

Supplementary Material

Gold/Prussian Blue-Based Nanocomposites with Dual Nanozyme Activities Exert a Synergistic Effect of Starvation Therapy and Sonodynamic Therapy in the Treatment of Liver Cancer

1. Supporting methods

Synthesis and characterization of thiolated hyaluronic acid (HA-SH)

A quantity of 0.5 mmol HA was dissolved in 50 mL PBS solution (pH=7.4) at room temperature. Then 0.4 mmol EDC and NHS were added in sequence to react with HA for 2 h to activate the carboxyl under continuous stirring. After activation, 5 mmol of Cys was added to the HA mixture and the reaction was carried out overnight. Afterward, the reaction mixture was dialyzed in deionized water for 24 hours in a dialysis bag with a molecular weight threshold of 3500 Da. Afterward, the pH of the aforementioned solution was carefully adjusted to 8.0 using 1 M NaOH. Then, 2.5 mmol DTT was introduced to the solution and left to stir overnight. Next, the acidity of the solution was modified to a range of 3.0-4.0 using HCl, and subsequently moved into a dialysis bag with a molecular weight cut-off of 3500 Da. The bag underwent dialysis against a 0.1 M NaCl solution (pH 3.0-4.0) for a duration of 24 hours, followed by dialysis against an aqueous solution with a pH range of 3.0-4.0 for an additional 24 hours. The purified solution was lyophilized to obtain white flocs, namely thiolated HA, and stored at 4 °C. The chemical structure of HA-SH was characterized by FT-IR and ¹H NMR (400 MHz).

2. Supporting figures

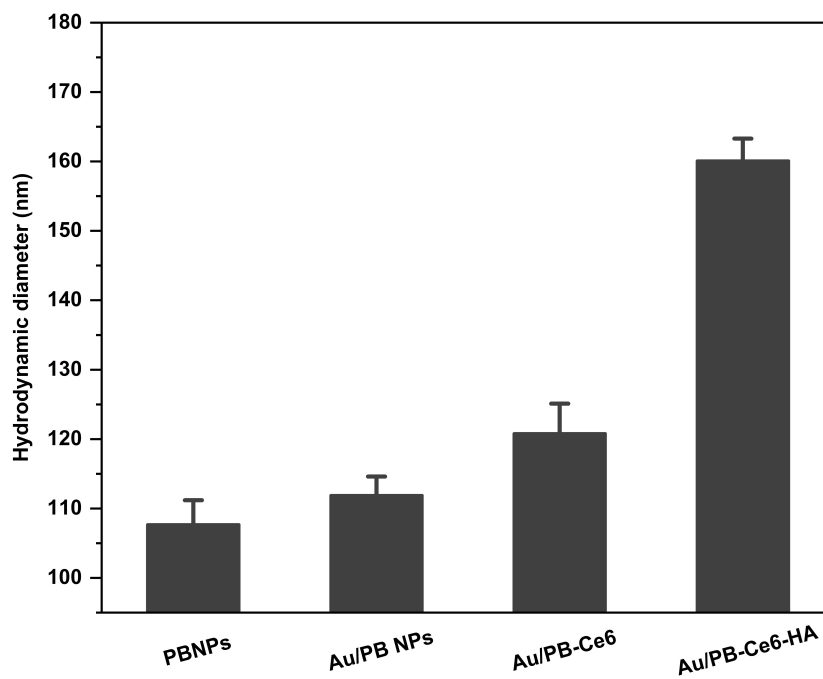


Figure S1 DLS result of PBNPs, Au/PB NPs, Au/PB-Ce6 and Au/PB-Ce6-HA.

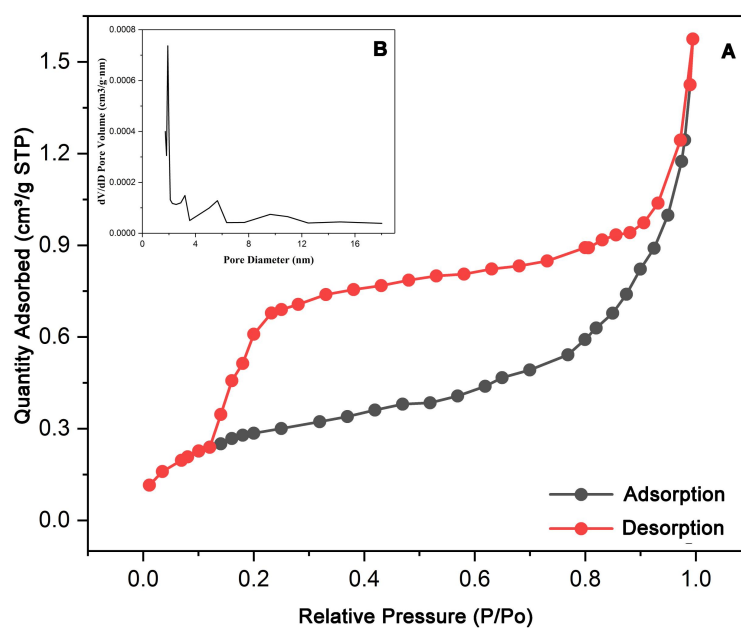


Figure S2 Nitrogen adsorption-desorption isotherm (A) and BJH pore size distribution (B) of PBNPs.

