

Supporting Information

siRNA-Based Carrier-Free System for Synergistic Chemo/Chemodynamic/RNAi Therapy of Drug-Resistant Tumors

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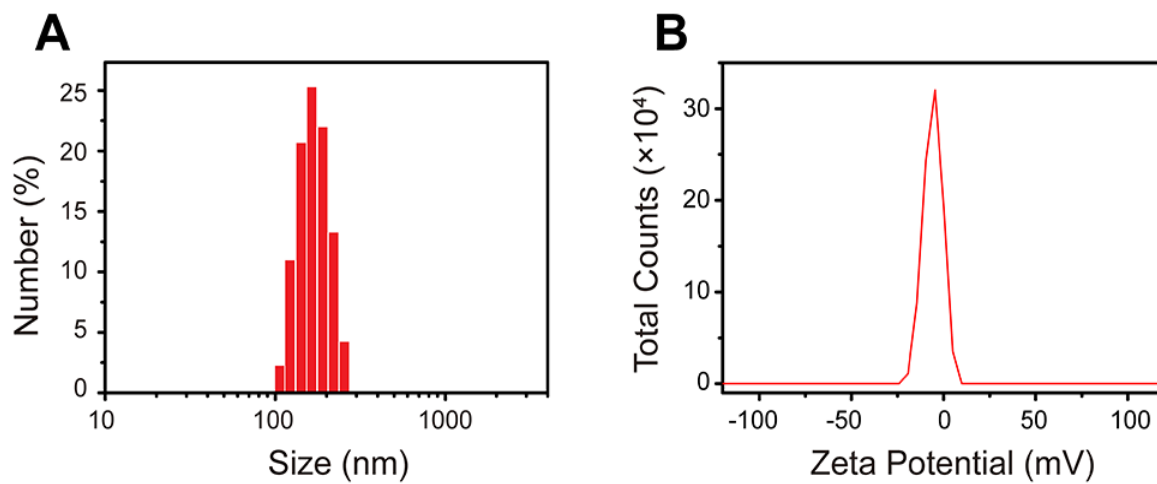


Figure S1. DLS results of Cu-siMDR-CDDP include size (A) and zeta potential (B).

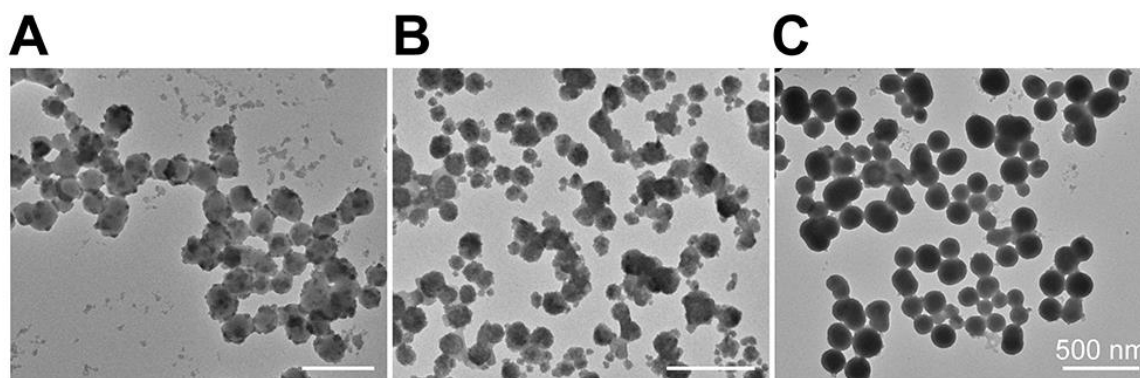


Figure S2. TEM images of (A) Cu-siMDR, (B) siMDR-CDDP, and (C) Cu-siNC-CDDP.

