

Supporting Information

Self-amplified ROS-responsive chemodrug-inhibitor conjugate for multi-drug resistance tumor therapy

Tingting Sun,^a Jie Xu,^a Tianbao Chen,^a Chunlai Tu,^a Lijuan Zhu*^b and Deyue Yan^{a, b}

a. School of Chemistry and Chemical Engineering, Frontiers Science Center for Transformative Molecules, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai, 200240, China.

b. Institute of Molecular Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, 160 Pujian Road, Shanghai, 200217, China

E-mail: lijuanzhu@sjtu.edu.cn

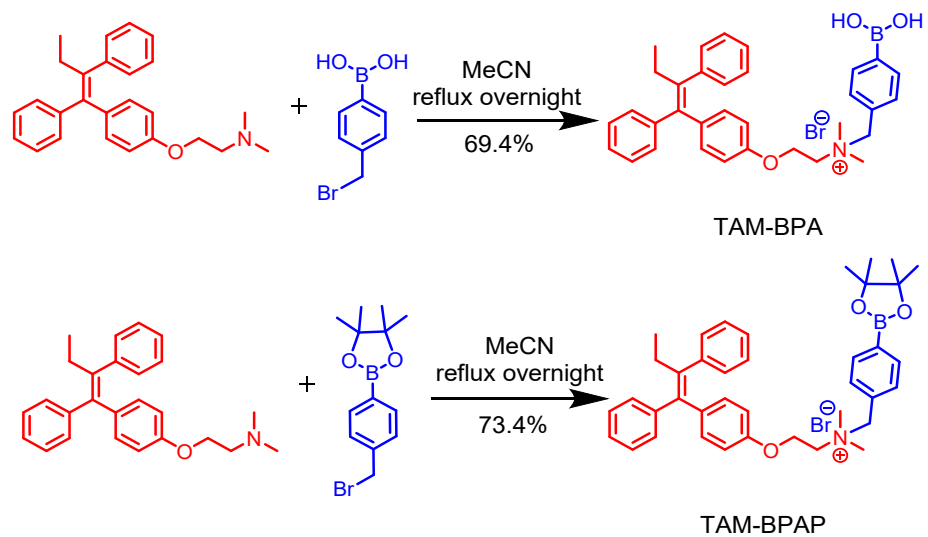


Fig. S1 Synthesis of the prodrugs: TAM-BPA and TAM-BPAP.

