Supporting Information

Convenient Tuning of the Elasticity of Self-assembled Nano-sized Triterpenoid to Regulate Their Biological Activities

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Table S1. Gelation time of different formulations determined by the tube-inversion method.

Ethanol content	OA concentration (wt%)	State[a]	Gel time
60%	0.025	S	-
	0.05	P	-
	0.75	P	-
	0.1	P	-
	0.15	G	4 min
	0.2	G	30 s
	0.3	G	18 s
	0.4	G	instant
50%	0.025	S	-
	0.05	P	-
	0.75	G	3 min
	0.1	G	140 s
	0.15	G	83 s
	0.2	G	5 s
	0.4	G	instant
40%	0.025	P	-
	0.05	P	-
	0.75	G	3 min
	0.1	G	3 min
	0.15	G	2 min
	0.2	G	instant
30%	0.025	P	-
	0.05	G	21 min
	0.75	G	17 min
	0.1	G	12 min
	0.15	G	10 min
	0.2	G	9 min
20%	0.025	P	-

	0.05	G	6 days
	0.75	G	5 days
	0.1	G	5 days
	0.15	G	3 days
	0.2	G	3 days
15%	0.025	P	12-24 h
	0.05	P	12 h
	0.1	P	12 h
	0.1	G	16 days
10%	0.025	P	7 days
	0.05	P	7 days
	0.1	P	6 days
5%	0.0125	P	14 days
	0.025	P	14 days
	0.05	P	11 days

[a]S: Solid; P: Partial gel; G: Gel.

Table S2. Size and PDI of different nanodrugs.

Ethanol content	OA concentration (wt%)	Diameter (nm)	Polydispersity index (PDI)
15%	0.025	288.6±10.0	0.40±0.06
	0.05	283.0±15.6	0.53±0.01
	0.1	305.1±29.3	0.48±0.02
10%	0.025	274.8±4.9	0.45±0.04
	0.05	339.0±11.3	0.55±0.12
	0.1	411.0±9.2	0.48±0.05
5%	0.025	147.0±2.4	0.34±0.04
	0.05	213.5±6.8	0.44±0.08
	0.1	223.9±5.6	0.48±0.06

