Supporting information

Enhancing Chemotherapy Efficacy of Platinum Prodrug Nanoparticles and Inhibiting Cancer Metastasis via Targeting Iron Homeostasis

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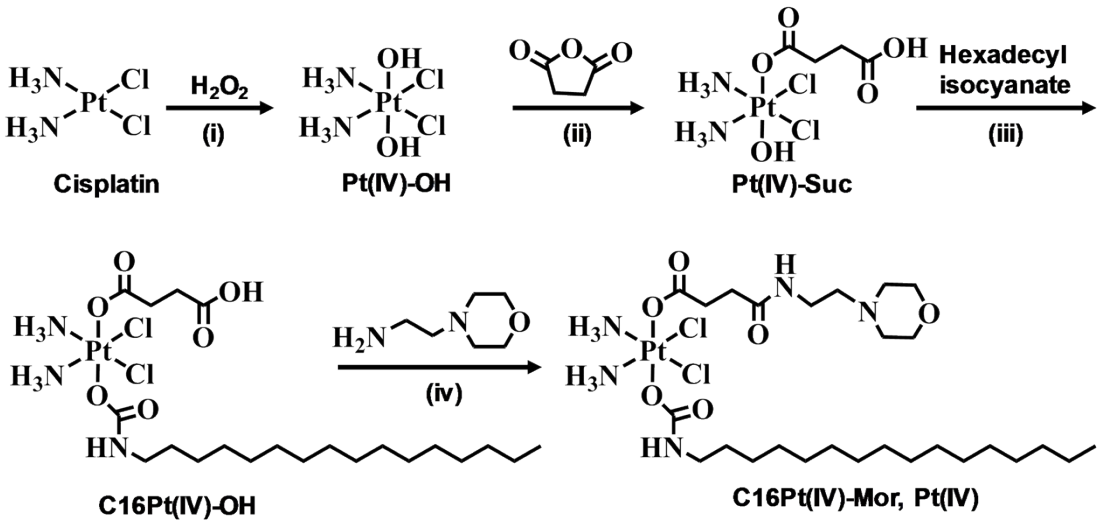
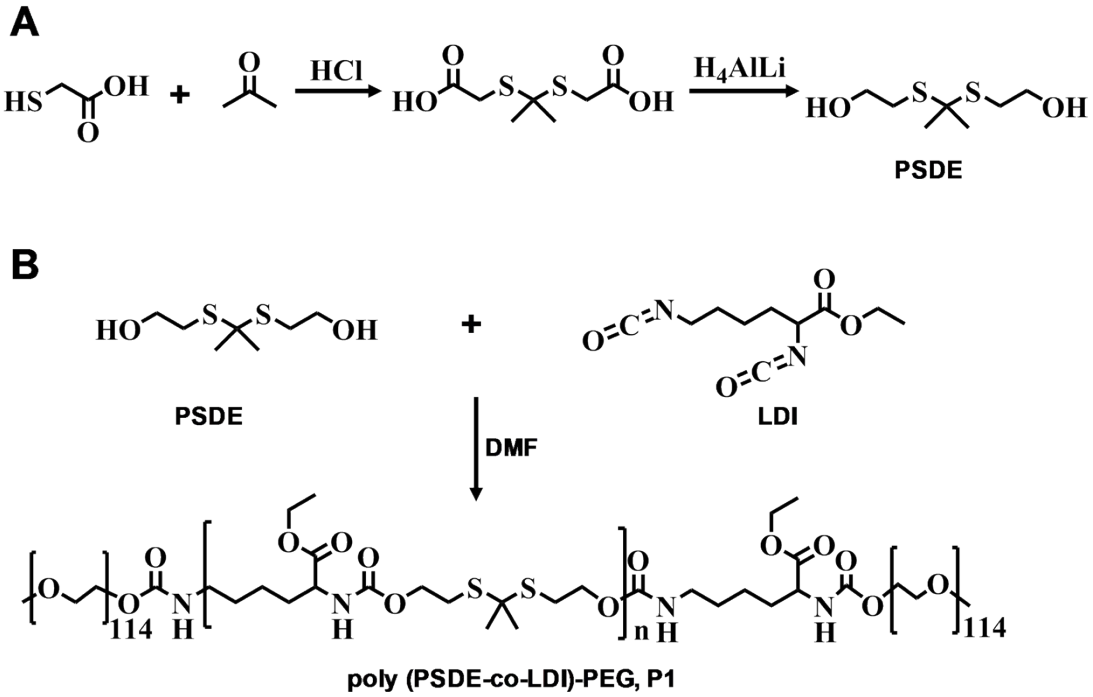