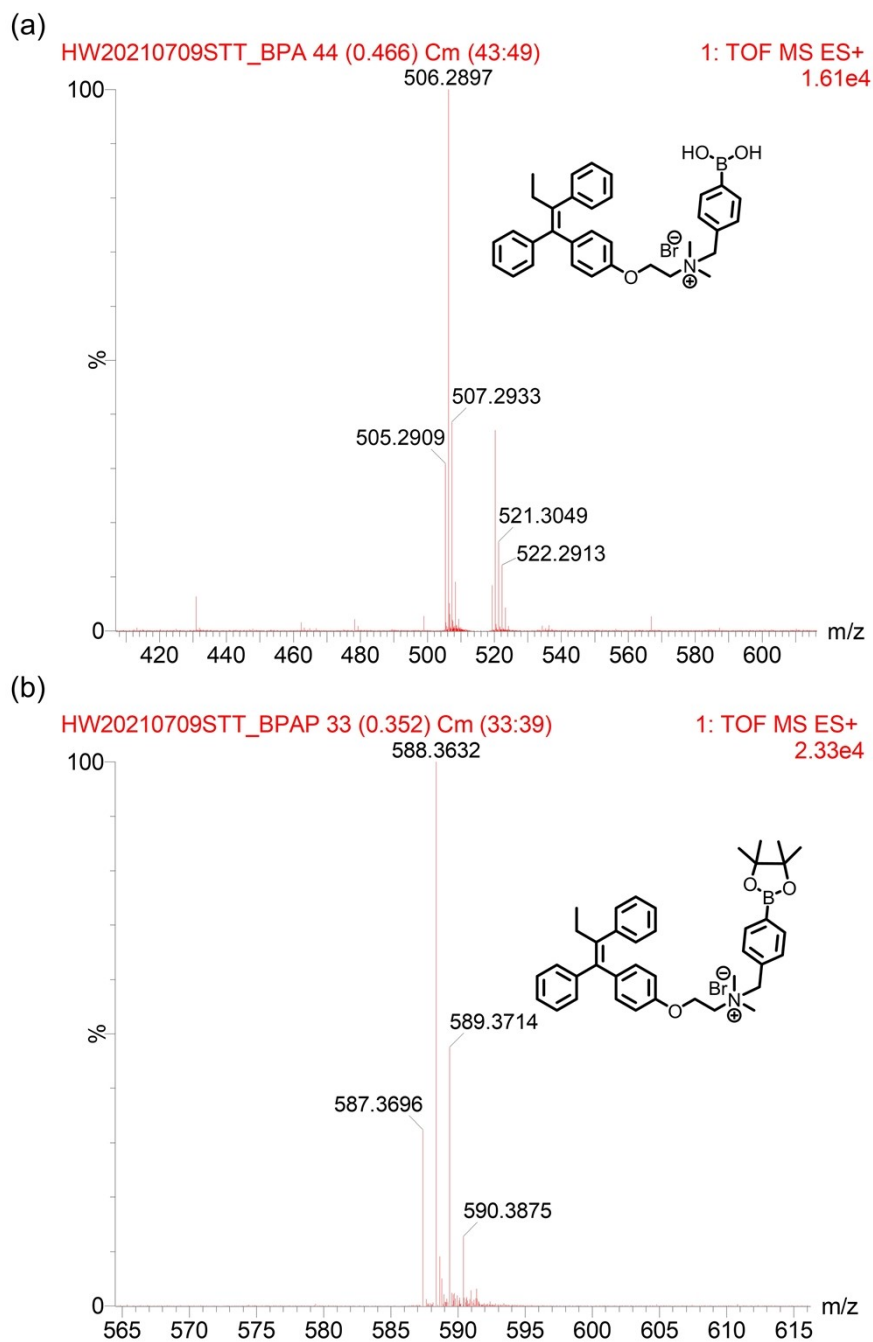


Fig. S2 (a) HRMS spectrum of TAM-BPA (calculated for $C_{33}H_{36}BNO_3$, $[M + H]^+$ m/z 506.2861, found 506.2897). (b) HRMS spectrum of TAM-BPAP (calculated for $C_{39}H_{46}BNO_3$, $[M + H]^+$ m/z 588.1929, found 588.3632).

