Supplementary materials

Ultrahigh SERS Activity of TiO_2@Ag Nanostructure Leveraged for Accurately Detecting CTCs in Peripheral Blood

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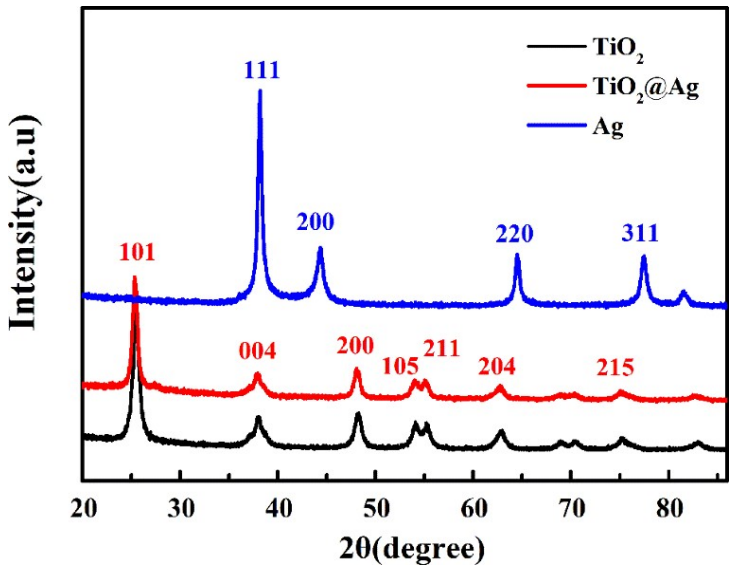

Fig. S1 X-ray diffraction (XRD) spectra of TiO_2, TiO_2@Ag, and Ag.

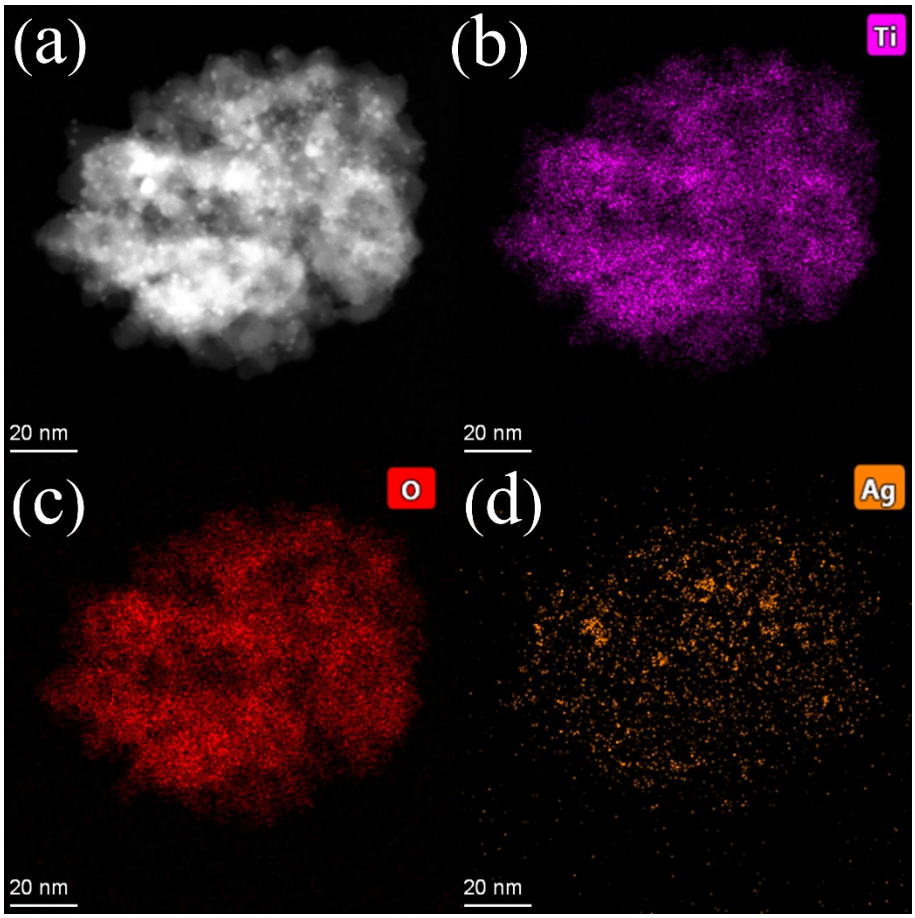

Fig. S2 Element distributions mapping images of Ti, O, and Ag in TiO_2@Ag nanostructures.

