Supplementary Information

Cell-Imprinted Biomimetic Interface for Intelligent Recognition and Efficient Capture of CTCs

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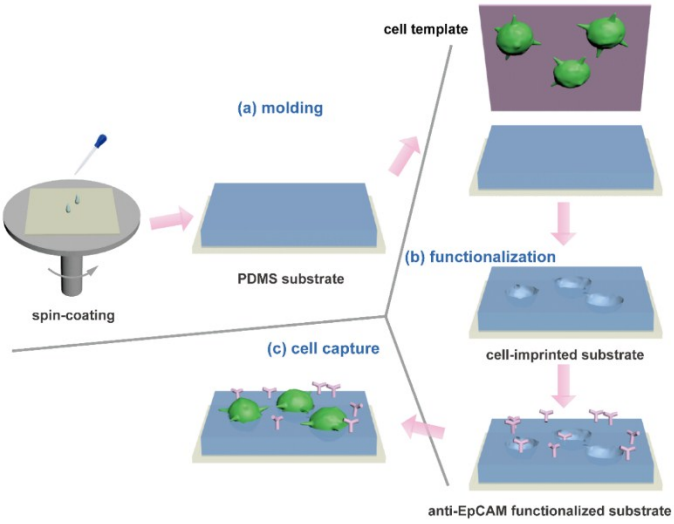

Figure S1. (a) Fabrication of PDMS substrates by spin-coating. (b) Preparation of cell-imprinted substrates by soft lithography and successful modification of anti-EpCAM on their surface. (c) Capture of tumor cells by anti-EpCAM-modified as-prepared cell-imprinted substrates.

Table S1. Quantification of AFM images of the cell-imprinted sites.

No.	Width/μm	Depth/μm	Average width/μm	Average depth/μm
1	20.0	5.9		
2	18.7	4.6		
3	22.5	5.7	18.9	5.7
4	14.8	7.4		
5	18.6	5.1		

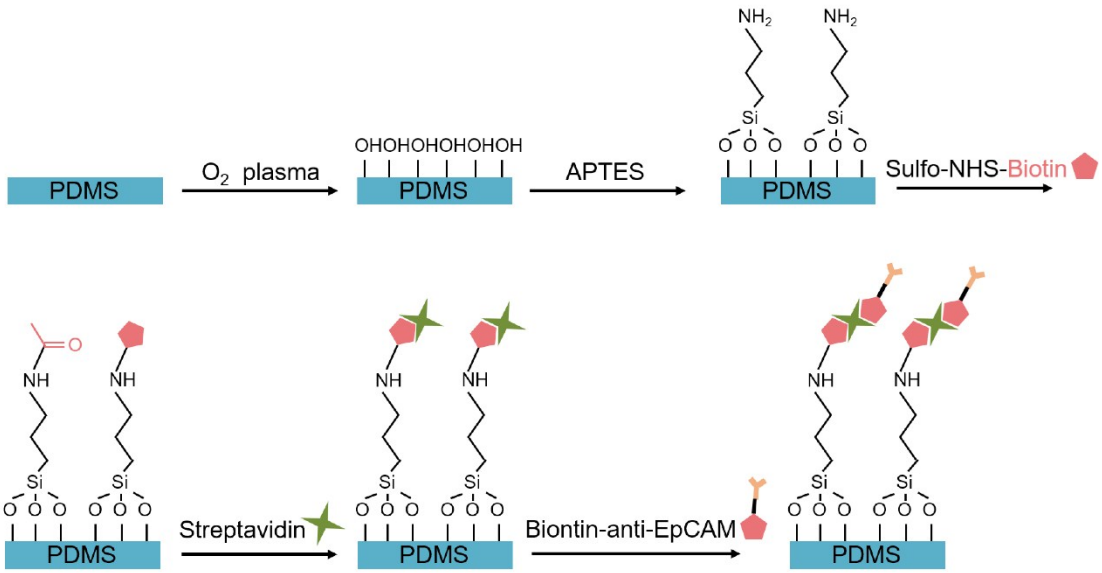

Figure S2. Schematic diagram of grafting of biotinylated epithelial-cell adhesion-molecule antibody (anti-EpCAM) onto cell-imprinted substrates.

