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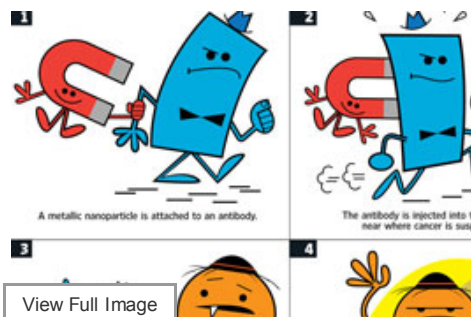
## Researchers Create Better Ways to Spot Cancer Cells

By SHIRLEY S. WANG



Cancer can be notoriously difficult to spot, so scientists are working to develop new techniques to better detect tumors in the body.

Such tools could potentially identify cancer cells more reliably and earlier than currently available methods, such as mammography, biopsies and magnetic resonance imaging, or MRI. Improved detection methods could help speed up treatment decisions and monitor whether a therapy is working.



Some cancer researchers are working with metal nanoparticles—tiny bits of matter that are 100,000 times smaller than the thickness of a sheet of paper—and sensitive magnetic fields to locate breast-cancer cells. The technique appears to be much more sensitive than current methods allow and eliminates fears of radiation from a mammogram. Other scientists are attempting to improve detection of melanoma skin cancers without taking painful biopsies that can leave unsightly scars.

Another research project, also involving nanoparticles, aims to identify the molecular "fingerprint" of cancer of the abdomen, which could reveal how invasive the cancer is and from what part of the body it may have

originated.

Current cancer-detection methods have limitations. Some technologies, like mammography used for screening for breast cancer, can only detect cancerous tumors after they have grown to a certain size. With biopsies, in which samples of tissue are removed for study, only a portion of the sample is examined; it is too time consuming and expensive to look at the entire biopsy. And, because tissues are sampled randomly from suspicious regions, it is hit-or-miss whether the biopsies actually capture any cancerous cells that may be present. MRIs are more sensitive than mammography but are more expensive and have some limitations on image quality.

With some types of cancer, like melanoma, distinguishing between a normal mole and cancerous skin tissue is extremely challenging, even for experienced medical professionals, says Mitchell Kline, a New York-based dermatologist and an expert in diagnostic tools for melanoma. There is a lot of variability in the appearance of skin tissue, he says. Recent research suggests that as few as 1 in 30 skin biopsies conducted turn out to be cancerous.

Edward Flynn, at the Los Alamos National Laboratory in New Mexico, and his colleagues are working with nanoparticles to detect breast-cancer cells. The technique involves attaching nanoparticles of iron oxide to certain antibodies, which are then injected into the patient. If a tumor is present, the antibodies, with the nanoparticles in tow, naturally recognize and bind to the HER-2 receptor of breast-cancer cells.

The patient is then surrounded with sensitive magnetic coils known as SQUID, for superconducting quantum interference device. A magnetic field is generated and all of the metal nanoparticles align in one direction. When the magnetic field is broken, the nanoparticles emit an electromagnetic signal as they relax back into their original state. By measuring the strength of the signal, doctors can tell how many metal particles, and therefore how many cancer cells, are present, and where in the breast they are located.

With mammography, which uses low doses of radiation to image the breast, approximately 100 million cancer cells—equal to a tumor about 6 to 8 millimeters in size—must be present before they show up on the film. Dr. Flynn says early tests of the SQUID technology in mice have shown that the technique can detect as few as 50,000 breast-cancer cells. That suggests a cancer could be detected 2½ years sooner using SQUID rather than a mammogram, he says. Dr. Flynn says he and his team plan to submit the data for publication soon.

Dr. Flynn, who also serves as chief executive of nanomedicine firm Senior Scientific LLC of Albuquerque, N.M., originally worked as a nuclear physicist at Los Alamos, studying how the atomic nucleus functions. He began wondering if the technology could be used to study the body, and he turned his attention to researching the brain and later to looking at cancer.

A key challenge of the SQUID technology is getting the nanoparticles, which are made in a lab using chemical techniques, into cancer cells at sufficient quantities to detect the magnetic charge, Dr. Flynn says. Another issue: making sure the antibodies bind only to cancer and not to normal cells. Only 30% to 40% of breast cancers contain the HER-2 receptor, the target in the current experiment. If more cancer-specific receptors can be identified, the technology's utility could grow, he says.

Dr. Flynn's team previously demonstrated that the SQUID technology could be used to assess the progress of leukemia patients. The process enables doctors to count cancer cells before and again after a chemotherapy treatment to gauge the effectiveness of the therapy. The results were published in a 2009 paper in the journal *Cancer Research*.

Jared Haun, a researcher at the Center for Systems Biology at Massachusetts General Hospital, and colleagues are running a program to analyze abdominal cancer. They take a biopsy of the tumor and, after attaching magnetic nanoparticles, examine the types of proteins the cancer cells produce. A "smart-phone"-like device using the same magnetic technology as an MRI can read the molecular "fingerprint" of cancer, potentially providing data about how invasive the cancer is, where in the body it originated and whether a treatment is working, says Dr. Haun. The findings, published last week in the journal *Science Translational Medicine*, showed the technology correctly identified that samples were cancerous in 44 of 50 patients.

Another cancer-detection effort is aimed at melanoma, which is normally diagnosed using skin biopsies. Bill Wachsman, a hematologist oncologist at the University of California, San Diego, and his colleagues have developed a Scotch-tape-like adhesive to remove dead cells from the skin for a sample of the genes that are active in skin cells in that region. Dr. Wachsman, who also serves as an advisor to La Jolla, Calif.-based biotech DermTech International, says the genes are then compared to a panel of 17 genes known to be common to various forms of melanoma. Similarities in the pattern indicate that melanoma is present.

Results from a recent study showed that the test was able to accurately diagnose 100% of malignant samples, but falsely identified 12% of the normal samples as positive for cancer. With biopsies, some 95% of clinically performed biopsies are false-positives, says Dr. Wachsman. The paper was published recently in the *British Journal of Dermatology*.

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