Scheme S1: Synthetic routes of Pt(IV) prodrug. (i) 30% H_2O_2; (ii) succinic anhydride and anhydrous DMF; (iii) hexadecyl isocyanate in anhydrous DMF at 75 ℃; (iv) morpholine in EDC/NHS anhydrous DMF.



Scheme S2: Synthetic routes of the polymer drug carrier P1. (A) preparation of PSDE; (B) Synthesis of the P1 in anhydrous DMF for 24 h.

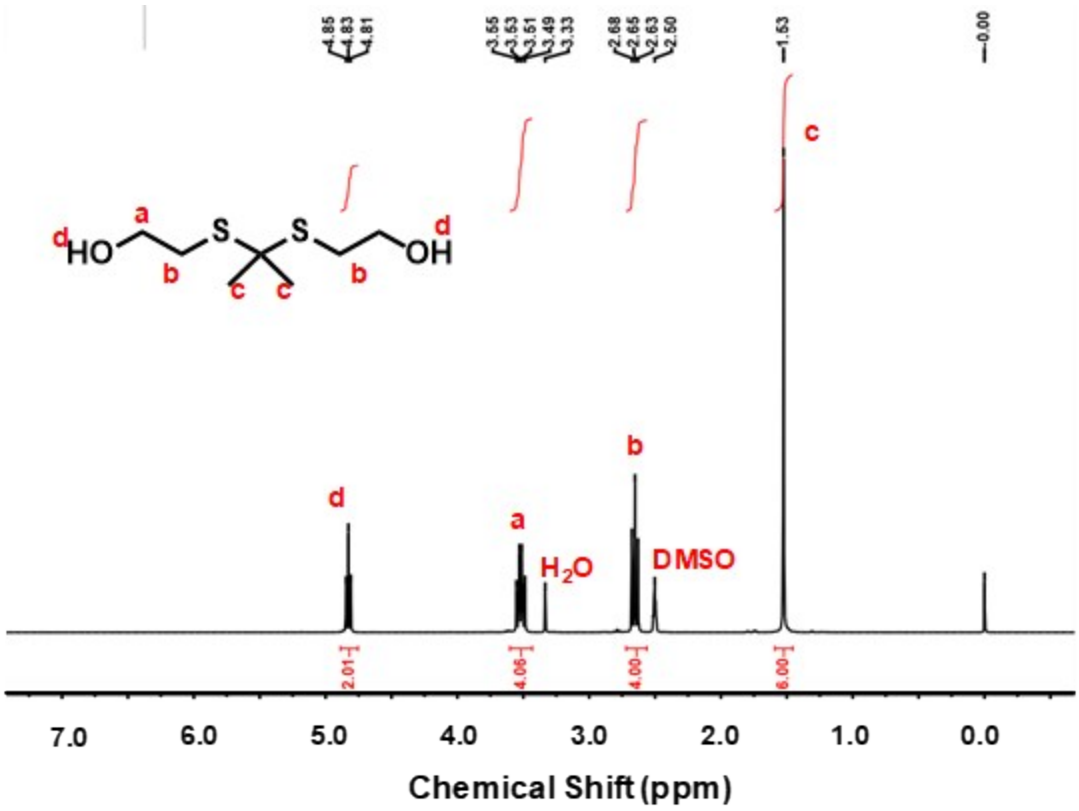


Fig. S1. ^{1}H NMR spectrum of PSDE in DMSO-d6.

