Nanoparticle study produces clearer understanding of kidney function

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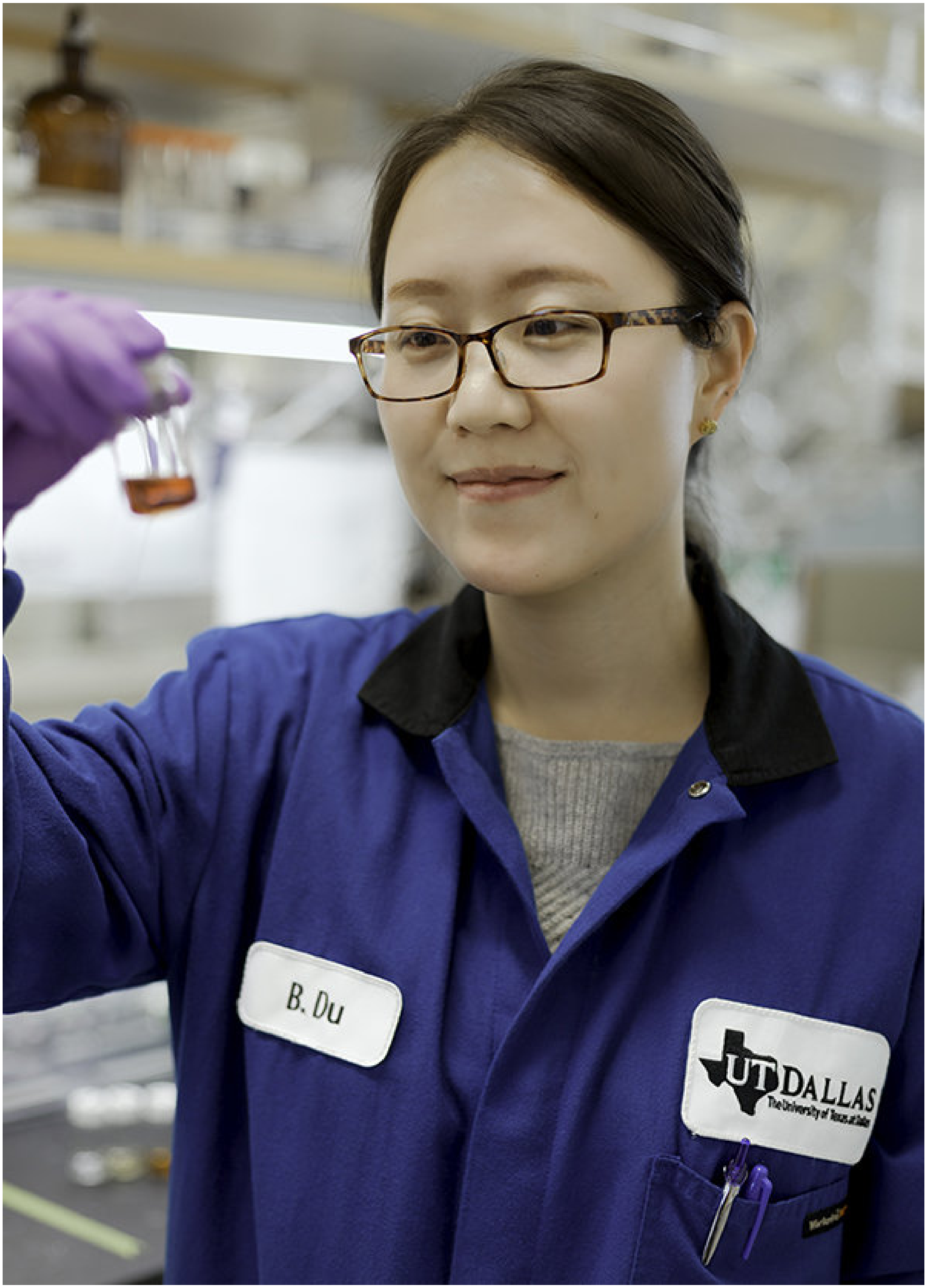
B. Du
UT DALLAS
The University of Texas at Dallas