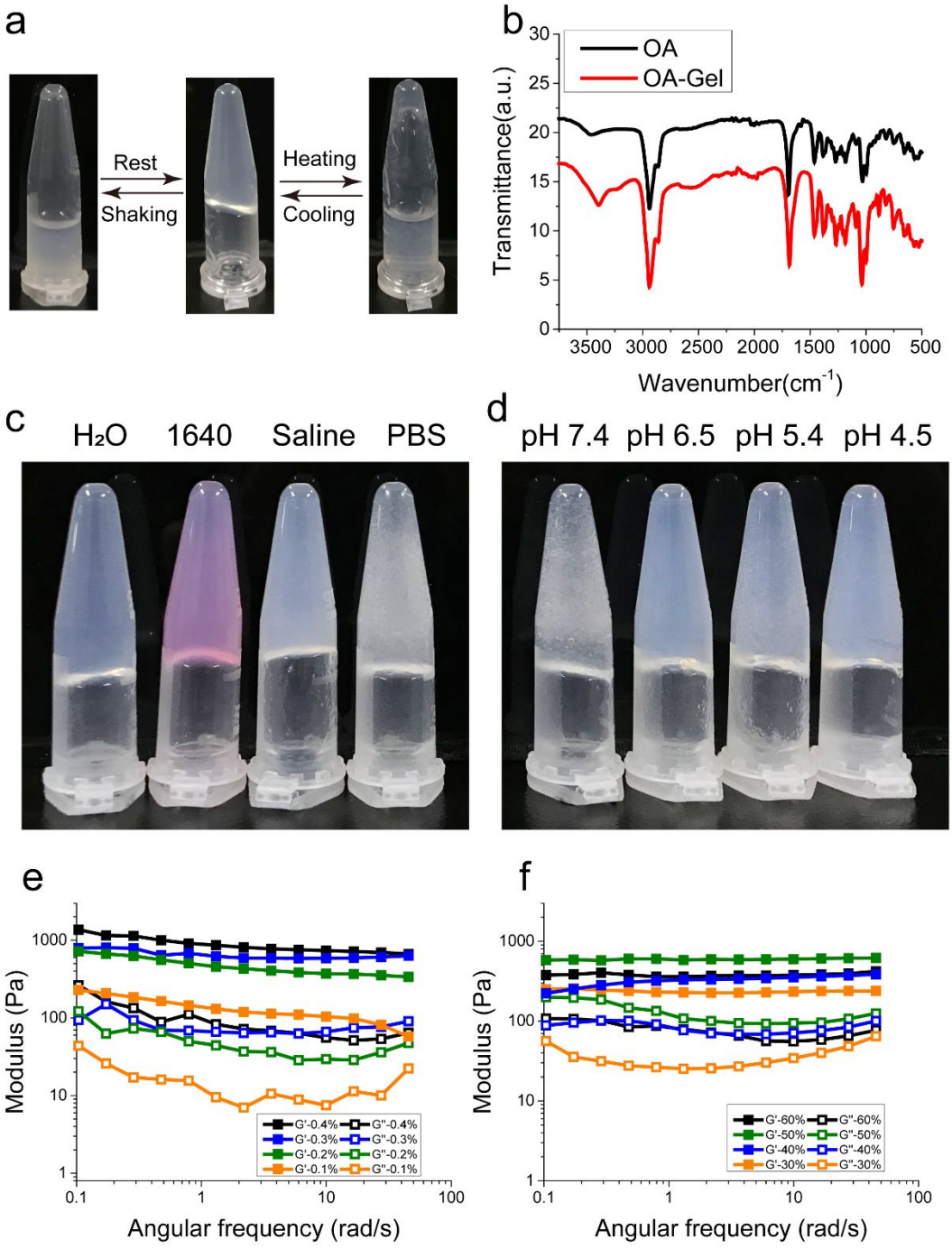

Figure S1. Characterization of OA-Gel. (a) Photographs of OA-Gel after different operation. The gel-to-sol transition temperature is 75 ℃. (b) FTIR of OA powder and OA-Gel. (c) Photographs of the OA-Gel in different ethanol/water-based medium (ethanol content: 50%). (d) Photographs of OA-Gel in PBS with different pH. (e) Storage and loss moduli of OA-Gel as functions of angular frequency at different OA concentrations. (f) Storage and loss moduli of OA-Gel as functions of angular frequency at different ethanol contents.

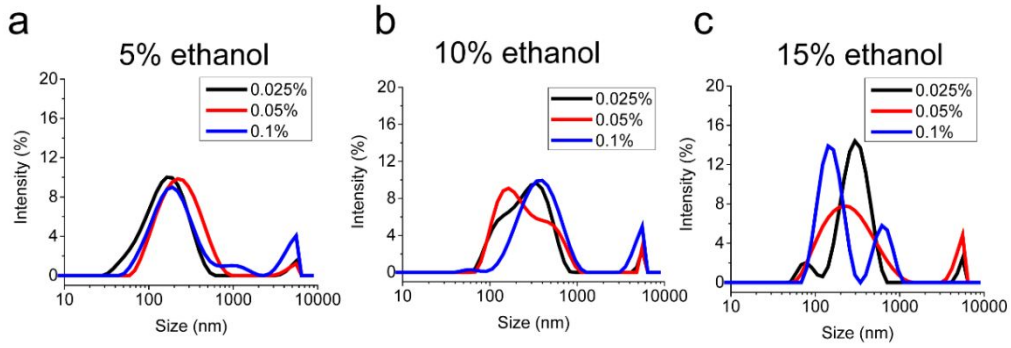

Figure S2. Size distributions of different nanodrugs with different ethanol contents.

