Supplementary Material

A Programmed Nanoparticle with Self-Adapting for Accurate Cancer Cell Eradication and Therapeutic Self-Reporting

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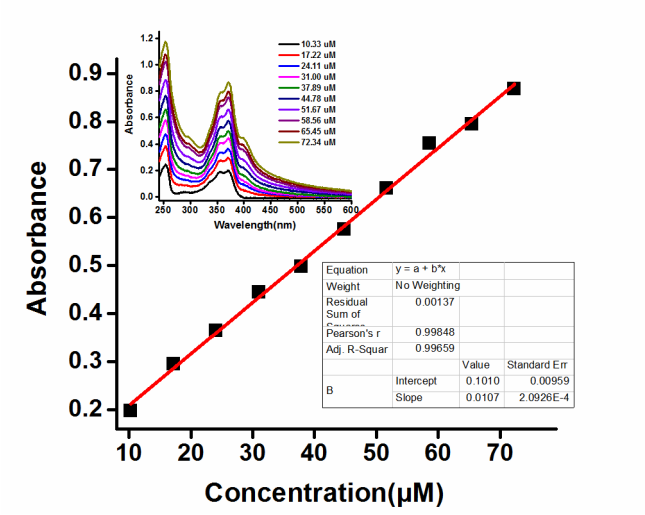

Figure S1. Absorption standard curve of CPT at 371 nm wavelength using UV-VIS method. Inset: absorption spectra of different concentrations of CPT.

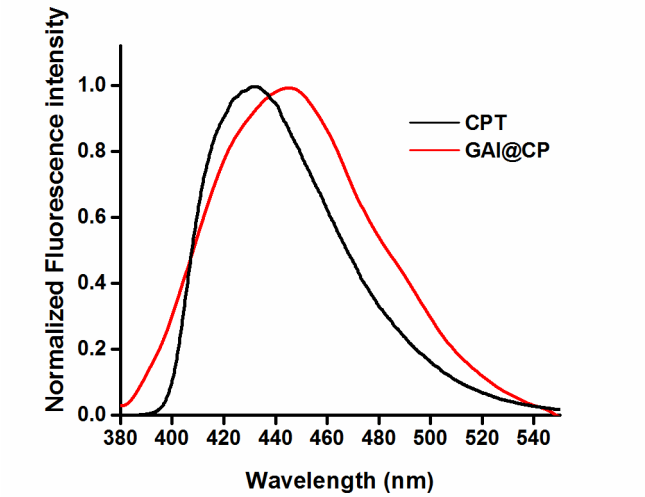

Figure S2. The fluorescence emission spectra of CPT and GAI@CP. The excitation was 370 nm and the emission was collected from 380 to 555 nm.

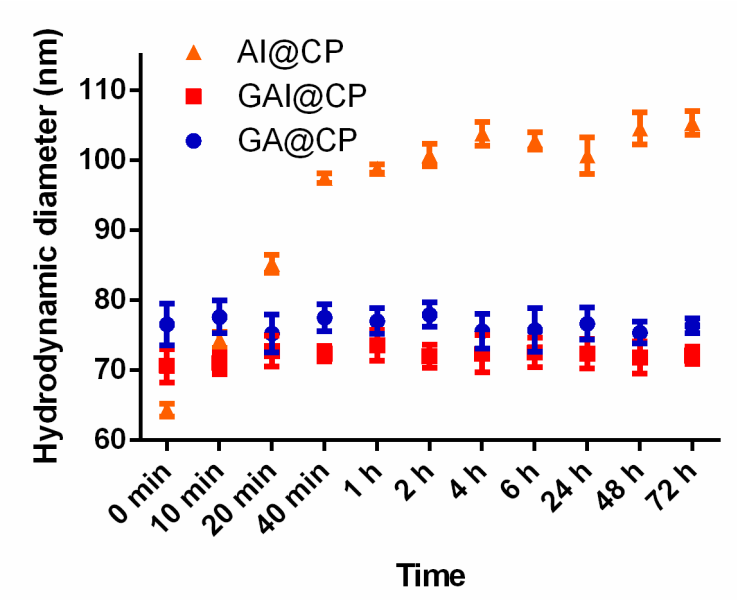

Figure S3. Stability of AI@CP, GAI@CP and GA@CP in PBS (pH 7.4) containing 10% fetal bovine serum (FBS) measured by dynamic light scattering. Data are means ± SD (n = 3).

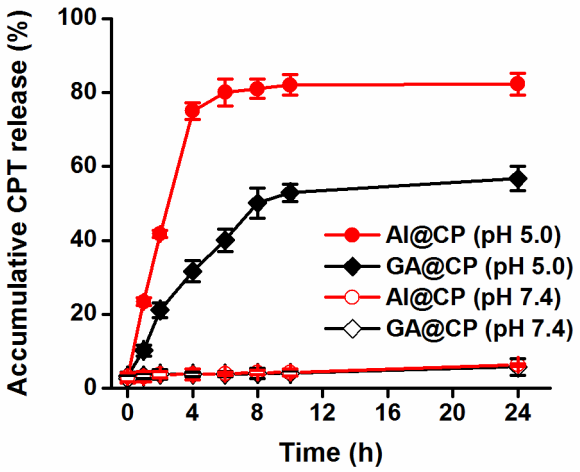

Figure S4. Accumulative release of CPT from AI@CP and GA@CP at pH 5.0 and 7.4 in citrate buffer containing 10% FBS, respectively.

