Novel ultrafast laser detection of cancer cells also may improve understanding of stem cells

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To investigate tumors, pathologists currently rely on labor-intensive microscopic examination, using century-old cell-staining methods that can take days to complete and may give false readings.
A lightning-fast laser technique, led by Sandia National Laboratories researcher Paul Gourley, has provided laboratory demonstrations of accurate, real-time, high-throughput identification of liver tumor cells at their earliest stages, and without invasive chemical reagents.

The technique generates a laser beam in single human cells pumped from a flask through tiny microchannels. The beam is altered by what it encounters. These changes, registered by an imaging spectrometer, instantly identify cancer-modified mitochondria in cells gone wrong. Mitochondria are known as the power pack of cells, energizing them like batteries do flashlight bulbs.

"There are hundreds of mitochondria, sometimes thousands, in a cell," says Gourley. "To see them in the old way requires a time-consuming process like fluorescent tagging or a chemical reagent. We've found we can see them immediately by light alone."

The techniques could be critical to advancing early detection, diagnosis, and treatment of disease.

More technically put, "To rapidly assess the health of a single mammalian cell," says Gourley, "the key discovery was the elucidation of biophotonic differences in normal and cancer cells by using

intracellular mitochondria as biomarkers for disease. This technique holds promise for detecting cancer at a very early stage and could nearly eliminate delays in diagnosis and treatment."

The technique is effective because "it measures changes in the cell architecture, especially those arising from alterations in protein density, cytoskeleton shape, and distribution of mitochondria - changes that occur when a cell becomes cancerous," says Gourley.

"One would think that if a cell became nonfunctional, it would become disorganized. In cancer, however, that's not the case. A cancer cell is like an insurgent terrorist with a very well-defined agenda. It rearranges the cytoskeleton and the arrangement of mitochondria in the cell. It's no longer a cooperative agent in a collection of cells but becomes malicious, tries to get outside the area, and hijacks the respiratory machinery of a cell."

The biocavity laser

It is these changes - a kind of beefing-up of the criminal forces - that Gourley's device, called a biocavity laser, detects.

A nano-thin layering of gallium aluminum arsenide combinations send up numerous tiny beams from a small cross-sectional generating area. These beams are reinforced or thwarted by the position and density of the mitochondria.

"The pictures we get from normal and cancer cells are very different," says Gourley. "Mitochondria conspire to cluster around the nucleus and work together to supply energy to the healthy, functioning cell. In contrast, the mitochondria in the cancer cell sit all over, isolated and balled up in a quiescent, non-functioning state. Apparently, the rapidly growing cancer cells derive energy from an alternative source such as

free glucose in the cell."

Fortunately, the mitochondrion is nearly the same size as the light wavelength of about 800 nanometers, a frequency otherwise little absorbed by the body. Because of this close match, the laser is exquisitely sensitive to subtle changes in the mitochondria size and effects of clustering. To date, the research team has found that 90 to 95 percent of light scatter generated is from optical properties of mitochondria.

Working with UCSD

According to Bob Naviaux, professor at the School of Medicine at the University of California at San Diego and co-director of its Mitochondrial and Metabolic Disease Center, "What's attractive about this novel optical method for identifying cancer cells is it's a very rapid and general method that potentially can be applied to cancer cells from solid tumors as well as hematological malignancies like leukemia."

Naviaux looks forward to examining a wider population of cancer cells to validate the method, combining the resources of his Center with Sandia's laser expertise.

A project proposal has been filed with Sandia to support collaborative work between the unique research capabilities of UCSD and Sandia. "There are 300 different cell types in the human body and different mitochondria for each different shape and arrangement," says Naviaux. "We want a library of spectra from different cell types and their cancers."

Aiding stem cell research

Of further interest is that the biocavity laser may be applied not only to identifying the spectra associated with cancer cells but also those associated with stem cells, and how these optical signals change as they differentiate into nerve, muscle, and other tissues. "At present, there's no rapid method for identifying the transitional states [of a stem cell] with the functional cell type it eventually becomes. That process is a mysterious sequence of metabolic and genetic changes." There are, he says, metabolic similarities between stem cells and cancer cells, and researchers would like to clearly identify the differences.

"Stem cells are therapeutic," says Naviaux. "How are their spectra distinct from cancer?"

A difficulty still ahead is viewing cancer cells in fluids taken directly from the body, rather than isolated by type in a flask. This problem will be solved by winnowing out unlikely particles through size and frequency.

Source: DOE/Sandia National Laboratories