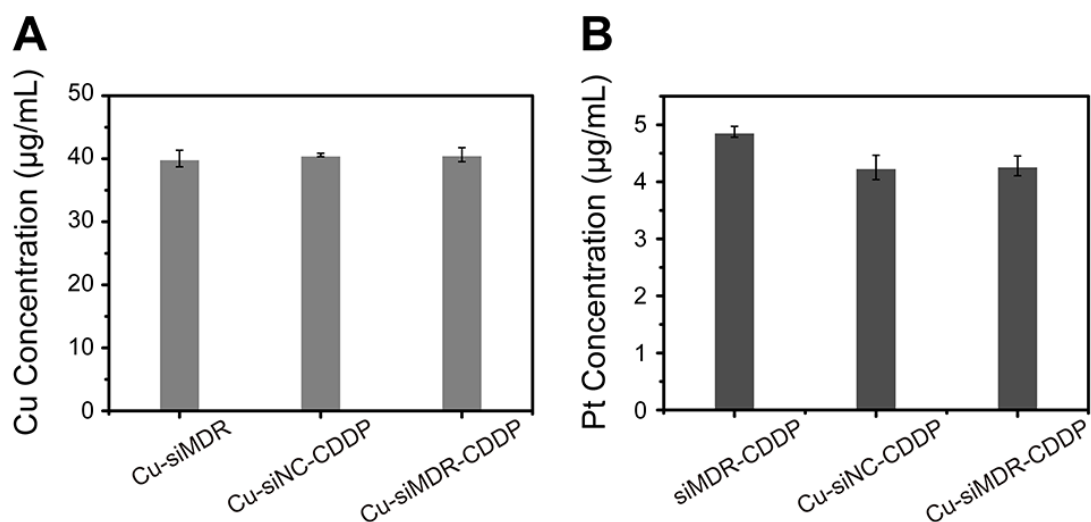


Figure S3. Elemental quantification by ICP-MS showed the Cu (A) and Pt (B) concentrations in different nanoparticles ($100 \mu\text{g mL}^{-1}$).

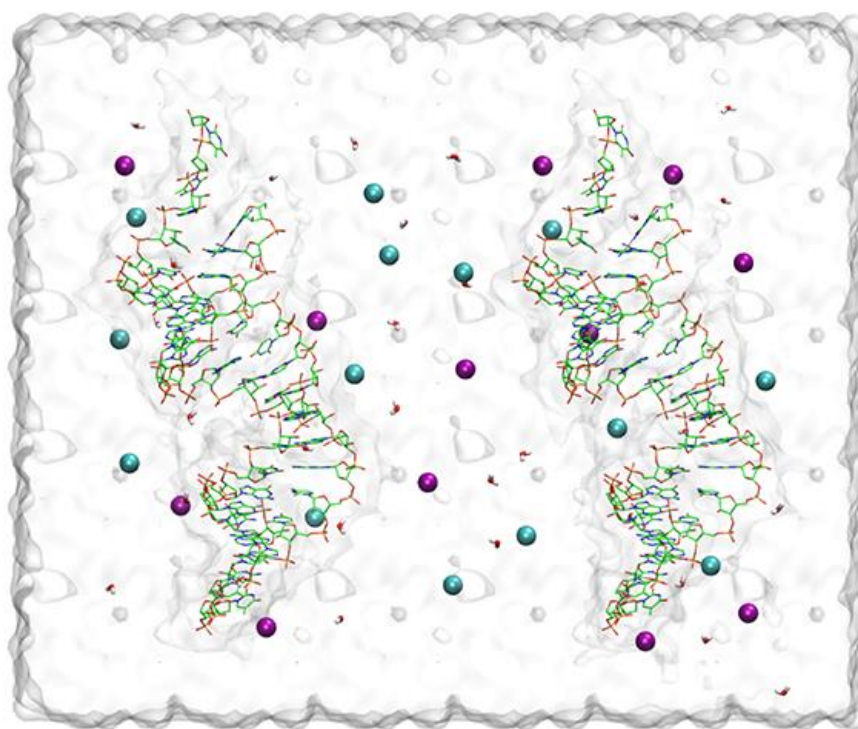


Figure S4. Two double-stranded siRNA-CDDP molecules were initially placed and solvated in the center of a truncated octahedral water box. Cu^{2+} and Cl^- ions were added to counterbalance the charge of the complex. The green, red, blue, orange, cyan, and purple represented the C, O, N, P, Cu^{2+} , and Cl^- .