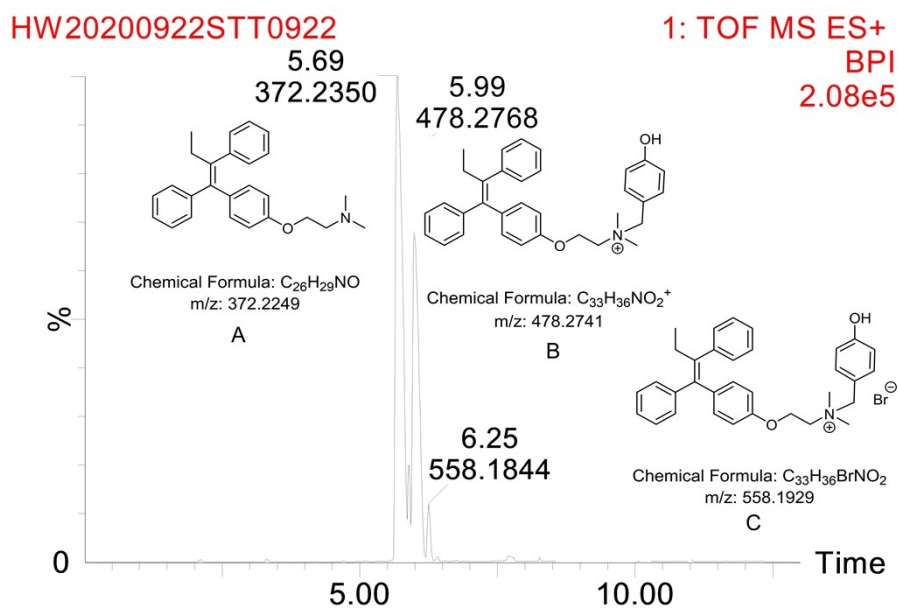


Fig. S3 LC-MS chromatogram spectrum of TAM-BPAP treated by 100 μ M H_2O_2 in methanol solution in 37°C for 12 h and its presumed intermediates.

