

Circulating tumor isolation strategy for personalized cancer therapy

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Metastasis the spread of cancer from a primary tumor to a distant site is largely responsible for cancer's lethality. Research into Circulating Tumor Cells (CTCs) has suggested an important role for these cells in metastatic spread, inspiring hope of new and more effective ways to diagnose and treat aggressive disease. Detection of these exceedingly rare cells within the circulation may provide important clues regarding cancer prognosis and progression, potentially advancing, too the assessment of anticancer drug treatment and optimization of individualized therapy. In developing CTC technology, the critical criteria are high recovery rates and high purity. Current isolation methods suffer from an inherent trade-off between these two goals. Moreover, ensuring minimal cell stress and robust reproducibility is also important for the clinical application of CTCs. In this study we introduce a method to decide optimal filter gap size satisfying both 100% theoretical recovery rate and purity, as determined by biomechanical analysis and Fluid-structure Interaction (FSI) simulations. Nano indentation experiments are conducted to measure the stiffness of leukocytes as compared to the microbead-conjugated cancer cells, with these parameters then being used in FSI. In addition, a novel rare cell isolation system, a centrifugal microfluidic technology, is demonstrated to satisfy full automation for circulating tumor cell isolation from blood. The disc-based device could process 10 ml of blood sample at a time and the purity of the finally isolated fraction was enough to work direct sequencing for mutation analysis. The systems represent a potentially significant advance towards ensuring highly efficient isolation of these sparsely populated target cells in microfluidic study contributing, therefore, to the sensitive and robust clinical validation of studies towards precision and personalized medicine.

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