Heterogeneity of Biomarker Expression in Clinical Urine Biopsies

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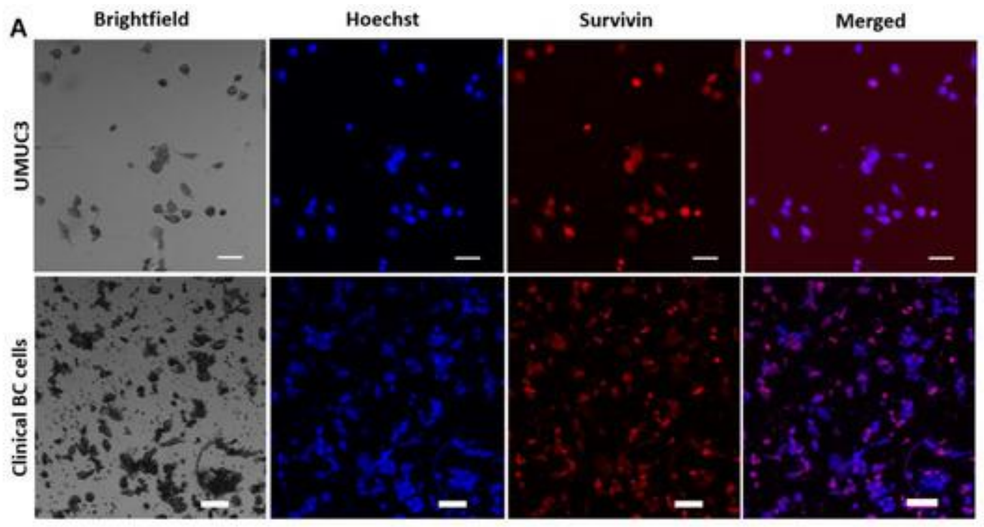
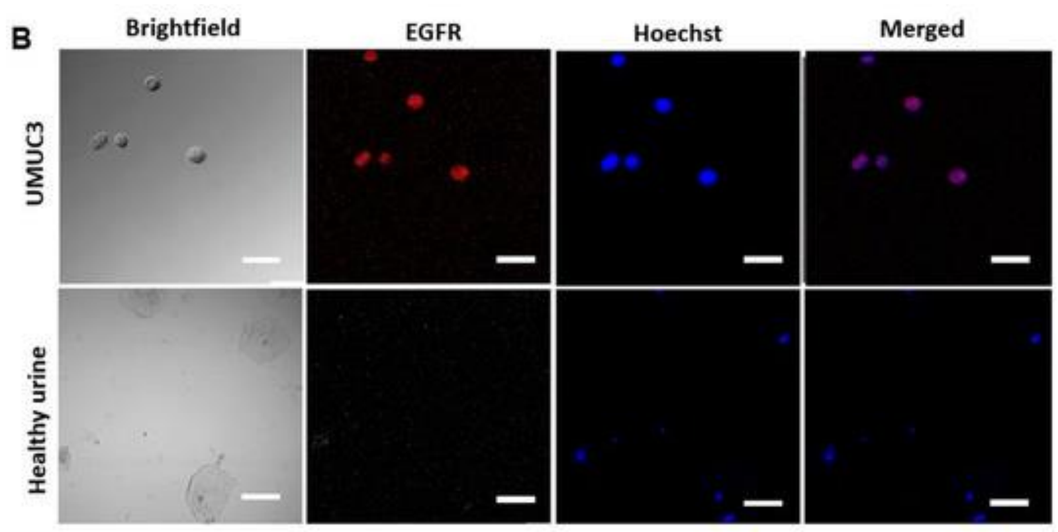
ABSTRACT