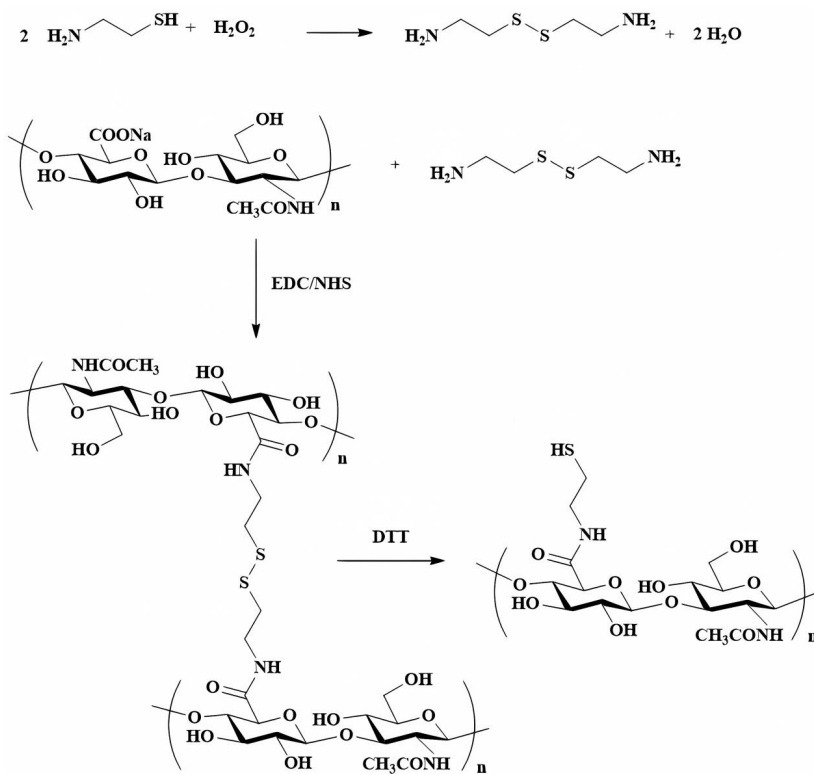


Figure S3 Synthetic route of HA-SH.

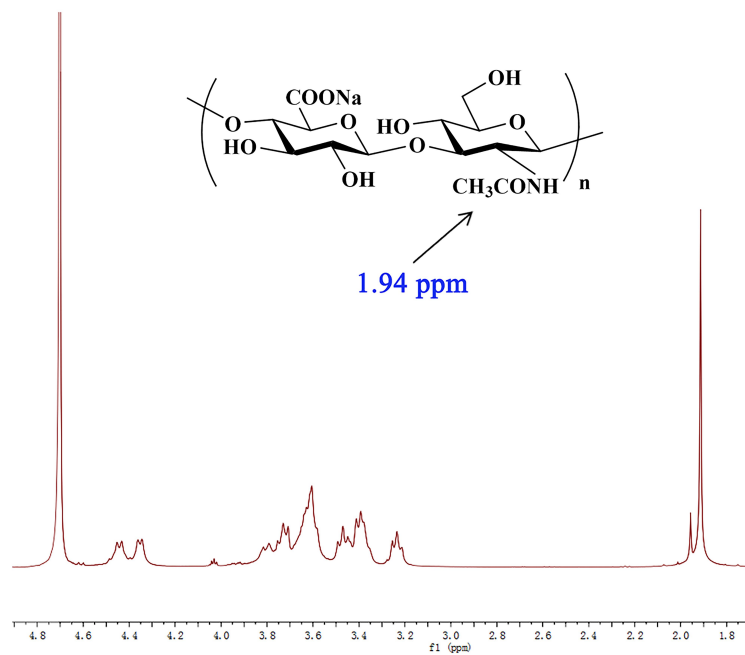


Figure S4 ^1H NMR spectra of HA in D_2O .

