

Supplementary Material

Redox dual-responsive and O₂-evolving theranostic nanosystem for highly selective chemotherapy against hypoxic tumor

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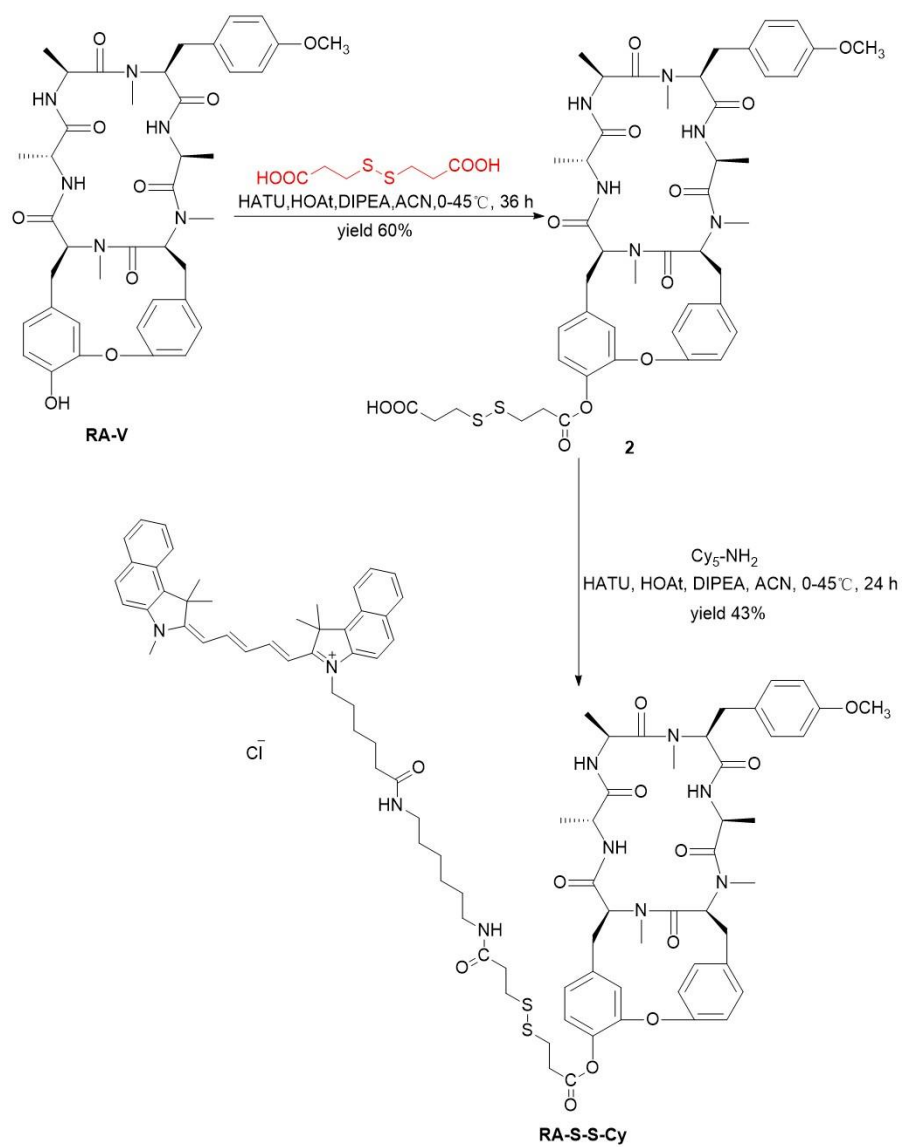
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- 10. Figure S9.** Drug released from RA-S-S-Cy (5 μM) as a function of time in the presence and absence of GSH (1 mM).
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Scheme S1. Synthesis of RA-S-S-Cy.