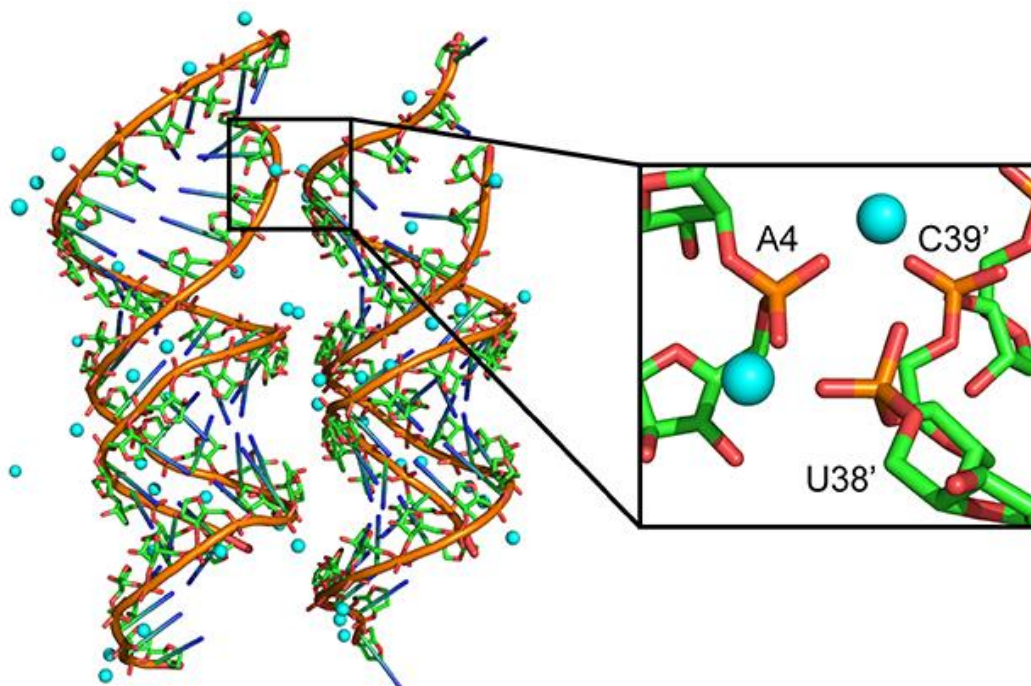


Figure S5. The simulation of Cu-siRNA complexes assembly process. The green, red, blue, orange, and cyan represented the C, O, N, P, and Cu atoms.

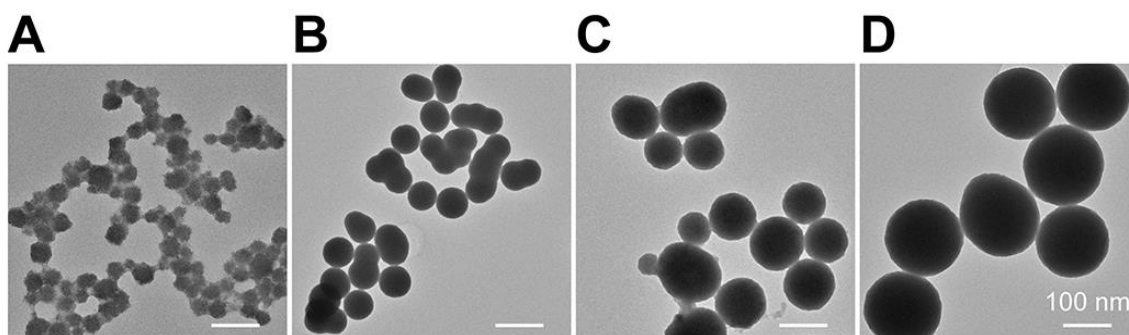


Figure S6. TEM images of intermediate products for different reaction times in the synthesis process of Cu-siMDR-CDDP. (A) 1 h (B) 6 h (C) 12 h (D) 24 h.

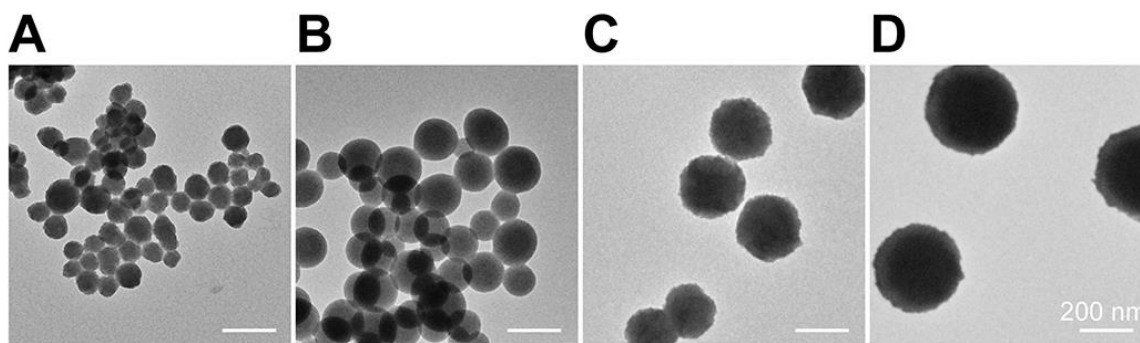


Figure S7. TEM images of the Cu-siMDR-CDDP synthesized at varying concentrations of siRNA. (A) 10 μ M (B) 20 μ M (C) 30 μ M (D) 40 μ M.

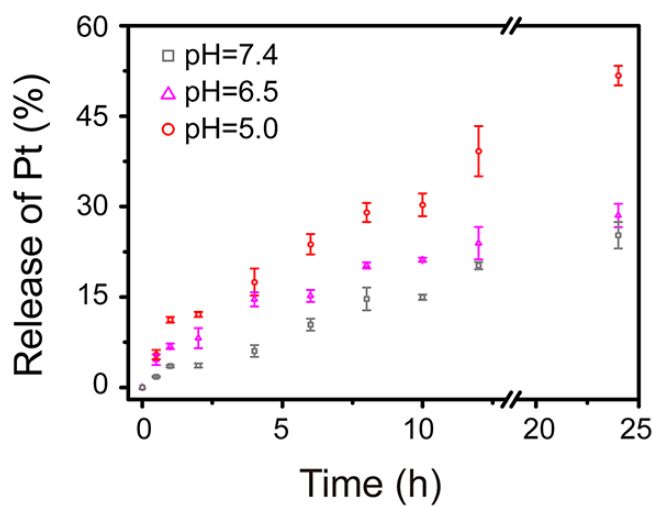


Figure S8. The cumulative release of Pt from Cu-siMDR-CDDP in the PBS solution at pH 7.4, 6.5, and 5.0, respectively.

