

# Nanoparticles Home in on Brain Cancer in rats

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Nanoparticles Home in on Brain Cancer

Call them laser-guided smart bombs for brain tumors. Researchers at the University of Michigan announced the testing of a drug delivery system that involves drug-toting nanoparticles and a guiding peptide to target cancerous cells in the brain. Their study finds that via this method more of the drug can be delivered to a tumor's general vicinity. They report their findings in the November 15 issue of *Clinical Cancer Research*.

The researchers used a pharmaceutical called Photofrin, which is photodynamic, meaning it is activated by a laser after it has entered the bloodstream. As its primary side effect, the drug renders patients photosensitive, and they must remain out of bright sunlight and even unshaded lamps for up to 30 days after receiving treatment. Despite this major drawback, Photofrin is used in the treatment of esophageal, bladder and skin cancers. But their novel delivery system, which relies on the intravenous delivery of 40-nanometer-wide particles to carry the drug, may actually avoid much of the photosensitivity, because less Photofrin circulates in the bloodstream thanks to a peptide called F3. A sequence of 31 amino acids broken off of the protein HMGN2 (high mobility group protein 2), F3 has the ability to penetrate cell membranes. "This peptide acts as a "zip code" in that it enables the binding of the nanoparticles only to blood vessels within the tumor and not normal blood vessels," says Alnawaz Rehemtulla, a radiologist and environmental health scientist who co-authored the study. F3 can detect the expression of a protein called nucleolin, which is a marker on the surface of tumor cells.

Another problem the researchers avoided was having to deliver their medicine in such a way that it could cross the blood-brain barrier, which keeps many substances from entering the brain from the bloodstream. Typical chemotherapies must penetrate this shield to treat tumors. In this case, however, the nontoxic polyacrylamide particles didn't have to cross over via the bloodstream. "The nanoparticles do not need to cross the blood-brain barrier as they were specifically designed to target the blood vessel cells within the tumor," explains radiologist Brian Ross, one of

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the study's authors. "The treatment should be thought of as an antivasular treatment thereby shutting off the tumor blood flow resulting in the death of the tumor cells through starvation of oxygen and energy sources."

To test the delivery method, researchers divided 34 rats—all who received injections of cancerous cells into their brains—into different groups. Those that received no treatment or got only the laser fared poorly, dying on average within 8.5 days. Those that got Photofrin either intravenously or encapsulated in nanoparticles had a median survival time of 13 days. The group that got F3 with the Photofrin-carrying nanoparticles came through the best: they lived for, on average, 33 days; three of the five in this grouping lived for 60 days, and two of those three appeared tumor-free after six months. By using iron oxide as a contrast agent—to more easily detect where the nanoparticles ended up via MRI—the group determined that twice as much drug with the F3 peptide attached reached the tumor site—10 percent of the total amount administered—compared with when nontargeted nanoparticles were injected.

Ross says that based on the success of the study, the team is investigating if this delivery technology will work for nonphotodynamic therapies. Rehemtulla adds that if other FDA-approved chemotherapeutic agents reach their targets as successfully as Photofrin did, "then we will have developed a way to make cancer drugs more 'tumor-specific,' because they will only get into tumor vasculature and not normal vasculature. This will spare patients from normal tissue toxicity that is commonly associated with almost all chemotherapy." —Nikhil Swaminathan