

## Albumin-templated Biomineralizing Growth of Composite Nanoparticles as Smart Nanotheranostics for Enhanced Radiotherapy of Tumors

Jiawen Chen<sup>1</sup>, Qian Chen<sup>1\*</sup>, Chao Liang<sup>1</sup>, Zhijuan Yang<sup>1</sup>, Lin Zhang<sup>3</sup>, Xuan Yi<sup>2</sup>, Ziliang Dong<sup>1</sup>, Yu Chao<sup>1</sup>, Youguo Chen<sup>3\*</sup> and Zhuang Liu<sup>1\*</sup>

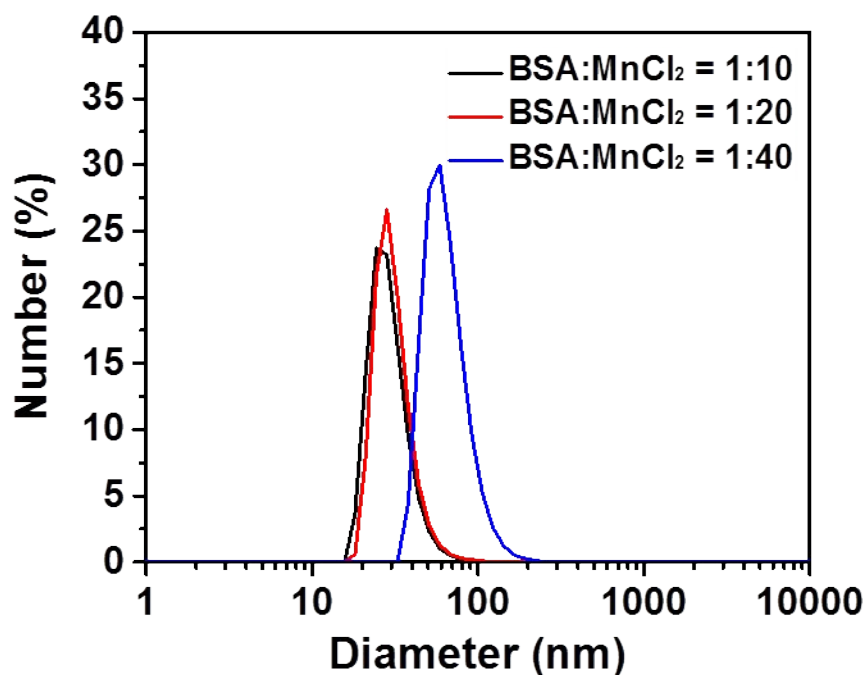
1, Institute of Functional Nano & Soft Materials (FUNSOM), Collaborative Innovation Center of Suzhou Nano Science and Technology, Jiangsu Key Laboratory for Carbon-based Functional Materials and Devices, Soochow University, Suzhou, Jiangsu, 215123, China

2, School of Radiation Medicine and Protection & School for Radiological and Interdisciplinary Sciences (RAD-X), Collaborative Innovation Center of Radiation Medicine of Jiangsu Higher Education Institutions, Soochow University, Suzhou 215123, China

