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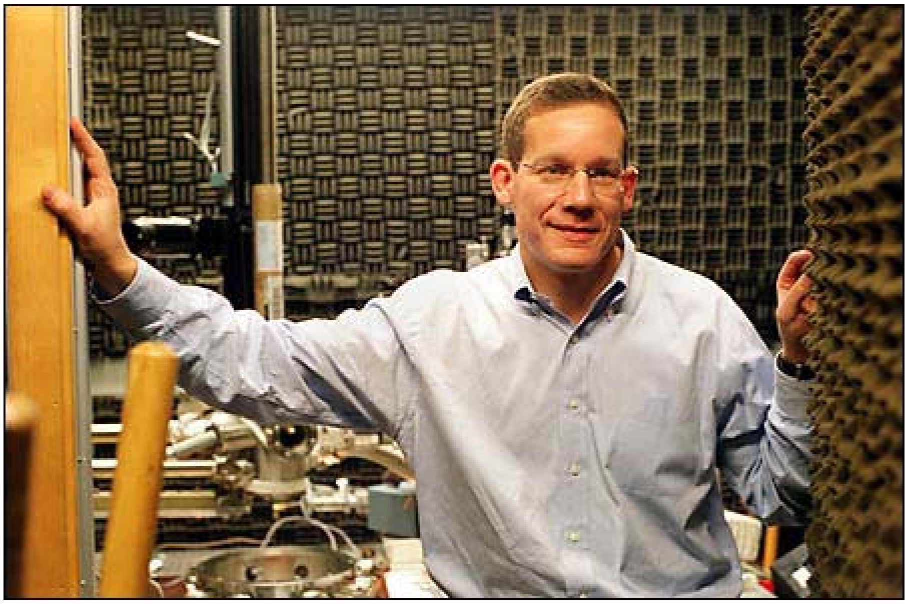

Charles Lieber has invented a new detector that may be small and fast enough to detect cancers while patients waits in a doctor's office. (Staff file photo Kris Snibbe/Harvard News Office)

New cancer detector developed that's fast, sensitive, reliable

By William J. Cromie
Harvard News Office

Cancers and many other diseases often reveal themselves by the presence of proteins absent or inactive in people who do not suffer from such ailments. Researchers are finding new biomarkers, as they are called, at a rapid pace, and they promise faster, more reliable ways to detect a disease earlier and to determine the prospect of recovering from it.

To take advantage of these "hot" new sources of information, researchers at Harvard University have developed a cracker-size electric sensor boasting wires thousands of times thinner than a human hair. In the near future, such sensors might test people for cancer while they wait in their doctor's office, or be implanted under their skin to monitor disease progression or the effectiveness of treatments.

"Our approach requires a minimum number of steps and very small samples [of blood]," says Charles Lieber, Hyman Professor of Chemistry, in whose lab the device was developed. "Tests done on human plasma samples show highly selective and unprecedented sensitivity to very small concentrations of protein markers that result from disease. The sensor detects multiple markers for the same or different diseases.

"These advantages lead to faster, possibly cheaper, and more reliable detection, which should greatly improve diagnosis and treatment of cancer and other complex diseases."

Higher sensitivity should also lead to earlier detection. The sooner treatment starts for cancers, the better the chances for survival.

Higher reliability equals fewer mistakes, so-called "false positives," that tell patients they have cancer or the AIDS virus when they do not.

Monitoring cancer

The disease detector works on a simple principle. Its ultrathin wires carry a tiny electric current and are coated with biochemicals that bind to the proteins. When that binding occurs, it increases or decreases the current. For example, prostate specific antigen (PSA), a well-known herald of prostate cancer, triggers an increase in current.

When men have their prostate tumors treated by surgery or radiation, tracking their PSA levels reveals whether their cancer is recurring. A sharp rise in this telltale protein signals that additional "salvage" treatment is needed.

Experts would like to have more than one test to detect and monitor such a widespread and deadly cancer - it kills about 30,000 men every year in the United States alone. High levels of PSA can lead to painful, expensive, and sometimes unnecessary biopsies when the cancer is slow growing, not to mention a great deal of worry for patients. That situation has led to a search for other biomarkers.

"The capability of our sensor to detect multiple markers simultaneously will enable it to handle new markers being developed by cancer biologists, and provide much more definitive diagnosis and monitoring of treatments," Lieber notes.

Laboratory tests that he and his colleagues have done show that known markers for breast and colon cancer can be found with this device. "As new and potentially better markers are developed, a multiplexed detector has a clear advantage for future health care," Lieber says. "Being able to screen for multiple markers for the same - or for different - diseases will lead to more reliable diagnoses than approaches that can check only one marker at a time."

While-you-wait results

The coated wires in this sensor also respond to proteins in urine, stool, saliva, and bits of tumor or tissue punched out by a biopsy needle. That capability is usable to detect a protein (enzyme) called telomerase, present in more than 80 percent of known human cancers. Other sensors can find this important enzyme, but not in so-called real time, that is, without any waiting. Finding telomerase immediately has advantages not only for detecting cancers but for studying it in laboratories.

Lieber claims that his instrument can "detect any protein or antibody expressed in the body as a result of disease." Antibodies are proteins released by the immune system to fight invasions by such diseases. That's how infections by HIV, the AIDS virus, are found and their severity measured.

Lieber believes that his instrument can do a better job than the present system used for a fast assay, called ELISA. That system requires more time-consuming steps, and, he says, "lacks the required sensitivity for early detection of HIV." He claims that his device "could perform earlier detection of the virus" and thus lead to earlier treatment and a better outcome.

Beside the potential for "while-you-wait" results in a doctor's office, Lieber envisions "development of under-skin implantable sensors which could be used by patients at home to continuously monitor their blood."

Details of how this would all work are described in the October issue of Nature Biotechnology. Authors of the report include Lieber, Gengfeng Zheng, Fernando Patolsky, Yi Cui, and Wayne Wang, all of the Department of Chemistry and Chemical Biology at

Harvard.

Lieber said that the sensor "could be available for everyday use with patients in the next two to five years."

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