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The Feel of Cancer Cells

Future diagnostic tests for cancer may probe cell stiffness.

By Katherine Bourzac

Aggressive cancer cells are about 70 percent softer than normal cells, according to research from the University of California at Los Angeles (UCLA). The UCLA researchers are the first to mechanically probe the physical properties of live cancer cells taken directly from a patient. The researchers suggest that such nanomechanical tests of cancer cells might be incorporated into future cancer diagnosis and treatment.

Using atomic-force microscopy, chemist [James Gimzewski](http://www.chem.ucla.edu/dept/Faculty/gimzewski/) and pathologist [Jianyu Rao](http://faculty.uclaaccess.ucla.edu/institution/physician?personnel_id=9187) measured the stiffness of living cells in samples taken from the fluid surrounding the lungs of patients with cancer. Any cancer cells found in these samples have left the patient's original tumor, indicating that the cancer is spreading. Gimzewski and Rao found that lung, breast, and pancreatic cancer cells in these samples were much softer than normal cells.

The finding is consistent with what is known about cancer cells. In order to spread and form new tumors, cancer cells "need to circulate through narrow blood capillaries and then ooze between other cells into normal tissue," says [Dennis Discher](http://www.seas.upenn.edu/~discher/), professor of chemical and biomolecular engineering at the University of Pennsylvania. Being soft and flexible might give aggressive, traveling cancer cells a physical advantage, says Discher.

Clinical detection of these spreading, or metastatic, cancer cells is problematic. Rao says that he examines about five such samples a day and that, under the microscope, some normal cells resemble cancer cells. "It's challenging to make a correct diagnosis of cancer," he says. By examining the shape of dead cells under the microscope, and by applying fluorescent dyes that highlight particular proteins on their surfaces, Rao says that pathologists can distinguish cancer cells with about 85 percent accuracy. He hopes that adding a mechanical test will lead to greater accuracy.

Biologists usually focus on the chemical properties of cells, not on their physical properties. In the past few years, nanotechnologist Gimzewski and engineers like MIT's [Subra Suresh](http://dmse.mit.edu/faculty/faculty/ssuresh/) have begun applying the tools of materials science and engineering to cells. In 2005, Suresh made some of the first measurements of the physical properties of cancer cells. He and other researchers have studied the physical properties of cells using many techniques, from squishing them between parallel glass plates, to stretching them with optical tweezers, to probing them with atomic-force microscopy, a nanomechanical tool used to study surfaces at high resolution. "This is only the beginning," says Suresh, referring to the use of mechanical tools to understand the physical properties of cancer cells.

Gimzewski and Rao use the ultrasharp tip of an atomic-force microscope probe to apply force to single cells and measure the resistance. Cancer cells have less resistance to such poking than normal cells do. Gimzewski and Rao's innovation is to study live cells taken directly from cancer patients, rather than cells grown in the lab.

The UCLA researchers are currently probing lung-fluid samples taken from patients with different types of cancer, including prostate and ovarian, and they will also test cells from primary tumors. Gimzewski says that he and his team will also test how cancer drugs affect cell stiffness. They hope that cell stiffness will help researchers determine how aggressive a patient's cancer is and predict whether it will respond to particular therapies.

[Sanford Barsky \(http://www.ibgp.org/faculty/profilepage.asp?ID=432\)](http://www.ibgp.org/faculty/profilepage.asp?ID=432), chief of pathology at the Ohio State University Medical Center, says that atomic-force microscopy is an "esoteric, high-power technique" that's unlikely to be widely adopted by hospitals. If further research supports Gimzewski and Rao's results, Barsky says, it will be important to find out what molecular changes are associated with cancer cells' structural changes. Detecting particular proteins in a clinical setting, says Barsky, is relatively routine; if the structural changes are caused by alterations in a protein, detecting that protein would be cheaper and easier than using atomic-force microscopy.

But Suresh agrees with Rao that cancer hospitals would adopt atomic-force microscopy if it proves clinically useful. The instruments cost about \$60,000--well within the budgets of many hospitals. Gimzewski says that he hopes future clinical instrumentation will incorporate automated atomic-force microscopy with the traditional optical microscopes used by pathologists.

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