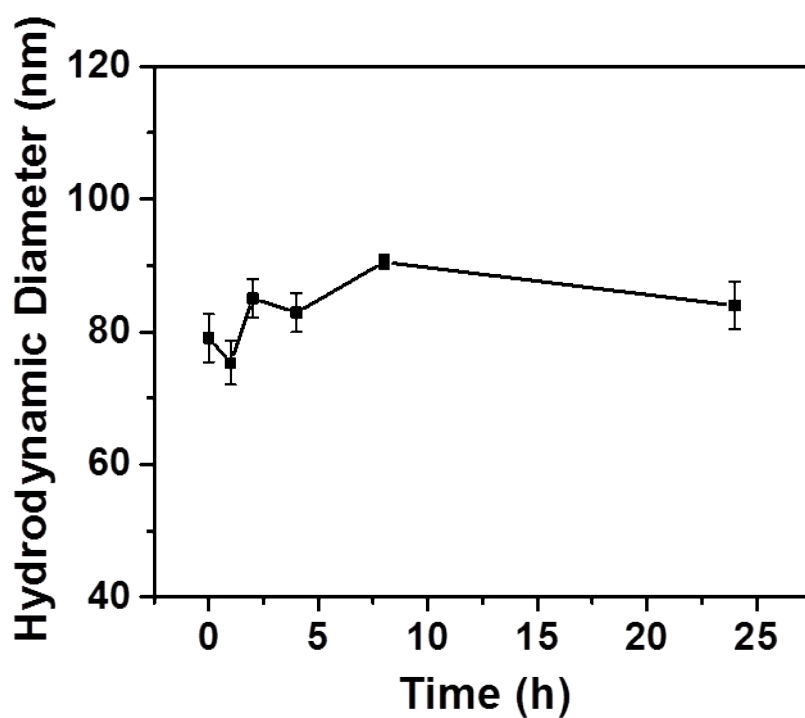
3, Department of Obstetrics and Gynecology, The First Affiliated Hospital of Soochow University, Suzhou 215006, China

\* Email: [zliu@suda.edu.cn](mailto:zliu@suda.edu.cn), [chenqiansuda@163.com](mailto:chenqiansuda@163.com), [chenyouguo@suda.edu.cn](mailto:chenyouguo@suda.edu.cn).

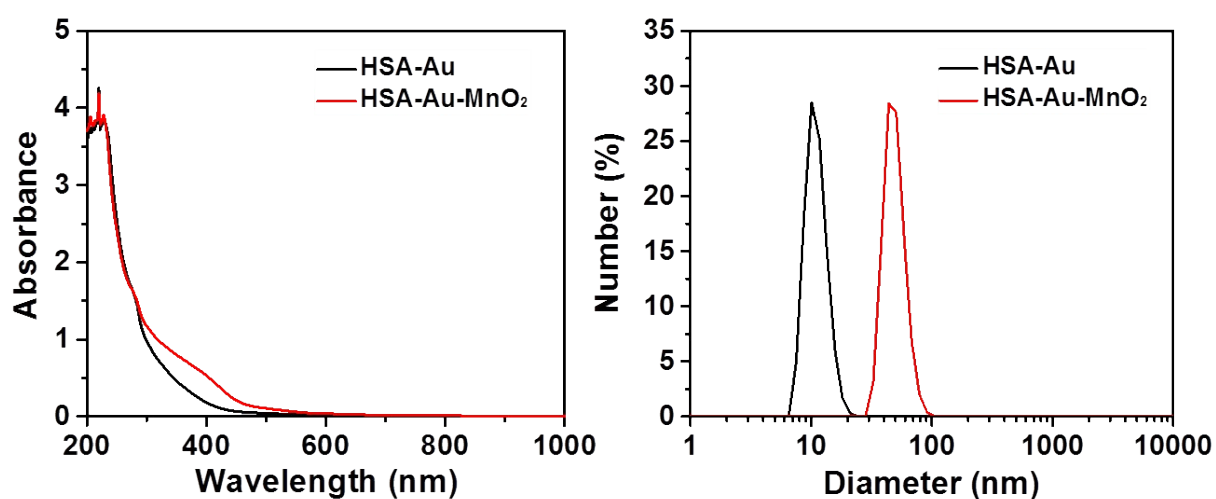
### Supporting Figures



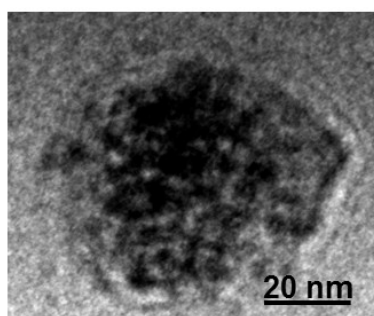
**Supporting Figure S1.** The hydrodynamic diameters of BSA-Au-MnO<sub>2</sub> prepared with different BSA : MnCl<sub>2</sub> feeding molar ratios (1:10, 1:20, 1:40).



