KIDNEY RESEARCH INSTITUTE

A collaboration between Northwest Kidney Centers and UW Medicine

ON THE HORIZON

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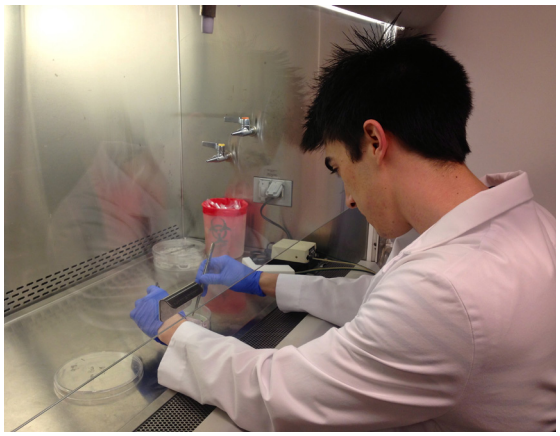

LEFT: Jacqui Seet, RN interviews a participant in the Preventing Early Renal Loss trial. Learn more about this trial that aims to identify a more effective treatment for diabetic kidney disease on page 2.

RIGHT: Ryan Nagao, a postdoctoral fellow, works on kidney microvessels as part of the kidney-on-a-chip project. Read more on page 3.

Updates from early 2015

A message from the director

DR. JONATHAN HIMMELFARB

There is much to report as we move into 2015. We recently made our annual presentation to Northwest Kidney Centers' Board of Trustees. We spoke about our continued focus on scientific themes geared to public health as well as new initiatives around dialysis innovation. Examples of some additional studies for 2015 include:

- developing needle-less vascular access for hemodialysis patients
- looking at activated vitamin D as a way to prevent cardiac events in chronic kidney disease patients
- reviewing options for the treatment of depression in patients undergoing hemodialysis
- investigating new methods to measure kidney function
- examining new methods for preventing drug dosing errors in kidney disease.

In this newsletter you'll read about an active clinical trial that's testing a drug that could slow down the progression of diabetic kidney disease, the latest on the kidney-on-a-chip project and a study that has brought critical care doctors at University of Washington into kidney research.

In addition, Northwest Kidney Centers (NKC), an organization that helped found the Kidney Research Institute in 2008 and one we still work closely with, is holding its 13th annual Breakfast of Hope on May 14. This year's event will support NKC's transplant support services and charity care program. Your support of the Kidney Research Institute and its partners makes it possible for us to continue our efforts around groundbreaking research, educational outreach and community involvement — all activities that align with our mission to improve the lives of people with kidney disease.

TRANSFORMING LIVES THROUGH INNOVATION AND DISCOVERY

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Kidney Research Institute joins large multi-center study, forms group to investigate new treatments for diabetic kidney disease

Diabetes is the leading cause of chronic kidney disease, but treatment for it is limited.

Dr. Maryam Afkarian is investigating the impact of allopurinol on people with diabetic kidney disease. She also leads a group of researchers working to find new ways to treat the disease.

"Right now, we tell people to control their blood sugar and blood pressure and take a group of medications called renin angiotensin inhibitors," says Dr. Maryam Afkarian, assistant professor of medicine at University of Washington and an investigator at the Kidney Research Institute, "but despite all of these treatments, many people progress to dialysis."

Afkarian and other investigators at the Kidney Research Institute hope their work on the Preventing Early Renal Loss trial — PERL for short — might help identify a more effective treatment for diabetic kidney disease. PERL, a large, multi-center clinical trial funded by the National Institutes of Health and the Juvenile Diabetes Research Foundation, aims to test the drug allopurinol to see if it slows down kidney disease in people with Type 1 diabetes.

"Allopurinol has been used for decades to reduce uric acid in people with gout and cancer," says Afkarian, "and small trials have shown it is also effective in slowing kidney disease progression. Now we need a large clinical trial to confirm this is an effective treatment in diabetic kidney disease."

Just 10 percent of people with diabetic kidney disease have Type 1 diabetes. The other 90 percent have Type 2.