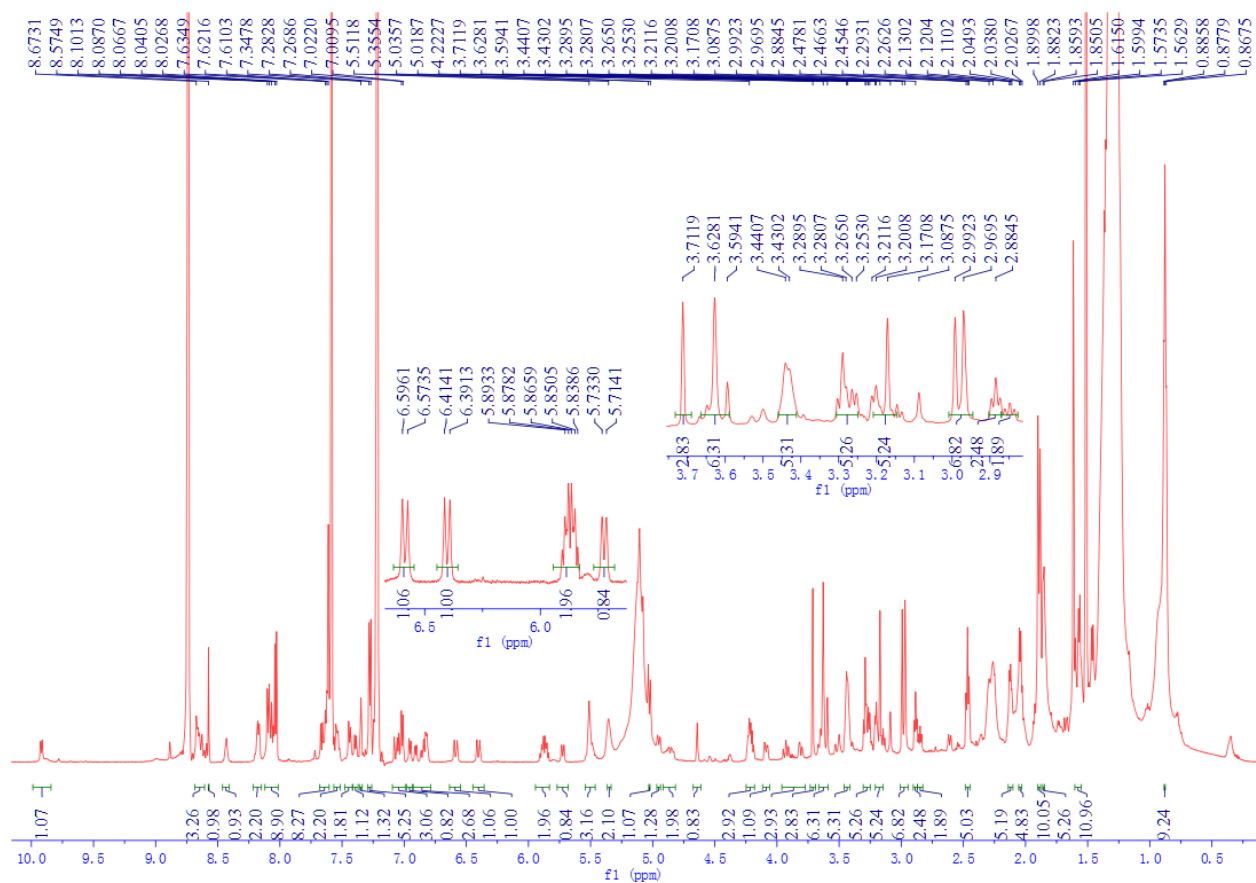


Figure S1. ^1H NMR spectrum of RA-S-S-Cy in $\text{C}_5\text{D}_5\text{N}$.

