

¹Supporting Information

NIR/Reduction Dual-sensitive Polymeric Prodrug Nanoparticles for Bioimaging and Combined Chemo-phototherapy

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Synthesis of DHP

According to reports in the literature[38], cisplatin (1.0 g, 3.33 mmol) was added to a 50 mL flask, 10 mL ultrapure water and 10 ml hydrogen peroxide (H₂O₂, 30%) were added, and stirred for 12 h in the dark. After the filtration and washing with ultrapure water and ice-cold acetone several times, the obtained solid cis,cis,trans-[Pt(NH₃)₂Cl₂(OH)₂] (DHP) was dried in vacuum to obtain 0.85g light yellow powder solid, the yield of DHP was 85%.

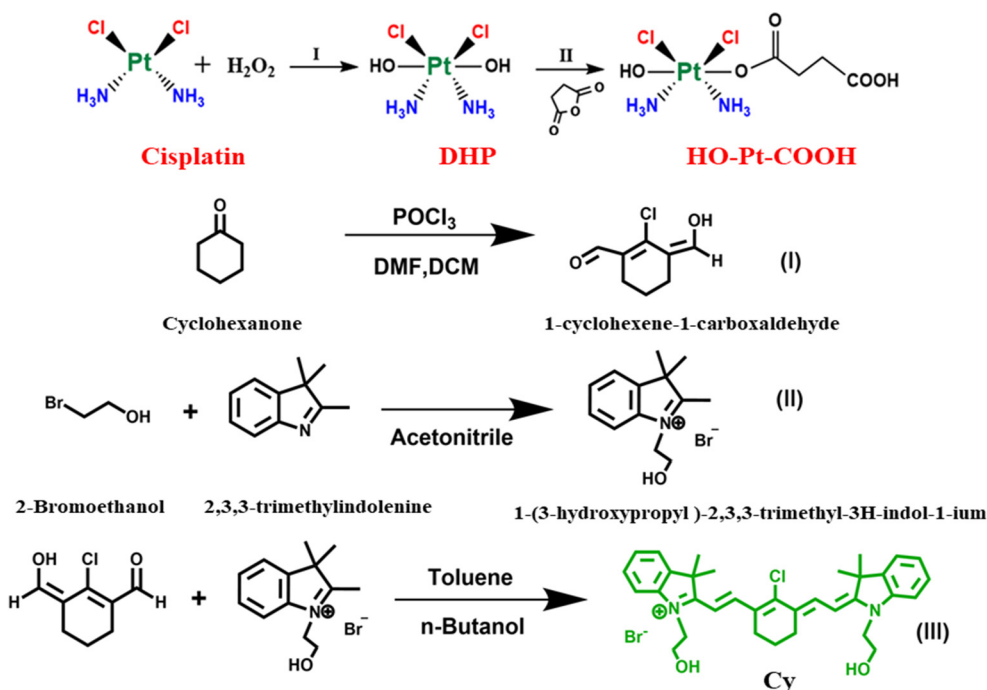
Synthesis of Pt(IV) prodrug HO-Pt-COOH

DHP (0.4g, 1.2mmol), succinic anhydride (0.12g, 1.2mmol), and DMSO (4ml) was added to the polymerization vial, with a light avoidance reaction at 30°C for 24h in the inert gas state [39]. After the reaction, the solvent was drained, dissolved with 2 mL methanol, then precipitated in ice-cold anhydrous diethyl ether, The obtained solid product was filtered and dried under vacuum, the product of cis,cis,trans-[Pt(NH₃)₂Cl₂(OH)(O₂CCH₂CH₂CH₂CO₂H)](HO-Pt-COOH) was 0.45g (87%).