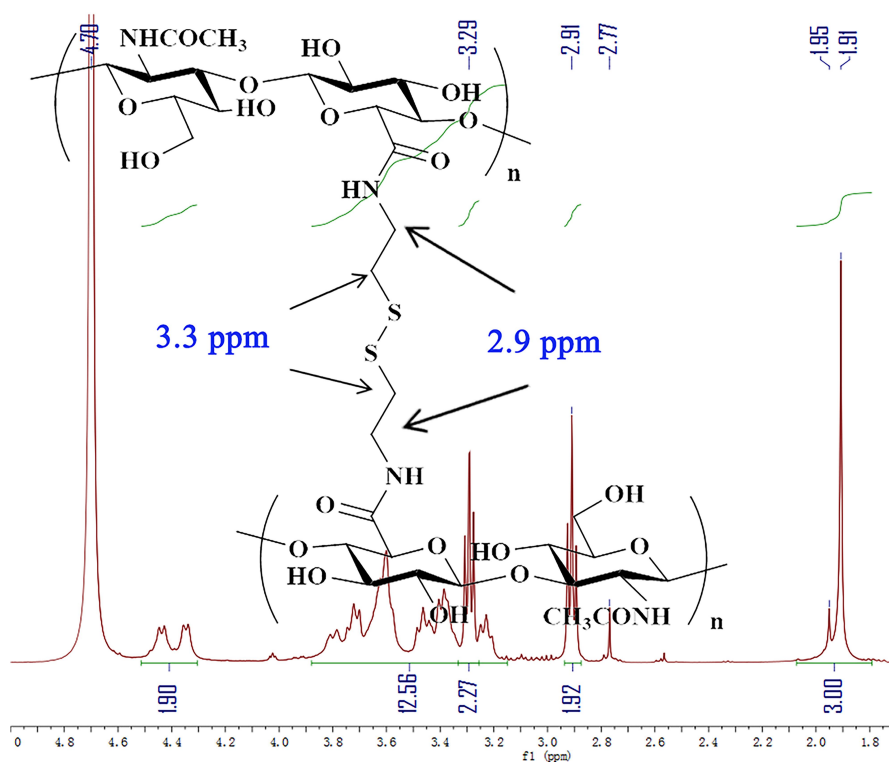


Figure S5 ^1H NMR spectra of HA-Cys in D_2O .

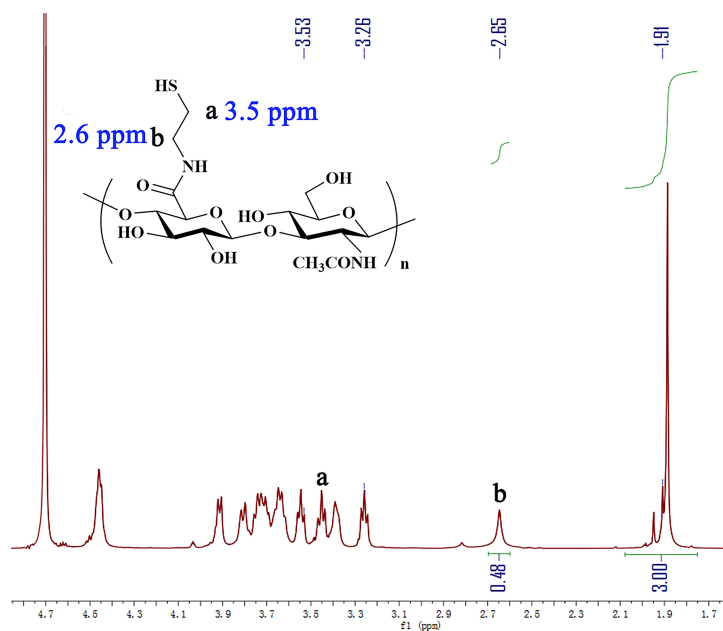


Figure S6 ^1H NMR spectra of HA-SH in D_2O .

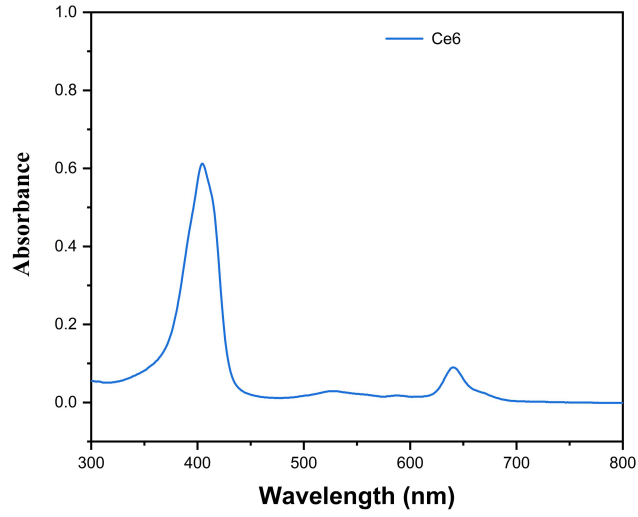


Figure S7 UV-Vis spectral scanning of Ce6 solutions.

