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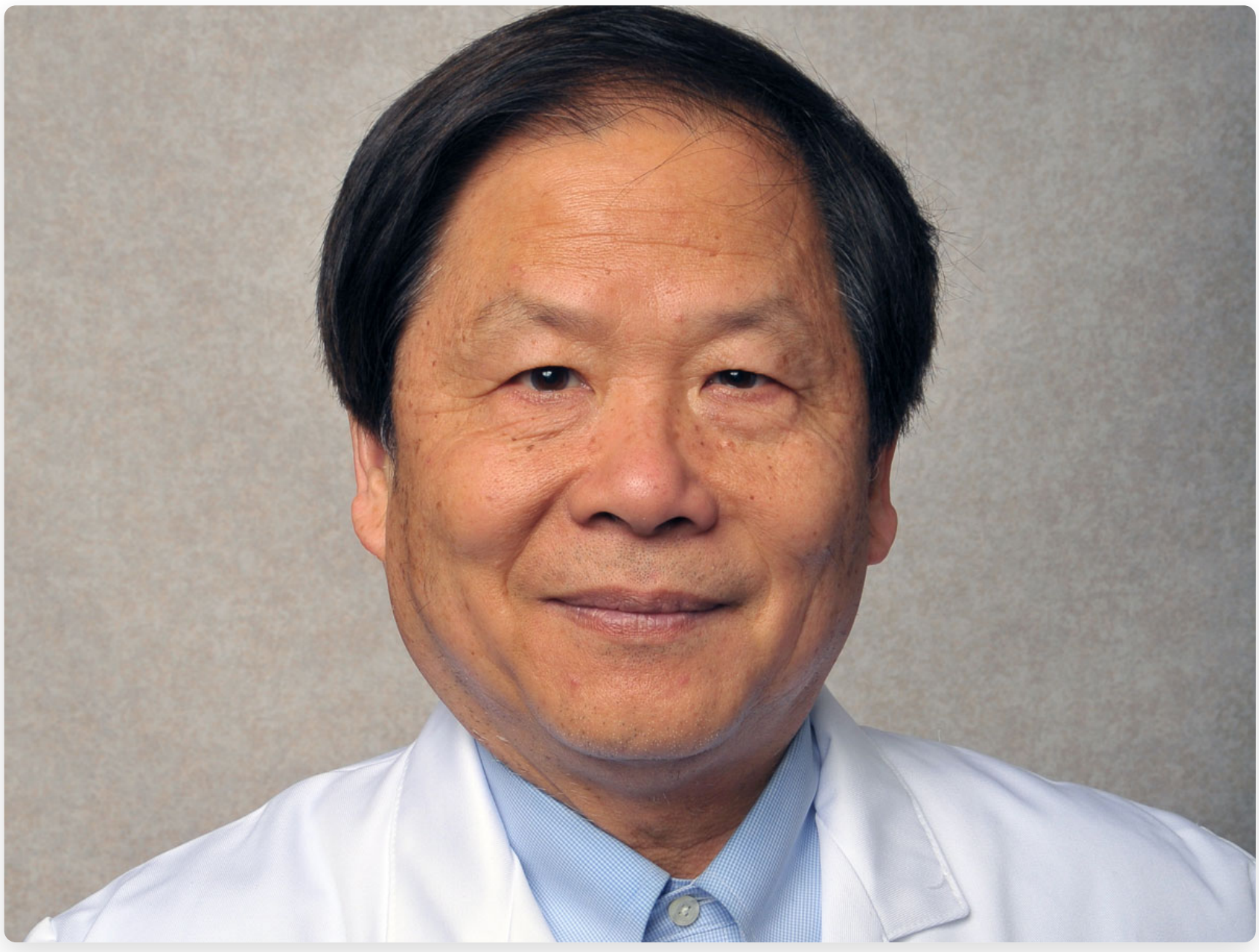
RNA Nanoparticles May Improve the Solubility, Delivery and Safety of Cancer Chemotherapy



COLUMBUS, Ohio – Two studies led by researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) suggests that RNA nanoparticles may vastly improve the solubility, delivery and safety of two chemotherapeutic drugs.

In one study, researchers used RNA nanoparticles to deliver the chemotherapeutic drug paclitaxel, commonly used to treat breast as well as many other cancers; that study is published in the journal *Nature Communications*.