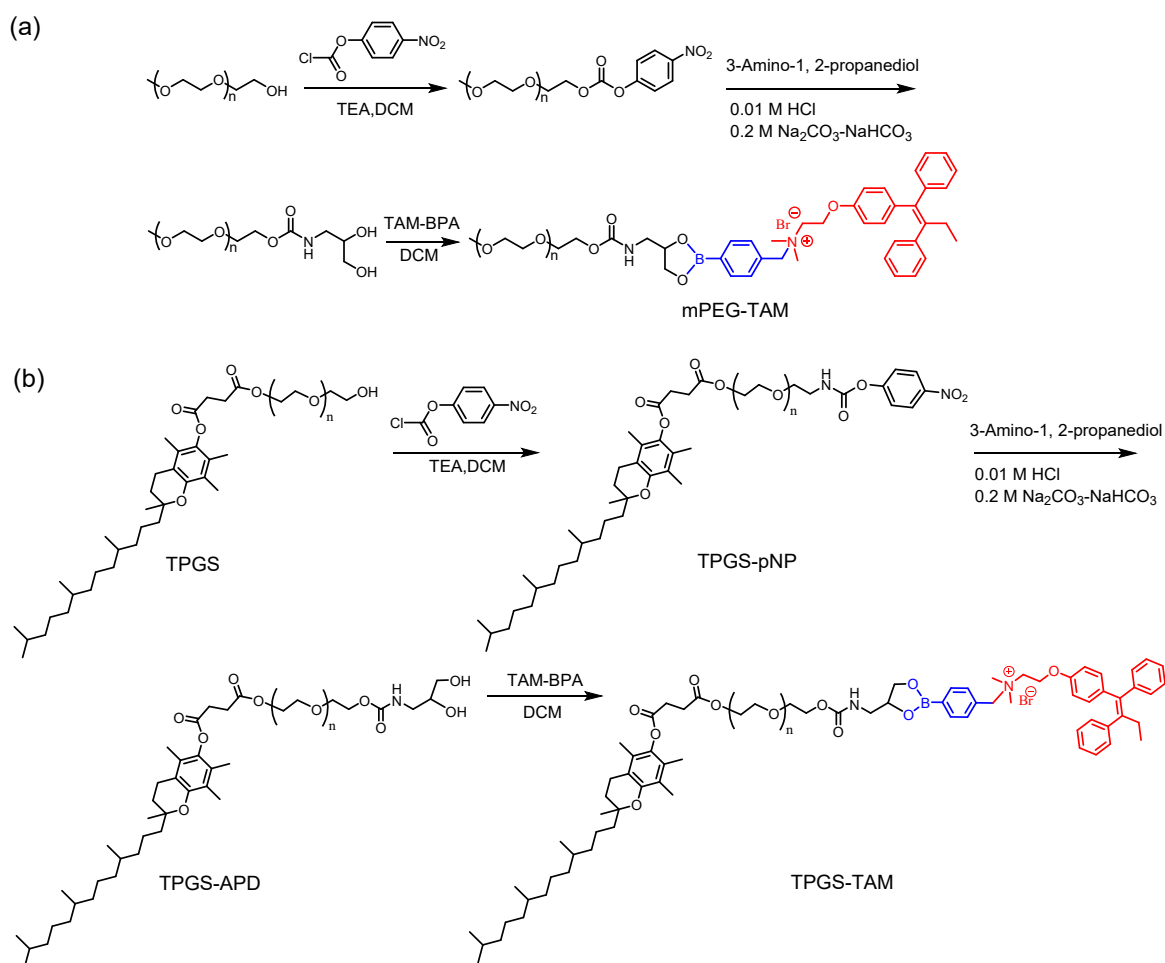


Fig. S4 The synthetic route of mPEG-TAM and TPGS-TAM conjugate.

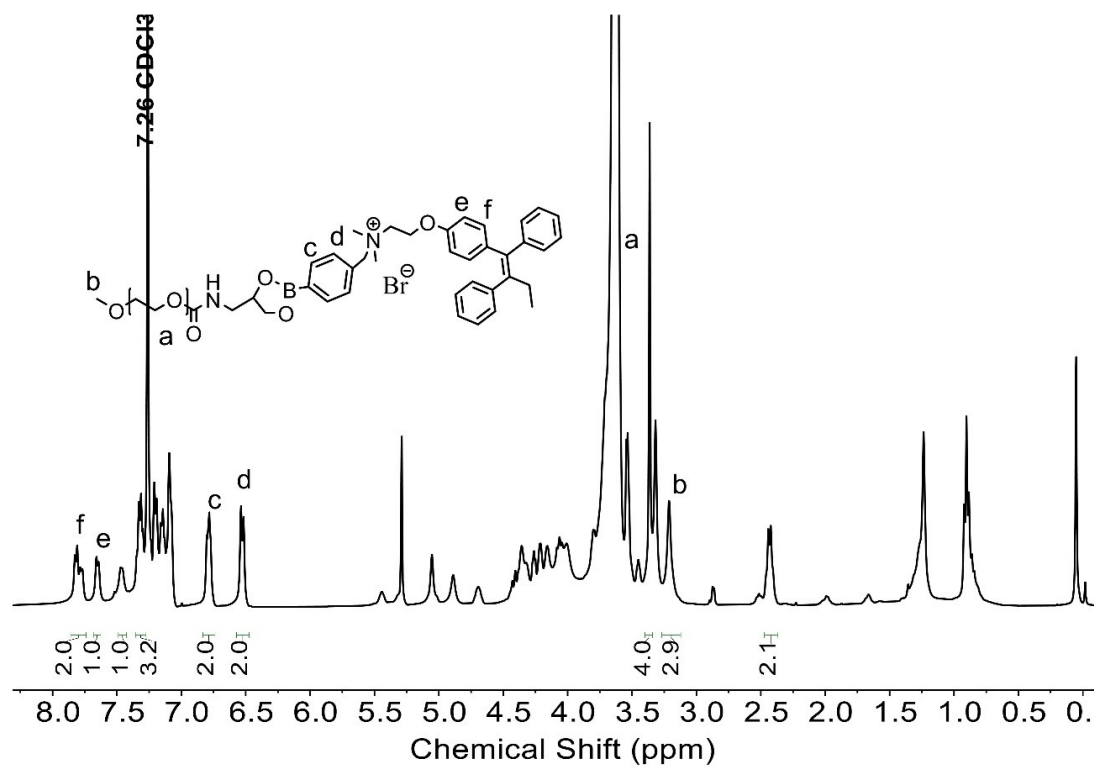


Fig. S5 ^1H NMR spectrum of mPEG-TAM in CDCl_3 .

