Researchers use nanoparticles to target brain cancer

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Tiny particles one-billionth of a meter in size can be loaded with high concentrations of drugs designed to kill brain cancer. What's more, these nanoparticles can be used to image and track tumors as well as destroy them, according to researchers at the University of Michigan Comprehensive Cancer Center.

Researchers incorporated a drug called Photofrin along with iron oxide into nanoparticles that would target cancerous brain tumors. Photofrin is a type of photodynamic therapy, in which the drug is drawn through the blood stream to tumor cells; a special type of laser light activates the drug to attack the tumor. Iron oxide is a contrast agent used to enhance magnetic resonance imaging, or MRI.

"Photofrin goes into tumor blood vessels and collapses the vasculature, which then starves the tumor of the blood flow needed to survive. The problem with free photofrin therapy is that it can cause damage to healthy tissue. In our study, the nanoparticle becomes a vehicle to deliver the drug directly to the tumor," says study author Brian Ross, Ph.D., professor of radiology at the U-M Medical School and co-director of Molecular Imaging at the U-M Comprehensive Cancer Center.

Photofrin has been used to treat several types of cancer, including esophageal, bladder and skin cancers. It works by traveling through blood vessels until it reaches the vessels supplying blood to the tumor. When activated by light, the Photofrin collapses these blood vessels, starving the tumor of the blood it needs to survive.

Results of the study appear in the Nov. 15 issue of *Clinical Cancer Research*.

"Thinking outside the box is a must for developing brain cancer treatments. Drugs don't get into the brain when delivered in the normal way, which explains in part why some current treatments for brain tumors are generally not effective. Targeting the tumor vasculature with nanoparticles containing a payload will overcome these issues," says study author Alnawaz Rehemtulla, Ph.D., professor of radiology and radiation oncology at the U-M Medical School and professor of environmental health sciences at the School of Public Health.

Treating brain tumors is traditionally difficult because of the blood-brain barrier, which prevents harmful substances from traveling through the bloodstream into the brain. In order for chemotherapy to treat a tumor, it must penetrate this barrier.

Researchers tested the nanoparticles in cell cultures and animal models. The studies showed the nanoparticles traveled to the tumor, resulting in less Photofrin exposure throughout the body and enhanced exposure within the tumor. This allowed a larger window for activating the drug with light. It also would eliminate a common side effect of photodynamic therapy, in which healthy skin becomes sensitive to light.

In rat studies, researchers found those treated traditionally with Photofrin survived 13 days, while rats treated with Photofrin incorporated into a nanoparticle survived an average of 33 days. Forty percent of the rats remained disease-free six months after treatment.

The researchers also found twice the amount of the contrast agent at the tumor site when using targeted nanoparticles, suggesting the nanoparticles were attracted to the tumor site.

The advantage of this delivery system is the ability to attack the tumor with higher doses of a drug while sparing normal tissue from a drug's toxic side effects.

"Our research suggests that you can take a drug that may be toxic to normal tissue – it could be any type of drug, not just photodynamic – and you could deliver higher doses of that drug for a more powerful punch," says Rehemtulla, co-director of Molecular Imaging at the U-M Comprehensive Cancer Center.

If nanoparticle delivery proves to be safe in humans, it will allow researchers to re-examine previously developed drugs that were discarded because they caused too many dangerous side effects in patients.

By combining the drug with a contrast agent, researchers were able using imaging techniques to determine whether the drug actually got to the tumor. This technique could have potential to diagnosis brain tumors early, as well as to help researchers determine when to deliver a drug or when to administer the next dose.

Further lab research is needed before the nanoparticle technology can be tested in clinical trials. More than 18,800 people will be diagnosed with brain cancer this year, and 12,820 will die from it. For information about treatments that are currently available, call U-M's Cancer AnswerLine at 800-865-1125.

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