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Division of Nephrology and the Center for Immunity, Inflammation & Regenerative Medicine (CIIR)

Chief & CIIR Director: Mark D. Okusa, MD

Since the first dialysis procedure in the Commonwealth of Virginia was performed at UVA on March 27, 1959, the University has been recognized for its excellence in treating kidney diseases. Today, patients receive comprehensive services and medical expertise through the Division of Nephrology and its clinical arm, UVA Kidney Center. The Division of Nephrology is nationally recognized for excellence in clinical care by *U.S. News & World Report's* list of top programs. In 2012 and 2013, the division was ranked as "high performing" in the "Best Hospitals" guide published by *U.S. News & World Report*.

The division, established the same year as UVA's first dialysis procedure, was directed for two decades by W. Kline Bolton. During his tenure (1988-2008), Dr. Bolton initiated an expansion of the division, including all aspects of the academic mission – clinical, educational, and research.

Mark Okusa, John C. Buchanan Distinguished Professor of Medicine, was appointed director of the newly created Center for Immunity, Inflammation and Regenerative Medicine in 2007, and became division chief in 2008. He is recognized internationally for his contributions to both basic and translational research in acute kidney injury, and was elected as Councilor to the American Society of Nephrology in 2012.

Today, the combined enterprises of the Division of Nephrology and the CIIR have 29 full-time faculty members (19 clinical, 10 research), nine clinical fellows, a number of postdoctoral fellows and graduate students, and over 800 dialysis patients. Nephrology faculty serve on national and international committees, advisory groups and editorial boards, and the division has emerged as a nationally recognized program in all facets of academic nephrology, including basic and clinical research.

HIGHLIGHTS

CLINICAL

As Nephrology's reputation has grown over the last decade, so has its clinical practice and patient referrals, reflected in a 27% increase in revenue and 20 percent increase in work RVUs over the last six years. The division has continued to expand its outreach through the establishment of new clinics and services in multiple locations in and around Charlottesville, providing care to patients from a wide swath of central Virginia and, through referrals, many more from elsewhere in Virginia and surrounding states – often for expert opinion, therapies (such as apheresis) and treatments (including experimental drugs) that are not available locally.

New clinical services launched in the last five years include:

- Chronic kidney disease clinic at UVA Orange Dialysis facility
- Kidney stone clinic at Augusta Medical Center
- Dialysis and consultation services at UVA HealthSouth Rehabilitation hospital
- Dialysis and consultation services at UVA Transitional Care Hospital
- Rapid Access Clinic located in the UVA Kidney Center, in which urgent referrals are seen within 24 to 48 hours
- Dialysis clinic in Alta Vista, and home hemodialysis programs, including short daily hemodialysis, in both Charlottesville and Lynchburg
- Transitional Extracorporeal Care Unit (TECU) to care for patients requiring temporary dialysis for acute kidney injury, or that require apheresis on an outpatient basis

The division plans to add urgent-start peritoneal dialysis and ultrafiltration services in the near future.

During FY 2013, all eight UVA dialysis centers, which together served over 800 dialysis patients, achieved "Five Diamond" status from the Mid-Atlantic Renal Coalition (MARC). The MARC program

consists of training modules and resources to help dialysis facilities meet Centers for Medicare & Medicaid Services (CMS) standards for patient and staff safety; each certified facility must complete at least five training modules every year to maintain five-diamond status. This is the third straight year that all of UVA Health System's dialysis clinics have garnered a top patient-safety honor from the MARC program. Only 21 dialysis centers in Virginia have five-diamond status.

Another patient safety-related effort, the Acute Kidney Injury (AKI) Risk Reduction initiative, initiated and managed by Dr. Charles H. Brooks, has decreased the risk-adjusted incidence of AKI, with significant cost savings and reduction in hospital length-of-stay.

Transplant programs: The kidney transplant program at UVA, started in 1967, is currently one of the busiest in the state; it has performed more than 1,800 transplants to date. Kidney transplant recipients come from all over Virginia, from other states, and from other countries; many such referrals involve high-risk recipients or otherwise extremely challenging cases that require state-of-the-art diagnostic and therapeutic approaches. The transplant program offers innovative translational research protocols, including transplantation for sensitized patients (those who are both ABO-incompatible and crossmatch-positive with their only available live donor), as well as donor advocacy and support for altruistic live donation.