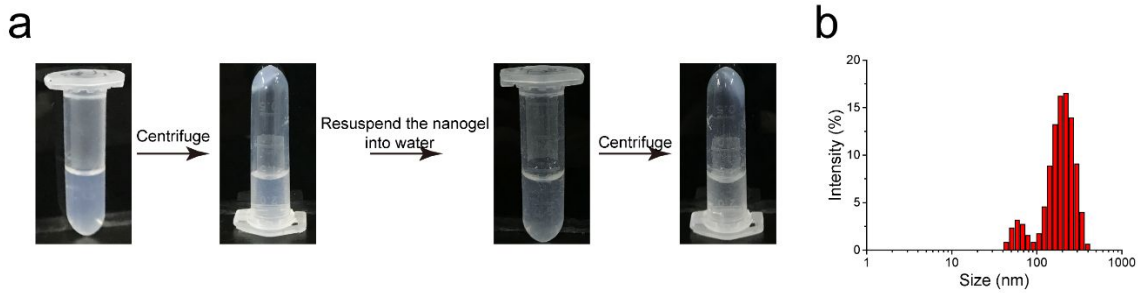

Figure S3. (a) Image of OA-NG after dilution. (b) Particle size distribution of OA-NG after dilution.

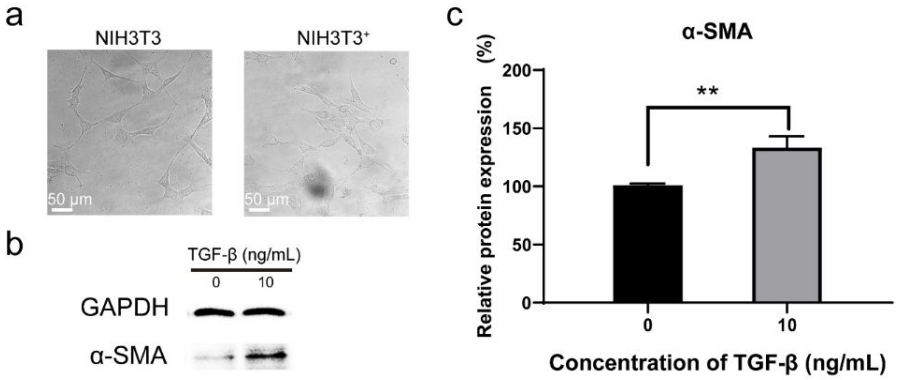

Figure S4. (a) The morphology of NIH3T3 and NIH3T3^{+} cells. (b) Western blot analysis of α-SMA in NIH3T3 cells after treatments with different TGF-β (10 ng/mL). (c) Relative protein expression of α-SMA in NIH3T3 cells analysed by Image J. **$p < 0.01$.