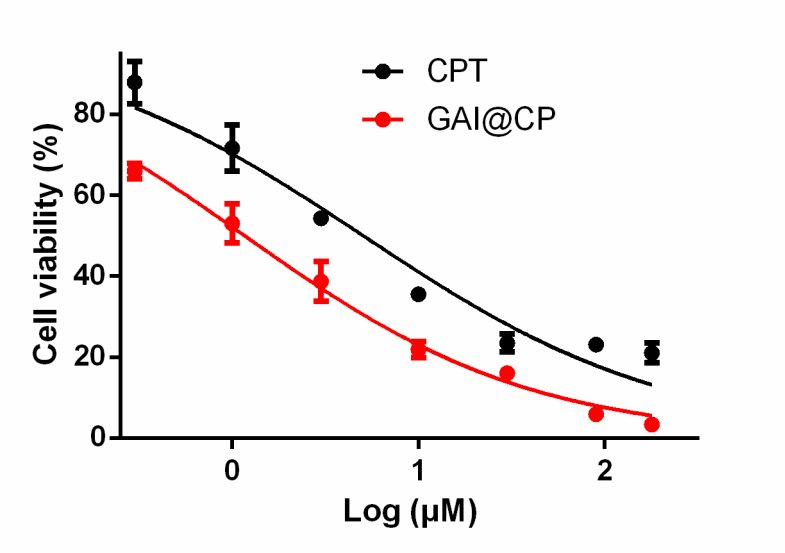

Figure S5. MTT assay for HeLa cells after incubated with free CPT and GAI@CP at different concentrations (CPT equiv.) for 24 h. Data are means ± SD (n = 5).

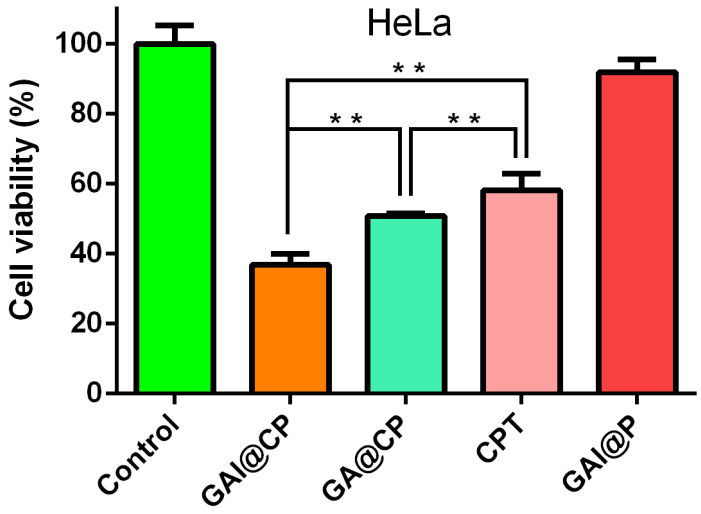

Figure S6. MTT assays for HeLa cells incubated with PBS as control, GAI@CP, GA@CP, free CPT and GAI@P (3.0 μM CPT equiv.). Data are means ± SD ($n \geq 3$, *$P < 0.05$, **$P < 0.01$ using a one-way ANOVA).