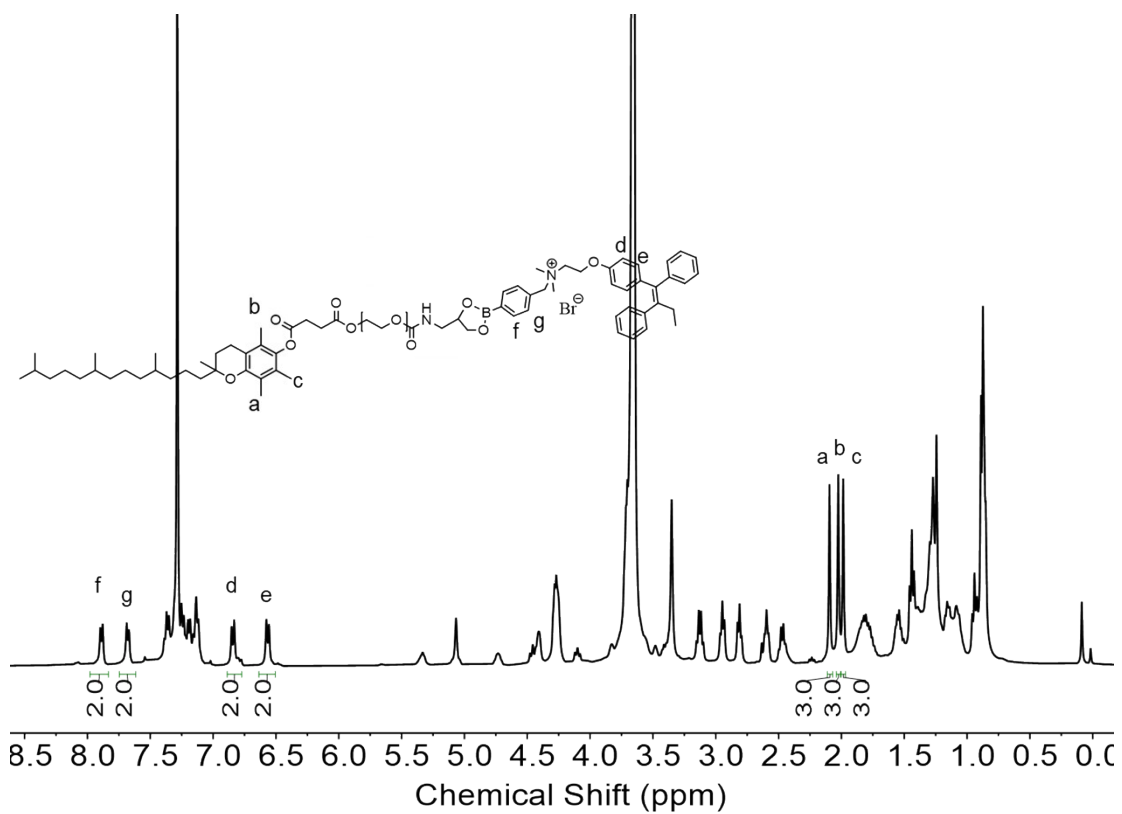


Fig. S6 ^1H NMR spectrum of TPGS-TAM in CDCl_3 .