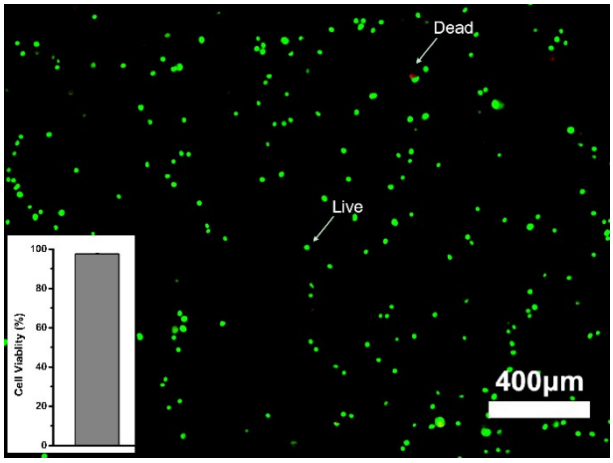

Figure S3. Fluorescent image of MCF-7 cells captured on anti-EpCAM modified substrates with Live/Dead staining.

To test the viability of the captured cells on the cell-imprinted substrates, we further performed live/dead staining of the captured tumor cells using acridine orange (AO) and ethidium bromide (BE) to analyze their viability. As can be seen from Figure S3,

the vast majority of the cells showed green fluorescence, indicating that those captured cells were still alive. The cell viability of MCF-7 cells was calculated to be as high as 97.6% ± 0.2%.

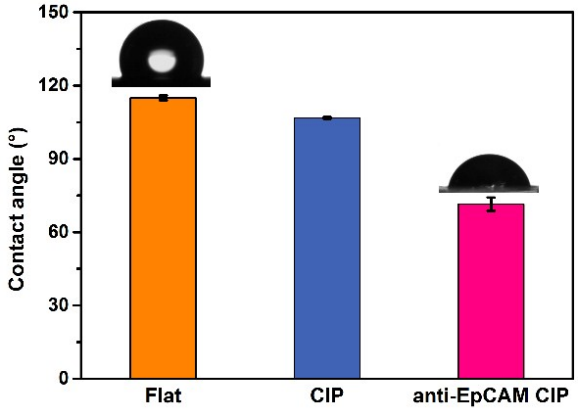

Figure S4. Contact angle measurements of the flat, CIP and anti-EpCAM modified CIP substrates.

Furthermore, we determined the wettability of the PDMS interfaces because it affects cell capture and adhesion properties. Wettability was determined by monitoring the contact angle (CA). As shown in Figure S4, the contact angle of cell-imprinted substrate decreased from 115° to 106.8° compared with flat PDMS interface. After modification with anti-EpCAM, the contact angle was further decreased to 71.5°. This significant decrease in contact angle indicated that the hydrophilicity and/or polarity of the interface increased. As reported in the previous studies, cells adhered well onto polymer surfaces presenting moderate wettability with water contact angles of 40-70°.[1, 2] Therefore, as-prepared cell-imprinted substrates, after modification with anti-EpCAM,

enhanced cell capture and adhesion due to the moderate wettability in addition to the specific recognition of the antigen-antibody.