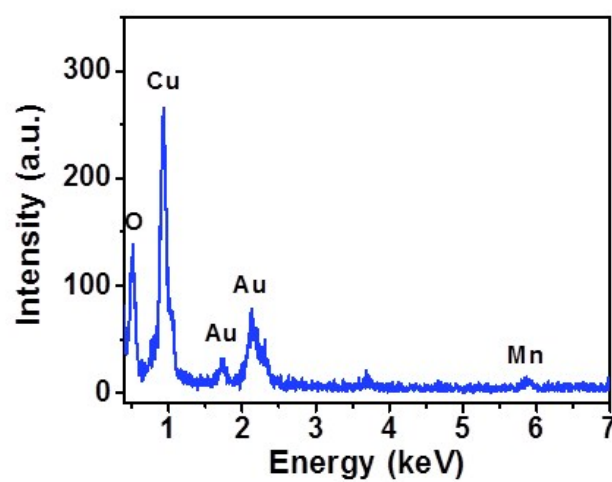
**Supporting Figure S2.** Hydrodynamic diameter change of BSA-Au-MnO<sub>2</sub> nanoparticles in FBS within 24 h.



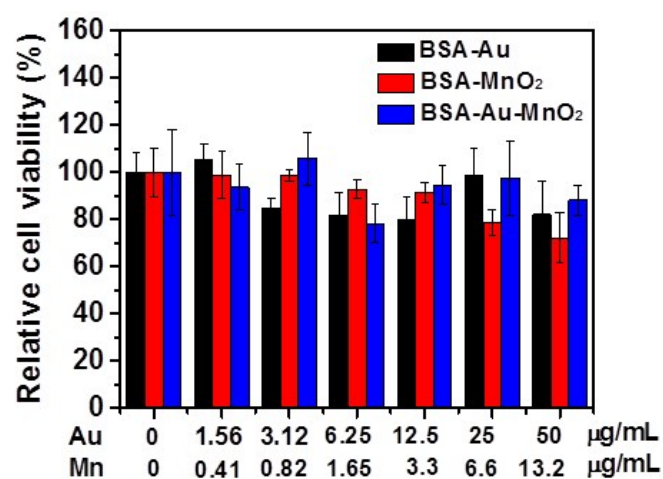
**Supporting Figure S3.** UV-vis-NIR spectra and hydrodynamic diameters of HSA-Au and HSA-Au-MnO<sub>2</sub> nanoparticles.



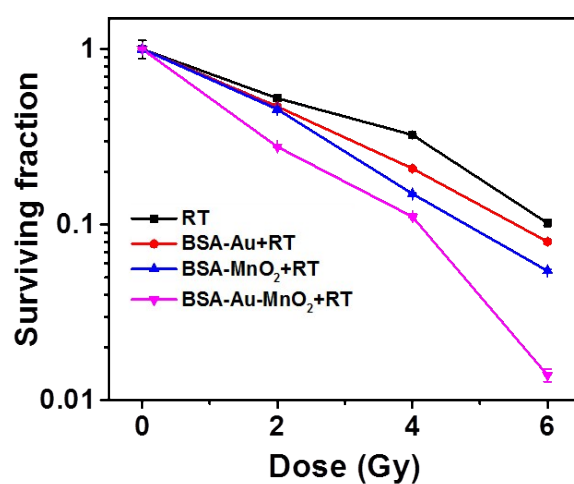
**Supporting Figure S4.** Magnified TEM image of BSA-Au-MnO<sub>2</sub>.



