Recirculating Microfluidic Device for Efficient Filtration and Enrichment of Circulating Tumor Cells

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Tumor cells invade the surroundings of the primary tumor and go into the circulatory system. The circulating tumor cells (CTCs) are believed to the cause for cancer metastases (Chaffer & Weinberg, 2011). The separation and enrichment of CTCs from whole blood have received widespread attention for potential applications on cancer diagnosis and treatment. Current CTCs isolation can be characterized into chemical and physical approaches. Bio-chemical method involves immunecytochemistry to isolate CTCs with high purity. These approaches are also typically expensive with rather low through put. Physical method such as membrane filtration, or size-based separation with complex fluid flow, are often limited by low efficacy.

In this work, we propose the fabrication and optimization of a PDMS lateral-flow microfilter device capable of isolating CTCs from the red blood cells (RBCs) and white blood cells (WBCs) from whole blood samples. The device is fabricated by stacking and bonding three layers of PDMS microfluidic channels with different structures in each layer, as shown in Fig. 1a. Figure 1b shows the SEM image of device's cross-section and Fig. 1c shows the top view of the device in optical microscope. The top layer contains large microfluidic channels for all fluid and particles to flow. The middle layer has lithographically defined pores for smaller particles to pass through. The bottom layer is for the fluid and smaller particles to flow. It also contains supporting posts to prevent the collapsing of the thin middle layer. For fluid input/output, the device has three ports. The input and output ports are connected to the top layer and the waste port is connected to the bottom layer.

The efficiency of the device was characterized using polystyrene (PS) microbeads, cells and blood samples. The flow rates at the three fluid ports can impact the filtration efficiency. CTCs trapping efficiency and blood cells passing efficiency were evaluated under different waste/input flow ratios (Fig.2). The lateral-flow microfilter device has achieved a passing efficiency of 77.3% for 4.5 μm PS microbeads (Fig. 2a) and a recovery efficiency of around 97% for 20 μm PS microbeads (Fig. 2b). The recovery efficiency deceases at higher waste/input ratio, which is ascribed to the deformation of the middle layer. The enlarged pore size in PDMS filtration membrane allows larger particles to pass through, resulting in a lower recovery rate for larger particles. A refined overall device design with high RBC and WBC passing efficiency and CTC trapping efficiency will be reported. Finally, recirculating flow setup will be constructed to further improve the overall efficiencies for practical application. With the novel later-flow filtration mechanism and the lithographically defined pore size in the middle layer, the microfilter device can achieve deterministic particle filtration without congestion.

References

Chaffer, C. L., & Weinberg, R. A. (2011). A Perspective on Cancer Cell Metastasis. *Science*, 331(6024):1559-64.

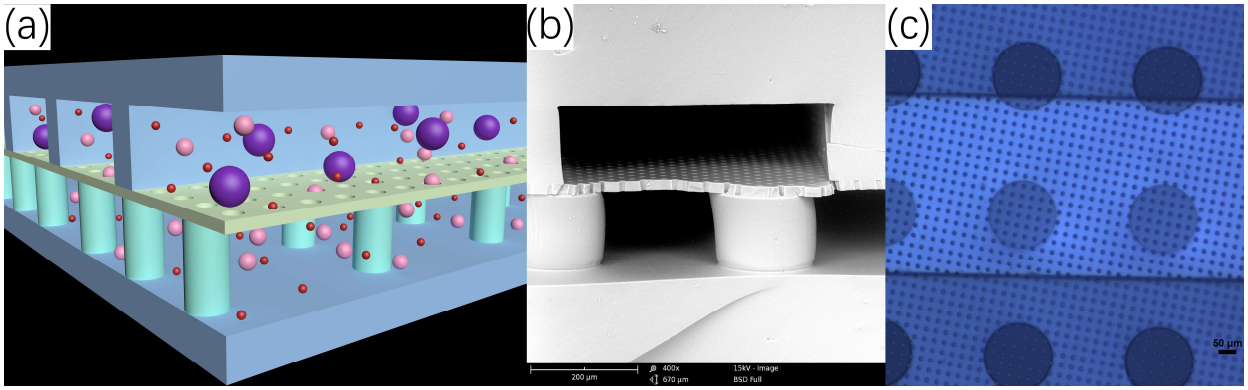

Figure 1: Images of the lateral-flow microfilter device: (a) The CTCs (purple) can only flow within the top channels while the RBCs (red) and the WBCs (pink) can pass through the filter membrane and enter the bottom channel. (b) The cross-sectional view of the PDMS microfilter membrane under SEM, and (c) the top view of the PDMS microfilter device in optical microscope.

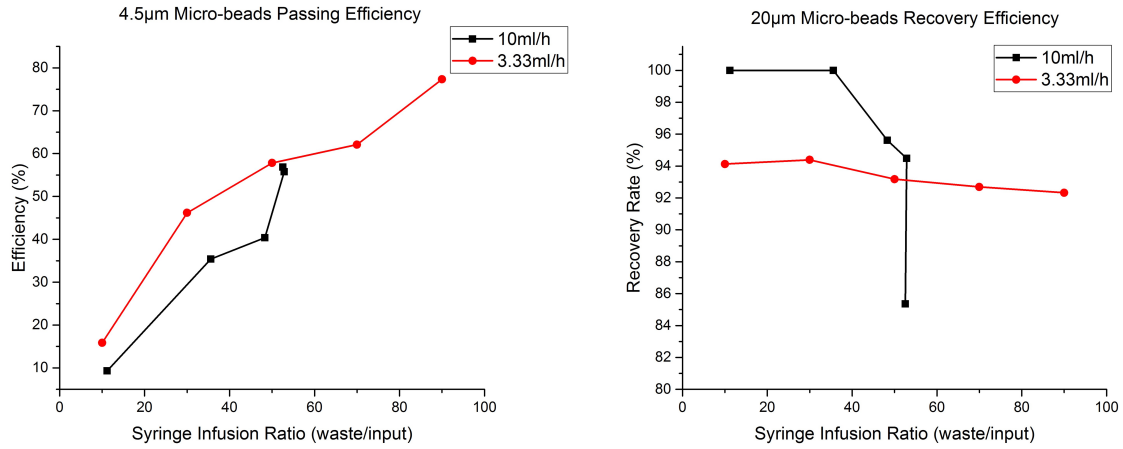

Figure 2: Efficiencies of the lateral-flow microfilter device: (a) The passing efficiency for 4.5 µm PS microbeads; and (b) the recovery efficiency for 20 µm PS microbeads. Due to the deformation of the PDMS filter membrane under large flow rate, syringe infusion ratio larger than 57% cannot be obtained with 10 ml/h input flow rate.