Gold nanoparticles may help improve understanding, detection of kidney disease

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UT Dallas scientists are developing an innovative research technique that

could help urologists better understand the early stages of kidney disease.

Dr. Jie Zheng, associate professor of chemistry and biochemistry at UT Dallas, and his colleagues have combined tiny gold nanoparticles with a technique called in vivo near-infrared fluorescence imaging to study early stage kidney disease in a live animal model.

The research, described in a recent study published in the journal *Angewandte Chemie*, overcomes a long-standing challenge to the study of kidney disease.

The Centers for Disease Control and Prevention estimates that 10 percent of adults in the U.S.—more than 20 million people—may have chronic kidney disease, a condition in which a person's damaged kidneys cannot effectively filter waste from the blood. Treating Medicare patients aged 65 or older with this disease cost the United States about $45 billion in 2012.

"They call kidney disease the silent killer, because in its early stages, most individuals show no symptoms and do not know anything is wrong," said Zheng, who is also an adjunct associate professor of urology at UT Southwestern Medical Center. "Since it is difficult to study in humans, early stage kidney disease is poorly understood."

Routine clinical tests of blood or urine are not sensitive enough to detect kidney disease in its earliest stages and may still register in the normal range even when 60 to 70 percent of normal kidney function has been lost, Zheng said.

"You have two kidneys, and if one kidney has a problem, the other kidney will adapt to try to make conditions normal," he said.

Noninvasive in vivo near-infrared fluorescence imaging is an inexpensive, highly sensitive and widely used laboratory technique for studying internal organs, the effectiveness of drugs and diseases such as cancer in small living animals, primarily mice. In this type of imaging, a fluorescent organic dye is introduced into the subject, which is then exposed to an external source of invisible near-infrared light that can penetrate the skin. When the light reaches the dye, the dye emits—or fluoresces—light of a different wavelength, which is then picked up by a detector or camera. Such preclinical studies help facilitate and inform eventual clinical investigations of disease in humans.

A Golden Solution

Using this technique for preclinical kidney disease studies has long been a challenge because organic dyes do not provide adequate contrast in the kidneys. They also are taken up by the skin, which results in the kidneys being obscured during the imaging process.

But Zheng and his colleagues have developed a way to make it work. The key is tiny gold nanoparticles less than 6 nanometers in size, small enough to clear completely out of the kidney through urination.

Zheng's team previously reported that such gold nanoparticles coated with glutathione, a small molecule found in plant and animal cells, work better than the dyes as fluorescence imaging agents for cancer detection. The nanoparticles are inexpensive—the amount of gold used is miniscule—and clear the body easily, Zheng said.

The ease by which the particles cleared the kidneys first inspired Zheng to adapt the technique to study the kidneys. The nanoparticles do not accumulate in the skin as conventional dyes do, and they provide a 50-fold increase in contrast, for a much sharper image.

"Using this technique, we can readily differentiate between various stages of kidney dysfunction in the animal model, and should be able to learn more about how these stages develop," Zheng said. "Our fluorescence imaging technique is noninvasive, and is much lower in cost than other imaging techniques used to study kidney disease in animal models. This should greatly expedite the advancement of our fundamental understanding of kidney diseases."

Four Years in the Making

Because the nontoxic gold nanoparticles stay in the body longer than other fluorescent dyes, Zheng said surgeons might use them to their advantage during kidney surgery.

"There are many, many blood vessels in the kidneys, and surgeons currently use fluorescent dye as a probe to guide surgery and minimize damage to the organ," Zheng said. "The problem is these dyes can clear out from the body really fast, so surgeons have to inject multiple times to be sure they can see the blood vessels clearly all the time. In the future, surgeons could improve their accuracy in fluorescence-guided surgery by using these nanoparticles."

Zheng said it took his research group four years to develop the technique.

"It was a long journey with great support from many colleagues and upper-level administration. UT Dallas is a great place to do cutting-edge research," Zheng said.

The project was initially supported by UT Dallas startup funds, and later funded by an R01 grant from National Institute of Diabetes and Digestive and Kidney Diseases, as well as an individual research award to Zheng from the Cancer Prevention and Research Institute of Texas.

More information: Mengxiao Yu et al. Noninvasive Staging of Kidney Dysfunction Enabled by Renal-Clearable Luminescent Gold Nanoparticles, *Angewandte Chemie International Edition* (2016). DOI: 10.1002/anie.201511148

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