"Every hope is that once we find out how allopurinol affects Type 1 diabetics with chronic kidney disease, we can then test it with people who have Type 2 diabetes and CKD," says Afkarian. "In the past, most medications that have worked for kidney disease in Type 1 diabetes have also worked in Type 2, so we are very hopeful the same would happen here."

To further research in this area, KRI investigators formed a diabetic kidney disease working group in 2011.

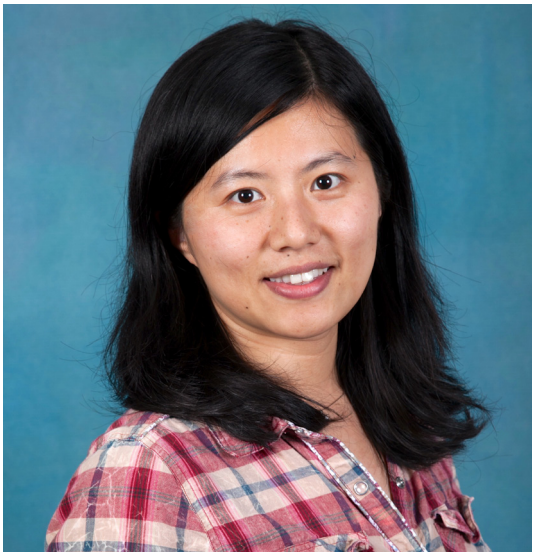
"We have many talented diabetes researchers in this area," says Afkarian, "at the KRI, Benaroya, UW and other institutions. The idea is to bring everyone together to exchange ideas, take data from basic research all the way to clinical settings to come up with new ways to treat and diagnose diabetic kidney disease, and implement a true translational approach to this disease that affects so many people."

The group meets once a month and "the ideas just keep rolling," says Afkarian. "It's great to work with such a talented and collaborative group. More importantly, I really think it's the only way to crack a complex problem like kidney disease."

Coordinators conduct PERL study visits at the Kidney Research Institute's space at Northwest Kidney Centers in Seattle, Wash.

Investigators make progress on kidney-on-a-chip and look to the future: 3D-printing a kidney

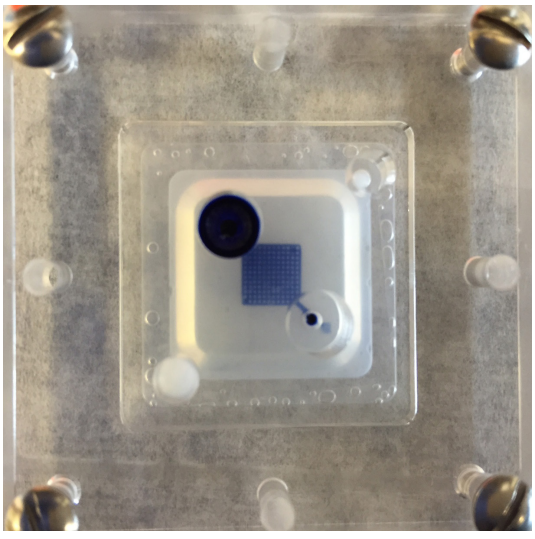
For Dr. Ying Zheng and her team of eight researchers, the last two and a half years have been busy.



Dr. Ying Zheng.

"We've continued to work on reconstructing kidney blood vessels onto a chip, creating a tiny model of this particular part of the kidney," says Zheng, an assistant professor of bioengineering at University of Washington. "We're now able to isolate, purify and characterize different components of peritubular microvascular cells. No one's ever done that before. We're starting to find out how different the cells in the kidney really are."

Zheng and her team of bioengineers are working on the kidney-on-a-chip project, which aims to create tissue chips that mimic the function of a live, working kidney. Scientists from University of Washington Departments of Medicine, Environmental Health and Pharmaceutics are currently building chips that show how different parts of the kidney function. Later, researchers will combine individual components to create chips that reflect an entire kidney and those chips will then be used to test how the kidney responds to different drugs.



A chip, the size of a dime, with microvessel networks.

