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Detection and Characterization of Circulating Tumor Cells

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Circulating tumor cells (CTCs) occur in blood below the concentration of 1 cell in a hundred thousand white blood cells and can provide prognostic and diagnostic information about the underlying disease. While numeration of CTCs has provided useful information on progression-free and overall survival, it does not provide guidance of treatment choice. Since CTCs are presumed contain features of the metastatic tissue, characterization of cancer markers on these cells could help selection of treatment. At such low concentrations, reliable location and identification of these cells represents a significant technical challenge. Automated digital microscopy (ADM) provides high levels of sensitivity, but the analysis time is prohibitively long for a clinical assay. Enrichment methods have been developed to reduce sample size but can result in cell loss. A major barrier in reliable enrichment stems from the biological heterogeneity of CTCs, exhibited in a wide range of genetic, biochemical, immunological and biological characteristics. We have developed an approach that uses fiber-optic array scanning technology (FAST) to detect CTCs. Here, laser-printing optics are used to excite 300,000 cells/sec, and fluorescence from immuno-labels is collected in an array of optical fibers that forms a wide collection aperture. The FAST cytometer can locate CTCs at a rate that is 500 times faster than an ADM with comparable sensitivity and improved specificity. With this high scan rate, no enrichment of CTCs is required. The target can be a cytoplasm protein with a very high expression level, which reduces sensitivity to CTC heterogeneity. We use this method to measure expression levels of multiple markers on CTCs to help predict effective cancer treatment.