Biochips can detect cancers before symptoms develop

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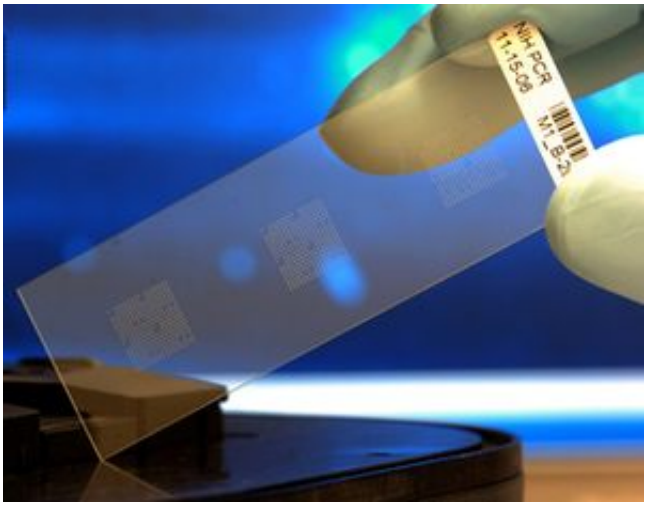

Biochips contain grids of small wells or "dots," each of which contains a protein, antibody or nucleic acid that can bind to a target antigen or DNA sequence.

In their fight against cancer, doctors have just gained an impressive new weapon to add to their arsenal. Researchers at the U.S. Department of Energy's Argonne National Laboratory have developed a chip that can save lives by diagnosing certain cancers even before patients become symptomatic.

The new technology, known as a biochip, consists of a one-centimeter by one centimeter array that comprises anywhere between several dozen and several hundred "dots," or small drops. Each of these drops contains

a unique protein, antibody or nucleic acid that will attach to a particular DNA sequence or antigen.

A tumor, even in its earliest asymptomatic phases, can slough off proteins that find their way into a patient's circulatory system. These proteins trigger the immune system to kick into gear, producing antibodies that regulate which proteins belong and which do not.

"Antibodies are the guardians of what goes on in the body," said Tim Barder, president of Eprogen, Inc., which has licensed Argonne's biochip technology to search for new biomarkers that indicate cancer. "If a cancer cell produces aberrant proteins, then it's very likely that the patient will have an antibody profile that differs from that of a healthy person. You can look for similarities and differences in autoantibody profiles to look for clues and markers that provide early indicators of disease."

In their hunt for cancer indicators, Eprogen uses a process called 2-dimesional protein fractionation, which sorts thousands of different proteins from cancer cells by both their electrical charge and their hydrophobicity or "stickiness."

The 2-D fractionation process creates 960 separate protein fractions, which are then arranged in a single biochip containing 96-well grids. Eprogen scientists then probe the microarrays with known serum or plasma "auto-antibodies" produced by the immune systems of cancer patients.

By using cancer patients' own auto-antibodies as a diagnostic tool, doctors could potentially tailor treatments based on their personal autoantibody profile. "This technology is really designed to take advantage of the information contained within the patient's own biology," Barder said. "What makes this technique unique is that

scientists can use the actual expression of the patient's disease as a means of obtaining new and better diagnostic information that doctors could use to understand and fight cancer better.

"We're starting to see a way of developing tests and therapies for cancer by bringing the bedside to the laboratory, rather than the other way around," he added.

Biochips have already shown promise in diagnostic medicine, according to Argonne biologist Daniel Schabacker, who developed the technology. In addition to Eprogen, three other companies have licensed biochips, he said. One of these companies, Akonni Biosystems of Frederick, Md., has already produced dozens of assays, which it markets under the TruArray® brand name. Another company, Safeguard Biosystems, licensed biochips for veterinary diagnostic applications.

When a biochip tailored to detect upper respiratory diseases is exposed to a swab taken from a patient's mouth, for instance, the binding patterns of the proteins or nucleic acids in the array cause the dots to "light up" when scanned and analyzed with a computer. Computer algorithms decode the dot pattern produced by the biochip, calculate the statistical likelihood of each possible infection and provide this information to the doctor.

"Suppose someone shows up to the hospital and they're sick with an upper respiratory infection," said Schabacker. "First thing a doctor is going to want to know is whether the infection is viral or bacterial; this is especially true in pediatrics. And ideally, they'd really like to have a single test that they can run very rapidly that will identify exactly which disease you have from a dozen top targets."

The development of products like TruArray will soon revolutionize doctors' ability to quickly diagnose a number of diseases, Schabacker

said. For example, while existing rapid strep tests performed by many pediatricians take only a few minutes to process, they yield so many false negatives that doctors routinely send out the samples for subsequent rounds of more thorough, time-consuming and expensive analysis.

"The unique advantage offered by the TruArray platform lies in the fact that we can screen a single sample for multiple viral and bacterial infections at the same time," said Charles Daitch, Akonni's president and CEO. "Soon, doctors will no longer need to order as many expensive and time-consuming tests, and can instead obtain accurate diagnoses that will enable them to quickly provide their patients with targeted treatment strategies."

Though the analysis of a sample on a biochip can take 30 minutes, scientists can have much more confidence in the accuracy of the diagnosis, according to Schabacker. "Biochips give us the ability to run a test that allows your doctor to figure out exactly what you're suffering from during the time that you're in his or her office," he said.

While biochips will allow doctors to more quickly and authoritatively explain your sniffles, they might also be used for patients who exhibit symptoms of much more serious infections. By adding just a few more drops to the chip's array, Schabacker claimed, lab technicians could test for a whole slate of biotoxins and especially virulent diseases from the plague to smallpox to anthrax.

Other infections, such as those caused by Multidrug-Resistant Tuberculosis (MDR-TB) and the often deadly Methicillin-resistant Staphylococcus aureus (MRSA), can be quickly diagnosed with biochips like Akonni's TruArray assay, according to Daitch.

"The most important thing with these types of infections is that you have

to be right and get the answer quickly," Schabacker said. "Some of the tests out there, though marginally quicker than ours, are so inaccurate that they're almost useless. Especially when you're talking about anthrax or plague, you have to be confident in your diagnosis or else risk causing a panic."

Source: Argonne National Laboratory