

NEPHROLOGY UPDATE

Kidney Translational Research Center Focuses on Development of Kidney Atlas

Sanjay Jain, MD, PhD, is in the middle of an ambitious research initiative—mapping what he calls “every major and sub-major functionally important kidney cell type” in the human body and then identifying the molecular features, spatial relationships, and differentiating factors in the cells throughout their entire life cycle, from childhood through adulthood in health and disease.

“We know the anatomy of the kidney and the major cell types that perform specific functions,” notes Dr. Jain. “What we don’t know is the molecular diversity of those different cell types across ethnicity, age groups, or gender. We also need to know more about how the kidney cells change after disease or injury. This knowledge is critical for precision medicine.”

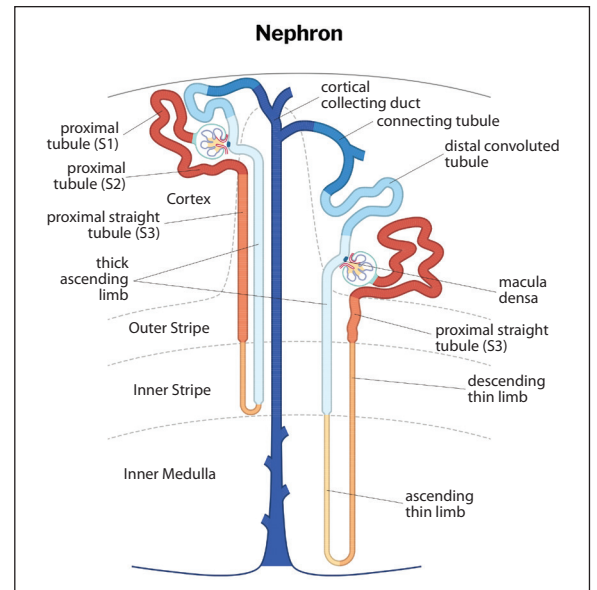
To create a comprehensive Kidney Atlas, Jain and colleagues have been awarded more than \$15 million in total grants from the National Institutes of Health. One is a prestigious Pediatric Center of Excellence grant, awarded to just three institutions in the United States. At Washington University, that grant is shared by the Department of Pediatrics and the Division of Nephrology. Other NIH grants fund the Kidney Precision Medicine Initiative and the Kidney Single Cell and Spatial Molecular Atlas Project (KIDSSMAP) as part of a Human Biomolecular Atlas Project (HuBMAP) funding by the NIH Common Fund and the Kidney Precision Medicine Project (KPMP) funded by the NIDDK.

“Our goal with KIDSSMAP, KPMP, and the other atlas projects is to create an anatomical and molecular ‘metaverse’ of the human kidney that integrates multiple spatial and single cell technologies from anatomical to microscopic scales,” Dr. Jain explains.

The Kidney Translational Research Center at Washington University School of Medicine is one of the key components of Dr. Jain’s atlas projects. Dr. Jain, after finishing his residency training in pathology, established the Center almost 15 years ago after he searched for genetic tissue repositories elsewhere to further his own research on the genetic basis of pediatric kidney diseases.

“We found none, so we established our own bio-repository to facilitate translational kidney disease research with support from the Division and the NIH-funded George O’Brien Center for Kidney Diseases,” Dr. Jain says. “With our dedicated colleagues and support from Pathology, Urology, Pediatric Nephrology, and Nephrology, we now have more than 4,000 patients enrolled with varying kidney and lower tract diseases. Currently two research personnel, Kristy Conlon and Amanda Knoten, help oversee the operations of this highly complex large-scale tissue repository.”

To date, more than 100 investigators worldwide have used the resources of the repository to look for biomarkers of kidney disease, validate basic research findings, and explore new scientific discoveries. Says Dr.

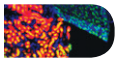


Schemata of the human nephron (short and long loop) developed by the Kidney Precision Medicine Project and the Human Biomolecular Atlas project. *Modified from Krizt and Bankir, Kidney International, 1988*

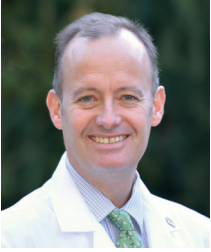
Jain, “One of the most gratifying aspects is that over the years, several trainees, junior and senior investigators, within and outside the university, through KTRC resources were able to secure independent funding and publish high impact papers in the field.”