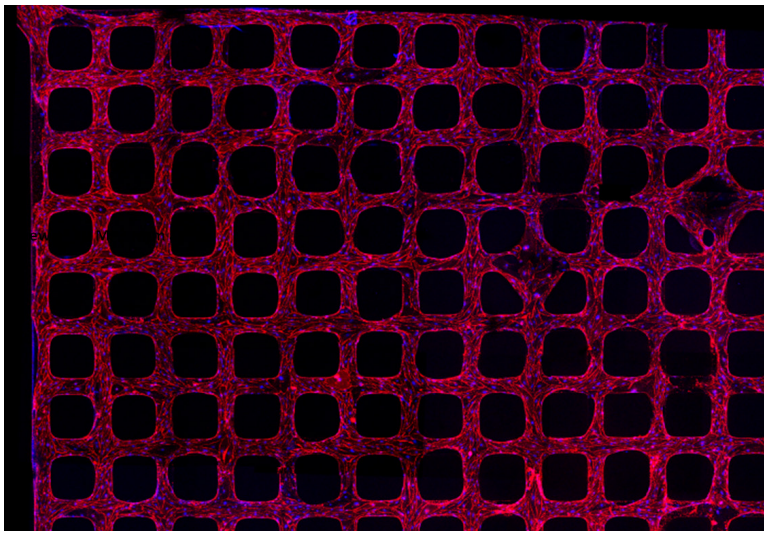
"Not much is known about how kidney blood vessels get injured," says Zheng. "We recently used the chips we've built to look at blood vessel response to a drug, making this the first study to show the toxicity of a drug on kidney blood vessels."

Zheng and her team tested an immunosuppressant given to patients who have had an organ transplant.

"What we're finding out is that kidney cells lack regenerative properties, meaning that once they're injured, they can't recover. We need to continue our work to better understand what these drugs do to kidney vessels. The next step, then, is to test different drugs, understand how the cells are being injured and then see what we can do to fix those injuries."

In 2015, Zheng introduced another potential tool for building kidney models to her lab — a 3D printing machine.

"If we could take advantage of 3D printing technology, we could design a model, print it and use that to explore the compartments and architecture of the kidney.



A close-up view of a chip with engineered human kidney microvessel network, with endothelial cells stained in red. Researchers are using chips to study the impact of drugs on human kidney blood vessels.

"The idea with 3D printing organs is similar [to the chip] — we need to build structures that mimic the actions of an actual kidney. For example, the kidney is an oxygen-deprived organ. Can we locally introduce oxygen? Can we introduce precursor cells? Will these actions help injured cells regenerate? Maybe. We just don't know. If we could perfect 3D printed kidneys, we could test many hypotheses before they go to trial."

Right now, investigators in Zheng's lab are testing the machine but they're hopeful 3D printing could eventually be used to build a complete kidney model.

"We know the technology, they [the KRI] know what we can make an impact on — it's the perfect match."

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'AKI is so prevalent in hospitals — 30 to 40 percent of patients in the ICU develop it — but we don't know how people develop it and what complications they experience after they leave.'

Critical care doctors study long-term effects of acute kidney injury in intensive care patients

Critical care doctors at University of Washington first teamed up with the Kidney Research Institute to study acute kidney injury back in 2010.

"We started participating in ASSESS-AKI, a consortium with clinical centers around the U.S., about five years ago," says Dr. Mark Wurfel, an associate professor at University of Washington and a critical care doctor at Harborview Medical Center in Seattle. "The study aims to discover the long-term effects of acute kidney injury."

Wurfel and his team completed initial recruitment for the study in February.

"We've enrolled 400 subjects and have followed many for three or four years already. We plan to continue to follow them for an additional seven or eight years. We're interested in what, if any, long-term renal dysfunction occurs and also if genetic factors might predict development of AKI."

ASSESS-AKI is the largest prospective cohort to study AKI and the only one to follow patients for such a long time.

"AKI is so prevalent in hospitals — 30 to 40 percent of patients in the ICU develop it — but we don't know how people develop it and what complications they experience after they leave."

Other critical care doctors at UW are also researching AKI's impact on patients in intensive care.

"We're hoping for ongoing funding for AKI research," says Wurfel. "I'm a critical care physician. Many of my patients would directly benefit from research into the causes of AKI."