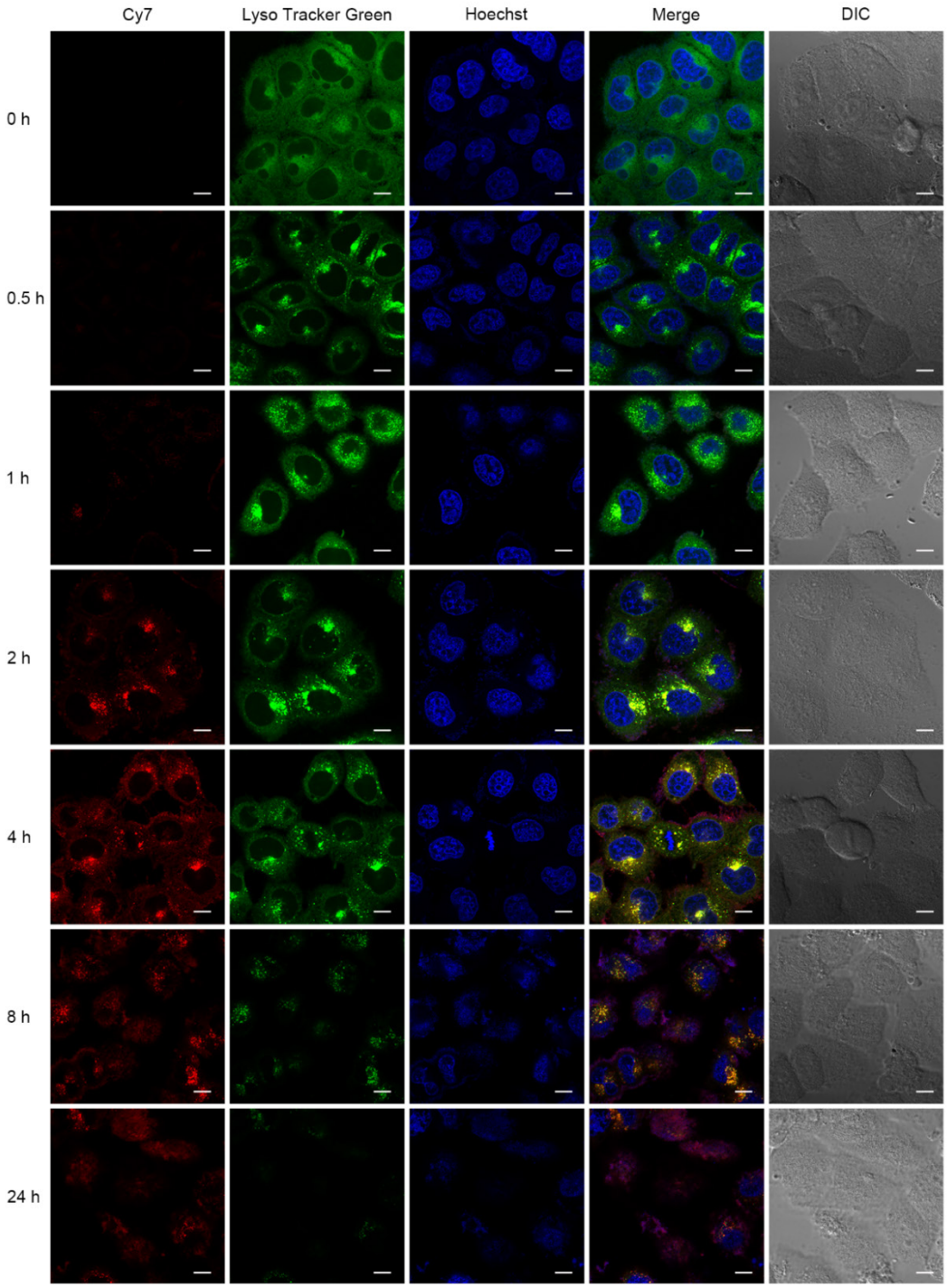

Figure S7. Confocal fluorescence images of HeLa cells stained with Lyso Tracker Green and Hoechst 33342 after cells were incubated with GAI@CP/Cy7 for 0, 0.5, 1, 2, 4, 6, 8 and 24 h, respectively. Scale bars: 10 μm.

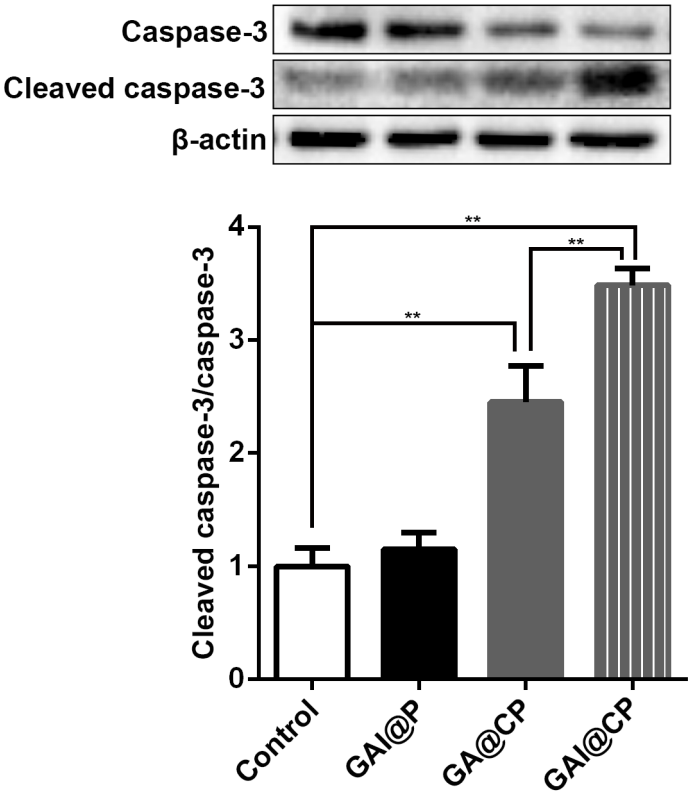

Figure S8. Protein expressions of GAI@P, GA@CP and GAI@CP treated HeLa cells were tested by western blot using *β*-actin as the loading control.

