (doi: 10.1111/apha.13227).

Dr. Carmen De Miguel received her B.S in Biochemistry and Molecular Biology from the Universidad Autónoma de Madrid (Spain), her Ph.D. in Renal Physiology from the Medical College of Wisconsin, and her M.S. in Cell and Molecular Biology from St. Cloud State University. Research in Dr. De Miguel's laboratory is focused on understanding how immune cells and immune mediators impact renal function and end-organ damage during hypertension, diabetes and high oxygen supplementation. Dr. De Miguel is especially interested in the interplay between the endothelin system and inflammation as well as sex differences possibly controlled by endothelin in these renal diseases. She is passionate about mentoring, science outreach and increasing diversity in the STEM field, as well as the use of social media to disseminate science.

Dr. De Miguel joined the Cardio-Renal Physiology and Medicine Section as a postdoctoral scholar in the lab of Dr. Jennifer Pollock when the section was started in 2014, and she became an Instructor in Medicine in 2017. In 2019, Dr. De Miguel was promoted to Assistant Professor of Medicine after being awarded a K01 Career Development Award and she started her independent laboratory. Since then, over 30 trainees (medical, graduate and undergraduate students, as well as gap year interns) have done research in her lab

Dr. Zhengrong Guan

Unveiling the Role of Sphingosine 1-Phosphate (S1P) in Renal Microvascular Function

Research from the laboratory of Dr. Zhengrong Guan has shed light on the intricate role of sphingosine 1-phosphate (S1P) in regulating vascular reactivity, particularly in the renal microvasculature, offering potential insights into the pathogenesis of renal diseases. S1P, a bioactive sphingolipid metabolite, acts through five distinct receptors, primarily S1P1 and S1P2, to modulate various physiological processes.

A groundbreaking study, published in the leading journal for kidney research, The Journal of the American Society of Nephrology, revealed that exogenous S1P exerts potent vasoconstriction on preglomerular microvessels, particularly afferent arterioles, without affecting efferent arterioles. This selective vasoconstrictive effect suggests a novel regulatory role for S1P in modulating glomerular hemodynamics.

The Guan team found that S1P-induced vasoconstriction of afferent arterioles is mediated primarily through S1P1 and S1P2 receptors, leading to calcium influx via L-type voltage-dependent calcium channels (L-VDCC). Importantly, pharmacological blockade of S1P2 receptors attenuated S1P-induced vasoconstriction, highlighting the therapeutic potential of targeting this receptor subtype in renal microvascular dysfunction.

The study also elucidated the distribution of S1P receptors in renal microvessels, with S1P1 and S1P2 receptors predominating in preglomerular microvessels and vascular smooth muscle cells. This localization underscores the specificity of S1P-mediated vasoconstriction and provides valuable insights into the signaling pathways involved.

These findings have significant implications for our understanding of renal physiology and pathology. Dysregulation of S1P signaling pathways has been implicated in various renal diseases, including ischemia-reperfusion injury, diabetic nephropathy, and hypertensive renal injury. Therefore, elucidating the role of S1P in renal microvascular function may pave the way for novel therapeutic strategies targeting S1P receptors to mitigate renal injury and improve patient outcomes.

Moving forward, further research is warranted to delineate the precise mechanisms underlying S1P-mediated vasoconstriction and its implications for renal disease progression. By unraveling the complexities of S1P signaling in the kidney, researchers aim to advance our understanding of renal microvascular regulation and identify potential targets for therapeutic intervention in renal pathologies.

Dr. Guan joined the CRPM in 2014 as an instructor and was promoted to an assistant professor soon after. She has a long-standing interest in the research of renal physiology, particularly in the mechanisms that are involved in the regulation of renal microvascular function, autoregulation, and hemodynamics, under physiological and variant pathophysiological conditions. CRPM has provided great opportunities to work and collaborate with other PIs who keep me motivated to succeed as much as possible. Our research project supported by Grant-in-Aid (GIA) from the American Heart Association (AHA) and NIH R01 grants focus on a potential signaling molecule S1P in regulating renal microvascular reactivity and contributing to the renal microvascular dysfunction in ischemia-reperfusion induced kidney injury (IRI). Current research studies reveal sex-associated differences in renal microvascular regulation, mitochondrial function and intracellular calcium handling. The lab equips with the cutting-edge facilities which are applied in the in vitro blood-perfused juxtamedullary nephron (JMN), and in vivo renal hemodynamic studies. We also use the fluorescence spectrophotometer to investigate intracellular calcium signaling in primary vascular smooth muscle cells isolated from preglomerular microvessels. We are proud of being a part of the CRPM family to celebrate the 10th anniversary.

Dr. Kelly Hyndman

Hyndman Study Reveals Critical Role of Kidney Epithelial HDACs in Maintaining Fluid-Electrolyte Balance and Blood Pressure Regulation

In a groundbreaking study published in JCI Insight, Dr. Kelly Hyndman and colleagues unveil a crucial link between kidney epithelial histone deacetylases (HDACs) and fluid-electrolyte balance maintenance, shedding new light on potential implications for cardiovascular and renal health. The research provides key insights into mechanisms governing fluid-electrolyte homeostasis and highlights therapeutic intervention implications in cardiovascular and renal diseases.

