Support Information

EXPERIMENTAL SECTION

Preparation of HATb

HA-Tb nanocrystals were synthesized by hydrothermal method. Briefly, a reaction formula, $(10 - x)\ Ca(NO_3)_2 + xTb(NO_3)_3 + Na_3PO_4 \rightarrow (Ca_{10-x}Tb_x)(PO_4)_6OH_2$, was adopted, in which x = 0 to 1. Briefly, octadecylamine (1 g) was dissolved in oleic acid (8 mL) and ethanol (32 mL) under magnetic stirring in a Teflon-lined autoclave (100 mL). Next, aqueous solutions of $Ca(NO_3)_2$ (3.6 to 4 mmol, 14 mL) and $Tb(NO_3)_3$ (0 to 0.4 mmol, 4 mL) were added and stirred for 5 min, followed by the addition of Na_3PO_4 (2.4 mmol, 14 mL) solution. Afterward, the resulting solution was agitated for 10 min and hydrothermally treated at 160 °C for 6 h. After cooling to room temperature, the white precipitate was collected through centrifugation (4000 r/min, 5 min), fully washed using cyclohexane, ethanol, and deionized water, and then freeze dried.

The degradability of HA-Tb NPs *in vitro*

HA-Tb degradation and phase evolution were investigated over up 5 weeks in PBS (pH = 7.4, 6.5, and 5.0). Briefly, 20 mg samples were immersed in 10 mL PBS and shaken at 150 rpm at 37 ℃. The release medium was withdrawn at 1, 2, 3, 4, and 5 weeks and replaced with an equal volume of the fresh medium. The absorbance of the solution at 610 nm was then measured, and the amount of cumulative calcium ions was calculated based on the standard curve. Moreover, these samples were centrifuged and lyophilized for later SEM-EDS and FTIR analysis after aging in 5 weeks.

Biocompatibility and chemotherapy effect *in vitro*

To investigate the biocompatibility of HATb and HATb-PDA, three kinds of cells (Cal-27, HSC-3, and HGF) were grown at 8×10^4 cells per well in 24-well plates, respectively. After attached and spread well, the three kinds of cells were incubated in the culture medium containing HATb or HATb-PDA nanoparticles with concentrations

up to 1 mg/mL for 24 h and 48 h. After washing with PBS to remove extracellular excess nanoparticles, the medium was replaced with 100 μL fresh DMEM (including 10 μL CCK-8 solutions). The supernatant was taken after 1.5 h incubation, and the absorbance at 450 nm was determined by microplate reader (MK3, Thermo, USA). Relative cell viability was calculated according to the standard method.

Moreover, to study the chemotherapy of DOX, cells (Cal-27, HSC-3, and HGF) were treated with different concentration of DOX (0, 0.125, 0.25, 0.5, 1, and 2 μg/mL) for 24 h and 48 h, the cell viability was measured by CCK-8 kit as described above. Subsequently, three kinds of cells were incubated with free DOX and HATb-PDA-DOX at equivalent DOX concentration (0.5 μg/mL) for 48 h to compare the chemotherapy effect.

About live cell staining, cells were cultured with calcein-AM reagent for 30 min after washing with PBS based on the manufacturer's protocol, and then observed by inverted fluorescence microscope.

