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Protein Shows Potential as Chemotherapy Carrier

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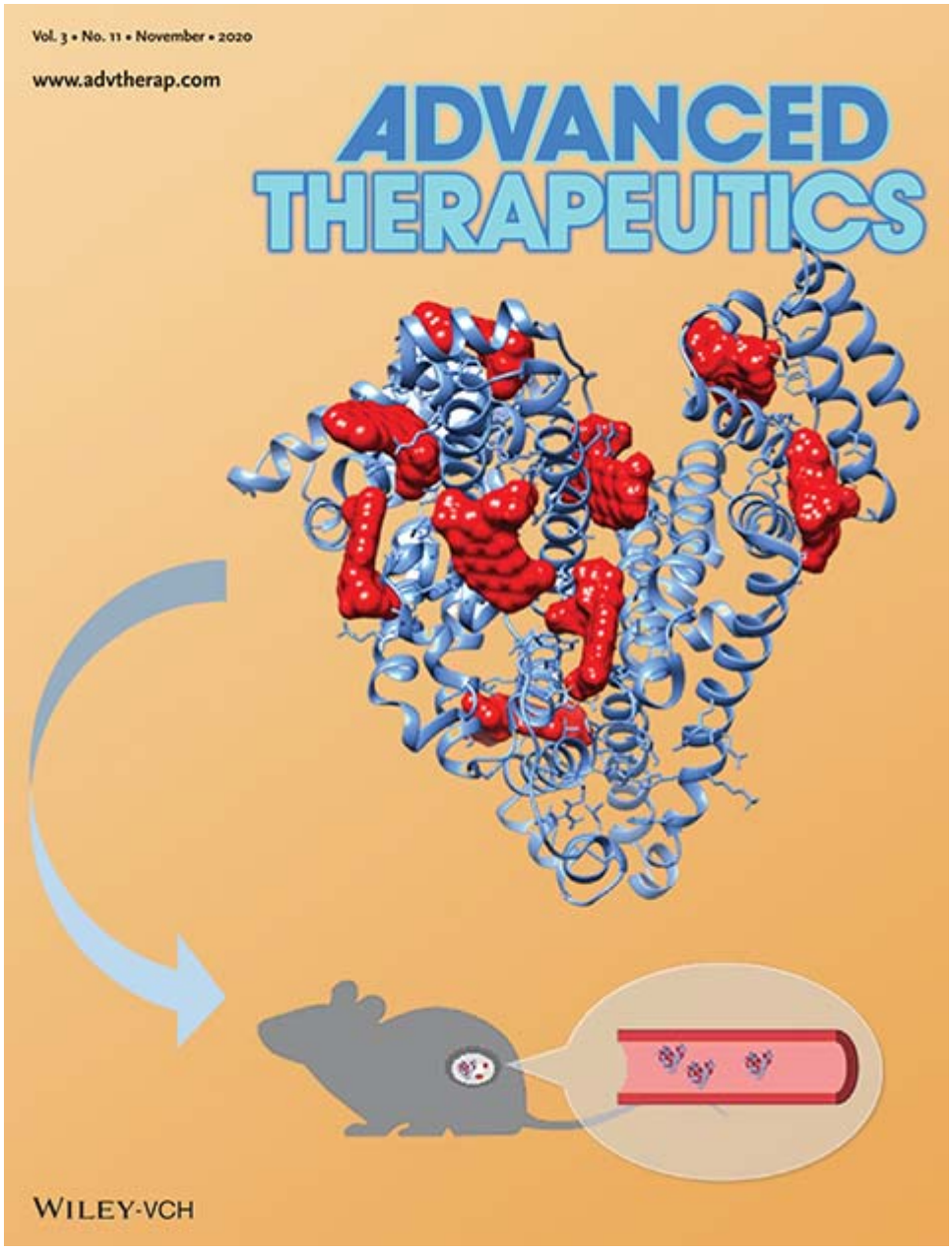