Synthesis of Cy

According to the literature reports [37], 20 mL anhydrous DMF and 20 mL

anhydrous DCM were added into a two-necked flask in an ice-water bath. Subsequently, 20 mL POCl₃ was slowly dropwised with a constant pressure dropping funnel, and then cyclohexanone (5 g, 51 mmol) was gradually pumped into the flask. Finally, the mixture was reacted for 7 hours at 55°C in the dark under N₂ atmosphere. After concentration and recrystallization, a yellow solid, 1-cyclohexene-1-carboxaldehyde was obtained (**I**). 2,3,3-trimethylindolenine (6 g, 37.7 mmol), 2-bromoethanol and 80 mL of anhydrous acetonitrile were added to a single-necked flask, the reaction was carried out at 85°C in the dark under N₂ atmosphere for 48h. After rotary evaporation and concentration, The crude product was settled in frozen ethyl acetate and dried to obtain a pink solid, 1-(3-hydroxy ethyl)-2,3,3-trimethyl-3H-indol-1-ium(**II**).



Scheme S1. Synthetic scheme of the DHP(**I**), HO-Pt-COOH(**II**) and Cy.

Dissolve 1-cyclohexene-1-carboxaldehyde (1.73 g, 10 mmol) and 1-(3-hydroxy ethyl)-2,3,3-trimethyl-3H-indol-1-ium (5.735 g, 20 mmol) in anhydrous n-butanol (70 mL) and toluene (30 mL), and react in N₂ atmosphere at 120°C in the dark for 12 h, the solvent was separated and collected by an oil-water separation device, and after cooling to room temperature, the crude product is separated and purified by a chromatographic column to obtain

1-(2-hydroxyethyl)-2-((E)-2-((E)-3-((E)-2-(1-(2-hydroxyethyl)-3,3-dimethylindolin-2-ylidene)ethylidene)-2-chlorocyclohex-1-en-1-yl)vinyl)-3,3-dimethyl-3H-indol-1-ium bromide (Cy)(III), the Cy was 3.48g, the yield was 47%.

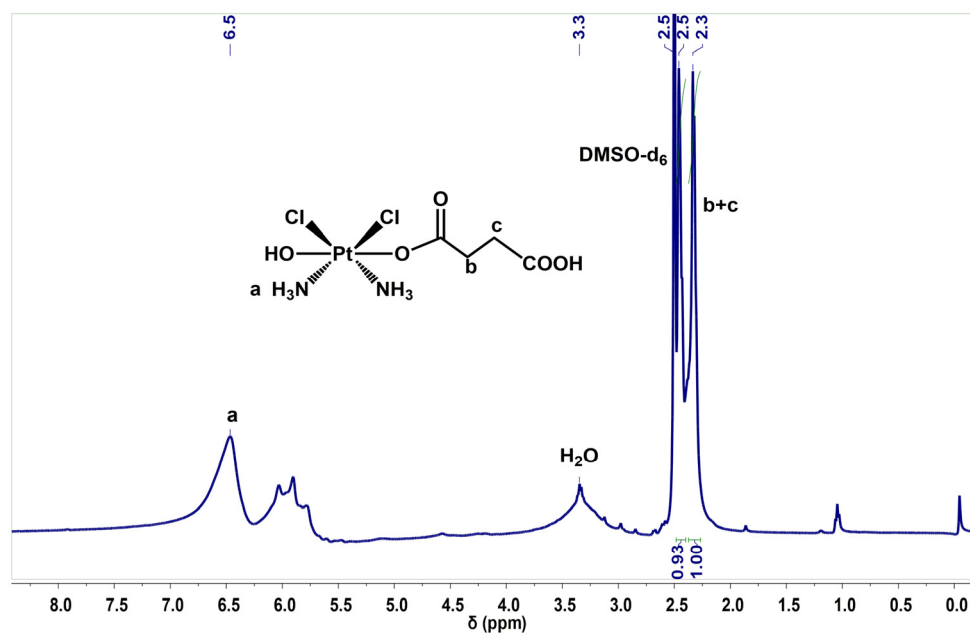


Figure. S1. ^1H NMR spectrum of HO-Pt-COOH in DMSO- d_6 .