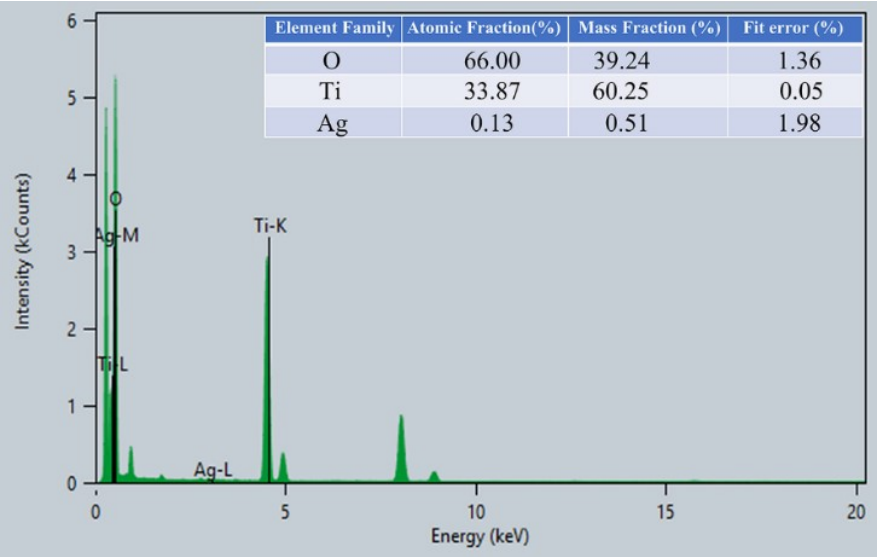

Fig. S3 Energy-dispersive spectroscopy (EDS) characterization of TiO_2@Ag.