Maintaining optimal fluid-electrolyte balance is vital for health, yet disruptions can lead to hypertension and kidney damage. The study explores the intricate interplay of physiological pathways, focusing on kidney epithelial HDACs.

"Our findings reveal renal medullary class I HDACs as critical mediators between high-salt diets and mechanisms to maintain fluid-electrolyte balance," says Dr. Hyndman. "This underscores their potential as therapeutic targets."

HDACs, particularly HDAC1 and HDAC2, regulate ion transporter/channels transcription and activity in kidney epithelium. They're crucial for high salt-induced NOS/NO pathway activation, impacting blood pressure control and fluid-electrolyte balance.

"Understanding kidney epithelial HDACs' role is a significant step in developing therapies," adds Dr. Hyndman. "By elucidating fluid-electrolyte regulation mechanisms, we aim to identify new therapeutic targets."

The study also warns of risks associated with HDAC inhibitors (HDACi) use. While promising for various diseases, including cancer, HDACi can cause adverse events like hyponatremia and hypokalemia. Monitoring fluid-electrolyte balance in patients undergoing HDACi therapy is crucial to prevent complications.

"As we explore HDAC inhibitors' therapeutic potential, we must consider their impact on fluid-electrolyte balance," stresses Dr. Hyndman. "Elucidating kidney epithelial HDACs' role may lead to safer treatments for cardiovascular and renal diseases."

This study was highlighted as a Featured Discovery by the Heersink School of Medicine in 2021.

Kelly Anne Hyndman, PhD Associate Professor of Medicine, Division of Nephrology, Section of Cardio-Renal Physiology and Medicine. Dr. Hyndman has always been curious about how the body maintains fluid-electrolyte balance in an ever-changing environment. Whether it is a fish that migrates daily between fresh and sea water or a human that consumes a lot of dietary sodium, she has used basic science models to understand mechanisms related to fluid-electrolyte balance. Dr. Hyndman received her PhD in Zoology from the University of Florida under the mentorship of Dr. David Evans. Her doctoral work focused on elucidating the evolution and physiology of the endothelin system in fishes. From here, she completed post-doctoral research at the Medical College of Georgia under the mentorship of Dr. Jennifer Pollock, where she tested the hypothesis that endothelin and nitric oxide work in the kidney to promote salt excretion. he found that if you cannot activate the endothelin system or nitric oxide system, that a salt sensitive hypertension will develop.

Now as a PI she has three focused areas of research: 1) Understanding the physiology and regulatory mechanisms of lysine acetylation in the kidney, and how enzymes in these pathways are critical to maintain fluid-electrolyte balance. 2) Understanding the pathophysiology of epigenetic regulating pathways in acute kidney injury and chronic kidney disease progression. 3) Using ‘omics to define novel regulatory pathways in the kidney during repeat exposure to dehydration. She is currently funded by multiple grants from the National Institutes of Health and has contributed to over 54 peer-review publications. She is involved in both local and national committees, include being the Co-Associate Director of the Nephrology Research and Teaching Center at UAB, and the chair of the American Physiological Society Renal Section Awards Committee.

She is a standing member of the NIH Study Section, PBKD and is the new Senior Editor for the Canadian Journal of Physiology and Pharmacology. She started her faculty appointment at UAB in the Section of Cardio-Renal Physiology and Medicine, and through the support of the section and division, has built strong research and education programs to help train the next generation of scientists.

Dr. Ed Inscho

Meeting the Challenge of Renal Microvascular Dysfunction

The Inscho lab has been a beacon in studying renal microvascular control, shedding light on renal function mechanisms, particularly the critical role of renal autoregulation in maintaining stable blood flow and filtration rates. Led by Dr. Inscho's PhD student, Justin van Beusecum, their groundbreaking study uncovers a concerning link between chronic low-dose lipopolysaccharide (LPS) exposure and impaired renal autoregulation, potentially aiding chronic kidney disease (CKD) understanding and treatment.

Renal autoregulation, crucial for maintaining renal function, adjusts vascular resistance to arterial pressure changes. However, subclinical Toll-like receptor 4 (TLR4) activation by low-dose LPS disrupts this balance, impairing kidney autoregulation.

Dr. van Beusecum, now at the Medical University of South Carolina, explains, "We investigated chronic, low-dose LPS impact on renal autoregulation and underlying mechanisms." Using rats to mimic low-grade inflammation, they administered low-dose LPS over 8 or 14 days. Despite stable physiological parameters like blood pressure, chronic low-dose LPS led to impaired autoregulation in kidney afferent arterioles (AAs), persisting for 14 days.

The study identifies TLR4-dependent mechanisms behind this impairment. Anti-TLR4 antibody co-treatment preserved AA autoregulation, highlighting TLR4 activation's pivotal role.Competitive antagonism of MHC-II-associated peptide (CLIP) using CAP treatment preserved and rescued AA autoregulation during LPS exposure, suggesting a potential therapeutic target for mitigating chronic inflammation's renal effects.

These findings are crucial for understanding CKD pathogenesis and related inflammatory renal disorders. "Subclinical inflammation and TLR4 activation must be considered in renal disease management," stresses Dr. Inscho.