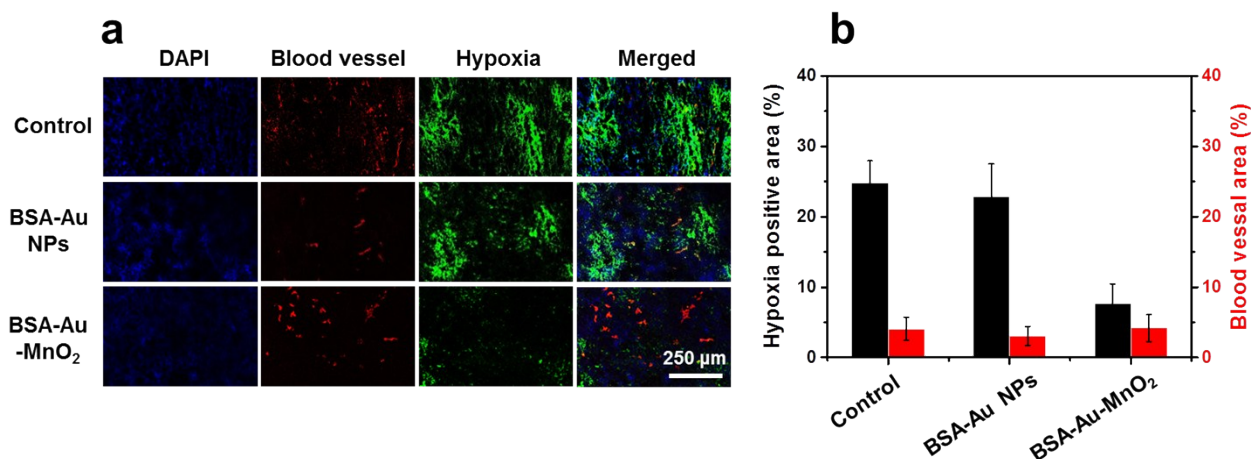
**Supporting Figure S5.** Energy-dispersive X-ray spectroscopy (EDX) spectrum of BSA-Au-MnO<sub>2</sub>.



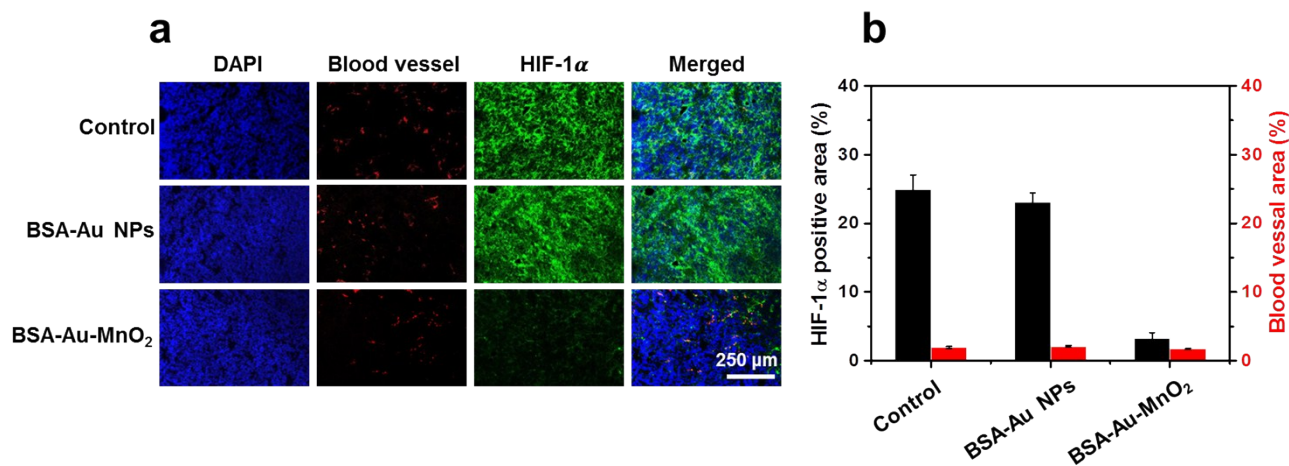
**Supporting Figure S6.** The relative viabilities of 4T1 cells incubated with various concentrations of BSA-Au, BSA-MnO<sub>2</sub> or BSA-Au-MnO<sub>2</sub> for 24 h.



