Microfluidic Devices Capture and Analyze Single Cancer Cells

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(PhysOrg.com) -- One of the grand goals in nanotechnology is to develop a single microfluidic device that integrates all of the components needed to perform polymerase chain reaction (PCR)-based nucleic acid analyses. Experts predict that such a device would enable researchers to develop rapid assays for cancer and other life-threatening diseases while a patient is in the doctor's office.

A team of investigators at the University of California, Berkeley not only has built such a device, but also has used it to measure changes in gene expression in individual cells following treatment with an agent designed to silence gene expression. The device features four distinct regions that capture single cells, break them apart, amplify the messenger RNA (mRNA) from the cells using reverse-transcriptase PCR, and then analyze and quantify the amplified nucleic acids. The team, led by Richard Mathies, Ph.D., and Carolyn Bertozzi, Ph.D., describes its new device in the journal *Proceedings of the National Academy of Sciences of the United States of America.*

Four complete devices reside on a glass wafer that is a mere 100 millimeters in diameter. A complete analysis, from cell capture to data output, takes less than 75 minutes. A fully integrated capillary electrophoresis system—a miniaturized version of a standard PCR analysis setup—is incorporated in each device and yields data in a format readily interpretable by anyone with PCR experience. The researchers note that the device should be capable of measuring the expression of 5 to 10 different genes simultaneously.

As a test of the device's capabilities, the researchers analyzed gene expression by Jurkat T-lymphocyte cells that were first treated with a small interfering RNA (siRNA) agent designed to reduce production of a protein known as GAPDH. When the cells were analyzed in bulk, using standard methods, the results showed that siRNA treatment reduced GAPDH expression to 21% of its original value before treatment. However, an analysis of individual cells showed that there were two populations of cells, one of which experienced complete silencing of GAPDH, whereas the other showed moderate gene silencing in which protein expression was cut in half.

One of main limitations of this device is that it uses a biochemical "trick" to capture cells. This trick involves growing the cells of interest in a special growth medium that enables the cell to present a specific chemical group on their cell membranes. This chemical group acts as a tether that can be used to capture the cells inside the microfluidic device. However, research by Weihong Tan, Ph.D., and his colleagues at the University of Florida details a different approach for capturing specific types of cancer cells, which could be used with the integrated mRNA analyzer.

Reporting its work in the journal *Analytical Chemistry*, Dr. Tan's group describes its use of aptamers to capture cancer cells in a microfluidic device. Aptamers are short, chemically synthesized pieces of DNA or RNA that bind strongly to protein targets, much like antibodies. Using the standard aptamer discovery technology known as SELEX, the researchers are able to quickly identify aptamers that bind to a specific cell type—in this case acute lymphocytic leukemia cells—while ignoring all others. The investigators then immobilized this aptamer on the surface of a microfluidic channel and used it to capture about 80 percent of the target cells in a mixture of cells. The purity of the captured cells was over 97%.

The study results from Dr. Mathies and his colleagues are detailed in the paper “Integrated microfluidic bioprocessor for single-cell gene expression analysis.” Investigators from the Howard Hughes Medical Institute and the Lawrence Berkeley National Laboratory also participated in this study. An abstract of this paper is available from the journal’s Web site.

The work from Dr. Tan’s group is described in the paper “Enrichment of cancer cells using aptamers immobilized on a microfluidic channel.” An investigator from Xiamen University in China also participated in this study. An abstract of this paper is available at the journal’s Web site.

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