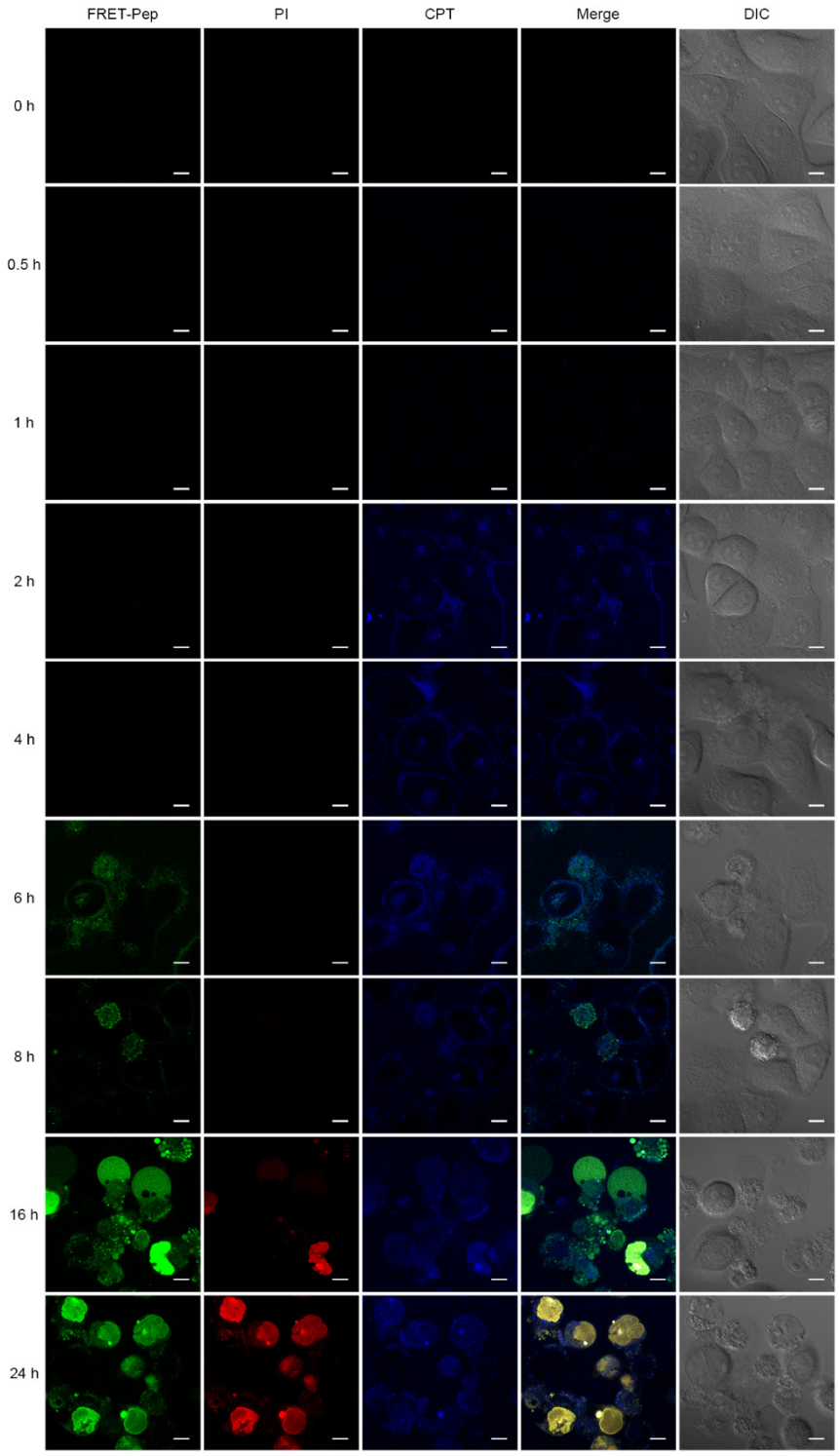

Figure S9. Confocal fluorescence images of HeLa cells stained with PI after cells were incubated with GAI@CP for 0, 0.5, 1, 2, 4, 6, 8, 16 and 24 h, respectively. Scale bars: 10 μm.

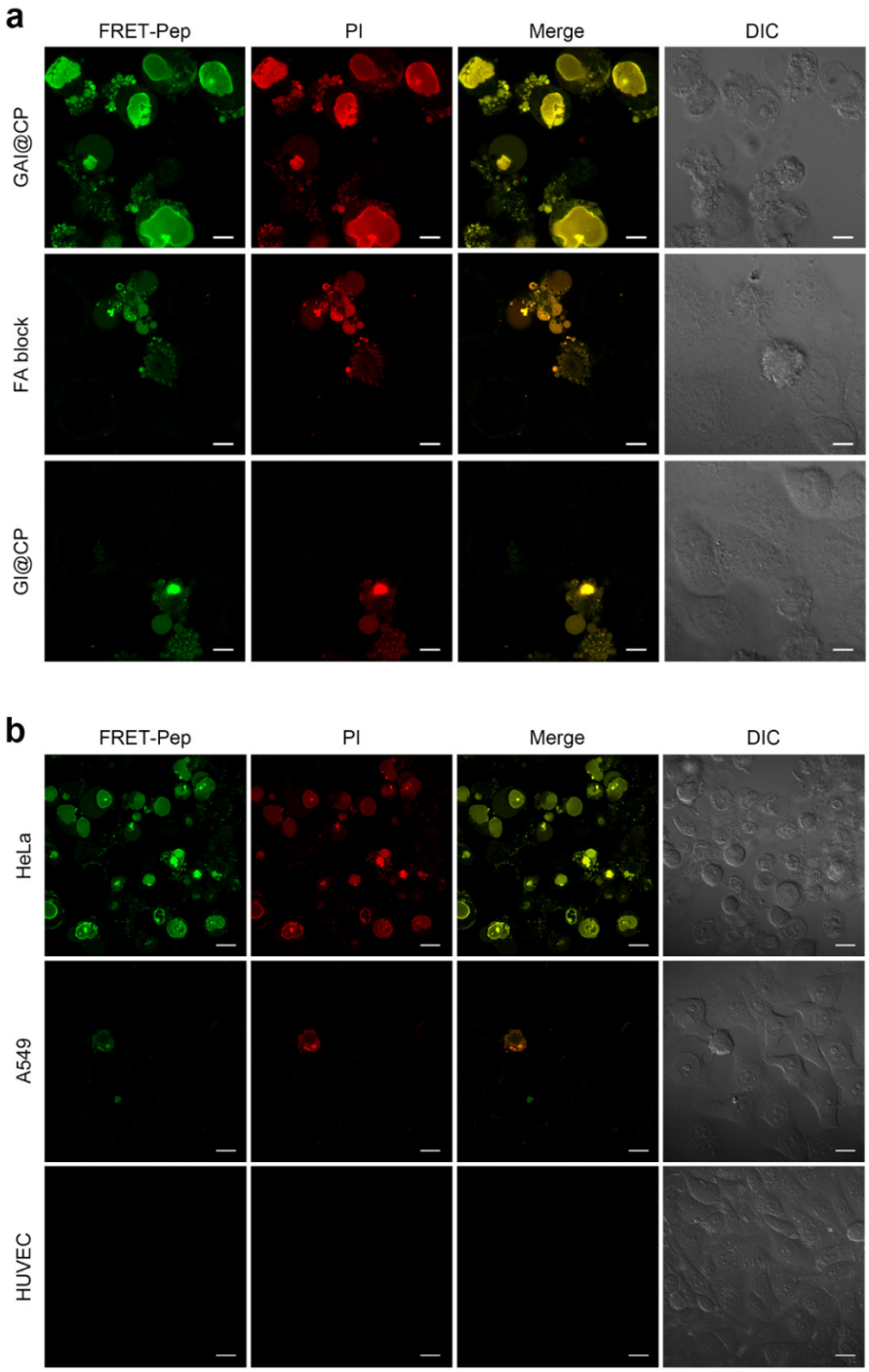

Figure S10. Confocal fluorescence images of (a) HeLa cells stained with PI after cells were incubated with GAI@CP for 24 h, pre-blocked by folate (FA) for 30 min following incubated with GAI@CP for 24 h and incubated with GI@CP for 24 h. Scale bars: 10 μm. (b) HeLa, A549 and HUVEC cells stained with PI after cells were incubated with GAI@CP for 24 h. Scale bars: 20 μm.