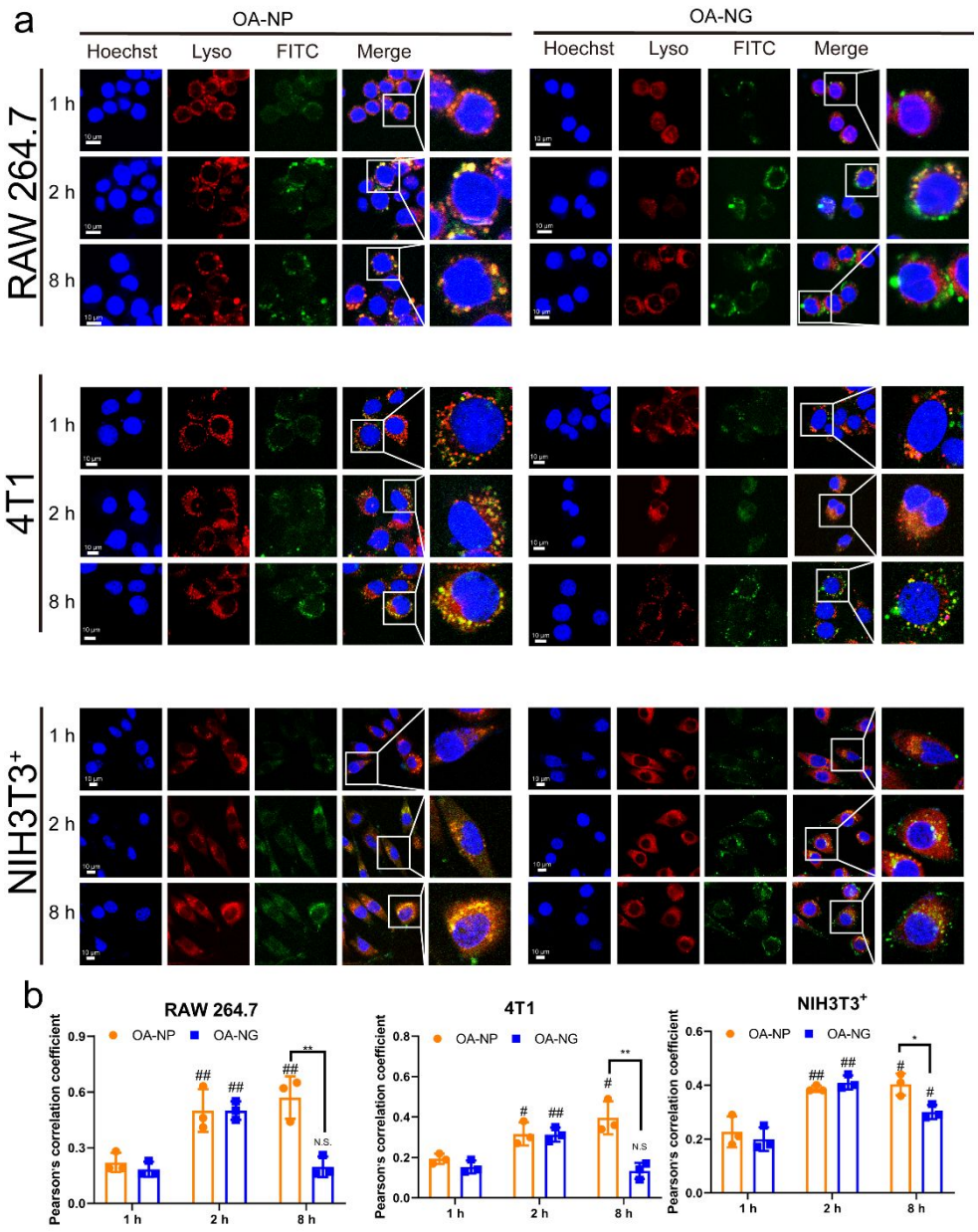

Figure S5. (a) Confocal laser scanning microscopic (CLSM) images and co-localization efficiencies (b) of RAW 264.7 cells, 4T1 cells, and NIH3T3^{+} cells after incubation with two nanodrugs for different times. Red color originates from LysoTracker Red probe. Green color originates from FITC entrapped in the nanoassemblies. The yellow color indicates co-localization of LysoTracker Red and FITC. N.S. (not significant), $^{\#}p<0.05$, $^{\#\#}p<0.01$ compared with the 1 h group. $^{*}p < 0.05$, $^{**}p < 0.01$ compared with the OA-NP group.

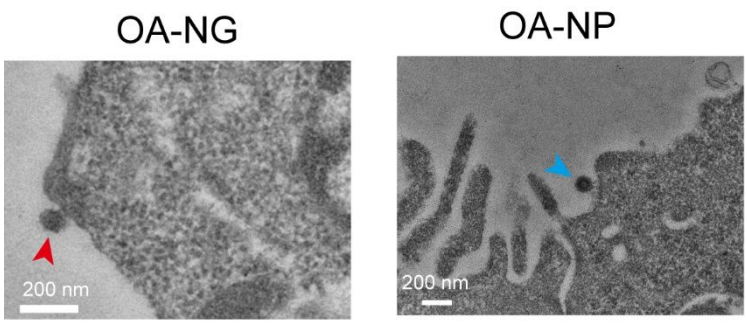

Figure S6. The morphology of OA-NG and OA-NP during the interactions with 4T1 cells observed by TEM. Red arrows: OA-NG with deformation. Blue arrows: OA-NP.