RESULTS SECTION

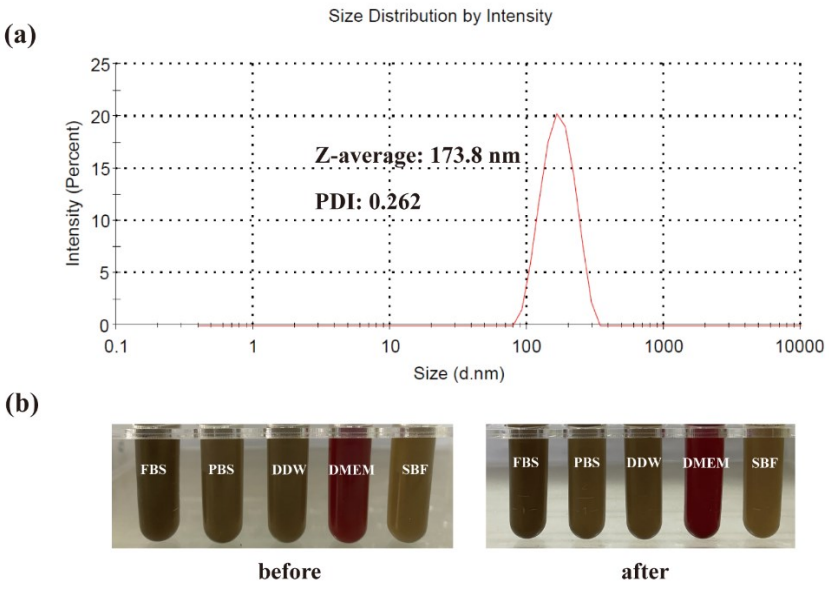

Figure S1. (a) The hydrodynamic size distribution of HATb-PDA-DOX. (b) The photos of stability of HATb-PDA-DOX in FBS, PBS, distilled water, DMEM and SBF before and after 1 month.

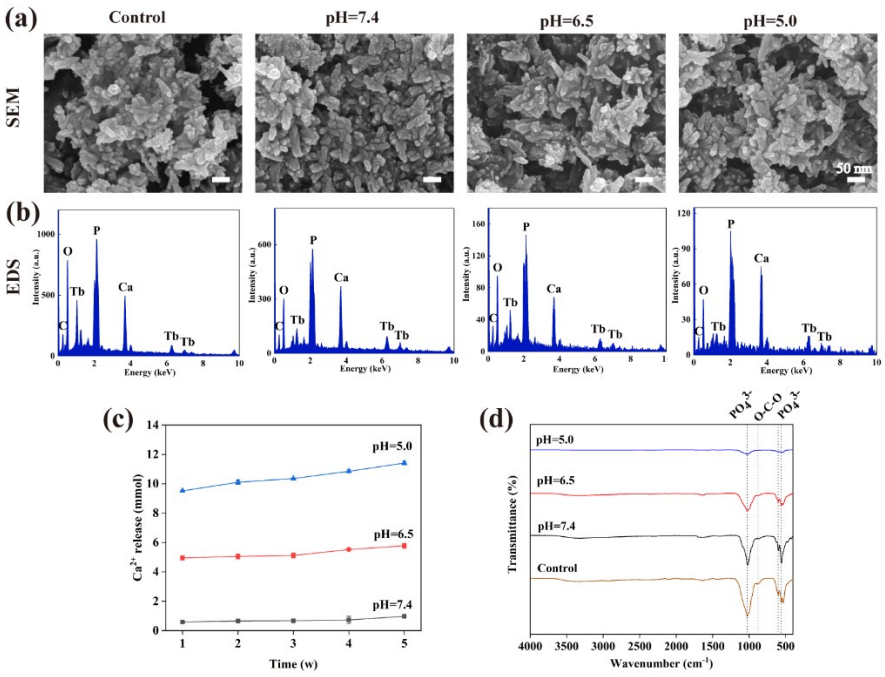

Figure S2. (a) SEM, (b) EDS, (c) Ca^{2+} release amount, and (d) FTIR of HA-Tb nanoparticles after immersion in PBS (pH = 7.4, 6.5, and 5.0) over 5 weeks.

