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Nanowires can detect molecular signs of cancer, scientists find

Use of minuscule devices to spot cancer markers could lead to ultra-powerful new diagnostics

CAMBRIDGE, Mass., Sept. 23, 2005 -- Harvard University researchers have found that molecular markers indicating the presence of cancer in the body are readily detected in blood scanned by special arrays of silicon nanowires -- even when these cancer markers constitute only one hundred-billionth of the protein present in a drop of blood. In addition to this exceptional accuracy and sensitivity, the minuscule devices also promise to pinpoint the exact type of cancer present with a speed not currently available to clinicians.

A paper describing the work will appear in October in the journal *Nature Biotechnology* and is now posted on the journal's web site.

"This is one of the first applications of nanotechnology to healthcare and offers a clinical technique that is significantly better than what exists today," says author Charles M. Lieber, Mark Hyman Jr. Professor of Chemistry in Harvard's Faculty of Arts and Sciences. "A nanowire array can test a mere pinprick of blood in just minutes, providing a nearly instantaneous scan for many different cancer markers. It's a device that could open up substantial new possibilities in the diagnosis of cancer and other complex diseases."

Lieber and his colleagues linked slender nanowires conducting a small current with antibody receptors for certain cancer markers -- such as prostate specific antigen (PSA), PSA-a1-antichymotrypsin, carcinoembryonic antigen and mucin-1. When these telltale proteins come into contact with a receptor, it sparks a momentary change in conductance that gives a clear indication of the marker's presence. The detectors differentiate among various cancer markers both through the specific receptors used to snag them and because each binds its receptor for a characteristic length of time before dislodging.

"Our results show that these devices are able to distinguish among molecules with near-perfect selectivity," Lieber says, adding that the risk of false readings is minimized by the incorporation of various control nanowires.

The scientists also fitted some nanowires in the arrays with nucleic acid receptors for telomerase, an enzyme inactive in most of the body's somatic cells but active in at least 80 percent of known human cancers. In testing of extracts from as few as 10 tumor cells, these receptors allowed real-time monitoring of telomerase binding and activity.

Lieber says nanowire arrays could easily be scaled up to detect many different cancer markers -- more of which are being found all the time, thanks to the current boom in proteomics. Widespread use of these cancer markers in healthcare will ultimately depend upon the development of techniques that allow rapid detection of many markers with high selectivity and sensitivity.

"Genomics and proteomics research has elucidated many new biomarkers that have the potential to greatly improve disease diagnosis," the scientists write. "The availability of multiple biomarkers is believed to be especially important in the diagnosis of complex diseases like cancer, for which disease heterogeneity makes tests of single markers inadequate. Patterns of multiple cancer markers might, however, provide the information necessary for robust diagnosis of disease ... [and] detection of markers associated with different stages of disease pathogenesis could further facilitate early detection."

While initial rounds of cancer testing today identify only whether or not cancer is present, nanowire arrays have the potential to immediately fill in details on exactly what type of cancer is present. Nanowires could also track patients' health as treatment progresses. Because the arrays detect molecules suspended in fluids, drops of blood could be tested directly, in a physician's office, without any need for biochemical manipulation.

Lieber's co-authors are Gengfeng Zheng, Fernando Patolsky, Yi Cui and Wayne U. Wang, all of Harvard's Department of Chemistry and Chemical Biology, Biophysics Program and Division of Engineering and Applied Sciences. The work was supported by the Defense Advanced Research Projects Agency and the National Cancer Institute.

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