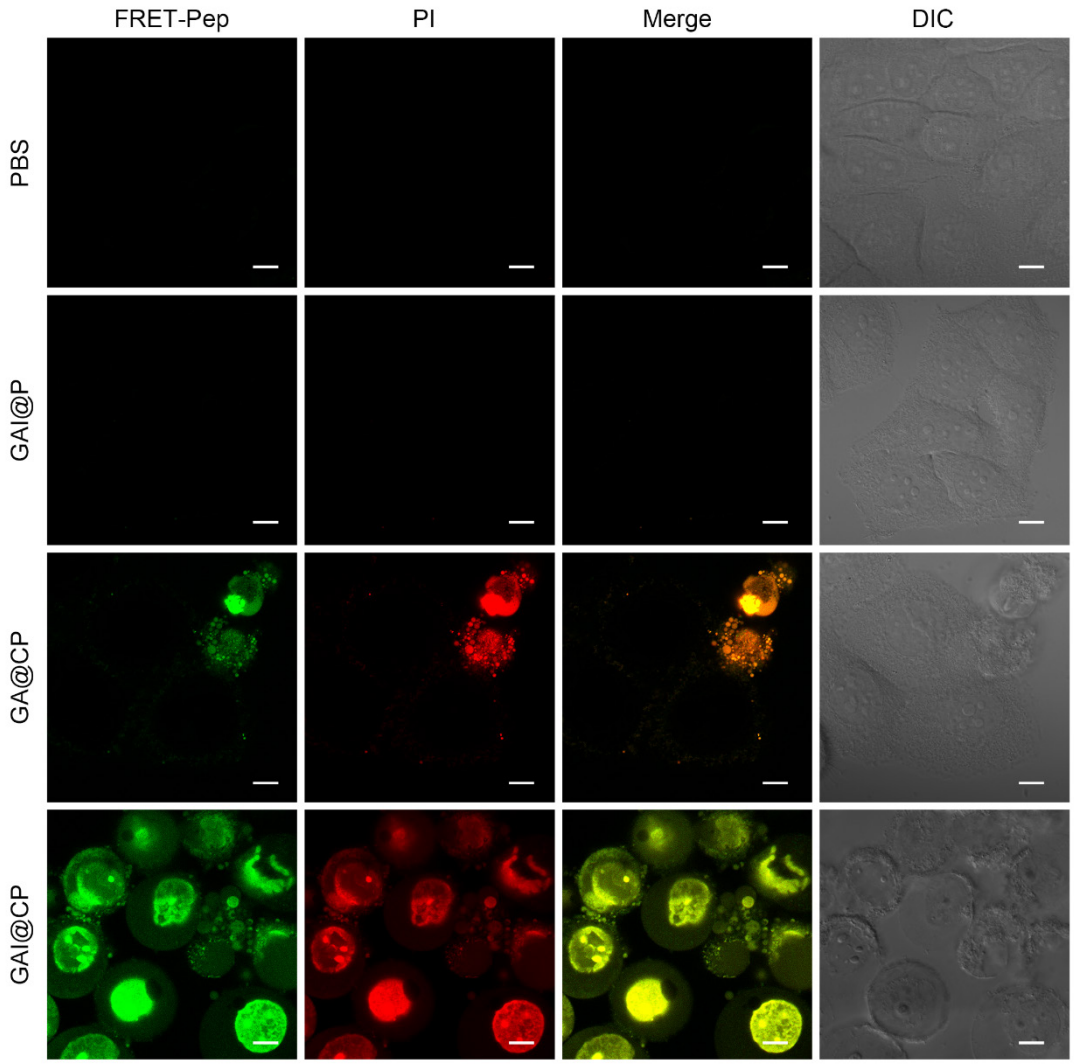

Figure S11. Confocal fluorescence images of HeLa cells stained with PI after cells were incubated with PBS, GAI@P, GA@CP and GAI@CP for 24 h. Scale bars: 10 μm.