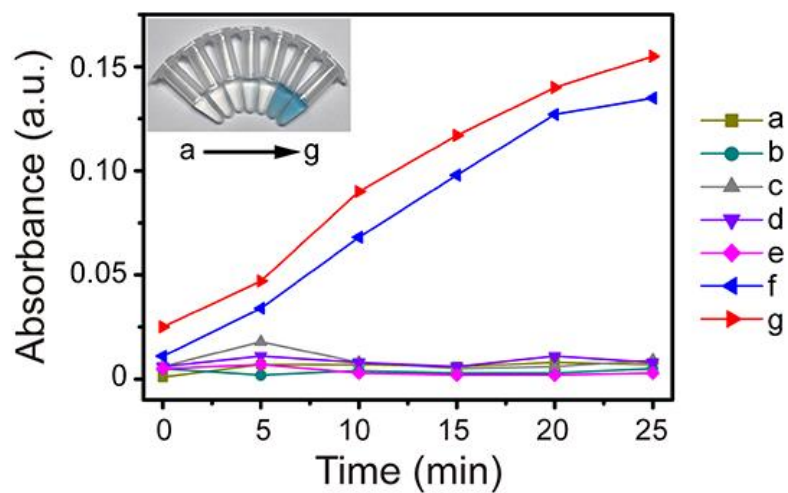


Figure S9. The HO[•] level in various groups in the PBS solution of pH = 5.0: (a) TMB, (b) TMB + GSH, (c) TMB + H₂O₂, (d) TMB + Cu-siMDR-CDDP, (e) TMB + Cu-siMDR-CDDP + GSH, (f) TMB + Cu-siMDR-CDDP + H₂O₂, (g) TMB + Cu-siMDR-CDDP + GSH + H₂O₂.

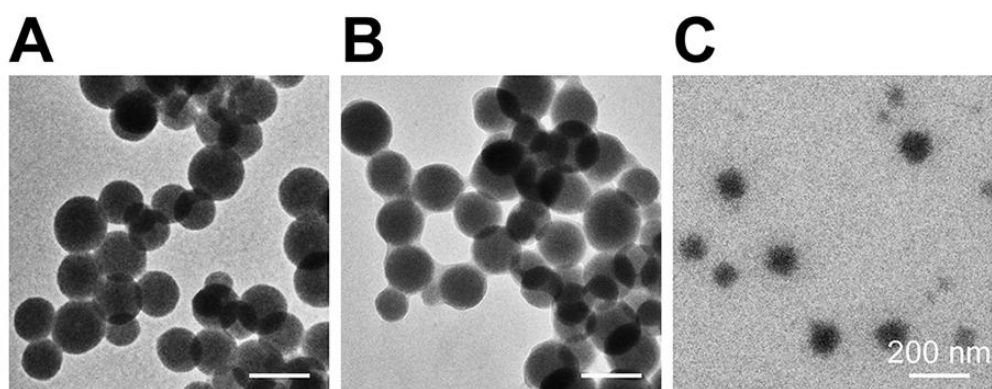


Figure S10. TEM images of Cu-siMDR-CDDP incubated with 10% FBS for (A) 1 h (B) 6 h (C) 12 h.

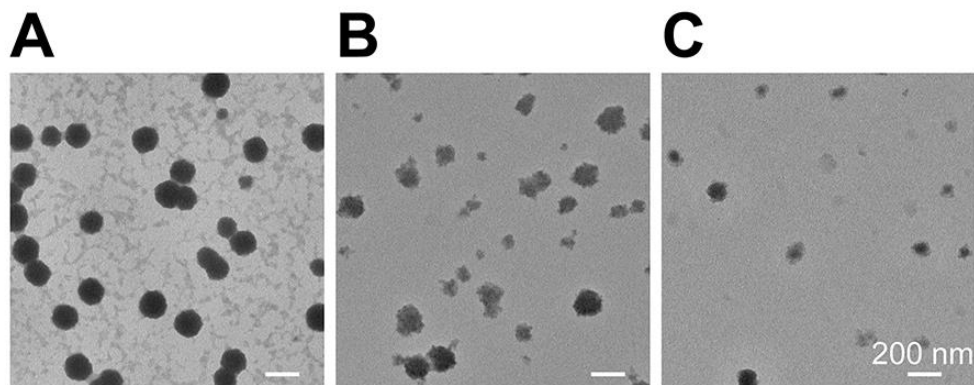


Figure S11. TEM images of Cu-siMDR-CDDP incubated with DNase I for (A) 1 h (B) 3 h (C) 6 h.