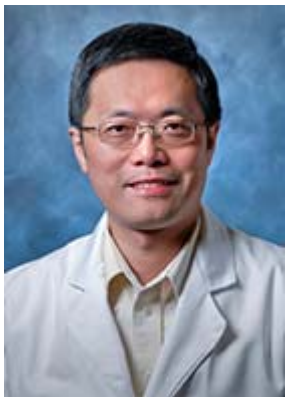
The recent cover of the journal Advanced Therapeutics, which published a multi-institutional study about a protein molecule that may help in the fight against cancer.

Enclosing drugs inside a protein molecule shows potential as a method to safely deliver more cancer-fighting treatment directly to the tumor, according to a recent multi-institutional study. In tests performed in laboratory mice, the buffering method unleashed powerful tumor-killing drugs into cancer cells while leaving healthy tissues alone.

If results from the study are duplicated in human trials, the protein-capsule delivery method potentially could be developed into a treatment that ferries more anticancer drugs to tumor sites and improves outcomes for patients with aggressive cancers.

The collaborative research involved investigators from Cedars-Sinai, the California Institute of Technology in Pasadena, the University of Southern Mississippi in Hattiesburg and City of Hope in Duarte, California. It was the cover story for the Nov. 6 issue of the journal *Advanced Therapeutics*.

In treating aggressive cancers, clinicians must carefully cap the maximum doses of tumor-killing drugs because of their severe side effects on healthy tissue.



Xiaojiang Cui, PhD

"Our goal in this study was to improve tumor suppression in aggressive cancers by directly targeting tumors while protecting against toxic side effects," said Xiaojiang Cui, PhD, associate professor of Surgery at Cedars-Sinai. Cui was co-corresponding author of the study, along with Changjun Yu, PhD, visiting scholar at the California Institute of Technology, who also was the first author.

The study team used the most abundant protein in blood called human serum albumin as a "cloak" and transport vehicle for doxorubicin, a potent, widely used chemotherapy drug. Doxorubicin is effective against both solid-tumor and blood cancers, but it also can infiltrate healthy tissues and organs, damaging the heart muscle and suppressing production of red blood cells.

Human serum albumin was chosen for the study because it binds easily with other substances, doesn't trigger immune responses and is readily taken in by cancer cells as a nutrient for growth and spread of tumors. In addition, it already had been used in various FDA-approved clinical applications and was commercially available.

The investigators bound together the cancer drug and the single-protein capsule and confirmed that the resulting complex substance, called SPEDOX, was stable and successfully infiltrated cancer tissue in the test tube. Then they tested the substance against tumors in laboratory mice with triple-negative breast cancer, a particularly aggressive malignancy that is difficult to treat.

The SPEDOX-treated mice showed more effective drug uptake and tumor supression than the mice treated with unformulated doxorubicin, Cui said.

To test whether SPEDOX reduced unwanted spillover of doxorubicin into healthy tissues, the team compared heart tissue harvested from mice treated with the buffered doxorubicin with heart tissue from mice treated with "free" unformulated doxorubicin.

The levels of doxorubicin in heart tissue in mice in the first group were four to eight times lower than levels in the second group, suggesting that heart toxicity may be substantially reduced by the new delivery system.

More research is needed to confirm the study's findings in human patients. To that end, the investigators are pursuing further testing to prepare for a potential clinical trial of SPEDOX.

The study's other co-authors included Galen Cook-Wiens, MS, senior biostatistician at the Cedars-Sinai Samuel Oschin Comprehensive Cancer Institute; Warren Chow, MD, from City of Hope; and Faqing Huang, PhD, from the University of Southern Mississippi.

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Conflict of Interest: Changjun Yu is a named inventor for patent applications regarding "Single Protein-Encapsulated Pharmaceutics for Enhancing Therapeutic Effects." The other authors declare no conflict of interest.

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