Hitting target in cancer fight now easier with new nanoparticle platform

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(PhysOrg.com) -- The ability to use nanoparticles to deliver payloads of cancer-fighting drugs to tumors in the body could herald a fundamental change in chemotherapy treatment. But scientists are still at a relatively early stage in the implementation of this technology.

Although developing nanoparticles that work as "magic bullets" — selectively targeting tumors while sparing normal, healthy tissues — is still the goal, the reality is that most of these nanocarriers are removed through the liver and spleen before ever reaching their intended target. And many of the encapsulated drugs can be lost while the carriers circulate in the blood or degraded on the way to tumors.

In a study recently published in the journal *ACS Nano*, UCLA scientists report that by using engineered mesoporous silica nanoparticles (MSNPs) as delivery vehicles, they were able to achieve significant increases in the percentage of drug-carrying nanoparticles that reach and are retained at tumor sites.

The MSNP platform allows for the introduction of multiple and customized design features that can help optimize the delivery of chemotherapeutic drugs to a variety of cancer types, said the researchers, led by Dr. Andre Nel, a professor of medicine, pediatrics and public health and chief of the nanomedicine division in the UCLA Department of Medicine, and Jeffrey Zink, a professor in the UCLA Department of Chemistry and Biochemistry. Nel and Zink are also members of the California NanoSystems Institute at UCLA.

A key challenge in enhancing drug delivery has been improving nanocarriers' access to tumors by capitalizing on features like the leakiness of abnormal tumor blood vessels, which allows nanoparticles to slip through and be retained at tumor sites. To achieve that, particles must be designed to be the ideal size, to remain in the blood stream long enough by temporarily evading the liver and spleen, and to stably bind the drug.

The dynamic design features employed by the UCLA research team include the manipulation of the size and surface properties of the nanoparticle to improve tumor biodistribution and protected delivery. The study demonstrates how, through an iterative design process, the first-generation MSNP was redesigned and optimized to deliver doxorubicin to a cancer xenograft in a mouse model.

The team demonstrated a significant increase in particle retention at the tumor site: Approximately 10 to 12 percent of all the drug-loaded particles injected intravenously reached the tumor site. This high tumor distribution is exceptionally good, compared with other polymer- and copolymer-based nanodelivery platforms for which the best passive tumor targeting is in the range of 3.5 to 10 percent of injected particles, the researchers said.

The study also demonstrated efficient drug delivery and tumor cell–killing using the redesigned and optimized MSNP system in mice.

"The amount of doxorubicin being delivered to the tumor site was considerably higher than what could be achieved by the free drug, in addition to allowing efficient delivery into the cancer cells at the tumor site," said Nel, who is also a member of UCLA's Jonsson Comprehensive Cancer Center.

Moreover, the improved drug delivery was accompanied by a significant

reduction in systemic side effects such as weight loss and reduced liver and renal injury.

"This is an important demonstration of how the optimal design of the MSNP platform can achieve better drug delivery in vivo," Nel said. "This delivery platform allows effective and protective packaging of hydrophobic and charged anticancer drugs for controlled and on-demand delivery. Not only are these design features superior to induce tumor shrinkage and apoptosis compared to the free drug, but they also dramatically improve the safety profile of systemic doxorubicin delivery."

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