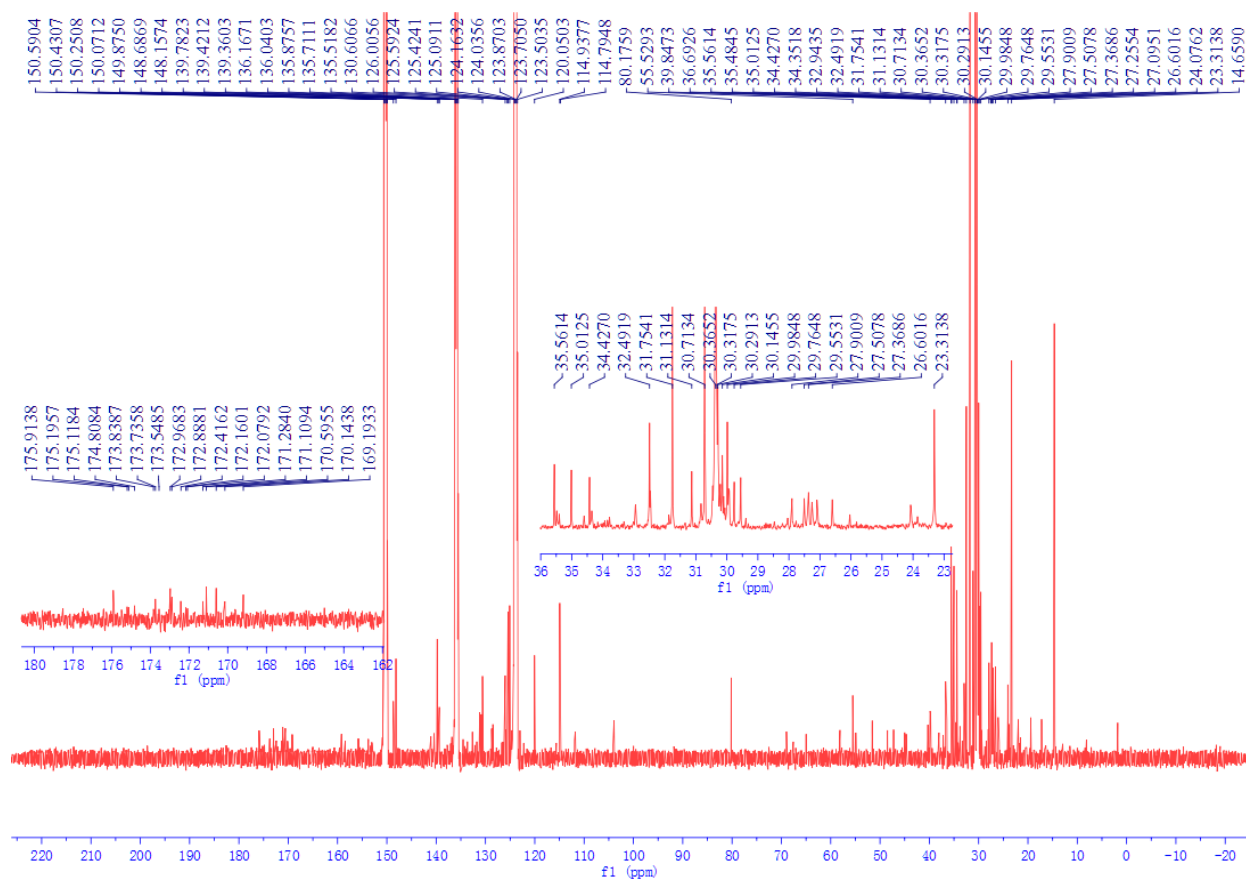


Figure S2. ^{13}C NMR spectrum of RA-S-S-Cy in $\text{C}_5\text{D}_5\text{N}$.

Qualitative Compound Report

Data File	RA-Cy.d	Sample Name	RA-Cy
Sample Type	Sample	Position	Vial 3
Instrument Name	Instrument 1	User Name	
Acq Method	method-POS1.m	Acquired Time	1/30/2018 2:16:26 PM (UTC+08:00)
IRM Calibration Status	Success	DA Method	1.m
Comment			
Sample Group			
Stream Name	LC 1	Info.	
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)	Acquisition Time (Local)	1/30/2018 2:16:26 PM (UTC+08:00)
TOF Firmware Version	17.643	TOF Driver Version	6.00.01

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	Hits (DB)
Cpd 1: C92 H111 N10 O12 S2; 0.278	0.278	1611.7806	76233	C92 H111 N10 O12 S2	1611.7824	-1.13	1

Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: C92 H111 N10 O12 S2; 0.278	806.8964	0.278	Find By Formula	1611.7806

Figure S3. HRMS spectrum of RA-S-S-Cy.