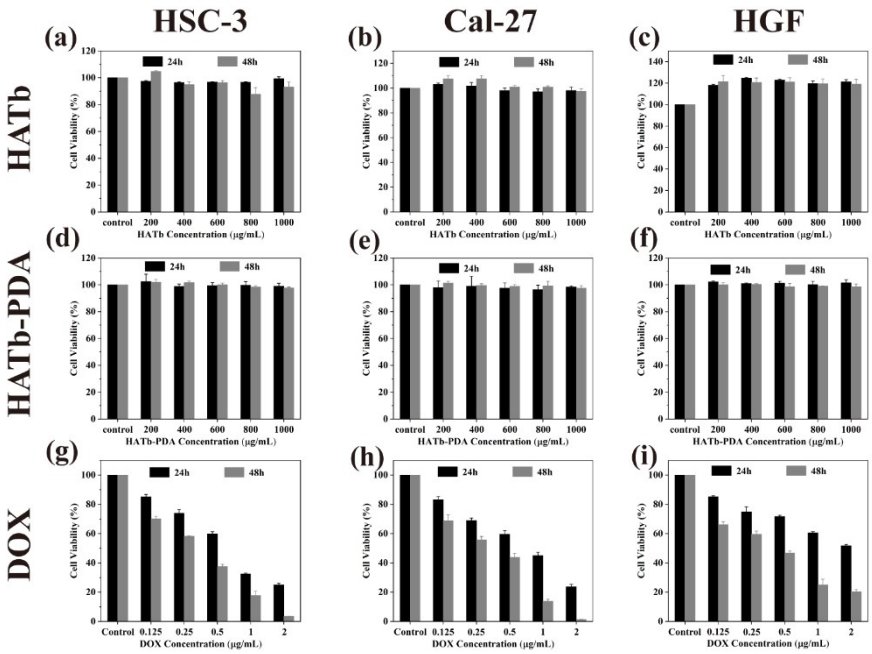

Figure S3. Cytotoxicity analysis to (a, d, g) HSC-3, (b, e, h) Cal-27, and (c, f, i) HGF cells of HA-Tb, HATb-PDA, and DOX with different concentrations for 24 and 48 h, respectively.

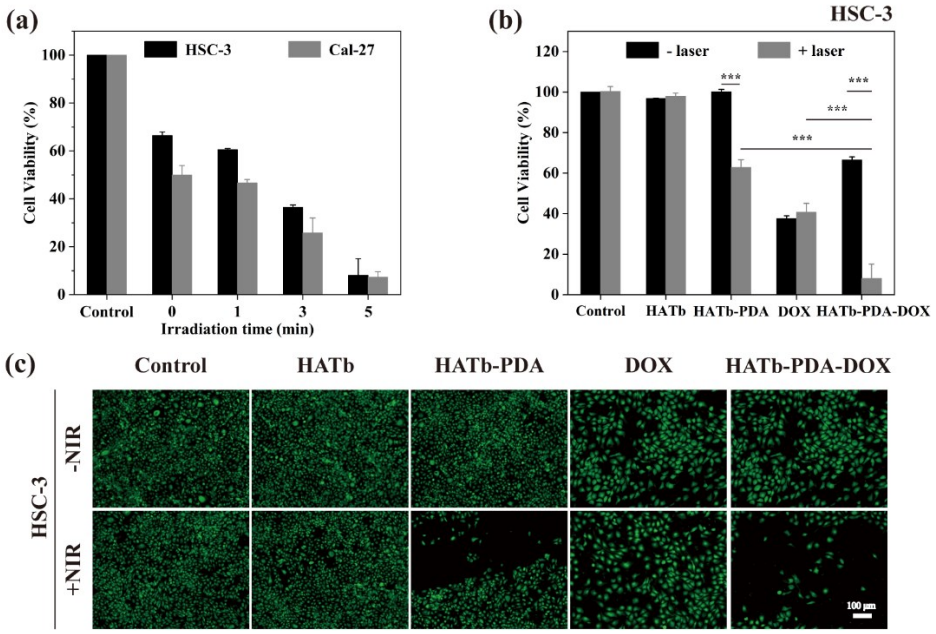

Figure S4. (a) HSC-3 cells and Cal-27 cells viability after being treated with HATb-PDA-DOX with NIR laser irradiation (808 nm, 1.4 W/cm^2) for different times. (b) Fluorescence images of live HSC-3 cells incubated with various samples treated with or without 808 nm laser (1.4 W/cm^2) for 5 min. (c) HSC-3 cells viability after being treated with HA-Tb, HATb-PDA, DOX, and HATb-PDA-DOX at the same DOX concentration level (in terms of HA-Tb or HATb-PDA, 500 μg/mL; DOX, 0.5 μg/mL) with or without NIR laser irradiation (808 nm, 1.4 W/cm^2, 5 min).