The first round of atlas grants helped Jain and his colleagues in Pathology (Dr. Gaut) and Urology (Dr. Kim) optimize methods for tissue collection and assay development as well as establish base protocol standards. Now under way is round two, which focuses heavily on integrating single cell technologies with 2D and 3D imaging of tissue samples from healthy, acute, and chronic kidney disease recipients to gain a deeper understanding of cell types and extracellular structures. The multidisciplinary team in these various atlas projects includes experts from Indiana University, University of

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Message from the Chief



Our cover story noted that more than 100 investigators have tapped into the resources of the Kidney Translational Research Center, established

15 years ago by Dr. Sanjay Jain. This is a powerful example of our Division's deep resources for investigative research. Our Division is proud to host 11 dedicated research labs all located together in fully renovated space. From basic cellular and molecular investigations to translational and clinical research, our faculty members are delving into the mechanisms

behind kidney disease and identifying promising targets and pathways for new therapeutics. Research such as this can change the course of patient care and improve outcomes. Examples include the research highlighted on page 6, all recently published in peer-reviewed journals.

As a physician scientist myself, it is rewarding to lead in an environment where critical thinking is nurtured and supported across the academic medical center. Collaborations with investigators from other divisions and institutions are common. Eagerness to learn new skills is also apparent, as in the recent activities among faculty and fellows

to train on the use of point-of-care ultrasound to enhance care at the bedside.

If you didn't get a chance to re-connect with our WashU nephrology faculty at the recent ASN meeting, reach out and let us know how you are doing and where your career path has taken you. We are always interested in updating readers on our alumni!

Benjamin D. Humphreys, MD, PhD
Joseph P. Friedman Professor and Chief
Division of Nephrology
Washington University School of Medicine

Thank You!

Thank you to the following individuals and organizations for graciously donating to our Division from March 2022 through September 2022:

American Heart Association-Dallas
ASN Foundation for Kidney Research
Central Society for Clinical Research
Chan Zuckerberg Initiative
Children's Discovery Institute

Dr. Aubrey R. Morrison
Dr. Eduardo Slatopolsky
Dr. John Mellas
Longer Life Foundation

Support the Division of Nephrology

If you would like to support our research and teaching mission or contribute to the Division of Nephrology's programs and services, please send your contribution to:

Washington University in St. Louis
Office of Medical Alumni and Development
Attn: Rachel A. Hartmann
7425 Forsyth Blvd.
Campus Box 1247
St. Louis, MO 63105

You may also contact Rachel A. Hartmann directly at 314-935-9715 or by email at rachel_hartmann@wustl.edu if you are considering supporting the Division through appreciated stocks, deferred giving, beneficiary plans or other assets.

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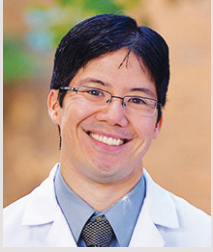
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Fellowship Notes



By Steven Cheng, MD
Director, Nephrology
Fellowship Program

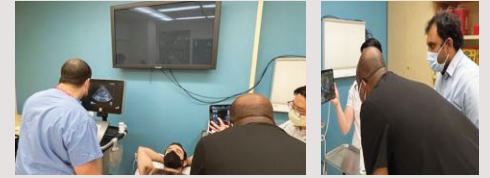
The fellowship training program has always prided itself in preparing trainees not only for the current state of practice in nephrology but for the future of the specialty. This year, for the first time, faculty members Andy Chuu, MD, and Gonzalo Matzumura, MD, presented a point-of-care ultrasound (POCUS) training workshop for nephrology fellows during their orientation boot camp. While POCUS already has been used in other specialties, it has not yet become a standard tool in nephrology. It has, though, the potential to provide significant insights in patient care. Dr. Matzumura noted that with recent advances in technology, POCUS can now be used to explore volume status, blood flow, and anatomic structure at the bedside, which enables nephrologists to tap into a wealth of precise and objective data that can help guide complex decision-making processes.

Both Dr. Chuu and Dr. Matzumura are graduates of our nephrology fellowship

program and have a passion for bringing new imaging techniques to the patient bedside. Already POCUS has been successfully integrated into other specialties such as emergency medicine and critical care medicine. With improvement of ultrasound technologies and, now, portability, Dr. Chuu told trainees that POCUS will become a standard component of patient evaluations in nephrology, too. One of our first-year fellows, Taha Mohamed Djirdeh, MD, commented that the fellows

enjoyed learning these new skills in the medical campus' simulation center and appreciated having a POCUS workshop early in the training curriculum.