The second study used RNA nanoparticles that were engineered in a slightly different way to carry camptothecin in an animal model; the findings are reported in the journal *Advanced Science*. Both studies were published by Peixuan Guo, PhD, and colleagues with the OSUCCC – James Translational Therapeutics Research Progra. The team established proof-of-concept for RNA nanotechnology more than two decades ago, describing how nano-meter scale RNA structures are assembled (*Mol Cell* 1998; 2:149; featured in *Cell*), opening a new pathway for research.

Both paclitaxel and camptothecin dissolve poorly in water and are highly toxic, resulting in serious side effects. Their toxicities are due in part to their low solubility, which requires that the two drugs be specifically formulated in a way that they are tolerable and safe to use in patients for cancer control.

Guo describes RNA nanotechnology as analogous to interconnecting building blocks like LEGOs. To harness this approach to drug delivery, RNA molecules are modified to, first, make them highly stable in water; second, carry a number of drug molecules; and third, display a molecule (i.e., an RNA aptamer) that targets a receptor on cancer cells.

“Our studies demonstrate the feasibility of using RNA nanoparticles to safely and efficiently deliver small-molecule chemotherapeutic drugs to tumor cells,” says Guo, who served as prinicipal investigator of the two studies and is a professor of Pharmacy and the Sylvan G. Frank Endowed Chair in Pharmaceutics and Drug Delivery in The Ohio State University College of Medicine. Guo also directs Ohio State’s Center for RNA Nanobiotechnology and Nanomedicine.

“In both studies, these therapeutic RNA nanoparticles were highly stable, had well-defined structure and showed precise drug loading and targeted delivery,” says Guo.

Guo noted that, once inside tumor cells, the drug was released from the RNA nanoparticles and retained its ability to kill cancer cells and inhibit tumor growth.

Key findings of the paclitaxel study:

- The paclitaxel RNA nanoparticle was composed of a four-way junction structure and carried 24 paclitaxel prodrug molecules;
- Using RNA nanoparticles increased the water solubility of paclitaxel 32,000-fold;
- The paclitaxel RNA nanoparticles displayed an RNA aptamer (sequence-dependent RNA structure domain) that binds epidermal growth factor receptor (EGFR), which is often overexpressed on breast cancer cells;
- In a triple-negative breast-cancer animal model, the targeted RNA-paclitaxel nanoparticles dramatically inhibited breast cancer growth, with nearly undetectable toxicity and no fatalities;
- The therapeutic RNA nanoparticles efficiently target to tumor with little accumulation in vital organs.

Key findings of the camptothecin study:

- Each RNA nanoparticle was composed of a three-way junction structure that carried seven camptothecin prodrug molecules;
- Using RNA nanoparticles increased the water solubility of camptothecin 1,000-fold;
- The RNA nanoparticles displayed cancer binding ligands as a way to target tumor cells that overexpress the receptors on their surface.

"The display of EGFR binding RNA aptamer on the nanoparticles specifically recognized the overexpressed TNBC EGF receptors on the tumor cell surface and increased the uptake of the nanoparticles into tumor cells," Guo says.

"Collectively," Guo says, "our data demonstrates the feasibility of RNA nanoparticles for the safe and effective targeted delivery of hydrophobic anti-tumor drugs."

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Authors in addition to Guo for the camptothecin report were Xijun Piao, Hongran Yin, Sijin Guo and Hongzhi Wang of The Ohio State University.

Authors for the paclitaxel report were Sijin Guo, Mario Vieweger, Hongran Yin, Hongzhi Wang, Xin Li, Shuiying Hu, Alex Sparreboom, Yizhou Dong, and Peixuan Guo, The Ohio State University; Kaiming Zhang, Shanshan Li and Wah Chiu, Stanford University; B. Mark Evers, University of Kentucky.

About the OSUCCC – James

The OSUCCC – James strives to create a cancer-free world by integrating scientific research with excellence in education and patient-centered care, a strategy that leads to better methods of prevention, detection and treatment. Ohio State is one of only 51 National Cancer Institute (NCI)-designated Comprehensive Cancer Centers and one of only a few centers funded by the NCI to conduct both phase I and phase II clinical trials on novel anticancer drugs sponsored by the NCI. As the cancer program's 356-bed adult patient-care component, The James is one of the top cancer hospitals in the nation as ranked by *U.S. News & World Report* and has achieved Magnet® designation, the highest honor an organization can receive for quality patient care and professional nursing practice. At 21 floors and with more than 1.1 million square feet, The James is a transformational facility that fosters collaboration and integration of cancer research and clinical cancer care. For more information, visit cancer.osu.edu

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