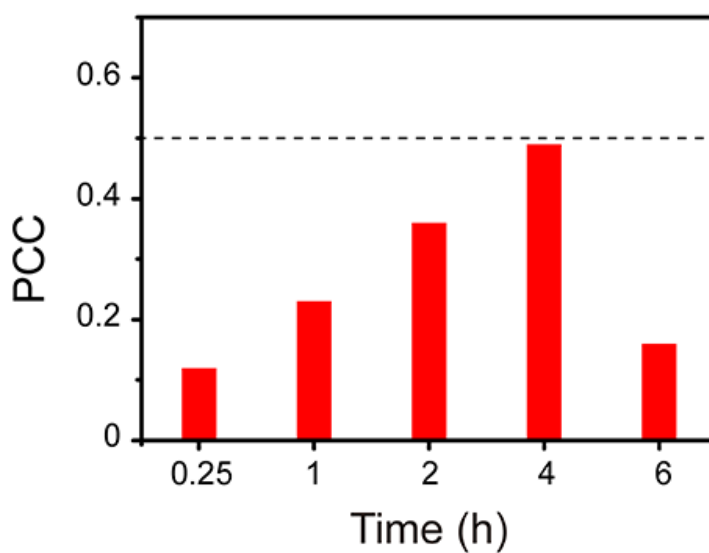


Figure S12. PCCs of Cu-siMDR-CDDP with lysosomes after incubating for different times. Data were obtained from Figure 5C and analyzed by ImageJ software.

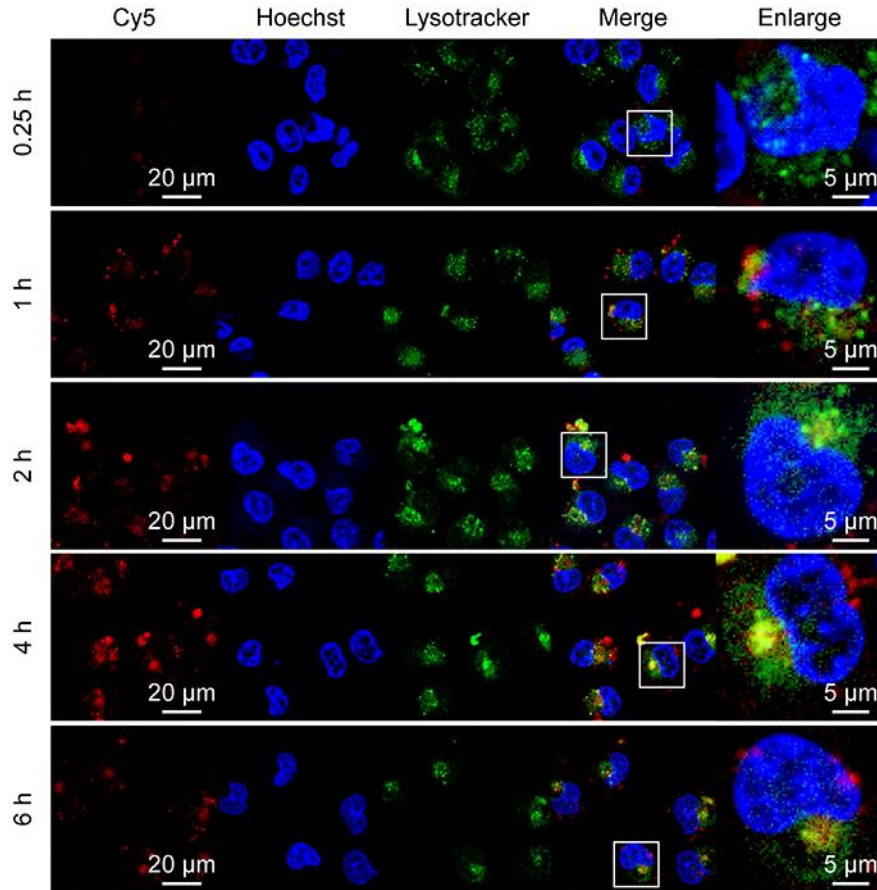


Figure S13. CLSM images of intracellular colocalization between Cu-siMDR-CDDP and lysosomes with the treatment of ROS scavenger NAC (5 mM). Blue: Hoechst 33342. Green: Lysotracker. Red: Cy5-labeled siRNA. Enlarge images were the framed regions expanded from merge images.

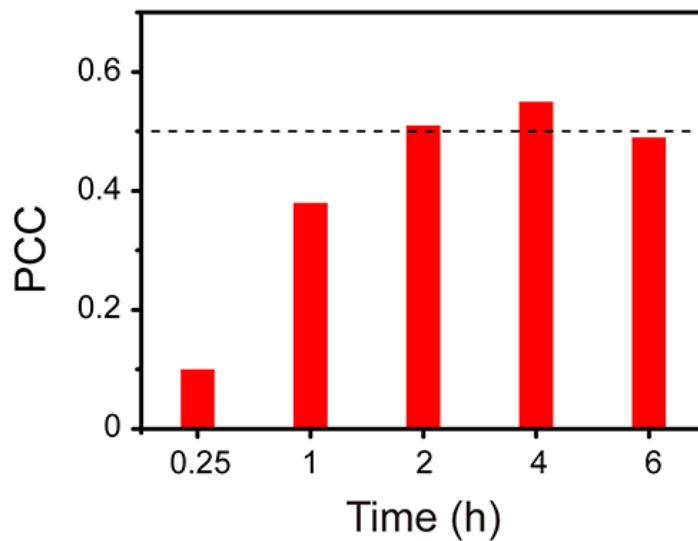


Figure S14. PCCs of Cu-siMDR-CDDP with lysosomes after incubating for different times in the presence of NAC. Data were obtained from Figure S13 and analyzed by ImageJ software.

