Supporting Information

Codelivery of a tumor microenvironment-responsive disulfiram prodrug and CuO₂ nanoparticles for efficient cancer treatment

Fen-Ting Cheng,^a Ya-Di Geng,^a Yun-Xiao Liu,^b Xuan Nie,^c Xin-Ge Zhang,^b Zhao-Lin Chen,^a Li-Qin Tang,^{*a} Long-Hai Wang,^{*c} Ye-Zi You,^{a,c} Lei Zhang^{*a,b}

^a Department of Pharmacy, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, 230001, China
^b Institute of Clinical Pharmacology, Anhui Medical University, Hefei, Anhui, 230032, China
^c Department of Polymer Science and Engineering, University of Science and Technology of China, Hefei, Anhui 230026, China
*To whom correspondence should be addressed.
E-mail: <u>zhanglei6@ustc.edu.cn (L. Z.)</u>
E-mail: tangliqin@ustc.edu.cn (L.-Q. T.)

E-mail: hiwang@ustc.edu.cn (L.-H. W.)



Fig. S1. ¹H-NMR spectrum of the prodrug in CD₃OD, 400MHz.



Fig. S2. Curve of particle size change of Cu@P-B nanoparticles in 7 days.



Fig. S3. TEM image of synthesized P-B NPs.



Fig. S4. The viability of 293T cells treated with different concentrations of CuO_2 , P-B, and Cu@P-B for 24 h.



Fig. S5. The hemolytic results of CuO2, P-B, and Cu@P-B at different concentrations.



Fig. S6. The relative percentage of apoptotic (lower-right quadrant plus upper-right quadrant in Fig. 3a), early apoptotic (lower-right quadrant in Fig. 3a), and late apoptotic (upper-right quadrant in Fig. 3a) cells (n = 3, *p < 0.05, **p < 0.01, and ***p < 0.001).



Fig. S7. Statistical analysis of cell migration indicated that treatment with Cu@P-B led to a significant decrease in cell migration when compared with the corresponding control, n = 3, *p < 0.05, **p < 0.01, ***p < 0.001.



Fig. S8. Statistical analysis of cell invasion showed that treatment with CuO_2 , P-B, Cu@P-B led to a dramatic decrease in cell invasion when compared with the control, n = 3, *p < 0.05, **p < 0.01, ***p < 0.001.



Fig. S9. Body weight changes of mice injected with different doses of Cu@P-B. n = 3.



Fig. S10. The distribution of Cu in the major organs (heart, liver, spleens, lung, and kidney) and tumors of 4T1 tumor-bearing mice after Cu@P-B NPs treatment for 12 h.



Fig. S11. Picture of the excised tumors after different treatments for 16 days.



Fig. S12. H&E results of tumor tissues and heart, liver, spleen, lung, and kidney harvested from corresponding mice after 16 days of various treatments. The scale bar is $200 \ \mu m$.