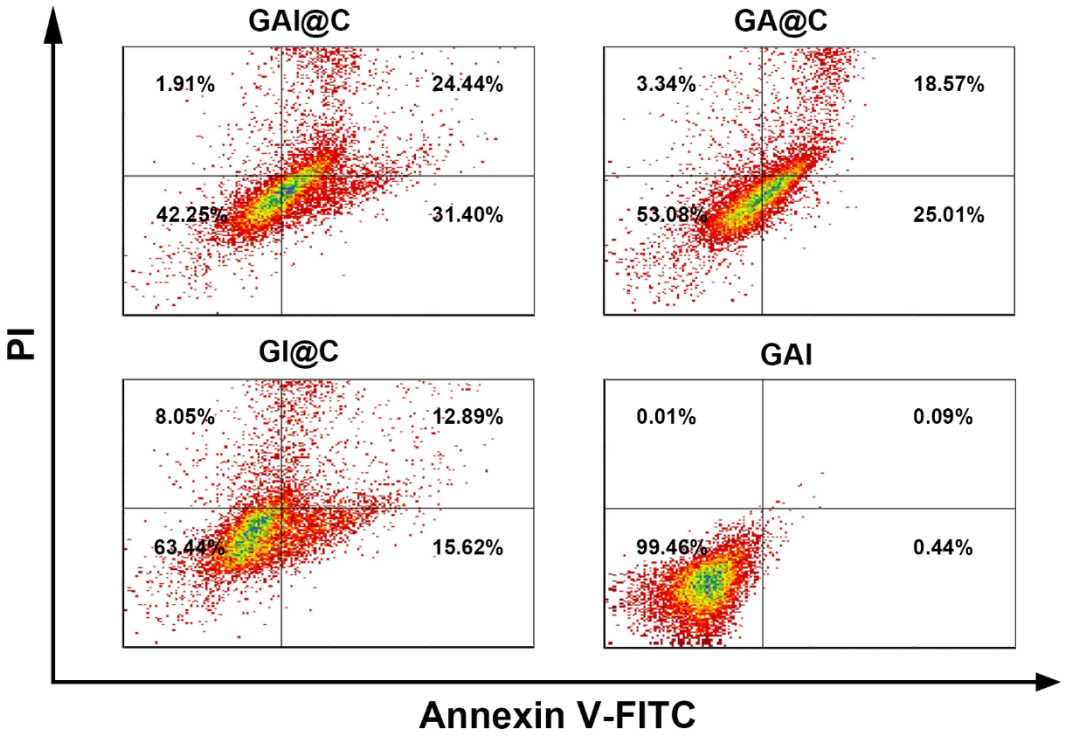

Figure S12. HeLa cells treated with GAI@C, GA@C, GI@C and GAI for 24 h and then stained with Annexin V-FITC and PI for flow cytometric assays.

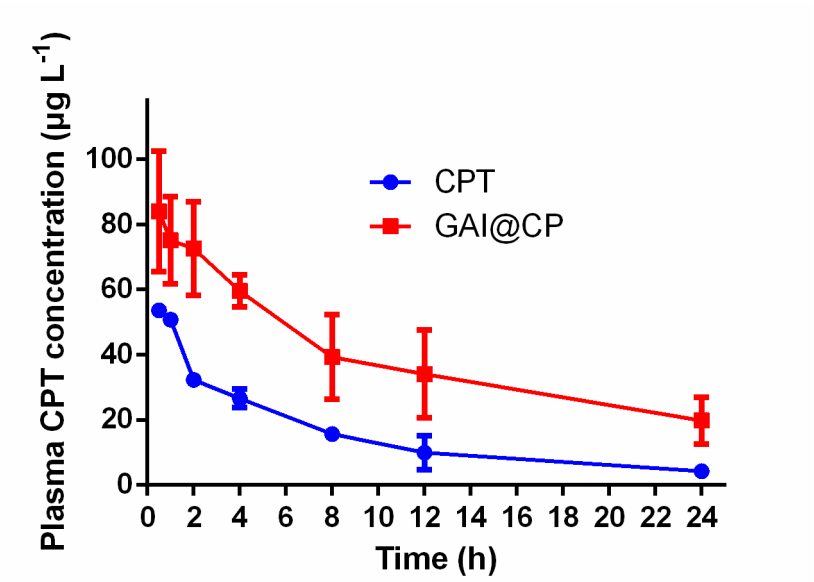

Figure S13. Pharmacokinetic profiles after intravenous injection of CPT and GAI@CP in Wister rats at a drug dose of 5 mg kg^{-1}. Data are means ± SD (n = 3).

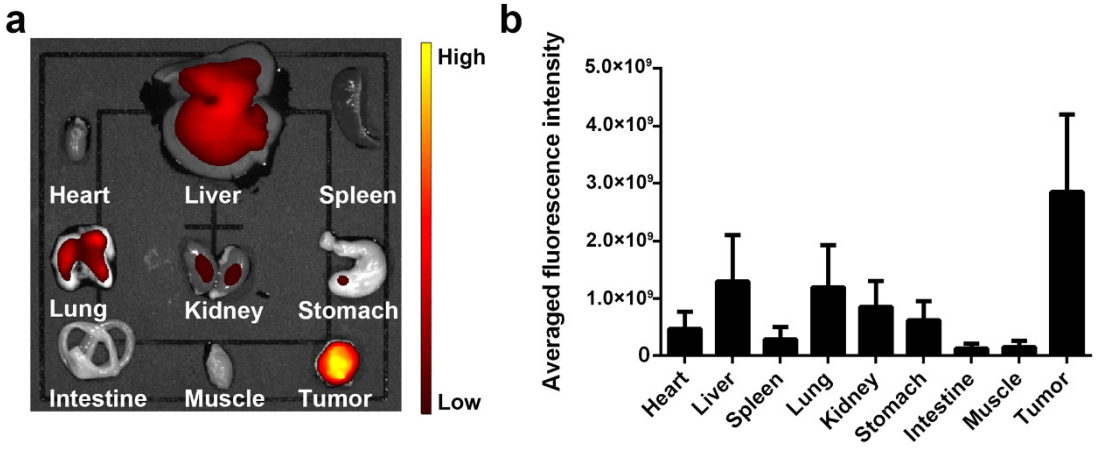

Figure S14. (a) Fluorescence image of major organs and tumor tissues after 48-h postinjection of GAI@CP/Cy7. (b) Cy7 fluorescence intensity at the major organs and tumor tissues of nude mice receiving GAI@CP/Cy7 via tail vein injection for 48 h. Data are means ± SD (n = 3).

