Nanostructured Integrated Circuit Detects Type and Severity of Cancer

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(PhysOrg.com) -- A team of investigators from the University of Toronto have used nanomaterials to develop an inexpensive microchip sensitive enough to quickly determine the type and severity of a patient's cancer so that the disease can be detected earlier for more effective treatment. Their work, reported in two papers published in the journals *ACS Nano* and *Nature Nanotechnology*, could herald an era when inexpensive yet sophisticated molecular diagnostics will become commonplace.

The researchers' new device can readily detect the signature biomarkers that indicate the presence of cancer at the cellular level, even though these biomolecules - genes that indicate aggressive or benign forms of the disease and differentiate subtypes of the cancer - are generally present only at low levels in biological samples. Analysis can be completed in 90 minutes, a significant improvement over the existing diagnostic procedures that generally take days.

"Today, it takes a room filled with computers to evaluate a clinically relevant sample of cancer biomarkers and the results aren't quickly available," said team co-leader Shana Kelley. "Our team was able to measure biomolecules on an electronic chip the size of your fingertip and analyse the sample within half an hour. The instrumentation required for this analysis can be contained within a unit the size of a BlackBerry."

The nanoelectrode device that Kelley, collaborator Edward Sargent, and their students created is able to detect disease-related genes without the

use of PCR to amplify low-level DNA. The electrodes, which are the key component of the device, have a novel highly-branched nanostructured shape that can detect attomolar concentrations of DNA. Using arrays of electrodes, each differing in the degree of nanostructured branching, the investigators were able to construct a device capable of sensing DNA molecules over six orders of magnitude, overcoming the dynamic range issue - the ability to detect both common and rare molecules - that has plagued other devices.

The investigators fabricated these devices using a standard microchip production process known as photolithography to create the basic electrode grid needed to measure multiple biomarkers simultaneously, and then used a second technique known as electrodeposition to grow the branched nanostructures on the electrodes, controlling the size of each electrode by varying the time over which electrodeposition occurred. With the electrodes in place, the investigators then coated them with various DNA-binding molecules known as peptide-nucleic acids, or PNAs, that can be designed to bind to a specific gene sequence. When a piece of DNA binds to its complementary DNA or RNA molecule, it triggers a chemical reaction that alters the electrical signal generated by the associated electrode.

Using their device, the investigators analyzed messenger RNA samples from prostate cancer biopsies. Their analysis showed that the device can detect gene fusions characteristic of prostate cancer. More importantly, the device was able to distinguish between gene fusions associated with either fast- or slow-growing forms of prostate cancer.

The paper describing the construction of this nanobiosensor is titled, "Programming the detection limits of biosensors through controlled nanostructuring." An abstract of this paper is available at the journal's Web site.

The paper detailing the use of the nanobiosensor to detect and characterize cancers is titled, "Direct Profiling of Cancer Biomarkers in Tumor Tissue Using a Multiplexed Nanostructured Microelectrode Integrated Circuit." An abstract of this paper is available at the journal's Web site.

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