Catching the early spread of breast cancer

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When cancer spreads from one part of the body to another, it becomes even more deadly. It moves with stealth and can go undetected for months or years. But a new technology that uses "nano-flares" has the potential to catch these lurking, mobilized tumor cells early on. Today, scientists presented the latest advances in nano-flare technology as it applies to the detection of metastatic breast cancer cells.

The report was one of more than 10,000 at the 247th National Meeting & Exposition of the American Chemical Society (ACS).

"We've taken perhaps the world's most important molecule, DNA, rearranged it into a spherical shape and modified it to detect specific molecules inside cells. These structures naturally enter cells and light up when they detect disease-causing molecules," said Chad Mirkin, Ph.D., who is collaborating with C. Shad Thaxton, M.D., Ph.D., to develop the new technology. "We're seeing if we can use nano-flares to create a new type of breast cancer diagnostic, and the early results are remarkable. Nano-flares could completely and radically change how we diagnose breast cancer."

Earlier is better when it comes to cancer detection, but sometimes, by the time a patient notices symptoms and visits a doctor, the first tumor has already spread from its original location in the body to another. It has undergone "metastasis," a state that causes many deaths related to cancer. Cancer took the lives of more than 8 million people worldwide in 2012.

To catch breast cancer—and possibly other types of cancers—earlier, the research groups built upon Mirkin's ongoing program that kicked off in the 1990s with the invention of "spherical nucleic acids" (SNAs). SNAs are usually made out of a gold nanoparticle core covered with densely packed, short strands of DNA.

"We thought that if we could get large amounts of nucleic acids to go inside cells, we could manipulate and measure things inside cells," said Mirkin, of Northwestern University. "Most people said we were wasting our time, but then out of curiosity, we put these particles in cell culture. Not only did we find that they go in, they went in better than any material known to man."

Taking advantage of their ability to enter cells easily, Mirkin's group set out to turn SNAs into a diagnostic tool—the nano-flare. Recently, he and Thaxton designed these particles, which enter circulating healthy and unhealthy cells in blood samples, but light up only inside breast cancer cells.

"Nano-flares can detect just a few cancer cells in a sea of healthy cells," Mirkin said. "That's important because when cancer spreads, only a few cells may break off from the original tumor and go into the bloodstream. An added bonus of these particles is that scientists may be able to sample the live cancerous cells and figure out what therapies they might respond to."

The groups have successfully tested the nano-flares' ability to identify metastatic breast cancer cells in blood samples from animals and are currently experimenting with human samples.

"If the work pans out, a commercial diagnostic test could be available in the near future," Thaxton said.

In addition to diagnostics, it turns out nano-flares can be used to perform other unique and valuable tasks.

"Nano-flares represent the only way to measure genetic content in live cells," Mirkin said. This kind of real-time observation could be useful in many areas of research and could lead to clinical advances. For example, using nano-flares, scientists can see how drugs target different genes. This would help them develop better treatments. One company, Millipore, has already commercialized the particles for use in research labs under the name SmartFlaresTM and offers more than 1,200 variations.

More information: Presentation: "Nano-flares" for the analysis of circulating cancer cells

Abstract
Cancer metastasis is the leading cause of mortality among cancer patients. Indeed, most traditional methods for diagnosing it rely on analysis of secondary tumor sites after metastasis has already occurred. Therefore, the ability to detect metastatic cancer cells from patient blood samples, before the development of secondary tumors, would represent a revolutionary advance in cancer diagnostics. We have designed and synthesized a nanoparticle-based system, which moves toward accomplishing this goal. Nano-flares are spherical nucleic acid (SNA)-gold nanoparticle constructs, which are bound to displaceable fluorescent reporter strands. These structures have the ability to efficiently enter cells without the use of transfection agents and provide an intracellular fluorescence signal correlated with the concentration of a target molecule. Therefore, they can be used to translate traditional extracellular diagnostic approaches to an intracellular environment. Advantageously, this nanoconjugate system exhibits all of the novel cooperative properties of SNA-gold nanoparticle conjugates, including enhanced target hybridization, resistance to enzymatic breakdown and

low immune response and can be easily combined with gene regulation technologies. Specifically, we have developed a functional assay for detecting multiple putative metastatic markers (such as Twist, vimentin and fibronectin) in circulating breast cancer cell populations. Furthermore, we have coupled nano-flare technology with flow cytometry to isolate these small breast cancer cell populations in cell culture and from whole blood samples for individual analysis. We are currently working to validate this novel nano-flare-based approach against traditionally-used assays, as well as to improve the sensitivity and specificity of nano-flares. We are also extending the capability of the system to address the need for multiplexed approaches, which allow for semi-quantitative detection of multiple mRNA targets simultaneously.

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