Electronic Supplementary Information

pH-sensitive self-assembling nanoparticles for tumor near-infrared imaging and chemo-photodynamic combination therapy

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Figure S1. Synthetic scheme of Cis-Aconityl-DOX (CAD) and TPGS-DOX (TCAD) conjugates.



Figure S2. Characterization of the nanoprobes. (A) UV–Vis absorption of TCAD NPs, (B) UV–Vis absorption of TCAD@Ce6 NPs.



Figure S3. Size distribution of TCAD NPs measured by DLS (A), TEM (B) and SEM (C).



Figure S4. Relationship between the fluorescent intensity ratio (I3/I1) and TCAD NPs or TCAD@Ce6 NPs concentration in water. The CAC value of TCAD was about 23.4 μ g/mL.



Figure S5. The fluorescence spectrum of DOX, TCAD NPs, Ce6 and TCAD@Ce6 NPs in the PBS (pH = 7.4) and the fluorescence spectral change of TCAD@Ce6 NPs in the mild acidic PBS (pH = 5.5). $\lambda ex = 405$ nm and 480nm for PL spectrum of DOX and TCAD, $\lambda ex = 405$ nm for PL spectrum of Ce6 and TCAD@Ce6. TCAD@Ce6-0 h: fluorescence spectral of TCAD@Ce6 in PBS (pH = 7.4) and TCAD@Ce6-24 h: fluorescence spectral of TCAD@Ce6 in PBS (pH = 5.5) for 24 h.



Figure S6. Confocal images of A549 cells exposed to free DOX or TCAD NPs for 4 h and 12 h, respectively. Scale bar, 100 μm.



Figure S7. Singlet oxygen detection test using a singlet oxygen sensor green (SOSG) reagent. Timedependent fluorescence spectra (λ ex =494 nm) of the SOSG/TCAD@Ce6 NPs mixture with light irradiation at 633 nm (50 mW/cm²).



Figure S8. Flow cytometry detection of ROS generation of free Ce6 or TCAD@Ce6 NPs in the presence of DCFH-DA.



Figure S9. *In vivo* therapeutic efficacy of TCAD@Ce6 NPs. Tumor images after photodynamic therapy with free Ce6 or TCAD@Ce6 NPs in A549 tumor -bearing mice



Figure S10. H&E stained tissue sections from the heart, liver, spleen, lung, and kidney of the mouse after 18 days post-treatment of TCAD@Ce6. Scale bar, 100 μm.