The division is working to strengthen its kidney transplant service through enhanced outreach efforts in regions across the state. Its newly renovated outpatient clinic in the West Complex will accommodate a higher volume of patient referrals, and the transplant nephrologists recently recruited to the faculty – Sundararaman Swaminathan, Gayle Vranic and Angie Nishio-Lucar – will further expand its clinical capacity. The goal for the program is at least 125 active patient listings per year, with a target of 5 percent growth each year after 2013. In FY 2013, the program exceeded its forecasted number of transplants. To offset the decreased availability of deceased-donor organs, the program is striving to increase the number of living-donor transplantations.

EDUCATION

The Division of Nephrology maintains a vigorous educational program that spans the spectrum from medical students to residents to fellows to continuing medical education for physicians. The division's post-graduate fellowship program, where future leaders and researchers in nephrology are mentored and taught, is the centerpiece of these efforts. Kambiz Kalantari was appointed director of the fellowship program in July 2012, and is currently revamping it to incorporate changes in ACGME curriculum requirements.

Mark D. Okusa, MD Division chief & CIIR director



Nephrology faculty members have received numerous teaching awards, including UVA's Robly Dungleison award and the American College of Physicians's Evergreen award. Educators from the division have played a leading role in developing the School of Medicine's "NextGen" curriculum, and medical students have given the Nephrology section an "outstanding" rating. The fellowship program's research component has been strengthened with the support of an NIH Training Grant.

Four or five fellows are selected each year for one of three training pathways:

- **Clinical pathway:** two years of training at UVA Medical Center and affiliated centers, with the goal of producing highly accomplished leaders in clinical nephrology
- **Clinical/research pathway:** three or more years of training, including one year of clinical training and two or more years in clinical or laboratory research, for those wishing to pursue independent research careers
- **Research pathway:** for those with advanced degrees (MD and/or PhD) interested in pursuing additional training in either basic or clinical research; supported by a training grant from the National Institutes of Health.

The first fellows to graduate from the division's transplant nephrology training program, a two-year program accredited by the American Society of Transplantation, were Gayle Vranic and Angie Nishio Lucar, who completed their training at the end of June 2013; Dr. Vranic joined the Nephrology faculty in November 2012, and Dr. Lucar joined the faculty in August 2013. Gabor Bodonyi-Kovacs is the third fellow accepted into the program, supported by a T32 research training grant.

Clinical Nephrology fellows for the 2012-2013 academic year were:

■ **Second year:** Samir Gautam, Daphne Harrington, Sana Khan, Hans Yehnert

■ **First year:** Mary Muoneke, Atul Bali, Rohit Arora, Helga Vamenta-Morris.

Current research fellows are Joseph Gigliotti and Pei-Lun Chu.

At the Mid-Atlantic Young Investigators Nephrology Forum, fellows have an opportunity to present their research to a panel of nationally recognized investigators as well as their peers. At the spring 2013 meeting, first prize in basic science was awarded to Joseph Gigliotti, a post-doctoral fellow in Mark Okusa's lab; second prize went to Katarzyna (Kasia) Jaworska, a student in Bert Kinsey's lab. Winners go on to compete in the National Young Investigators Forum held in conjunction with the annual National Kidney Foundation meeting.

Division faculty provide continuing medical education content and other educational opportunities for professionals through a variety of venues, including:

■ **Renal Grand Rounds and Fellows conference:** A weekly division conference that is broadcast to telemedicine affiliates in Lynchburg, Augusta, Salem and Culpeper.

■ **Therapeutic Apheresis Academy:** A division-sponsored two-and-a-half-day conference, offered annually since 2008 and designed for physicians in nephrology, hematology,

NEW DISCOVERIES:

Ultrasound may prevent injuries to kidney during surgery



Nephrology post-doctoral fellow Joseph Gigliotti

Joseph Gigliotti, a postdoctoral fellow in the lab of Nephrology division chief

Mark Okusa, recently discovered that ultrasound appears to have a therapeutic use in preventing acute kidney injury, which can sometimes result from heart surgery, abdominal surgery or other major procedures. He has tested the discovery in mice, and he and Okusa are excited about the promise it could hold for humans.

"A patient having cardiac surgery or other procedures with a high risk for acute kidney injury could potentially benefit from the application of a simple ultrasound procedure as a protective measure," says Okusa. "Noninvasive, no drugs, simple and portable – yet capable of protecting the kidneys from injury."

Acute kidney injury may result from a loss of blood flow to the kidneys, causing a loss of kidney function and potentially prompting a cascade of serious, even life-threatening complications.

Okusa's lab, supported by an NIH grant, was investigating the use of microbubble-mediated, contrast-enhanced ultrasound to deliver drugs directly to the kidney, when the research team discovered the protective benefit from ultrasound alone.

