Nanoparticles Detect Telomerase Activity

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Telomerase, an enzyme that prevents chromosomes from shortening when they divide, is widely suspected of playing a key role in making cancer cells immortal. Though researchers have developed a variety of methods for measuring the activity of this enzyme, none of these methods have proved suitable for use in diagnostic assays for cancer or in efforts to develop drugs that block telomerase activity.

Now, a team of investigators at Northwestern University's Nanomaterials for Cancer Diagnostics and Therapeutics has developed a new type of nanoparticle-based assay that appears to be both accurate and sensitive enough for clinical use.

Chad Mirkin, Ph.D., principal investigator of the National Cancer Institute-supported Center for Cancer Nanotechnology Excellence at Northwestern, led the research team that developed the new assay. Their results appear in the Journal of the American Chemical Society.

The assay system consists of gold nanoparticles coated with short stretches of DNA that can serve as a substrate for telomerase. When a sample containing this enzyme is mixed with these nanoparticles, telomerase binds to the DNA sequences and begins adding repeated stretches of six specific nucleotides to the end of the DNA. After a short time, the investigators wash off any telomerase and then add magnetic microparticles coated with a piece of oligonucleotide that is complementary to the sequence added by telomerase.

The coated magnetic microparticles bind to any elongated DNA and

enable the researchers to separate those complexes from the rest of the gold nanoparticles by using a magnetic field. Next, the DNA sequences are removed from the gold nanoparticles and are detected using a silver development process and automated reader that Dr. Mirkin's team invented for a related assay system, known as the biobarcode assay.

Using this assay, the investigators were able to reliably detect telomerase activity in as few as 10 to 1,000 tumor cells grown in culture. The researchers then showed that they could detect changes in telomerase activity after the addition of a known inhibitor of the enzyme, suggesting that this assay could help in efforts to develop telomerase inhibitors as anticancer agents.

This work, which was supported in part by the National Cancer Institute's Alliance for Nanotechnology in Cancer, is detailed in the paper "A New Approach to Amplified Telomerase Detection with Polyvalent Oligonucleotide Nanoparticle Conjugates."

Source: National Cancer Institute