Rubbery properties help RNA nanoparticles target tumors efficiently and quickly leave body

September 14 2020

Peixuan Guo, PhD, is a researcher with The Oho State University Comprehensive Cancer and The Ohio State University College of Pharmacy. Credit: The Ohio State University

A new study by researchers at The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Richard J. Solove

Research Institute (OSUCCC—James) shows that RNA nanoparticles have elastic and rubbery properties that help explain why these particles target tumors so efficiently and why they possess lower toxicity in animal studies.

RNA nanoparticles show great promise for the targeted delivery of anticancer drugs. Understanding their structure and behavior is essential for their possible future use.

This study, published in the journal *ACS Nano*, reveals that RNA nanoparticles have elastic and rubbery properties that enable the molecules to stretch and return to their normal shape. Researchers say that these properties could help the particles target tumors by enabling them to slip through the poorly formed walls of tumor blood vessels and enter a tumor mass.

The researchers further proved that the same rubbery properties enable the RNA nanoparticle to slip through the kidney filters to excrete into the urine half hour after systemic injection, thereby eliminating them from the body relatively quickly. That, in turn, could reduce retention of the anticancer agent in vital organs, lowering an agent's toxicity.

"We show that RNA nanoparticles have a flexibility that allows for the assembly of molecular structures that have stretchable angles," says study leader and corresponding author Peixuan Guo, Ph.D., professor in the College of Pharmacy and the Sylvan G. Frank Endowed Chair in Pharmaceutics and Drug Delivery. Guo also is in the OSUCCC—James Translational Therapeutics Research Program.

"These findings demonstrate the rubbery properties of RNA nanoparticles and why these molecules hold great promise for industrial and biomedical applications, especially as carriers for targeted delivery of anticancer drugs," says Guo, who directs Ohio State's Center for RNA

Nanobiotechnology and Nanomedicine.

For this study, Guo and his colleagues tested the elasticity of nucleic acid polymers by stretching and relaxing individual RNA nanoparticle , while subjecting RNA nanoparticles to elasticity studies using dual-beam optical tweezers built in Guo lab. Finally, they used animal models to study the biodistribution, excretion and retention of RNA nanoparticles. This included measuring excretion of the particles in urine, along with the study on the effect of their shape and size.

Key findings include:

- RNA nanoparticles are stretchable and shrinkable, like rubber, even after repeated extension and relaxation with multiple repeats by optical tweezers.
- In animal models, RNA nanoparticles show stronger cancer targeting and lower accumulation in healthy organs when compared to gold and iron nanoparticles of similar size.
- Also in animal models, within half hour after systemic injection, RNA nanoparticles that were 5, 10 and 20 nm in size were filtered by the kidneys and retained their original structure in urine, even though the upper limit of kidney pore size for filtration is generally 5.5 nm. This suggests that the larger RNA nanoparticles slipped like rubberl and amoeba through filtration pores, then returned to their original size and shape in urin.

"Overall," Guo says, "we believe these findings further support the development of RNA nanoparticles for targeted delivery of anticancer drugs or therapeutic RNA."

Other researchers involved in this study were Chiran Ghimire, Hongzhi Wang, Hui Li, Mario Vieweger and Congcong Xu, The Ohio State University.

More information: Chiran Ghimire et al, RNA Nanoparticles as Rubber for Compelling Vessel Extravasation to Enhance Tumor Targeting and for Fast Renal Excretion to Reduce Toxicity, *ACS Nano* (2020). DOI: 10.1021/acsnano.0c04863

Provided by Ohio State University Medical Center