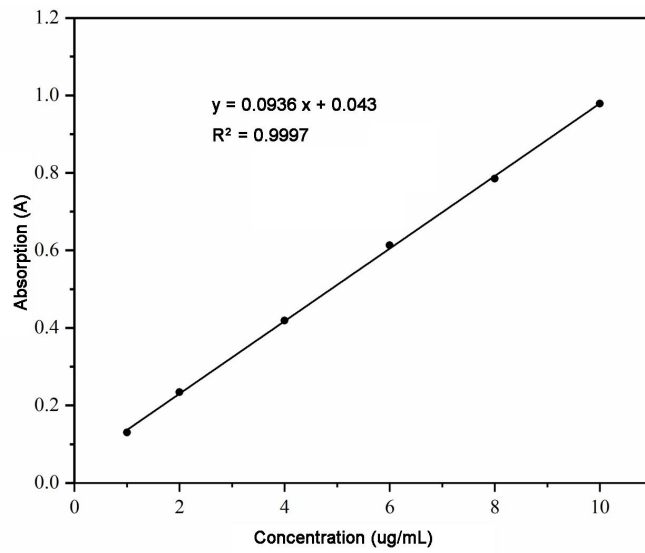


Figure S8 The standard curve of Ce6.

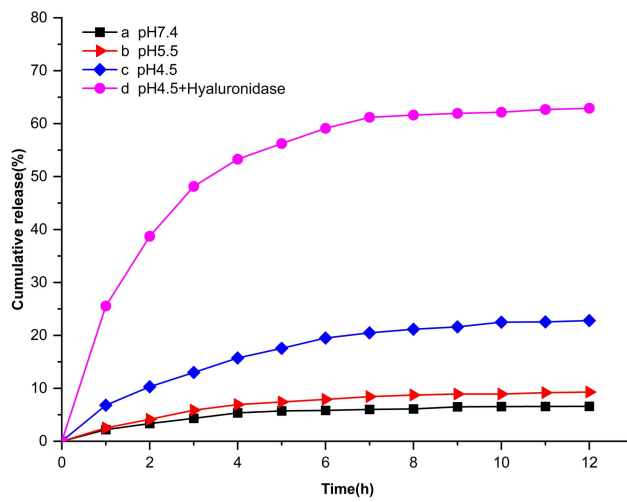


Figure S9 The release curve of Ce6.