Further research is needed to explore TLR4 and MHC-II therapeutic potential in preserving renal autoregulation and preventing kidney disease progression. By unraveling inflammation's complex role in renal function, these findings offer hope for novel CKD treatment strategies.

Dr. Inscho has spent his career investigating the physiology and pathophysiology of renal microvascular function. He has the training, expertise, leadership, and motivation necessary to successfully execute the experiments outlined in the current proposal. He has a broad background in renal, cardiovascular and endocrine physiology as well as a contemporary view of where the field of renal microvascular physiology is today. His research has focuses mainly on understanding the physiological mechanisms that underpin normal renal hemodynamics and how pathophysiological conditions such as hypertension, inflammation or excess dietary salt negatively impact on those mechanisms. He has secured peer-reviewed research support from NIH, AHA, NKF and other sources to support his work over the last 28+ years, and used those funds to expand our understanding of how healthy kidneys control their own blood flow. Over the past two decades, he has focused on the roles of P2 receptors, inflammation and the endothelin system in influencing renal microvascular function, renal hemodynamics and renal injury in hypertension. Some key publications that have come from that work are listed below. In addition, Dr. Inscho has overseen and administered his independently funded laboratory while retaining his laboratory staff from between 9 and 27 years attesting to the success and stability of the laboratory program. Dr. Inscho has also been heavily engaged in training aspiring young investigators. To date, he has trained or co-trained approximately 28 undergraduate students, graduate students, medical students and postdocs. Most of these trainees remain professionally involved in research, medicine or education.

Dr. Malgorzata Kasztan

Kasztan Attacks the Growing Problem of Kidney Disease in Sickle Cell Disease

Sickle cell disease (SCD), a prevalent genetic blood disorder, poses significant renal complications, yet effective treatments have been scarce. Despite its prevalence, efforts to uncover kidney-specific mechanisms and therapies have been lacking. However, Dr. Malgorzata Kasztan's groundbreaking study provides hope by targeting endothelin receptors as a potential therapeutic strategy.

The study delves into the intricate pathophysiology of SCD-related renal complications, focusing on endothelin-1 (ET-1) signaling. Elevated ET-1 levels in SCD patients' plasma and urine suggest its role in renal injury. Meticulous experimentation in mouse models reveals ET-1's crucial role, particularly its interaction with endothelin A (ETA) receptors, in sickle nephropathy development and progression.

Selective ETA receptor antagonism prevents glomerular and tubular pathologies associated with SCD nephropathy. Short-term treatment with ETA receptor antagonists shows promise in reducing established nephropathy severity.

While dual ETA/B receptor antagonism, used in pulmonary arterial hypertension, provides some renal protection, it's less effective than selective ETA receptor antagonism, highlighting the need for precise targeting in therapeutic interventions.

These findings warrant further exploration of endothelin receptor antagonism for sickle nephropathy treatment. With endothelin receptor antagonists already approved for other conditions, clinical translation prospects are promising, offering hope for improved SCD renal complication outcomes and quality of life.
Initial work, published in the Journal of the American Society of Nephrology, received editorial highlight.

Malgorzata Kasztan, M.S., Ph.D. earned her medical research degree in laboratory medicine from the Medical University of Gdansk, Poland, in 2014. During her graduate studies, she developed research skills in renal physiology and determined that extracellular nucleotides via purinergic receptors activation increase glomerular permeability to albumin in physiological and pathophysiological conditions (low sodium diet, diabetes). This led to her moving to UAB as a post-doctoral fellow in the laboratory of Dr. David Pollock.

During her fellowship, Dr. Kasztan led the study that demonstrated a critical role of endothelin-1 in the development and progression of sickle cell nephropathy. This included a novel study that endothelin A receptor antagonism rescued kidney from injury by preserving kidney structure and function of sickle cell mice. This pre-clinical work provided key evidence and rational for phase 1 clinical trial in patients with sickle cell kidney disease. Additionally, in collaboration with Dr. Lebensburger in the Department of Pediatrics, she conducted longitudinal study to demonstrate that hyperfiltration is a determinant as well as predictor of the onset of long-term kidney damage in both pediatrics and murine sickle cell anemia.

Dr. Kasztan and colleagues have pioneered studies on sex-specific discrepancies in sickle cell-associated renal involvement. This work undoubtedly has advanced basic science as well as clinical research and encouraged more comprehensive prospective studies on progression of sickle cell kidney disease. More recent work has focused on identifying mechanisms of renal iron handling in the acute and the progressive sickle cell kidney disease.

Dr. Kasztan's research has led to a better understanding of mechanisms that lead to progressive sickle cell disease-associated nephropathy that have important implications for a broader understanding of chronic kidney disease, hypertension and diabetes. In this area, she over 35 peer-reviewed manuscripts in top-tier journals, including but not limited to the Journal of American Society of Nephrology, Blood Advances and Hypertension.

In her yet brief career, Dr. Kasztan has already received numerous grants including an AHA post-doctoral fellowship, an ASN Joseph A. Carlucci Research Fellowship, and an AHA Career Development Award. In 2019, she was awarded a K99/R00 grant from NHLBI that led to her recruitment into the UAB Department of Pediatrics, Hematology and Oncology Division where she is now an Assistant Professor. In 2023, Dr. Kasztan received an ASN Gottschalk Award and was named a UAB Pittman Scholar.