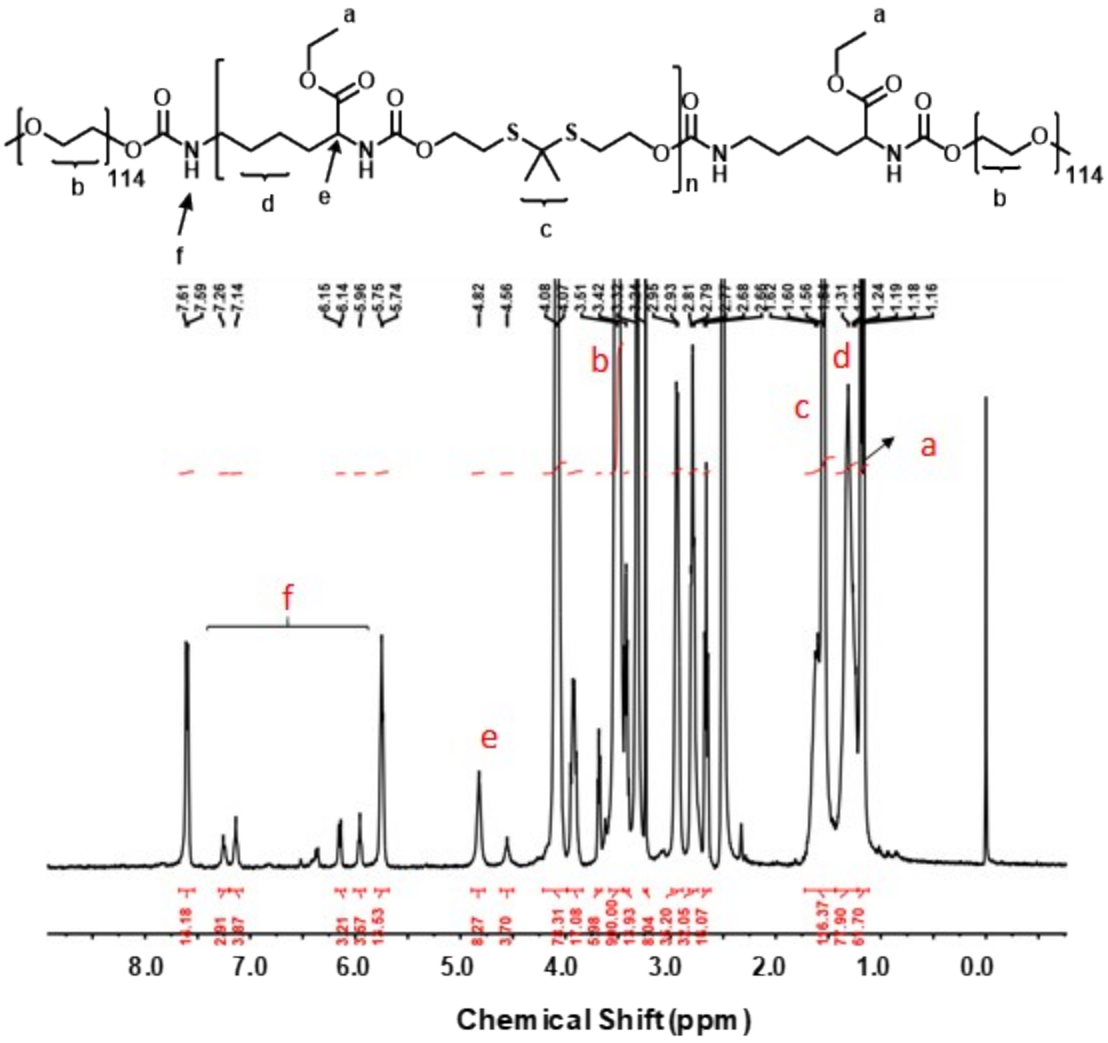


Fig. S2. ^{1}H NMR spectrum of P1 in DMSO-d6.