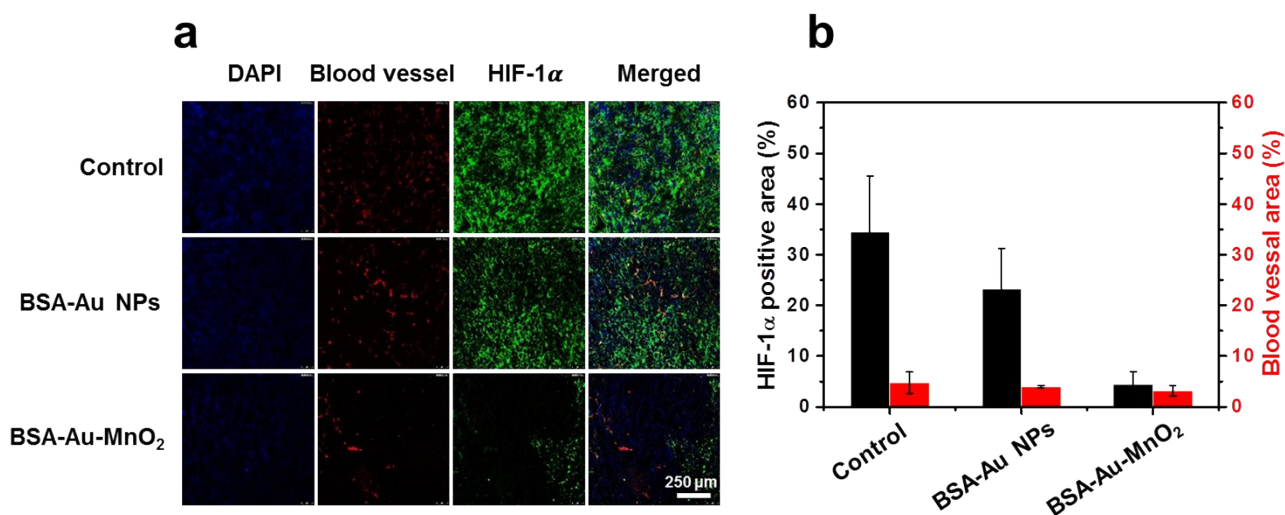
**Supporting Figure S7.** Clonogenic survival assay of NIH 3T3 cells treated with BSA-Au, BSA-MnO<sub>2</sub> or BSA-Au-MnO<sub>2</sub> under different radiation doses at 0, 2, 4, or 6 Gy.



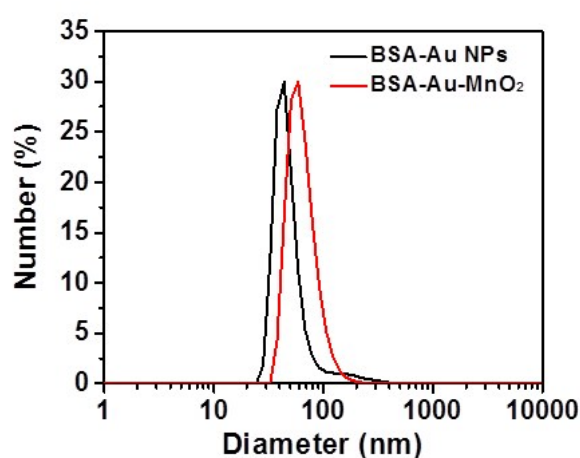
**Supporting Figure S8.** (a) Representative immunofluorescence images of tumor slices stained by the hypoxia-probe collected at 24 h after i.v. injection. Cell nuclei, blood vessels and hypoxia areas were stained by DAPI (blue), anti-CD31 antibody (red) and antipimonidazole antibody (green), respectively. (b) Quantification of hypoxia positive areas and blood vessel areas recorded from more than 10 images for each group.