Ultrasound does not appear to act on the kidney but rather on the spleen, an organ that helps regulate immune system responses. "During acute kidney injury, the spleen sends out inflammatory signals that lead to further injury to the kidney," Okusa explains. "Exposing the spleen to ultrasound blocks these inflammatory signals and preserves kidney function."

They found that an ultrasound could be administered up to two days before an injury and still have a protective effect; after that, the benefits begin to wane. In the next stage of research, UVA Nephrology colleague Kambiz Kalantari will lead human studies of ultrasound treatment to prevent acute kidney injury.

The study, published in the *Journal of the American Society of Nephrology*, was accompanied by an editorial saluting the discovery: "We believe that splenic ultrasound stimulation has a bright future ahead," the editors wrote.

Reference:

Joseph C. Gigliotti, Liping Huang, Hong Ye, Amandeep Bajwa, Krypt Chattrabuthi, Sangju Lee, Alexander L. Kilbanov, Kambiz Kalantari, Diane L. Rosin and Mark D. Okusa. Ultrasound prevents renal ischemia-reperfusion injury by stimulating the splenic cholinergic anti-inflammatory pathway. *J Am Soc Nephrol* 2013 Sep;24(9):1451-60.

pathology/blood banking and other allied health professionals. It is chaired by Rasheed Balogun and taught by members of the Nephrology faculty.

■ Recent Advances in Internal Medicine: Annual Department of Medicine conference (sponsored by UVA Office of Continuing Medicine Education and School of Medicine) with Nephrology faculty participation.

■ National Kidney Foundation of the Virginias clinical meetings: Nephrology faculty provide educational content.

RESEARCH

The Division of Nephrology and the Center for Immunity, Inflammation and Regenerative Medicine (CIIR), are at the forefront of basic and translational research in kidney disease,



immunity, autoimmunity, inflammation and regenerative medicine. Together, they have generated more than \$20 million in research and training awards over the last five years. The CIIR, established in 2007, facilitates the transition of immunological concepts underlying

human disease to clinical trials; research labs for both the division and the CIIR are housed in approximately 9,000 square feet of renovated, state-of-the-art space in Jordan Hall. The center serves as an important training ground for undergraduate, graduate and medical students, and postdoctoral fellows and visiting scientists in nephrology and allied fields. The division has internationally recognized research programs in acute kidney injury, Goodpasture's syndrome, genetics of hypertension, pathogenesis of lupus nephritis, biology of natural killer T cells, dendritic cells and macrophages, and immunobiology of transplantation. Biostatistical support for division research is provided in part by Jennie Ma, PhD, who has a joint appointment in Nephrology and the Department of Public Health Sciences.

Division and CIIR faculty have a total of 17 active NIH grants, including 10 R01 (research) awards; three R21 (exploratory/developmental) research awards; two career development ("K") awards; a T32 training grant, renewed until 2016; and a U19 (cooperative agreement) research program award. With the shrinking of NIH dollars, younger faculty member have to work harder than ever to secure research support, so it is particularly noteworthy that assistant professors Amandeep Bajwa and Gilbert Kinsey were both able to obtain NIH career development awards.

MORE HIGHLIGHTS:

Harini Bagavant: received one-year grant from National Kidney Foundation to study pathogenesis of lupus

Umesh Deshmukh: completed second of two-year NIH R21 (exploratory research) award to study "Innate immunity activation in pathogenesis of Sjogren's syndrome"(5R21DE019883-02)

Shu Man Fu: received \$195K grant from the Alliance for Lupus Research to study "Progressions and biomarkers of proliferative lupus nephritis"

Mark Okusa: renewed NIH grant on "Leukocyte trafficking in acute renal failure," now in its tenth year, for additional four-year period

Sundararaman Swaminathan: received a Pilot and Feasibility Grant from UVA entitled "Role of Myeloid Osteogenic Cells in Vascular Calcification of End Stage Renal Disease"

Active NIH awards (for clinical trials, see box):

Amandeep Bajwa, PI:

■ K01DK091444-01A1 – Sphingosine-1-phosphate receptor 1

A busy year for Rasheed Balogun

Rasheed A. Balogun, MBBS, was appointed to the board of directors of the American Society for Apheresis at the ASFA's annual meeting in May 2013. The Society advances apheresis medicine for patients, donors and practitioners through education, evidence-based practice, research and advocacy.



Additionally, Dr. Balogun directed the Division of Nephrology's Sixth Annual Therapeutic Apheresis Academy in September 2013. The Academy, held in Charlottesville and sponsored by the UVA Office of Continuing Medical Education, is designed for physicians in nephrology, hematology and related disciplines. Therapeutic apheresis is the separation of whole blood into its major components and removal of the abnormal, pathogenic component; apheresis procedures are performed for various hematologic, neurological, renal, and other disorders – usually as a measure of last resort.