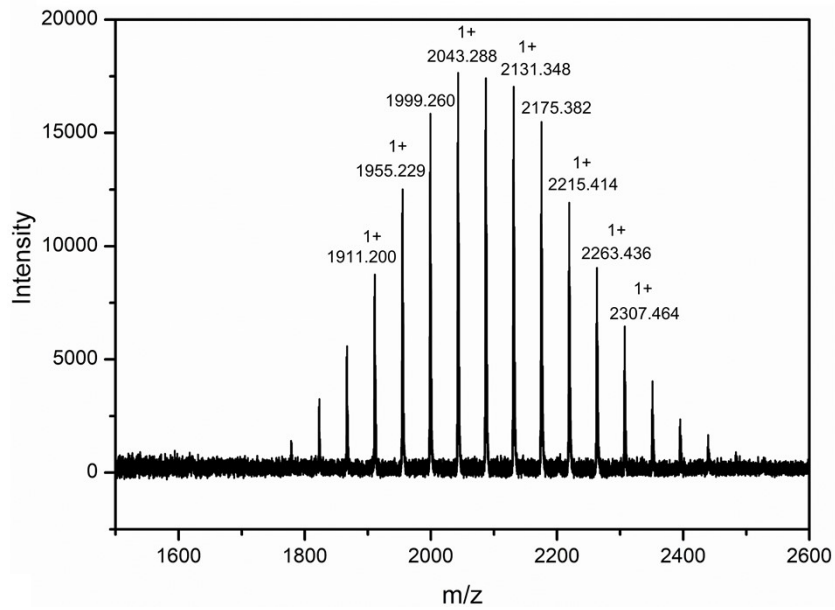


Fig. S7 MALDI-TOF spectrum of TPGS-TAM, the instrument was run in a positive ion reflection mode using a-cyano-p-hydroxycinnamic acid (CHCA) as a matrix.

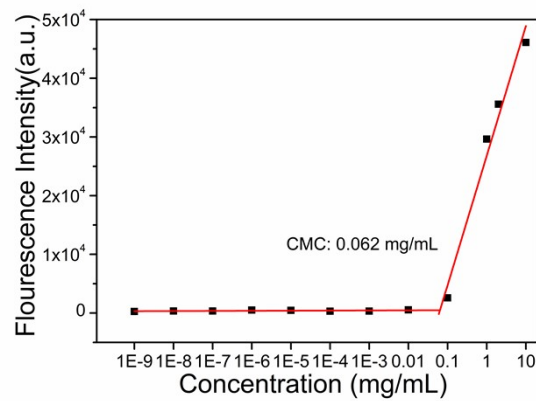


Fig. S8 The CMC values of TPGS-TAM determined by employing Nile red as a fluorescent probe.