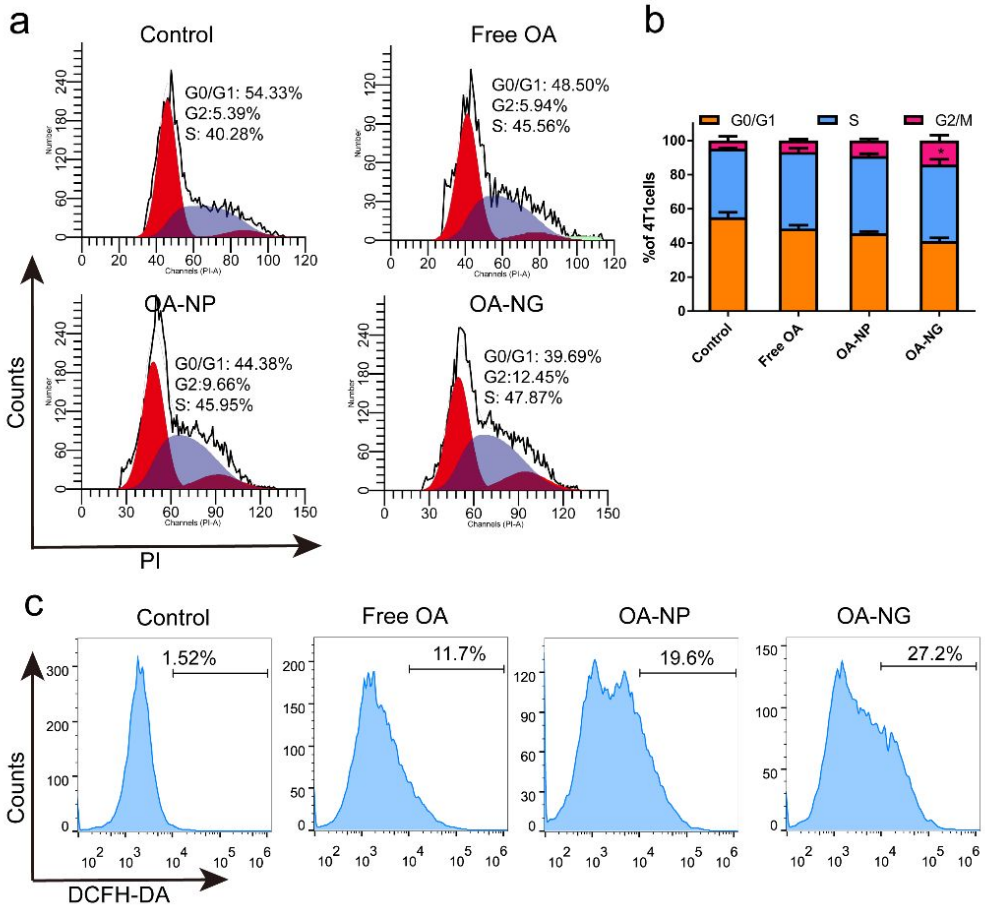

Figure S7. Anti-tumor mechanisms of OA nanoassemblies. (a) Flow cytometry analysis of the cell cycle distribution of 4T1 cells after being treated with free OA, OA-NP, and OA-NG for 24 h. (b) The proportions of G0/G1, S, and G2/M phase cells were quantitatively determined and presented. *$p < 0.05$ compared with the Control group. (c) Flow cytometry analysis of ROS generation in 4T1 cells after the treatment of free OA, OA-NP and OA-NG (50 μg/mL of OA concentration) for 24 h.