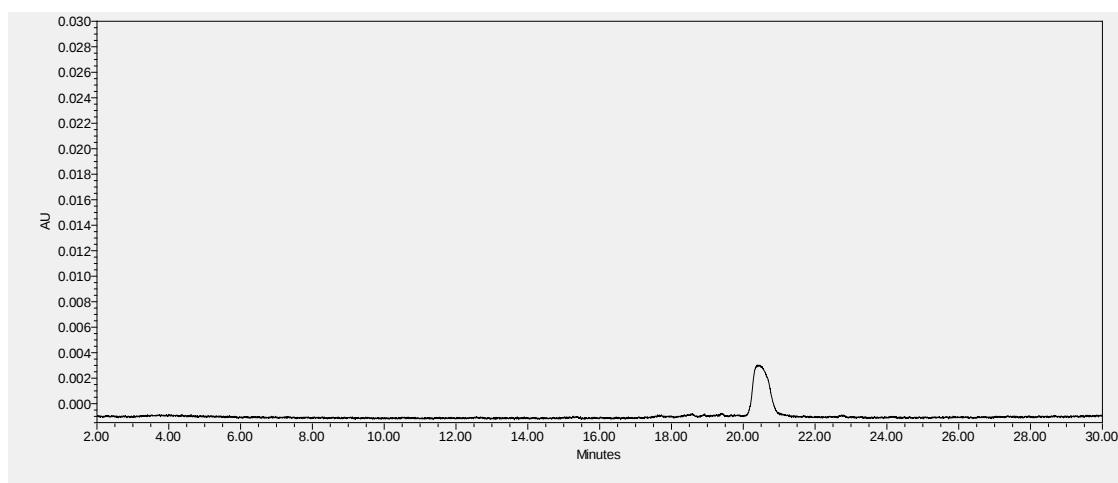


Figure S4. HPLC analysis of RA-S-S-Cy.

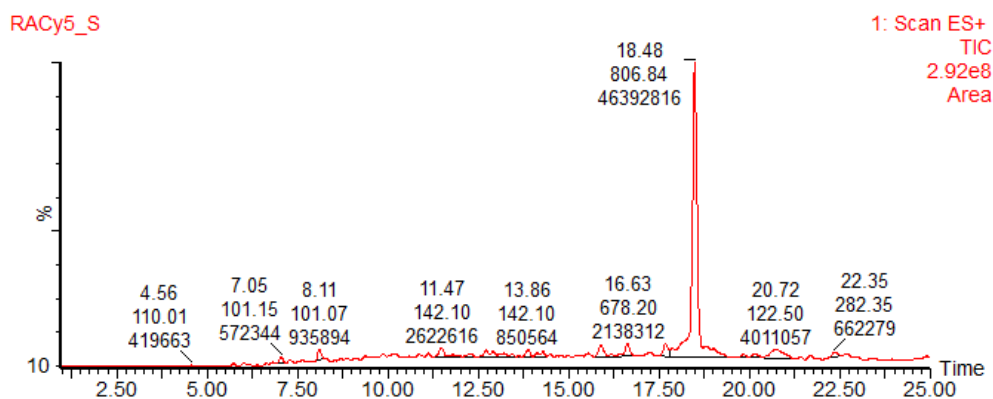


Figure S5. LCMS analysis of RA-S-S-Cy.

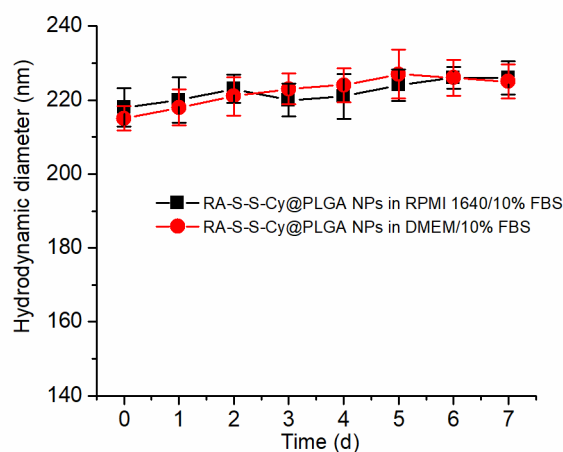


Figure S6. Long-term-stability study of the size of RA-S-S-Cy@PLGA NPs in RPMI 1640 or DMEM with 10% FBS.