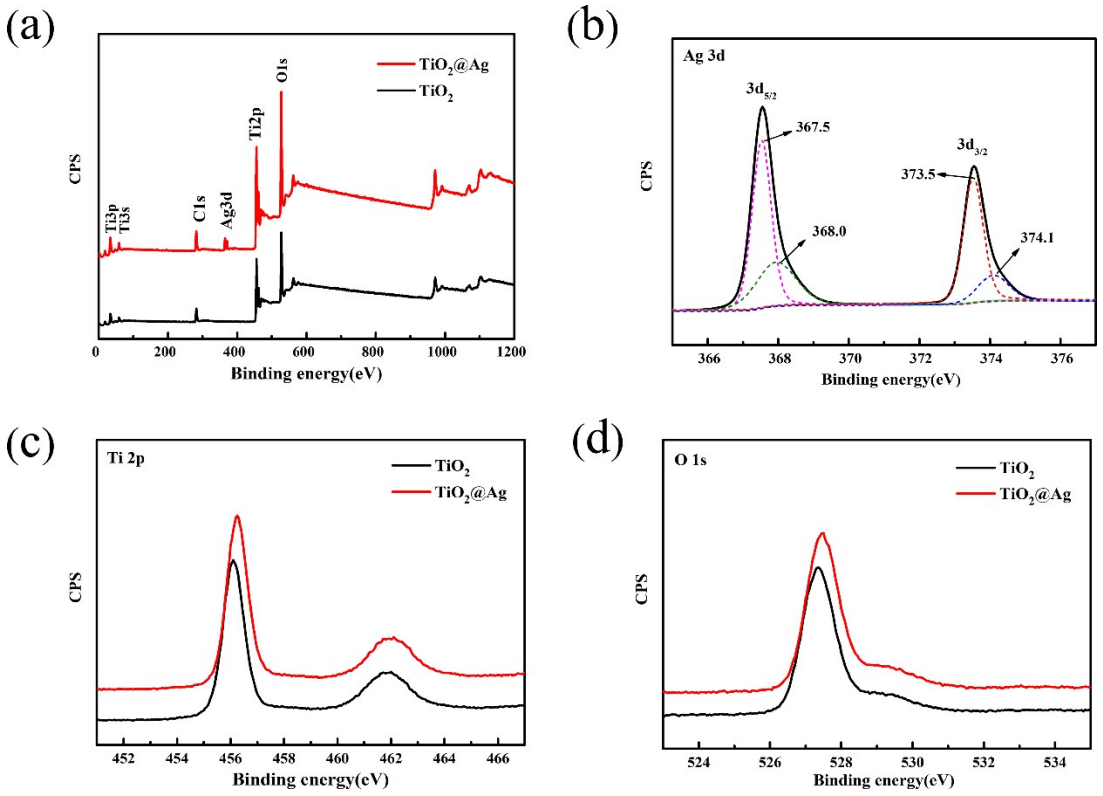

Fig. S4 XPS spectra of survey spectrum (a), Ag 3d (b), Ti 2p (c), and O 1s (d) of TiO_2 and TiO_2@Ag samples, respectively.

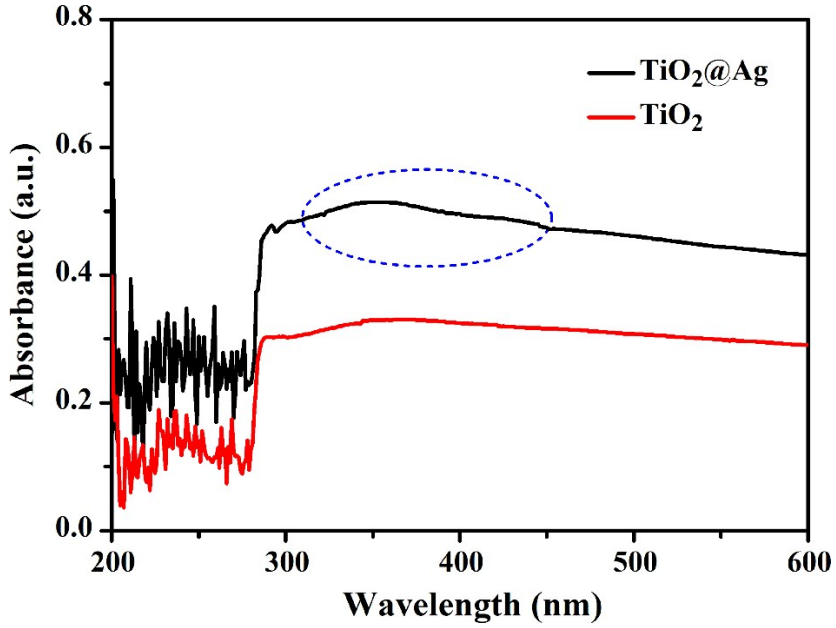

Fig. S5 UV-vis spectroscopy of TiO_2@Ag, and TiO_2.

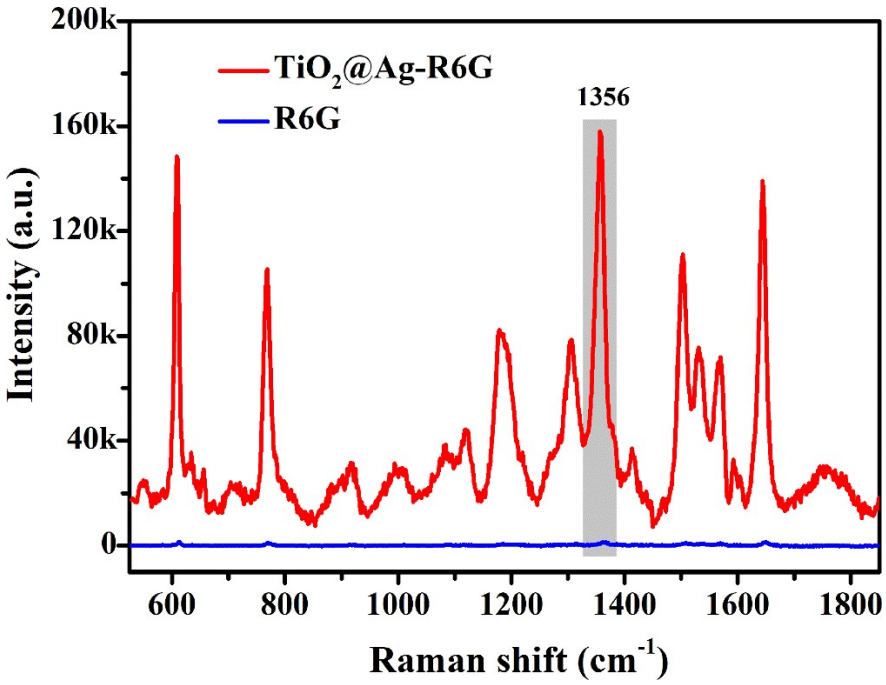

Fig. S6 Raman spectra of R6G molecule (5×10^{-5} M) adsorbed on TiO_2@Ag NPs and pure SERS signal of R6G molecules (5×10^{-2} M).