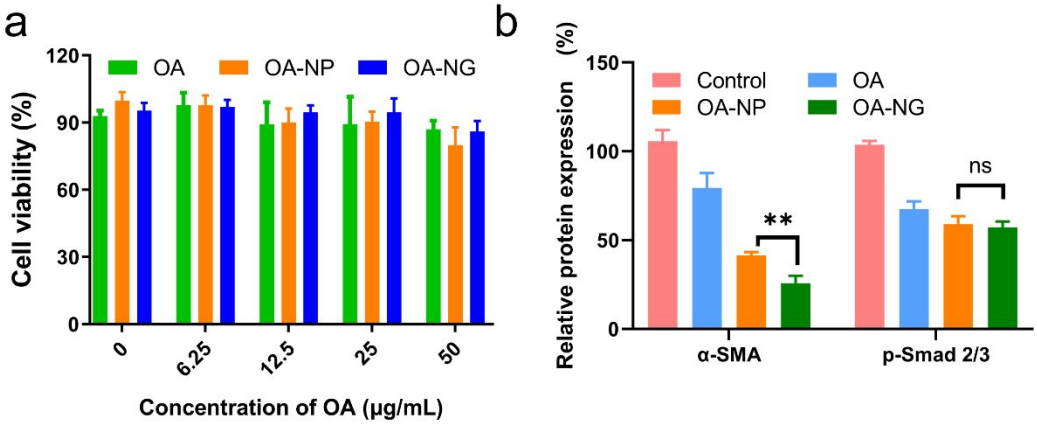

Figure S8. (a) *In vitro* cytotoxicity of free OA, OA-NP and OA-NG against NIH3T3^{+} cells. (b) Relative protein expression of α-SMA, p-Smad 2/3, and GAPDH in NIH3T3^{+} cells after different treatments analyzed by Image J. N.S. (not significant), **p < 0.01 compared with the OA-NPgroup.

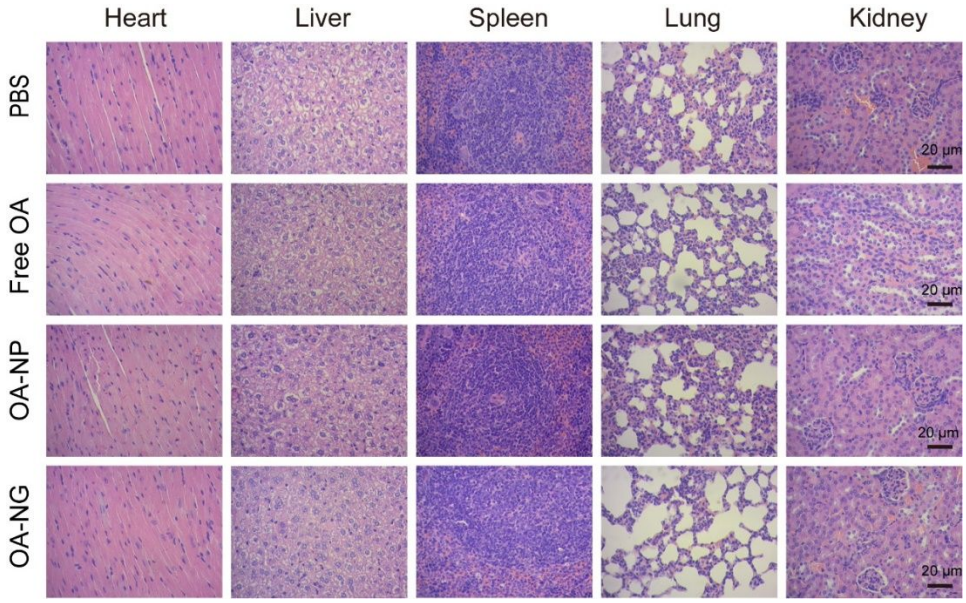

Figure S9. Hematoxyline and eosin staining assay of major organs from tumor-bearing mice after various treatments.