On the global front, Dr. Balogun serves in the International Society of Nephrology's Educational Ambassador Program, which works to advance nephrology medicine in developing countries through hands-on training while involving younger nephrologists in shaping national renal programs and policies. He is also on the council of the International Society for Blood Purification, and the editorial boards of the *Journal of Clinical Apheresis* and the *Journal of the American Society of Artificial Internal Organs*.

NEPHROLOGY CLINICAL TRIALS

W. Kline Bolton, PI:

■ Study to Evaluate the Long-Term Efficacy & Safety of Oral Tolvaptan Tablet, Protocol 156-08-271

■ A Three-period, 58-week safety and efficacy trial of KRX-0502 (ferric citrate) in patients with end-stage renal disease on dialysis, KRX-0502

■ Celgene Renal Anemia Study, ACE-011-REN-001

■ A Long-Term Safety Extension Trial of KRX-0502 in Patients with End-Stage Renal Disease on Dialysis, KRX-0502

Charles H. Brooks, PI:

■ A randomized, multicenter, double-blind, placebo controlled study of AC607 for the treatment of acute kidney injury in cardiac surgery subjects (Phase 2), AC6071103

Mitchell Rosner, PI:

■ MD-INMD Covance, Inc. – Tolvaptan PKD-156-09-290, 156-09-29.

and 3 as novel targets in transplantation

Umesh Deshmukh, PI:

■ 1R21DE022977-01 – Adenosine receptors and restoration of salivary gland in Sjogren's syndrome

■ 5R01AI079621-04 – T cell epitope mimicry for autoimmune responses in systemic lupus erythematosus (SLE)

Shu Man Fu, PI:

■ 5R01AR047988-12 – Cellular and genetic basis of systemic lupus

■ 5R01AR049449-08 – HLA-D region in systemic lupus erythematosus pathogenesis



■ Alliance for Lupus Research – “Progressions and biomarkers of proliferative lupus nephritis”

Kambiz Kalantari, PI:

5K23DK074616-05 – Adenosine 2a Receptor Agonist in Diabetic Nephropathy

Gilbert Kinsey, PI:

5K01DK088967-03S1 – Regulatory T Cells as a Novel Therapeutic Agent/Target for Acute Kidney Injury

Thu Le, PI:

■ 5R01DK094907-02 – Contribution of GSTM1 to the severity of hypertension and chronic kidney disease

Li Li, PI:

■ American Heart Association Scientist Development Grant #0835258N – Type I and type II NKT cells: immunity and tolerance in kidney ischemia/reperfusion injury”

Peter Lobo, PI (Mark Okusa, co-PI):

■ 5R01DK083406-04 – Naturally occurring IgM anti-leucocyte autoantibodies protect against renal ischemia-reperfusion injury

Mark D. Okusa, PI:

■ 5R01DK085259-04 – Sphingolipids in acute kidney injury

■ 5R21DK093841-02 – Nanotherapeutics for acute kidney injury

■ 2R01DK062324-10A1 – Leukocyte trafficking in acute renal failure

FACULTY RECRUITMENT, RECOGNITION & SERVICE

During the 2012–2013 academic year, the division welcomed six new faculty members: Daniel Hu and Sundararaman Swaminathan (associate professors); Gayle Vranic (assistant professor, former UVA fellow in kidney transplantation); and John Hayes and Joshua King (instructors). In addition, three assistant professors were hired to start in July and August 2013: Brendan Bowman, Angie Nishio-Lucar and Jwalant Patel.

Division faculty members received numerous awards and recognition from peers and colleagues during the 2012–2013 academic year. At the Department of Medicine awards ceremony in August 2012, Thu Le received the Outstanding Research award; Garland Campbell, the Outstanding Clinical Activity award; and Kambiz Kalantari, the Outstanding Educator award. Kambiz Kalantari was also named to the School of Medicine’s Academy of Distinguished Educators. W. Kline Bolton was inducted into the MilliPub Club by UVA’s Claude Moore Health Sciences Library searchers, in recognition of a single paper that has been cited over 1,000 times.

The 2013 “Best Doctors in America” list included four Nephrology faculty members (Bolton, Kalantari, Okusa, Rosner), as did the Castle Connolly “Top Doctors in America” list (Balogun, Bolton, Erdbruegger, Okusa). Other notable achievements:

Rasheed Balogun was appointed to the board of the American Society for Apheresis; Council member, International Society for Blood Purification

Shu Man Fu received a 2012 Distinguished Basic Investigator Award from the American College of Rheumatology, for outstanding contributions to the field of rheumatology.

