

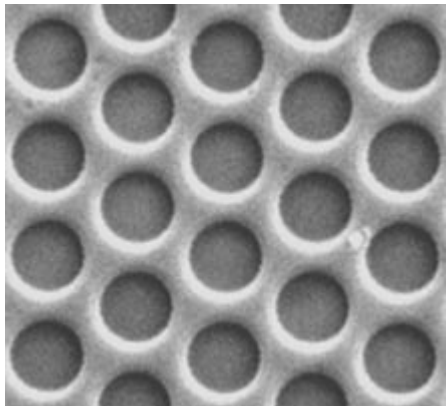
Next-Generation Diagnostics

A startup can detect tiny traces of cancer markers in blood samples.

By Katherine Bourzac

May 13, 2008

One of the loftier dreams of personalized medicine is to detect and eliminate tumors before they become life threatening—before they are even visible on medical images. Now a Cambridge, MA, startup called [Quanterix](#) is developing an extremely sensitive protein-detection technology that can count single molecules—and could potentially detect the trace amounts of characteristic proteins that tiny tumors release into the blood.



Lab on a tip: Wells carved into the tip of an optical fiber allow researchers to detect single proteins in blood samples. Each well in this image is about 2.5 micrometers in diameter and sits at the tip of an individual thread of an optical fiber.

“The premise is to get diagnostics to the most sensitive level possible,” says [David Walt](#), a chemist and Howard Hughes Medical Institute professor at Tufts University, who developed the Quanterix technology. Trace proteins in the blood could also reveal early signs of heart disease, Alzheimer’s, and other ailments, and enable noninvasive fetal diagnostics.

“If we could understand the baseline levels of proteins in the serum, it could be used to track the integrated health of a person over the course of life,” says [Christopher Love](#), a chemical-engineering professor at MIT who is not involved with Quanterix.

With current clinical technologies, hospital labs can detect only the most abundant proteins—only a quarter of all those known to be present in the blood. Because proteins are present in the blood at a range of different concentrations spanning about 16 orders of magnitude, abundant proteins mask the rare ones. “It’s like trying to look for a slightly different piece of hay in the haystack,” says [Forest White](#), a biological engineer at MIT.

The current detection limit is 10 picograms of protein per milliliter of blood. But Walt has developed a detection technique that allows him to count individual protein molecules present in the blood using specially treated optical fibers. A single optical fiber is a bundle made up of thousands of individual glass threads, each of which carries a distinct stream of light. By dipping optical fibers in acid, Walt etches them with tens of thousands of microwells, one at the tip of each thread. That effectively makes each fiber into a large array of nanoscale test tubes, each of which is then coated with thousands of protein-capturing antibodies.

The tip of the fiber is dipped into a droplet containing a blood sample and a protein-targeting enzyme. If the protein is present in the blood trapped inside an individual well, it will be captured between the antibody and the enzyme like the meat inside a sandwich. When Walt sends light down the optical fiber, the sandwiched antibody and enzyme undergo a reaction that produces red or yellow fluorescent light. The light travels back up the optical fiber.

By counting how many microwells light up, Walt can determine the concentration of a protein in a blood sample. In an unpublished proof-of-principle experiment, Walt says that his optical-fiber method was able to detect a human cancer biomarker in cow's blood at concentrations 250 times lower than that possible using clinical techniques.

So little is known about the 800 or more remaining blood proteins that fall under current detection limits that scientists can only speculate on their clinical relevance. "We're talking to clinicians to figure out what makes sense to test for," says Walt. Once the company picks target proteins, they'll draw on blood samples archived at hospitals and try to correlate protein levels with clinical outcomes. "Every time a more sensitive technology has become available, it has opened up new diagnostics and led to advances in treatment," says Walt.

Early detection can have a downside. "We don't want to scare people by telling them, 'You have an early tumor,'" says Walt. "It may be that the immune system takes care of small tumors." So any potential biomarkers will have to be carefully validated. But even if the new method only leads to a test for a single cancer biomarker, Walt hopes that it will improve survival rates for a large number of people.

"We believe this has the potential for transforming diagnostics," Walt says.

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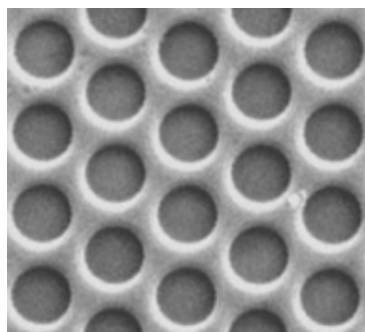
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