Multifunctional Nanoparticles Image and Treat Brain Tumors

December 4 2006

Combining two promising approaches to diagnosing and treating cancer, a multidisciplinary research team at the University of Michigan has created a targeted multifunctional polymer nanoparticle that successfully images and kills brain tumors in laboratory animals. This work was conducted as part of the National Cancer Institute's Unconventional Innovations Program, an effort that first showed the promise of nanotechnology for diagnosing and treating cancer.

Writing in the journal *Clinical Cancer Research*, the research team led by Brian Ross, Ph.D., Alnawaz Rehemtulla, Ph.D., Raoul Kopelman, Ph.D., and Martin Philbert, Ph.D., describes its development of a 40-nanometer-diameter polyacrylamide nanoparticle loaded with a photosensitizing agent, known as Photofrin, and iron oxide. When irradiated with laser light, Photofrin, which is used to treat several types of cancer, including esophageal, bladder, and skin cancers, triggers the production of reactive oxygen species that destroy a wide variety of molecules within a cell. The iron oxide nanoparticles function as a magnetic resonance imaging (MRI) contrast agent.

As the targeting agent, the researchers used a 31-amino-acid long peptide that had been developed by members of the NCI-funded Center of Nanotechnology for Treatment, Understanding, and Monitoring of Cancer at the University of California, San Diego. This peptide targets an unknown receptor found on the surface of new blood vessels growing around tumors and also triggers cell uptake of nanoparticles attached to it.

"Photofrin goes into tumor blood vessels and collapses the vasculature, which then starves the tumor of the blood flow needed to survive," explains Ross. "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."

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.

"Thinking outside the box is a must for developing brain cancer treatments," says Rehemtulla. "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."

Researchers tested the nanoparticles in cell cultures and animal models. The studies showed that 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, which was accomplished by threading a fiber optic laser into the brain. In humans, this approach could reduce or eliminate a common side effect of photodynamic therapy, in which healthy skin becomes sensitive to light.

In rat studies, researchers found that 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. Using MRI, the researchers also found twice the amount of the contrast agent at the tumor site when using targeted nanoparticles, compared to

nanoparticles lacking the targeting peptide, suggesting the nanoparticles were concentrating at the tumor site.

This work, which was funded by the National Cancer Institute, is detailed in a paper titled, “Vascular targeted nanoparticles for imaging and treatment of brain tumors.” An abstract of this paper is available through *PubMed*.

Source: National Cancer Institute