Dr. Paramita Pati

Pati and colleagues uncover key mechanisms for the benefits of strict meal timing

Working with a large team of investigators from several UAB departments, Dr. Paramita Pati, investigated the impact of time-restricted feeding (TRF) on cardiovascular health in mice with diet-induced obesity. The study aimed to understand how restricting food availability to specific time windows could improve cardiovascular disease risk factors.

The researchers began by highlighting the influence of feeding-fasting cycles on metabolic and vascular health, emphasizing disruptions in these cycles as potential contributors to neural and endocrine dysfunction. They noted that mice fed a high-fat diet (HFD) ad libitum exhibited altered glucose and leptin rhythms, along with increased risk of metabolic and vascular diseases.

Previous studies have shown the beneficial effects of TRF on cardiometabolic health in both animals and humans. TRF restricts food intake to specific time windows without reducing daily caloric intake, leading to improvements in metabolic diseases and cardiovascular risk factors.

Dr. Pati and colleagues hypothesized that restricting food availability to the dark phase in mice with established diet-induced obesity would improve cardiovascular health. They conducted experiments involving 8-week-old mice fed either a normal diet or HFD for 18 weeks, followed by 2 weeks of ad libitum feeding or TRF (food available only during the 12-hour dark phase).

Their findings revealed that TRF intervention for 2 weeks effectively restored or substantially improved various cardiovascular health parameters compared to ad libitum HFD feeding. Notably, TRF did not reduce caloric intake or body weight but improved whole-body energy metabolic rhythms. It also restored blood pressure and heart rate dipping, enhanced aortic endothelial function, reduced aortic wall thickness and stiffness, and mitigated kidney damage.

The study provided new evidence supporting the efficacy of short-term TRF intervention in improving cardiovascular health in mice with diet-induced obesity. TRF restored metabolic rhythms, improved blood pressure regulation, enhanced endothelial function, and reduced organ damage, suggesting its potential as an effective intervention for obesity-related cardiovascular diseases.

This work was supported by a grant from the HSOM AMC21 program awarded to Drs. Jennifer Pollock, David Pollock, Shannon Bailey (Department of Pathology), and Karen Gamble (Department of Psychiatry and Behavioral Neurobiology).

Dr. Paramita Pati is an Instructor of Medicine in the CRPM. She has had a long-standing interest in studying the circadian mechanisms of cardiovascular disease commenced during their dissertation studies in the Department of Pharmacology at Augusta University under the direction of Dr. R. Daniel Rudic. Following this, she undertook postdoctoral training in the laboratory of Jennifer S. Pollock in the Cardio-Renal Section of the Division of Nephrology, serving as a postdoctoral fellow from 2016 to 2021. During this period, she broadened her research expertise in cardiovascular and renal pathophysiology that includes the role of nitric oxide in the vascular endothelium and control of kidney function. In 2021, she was promoted to faculty status, assuming an Instructor position. Dr. Pati's research has been supported by a Career Development Award from the American Heart Association.

Dr. David Pollock

WHEN you eat may be as important as what you eat

Recent work from the David Pollock lab unveils a pivotal discovery in the intricate connection between meal timing and blood pressure rhythms. Led by Dr. Pollock's PhD student, Dingguo Zhang, the study elucidates how meal timing impacts the body's circadian rhythms and blood pressure regulation.

In healthy individuals, blood pressure naturally dips during nighttime, known as "BP dipping," vital for cardiovascular health. Disruptions in this pattern, such as non-dipping blood pressure, elevate cardiovascular risk.

The study investigates the mechanisms behind BP dipping, focusing on the kidney's role in sodium excretion and fluid-volume regulation. While prior research linked circadian rhythms and kidney function, this study explores how meal timing influences these processes.

Using mouse models, Zhang and team found that restricting food intake to the inactive phase alters the blood pressure rhythm without changing the 24-hour average. This underscores the critical role of meal timing in modulating blood pressure rhythms, independent of internal clock genes. Interestingly, renal excretory rhythms remained intact regardless of meal timing, suggesting the kidney's molecular clock operates independently of eating behavior, challenging previous assumptions.

Experiments with mice lacking the gene Bmal1 show that meal timing overrides internal clock genes, influencing blood pressure rhythms. Dr. Pollock remarks, "We've uncovered a fascinating interplay between meal timing, circadian rhythms, and blood pressure regulation," opening new avenues for exploring diet's impact on cardiovascular health.

The study, titled "Timing of food intake drives the circadian rhythm of blood pressure," was published in the journal Function in 2020.

David M. Pollock, Ph.D. is the James A. Schafer Professor of Medicine and Director of the Cardio-Renal Physiology & Medicine Section at the University of Alabama at Birmingham (UAB) and Co-Director of the UAB Hypertension Research Center. He earned his bachelor's degree in biology and chemistry from the University of Evansville and his Ph.D. at the University of Cincinnati. This was followed by a post-doctoral fellowship at the University of North Carolina at Chapel Hill. Dr. Pollock spent two years as an Investigator at the Institute for Circadian Physiology at Harvard University before working in drug discovery at Abbott Laboratories in Chicago. In 1995, he accepted a faculty position at the Medical College of Georgia (now known as Augusta University) where he eventually became a Regents' Professor and Head of Experimental Medicine in the Department of Medicine. In 2014, he moved to UAB to assume his current role.