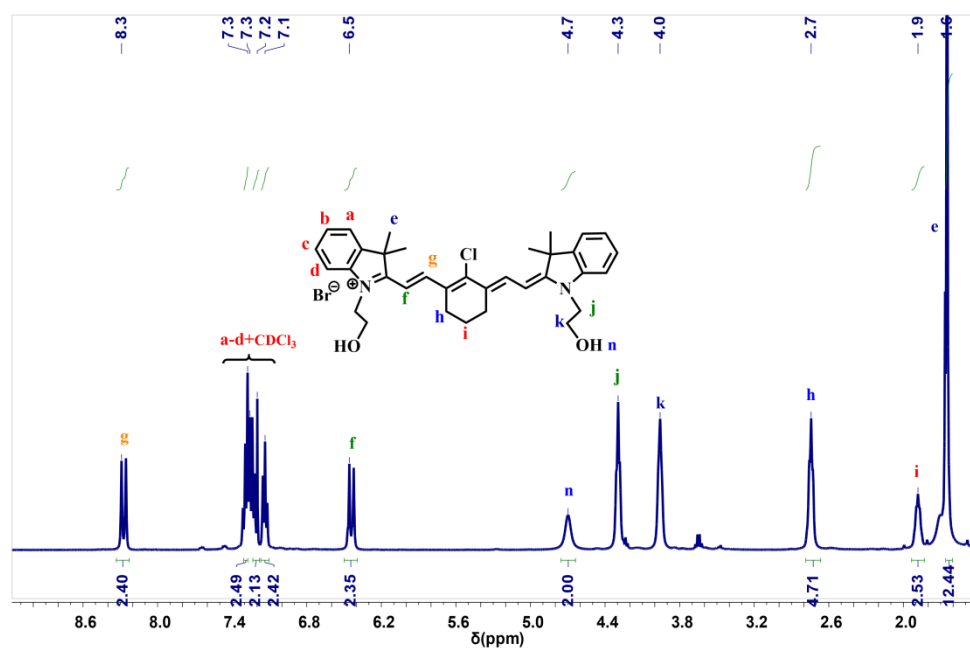


Figure. S2. ^1H NMR spectrum of Cy in CDCl_3 .

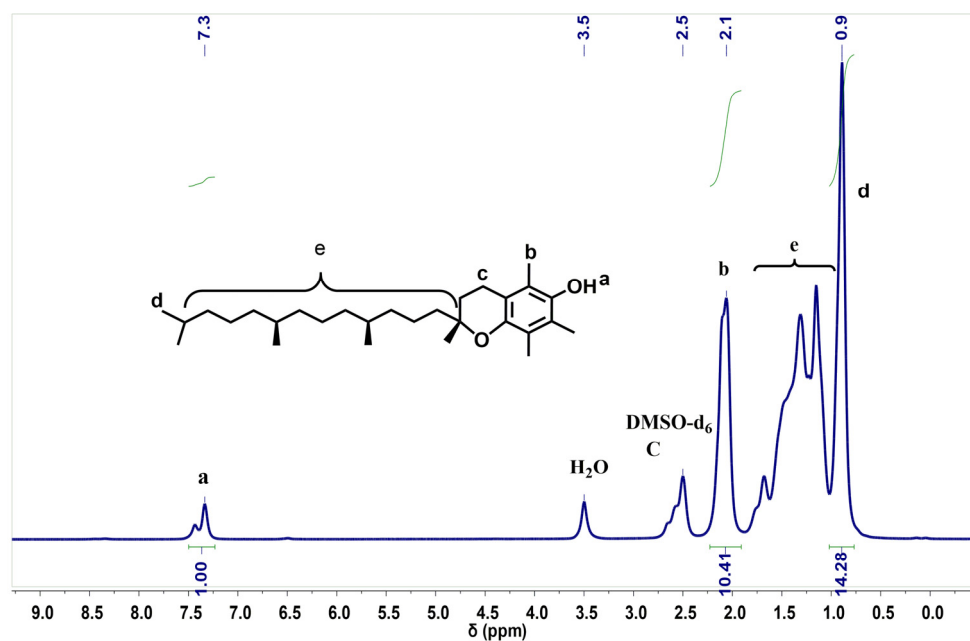


Figure S3. ^1H NMR spectrum of α -tocopherol in DMSO-d_6 .