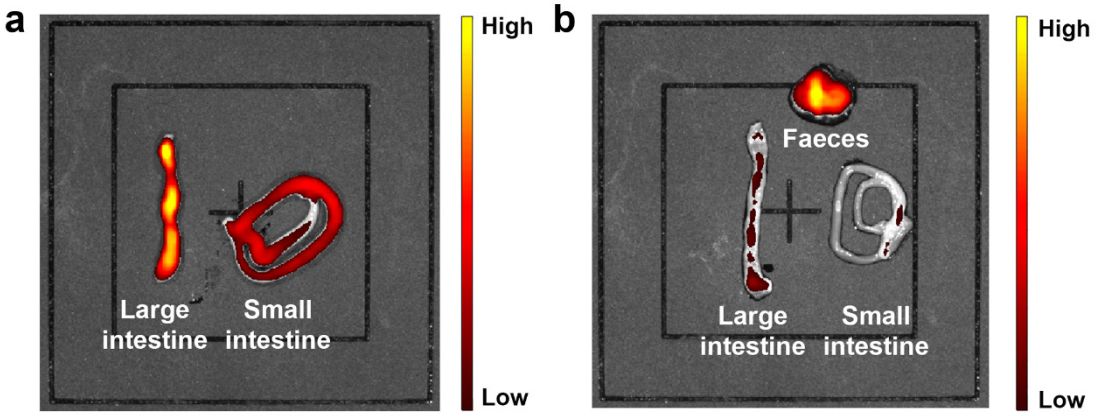

Figure S15. Cy7 fluorescence imaging at large intestine and small intestine of the nude mice receiving GAI@CP/Cy7 after 48-h tail vein injection (a) before and (b) after extrusion faeces.

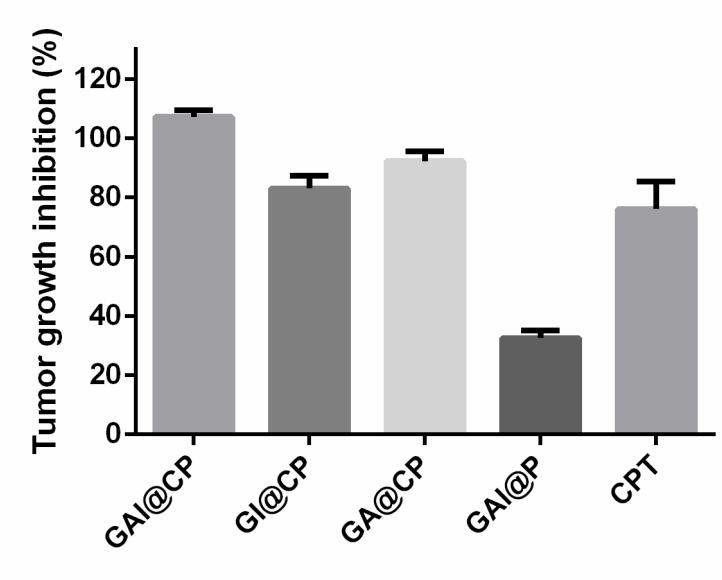

Figure S16. Tumor growth inhibition after treatment with GAI@CP, GI@CP, GA@CP, GAI@P and free CPT over 15 d, respectively. Data are means ± SD (n = 12).

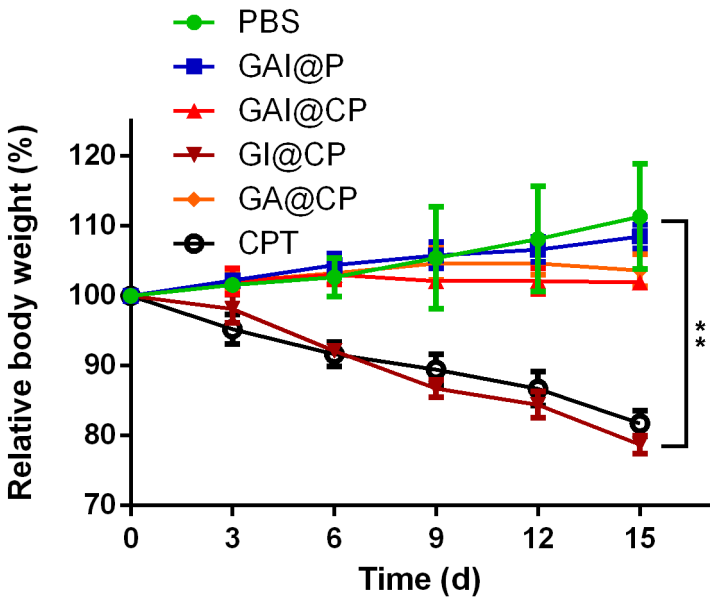

Figure S17. Body weight changes of BALB/c mice bearing HeLa cells with PBS, GAI@P, GAI@CP, GI@CP, GA@CP and free CPT over 15 d, respectively. Data are means ± SD (n = 12, *P < 0.05, **P < 0.01).