Enhancement factor (EF) calculation of TiO_2@Ag NPs was based on equation (1):

$$EF = (I_{SERS} / N_{ads}) / (I_{bulk} / N_{bulk}) \quad (1)$$

Where N_{ads} and N_{bulk} imply the number of R6G molecules adsorbed on the TiO_2@Ag NPs substrate and R6G molecules in normal Raman substrate, respectively. I_{SERS} and I_{bulk} are the vibration peak (1356 cm^{-1}) intensity of R6G molecules on TiO_2@Ag NPs substrate, and normal Raman spectrum of R6G molecules, respectively.

During the SERS experiment, 100 μL of ethanol aqueous R6G solution (5×10^{-2} M) was dried onto 0.4 cm × 0.4 cm^{-2} silicon wafer. N_{Raman} was lied on equation (2).

$$N_{bulk} = 100\ \mu L \times 5 \times 10^{-2}\ mol/L \times 8 \times 6.02 \times 10^{23}\ mol^{-1} \times 1.3\ \mu m^2 / 0.16\ cm^{-2} \quad (2)$$

where *d* is the diameter of the light spot estimated as $d = 1.22\ \lambda/NA$, λ is incident wavelength 532 nm, the numerical aperture of the objective lens $N_A = 0.5$, the laser spot is ~ 1.3 μm^2. On the basis of equation (2), N_{bulk} was estimated as ~1.95×10^{12}.

In addition, N_{ads} is synergistically determined by laser spot illuminating the TiO_2@Ag-R6G substrate, and the density of R6G molecules, N_{ads} is concluded as:

$$N_{ads} = \sigma \times 1.3\ \mu m^2 \times 6.02 \times 10^{23}\ mol^{-1} \quad (3)$$

Where σ is the density of R6G molecule absorbed onto TiO_2@Ag substrate, which is approximated to ~0.5 nM cm^{-2}(3). N_{ads} is concluded as ~ 3.91×10^6. I_{SERS} is the Raman peak intensity at 1356 cm^{-1} of R6G molecules on TiO_2@Ag NPs, while I_{bulk} represents the Raman peak intensity at 1356 cm^{-1} of pure R6G molecule (fig S6). I_{SERS} = ~ 135065 and I_{bulk} = ~ 882. Substituting these values into equation (1), EF of TiO_2@Ag NPs was concluded to be ~ 7.61×10^7.

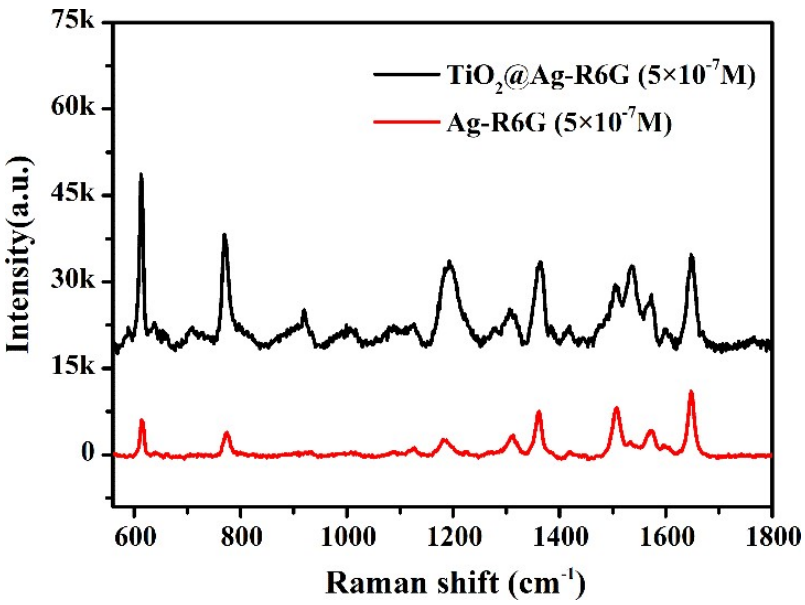

Fig. S7 SERS signal of R6G (5×10^{-7}M) molecule adsorbed on TiO_2@Ag nanostructure, and Ag NPs.

