World's fastest camera used to detect rogue cancer cells

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Optical microscope with world's fastest camera

(Phys.org) -- The ability to distinguish and isolate rare cells from among a large population of assorted cells has become increasingly important for the early detection of disease and for monitoring disease treatments.

Circulating cancer tumor cells are a perfect example. Typically, there are only a handful of them among a billion healthy cells, yet they are precursors to metastasis, the spread of cancer that causes about 90 percent of cancer mortalities. Such "rogue" cells are not limited to cancer — they also include stem cells used for regenerative medicine and other cell types.

Unfortunately, detecting such cells is difficult. Achieving good statistical accuracy requires an automated, high-throughput instrument that can examine millions of cells in a reasonably short time. Microscopes equipped with digital cameras are currently the gold standard for analyzing cells, but they are too slow to be useful for this application.

Now, a new optical microscope developed by UCLA engineers could make the tough task a whole lot easier.

"To catch these elusive cells, the camera must be able to capture and digitally process millions of images continuously at a very high frame rate," said Bahram Jalali, who holds the Northrop Grumman Endowed Opto-Electronic Chair in Electrical Engineering at the UCLA Henry Samueli School of Engineering and Applied Science. "Conventional CCD and CMOS cameras are not fast and sensitive enough. It takes time to read the data from the array of pixels, and they become less sensitive to light at high speed."

The current flow-cytometry method has high throughput, but since it relies on single-point light scattering, as opposed to taking a picture, it is not sensitive enough to detect very rare cell types, such as those present in early-stage or pre-metastasis cancer patients.

To overcome these limitations, an interdisciplinary team of researchers led by Jalali and Dino Di Carlo, a UCLA associate professor of bioengineering, with expertise in optics and high-speed electronics, microfluidics, and biotechnology, has developed a high-throughput flow-through optical microscope with the ability to detect rare cells with sensitivity of one part per million in real time.

This technology builds on the photonic time-stretch camera technology created by Jalali's team in 2009 to produce the world's fastest continuous-running camera.

In the latest issue of the journal *Proceedings of the National Academy of Sciences*, Jalali, Di Carlo and their colleagues describe how they integrated this camera with advanced microfluidics and real-time image processing in order to classify cells in blood samples. The new blood-screening technology boasts a throughput of 100,000 cells per second, approximately 100 times higher than conventional imaging-based blood analyzers.

"This achievement required the integration of several cutting-edge technologies through collaborations between the departments of bioengineering and electrical engineering and the California NanoSystems Institute and adds to the significant technology infrastructure being developed at UCLA for cell-based diagnostics," Di Carlo said.

Both Jalali and Di Carlo are members of the California NanoSystems Institute at UCLA.

Their research demonstrates real-time identification of rare breast cancer cells in blood with a record low false-positive rate of one cell in a million. Preliminary results indicate that this new technology has the potential to quickly enable the detection of rare circulating tumor cells from a large volume of blood, opening the way for statistically accurate early detection of cancer and for monitoring the efficiency of drug and radiation therapy.

"This technology can significantly reduce errors and costs in medical diagnosis," said lead author Keisuke Goda, a UCLA program manager in electrical engineering and bioengineering.

The results were obtained by mixing cancer cells grown in a laboratory with blood in various proportions to emulate real-life patient blood.

"To further validate the clinical utility of the technology, we are currently performing clinical tests in collaboration with clinicians," said Goda, also a member of the California NanoSystems Institute. "The technology is also potentially useful for urine analysis, water quality monitoring and related applications."

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