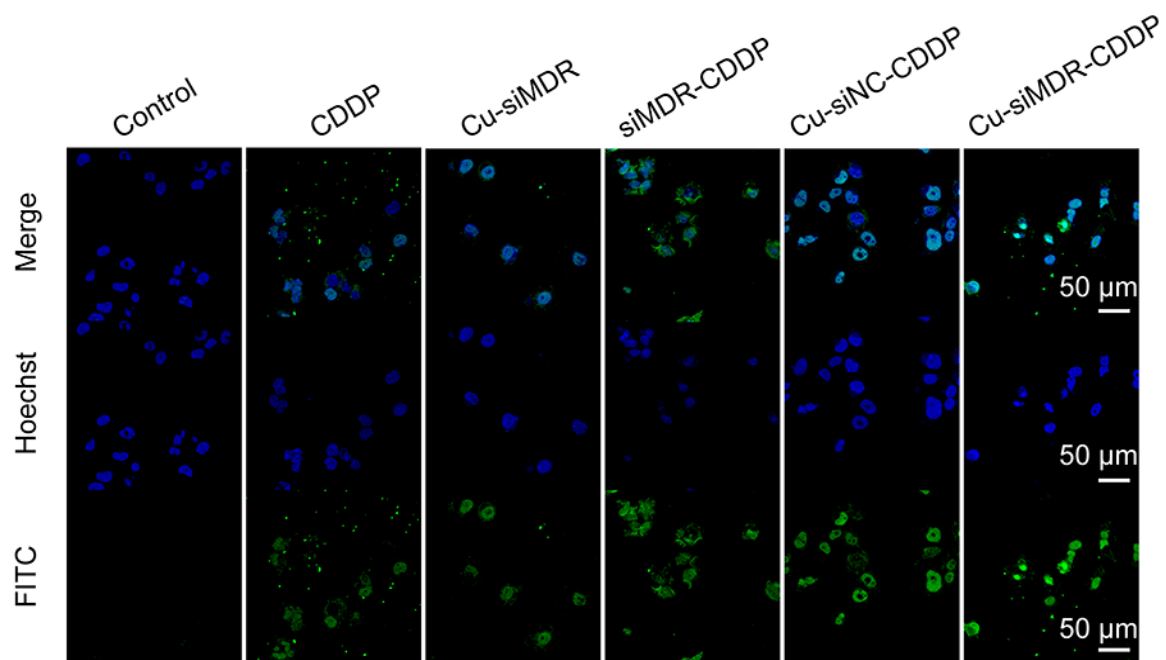


Figure S15. TUNEL staining of MCF-7/CDDP cells after treating with different groups at 12 h.

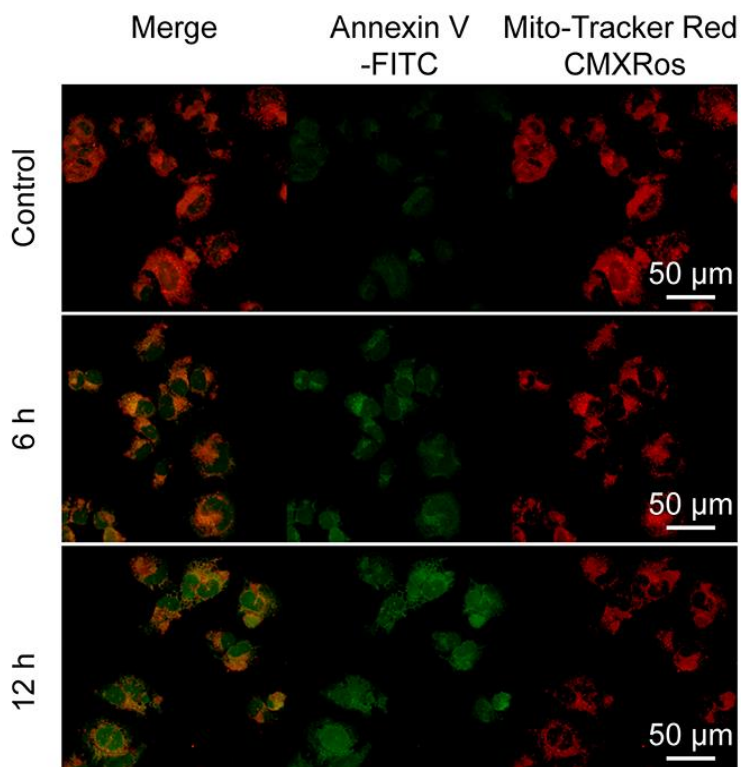


Figure S16. The mitochondrial membrane potential (MMP) of MCF-7/CDDP cells treated by Cu-siMDR-CDDP for 6 h and 12 h.