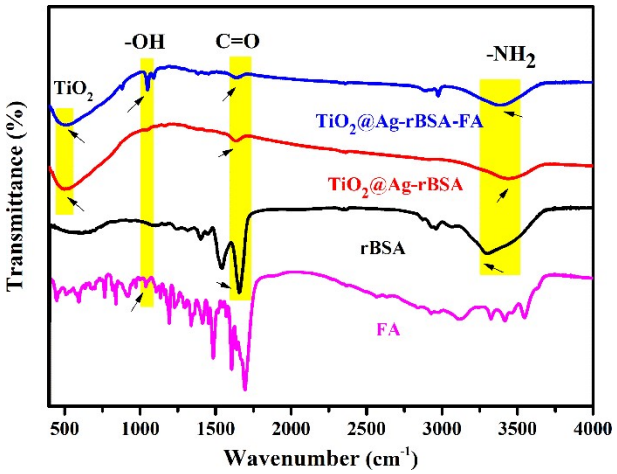

Fig. S8 FI-TR spectra of FA, rBSA, TiO_2@Ag-rBSA, and TiO_2@Ag-rBSA-FA.

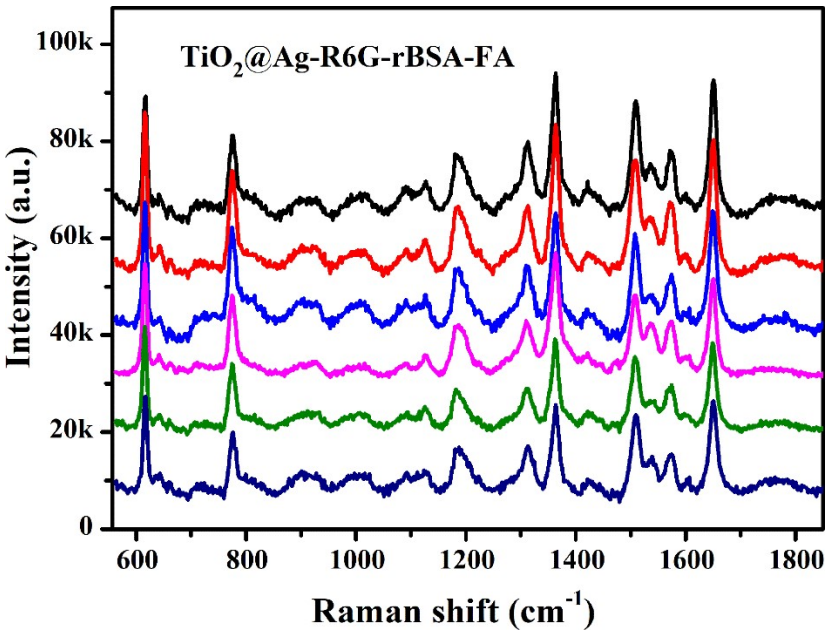

Fig. S9 SERS spectra of R6G (5×10^{-3} M) molecule collected from six TiO_2@Ag-rBSA-FA SERS bioprobes; Excitation wavelength: 532 nm; Laser power: 0.1 mW; Lens: 50× objective; Accumulations: 10 s.

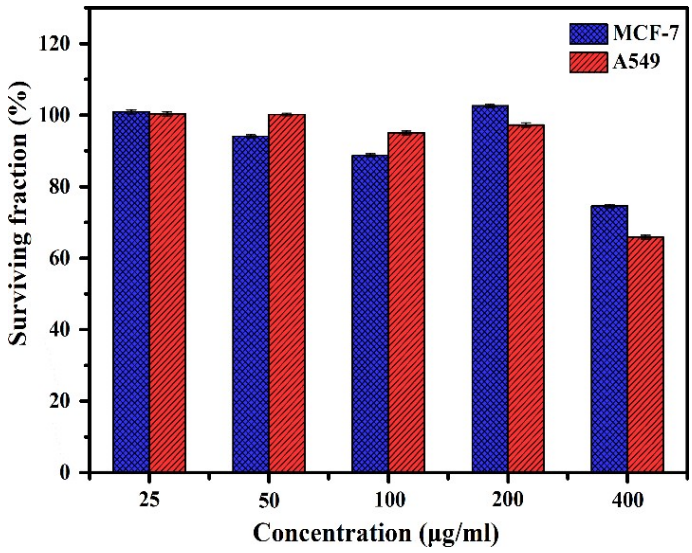

Fig. S10 Cell viability of A549 and MCF-7 cells co-incubated with TiO_2@Ag-R6G-rBSA-FA bioprobe for 24 h with different TiO_2@Ag concentrations.