Dr. Pollock's wide range of research interests focuses on high blood pressure and kidney disease. Dr. Pollock's lab has uncovered how endothelin regulates renal handling of high salt diets as well as key preclinical evidence for use of endothelin antagonists in the treatment of diabetic and sickle cell nephropathy. Since coming to UAB, most of his recent work has focused on circadian-related mechanisms contributing to blood pressure control and end-organ damage as well as the relationship between organ-specific molecular clocks following changes in diet. This includes a clinical study examining how the time-of-day salt is consumed on blood pressure rhythms and nocturnal hypertension.

Dr. Pollock has held many service leadership positions including several journal editorships and served as the 87th President of the American Physiological Society. In 2013, Dr. Pollock received the Lewis K. Dahl Award from the American Heart Association, and in 2016, was awarded the Ernst Starling Lectureship from the American Physiological Society. Dr. Pollock also received the 2020 Max Cooper Award for Career Excellence in Research from the UAB Department of Medicine.

Dr. Jennifer Pollock

Addressing Childhood Adversity and Cardiovascular Health: A Call to Action

Childhood adversity, encompassing abuse, neglect, and household dysfunction, has enduring impacts on individuals and society. Research links traumatic childhood experiences to adult health challenges like ischemic heart disease, autoimmune disorders, and premature mortality. Recent studies extend this understanding, showing childhood maltreatment's influence on health outcomes such as diabetes mellitus and hypertension, including the long-term effects of historical events like wartime evacuations.

Animal studies elucidate the mechanisms underlying these associations. Rodents exposed to early life stress exhibit changes in the central nervous, endocrine, and immune systems, mirroring human experiences. Dr. Jennifer Pollock's lab discovered that maternal separation in rats elevates endothelin-1 levels, a vasoconstrictor associated with cardiovascular dysfunction.

Collaborating with the Georgia Stress and Heart Study, Dr. Pollock's team investigated adverse childhood experiences (ACEs) in adolescents and young adults. They found ACEs linked to adverse hemodynamic parameters, indicating early cardiovascular risk factors in those with childhood adversity.

These findings emphasize the importance of exploring pathways like endothelin to understand childhood adversity's impact on cardiovascular health. They also highlight societal factors such as ethnicity and socioeconomic status influencing cardiovascular risk.

Longitudinal studies and targeted interventions offer promise in addressing the complex relationship between childhood adversity and cardiovascular health. By identifying the root causes of poor cardiovascular health resulting from childhood adversity, these efforts aim to safeguard future generations' well-being.

Supported by a 5-year, $11 million Program Project Grant from the National Heart Lung and Blood Institute, this work involves collaborators across the UAB campus, including the Departments of Pediatrics and Psychology.

Jennifer Pollock, PhD, FAHA, FAPS, trained in protein chemistry at UNC-Chapel Hill examining structure-function of prothrombin activation. Her postdoctoral studies with Dr. Ferid Murad, 1998 Nobel Laureate, were the first descriptions of NO synthase in the vasculature and provided a basis for continuing studies on the regulation of NO in cardiovascular disease. Her research has focused on endothelial function and, especially how early life stress mediates vascular disease as well as control of sodium handling by the kidney. With over 250 publications and an H-index of 63, Dr. Pollock has made a lasting impact on the fields of vascular biology and kidney physiology.

Dr. Pollock is an Endowed Professor in the Department of Medicine, Co-Director of Cardio-Renal Physiology & Medicine Section, Associate Director of the Center for Free Radical Biology, and a member of the MSTP Advisory committee at UAB. She also serves as the Pre-doctoral T32 Institutional Training Program Director for the Center for Clinical and Translational Science (CCTS) Partner Network, and more recently, Director of the Professional Development Core of the Deep South Interdisciplinary Mentored Education Program (KUH PRIME).

Over the past 20+ years, she been a leader and/or team member of 5 multi-investigator, multi-disciplinary, translational NIH grants of which 4 are currently active. She has also received multiple AHA grants as PI as well as numerous AHA fellowship grants for her trainees. Dr. Pollock has mentored over 100 undergraduate, medical, and graduate students as well as fellows and junior faculty. She has been PI of multiple NIH training grants including an active T32 and two R25's as well as TL1 leader for the UAB CCTS.

Dr. Pollock has held many leadership roles within her university and national societies including the current Past-President of the American Physiological Society. She received numerous honors for her research and mentoring including the AHA Lewis K. Dahl Memorial Lecture and the APS Bodil Schmidt-Nielsen Distinguished Mentor and Scientist Award.In 2022, she was awarded the Max Cooper Award for Research Excellence.

Dr. Takamitsu Saigusa

Saigusa Focuses on Discovering Key Mechanisms Driving Cyst Growth in Autosomal Dominant Polycystic Kidney Disease (ADPKD)

As a physician scientist, Dr. Takamitsu Saigusa has been trying to understand the causes of cyst growth in autosomal dominant polycystic kidney disease (ADPKD). ADPKD affects millions worldwide and is characterized by the formation of fluid-filled cysts in the kidneys, leading to kidney enlargement and eventual failure.

