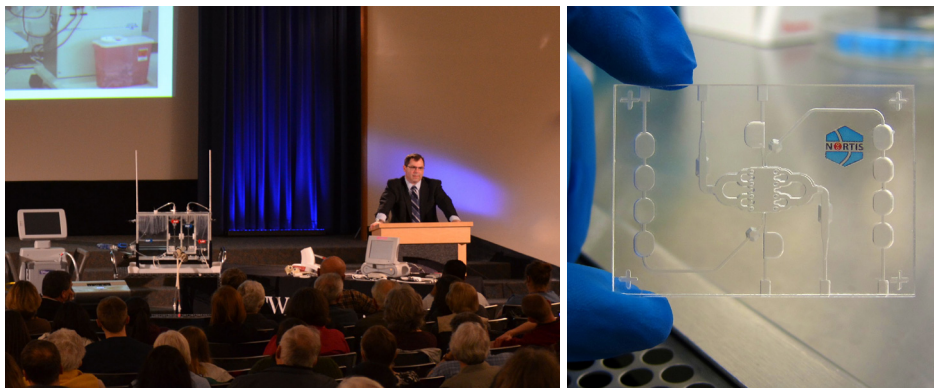


A collaboration between Northwest Kidney Centers and UW Medicine



LEFT: Dr. Jonathan Himmelfarb spoke about two exciting projects, the wearable artificial kidney and the human kidney-on-a-chip, at UW Medicine's Mini-Medical School March 12.

RIGHT: A close-up of a kidney-on-a-chip. Read more about this project below.

Ten top studies impacting patient care

A message from the director

DR. JONATHAN HIMMELFARB

The Kidney Research Institute was developed in response to growing concerns over the public health implications of kidney disease. More than 20 million people in the United States are affected by kidney disease, while major gaps in our knowledge base hinder the delivery of optimal medical care to affected people. **Our mission** is to conduct research that has high potential to tangibly improve the lives of those with kidney disease. **Our vision** is that every person with kidney disease will be informed about, participate in, and benefit from research. **Our goal** is to bring the best science to the bedside. We continue to focus efforts on early detection, prevention and treatment of kidney disease and its complications, consonant with the public health component to our mission.

Below are ten active, ongoing or planned studies that have high potential to significantly impact patient care.

1. Preventing acute kidney injury in children undergoing open heart surgery. The Seattle Cardiorenal Remote Ischemic Preconditioning Trial (SCRIPT) study, led by Dr. Christine Hsu, looks at whether remote ischemic preconditioning, a novel non-invasive intervention, can prevent acute kidney injury in children undergoing cardiac surgery. Acute kidney injury in children undergoing cardiac surgery is common and dramatically increases the risk of mortality. Currently there are no effective strategies to prevent this complication in these children. We anticipate results by the end of 2013.

2. Improving outcomes by enhancing healthy lifestyle interventions in people with moderate to severe chronic kidney disease. The Aerobic Exercise and Diet for Enhancing Metabolic Improvement (RESTORATIVE) clinical trial is a landmark study evaluating the value of aerobic exercise and lower calorie diets in people living with chronic kidney disease. We anticipate results in 2014.

3. Enhancing drug safety in kidney disease by developing a human kidney-on-a-chip. The kidney-on-a-chip uses an in vitro three-dimensional system to create tissue chips that mimic critical functions of a living human kidney. The kidney-on-a-chip project is designed to improve drug safety testing, and can be used to identify new strategies for preventing kidney injury by drugs and environmental toxins.

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ON THE HORIZON

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**TRANSFORMING LIVES THROUGH
INNOVATION AND DISCOVERY**

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Ten top studies

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4. Clinical trials of a wearable artificial kidney. A wearable artificial kidney has been a dream of patients, physicians and scientists since the inception of dialysis. We will play a major role in the first U.S. trials of this machine, trials conducted under the auspices of the federal Food and Drug Administration's new Innovations Pathway program. The device, which weighs less than 10 pounds and is worn in a belt around the waist, delivers dialysis therapy on an ongoing basis, an ideal alternative to in-center dialysis.

5. Improving outcomes of diabetic kidney disease. Novel diagnostics and therapeutic targets are needed to prevent complications of diabetic kidney disease. Our ongoing Study of Glucose and Insulin in Renal Disease (SUGAR), led by Dr. Ian de Boer, evaluates how chronic kidney disease effects the body's ability to metabolize glucose. The Vitamin D and Omega-3 (VITAL) trial, also led by de Boer, studies whether vitamin D administration can prevent early diabetic kidney disease.

6. Bioengineering to improve dialysis technology. We are currently working with the University of Washington School of Bioengineering to improve dialysis technology. Projects are underway or in planning to do the following: bioengineer dialysis membranes resistant to clotting, use anticoagulants to help prevent bleeding complications, engineer dialysis catheters highly resistant to infection, and enhance the use of fistulas for dialysis.

7. Enhancing the success of home dialysis therapies. Home dialysis modalities are an underutilized method of dialysis with the potential to provide patients with better quality of life and better opportunities for rehabilitation compared to in-center dialysis. Led by Dr. Raj Mehrotra, KRI investigators are developing new tools to enhance the use of home therapies, and to improve outcomes of peritoneal dialysis through local and international studies.



Laboratory manager John Ruzinski centrifuging samples in the lab.

8. Improving cardiovascular outcomes in people with chronic kidney disease. In an effort to reduce the high rate of cardiovascular events in people with chronic kidney disease, Dr. Bryan Kestenbaum and other KRI investigators are conducting clinical trials and studies on new therapies designed to prevent calcification in the heart and blood vessels and reduce inflammation and oxidative stress.

