Nanoparticles help disrupt tumor blood supply, destroy tumors

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(Phys.org) —In recent years, cancer researchers have been developing agents that destroy the blood vessels surrounding tumors with the goal of starving tumors to death. Some of these agents, such as tumor necrosis factor-alpha (TNF-α) have shown promising results, but often their toxicity has proven too great to be clinically useful. Using gold nanoparticles as a delivery vehicle for TNF-α has reduced this toxicity and the resulting construct has already completed a phase I clinical trial in humans.

Now, a team at the University of Minnesota headed by John Bischof, has shown that they can use this gold nanoparticle-TNF-? system to enhance the effects of either thermal therapy or cryosurgery. Moreover, the researchers demonstrated that they can use standard magnetic resonance imaging technology to visualize tumor destruction. Dr. Bischof and his colleagues reported their findings in the journal *Molecular Pharmaceutics*.

Experiments in a mouse model of human prostate cancer showed that the gold nanoparticle-TNF-? system disrupted blood flow into tumors within 90 minutes of injection, an effect that lasted up to six hours. Using a technique known as dynamic contrast-enhanced MRI, Dr. Bischof's team was able to clearly image the changes in blood flow into and around the tumor following nanoparticle treatment. The researchers note that in human patients, a simple five-minute MRI scan would be sufficient to detect a meaningful change in tumor blood vessel function.

Once the tumor blood vessels had been "preconditioned," Dr. Bischof and his collaborators treated the animals with either thermal therapy or cryosurgery, both of which produced marked reductions in tumors. They noted that none of the animals treated with thermal therapy died, an important finding given that an equivalent dose of TNF-? with no gold nanoparticle attached followed by thermal therapy was found to be lethal in a large percentage of animals. The researchers also showed that nanoparticle-delivered TNF-? did not trigger inflammatory reactions associated with activated neutrophils, something that does occur when tumors are treated with native TNF-?.

This work, which was supported in part by the National Cancer Institute, is detailed in a paper titled, "Nanoparticle delivered vascular disrupting agents (VDAs): use of TNF-alpha conjugated gold nanoparticles for multimodal cancer therapy." Investigators for the University of Arkansas for Medical Sciences also participated in this study. An abstract of this paper is available at the journal's website.

More information: doi:10.1021/mp300505w" target="_blank">dx.doi.org/doi:10.1021/mp300505w

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