**Supporting Figure S9.** (a) Representative immunofluorescence images of tumor slices with nuclei, blood vessels and HIF-1 $\alpha$  stained by DAPI (blue), anti-CD31 antibody (red) and anti-HIF-1 $\alpha$  antibody (green), respectively. (b) Quantification of HIF-1 $\alpha$  positive areas and blood vessel areas recorded from more than 10 images for each group.

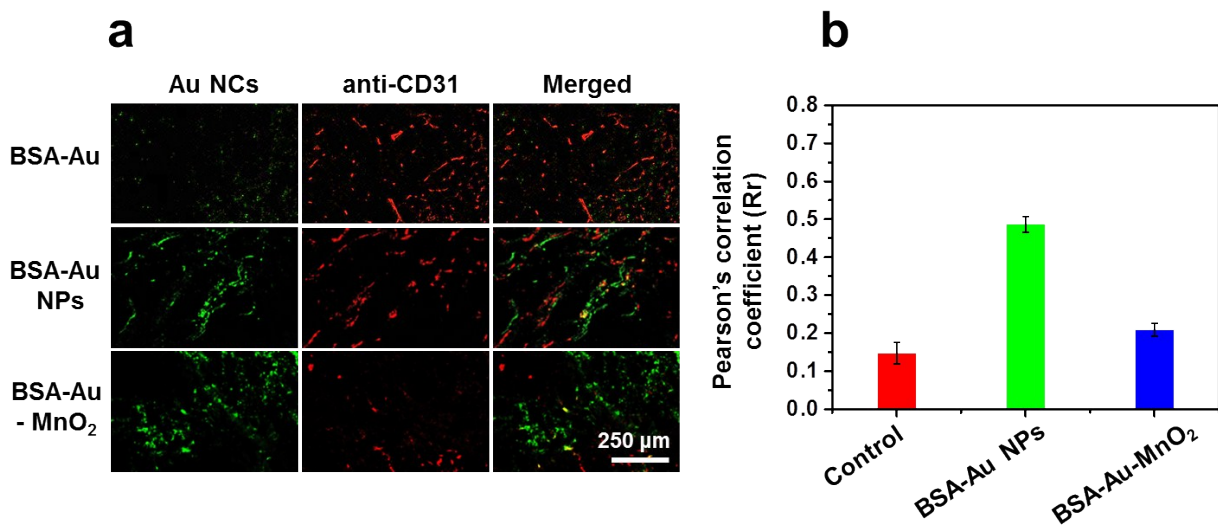


**Supporting Figure S10.** (a) Representative immunofluorescence images of tumor slices collected at 24 h with nuclei, blood vessels and HIF-1 $\alpha$  stained by DAPI (blue), anti-CD31 antibody (red) and anti-HIF-1 $\alpha$  antibody (green), respectively. (b) Quantification of HIF-1 $\alpha$  positive areas and blood vessel areas recorded from more than 10 images for each group.

