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Reducing WBC background in cancer cell separation products by negative acoustic contrast particle immuno-acoustophoresis

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Abstract

Cancer cells display acoustic properties enabling acoustophoretic separation from white blood cells (WBCs) with 2-3 log suppression of the WBC background. However, a subset of WBCs has overlapping acoustic properties with cancer cells, which is why label-free acoustophoretic cancer cell isolation needs additional purification prior to analysis. This paper reports for the first time a proof of concept for continuous flow acoustophoretic negative selection of WBCs from cancer cells using negative acoustic contrast elastomeric particles (EPs) activated with CD45-antibodies that specifically bind to WBCs. The EP/WBC complexes align at the acoustic pressure anti-nodes along the channel walls while unbound cancer cells focus to the pressure node in the channel center, enabling continuous flow based depletion of WBC background in a cancer cell product. The method does not provide a single process solution for the CTC separation challenge, but provides an elegant part to a multi-step process by further reducing the WBC background in cancer cell separation products derived from an initial step of label-free acoustophoresis. We report the recorded performance of the negative selection immuno-acoustophoretic WBC depletion and cancer cell recovery. To eliminate the negative impact of the separation due to the known problems of aggregation of negative acoustic contrast particles along the sidewalls of the acoustophoresis channel and to enable continuous separation of EP/WBC complexes from cancer cells, a new acoustic actuation method has been implemented where the ultrasound frequency is scanned (1.991 MHz $\pm$100 kHz, scan rate 200 kHz msec^{-1}). Using this frequency scanning strategy EP/WBC complexes were acoustophoretically separated from mixtures of WBCs spiked with breast and prostate cancer cells (DU145 and