The Circulating Tumor Cells Chip

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BACKGROUND:

Cancers arise within the cells of an organ, such as the breast or pancreas, but cause death by disseminating throughout the bloodstream, leading to distant metastases in the bone, liver, lungs or brain.

Cancer cells that spread from the primary tumor can be found in the blood of patients with cancer. These circulating tumor cells (CTCs) are extraordinarily rare, estimated at one CTC per billion normal cells, but the ability to detect and analyze them would allow for significant advances in detecting and treating cancers as well as understanding the fundamental mechanisms by which cancers spread.

To date, available technology has not provided either the sensitivity or the reliability to be useful in guiding treatment decisions.

In this project, a collaboration of clinicians, bioengineers and molecular biologists has developed a novel and radically different approach to detecting and isolating CTCs. This technology takes advantage of microscopic fluid dynamics to construct a Chip with 100 times greater sensitivity than existing technologies.

The CTC-Chip, which is the size of a business card, contains 78,000 microscopic columns, each coated with material capable of attaching to CTCs while allowing normal blood cells to flow through unimpeded.

The CTC-Chip can capture approximately 200 CTCs from a teaspoon of blood taken from a cancer patient, thereby making these cells available for scientific analysis, providing an important tool for clinical investigation, and ultimately leading to improved clinical care for patients with cancer.

THE GOALS:

The first goal is to optimize the technology of the CTC-Chip to make it more sensitive and assure that it can be used reliably and efficiently in a large-scale clinical setting. The new Chip will be faster, increase the purity of the recovered cells and allow for analysis of the cells in assays away from the Chip itself.

The project's second goal is to conduct clinical trials to assess the value of the Chip in detecting cancers early or monitoring tumor response to treatment. The CTC-Chip has proven efficacy in monitoring specific EGFR mutations in lung cancer patients that predict their responsiveness to targeted drugs. The new trials will involve a wide range of cancers, including breast, pancreatic, prostate and colon.

SIGNIFICANCE:

The potential clinical applications of this technology are widespread and have the potential to revolutionize the ways in which cancers are detected and treated.

The CTC-Chip could make it possible to analyze cancers of the internal organs in real time, non-invasively, both at the time of diagnosis and throughout treatment. This would enable clinicians to match patients to effective therapies and monitor the response to treatments.

The CTC-Chip would provide a reliable means not only of detecting resistance when it occurs but also of analyzing the specific genetic alterations that lead to resistance. The Gleevec experience has demonstrated that tumors often become resistant to highly effective targeted therapies, leading to relapses, and the need for secondary approaches.

An additional goal for the CTC-Chip is to make it sufficiently sensitive to detect cancers at an earlier stage. Studies indicate that tumors may start shedding CTCs into the bloodstream long before they actually metastasize to distant organs, opening the door for early detection and screening strategies.

THE QUOTE (ATTRIBUTE TO DANIEL HARBER):

“When patients develop cancer and it has spread, there is often no good way of following the cancer during treatment. You have a biopsy that is done early in your treatment, and then we somewhat improvise with different treatments, some work, some don’t, but it’s really a bit of guess work.

“If you had a way of doing a blood test and questioning the tumor cells, looking at what genes are abnormal, whether they are likely to respond to this drug versus that drug, and being able to do that repeatedly through the course of a patient’s treatment, then you really have a way of following the kind of interventions we do in real time. That would really direct the kind of treatments, particularly the new and more focused treatments, the smart drugs or targeted treatments that we have for cancer.

“The other clinical application is that we’re getting indications that cancers tend to send out these cells into the blood relatively early when they become invasive. The great hope is that we could use this eventually to pick up cancer earlier, at a time when it could still be cured.

“I think the excitement about bringing technology into a question like this is all of a sudden you can ask questions you could never ask before. We all know that cancer spreads; it goes from the breast to the lungs, or from the colon to the liver, but you could never see that transit. You could never see the cells in the act of spreading, which is what we can do now. The very questions that you can ask, some very simple, some very profound, are all dependent on technology.”