Researcher uses Jell-O-like substance to attract and kill cancer cells

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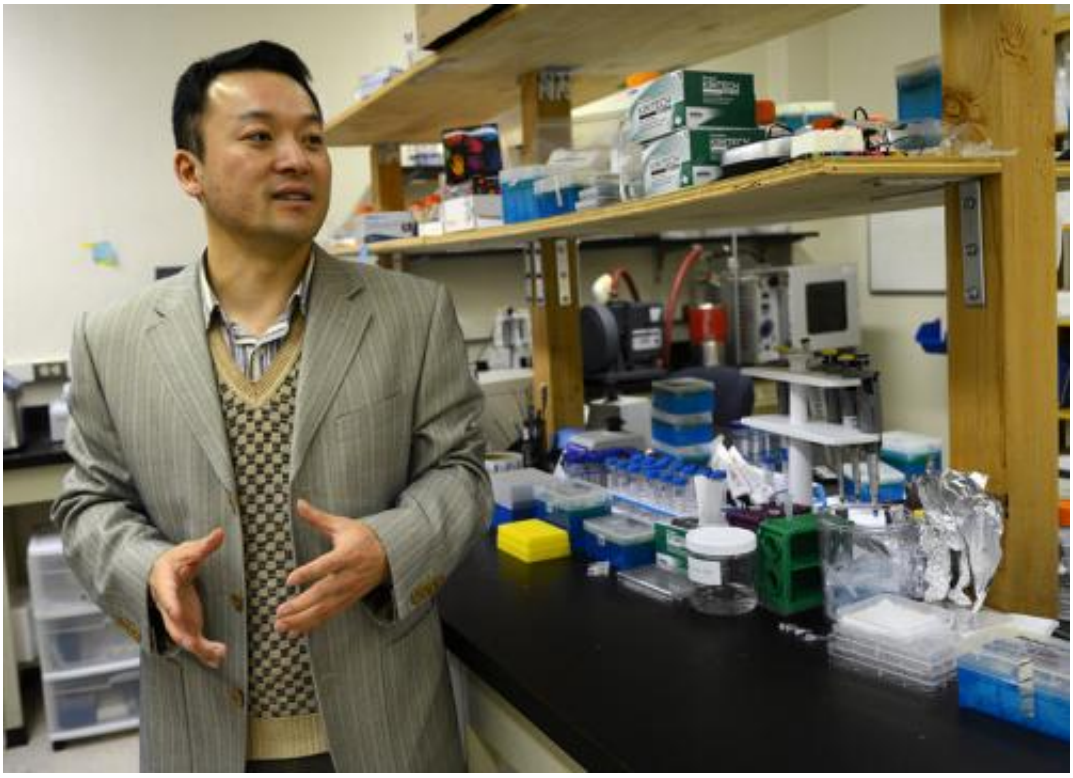

Yong Wang's work focuses on developing biomaterials that can attract cancer cells like a magnet and then entrap them. Credit: Curtis Chan

(Phys.org) —Chasing cancer cells with chemotherapy drugs can save lives, but there's no guarantee that the treatment will kill every run-away cancer cell in the body.

What if, instead of hunting those metastatic cells, a treatment could lure them out of hiding—every last one of them—and eliminate them in one swift blow?

Yong Wang, associate professor of bioengineering at Penn State, has created such a therapy—a tissue-like biomaterial that attracts cancer cells, like bits of metal to a magnet, and entraps them.

"Once we trap the cancer cells, we can deliver anticancer drugs to that specific location to kill them," he said. "This technique would help avoid the need for systemic medications that kill not only cancer cells, but normal cells as well. Systemic chemotherapy drugs make patients devastatingly sick and possibly leave behind cancer cells to wreak havoc another day. If our new technique has any side effects at all, it would be only local side effects and not whole-body systemic side effects."

Wang's idea to trap cancer cells began with a few tiny molecules called monomers, which he purchased from a company. From these, he and his Penn State colleagues—which include Cheng Dong, distinguished professor and head of the Department of Biomedical Engineering, and graduate students Shihui Li and Erin Richards—built polymers, or strings of monomers, and then wove these polymers into three-dimensional networks, called hydrogels.

