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Nanoparticles Enable Surgical Strikes against Cancer

Microscopic instruments that target only cancerous cells could replace less precise methods that also kill healthy tissue

By Larry Greenemeier

In a bid to progress beyond the shotgun approach to fighting cancer—blasting malignant cells with toxic chemicals or radiation, which kills surrounding healthy cells in the process—researchers at the Harvard-MIT Division of Health Sciences and Technology (HST) are using nanotechnology to develop seek-and-destroy models to zero in on and dismantle tumors without damaging nearby normal tissue.

HST takes an interdisciplinary approach to biomedicine. It consists of physicians, scientists and students from the Massachusetts Institute of Technology, Harvard Medical School, Harvard University, Boston-area teaching hospitals and other research centers. A team of researchers, led by Sangeeta Bhatia, an associate professor at HST and in M.I.T.'s department of electrical engineering and computer science, report in *Advanced Materials* that they have developed and tested injectable multifunctional nanoparticles—particles billionths of a meter in size—that they expect to become a new, potent weapon against cancer. (To provide some perspective, the width of a human hair is about 80,000 nanometers, or 0.003 inches.)

Nanoparticles could help treat cancer in a number of ways. They could be introduced into the bloodstream to locate and map tumors so that physicians would know what they were up against. Nanoparticles could also be designed to carry a payload of drugs that could be released near or even inside tumors to shrink or eliminate them.

HST researchers have experimented with polymer-coated iron oxide nanoparticles held together by DNA tethers to help them create a visual image of a tumor through magnetic resonance imaging. To test the particles, the researchers implanted mice with a tumorlike gel saturated with nanoparticles and placed those mice into the wells of cup-shaped electrical coils, which activated the nanoparticles via magnetic pulses.

The researchers subjected the metallic iron oxide particles to radiation until the DNA bonds holding them together broke, releasing fluorescent materials. "We just wanted to focus on characterizing the kinetics and temperature sensitivity using a payload we could detect," says Geoff von Maltzahn, an HST graduate student who has been working on the project since its inception in 2004.

The researchers are studying DNA sequences to gauge the point at which heat activates the nanoparticles after they have reached tumors in the body. One advantage of a DNA tether, the HST team members say, is that its melting point is tunable—scientists would be able to control when the bonds between the nanoparticles break by creating links of varying lengths with different DNA sequences.

Exposing the nanoparticles to a low-frequency electromagnetic field causes them to radiate heat that, in turn, erases the tethers and releases the drugs. The waves in the magnetic field used by the HST researchers have the same frequency range as radio waves (between 350 and 400 kilohertz). These waves pass harmlessly through the body and heat only the nanoparticles. In comparison, microwaves, which would cook tissue, are about a million times more powerful with frequencies measured in the gigahertz range.

Von Maltzahn and six other researchers, including Bhatia, wrapped up their initial study about a year ago and are now planning to replace the original fluorescent payload with a more therapeutic one, such as an enzyme that could be injected directly into the tumor to attack it from the inside out. Their goal is to eventually be able to release nanoparticles intravenously into the bloodstream and activate those particles by heat or magnetism as needed.

One open question is: What will happen to the nanoparticles after they are used? Since the particles are biodegradable, von Maltzahn says, the polymers would most likely make their way to the liver and be eliminated; the iron would probably be absorbed by the blood. Despite the potential of nanosize treatments for cancer, the researchers are unable to predict when such treatments might be available.