Improved device provides more rapid, comprehensive analysis of circulating tumor cells

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Technical improvements to a microchip-based device for detecting and analyzing tumor cells in the bloodstream are revealing cellular differences that may reflect a tumor's aggressiveness and long-term response to treatment. A report from the Massachusetts General Hospital (MGH) Center for Engineering in Medicine in the March 31 *Science Translational Medicine* describes refinements to the MGH-developed CTC-chip, which measures levels of circulating tumor cells (CTCs) in the blood stream, that may allow better monitoring of how CTC levels react to treatment for prostate cancer and reveal key biological properties of the cells.

"The earlier versions of the CTC-chip required hand-counting of thousands of microscopic images, which was sufficient for the initial proof-of-principle studies but far too time-intensive for handling high volumes of patient samples," says Shannon Stott, PhD, of the MGH Center for Engineering in Medicine, the study's lead author. "We also were limited in our ability to analyze cellular factors that could be markers for important properties of the tumors."

CTCs are living solid-tumor cells found at extremely low levels in the bloodstream. Until the 2007 development of the CTC-chip by researchers from the MGH Cancer Center and Center for Engineering in Medicine, it was not possible to get information from CTCs that would be useful for clinical decision making. The updated system described in the current report incorporates improved imaging technology, allowing more complete visualization of cells captured by the device, and new software that automates the identification of CTCs using criteria specific to the particular type of tumor.

The MGH team used the automated system to analyze CTCs from two groups of prostate cancer patients. After the cells were initially captured on the CTC-chip, which is covered with microscopic posts coated with antibody to a common tumor protein, the cells were tagged using an antibody to prostate-specific antigen, allowing rapid scanning and more comprehensive visualization of the CTCs. Samples taken from a group of men with localized prostate cancer right before and at several intervals after surgical removal showed that, while CTCs disappeared immediately after surgery in some patients, CTC levels dropped only modestly in others. Analyzing CTCs from a group of patients being treated for metastatic prostate cancer revealed that, among patients whose tumors were responding to treatment, only a few CTCs displayed a marker found on proliferating cells. But in patients whose tumors were not responding, the majority of CTCs displayed the proliferation marker.

"Further studies are needed to determine whether the differences seen in our study actually reflect which tumors are more invasive, in the case of the persistance/disappearance observation, or reveal important biological properties of the tumor," says Stott, who is a research fellow in Surgery at Harvard Medical School. "We are also working to create a 'plug-and-play' version of the machine that will be easy to use clinically, exploring options for large-scale production of the CTC-chip, and continuing to optimize the device to increase its speed and efficiency."

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