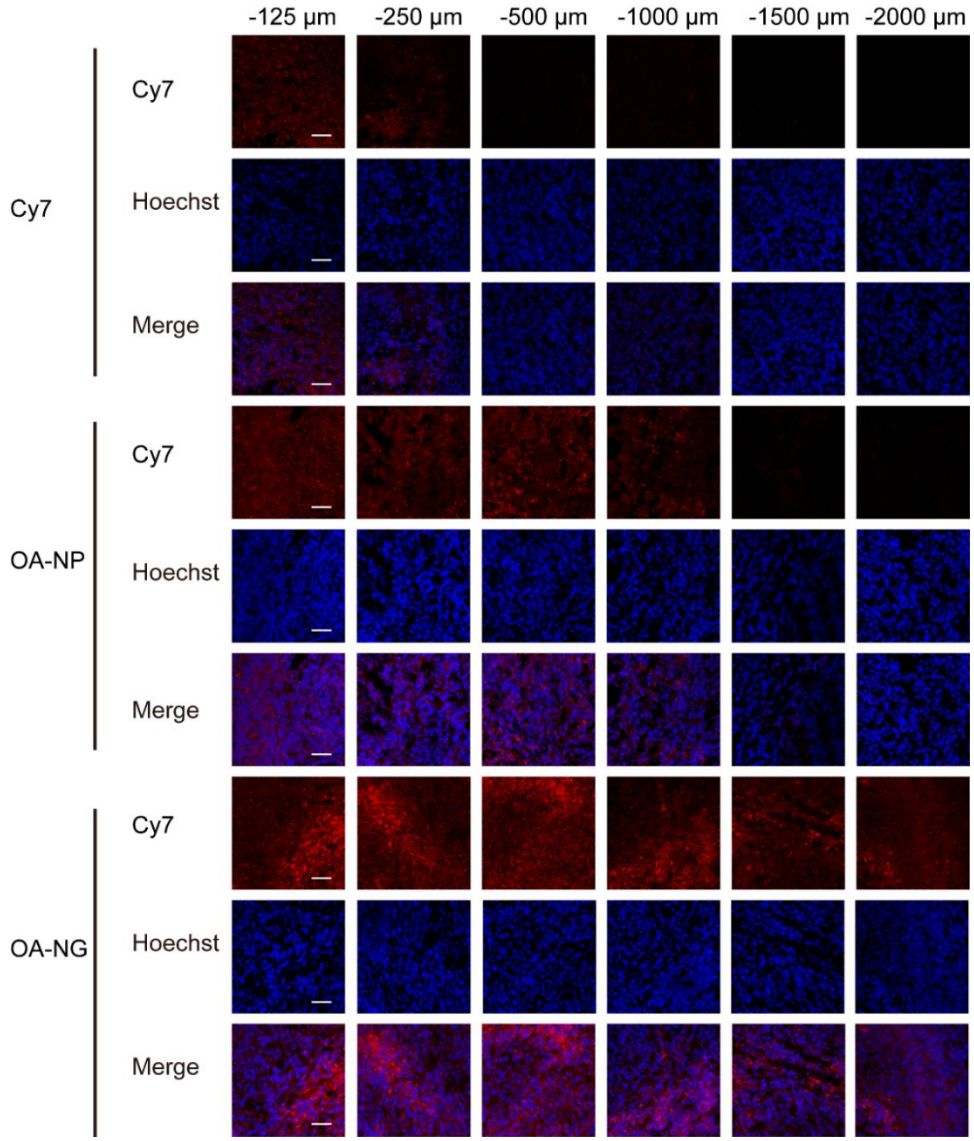

Figure S10. *In vivo* tumor penetration of Cy7, OA-NP/Cy7, and OA-NG/Cy7 with equal Cy7 concentration of 0.2 mg/kg at 24 h after intratumorally injection. The scale bars represent 50 μm.

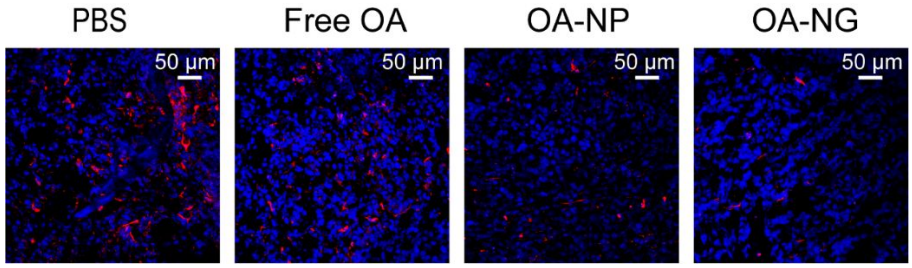

Figure S11. Immunofluorescence staining of α-SMA of tumor sections after treatment for 14 days.