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Tumor Cell Detection, Isolation and Monitoring Using Bi-Layer Magnetic Microfluidic Chip

Authors : Amir Seyfoori, Ehsan Samiei, Mohsen Akbari

Abstract : The use of microtechnology for detection and high yield isolation of circulating tumor cells (CTCs) has shown enormous promise as an indication of clinical metastasis prognosis and cancer treatment monitoring. The Immunomagnetic assay has been also coupled to microtechnology to improve the selectivity and efficiency of the current methods of cancer biomarker isolation. In this way, generation and configuration of the local high gradient magnetic field play essential roles in such assay. Additionally, considering the intrinsic heterogeneity of cancer cells, real-time analysis of isolated cells is necessary to characterize their responses to therapy. Totally, on-chip isolation and monitoring of the specific tumor cells is considered as a pressing need in the way of modified cancer therapy. To address these challenges, we have developed a bi-layer magnetic-based microfluidic chip for enhanced CTC detection and capturing. Micromagnet arrays at the bottom layer of the chip were fabricated using a new method of magnetic nanoparticle paste deposition so that they were arranged at the center of the chain microchannel with the lowest fluid velocity zone. Breast cancer cells labelled with EPCAM-conjugated smart microgels were immobilized on the tip of the micromagnets with greater localized magnetic field and stronger cell-micromagnet interaction. Considering different magnetic nano-powder usage (MnFe2O4 & gamma-Fe2O3) and micromagnet shapes (ellipsoidal & arrow), the capture efficiency of the systems was adjusted while the higher CTC capture efficiency was acquired for MnFe2O4 arrow micromagnet as around 95.5%. As a proof of concept of on-chip tumor cell monitoring, magnetic smart microgels made of thermo-responsive poly N-isopropylacrylamide-co-acrylic acid (PNIPAM-AA) composition were used for both purposes of targeted cell capturing as well as cell monitoring using antibody conjugation and fluorescent dye loading at the same time. In this regard, magnetic microgels were successfully used as cell tracker after isolation process so that by raising the temperature up to 37^0 C, they released the contained dye and stained the targeted cell just after capturing. This microfluidic device was able to provide a platform for detection, isolation and efficient real-time analysis of specific CTCs in the liquid biopsy of breast cancer patients.

Keywords : circulating tumor cells, microfluidic, immunomagnetic, cell isolation
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