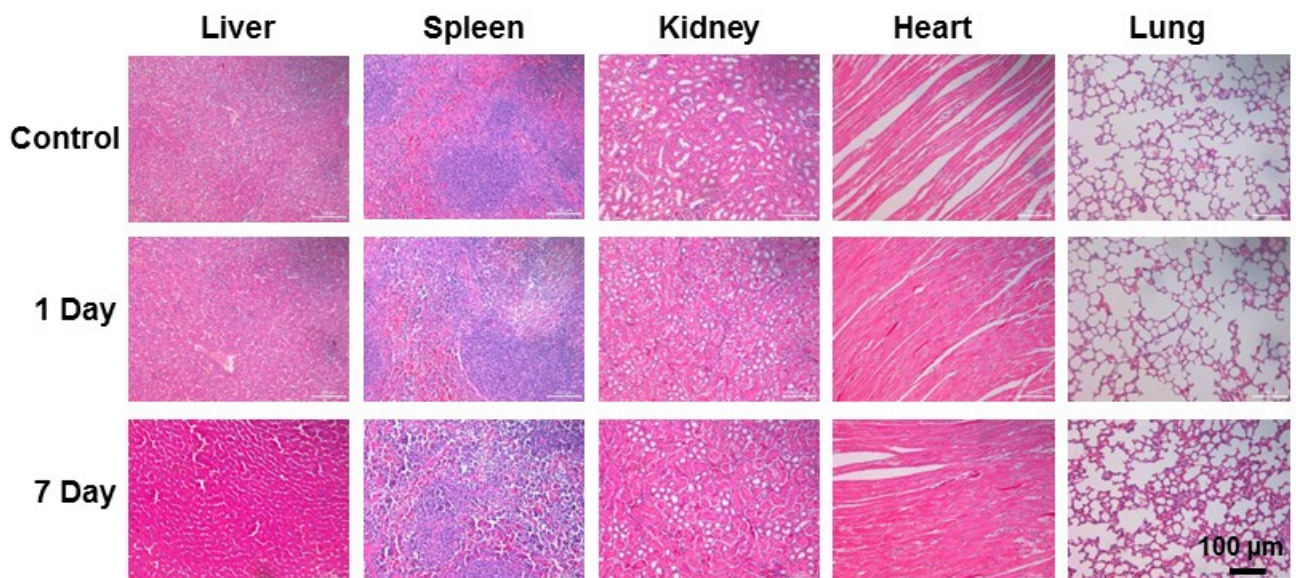


**Supporting Figure S11.** Hydrodynamic diameters of BSA-Au NPs and BSA-Au-MnO<sub>2</sub> measured by DLS.

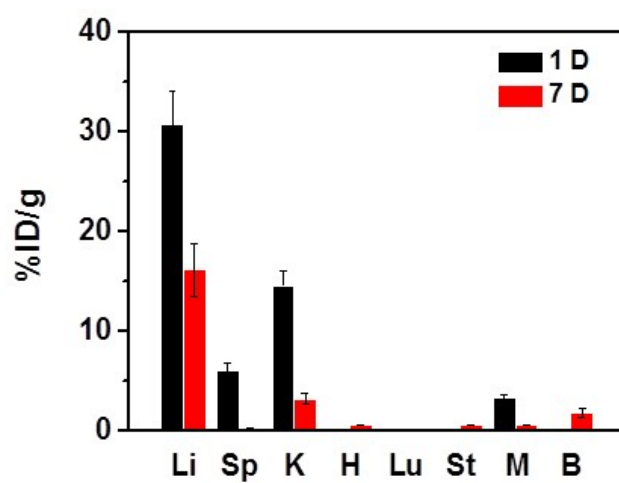




**Supporting Figure S12.** (a) Confocal images of tumor slices dissected from mice at 24 h post i.v. injection of BSA-Au, BSA-Au NPs, or BSA-Au-MnO<sub>2</sub>. Blue, red and green signals are from the fluorescence of DAPI, anti-CD31-stained blood vessels and AuNCs, respectively. (b) Pearson's correlation coefficient (Rr) calculated based on the images shown in (a).



**Supporting Figure S13.** Micrographs of H&E stained slices of major organs (liver, spleen, kidney, heart and lung) collected from mice at the 1st day and 7rd day after i.v. injection of BSA-Au-MnO<sub>2</sub>. Mice without any treatment were used as the control.



**Supporting Figure S14.** Biodistribution of BSA-Au-MnO<sub>2</sub> in different organs 1 day or 7 days after i.v. injection. (Li: liver, Sp: spleen, K: kidney, H: heart, Lu: lung, St: stomach, M: muscle, and B: bone).