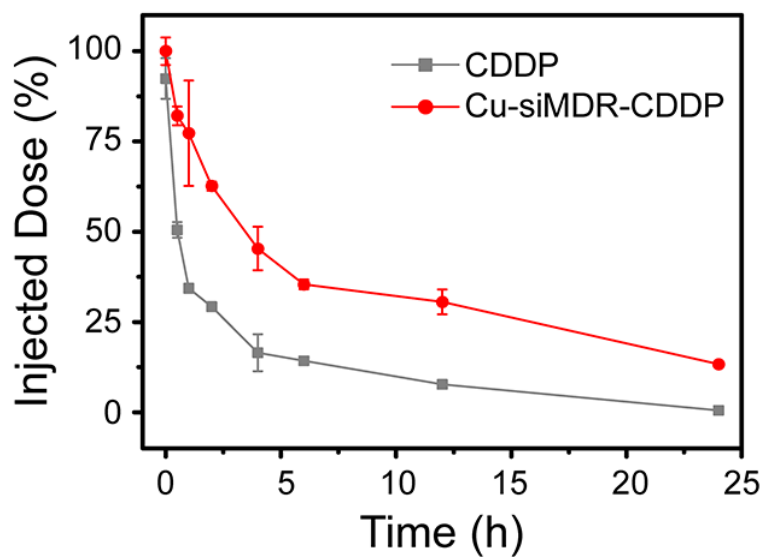


Figure S17. The plasma concentration-time curves of CDDP (Gray) and Cu-siMDR-CDDP (Red) after intravenous administration in mice. Data were shown as mean \pm S.D. (n = 3)

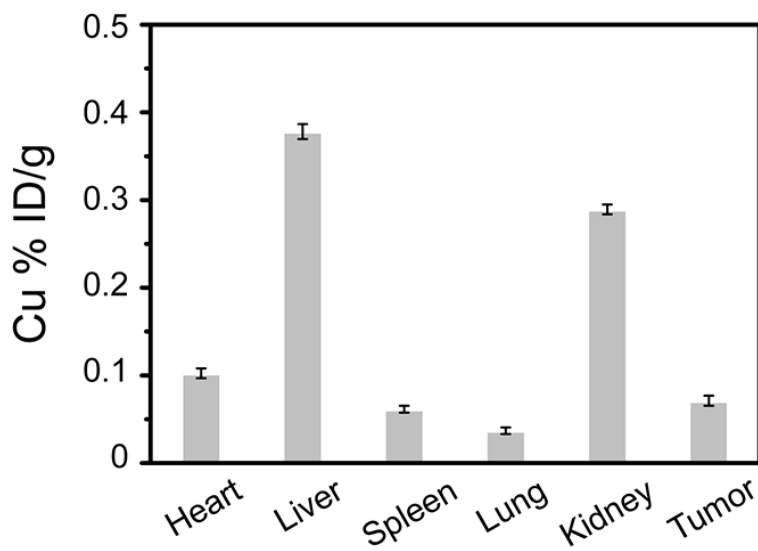


Figure S18. Quantitative analysis of Cu content in heart, liver, spleen, lung, kidney, and tumor at 24 h after injection of Cu-siMDR-CDDP.

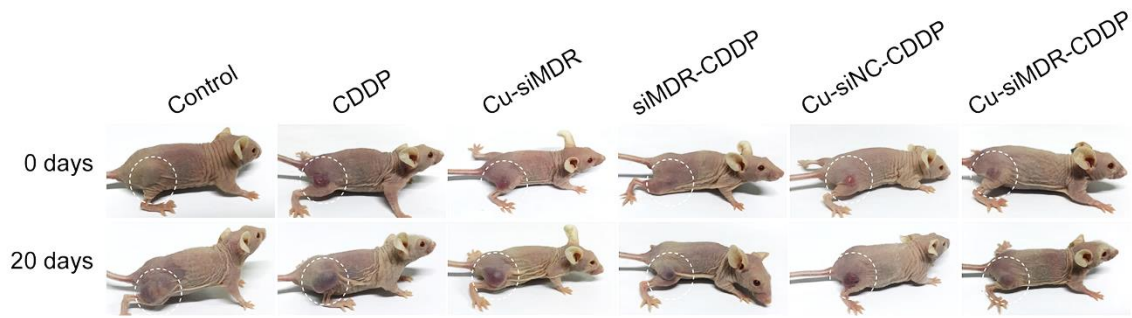


Figure S19. Digital photos of mice in different groups on the 20th day.