We are committed to providing our fellows with the focused didactics, supervised image acquisition, and clinical integration training needed to feel comfortable integrating POCUS into their everyday practice. By all accounts, our first POCUS training session exceeded our expectations.



Images from our first POCUS training workshop

Egress

We congratulate the following fellows for completing their training in our Nephrology Fellowship and now moving on to the next phase of their careers:

Joining the Division of Nephrology



Karen Flores, MD
 Assistant Professor
 of Medicine
 Transplant Nephrology
 Washington University
 School of Medicine

Moving on to Advanced Fellowships:



Jason Cummings, MD
 Critical Care Medicine
 Fellowship
 Washington University
 School of Medicine

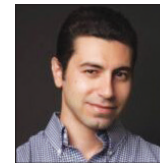


Gaurav Rajashekar
 Transplantation
 Nephrology Fellowship
 Washington University
 School of Medicine



Bharat Neelam Raju, MD
 Critical Care Medicine
 Fellowship
 Stonybrook University
 New York

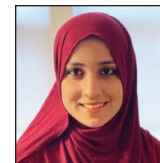
New Career Paths



Mohamed Ibrahim, MD
 Clinical Transplant
 Nephrologist
 Nephrology researcher
 University of Maryland



Hassaan Iftikhar, MD
 Private Practice
 Owensboro, KY



Maryam Saleem, MD
 Private Practice
 Owensboro, KY

Alumni Connections

Munis A. Mattu, MD

*Clinical Associate Professor,
University of South Dakota
Sanford School of Medicine &
Medical Co-Director, Kidney-Pancreas
Program, Avera Transplant Institute
Sioux Falls, South Dakota
2020 Fellow, Transplant Nephrology*



Munis Mattu, MD, has long equated the wonders of nature with the wonders of transplantation.

“My favorite hobby

is gardening, and I like immersing myself in nature,” he says matter-of-factly. “It’s akin to the sensitive care and nurture transplant patients need while preserving the biome.”

Dr. Mattu, a transplant nephrologist, is medical co-director of the Kidney Pancreas Program at the Avera Transplant Institute, located at Avera McKennan Hospital and the University of South Dakota Sanford School of Medicine, where he also serves as a clinical associate professor. The Institute was the first in the South Dakota region to offer kidney transplantation and is the only center there that also has a pancreas transplant program.

“My core responsibilities are patient care and educating internal medicine residents and medical students while they are on their nephrology and transplant rotations,” he says. “We also train interns enrolled in the

Avera Abdominal Transplant Undergraduate Internship Program.”

Dr. Mattu has been a practicing nephrologist in Sioux Falls, SD, since 2017. In 2020, he came to Washington University School of Medicine to complete a one-year advanced fellowship in Transplant Nephrology. The Division accepts two transplant nephrology fellows annually. Dr. Mattu says he was drawn here because the University and Barnes-Jewish Hospital have one of the largest and most respected kidney and kidney/pancreas transplant programs in the United States.

“It was a very rewarding and enriching time in the WashU Kidney and Pancreas transplant program because of its vast experience in treating a diverse spectrum of multi-solid organ transplant patients,” he says. “That experience, under the guidance of world class faculty, improved my clinical expertise to be able to optimize kidney and pancreas transplant care.”

He earned his medical degree from Jawaharlal Nehru Medical College in Belgaum, India, and completed a residency in Internal Medicine at the University of Buffalo in New York and a fellowship in Nephrology at the University Of Kansas School Of Medicine in Kansas City. He went on to serve as a staff nephrologist at the Veterans Affairs Medical Center in

Kansas City from 2014 to 2017. In addition to nephrology training, Dr. Mattu also has three years of emergency medicine clinical experience while serving in the Emergency Department of Riyadh Central Hospital, a Level I trauma center in Saudi Arabia and two years of clinical Nephrology experience at Riyadh Armed Forces Hospital, considered one of the most advanced centers in the Middle East.

When he joined our transplant nephrology training program, Dr. Mattu often talked of his passion for gardening, noting “Sow and nurture the seeds with care.”

While it may be colder this time of year in South Dakota and gardening time is less, Dr. Mattu says that it has been a pleasure working within the Avera Health Care system, a university affiliated healthcare system. In addition to gardening, he spends time with his wife and his two children, whenever they are home from college. “I’m very thankful for the support of the WashU nephrology faculty in enhancing my clinical experiences. My time there was memorable and I was pleased to be able to use that advanced knowledge in my current positions.”