One of his recent studies published in Kidney 360 uncovered how a transcription factor called IRF5 drives cyst growth by promoting inflammation in kidney-resident macrophages. These macrophages, part of the innate immune system, play a significant role in cyst development by releasing proinflammatory cytokines that stimulate cyst formation and progression.

"We have identified a novel therapeutic target for slowing kidney cyst growth in ADPKD," said Dr. Saigusa, senior author of the study. "By targeting IRF5 with antisense oligonucleotides (ASOs), we were able to reduce inflammation, cytokine production, and cystic severity in mouse models of ADPKD."

The study further elucidates the connection between kidney injury and cystogenesis, showing that factors triggering compensatory renal hypertrophy, such as unilateral nephrectomy, accelerate cyst growth by promoting macrophage activation and cytokine release.

"These findings have important implications for patients with ADPKD," said lead author and postdoctoral fellow Kurt Zimmerman (now on the faculty at the University of Oklahoma). "Slowing the rate of cyst growth may have significant clinical benefits and improve patient outcomes."

The research team is now exploring the therapeutic potential of IRF5-targeted ASOs in human patients with ADPKD, offering hope for new treatments to slow disease progression and improve quality of life.

Dr. Saigusa is a physician-scientist/Associate Professor in the Cardio-Renal Physiology and Medicine (CRPM) Section, Division of Nephrology at UAB. He received his MD degree in Japan and completed Internal Medicine and Nephrology training in both Japan and the US. After completing his T32 Nephrology Fellowship at the Medical University of South Carolina (MUSC) he joined the Division of Nephrology as a faculty at MUSC. Dr. Saigusa received a K08 career development award from the NIDDK under the mentorship of now Emeritus Professor, Dr. P. Darwin Bell, who supported him throughout his training as a fellow and faculty. Dr. Saigusa moved to UAB in 2016 and has been a member of the CRPM since then. Several summer students from the kidney pipeline program KURE and PROMOTE have been mentored by Dr. Saigusa and his lab.

Other mentees include postdoctoral fellow, Dr. Randee Sedaka, a former trainee of Dr. Jennifer Pollock's lab, who came to his lab as a T32 fellow and is currently a key member of the lab. Dr. Saigusa serves as a physician advisor for the Kidney Disease Screening and Awareness Prevention (KDSAP). Over the years, CRPM has held monthly meetings to discuss research projects among the CRPM members. The feedback received from these meetings was valuable and it helped him obtain successful research grants.

Recently, Dr. Saigusa was awarded an R03 and a R01 from the NIDDK. His research interest is to study how plant-based protein compared to animal-based protein diet, mitigates immune response, inflammation and slows kidney cyst growth in murine models of polycystic kidney disease (PKD). Dr. Saigusa sees general Nephrology patients at the UAB Gardendale Clinic and PKD patients at the Kirklin Clinic.

Dr. Michael Seifert

Subclinical inflammation phenotypes and long- term outcomes after pediatric kidney transplantation

Kidney transplantation stands as the gold standard for treating end-stage renal disease (ESRD), yet challenges persist in ensuring long-term allograft survival. In a study published in American Journal of Transplantation, led by Dr. Michael Seifert, investigators shed light on a pivotal aspect of this issue: the detection and implications of subclinical allograft injury in pediatric kidney recipients.

The research unveils the critical role of early surveillance biopsies in identifying subclinical inflammation—specifically, borderline T cell–mediated rejection (B-TCMR) or acute T cell–mediated rejection (SC-TCMR)—prior to the onset of clinical dysfunction. By implementing universal surveillance biopsies at 3 and/or 6 months posttransplant, the team uncovered insights into the relationship between early subclinical inflammation and late acute rejection, as well as allograft loss in pediatric kidney transplant patients.

"Our findings underscore the importance of proactive surveillance in pediatric kidney transplantation," says Dr. Seifert. "Detecting and addressing subclinical allograft injury before clinical dysfunction emerges could be paramount in improving long-term outcomes for these young recipients."

The study, conducted on a racially diverse cohort of pediatric kidney transplant patients receiving modern immunosuppression, challenges conventional paradigms by demonstrating a clear association between early subclinical inflammation and adverse late outcomes. This research not only deepens our understanding of the complexities surrounding pediatric kidney transplantation but also paves the way for targeted interventions aimed at mitigating allograft loss and enhancing patient outcomes.

While the debate on the impact of detecting and treating subclinical allograft injury continues, the findings by Dr. Seifert and colleagues provide compelling evidence for the proactive identification of these early markers. By doing so, the possibility of significantly extending life expectancy and improve the quality of life for children battling ESRD may be realized in the future.

Dr. Michael Seifert is a Professor of Pediatrics and Medicine at the University of Alabama Heersink School of Medicine in Birmingham (UAB), where his laboratory focuses on the role of endothelial injury and vascular inflammation in kidney transplant outcomes among children and young adults. With expertise in spatial and bulk molecular profiling of gene expression in kidney transplant biopsies using the NanoString GeoMx and nCounter platforms, his lab also investigates surrogates for future cardiovascular risk, conducts flow cytometry of circulating immune cells, and analyzes biomarkers of vascular inflammation derived from blood, urine, and tissue samples.