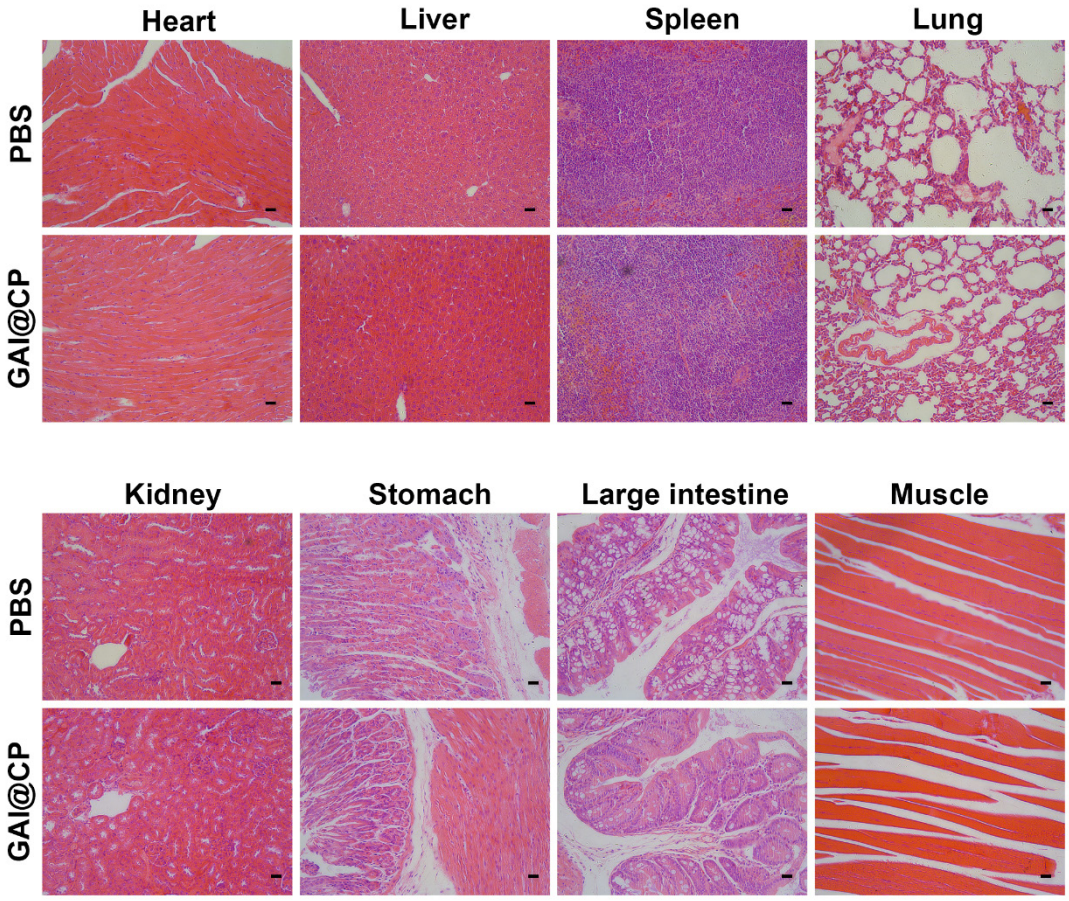

Figure S18. H&E stained tissue sections of major organs in BALB/c mice bearing HeLa subcutaneous xenograft after administration with PBS and GAI@CP for 15 d. Scale bars: 100 μm.

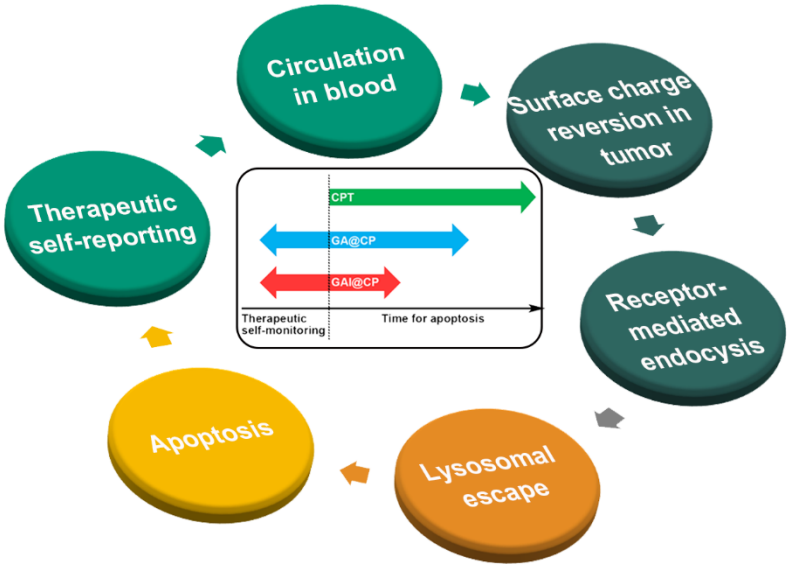

Figure S19. Schematic diagram demonstrating the programed steps of GAI@CP and its distinct advantages compared with other groups (such as CPT and GA@CP).

Table S1. The zeta potential, size determined by dynamic light scattering (DLS), polydispersity index (PDI), drug loading content (LC) and encapsulation efficiency (EE) of nanoparticles prepared with different proportions of PLGA-PEG, PLGA-PEI and DSPE-PEG-FA.

PLGA-PEG: DSPE-PEG-FA: PLGA-PEI	Zeta potential (mV)	DLS (nm)	PDI	LC (%)	LE (%)
9:1: 0	−27.55 ± 1.75	87.62 ± 4.82	0.029 ± 0.003	13.51 ± 0.04	97.61 ± 0.37
7: 1: 2	−26.17 ± 2.04	82.25 ± 4.79	0.034 ± 0.001	13.40 ± 0.02	96.72 ± 0.16
6: 1: 3	−25.20 ± 1.92	76.13 ± 5.50	0.038 ± 0.004	13.51 ± 0.15	97.61 ± 1.25
5: 1: 4	−22.59 ± 3.69	73.82 ± 4.94	0.038 ± 0.002	13.49 ± 0.01	97.43 ± 0.07
4: 1:5	−9.3 ± 1.07	71.57 ± 4.99	0.034 ± 0.001	13.31 ± 0.03	95.93 ± 0.24
3: 1: 6	+7.42 ± 1.49	71.93 ± 0.98	0.028 ± 0.006	13.47 ± 0.03	97.29 ± 0.28
0: 1: 9	+15.04 ± 3.90	59.50 ± 2.76	0.035 ± 0.003	13.66 ± 0.06	98.85 ± 0.52

Table S2. Pharmacokinetic parameters of CPT after intravenous injection of CPT and GAI@CP at a dose of 5 mg CPT per kg of mouse body weight (n = 3).

Parameter	Unit	CPT	GAI@CP
$t_{1/2Alpha}$[a)]	h	1.03	4.50
$t_{1/2Beta}$[b)]	h	7.51	36.84
AUC_{0-t}[c)]	μg h/L	364.69	930.69
MRT[d)]	h	9.67	44.07
CL[e)]	(mg/kg)/(μg/L)/h	0.012	0.003

[a)]distribution half-life time, [b)]elimination half-life, [c)]area under the curve, [d)]mean residence time, [e)]clearance.