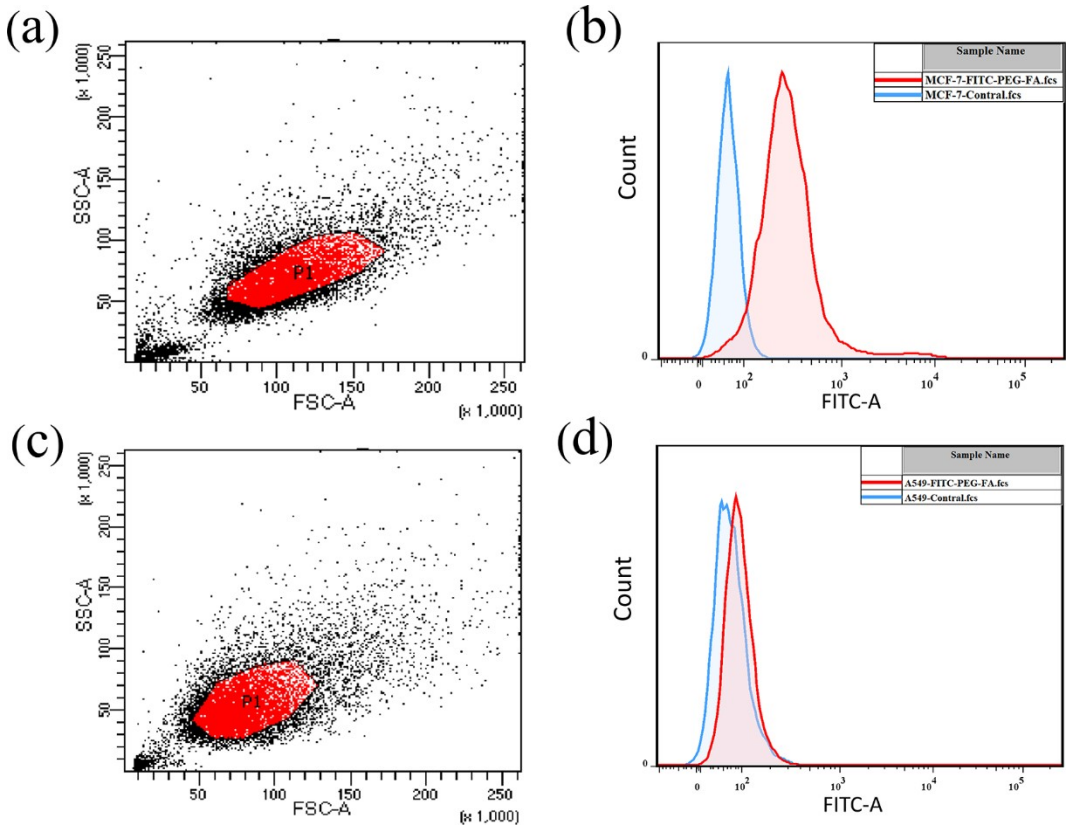

Fig. S11 FCS analysis of MCF-7 and A549 cells incubated with 20 μL FA-PEG-FITC (red) and PBS (blue).