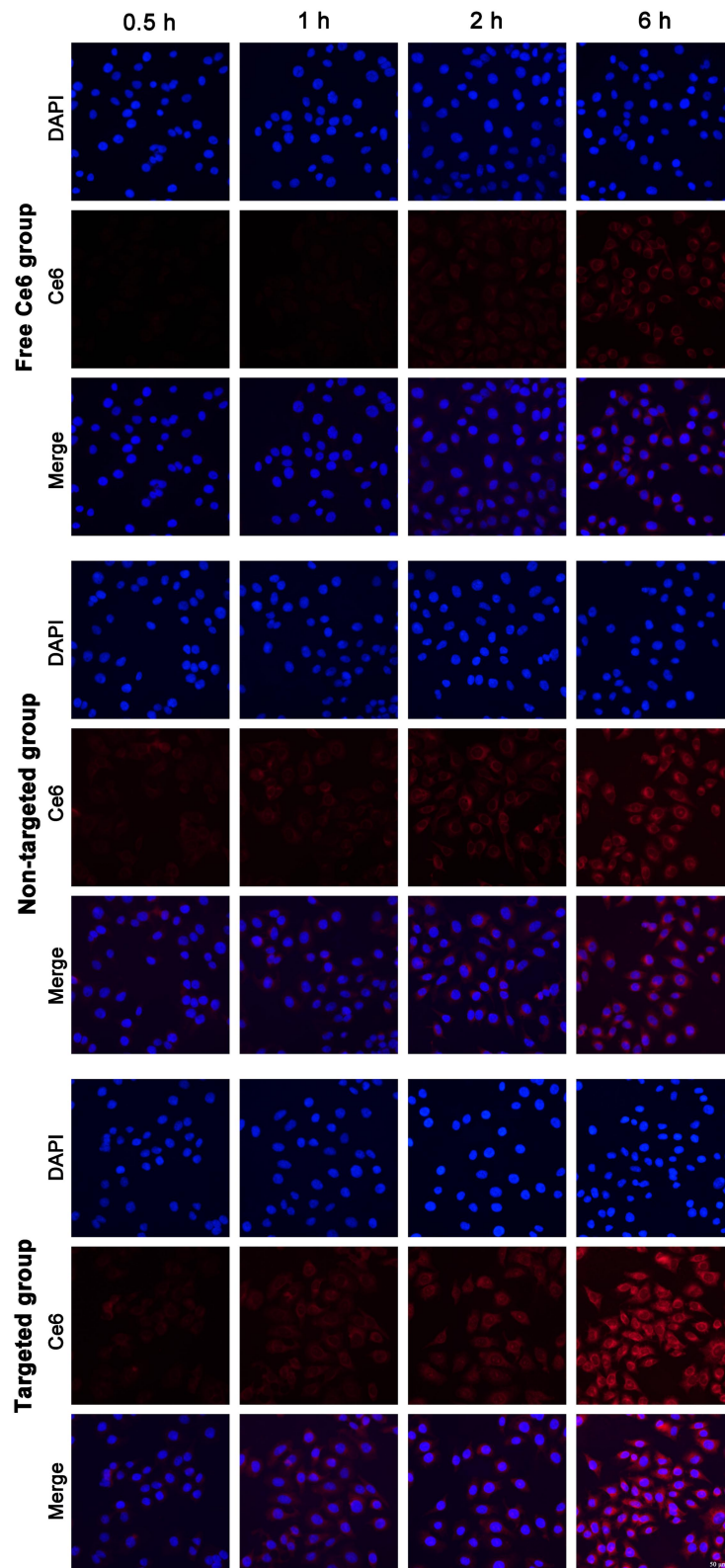


Figure S10 Cellular uptake of different drug administration groups by HepG2 cells. Free group: Ce6; Non-targeted group: Au/PB-Ce6; Targeted group: Au/PB-Ce6-HA. The concentration of Ce6 was $10 \mu\text{g mL}^{-1}$ (scale bar, $50 \mu\text{m}$).

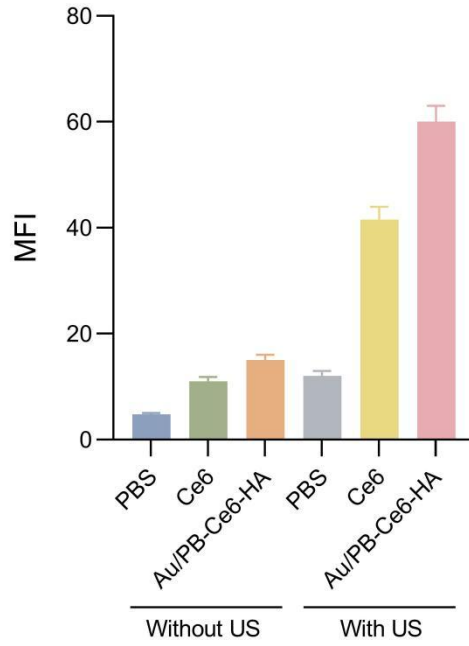


Figure S11 Mean fluorescence intensity (MFI) of cells treated with PBS, Ce6, or Au/PB-Ce6-HA, with or without ultrasound radiation, respectively.

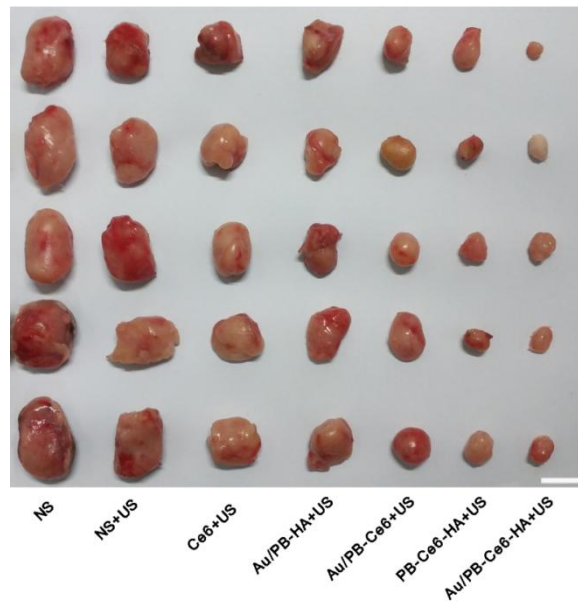


Figure S12 Photos of tumor tissue of H22 tumor-bearing mice treated with different groups (Scale bar = 1 cm).