Multifunctional Gold Nanoparticles Show Promise in Combination Therapy

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Gold nanoparticles, which can turn light into intense heat, are showing significant promise as targeted nanoscale thermal scalpels capable of killing cancer cells without damaging healthy tissue. Two new reports now suggest that gold nanoparticles may also be able to deliver additional therapeutic payloads to provide a simultaneous two-pronged attack on malignant cells.

In the first report, John Bischof, Ph.D., and his colleagues at the University of Minnesota used coated gold nanoparticles to deliver a molecule known as tumor necrosis factor-alpha (TNF-α) to breast tumors in mice. TNF-α, which plays a role in the body's normal immune response, has shown potent anticancer activity but also significant toxicities when administered in an untargeted manner. TNF-α kills tumors by enhancing the injury that can result when cells are heated above normal body temperature.

Writing in the journal Molecular Cancer Therapeutics, the investigators report that they were able to incorporate several hundred molecules of TNF-α per gold nanoparticle. These nanoparticles, when injected into tumor-bearing mice, triggered a marked reduction in tumor growth and size, but when the animals were placed in a water bath to raise their temperatures, the impact on tumor size and growth was magnified substantially. Indeed, 99.995 percent of tumor cells did not survive 18 hours after thermal therapy. This therapy also reduced blood flow to tumors and did not produce the type of side effects seen when free TNF-α is administered in conjunction with thermal therapy.

One item of note concerning this study is that although gold nanoparticles have been used to generate cell-killing heat in tumors, this study relied on an external heat source. Future work could use light to trigger the generation of heat by the nanoparticles themselves, but that was not the focus of the current work.

In a second report, published in the journal Nano Letters, a research team headed by David Curiel, M.D., Ph.D., at the University of Alabama at Birmingham details its initial efforts to use gold nanoparticles in conjunction with a virus that targets tumor cells to deliver thermal therapy and gene therapy to malignant cells. This approach entailed creating a virus-nanoparticle hybrid that would harness the targeting and gene-carrying capabilities of the virus with the light-activated heat generating properties of the gold nanoparticle.

To create the virus-nanoparticle hybrid, the investigators had to develop a method of linking the two nanoscale particles that would not compromise the ability of the virus to infect cancer cells. The virus the researchers chose is an adenovirus designed to bind to the tumor-associated carcino embryonic antigen (CEA), which is found on the surface of several types of cancer, including colon cancer. In the end, the investigators were able to attach 1,000 gold nanoparticles to each virus particle without affecting the virus's ability to target CEA. Investigations of the tumor-killing activities of this hybrid are now underway.

The work using nanoparticles to carry TNF-α to tumors, which was funded in part by the National Cancer Institute, is detailed in a paper titled, "Enhancement of tumor thermal therapy using gold nanoparticle-assisted tumor necrosis factor- a delivery." An investigator from Cytimmune Sciences in Rockville, MD, also participated in this study. An abstract of this paper is available through PubMed.

The work on virus-linked nanoparticles, which was also funded by the

National Cancer Institute, is detailed in a paper titled, “Covalently linked Au nanoparticles to a viral vector: potential for combined photothermal and gene cancer therapy.” Investigators from Groningen University in Groningen, The Netherlands, the University of Alabama at Tuscaloosa, and the University of Arkansas for Medical Sciences, in Little Rock, also participated in this study. An abstract of this paper is available through PubMed.

Source: National Cancer Institute