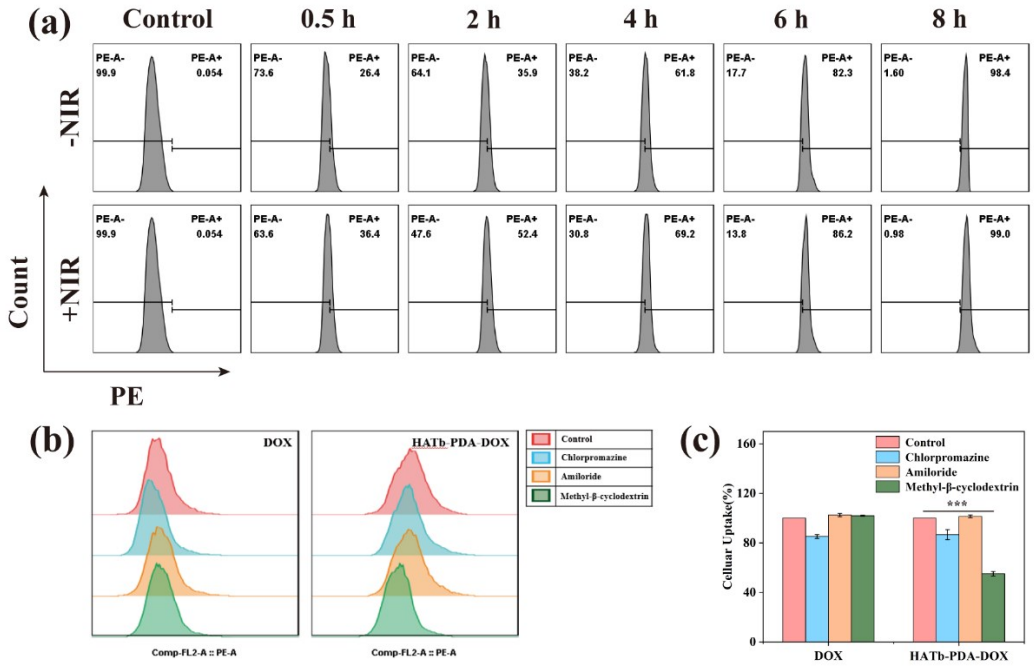

Figure S5. (a) Flow cytometry profiles of HSC-3 cells incubated with HATb-PDA-DOX (DOX concentration was 0.5 μg/mL) without or with NIR irradiation (808 nm, 1.4 W/cm^2, 5 min) for 0.5 h-8 h. (b) Cellular uptake of free DOX HATb-PDA-DOX after different inhibitors treatments in HSC-3 cells by flow cytometry analysis. (c) Relative fluorescent intensity of various inhibitors treatments in HSC-3 cells. Relative fluorescent intensity = MFI (experimental group) / MFI (control group) ×100%.