"To create a tissue-like biomaterial, you have to find a material that has a lot of similarities to human tissue," he said. "Hydrogel is soft and flexible, like Jell-O, and it contains a lot of water, so when you put it into the body, the body likes it. With other implants, the body often tries to get rid of them through the immune response. We want to make sure the materials we are using are compatible in the body."

Next, the team created synthetic biomolecules, called nucleic acid aptamers, which they engineered to bind to cancer cells. The researchers

then attached these aptamers to the hydrogels. Once in cell culture or in the body, the hydrogels secrete biochemical signal-only molecules to notify cancer cells of their presence. Alerted, the cancer cells come running, so to speak. The aptamers then bind to the cells, ensnaring them in a permanent "headlock."

To kill the cancer cells, Wang and his colleagues created an oligonucleotide, or single-stranded fragment of DNA, that binds to the protein-binding site of the aptamer and emits a trigger molecule that induces the release of anticancer drugs at the appropriate time.

According to Wang, previous drug-delivery implants could be externally triggered to release medication, but could deliver only a single drug. Wang's research, which is funded by the U.S. National Science Foundation, has demonstrated the ability to deliver several drugs at certain times.

"We can control when the process of releasing the drugs will begin by injecting the hydrogel with the oligonucleotide," Wang said. "It's like a knob for a light; you turn it on and the drugs will be released, you turn it off and the drugs will not be released."

The researchers built their hydrogels in a container and then characterized them using a high-powered microscope. To test the efficacy of their product in trapping cancer cells, they added them to cancer-cells cultures. According to Wang, the hydrogels successfully trapped the cancer cells in culture every time.

"This is different from what anyone else is doing," he said. "It's a completely new research direction."

Wang published some of the initial results of his research in the *Journal of the American Chemical Society* in 2012, and he presented his most

recent results at the Society for Biomaterials Meeting & Exposition in April 2014.

Wang said he thinks the technique has the potential to forever change the way metastatic cancer is treated. Seeing this happen, he added, would be incredibly satisfying.

"I started out as an environmental science major in college, but eventually switched to life science," he said. "I realized that as a researcher, I wanted to see things happen in my life. When you apply engineering knowledge to life science problems you have a chance of seeing some outcomes of the technologies you create. I think the project we are working on has the chance to make a difference for humanity."

The next step in the process, Wang said, is to design an in vivo study in mice.

Wang has another project that is already in the animal-testing phase. He is using mice to test the functionality of a hydrogel to regenerate tissues in the body. This time, he has designed the hydrogel to bind not to cancer cells, but to damaged tissues. He then delivers nutrients and/or necessary signal molecules to the area to help the tissue cells regrow.

His other work includes the use of biomolecules to develop biomimetic systems. In one project, he and his colleagues are creating artificial antibodies.

"There are a lot of reasons why we want to design artificial antibodies," he said. "For one, natural antibodies have some shortcomings; they can denature when you're trying to do a special application, like drug delivery, and, for some applications, they are too large. We have figured out how to make them smaller and much more stable. For example, when we try to congregate them to any other materials for drug delivery,

they do not lose their bioactivity."

In another project, Wang is designing biomimetic materials to control the delivery of protein drugs. He is trying to figure out how to deliver therapeutic biomolecules to a specific location in the body and with a pattern similar to the way it occurs in nature. As an example, he discusses insulin regulation.

"Our pancreas secretes insulin during or after a meal," he explained. "After a certain period of time, the level of insulin secreted decreases. The process happens again at the next meal. So you see a peak, valley, peak, valley in insulin level. If our bodies always had a very high concentration of insulin, we would die. When we design a drug delivery system to deliver therapeutic protein drugs we have to mimic this kind of natural pattern to ensure protein drugs will not induce any toxicity or side effects in our body."

Wang is quick to say that it is a constant struggle to create artificial materials that do their intended jobs without triggering any unwanted side effects. When successful, though, the effect is incredible.

"It sounds like fiction, but this is real," he said. "And I think it has the potential to change the way we approach medicine."

Provided by Pennsylvania State University