Dr. Mattu (right) with his family

Program Spotlight

Nephrology Services at St. Louis Veterans Affairs Medical Center

Seven years ago, the Division of Nephrology at Washington University School of Medicine had no presence at the St. Louis Veterans Affairs Medical Center. Today, the number of faculty providing care and conducting research at the VA stands at seven, with the Division hard at work to expand the scope of services offered to veterans.

“My overall vision is to make the VA program as full service as possible for veterans,” says Michael Rauchman, MD, the St. Louis VA’s Section Chief of Nephrology. “In general, veterans want coordinated and comprehensive care.”

Dr. Rauchman, professor of medicine in WashU’s Division of Nephrology, has worked at the VA since 1999, first as part of the faculty at Saint Louis University School of Medicine (SLU). When he came to WashU in 2018, he lobbied for the Division to also serve the VA. Division Chief Benjamin Humphreys, MD, PhD, agreed. Now, faculty from both academic medical centers work collaboratively at the VA in a joint nephrology program. Under Dr. Rauchman’s leadership, services have broadened to serve more patients throughout the region. He also helped to establish a Kidney Transplant Clinic at the VA that is directed by Anuja Java, MD.

“In the past year, we have made a big push to grow the home dialysis

program, starting with peritoneal dialysis, which not every VA provides,” says Dr. Rauchman. “That program is directed by Geetha Maddukuri, MD, from SLU. The goal is for a home hemodialysis program to get under way soon that will be under the direction of SLU nephrologist Stephanie Shieh, MD, and for that we also are tapping into the expertise of Manasa Metireddy, MD, Manasa Metireddy, MD, one of the hemodialysis program directors at WashU. These programs highlight the collaborative partnership between WU and SLU.”

Another specialized program led by WashU’s Andy Chu, MD, and Kelly Feigh, PA, is a Hypertension Clinic, which is a critical service because of the large number of VA patients diagnosed with hypertension. Point-of-care ultrasound also is on track to be offered in the coming year. Already, Dr. Chu is training SLU nephrology fellows on its use.

A hallmark of the VA program is the presence of a full-time dietitian and pharmacist dedicated to nephrology. Telehealth services also are offered. Dr. Rauchman hopes that more services will be added, including specialty clinics for the care of patients with kidney stones and glomerular diseases. In a few months, a new outpatient clinic at Jefferson Barracks in south St. Louis County will debut, staffed by Drs. Java and Chu. It will complement an outpatient clinic in north St. Louis County that opened two years ago. “We looked at the



Michael Rauchman, MD, (second from left), with the nephrology team at the St. Louis Veterans Medical Center.

patient demographics and the majority of patients reside in North County and the City,” says Dr. Rauchman. “And with Jefferson Barracks serving as the regional rehabilitation hospital for the VA, it makes sense to provide services closer to where they are needed.”

In addition to patient care, Dr. Rauchman notes the depth and breadth of nephrology research under way at the VA. He is a site investigator for the Million Veteran Program (MVP), a national effort to use electronic medical records to better understand how genetics, lifestyle and military exposures affect health and illness. Other clinical studies focus on diabetic kidney disease. Other WashU researchers that have received VA grants include Leslie Gewin, MD, and Andreas Herrlich, MD, PhD. “There have been landmark clinical trials at the VA that have changed or set standards of care,” says Rauchman, “Therefore, we want to continually expand and enhance the research we conduct.”

Translational Research Center continued from page 1

California-San Diego, University of Nebraska Medical Center, University of Rochester-Minnesota, and Altos Labs in San Diego.

The scientific work already has led to the development of a novel collection

process for tissue specimens for the repository. Dr. Jain and his team now are “tweaking” the method so that they can do more pathology and molecular testing with a single, smaller piece of tissue. “In one biopsy, we can conduct 10 different types of molecular, morphological, spatial, and single cell studies,” says Jain. “That was unheard

of a decade ago. This will significantly enhance the field of diagnostic pathology.”

The goal is for the various research efforts to create a worldwide, diverse atlas of healthy and diseased kidneys. “Our efforts are designed to inform clinical care,” says Jain. “But first you have to have a comprehensive map or atlas as a guide.”