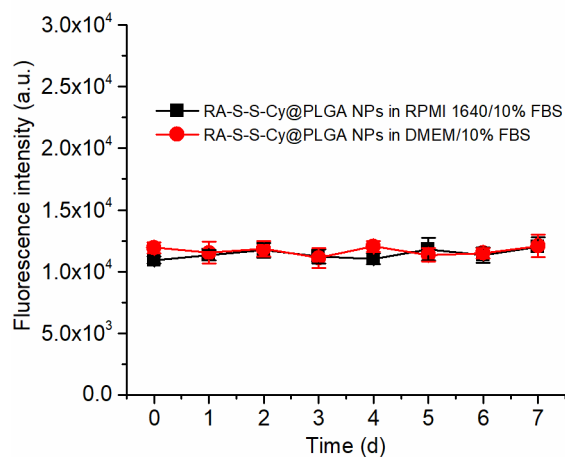


Figure S7. Long-term-stability study of the fluorescence of RA-S-S-Cy@PLGA NPs in RPMI 1640 or DMEM with 10% FBS.

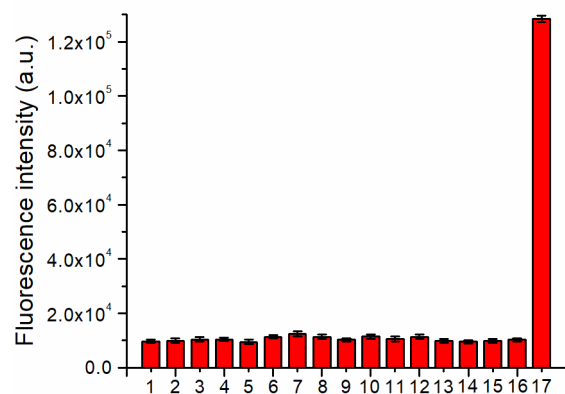


Figure S8. Specific selectivity of RA-S-S-Cy for GSH. 1, control; 2, Gln; 3, Lys; 4, Glu; 5, His; 6,

Leu; 7, Arg; 8, Gly; 9, Met; 10, DTT; 11, Hcy; 12, Cys; 13, Asp; 14, Trp; 15, Ser; 16, GSSG; and 17, GSH (1 mM). Concentration of interference: 100 mM.

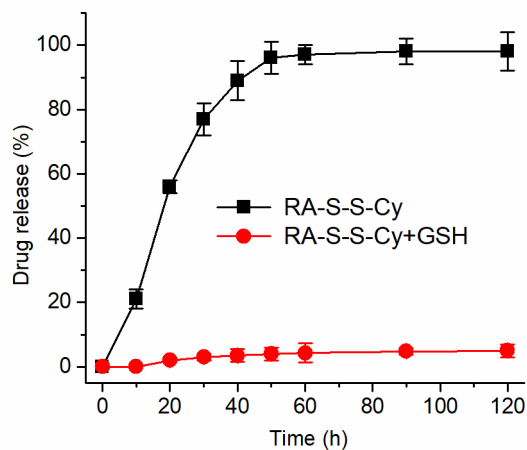


Figure S9. Drug released from RA-S-S-Cy (5 μM) as a function of time in the presence and absence of GSH (1 mM).

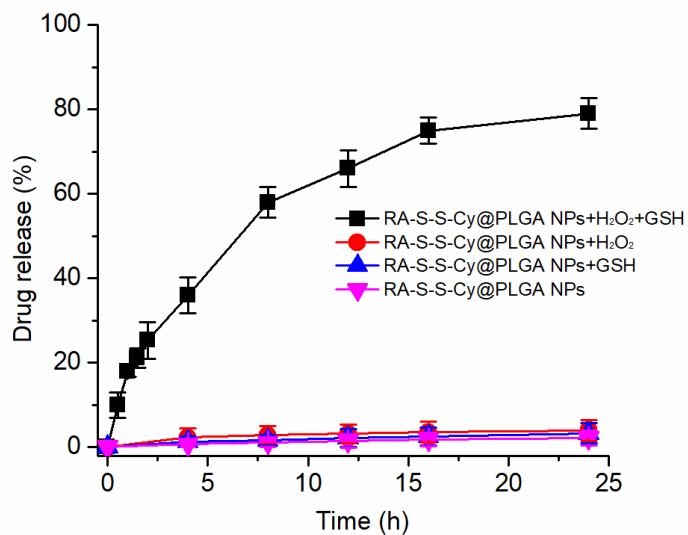


Figure S10. Drug released from RA-S-S-Cy@PLGA NPs as a function of time in the presence and absence of GSH (1 mM) and H₂O₂ (50 μM).