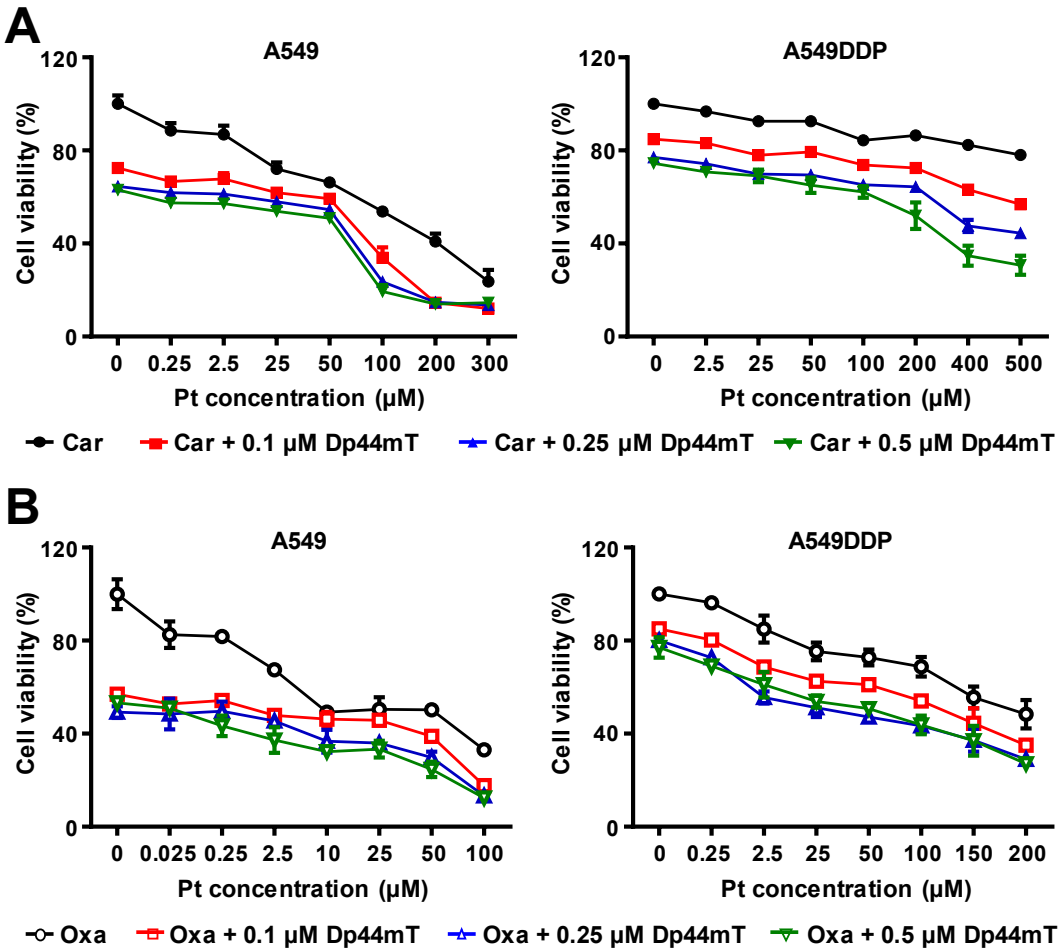


Fig. S3 *In vitro* cytotoxicity of Dp44mT with Carboplatin or Oxaliplatin against A549 and A549DDP cells. (A) The relative cell viabilities of A549 and A549DDP cells exposed to **Carboplatin (Car)** in the presence of different concentrations of Dp44mT for 48 h. (B) The relative cell viabilities of A549 and A549DDP cells exposed to **Oxaliplatin (Oxa)** in the presence of different concentrations of Dp44mT for 48 h.

Table S1 IC_{50} values of cisplatin and Dp44mT in A549 and A549DDP cells.

Cell lines	Cisplatin	Cisplatin	Cisplatin	Cisplatin
		0.1 μM Dp44mT	0.25 μM Dp44mT	0.5 μM Dp44mT
A549	3.92	1.32	0.24	0.10
A549DDP	30.15	3.82	0.42	0.10

** Cells were incubated with these above drug formulations for 48 h. The IC_{50} values were determined by MTT assay.

Table S2 IC_{50} values of Pt(IV) and Dp44mT in A549 and A549DDP cells.

Cell lines	Pt(IV)	Pt(IV)	Pt(IV)	Pt(IV)
		0.1 μM Dp44mT	0.25 μM Dp44mT	0.5 μM Dp44mT
A549	6.40	2.67	1.01	0.09
A549DDP	3.41	0.60	0.24	0.10

** Cells were incubated with these above drug formulations for 48 h. The IC_{50} values were determined by MTT assay.

Table S3 IC_{50} values of Pt(IV), NPs and Dp44mT in various cell lines.