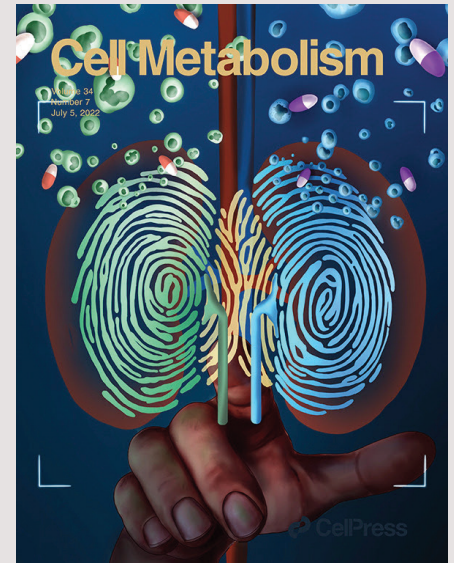
Mapping the Single-Cell Transcriptomic Response of Murine Diabetic Kidney Disease

A recent study led by Washington University investigators has found that combination therapies may be more beneficial than single therapeutics to treat diabetic kidney disease (DKD). The study, published July 5 in *Cell Metabolism*, highlights the complexity of DKD and notes that the various cell types in the kidney need to be targeted by different drug classes to be effective in treating the disease. The research is significant because DKD develops in an estimated 40 percent of patients with diabetes. It can progress to end stage kidney disease and cause early mortality.

Using a murine DKD model to test five treatment regimens using single-cell RNA sequencing, lead author Haojia Wu, PhD, and colleagues from the research lab of Division Chief Benjamin Humphreys, MD, PhD, as well as collaborators from

Janssen Cardiovascular and Metabolic Discovery Research, found that the therapies, including monotherapy and combination therapies, targeted “strikingly different” cell types and induced distinct and non-overlapping transcriptional changes in laboratory models. Combination therapy had the largest effects, but researchers noted that in those cases, the therapy still targeted distinct cell types and were non-overlapping. Investigators also found that sodium-glucose cotransporter-2 inhibitors (SLT2is) induce a state of fasting mimicry and hypoxia responses in the S1 segment of the proximal tube, which suggests a potential target for a new drug class.

Researchers tapped into their 1 million-cell atlas to discern the responses, which they note is the largest mouse kidney single-cell atlas to date. As part of the study, they also generated a data visualization



This cover image in *Cell Metabolism* highlights the research of Haojia Wu, PhD, and colleagues. The image depicts two fingerprints resembling two kidneys that are dissolving into different cell types whose transcriptional responses to therapy were measured. Cover art by Drawimpacts.

tool for use by others conducting DKD research. That tool is available online at <http://humphreyslab.com/SingleCell/>.

Novel Culturing Technique Developed to Study Podocytes

Research into cures for chronic kidney disease (CKD) has been severely hampered because of the difficulty in studying highly specialized cells of the kidney, particularly podocytes, outside their native microenvironment. Now, a novel culturing technique, developed through a collaboration of scientists from the Division of Nephrology and the WashU McKelvey School of Engineering allows for reconstitution of that microenvironment. The technique,

published Aug. 31 in *Science Advances*, highlights a new hydrogel culturing system that preserves the biochemistry and mechanical environments of cultured podocytes. As a result, kidney podocytes can be cultured and rapidly adopt new shapes and express new protein structures that are associated with injury, thereby enabling researchers to identify methods that may control how cells heal themselves. First author of the study is Shumeng Jiang, a doctoral student

in mechanical engineering at the WashU McKelvey School of Engineering. Senior authors include Hani Suleiman, MD, PhD, and Jeffrey Miner, PhD, in the Division of Nephrology and Gey Genin, MS, PhD, co-director of WashU's National Science Foundation Science and Technology Center for Engineering Mechanobiology. This past summer, Dr. Suleiman also was awarded a four year, \$1.37 million R01 grant from the NIDDK to study the “Molecular Determinants of Kidney Podocyte Architecture in Health, Injury, and Recovery.”

Research May Spark Development of Proteinuric Kidney Disease Therapeutics

A recent study by researchers from Washington University School of Medicine provides new insight into a possible novel drug target to treat proteinuric kidney disease. Using a genetic model of nephrotic syndrome (NS) and an acquired model of focal segmental glomerulosclerosis,

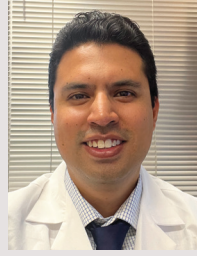
post-doctoral fellow Sun-Ji Park, PhD, and colleagues in the laboratory of Y. Maggie Chen, PhD, identified CHOP (C/EBP homologous protein)-TXNIP (thioredoxin-interacting protein) as critical molecular linkages between albuminuria-induced

ER dysfunction and mitochondria dyshomeostasis. Researchers found that TXNIP relocates from the nucleus to mitochondria when CHOP is induced by albuminuria. Blocking that transfer reduces albuminuria and mitigates kidney injury that occurs as a result of NS. The research was published Aug. 22 in the *Proceedings of the National Academy of Science*.