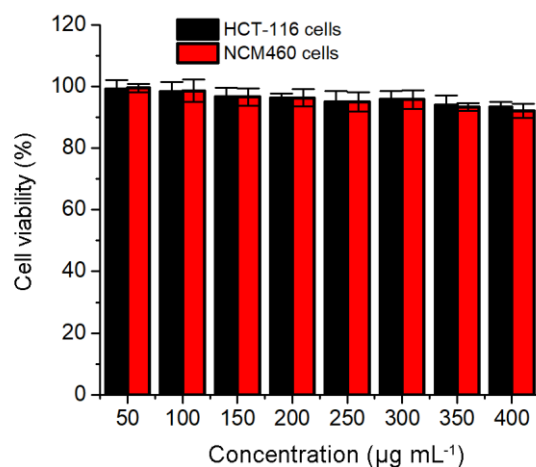


Figure S11. MTT assay of NCM460 and HCT-116 cells in the presence of different concentrations of empty NPs.

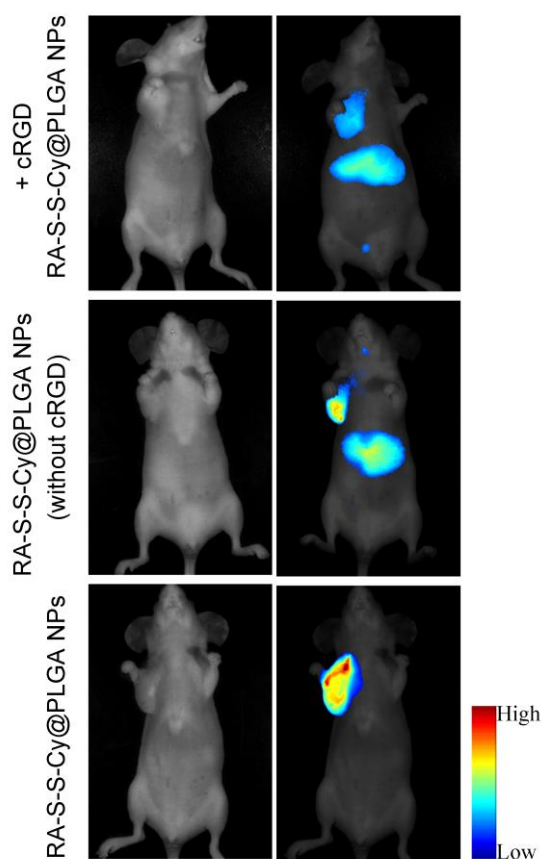


Figure S12. In vivo fluorescence images of subcutaneous HCT-116 tumor-bearing mice after i.v. injection of 10 mg kg^{-1} RA-S-S-Cy@PLGA NPs, or RA-S-S-Cy@PLGA NPs (without catalase); Mice pretreated with excessive free cRGD, followed by injection of 10 mg kg^{-1} RA-S-S-Cy@PLGA NPs. The fluorescence images were acquired using IVIS Spectrum instrument equipped with 675/30 nm excitation and 720/20 nm emission filters.

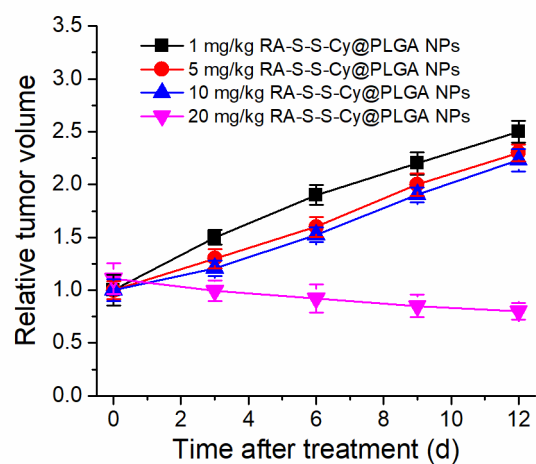


Figure S13. Change of relative tumor volume (V/V_0) upon treatments with different concentrations of RA-S-S-Cy@PLGA NPs on tumor-bearing mice.