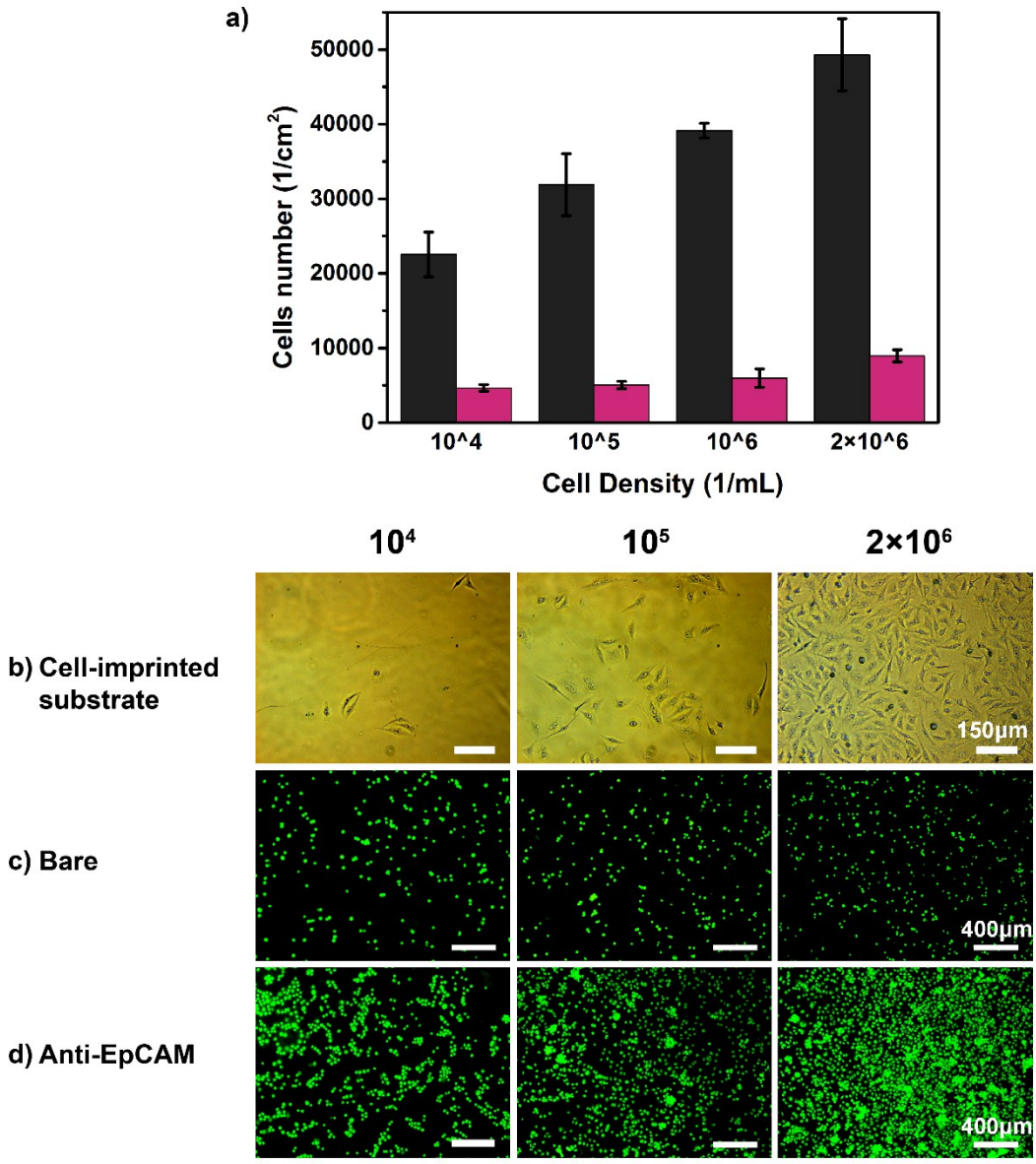

Figure S5. a) MCF-7 cell capture capacity of cell-imprinted substrates with different cell densities. The black represents anti-EpCAM modified cell-imprinted interfaces and the red indicates the original cell-imprinted interfaces. Error bars represent standard deviations, n=5. b) Optical images of cell-imprinted substrates with different cell

densities. (c, d) Fluorescent images of captured MCF-7 cells on cell-imprinted substrates. Cells were stained with AO/EB fluorescent dye.