Directed by Dr. Seifert, the laboratory conducts clinical and translational studies targeting cardiovascular and kidney transplant endpoints. These endeavors have been supported by a K23 Career Development Award (K23 DK101690) and subsequently an R01 award (R01 DK126907) aimed at studying clinical and molecular biomarkers of endothelial injury and vascular inflammation in pediatric and young adult kidney transplant recipients. Recognizing the power of team science, Dr. Seifert has served as Principal Investigator for multi-center studies within pediatric nephrology research networks such as the Pediatric Nephrology Research Consortium (PNRC) and the Improving Renal Outcomes Collaborative (IROC).

Additionally, Dr. Seifert holds significant research and administrative leadership roles, serving as the Medical Director of the UAB Pediatric Kidney Transplant Program locally and as the Clinical Studies Co-Chair of CTOT-41 (U01 AI163072) nationally. His background in endothelial injury and vascular inflammation traces back to his pediatric nephrology fellowship at Boston Children's Hospital, where he cultivated a passion for investigating the underlying mechanisms of cardiovascular and kidney transplant diseases from childhood into adulthood. Dr. Seifert emphasizes the importance of structured mentoring programs and has mentored numerous pre-doctoral medical/pharmacy students and post-doctoral clinical/basic science fellows, contributing to NIH/NIDDK-funded pipeline training programs at UAB such as KURE (R25 DK115353), PROmoTE (R25 DK112731), and T32 DK007545.

Recent Career Development Success

Dr. Keri Kemp

Early life stress (ELS) has well-documented long-term health consequences, increasing the risk of chronic diseases later in life. While its effects on adult health are extensively studied, less is known about its impact during early developmental stages, particularly on gastrointestinal (GI) tract microbial colonization. Recent research suggests ELS may influence microbial composition, potentially contributing to disease development.

Human neonatal intestine microbial colonization is shaped by maternal and environmental factors in the first years of life. Rodent models highlight maternal microbiota transfer's critical role. Perturbations in this process impact immune, gastrointestinal, and neurological development, leading to health issues.

In a study led by postdoctoral fellow Keri Kemp in Dr. Jennifer Pollock's lab, the effects of ELS on gut microbiota development were investigated using the maternal separation with early weaning (MSEW) mouse model. MSEW induced neonate mouse microbial composition changes by postnatal day 28 (PD28), independent of maternal microbiota.

MSEW-exposed mice exhibited harmful microbial expansion and beneficial taxa reduction, potentially promoting inflammation and affecting gut health. These alterations may contribute to "loss of function dysbiosis," disrupting gut barrier function and immune regulation.

This study underscores ELS's impact on early gut microbiota development and its implications for long-term health. Understanding these mechanisms may lead to novel strategies for preventing or mitigating adverse outcomes associated with ELS.

Published in the American Journal of Physiology in 2021, this study formed much of the basis for Dr. Kemp's recent 5-year K99/R00 grant from the National Heart Lung and Blood Institute.

Dr. Eman Gohar

Former post-doctoral fellow, Eman Gohar, has made seminal contributions to our understanding of sex differences in acclimation to high-salt (HS) diets and its implications for blood pressure regulation. Despite extensive research on sodium handling in men, understanding sex-specific regulation remains limited. Previous studies suggest faster natriuretic responses in females, but mechanistic pathways are poorly characterized.

The kidney's endothelin-1 signaling system plays a vital role in sodium homeostasis and exhibits sex-specific differences. While endothelin receptor expression varies between sexes, ETA receptors seem more active in females. The study aims to elucidate sex-specific renal adaptations to HS diets and the involvement of endothelin-1.

Results show that females respond more rapidly to HS diets, exhibiting increased urinary sodium excretion from day 1. Water intake and urine output are also more pronounced in females. Interestingly, serum sodium concentration remains stable in females but increases in males during HS acclimation, suggesting females may better maintain circulating sodium levels.

While no significant changes are observed in sodium transporter expression, females show higher abundance of phosphorylated NCC, contradicting presumed activity levels. Additionally, urinary endothelin-1 excretion increases in males upon HS challenge, indicating sex-specific endothelin-1 system activation.

Human studies confirm higher urinary endothelin-1 excretion in women, suggesting their enhanced ability to handle sodium challenges. These findings underscore sex-specific mechanisms in fluid and electrolyte homeostasis, potentially leading to sex-specific therapies for salt-sensitive hypertension. Women's superior ability to manage sodium intake may contribute to their lower hypertension risk premenopause, highlighting the importance of considering sex differences in hypertension research and treatment.

Recent Trainee Publication Highlights

Cailin Kellum

As an example of how trainees can participate in a collaborative effort between various departments, PhD candidate Cailin Kellum from Dr. Jennifer Pollock's lab partnered with investigators from Pediatrics, Psychology, and Medicine to delve into the association between adverse childhood experiences (ACEs) and the risk of cardiovascular, metabolic, and kidney diseases.

ACEs encompass traumatic events occurring before the age of eighteen, such as parental separation, household dysfunction, and maltreatment. Over 60% of US adults report experiencing at least one ACE, linking ACEs to cardiovascular disease (CVD) risk factors including hypertension, diabetes, and kidney diseases.