UT Dallas researcher Bujie Du looks at one of the samples she used to determine how quickly the body eliminates ultra-small nanoparticles from the kidneys. Du was the lead author of the *Nature Nanotechnology* study. Credit: University of Texas at Dallas

New research findings from The University of Texas at Dallas unveil how kidneys filter ultra-small engineered particles, which may lead to new ways of developing targeted therapy for the detection and treatment of kidney diseases and cancers.

The team, led by Dr. Jie Zheng, associate professor of chemistry in the School of Natural Sciences and Mathematics, synthesized a series of gold nanoclusters with specific numbers of atoms, creating different sizes of gold particles. They investigated how the kidney eliminates each of the particles, which are smaller than 1 nanometer, from the body.

"We were surprised to find that smaller gold nanoparticles were filtrated four to nine times slower than just a few atom-larger ones in the early elimination stage," Zheng said. "These findings help further improve our understanding of kidney filtration in the sub-nanometer regime and show how precisely the kidney can respond to the ultra-small nanoparticles. We hope this new knowledge can potentially help in the creation of therapies that can target kidney diseases."

The team identified a size cutoff filter that trapped small nanoparticles but allowed the larger particles to travel through quickly. The results appear in the journal *Nature Nanotechnology*.

"The whole-body X-ray imaging of the differing gold particles clearly showed their different transportation rates from the kidney to the bladder," Zheng said.

The smallest gold particle was eliminated through the kidneys into the bladder much more slowly than larger ones, which seems counterintuitive to our understanding of how the kidneys function.

"In our physiology textbooks, what we often know is that the smaller particles are eliminated faster than big ones, which is true for particles larger than 1 nanometer," Zheng said. "However, once the nanoparticles are smaller than that, this size-scaling law changes."

The researchers focused on the glomerulus, a network of capillaries that form a basic unit of the kidneys' filtration system. The glomerular filtration barrier is a multiple layer structure through which blood plasma is filtered. By comparing the distribution of nanoparticles in the glomerulus, researchers found that one layer in particular—the glomerular endothelial glycocalyx—more readily traps the smaller gold nanoclusters.

The glycocalyx is not only a major component of the glomerulus but also extensively lines blood vessels where the researchers discovered similar trends in filtration rates.

This observation provides new insights for the diagnosis of diseases such as chronic renal failure and atherosclerosis, which is caused by fatty deposits within blood vessel walls.

Nanoparticles have many potential biomedical applications, such as assisting in cancer diagnosis and treatment. Zheng's group found that reducing particle size into the sub-nanometer range could be a valuable strategy for enhancing the tumor-targeting capabilities of nanomedicine.

"The comprehensive understanding of how the body interacts with engineered nanoparticles, especially in sub-nanometer regime, could potentially bring future breakthroughs to nanomedicine in the realm of cancer treatment efficacy," said Bujie Du, UT Dallas doctoral student and lead author of the paper. "It also helps pave the road for the future medical applications of ultra-small nanomedicine."

Du spent four years working on the project with her fellow UT Dallas researchers.

"We definitely learned a lot about how the kidney works during this long journey, and I am very happy to see that the hard work was paid back," she said.

Other authors from Zheng's research group were UT Dallas graduate students Xingya Jiang and Qinhan Zhou and research assistant professor Dr. Mengxiao Yu.

"The important discovery was made possible because of the collaboration with Professor Rongchao Jin and his student Anindita Das from Carnegie Mellon University," Zheng said. "We have a great team."

More information: Bujie Du et al. Glomerular barrier behaves as an atomically precise bandpass filter in a sub-nanometre regime, *Nature Nanotechnology* (2017). DOI: 10.1038/nnano.2017.170

Provided by University of Texas at Dallas

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