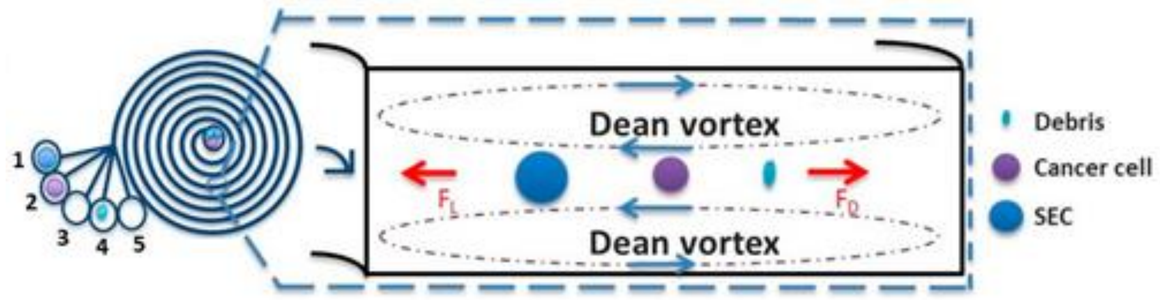
Bladder cancer (BC) often requires lifetime monitoring due to its high recurrence rate. Exfoliated bladder cancer cells (EBCCs) may express a series of different biomarkers according to their epithelial-mesenchymal transition (EMT) status, a phenomenon characterized by loss of intercellular adhesion, enhanced cell motility, and cancer invasion. Here, we demonstrated the clinical heterogeneity of EBCCs using an integrated microfluidic assay to separate various EMT subtypes of EBCCs in real-time and under high-throughput based on the principle of inertial focusing.

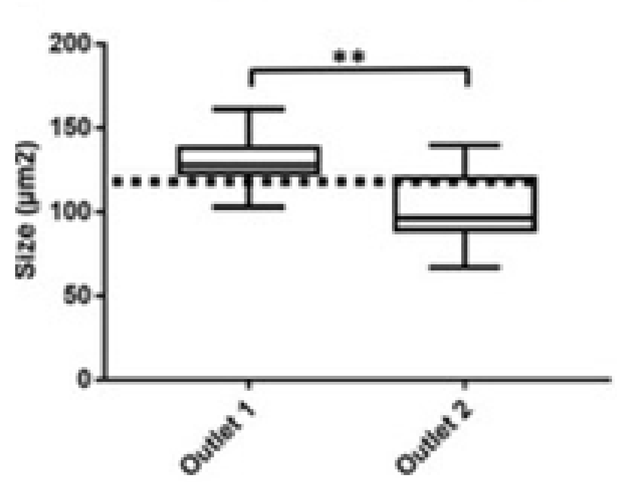




METHODS

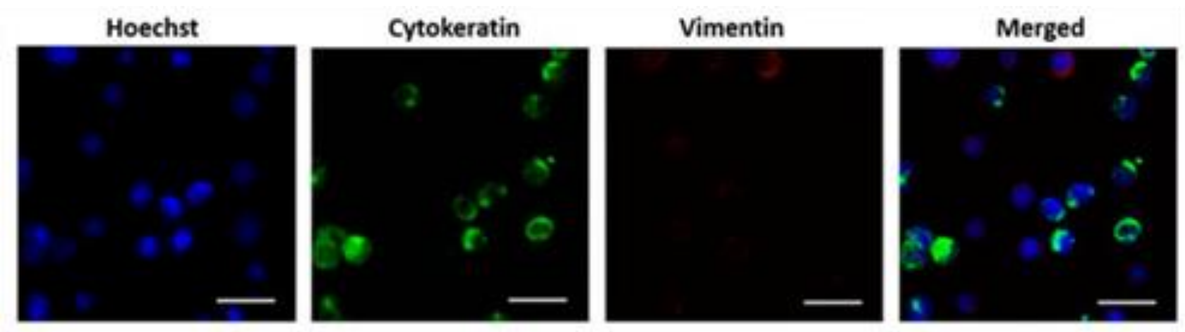
Enriched cells from BC patient-derived urine bladder wash samples were isolated based on cell size and characterized by antibodies targeting EMT biomarkers such as cytokeratin (CK), vimentin (VIM), survivin, and epidermal growth factor receptor (EGFR).



