Circulating tumor cell (CTC) enrichment and analysis enabled by a flexible micro spring array (FMSA) device

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The dissemination of circulating tumor cells (CTCs) implicated in the metastatic spread of cancer accounts for the majority of cancer-related deaths. CTCs have been established as a prognostic biomarker and are associated with worse survival outcomes in various cancer types. Microfiltration can be an efficient and antigen-independent method for CTC enrichment. We have developed several generations of microfabricated filtration devices for CTC enrichment. The latest device is a flexible micro spring array (FMSA) device for label-free viable mechanical enrichment of CTCs from whole blood samples obtained from patients with advanced and metastatic carcinoma. Unlike previous microfiltration devices, flexible structures at the microscale minimize cell damage to preserve viability, while maximizing throughput to allow rapid enrichment directly from whole blood with no need for sample pre-processing. The FMSA device can enrich tumor cells with 90% capture efficiency, higher than $10^4$ enrichment, and better than 80% viability from 7.5 mL whole blood samples in less than 10 minutes on a 0.5 cm$^2$ device. CTCs were enriched and analyzed qualitatively and quantitatively based on immunocytochemical determination of phenotype and morphological characteristics. Follow up samples were analyzed during the course of therapy and CTC results were correlated to patient survival and tumor burden. FMSA enriched CTCs obtained from a blood sample may prove to be a prognostic biomarker for advanced cancer. The FMSA device as a versatile platform is capable of viable enrichment and analysis of CTCs from clinically relevant volumes of whole blood.