Supporting Information

HMCuS@MnO₂ Nanocomplex Responsive to Multiple Tumor Environmental Clues for Photoacoustic/Fluoresence/Magnetic Resonance Trimodal Imaging-Guided and Enhanced Photothermal/Photodynamic Therapy

Qian Li^{a, b, ‡}, Junjie Ren^{a, ‡}, Qiubing Chen^{a, b, ‡}, Weiwei Liu^c, Zhigang Xu^a, Yang Cao^{c, *}, Yuejun Kang^a, Peng Xue^{a, *}

^a Institute for Clean Energy and Advanced Materials, School of Materials and Energy, Southwest University, Chongqing 400715, China.

^b Medical Research Institute, Wuhan University, Wuhan, Hubei 430071, China.

^c Chongqing Key Laboratory of Ultrasound Molecular Imaging, Institute of Ultrasound Imaging, Second Affiliated Hospital, Chongqing Medical University, Chongqing 400010, China.

[‡]These authors contributed equally to this work.

*Corresponding authors: <u>xuepeng@swu.edu.cn (P. Xue)</u>, <u>yangcao@cqmu.edu.cn</u> (Y. Cao)



Fig. S1 (a) A typical TEM image of HMCuS NP; (b) linear scanning results of the cross-section of individual HMCuS NP through EDS analysis.



Fig. S2 Core level XPS spectra of (a) Cu and (b) S in HMCuS NPs, as well as (c) Cu, (d) S and (e) Mn in CMC NPs.



Fig. S3 Hydrodynamic size of CMC NPs being incubated in PBS or DMEM (with 10% FBS) for 7 days.



Fig. S4 (a) Pore diameter distribution and (b) N_2 adsorption-desorption isotherm of HMCuS NPs; (c) pore diameter distribution and (d) N_2 adsorption-desorption isotherm of CMC NPs.



Fig. S5 (a) UV-vis-NIR absorption spectra of CMC NPs (equivalent Ce6 concentration: 10 μ g·mL⁻¹) containing DPBF exposed to a 660 nm laser (1 W·cm⁻²) for different periods; (b) decay of the normalized peak absorbance intensity of Ce6 and CMC NPs (equivalent Ce6 concentration: 10 μ g·mL⁻¹) at 417 nm over 5 min.



Fig. S6 Confocal images of 4T1 cells after being treated by CMC NPs (equivalent Ce6 concentration: $10 \ \mu g \cdot mL^{-1}$) for 1, 2, 4 and 6 h (scale bar: $20 \ \mu m$).



Fig. S7 Tumor to normal (TNR) ratio after intravenous injection of CMC NPs corresponding to Figure 6j.



Fig. S8 H&E stained tumor slices excised from major organs after the mice receiving various treatments (scale bar: $200 \ \mu$ m).



Fig. S9 Hemolysis rate by incubating RBCs with DI water (positive control), PBS (negative control) or CMC NPs under various concentrations. (Inset: corresponding digital photos of centrifuge tube containing different samples).



Fig. S10 Primary indicators of blood routine test after KM mice being injected with CMC NPs. The pink hatched areas represent the reference ranges of hematology index of healthy mice.