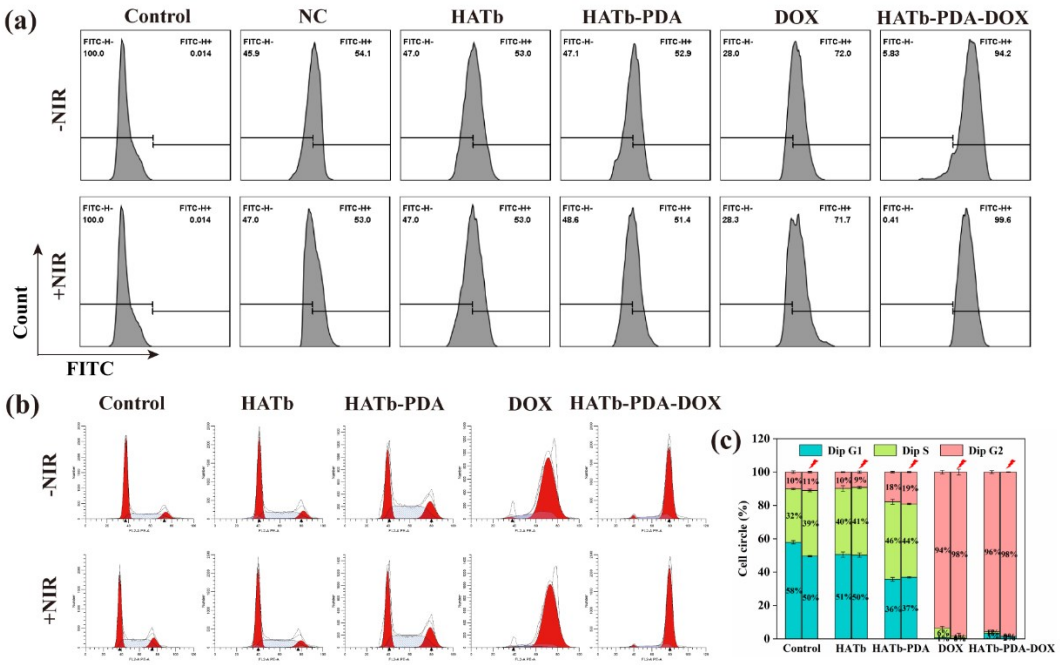

Figure S6. (a) Flow cytometry based intracellular ROS generation analysis on HSC-3 cells incubated with HA-Tb, HATb-PDA, DOX, and HATb-PDA-DOX at the same DOX concentration level (in terms of HA-Tb or HATb-PDA, 500 μg/mL; DOX, 0.5 μg/mL) with or without NIR laser irradiation (808 nm, 1.4 W/cm^2, 5 min). Control (no sample stimulation and no fluorescent probe), NC (no sample stimulation but fluorescent probe). (b, c) Cell cycle phases were determined by flow cytometry of HSC-3 cells after incubation with different samples without or with NIR laser irradiation (808 nm, 1.4 W/cm^2, 5 min).

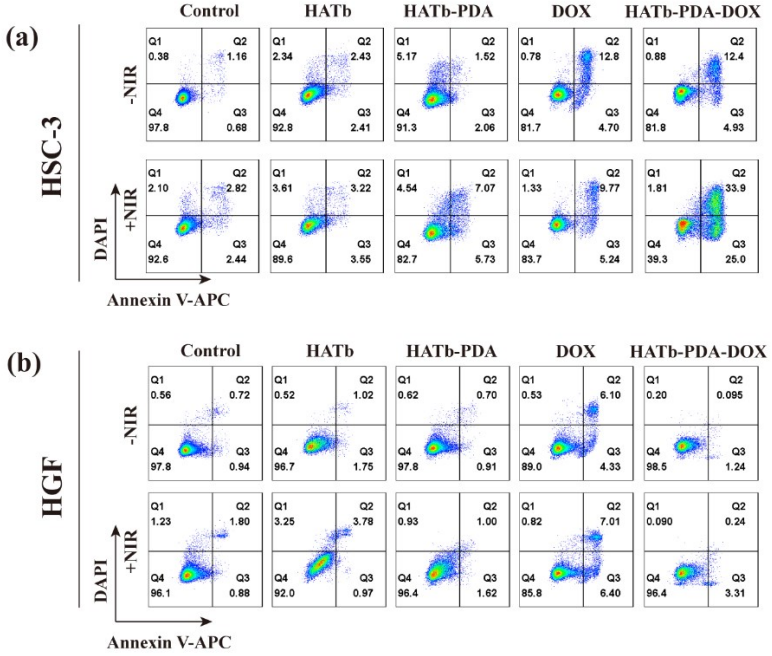

Figure S7. Cell apoptosis was evaluated by flow cytometry of HSC-3 cells (a) anf HGF cells (b) stained with CFSE and Annexin V-APC/DAPI after treatment with different samples without or with NIR laser irradiation (808 nm, 1.4 W/cm^2, 5 min).