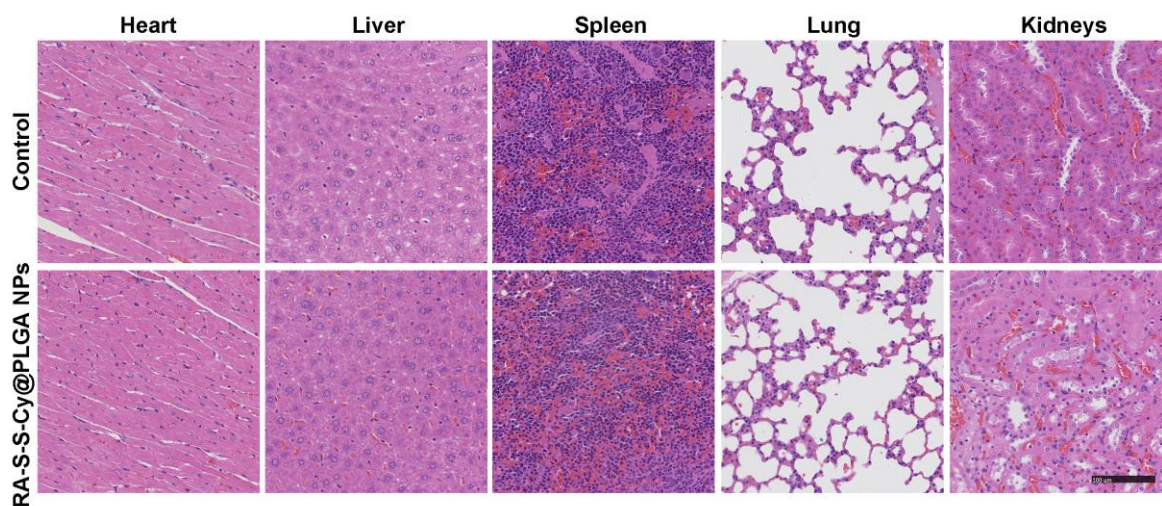


Figure S14. H&E stained images of tissue sections from different organs of mice after RA-S-S-Cy@PLGA NPs treatment and the age-matched healthy mice without treatment (control). Scale bars: 100 μ m.

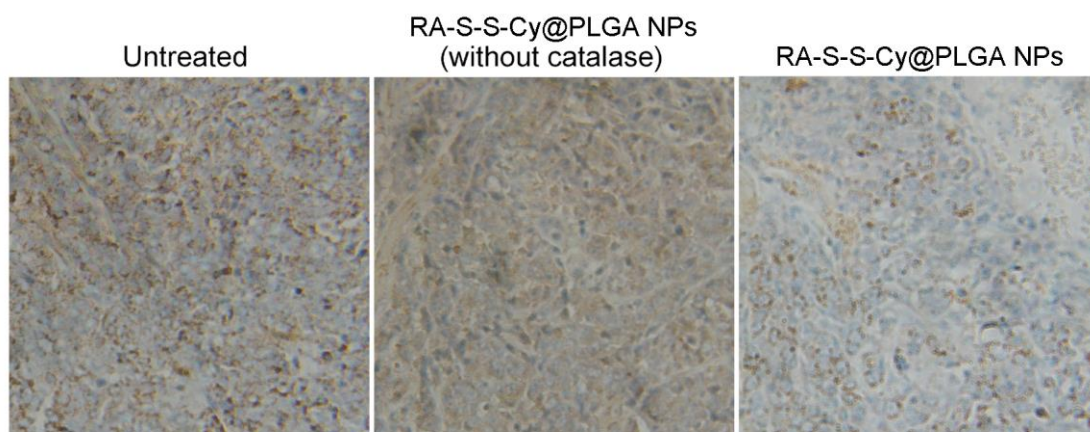


Figure S15. Immuno fluorescence staining with HIF-1 α antibodies and corresponding HIF-1 α staining of tumor slides from HCT-116 tumor-bearing mice treated with RA-S-S-Cy@PLGA NPs or RA-S-S-Cy@PLGA NPs (without catalase) at a dose of 10 mg kg⁻¹.