9. Improving kidney disease outcomes in the urban poor. Led by Dr. Yoshio Hall, KRI investigators have published landmark papers characterizing the impact of health organizational characteristics on the quality of kidney disease care for the urban poor. Hall is now developing patient-centered interventions to improve the delivery of chronic kidney disease care to diverse populations. Led by Dr. Bessie Young, investigators are also developing new tools for educating African Americans about preventing kidney disease.

10. Development of a patient registry and biorepository. Our patient registry includes participants interested in being contacted about research, allowing us to better determine eligibility for existing and future studies. Our expansive data and tissue repository currently holds more than 100,000 samples of blood, urine, tissue specimens and DNA. We expect to add many new samples every year.

Study finds increased risk of mortality among type 2 diabetics with kidney disease



Dr. Maryam Afkarian.

Kidney Research Institute investigator Dr. Maryam Afkarian's recent study investigated the impact kidney disease has on the mortality of those with type 2 diabetes.

"We wanted to figure out just how big a role kidney disease plays in people with type 2 diabetes," says Afkarian. "What we found was that yes, type 2 diabetics who also have kidney disease have a much higher rate of mortality than those who do not have kidney disease."

Just how much of an increased risk does kidney disease add? Afkarian studied mortality rates over a 10-year period in more than 15,000 adults, some with both diseases and some with just type 2 diabetes.

The mortality rate for people with diabetes but no kidney disease was 11.5 percent. This increased dramatically to 31.1 percent for those who suffer from both diabetes and kidney disease.

"Now that we know just how big an impact kidney disease has on people with type 2 diabetes, we can focus more efforts on preventing kidney disease from ever developing in this group of people," says Afkarian. "This could be a powerful way of reducing deaths among people with diabetes."

Results from this study were published in the February issue of the *Journal of the American Society of Nephrology*.

Exploring the connection between cardiovascular disease and kidney health

Dr. Rick Newitt is using the powerful analytical tools of mass spectrometry to help answer questions about the causes of kidney disease.



Dr. Rick Newitt.

Newitt and other KRI scientists are currently probing the close association between poor cardiovascular health and kidney disease. Cardiovascular events like heart attacks and strokes are a major cause of premature mortality in patients with kidney disease. Past studies have shown links between the levels of choline and its metabolites, particularly trimethylamine oxide (TMAO), and the presence of cardiovascular disease. People with chronic kidney disease also accumulate TMAO. The more we understand about these metabolites, the better we will be at identifying kidney disease patients who may go on to develop cardiovascular problems.

Investigators are currently studying hepatic flavin monooxygenases, focusing on FMO3, which is known to play a role in the accumulation of TMAO in humans.

With 15 years of mass spectrometry experience in small molecule, proteomics and protein characterization at universities, private biotech companies and non-profits in the Seattle area, Dr. Rick Newitt aims to provide new in-house resources to the kidney research community.

Newitt and other KRI

“In collaboration with Dr. Cathy Yeung, we are using FMO3 genotype analysis and mass spectrometry to assess the levels of TMAO and other choline metabolites in patients with progressive kidney disease,” says Newitt. “The goal is to establish a clear association between elevated levels of uremic toxins to clinical cardiovascular outcomes, as patients with higher levels of TMAO and other compounds may indicate they are more likely to develop cardiovascular disease.”

Understanding the causes of cardiovascular disease in kidney disease patients will enable us to improve the health of these patients in the future.



The mass spectrometer, a useful tool available for Kidney Research Institute investigators to use for analyzing specimens. We anticipate that more and more KRI research projects will be utilizing this valuable resource in the future.

Recent papers by two Kidney Research Institute fellows



Dr. Baback Roshanravan.

ASSOCIATION BETWEEN PHYSICAL PERFORMANCE AND ALL-CAUSE MORTALITY IN CKD

Journal of the American Society of Nephrology, upcoming issue

Dr. Baback Roshanravan, senior fellow

Roshanravan's recent study results show an increased risk of mortality in chronic kidney disease patients who have a slower gait.



Dr. Bernadette Thomas.

GEOGRAPHIC VARIATION IN BLACK-WHITE DIFFERENCES IN END-OF-LIFE CARE FOR PATIENTS WITH END-STAGE RENAL DISEASE

Clinical Journal of the American Society of Nephrology, upcoming issue

Dr. Bernadette Thomas, senior fellow

Thomas's study results demonstrate significant racial disparities in the end of life care that kidney failure patients in the United States receive.

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Life doesn't end
because you have
renal disease.

The heart of research: why one man joined a Kidney Research Institute study

When Michael E. Wiley, Sr. found out his kidneys were failing in 2000, he knew he needed to make some serious lifestyle changes. By controlling his blood pressure and changing his diet, he managed to hold off on dialysis for more than ten years.

On dialysis for a year and a half now, Wiley, 55, is currently involved in his second Kidney Research Institute study.

"I'm always willing to be involved," says Wiley, an ordained deacon. "All I do is take a pill every day. It's painless and really could help."

The Endothelial Dysfunction Nitric Oxide and Renal Failure study tests the hypothesis that certain drugs differ in their long-term effects on cardiovascular events in chronic kidney disease patients undergoing maintenance hemodialysis.

In short, we know there is a link between cardiovascular disease and kidney disease. The hope with this study is to learn more about which drugs work better in preventing heart problems in dialysis patients who, like Wiley, have high blood pressure.

On the kidney transplant list, Wiley undergoes dialysis three times a week at a Northwest Kidney Centers' facility in Seattle.

"I'm hoping they find something in the future so people don't have to go through dialysis," says Wiley. "But for now, I want to show people life doesn't end because you have renal disease. Research is one way to give back — it might not help me but it could help others down the road."