Faculty News and Awards

Portales-Castillo Joins Faculty

Ignacio Portales-Castillo, MD, has joined the division as Assistant Professor. He earned his medical degree from the Universidad Autonoma de San Luis Potosi in San Luis Potosi, Mexico. Following a residency in internal medicine at Rochester General Hospital in New



York, he completed a nephrology fellowship at Brigham and Women's Hospital and Massachusetts General Hospital in Boston. While in Rochester, he was a 2019 recipient of the Clinical Excellence Award. Dr. Portales-Castillo will provide both inpatient

and outpatient nephrology consults at Barnes-Jewish Hospital. He also will be conducting research related to parathyroid hormone receptor function in the laboratory of Roberto Civitelli, MD, the Sydney M. and Stella H. Schoenberg Professor of Medicine and Chief of the Division of Bone and Mineral Diseases.

Alhamad Presents at International Transplant Meeting

Tarek Alhamad, MD, MS, Director of Transplant Nephrology and Medical Director of the Kidney and Pancreas Transplant Programs at Barnes-Jewish Hospital, offered numerous research presentations at the 2022 international symposium of The Transplantation Society (TTS). TTS focuses on advancements in translational science and clinical practice as well as continuing education on transplantation issues. At this year's gathering, held in Argentina, Dr. Alhamad discussed recent research by he and his colleagues related to the Assessing Donor-derived cell-free DNA Monitoring Insights of kidney Allografts with Longitudinal Surveillance (ADMI-



RAL) study. The research was published in the April 2022 edition of *Kidney International* and found that the use of routine monitoring of donor-derived cell-free DNA after kidney transplant may be beneficial in early identification and treatment of

allograft injuries. Dr. Alhamad also made three other presentations, including one research study that showed mildly obese patients with diabetes mellitus could undergo kidney-pancreas transplants without an increase of mortality or allograft failure. That research could broaden the number of patients qualifying for transplantation. Dr. Alhamad has investigated outcomes and factors that lead to acute or chronic rejection in both kidney and pancreas transplants. He also is the site principal investigator for the NIH's Clinical Trials in Organ Transplantation (CTOT), a national research consortium dedicated to improving transplantation outcomes.

Java Receives NKF Award of Excellence

Anuja Java, MD, Associate Professor of Medicine in the Division of Nephrology and Director of the Kidney Transplant Program at the John Cochran Veterans Affairs Medical Center in St. Louis, was honored with the 2022 Award of Excellence from the National Kidney Foundation (NKF)'s local chapter. The award, the highest honor given by a local chapter, is in recognition of Dr. Java's work to develop new guidelines that improve

early diagnosis and management of chronic kidney disease in high-risk populations in Missouri. The project is part of the Show Me MO CKD Intercept™ initiative to ensure that individuals with CKD receive timely diagnoses, access to high quality care, and educational materials to help inform health-care choices.

Dr. Java is involved in several work groups and committees both nationally and internationally to better define guidelines



for kidney care. She recently was appointed as leader of a new transplant advisory committee for the Veterans Administration's Kidney Medicine Program. In this role, Dr. Java will work to improve quality metrics and standards for kidney transplant programs in the VA system.

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#NephStrong Still Going Strong

After the debut of our #NephStrong t-shirts during the pandemic, the phrase and logo are still going strong! At Renal Grand Rounds in September, Washington University Chancellor Andrew Martin, PhD, was spotted in our t-shirt hanging out with Matthew Sampson, MD, MSCE.

Dr. Sampson, an Associate Professor of Pediatrics at Harvard Medical School and a pediatric nephrologist at Boston Children's Hospital, is a friend of Chancellor Martin's, having spent time together at the University of Michigan. Dr. Sampson served as our visiting professor and keynote speaker for Renal Grand Rounds in September and presented on "Dissecting the Genomics of Steroid-Sensitive Nephrotic Syndrome." He liked his time so much at Washington University he took this photo and posted it on his Twitter feed! Thanks for the shout out! And we're so pleased to see the Chancellor's support for our Division!