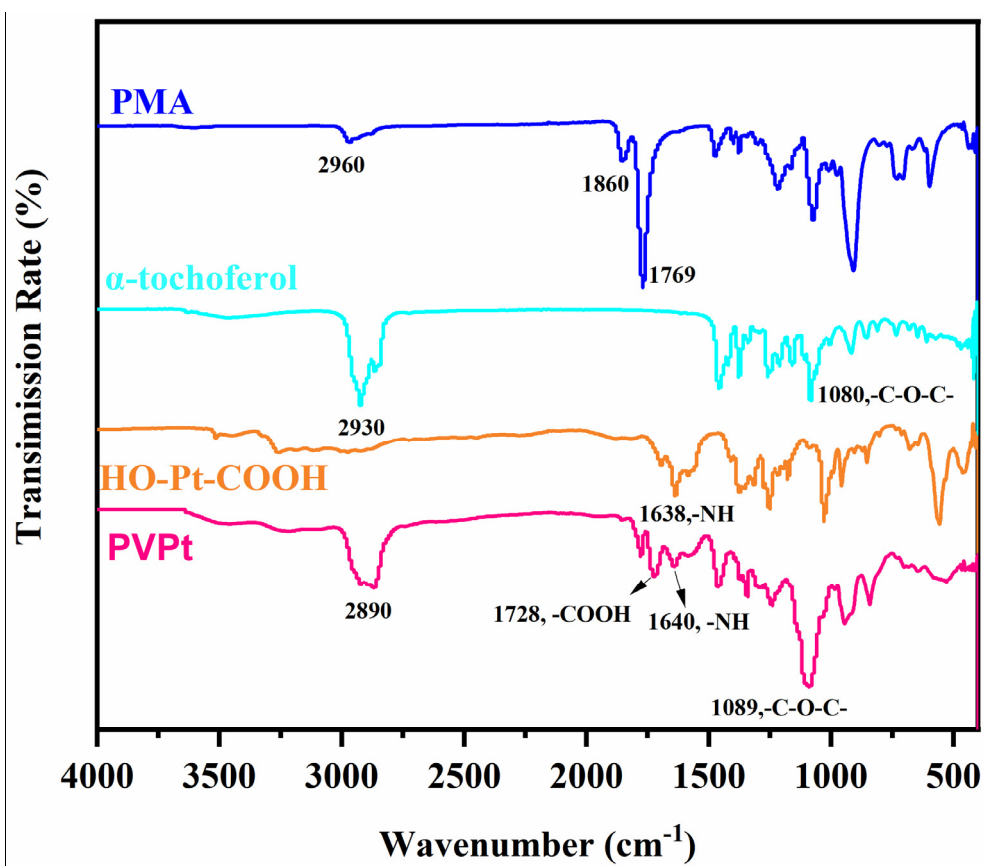


Figure S4. FT-IR spectra of PMA, α -tocopherol, HO-Pt-COOH and PVPt.

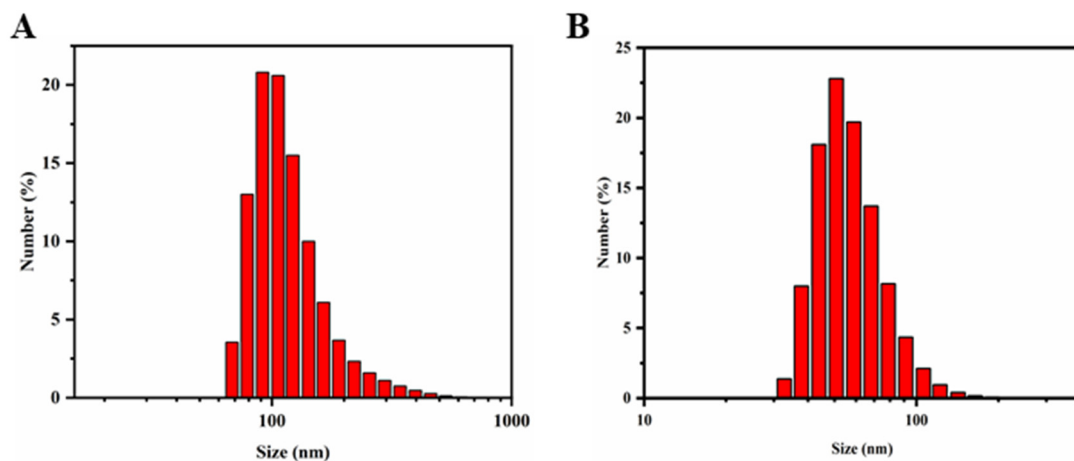


Figure S5. Hydrodynamic size of PVPt NPs (A) and PVPt@Cy NPs (B) after re-dispersion.