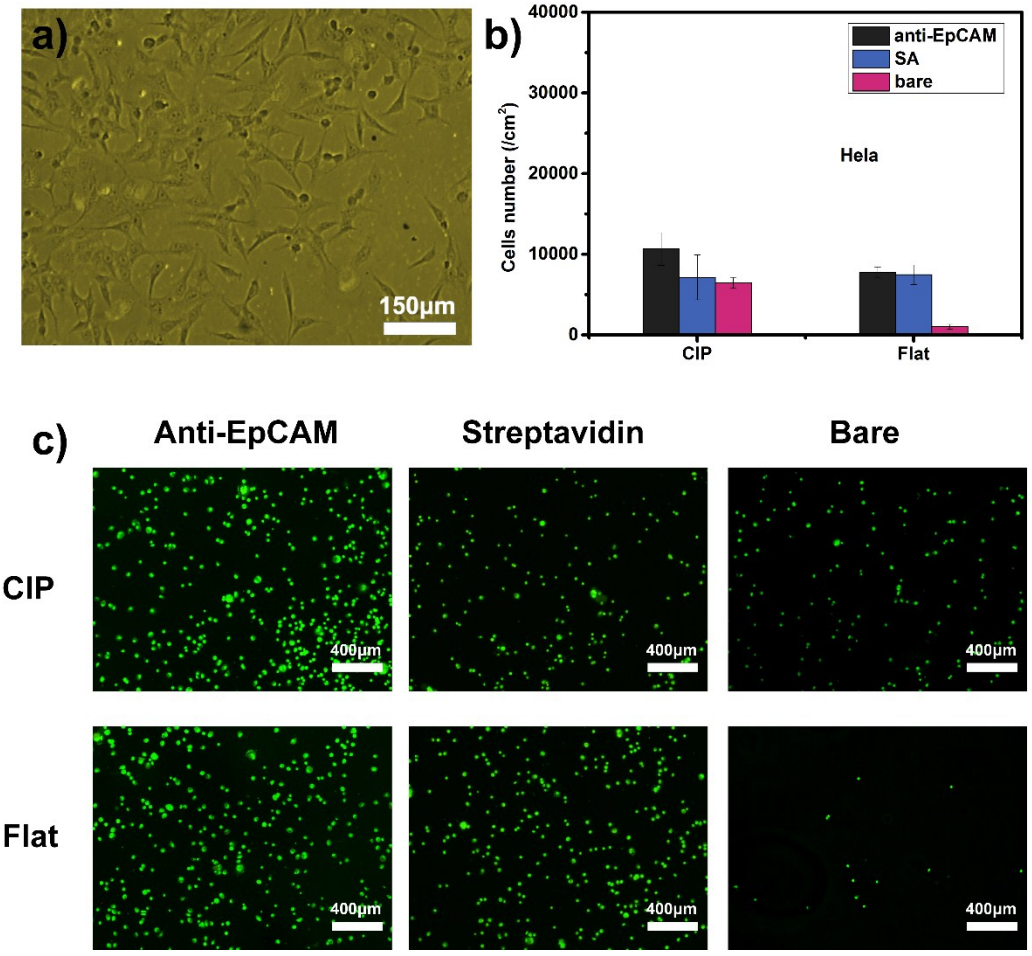

Figure S6. a) Optical image of HeLa cell imprinted substrates. b) Quantitative evaluation of HeLa cell capture performance on PDMS substrates (both cell imprinted and flat morphology) with various surface modification. Error bars represent standard deviations, n=5. c) Fluorescent images of captured HeLa cells on PDMS substrates. Cells were stained with AO/EB fluorescent dye.

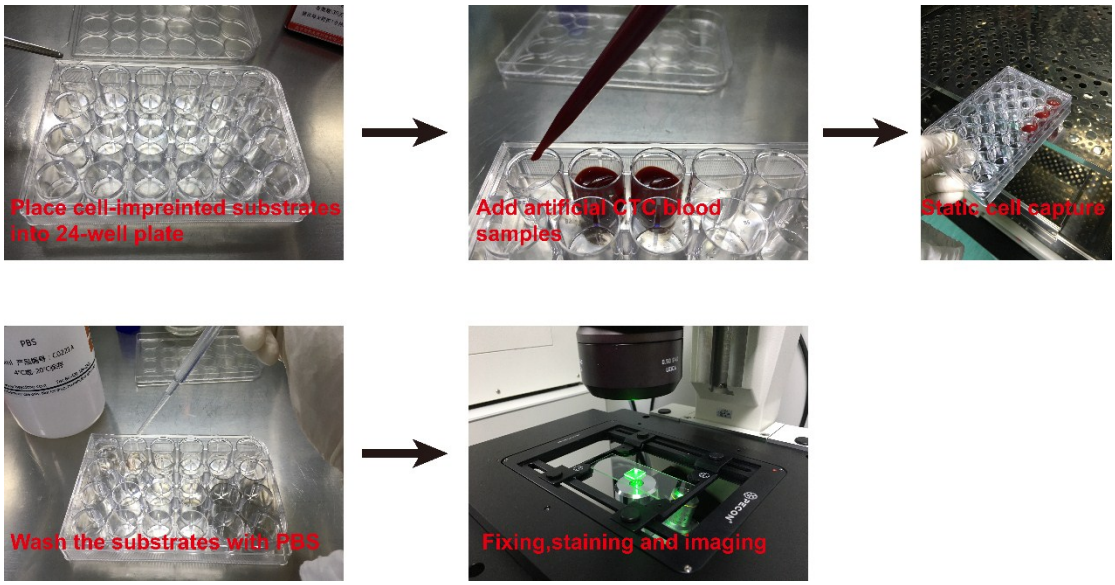

Figure S7. Schematic diagram of the simple and convenient procedures of cell capture experiments using the cell-imprinted substrates.

Table S2. Cell capture efficiencies of anti-EpCAM-modified cell-imprinted substrates by spiking rare number of MCF-7 cells into rabbit whole blood samples.

		Cell number/mL	20	50	100	250
MCF-7 cells	**Diluted with 1mL rabbit whole blood**	Capture efficiency	80%±4%	73%±9%	60%±13%	58%±5%
		Successful detection out of total samples	3/3	3/3	3/3	3/3

Table S3. Summary of various CTC isolation technologies.

Surface structure	Ways to obtain surface structure	Capture performance （cells cm^{-2}）	Ref.
PEDOT-COOH nanodots	Electropolymerization	$(2.4 \pm 0.2) \times 10^4$	[3]
Polypyrrole nanowires	Potentiostatic electrodeposition	$(1.8 \pm 0.2) \times 10^4$	[4]
Silicon nanopillar array	Wet chemical etching	$(1.2 \pm 0.5) \times 10^4$	[5]
Hierarchically Structured surface	A replication method with natural rose petals as the template	$(4.7 \pm 0.3) \times 10^4$	[6]
Nanofibers	Electrospinning	$(4.6 \pm 0.3) \times 10^4$	[7]
Cell-imprinted substrate	Cell-imprinting technology	$(4.9 \pm 0.9) \times 10^4$	This work

References

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