Smart Self-assembly of Multifunctional Theranostic Nanozyme for Self-enhanced Precise Chemo/Chemodynamic Therapy

Jin Tao^{1†}, Junhui Wei^{1†}, Junnan Kan², Kai Qi,¹ Tingting Wang¹, Ailing Wang³, Wenxin Pei¹, Haiyan Gao⁴, Caixia Yang^{1*}, Xianglin Li^{1*}

¹ School of Medical Imaging, Binzhou Medical University, Yantai, Shandong, China

² Department of Radiology, Yantai Affiliated Hospital of Binzhou Medical University, Yantai, Shandong, China

- ³ Department of Clinical Laboratory, Yantai Affiliated Hospital of Binzhou Medical University, Yantai, Shandong, China
- ⁴ School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, China

* Corresponding author. E-mail: <u>caixiacx@outlook.com</u> (Caixia Yang); <u>xlli@bzmc.edu.cn</u> (Xianglin Li).

[†] These authors have contributed equally to this work.



Figure S1. TEM image and particle size distribution of Leu/Mn nanoparticles.



Figure S2. TEM image and particle size distribution of His/Mn nanoparticles.



Figure S3. TEM image and particle size distribution of Glu/Mn nanoparticles.



Figure S4. Standard curve of GOX-FITC according to the absorbance of FITC at 486 nm.



Figure S5. Standard curve of TPZ according to the fluorescence intensity of TPZ (ex: 475 nm, em: 575 nm)



Figure S6. Changes in hydrodynamic diameter and PDI of Cys/Mn@GOX/TPZ in RPMI 1640 medium with 10% FBS over a period of 7 d at 37 °C .



Figure S7. Images of Cys/Mn@GOX/TPZ before and after treatment with GSH (5 mM) in PBS at 37 °C over a period of 12 h.



Figure S8. TEM image of Cys/Mn@GOX/TPZ after treatment with GSH (5 mM) in PBS at 37 °C over a period of 12 h.



Figure S9. Quantification of the degradation percentage of Mn with in Cys/Mn@GOX/TPZ after treatment with GSH (1 mM) for 12 h.



Figure S10. TPZ release profile of Cys/Mn@GOX/TPZ after treatment with GSH (1 mM) for 12 h.



Figure S11. ESR spectra demonstrating the •OH generation of Cys/Mn@GOX/TPZ + Glucose, Cys/Mn + H_2O_2 , and H_2O_2 only.



Figure S12. Cytotoxicity of Cys/Mn@GOX/TPZ ($[Mn^{2+}] = 0, 0.25, 0.5, 1, 2, 4 \mu M$) on L929 normal cells in normoxic conditions.



Figure S13. (A) Cellular •OH generation of Cys/Mn@GOX/TPZ in different conditions detected by APF. Scale bar: 50 μ m. (B) The corresponding quantified intracellular fluorescence intensities of APF.



Figure S14. (A) Examination of the ROS levels in 4T1 tumor tissue using DCFH-DA as an indicator. Scale bar: 50 μ m. (B) The corresponding quantified intracellular fluorescence intensities of DCF.