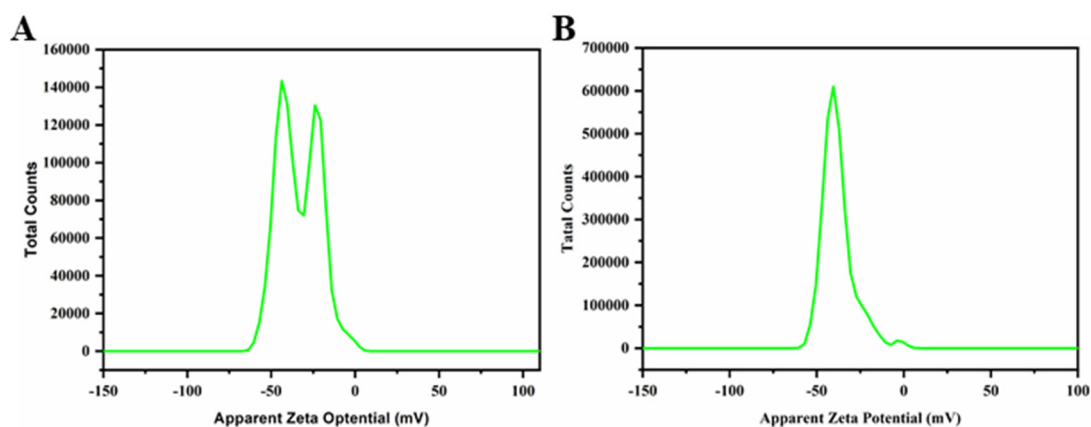


Figure S6. Zeta potential measurement of PVPt NPs(A) and PVPt@Cy NPs(B).

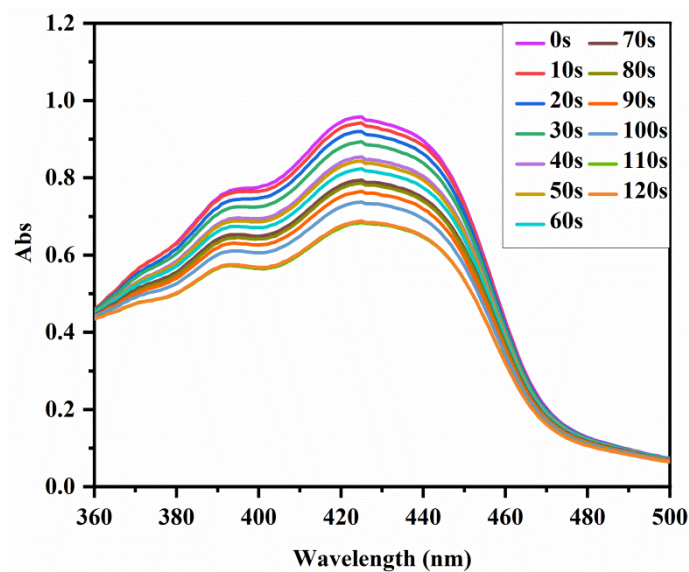


Figure S7. Absorption spectra of DPBF solution incubated with PVPt@Cy NPs in the dark (A) or under 808 nm irradiation (B) for different times.