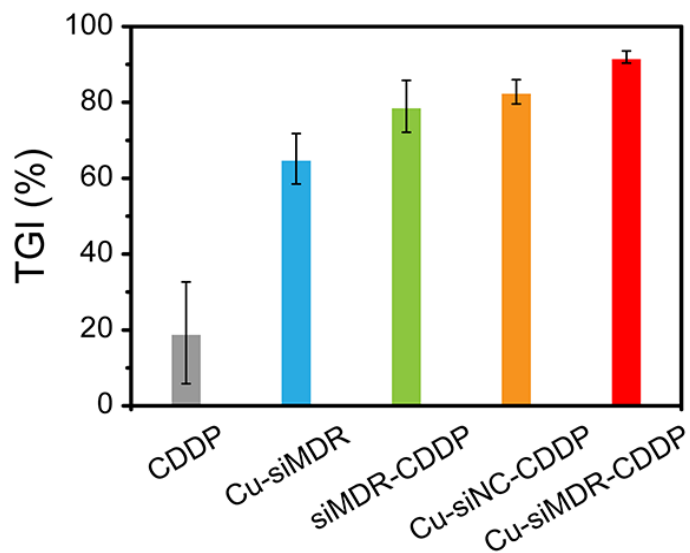


Figure S20. TGI values of different groups on the 20th day, including CDDP, Cu-siMDR, siMDR-CDDP, C-siNC-CDDP, and Cu-siMDR-CDDP. Data were calculated by the equation: $TGI = [1 - RTV(\text{Experiment group}) / RTV(\text{PBS-treated group})] \times 100\%$. RTV represented relative tumor volume between the start and end of treatment.

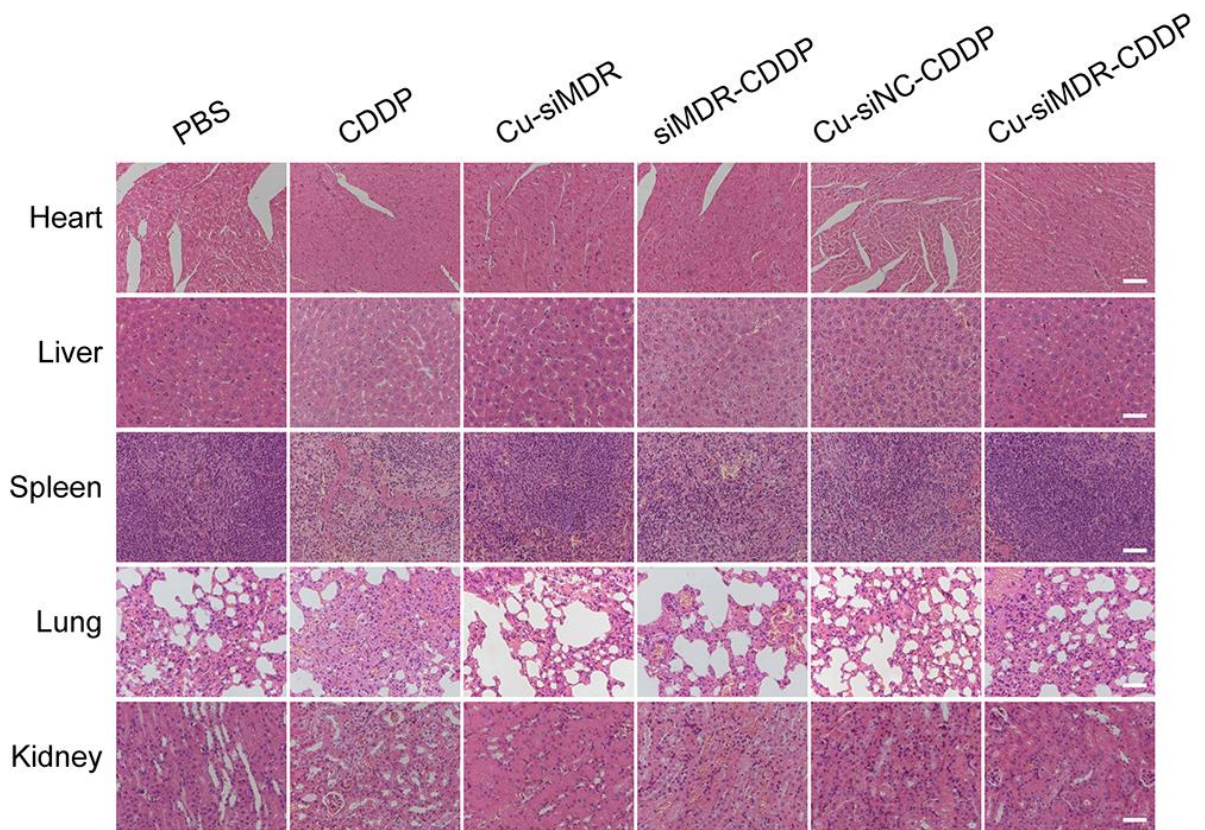


Figure S21. H&E staining of the major organs (heart, liver, spleen, lung, and kidney) on the 20th day from different groups. Scale bars: 100 μ m.