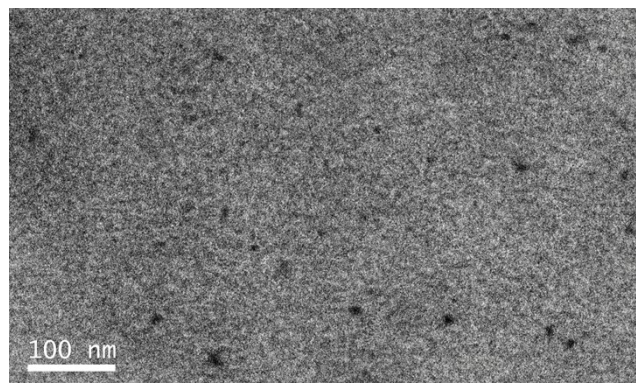


Fig. S9 TEM image of TPGS-TAM NPs treated with 100 μM H_2O_2

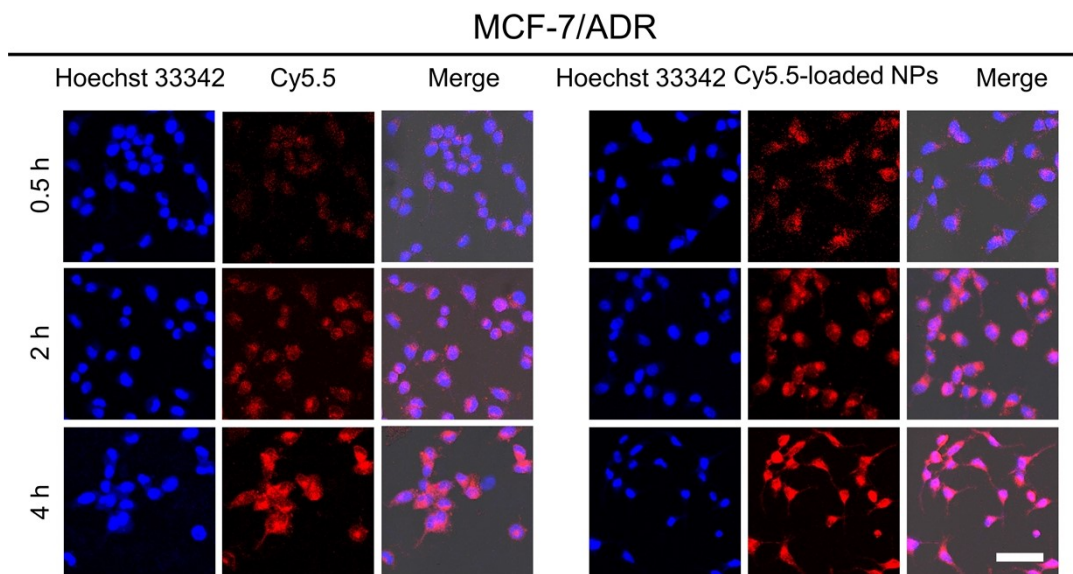


Fig. S10 CLSM images of MCF-7/ADR cells incubated with Cy5.5-loaded TPGS-TAM NPs for 0.5 h, 2 h, and 4 h respectively with a Cy5.5 concentration of 500 nM, the scale is 50 μ m.

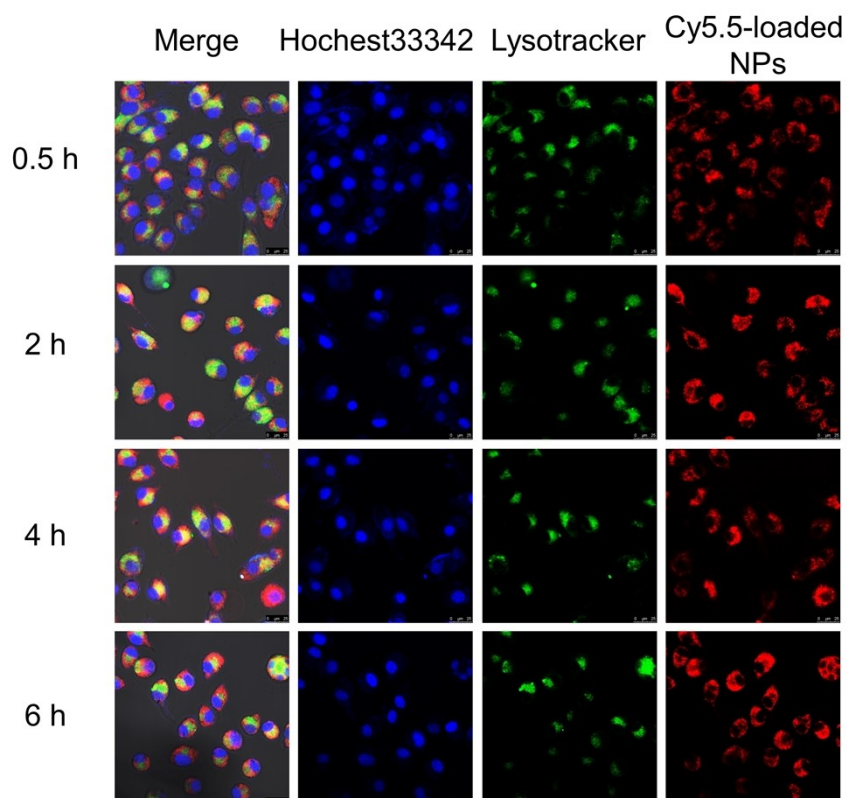


Fig. S11 CLSM images of MCF-7/ADR cells treated with Cy5.5-loaded NPs for 0.5 h, 2 h, 4 h and 6 h at 37 $^{\circ}$ C. The cell nuclei were stained with Hoechst 33342 and endo lysosomes were stained with Lysotracker Green.

