A Revolutionary Blood Test Catapults Cancer Treatment

By [redacted]

A revolutionary blood test could advance cancer treatment with warp speed. The little device, designed by a team working at Mass General Hospital, is a 1-inch by 3-inch silicon wafer called the CTC-iChip, the first of its kind to filter out thousands of cancer cells for genetic analysis.

CTC stands for "circulating tumor cells," which are found in the blood of anyone with metastatic cancer. Today, the sole Food and Drug Administration-approved CTC blood test, called CellSearch, can only roughly count cancer cells in the blood. And while counting cancer cells is helpful in determining whether a treatment is working, the CTC-iChip's new ability to extract thousands of cancer cells for mutation analysis will allow patients to have a far more tailored and less toxic treatment by targeting only those mutations that are causing the cancer. Today, this is done with drugs that block a pathway unique to a mutated cell's surface, or in the field of immunology, block the specific proteins that disguise the cancer cell from the immune system.

Research over the last decade has shown that cancer types are not limited to the larger categories we usually think of — prostate, breast, colon, and so on. Nor are they limited to the various cell types within an organ, bone or muscle, such as the lining of the kidney or its base. Each cell type typically has a variety of genetic mutations. For example, non-small cell lung cancer cells have about three known mutation types or a combination of them, with each responding differently to drugs. On top of this, some of these mutations drive cancer growth, while others can be latent, making our understanding of them a key piece in designing personalized treatment.

To date, most genetic analysis of tumors is done by way of a biopsy. The biopsy procedure, however, can be very difficult for a patient, especially if the tumor is in the bone, and is not possible for all cancers such as Leukemia, when tumors rarely form. Furthermore, a biopsy cannot

keep up to date with rapidly evolving mutations and rarely reveals the diversity of mutations that exists within tumors or from one tumor to another.

The CTC-iChip, on the other hand, is less invasive than a biopsy, and more effective at capturing the range of cancer cell mutations and the dynamic changes that occur amongst them. It works by filtering out everything from the blood except cancer cells. As blood enters the credit-card sized tray, magnetic beads coated with antibodies attach to the white blood cells. Red blood cells, platelets, and other smaller particles are then filtered out, while larger cells, including CTCs, pass through a magnetic field separating out the beaded white cells from the rest. What ultimately remains is a purified solution of circulating tumor cells.

"The CTC-iChip test allows patients to be tested easily, with liquid biopsies, more accurately and in genetic real time as cells evolve," says Mehmet Toner, PhD, Director of BioMicroElectroMechanical Systems at Mass General Hospital and one of the principal designers of the CTC-iChip.

The CTC-iChip can also test for mutations that are resistant to treatment, preempt them as fast as possible, and fine-tune its database of what drugs should be taken in combination to minimize resistance in the first place. Indeed, the need for a multi-drug cocktail approach to reduce resistance is becoming increasingly apparent as it was with HIV. A few years ago, the Program for Evolutionary Dynamics at Harvard University came out with a pivotal study showing that one resistant cell out of a million cancer cells in the body, can quickly grow to tumor level within months.

Fortunately, the iChip2 blood test is emerging at a critical time in cancer research with the FDA's first approval of combined cancer inhibitor drugs as a single pill. Last January 2014, the FDA approved the first combined inhibitor drug for melanoma: Dabrafenib and Trametinib, designed to block certain BRAF enzyme pathway mutations and resistant mutations. In July 2014, the FDA approved combined inhibitors idelaisib and rituximab to treat relapsed chronic lymphocytic leukemia. And while the FDA has taken baby steps towards combining inhibitors (and protein

inhibitors in the rapidly advancing field of immunology oncology), there are a slew of successful advanced phase clinical trials pressuring the FDA to approve more.

Researches are also making huge progress in screening CTC cells in the lab. At Massachusetts General, researchers using the iChip can screen over 1,000 genes for each cell instead of the standard 25 used to analyze tumor samples. The group has also vastly improved growing CTC's as a sphere of suspended cells vs attached as a monolayer to a petri dish, a technique that stops cells from mutating, a common problem when trying to test them.

Today, the CTC-iChip has already identified more than 1,400 cancer causing mutations, referenced by drug developers worldwide. And as the iChip continues to catalog the vast constellation of genetic mutations that lead to cancer, it provides real hope in outwitting this ever dreadful disease.