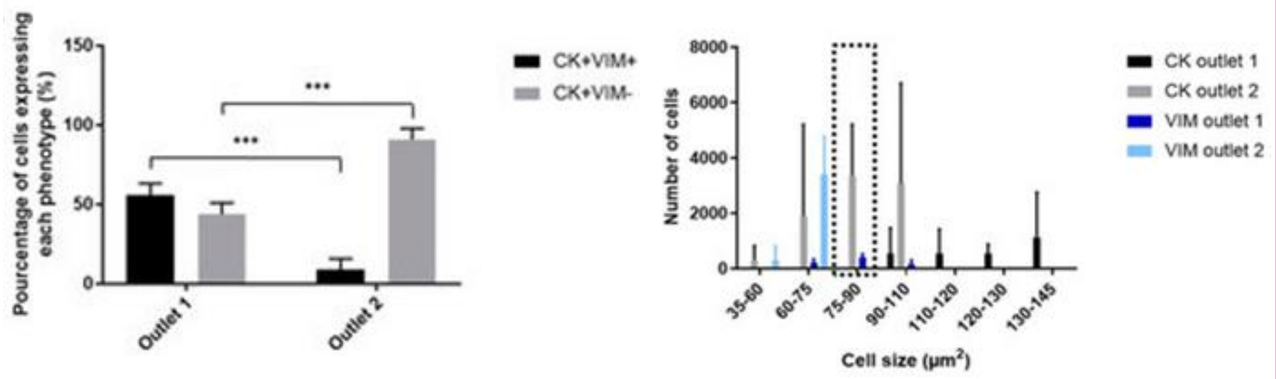


RESULTS

This rapid, non-invasive method demonstrates high efficiency of cancer cell recovery under the optimal flow rate and the specific retrieval of various EMT phenotype cell fractions from respective device outlets.

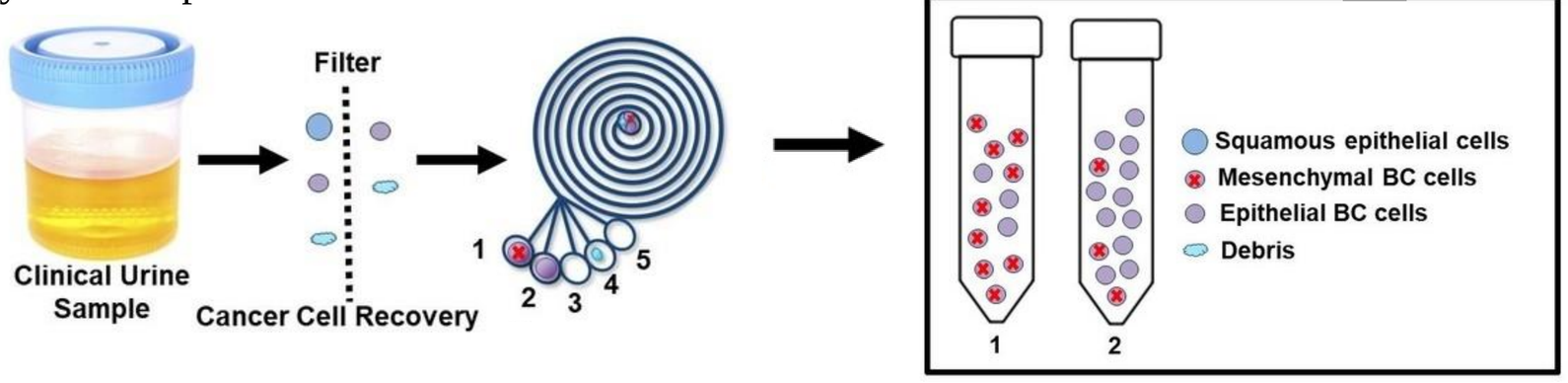


Among them, we observed cells with an intermediate EMT phenotype (CK + VIM+), which were isolated mainly in the first outlet (56.1% ± 8.99%). However, clinical EBCCs with an epithelial-like phenotype (CK + VIM−) were mostly isolated in the second outlet (90.9% ± 7%).



CONCLUSIONS

The evaluation of clinical samples revealed a vast amount of tumor heterogeneity, reflecting different EMT phenotypes, which can correlate with drug resistance and tumor dormancy. Overall, the separation of heterogeneous clinical samples can better facilitate routine screening procedures and greatly enhance personalized treatment.



ABBREVIATIONS

BC	Bladder Cancer	CK	Cytokeratin
EBCCs	Exfoliated Bladder Cancer Cells	VIM	Vimentin
EMT	Epithelial to Mesenchymal Transition	EGFR	Epidermal Growth Factor Receptor

REFERENCES

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