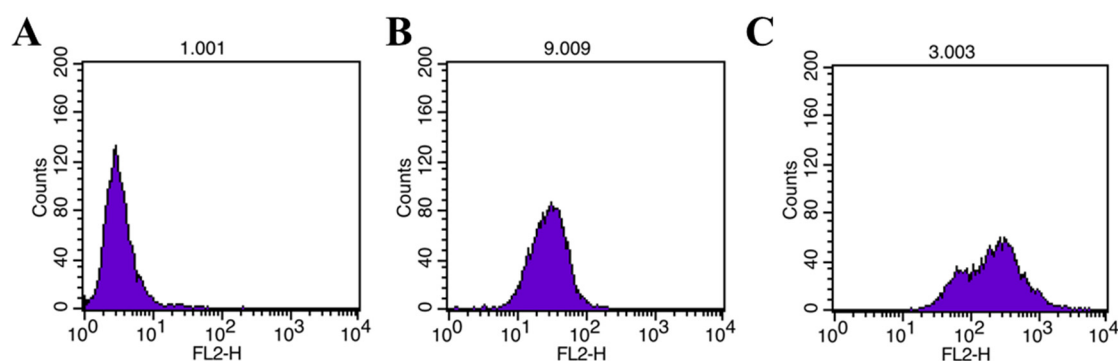


Figure S8. Flow cytometric histogram for quantitative comparison of the cellular uptake of control (A), PVPt@Cy NPs for 2 h (B), and PVPt@Cy NPs for 12 h (C).

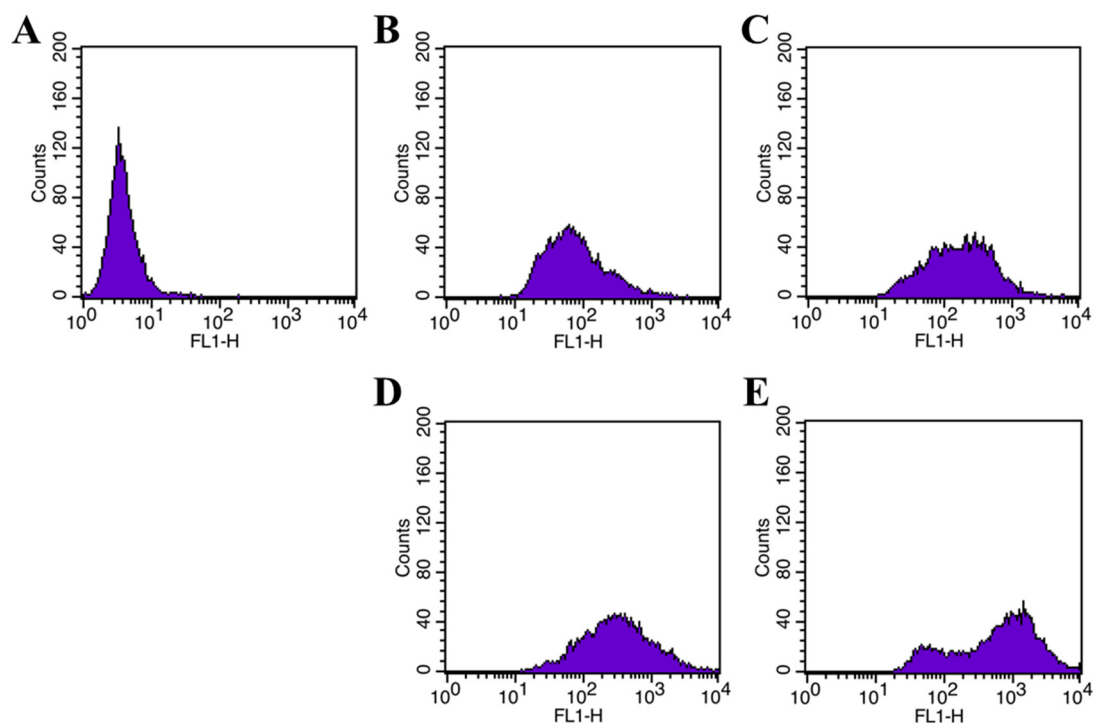


Figure S9. Flow cytometric histogram for quantitative comparison of the intracellular ROS generation of control (A), Cy in the dark (B), PVPt@Cy NPs in the dark (C), Cy with 808 nm irradiation (D), and PVPt@Cy NPs with 808 nm irradiation (E).