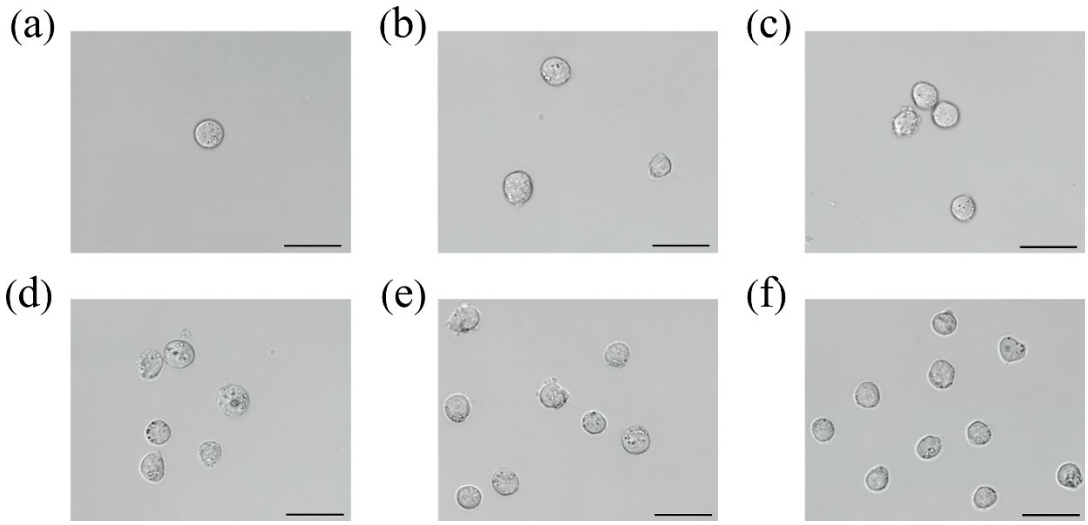

Fig. S12 HeLa cell count of bright field under laser scanning confocal microscope. Scale bar: 25 μm.

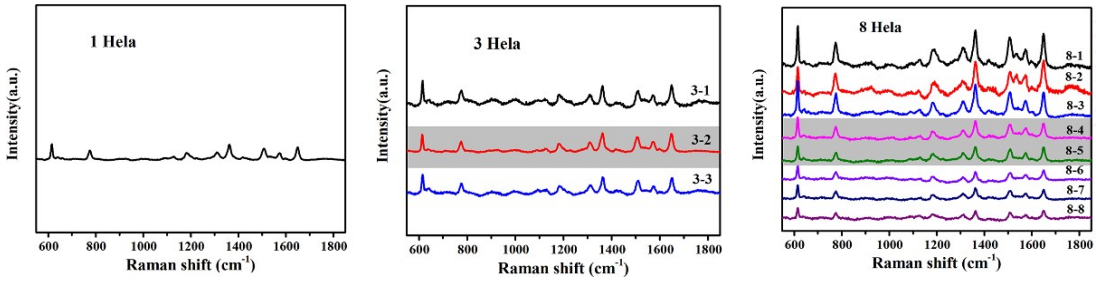

Fig. S13 Detection sensitivity of the TiO_2@Ag-R6G-rBSA-FA SERS bioprobe for different numbers of HeLa cells in the rabbit blood.

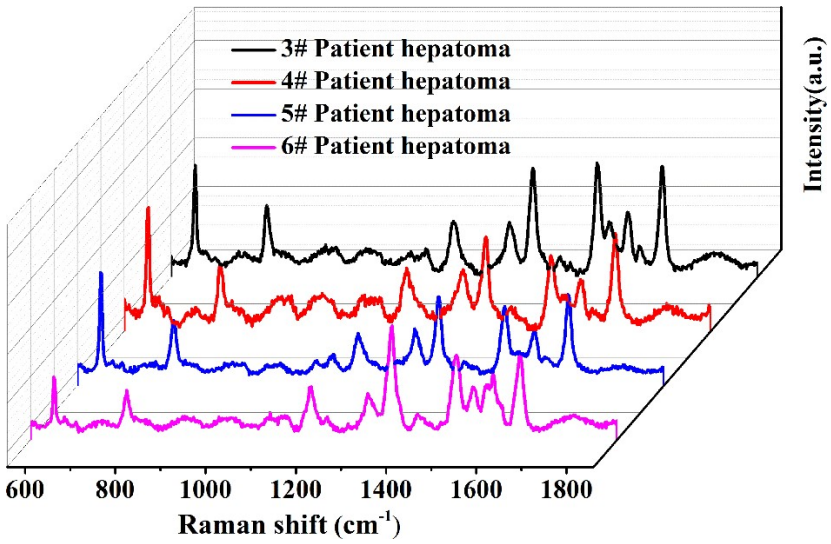

Fig. S14 TiO_2@Ag-R6G-rBSA-FA SERS bioprobe was utilized for CTCs detection in peripheral blood of four liver cancer patients.