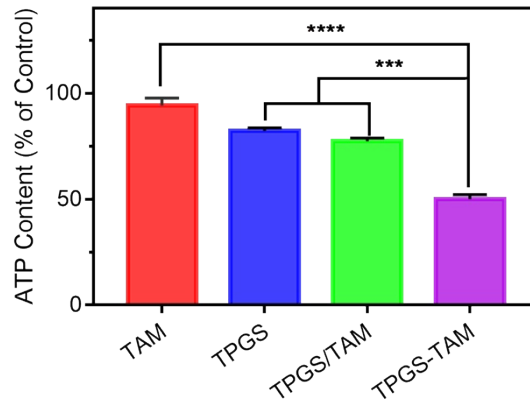


Fig. S12 Intracellular ATP level after treated with TAM, TPGS, TPGS/TAM and TPGS-TAM for 6 h in MCF-7/ADR cells. Significance is defined as *** $p < 0.001$, **** $p < 0.0001$.

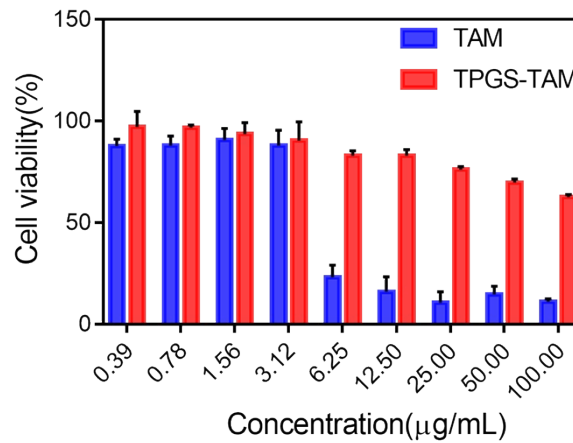


Fig. S13 Cell cytotoxicity of TPGS-TAM NPs to L929 evaluated by MTT assays with various TAM concentrations from 0.39 µg/mL to 100 µg/mL, the same amount of TAM was used as a control.



Fig. S14 Photographs of MCF-7/ADR tumor bearing mice after i.v. administration of different drugs from day1 to day 19.

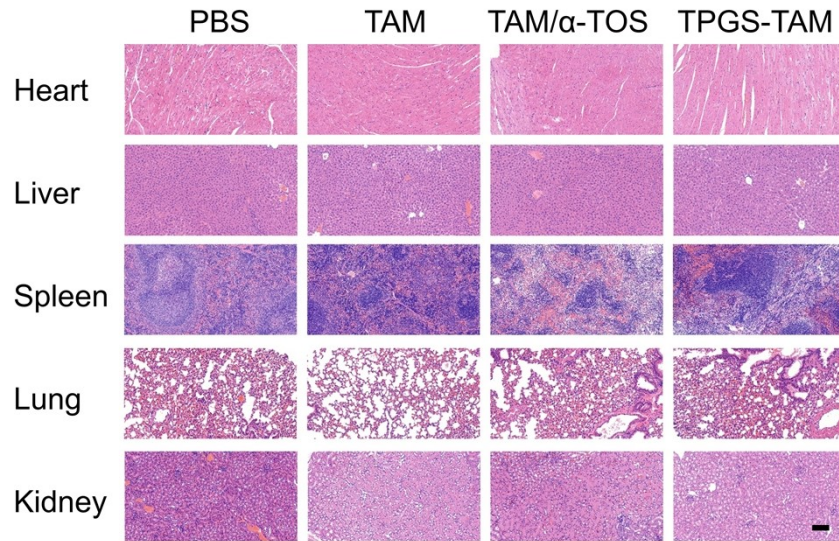


Fig. S15 H&E staining images of organs excised from MCF-7/ADR xenograft tumor bearing mice after treatment for 18 days (scale bar: 100 μ m).