Magnetic nanochain detonates chemo barrage inside tumors

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Medicine-toting nanochains slip into tumors and explode a chemotherapy drug into hard-to-reach cores of cancer, engineers and scientists at Case Western Reserve University report.

In tests on rats and mice, the technology took out far more cancer cells, inhibited tumor growth better and extended life longer than traditional chemotherapy delivery.

All the while, the targeted delivery system used far less of the drug doxorubicin than the amount used in traditional chemotherapy, saving healthy tissue from toxic exposure.

The new delivery system and results are described in the online edition of The American Chemical Society journal *ACS Nano*.

"Other nanotechnology has been used to get a drug inside a tumor, but once the drug gets in the door, it stays by the door, missing most of the building," said Efstathios Karathanasis, a biomedical engineering professor and leader of the research team. "We used a different kind of nanotechnology to smuggle the drug inside the tumor and to explode the bomb, releasing the drug in its free form to spread throughout the entire tumor."

The key to the new delivery system is the tail on the doxorubicin bomb.

Karathanasis' team took magnetic nanoparticles made of iron oxide and

modified the surfaces so that one would link to the next, much like Lego building blocks.

They linked three together and chemically linked a liposome sphere filled with the drug.

They then injected rat and mouse models with the nanochains, which carried only 5 to 10 percent of doxorubicin used in standard chemotherapy. The two rodents are models of two different strains of what is called triple-negative breast cancer, a highly-aggressive form of cancer treatable only with harsh chemotherapy.

The researchers started with an aggressive form, believing if the technology works on the least treatable cancers, it is likely to work with other drugs on other forms of cancers.

A day later, after nanochains had slipped from the blood stream and congregated in the tumor, the researchers placed a wire coil, called a solenoid, outside the animal models, near the tumor. Electricity passed through the solenoid creates a radiofrequency field. The field caused the magnetic tails to vibrate, breaking open the liposome spheres.

Two weeks after treatment, tumor growth in rats that received the new drug delivery was less than half that of rats treated traditionally. In rats that received two of the new treatments, tumor growth was reduced to one-tenth that of rats treated traditionally (for example clinically used doxorubicin or liposomal doxorubicin).

Rats that received one new treatment survived an average of 25 days and those treated twice, 46 days, compared to 15 days for traditionally treated rats.

Cell death, called apoptosis, within the tumor was at least 10 times

greater after one treatment with the new delivery system compared to traditional treatment.

The researchers tested only for apoptosis in mice with a different triple-negative cell line. The new treatment caused nearly a 4-fold increase in cell death within the tumor.

In both the mice and rats, the drug and resulting cell death was far more widely distributed throughout the tumors with the nanochain delivery.

"There are probably different mechanisms of growth in the different models, which indicates this technology will probably work in different types of cancer," said Ruth Keri, associate professor and vice chair of the Department of Pharmacology at Case Western Reserve School of Medicine. Keri, who is also associate director for basic research at Case Comprehensive Cancer Center, assisted in the investigation.

"This is a really clever and novel approach to targeted delivery. But, we need much more testing."

During their experimenting, the team found they could control the rate of drug release by adjusting the radiofrequency used to vibrate the chain.

They plan to further explore this capability and test whether the system can block the ability of the tumor to metastasize, which is the most common cause of cancer deaths. They will also optimize the system to provide more efficient and rapid drug release, and further evaluate the effect of size and shape of the nanochains on blood circulation and tumor penetration.

Provided by Case Western Reserve University