Identifying and Subtyping Circulating Tumor Cells (CTCs) from breast, prostate and pancreatic cancer patients based on distinct morphology

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ABSTRACT

Microfiltration is an increasingly popular method for isolating circulating tumor cells (CTCs) from the peripheral blood of cancer patients with solid tumors2-4. The microfiltration approach can be used on peripheral blood as a non-invasive “liquid biopsy” for precision cancer detection, regardless of surface marker expression2-4. Here we describe the use of CellSieve™ microfilters to isolate and subtype CTCs from the peripheral blood of breast, prostate and pancreatic cancer patients. As it is accepted that CTCs isolated from patient samples represent a highly heterogeneous population with varying degrees of epithelial/mesenchymal differentiation, microfiltration may be optimal for the purification of all CTC subtypes. We hypothesize that CTCs from three different epithelial malignancies can be identified and grouped into distinct subtypes by morphological characterization.

RESULTS

Blood from breast, prostate, and pancreas cancer patients were provided by Northwestern University, Fox Chase Cancer Center, University Maryland-Greenbaum Cancer Center, and Medical College of Wisconsin, and analyzed by Creativ Micro-Tech. Microfilters are fabricated with 7 micron diameter pores and uniform array of 160,000 pores over a 9 mm diameter area. 7.5 mL of whole blood was mildly pre-fixed and filtered through CellSieve™ microfilters (~3 min). CTCs collected were then fixed, permeabilized, and stained with DAPI, and antibodies to cytokeratin (CK) 8, 18 and 19 (FITC), EpCAM (PE), PSMA (DyLight 594) and CD45 (DyLight 649). CTCs were classified by their morphology, nuclear profile and the expression patterns of cytokeratin, PSMA and EpCAM.

CONCLUSIONS

- Microfiltration captures CTCs regardless of surface marker expression
- CTCs have multiple distinct phenotypes
- CTC phenotypes differ between malignant diseases
- Microfiltration captures weakened and apoptotic CTCs.
- CTC subtypes may indicate definable traits which may be exploited for personalized treatment of cancer patients

References