'Barcode Chip' Enables Cheap, Fast Blood Tests

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(PhysOrg.com) -- A new barcode chip developed by a multi-institutional team of investigators promises to revolutionize diagnostic medical testing. In less than 10 minutes and using just a pinprick's worth of blood, the chip can measure the concentrations of dozens of proteins, including those that herald the presence of diseases such as cancer and heart disease.

The device, known as the Integrated Blood-Barcode Chip (IBBC), was developed by members of the Nanosystems Biology Cancer Center, one of eight Centers of Cancer Nanotechnology Excellence (CCNEs) funded by the National Cancer Institute's (NCI) Alliance for Nanotechnology in Cancer initiative. This team was led James R. Heath, Ph.D., California Institute of Technology (Caltech), and Leroy Hood, M.D., Ph.D., Institute for Systems Biology. The group's work was published in the journal *Nature Biotechnology*.

An IBBC is about the size of a microscope slide and is made out of a glass substrate covered with silicone rubber. The chip's surface is molded to contain a microfluidics circuit. After a pinprick of blood is injected into this system of microscopic channels, the device separates the blood into protein-rich plasma and then measures a panel of protein biomarkers.

The chip offers a significant improvement over the cost and speed of standard laboratory tests that analyze proteins in the blood. In traditional tests, one or more vials of blood are removed from a patient and taken to

a laboratory, where the blood is centrifuged to separate whole blood cells from the plasma. The plasma is then assayed for specific proteins. “The process is labor intensive, and even if the person doing the testing hurries, the tests still take a few hours to complete,” said Dr. Heath. A kit to test for a single diagnostic protein costs about $50.

“We wanted to dramatically lower the cost of such measurements, by orders of magnitude,” he stated. “We measure many proteins for the cost of one. Furthermore, if you reduce the time it takes for the test, the test is cheaper, since time is money. With our barcode chip, we can go from pinprick to results in less than 10 minutes.”

A single chip can simultaneously test the blood from eight patients, and each test measures many proteins at once. The researchers reported on devices that could measure a dozen proteins from a fingerprick of blood, and their current assays are designed for significantly more proteins. “We are aiming to measure 100 proteins per fingerprick within a year or so. It’s a pretty enabling technology,” stated Dr. Heath.

To perform the assay, a drop of blood is added to the IBBC’s inlet, and then a slight pressure is applied, which forces the blood through a channel. As the blood flows, plasma is skimmed into narrow channels that branch off from the main channel. This part of the chip is designed as if it were a network of resistors, which optimizes plasma separation.

The plasma then flows across the barcodes, which consist of a series of lines, each 20 micrometers across and patterned with a different antibody that allows it to capture a specific protein from the plasma passing over. When the barcode is “developed,” the individual bars emit a red fluorescent glow, whose brightness depends on the amount of protein captured.

The researchers have used the chip to measure variations in the

concentration of human chorionic gonadotropin (hCG), the hormone produced during pregnancy. “The concentration of this protein increases by about 100,000-fold as a woman goes through the pregnancy cycle, and we wanted to show that we could capture that whole concentration range through a single test,” Dr. Heath said.

The scientists also used the barcode chip to analyze the blood of breast and prostate cancer patients for a number of proteins that serve as biomarkers for disease. The types and concentrations of the proteins vary from disease to disease and among different individuals. A woman with breast cancer, for example, will produce a different suite of biomarkers than will a man with prostate cancer, whereas a woman with an aggressive form of cancer may produce proteins that are different from those of a woman with a less deadly cancer.

Those proteins can also change as a patient receives therapy. Thus, determining these biomarker profiles can allow doctors to create individualized treatment plans for their patients and improve outcomes. The ease and the speed with which results can be obtained using the IBBC also will potentially allow doctors to assess their patients’ responses to drugs and to monitor how those responses evolve with time, much as a diabetic patient might use a blood glucose test to monitor insulin delivery.

The IBBC is now being tested in human clinical trials on patients with glioblastoma, a common and aggressive form of brain tumor. The researchers are also using the chips in studies of healthy individuals to determine how diet and exercise change the composition of proteins in the blood.

Currently, the barcoded information is “read” with a common laboratory scanner that is also used for gene and protein expression studies. “But it should be very easy to design something like a supermarket UPC scanner

to read the information, making the process even more user friendly," said Rong Fan, Ph.D., Caltech, the lead author of the paper.

"As personalized medicine develops, measurements of large panels of protein biomarkers are going to become important, but they are also going to have to be done very cheaply," Dr. Heath stated. "It is our hope that these IBBCs will enable such inexpensive and multiplexed measurements."

This work, which was detailed in the paper "Integrated barcode chips for rapid, multiplexed analysis of proteins in microliter quantities of blood," was supported in part by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. An abstract of this paper is available at the journal's Web site. (dx.doi.org/doi:10.1038/nbt.1507)

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