Scientists can predict nano drug outcome

February 5 2009

Scientists including one from The University of Texas Health Science Center at Houston successfully predicted the outcome of a nano drug on breast tumors in a pre-clinical study. Their research could help determine which patients will respond best to cancer-fighting nano drugs.

Researchers from the Georgia Institute of Technology and Emory University also participated in the study, which appears in the February issue of *Radiology*.

The investigators used contrast agents encapsulated in tiny fat bubbles called liposomes to determine if breast tumors in rodents could be breached by liposomes loaded with a cancer drug called liposomal doxorubicin. The liposomes were administered intravenously.

When scientists X-rayed the rodents, the investigators received good images of porous breast tumors which had absorbed the contrast agents. On the other hand, poor images indicated the contrast agents had not substantially penetrated the tumor. When liposomal doxorubicin was administered, it was associated with better therapeutic results in the tumors with superior images.

"We can tell if the animals are candidates for the treatment or not," said Ananth Annapragada Ph.D., one of two senior authors and an associate professor at The University of Texas School of Health Information Sciences at Houston.

Higher uptake of the probe by the tumor, indicating leakier vasculature, was associated with a slower tumor growth rate, suggesting a better therapeutic outcome with liposomal doxorubicin, the authors wrote. A nanometer is a billionth of a meter and a liposome is about 100 nanometers.

Nano drugs for cancer like liposomal doxorubicin are designed to increase the amount of drug reaching tumors. Currently, when an intravenous cancer drug is administered, very little reaches its intended target. The remaining drug circulates in the bloodstream and can cause side effects.

Liposomes carrying drugs infiltrate leaky tumors that have pores up to eight times the size of these miniaturized drug carriers. If a liposome with contrast agents can penetrate a tumor and be detected by X-rays, there is a good chance that a liposome with anti-cancer agents can enter the tumor, too. "We found that different tumors light up differently. The tumors that light up well take up the agent. Consequently, these are the tumors most likely to respond to liposomal doxorubicin," Annapragada said.

The current clinical protocols for liposomal doxorubicin consist of a standard dose every three to four weeks, the authors wrote. No prior knowledge of tumor vessel status, especially leakiness, is taken into account for the dose scheduling. However, it is well known that the degree of tumor vasculature leakiness differs not only among same-type tumors, but even spatially in the same tumor.

"This new information could help personalize the treatment of cancer with liposomal doxorubicin," Annapragada said.

In addition to predicting the outcome of liposomal doxorubicin on breast tumors, liposomes can be used for live monitoring of anti-cancer agents

in action. When loaded with both contrast agents and liposomal doxorubicin, the liposomes provide information on tumor leakiness, which can be used in tumor prognostication. A pre-clinical study on multi-functional liposomes by many of the same researchers was published in Biomaterials in December.

Annapragada and the study's other senior author, Ravi V. Bellamkonda, Ph.D., of the Georgia Institute of Technology/Emory University, are involved in a UT Health Science Center at Houston portfolio start-up company called Marval Biosciences that is working to translate these enhanced medical imaging techniques into patient diagnostics.

Source: University of Texas Health Science Center at Houston