Despite previous studies indicating increased blood pressure trajectories and pulse wave velocity (PWV) in individuals with ACEs, few studies focused on adolescents, and none utilized ambulatory blood pressure monitoring (ABPM), the gold standard for abnormal blood pressure assessment. To address these gaps, the study employed non-invasive techniques like PWV and aortic augmentation index (AIx75) to assess vascular stiffness in adolescents.

Results showed higher AIx75 in individuals with ACEs, suggesting early vascular changes before alterations in blood pressure. While PWV did not differ significantly between groups, the relationship between ACEs and PWV was BMI-dependent, with ACE exposure weakening the association between BMI and PWV.

These findings highlight the importance of early identification and intervention in mitigating future cardiovascular risks associated with ACEs. Further research is needed to elucidate the specific pathways linking ACEs to vascular dysfunction and hypertension, particularly focusing on abuse type and its relative impact on cardiovascular outcomes.

Van Huynh

PhD candidate Van Huynh has already published her initial first author paper in the American Journal of Physiology: Renal Physiology despite only being in the Hyndman lab a short time. Her work is based on observations that mild dehydration prompts significant transcriptional changes across various kidney cell types. Yet, chromatin accessibility and numerous positive associations between DNA peaks and RNA expression reveal the complexity of cis- and trans-regulatory factors.

In response to mild dehydration, mechanisms like osmosensors detecting plasma osmolality changes trigger the release of vasopressin (AVP) from the pituitary, enhancing water reabsorption through water channel expression. However, we observed no significant effect of dehydration on AVP receptors at the RNA level. Yet, downstream genes Aqp2 and Aqp3 exhibited increased expression, suggesting a compensatory response.

Additionally, the top gene differentially expressed in cortical collecting duct principal cells (CDPCs) was Grem2, involved in kidney development. It may play a role in cAMP activation and inflammation regulation. Transcription factor Crem, also upregulated in CDPCs, may further mediate cAMP-related responses to dehydration.

Interestingly, Pde10a, associated with cAMP degradation, showed increased expression in dehydrated mice, potentially regulating kidney metabolism during dehydration. Sex-specific gene expression differences were also evident, reflecting distinct pathways related to lipid and organic acid metabolism between males and females.

Despite these insights, the transient nature of some transcripts due to the single timepoint sampling remains a limitation. Future studies will elucidate the functional implications of these transcriptional changes, shedding light on kidney adaptation to dehydration.

Special Awards & Honors

Dr. Ijeoma Obi Near Peer Mentoring Award

The Dr. Ijeoma Obi Near Peer Award is a heartfelt tribute created to honor an extraordinary individual who personified unwavering support and unwavering encouragement. This award honors Pipeline Near Peers who fostered a nurturing environment, helping their mentees to overcome hurdles and achieve their goals, all while spreading joy and optimism.

Dr. James Schafer Summer KURE Award

Dr. Schafer was a founding member of the Division of Nephrology at UAB and internationally recognized for his technically innovative research program that made many significant advances in the field of ion transport. He received many honors and awards including service as the President of the American Physiological Society and a member of the Council of the American Society of Nephrology. Dr. Schafer was also known for his humility and generosity and always being eager to help others are create a thriving and welcoming research environment.

Therefore, this award is given to the KURE scholar who embodies the characteristics exemplified by Dr. Schafer, reflects a commitment to excellence, humility, generosity, and a strong sense of community. They are deserving of this recognition for their significant contributions to the field and for upholding the principles that Dr. Schafer represented throughout his career.

DOM: Jennifer S. Pollock Trainee Travel Award

The Department of Medicine Jennifer Pollock Trainee Travel Award provides trainees with supplemental costs associated with attending and presenting his/her scholarly work at prestigious national or international conferences. This Award was named for Dr. Jennifer Pollock in 2023.

Thank you!

We would like to thank all our sponsors, speakers, faculty, and students who have made this a decade to celebrate. We would like to thank the University of Alabama at Birmingham, Department of Medicine, Division of Nephrology for the support of the section, and look forward to the future of cardiorenal research - it certainly is bright!

PATRICIA E. MOLINA, MD, PHD

LSU Health Sciences Center

FRIEDRICH C. LUFT, MD

Charité – Universitätsmedizin Berlin

GREG FINK, PHD

Michigan State University

MICHELLE L. GUMZ, PHD

University of Florida

MARK KNEPPER, MD

National Heart Lung and Blood Institute

RAJAT M. GUPTA, MD

Harvard Medical School

A special thank you to the Kidney PIpeline Administrative Team for their efforts in planning the symposium

UAB NUTRITION OBESITY RESEARCH CENTER
The University of Alabama at Birmingham

UAB HEERSINK SCHOOL OF MEDICINE
The University of Alabama at Birmingham
Department of Medicine | Division of Nephrology

UAB Nutrition Obesity Research Center - UAB

- Fisher Scientific - UAB Heersink School of Medicine -

THANK YOU

SPONSORS

- HSOM Department of Medicine | Division of Nephrology -

UAB Nephrology Research and Training Center

fisher scientific

UAB HEERSINK SCHOOL OF MEDICINE
The University of Alabama at Birmingham

UAB NEPHROLOGY RESEARCH & TRAINING CENTER
The University of Alabama at Birmingham