Thu Le was elected a fellow of the American Heart Association.

Mark Okusa was elected a Councilor of the American Society of Nephrology.

David E. Simmons Jr. received the 2012 Trailblazer Award from the National Black Nurses Association.

Additional service:

■ **NIH/Center for Scientific Review committees, and other grant review committees**

• **Harini Bagavant:** NIH Immunobiology study section

• **Michael Brown:** NIH Immunity and Host Defense study section

• **Umesh Deshmukh:** NIH Special Emphasis panel ZDE1 RK (05)

• **Thu Le:** NIH Genetics of Health and Disease study section
Mark Okusa: Member, NIH/NIDDK-F subcommittee on F-Awards

• **Mitch Rosner:** NIH Special Emphasis Panel ZDK1 GRB-J O2

• **Shu Man Fu:** NIH Arthritis, Connective Tissue and Skin Study Section; Department of Defense CDMPP review panels on lupus and immunology

■ **Professional organizations**

• **Emaad Abdel-Rahman:** Geriatric Nephrology advisory group and organizing committee; Advances in Geriatric Nephrology scientific committee and course

• **Mitch Rosner:** co-director, American Society of Nephrology (ASN) board review course (San Francisco, August 2012); member, Education Executive Committee, ASN; member, Board of Advisors, Renal Physicians Association; member, Program Committee, Association of Professors of Medicine; co-organizer (with Mark Okusa) of the 2014 Acute Dialysis Quality Initiative (to be held at UVA)

• **Mark Okusa:** Councilor, ASN; Public Policy Committee, ASN; Acute Kidney Injury Advisory Group, ASN; Acute Kidney Injury Network

■ **Journal editorial boards**

• **Rasheed Balogun:** Journal of Clinical Apheresis; Journal of the American Society of Artificial Internal Organs

• **W. Kline Bolton:** Clinical Journal of the American Society of Nephrology

• **Shu Man Fu:** Cellular and Molecular Immunology; Clinical Immunology; F1000 Research (Immunology)

• **Thu Le:** American Journal of Physiology; Renal Physiology (associate editor)

• **Mark Okusa:** Kidney International; Journal of the American Society of Nephrology; American Journal of Nephrology

• **Mitch Rosner:** American Journal of Kidney Disease (section editor); Clinical Journal of the American Society of Nephrology; Kidney International; Nephron Clinical Practice

• **Sundararamn Swaminathan:** Kidney International

• **Rahul Sharma:** Modern Research in Inflammation; Advances in Medicine: Immunology section

SELECTED PUBLICATIONS 2012

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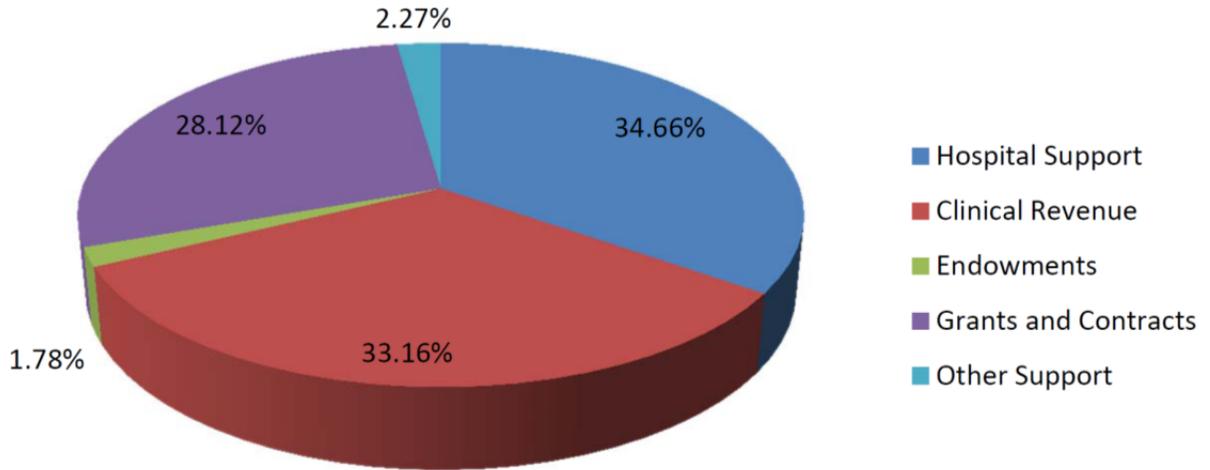
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Nephrology by the Numbers...

Sources of Revenue \$12,366,681



Grants and Contracts \$3,478,041

