# New Approaches Target Nanoparticles to Cancer Cells

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One of the major goals of cancer nanotechnology research is to develop nanoparticles that deliver cancer imaging agents and anticancer drugs specifically to tumors. Two new reports in the literature highlight new approaches to creating targeted nanoscale devices for diagnostic and therapeutic applications in cancer.

Writing in the journal *Nano Letters*, Elizabeth Singer, Ph.D., and Steven Smith, Ph.D., both at the City of Hope Medical Center, describe their use of a bacterial enzyme known as methyltransferase to attach as many as three different targeting molecules to a piece of Y-shaped DNA. The researchers engineered the Y-shaped DNA so that it contains a specific nucleic acid, known as 5-fluorocytosine, at the end of each arm. 5-Fluorocytosine tricks the enzyme into forming a chemical bond between the enzyme itself and the DNA molecule. Normally, this enzyme merely attaches individual methyl groups ($-CH_3$) to specific sequences of DNA, a process involved in gene regulation.

Methyltransferase itself is not a targeting molecule, but the researchers were able to create so-called fusion proteins between methyltransferase and proteins, such as thioredoxin, that do bind to malignant cells. Computer modeling studies enabled the investigators to determine in advance how best to link thioredoxin to methyltransferase without destroying the activity of the enzyme or the tumor-targeting ability of thioredoxin. The researchers also attached a fluorescent molecule to a different part of the DNA molecule in order to have the ability to image the nanoscale device.

Using a variety of cell lines growing in culture, the investigators then tested whether this nanoscale device could target prostate cancer cells expressing the thioredoxin receptor on their surfaces and distinguish among those cells and those not expressing this particular receptor. Indeed, fluorescence imaging showed that this nanoscale construct did bind only to those cells expressing the thioredoxin receptor, suggesting to the investigators that their nanoscale device could be useful in histological tumor typing assays. The researchers also note that the methods they developed can be tailored to attach a different molecule to each arm of the Y-shaped DNA molecule.

The second report, from Ronald Andres, Ph.D., and his colleagues at Purdue University, describes the development of folic acid-based targeting agents for use with gold nanoparticles. The goal of this project was to further efforts aimed at using gold nanoparticles as light-activated thermal scalpels for killing malignant cells, many of which overexpress a receptor for folic acid on their cell surfaces. This paper was published in the journal *Bioconjugate Chemistry*.

The investigators began their work with poly(ethylene glycol), a biocompatible, water-soluble polymer that can “hide” nanoscale objects from the immune system. To one of the polymer, the researchers attached one molecule of folic acid. They also added thioctic acid, a molecule that contains two sulfur atoms situated at the ends of what looks like molecular tweezers, to the other end of the polymer. Sulfur atoms are notorious for binding avidly to gold, and as expected, when added to gold nanoparticles this engineered polymer formed a tightly attached surface coating. The resulting coated gold nanoparticles had an average diameter of 10 nanometers and were soluble in water.

Using transmission electron microscopy, the investigators were able determine that these gold nanoparticles were taken up efficiently by tumor cells expressing the folic acid receptor. Other types of cancer cells

that lack surface folic acid receptors did not take up the nanoparticles.

The work with nanodevices made from Y-shaped DNA, which was supported by the National Cancer Institute, is detailed in a paper titled, "Nucleoprotein assemblies for cellular biomarker detection." This paper was published online in advance of print publication. An abstract of this paper is available at the journal's website.

The work with folate targeting is detailed in a paper titled, "Synthesis and grafting of thioctic acid-PEG-folate conjugates onto Au nanoparticles for selective targeting of folate receptor-positive tumor cells." This paper was published online in advance of print publication. An abstract of this paper is available at the journal's website.

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