New arsenic nanoparticle blocks aggressive breast cancer

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You can teach an old drug new chemotherapy tricks. Northwestern University researchers took a drug therapy proven for blood cancers but ineffective against solid tumors, packaged it with nanotechnology and got it to combat an aggressive type of breast cancer prevalent in young women, particularly young African-American women.

That drug is arsenic trioxide, long part of the arsenal of ancient Chinese medicine and recently adopted by Western oncologists for a type of leukemia. The cancer is triple negative breast cancer, which often doesn't respond well to traditional chemotherapy and can't be treated by potentially life-saving targeted therapies. Women with triple negative breast cancer have a high risk of the cancer metastasizing and poor survival rates.

Prior to the new research, arsenic hadn't been effective in solid tumors. After the drug was injected into the bloodstream, it was excreted too rapidly to work. The concentration of arsenic couldn't be increased, because it was then too toxic.

A new arsenic nanoparticle -- designed to slip undetected through the bloodstream until it arrives at the tumor and delivers its poisonous cargo -- solved all that. The nanoparticle, called a nanobin, was injected into mice with triple negative breast tumors. Nanobins loaded with arsenic reduced tumor growth in mice, while the non-encapsulated arsenic had no effect on tumor growth. The arsenic nanobins blocked tumor growth by causing the cancer cells to die by a process known as apoptosis.

The nanobin consists of nanoparticulate arsenic trioxide encapsulated in a tiny fat vessel (a liposome) and coated with a second layer of a cloaking chemical that prolongs the life of the nanobin and prevents scavenger cells from seeing it. The nanobin technology limits the exposure of normal tissue to the toxic drug as it passes through the bloodstream. When the nanobin gets absorbed by the abnormal, leaky blood vessels of the tumor, the nanoparticles of arsenic are released and trapped inside the tumor cells.

"The anti-tumor effects of the arsenic nanobins against clinically aggressive triple negative breast tumors in mice are extremely encouraging," said Vince Cryns, associate professor of medicine and an endocrinologist at Northwestern Medicine and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. "There's an urgent need to develop new therapies for poor prognosis triple negative breast cancer."

Cryns and Tom O'Halloran, director of the Chemistry of Life Processes Institute at Northwestern, are senior authors of a paper on the research, which will be published July 15 in *Clinical Cancer Research* and featured on the journal cover. Richard Ahn, a student in the medical scientists training program at Northwestern, is lead author.

"Everyone said you can't use arsenic for solid tumors," said O'Halloran, also associate director of basic sciences at the Lurie Cancer Center. "That's because they didn't deliver it the right way. This new technology delivered the drug directly to the tumor, maintained its stability and shielded normal cells from the toxicity. That's huge."

The nanoparticle technology has great potential for other existing cancer drugs that have been shelved because they are too toxic or excreted too rapidly, Cryns noted. "We can potentially make those drugs more effective against solid tumors by increasing their delivery to the tumor

and by shielding normal cells from their toxicity," he said. "This nanotechnology platform has the potential to expand our arsenal of chemotherapy drugs to treat cancer."

"Working with both professors O'Halloran and Cryns has enabled us to develop the nanobins and hopefully create a new platform for the effective treatment of triple negative breast cancer," Ahn said. "Having both a basic science mentor and breast cancer mentor is ideal training for me as a future physician-scientist."

Looking ahead, the challenge now is to refine and improve the technology. "How do we make it more toxic to cancer cells and less toxic to healthy cells?" asked Cryns, also the director of SUCCEED, a Northwestern Medicine program to improve the quality of life for breast cancer survivors.

Northwestern scientists are working on decorating the nanobins with antibodies that recognize markers on tumor cells to increase the drug's uptake by the tumor. They also want to put two or more drugs into the same nanobin and deliver them together to the tumor.

"Once you fine-tune this, you could use what would otherwise be a lethal or highly toxic dose of the drug, because a good deal of it will be directly released in the tumor," O'Halloran said.

Provided by Northwestern University