Cell lines	Pt(IV)	Pt(IV)+Dp44mT	NPs	NPs+Dp44mT
A549	2.22	0.31	0.81	0.17
A549DDP	4.50	1.25	1.99	0.75
4T1	4.15	1.03	0.29	0.13

** Cells were incubated with these above drug formulations for 48 h. The IC_{50} values were determined by MTT assay.

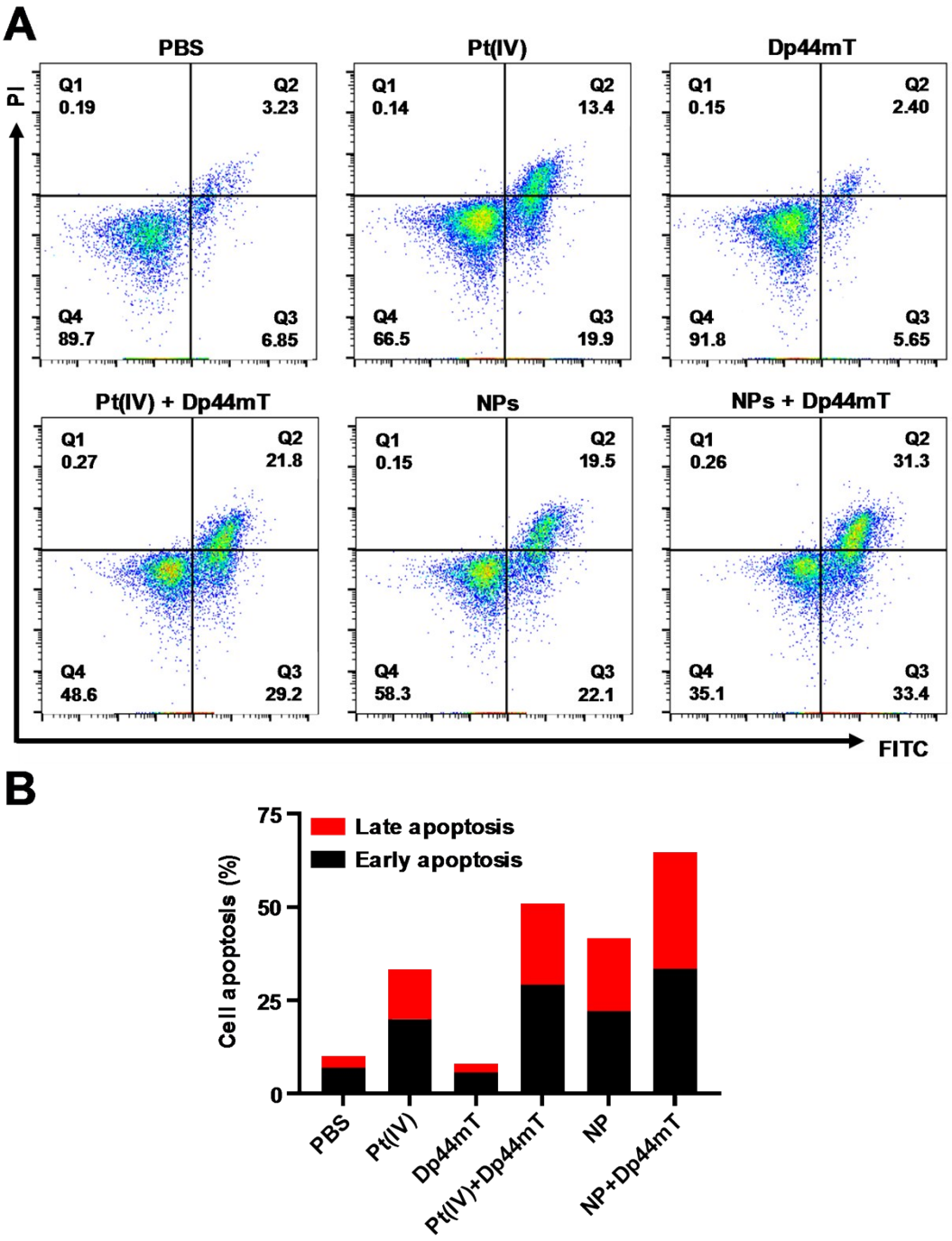


Fig. S4 Apoptosis and the statistical analysis of 4T1 cells with various treatments for 24 h: PBS, 2.5 μM Pt(IV), 0.25 μM Dp44mT, 2.5 μM Pt(IV) + 0.25 μM Dp44mT, 2.5 μM NPs and 2.5 μM NPs + 0.25 μM Dp44mT.

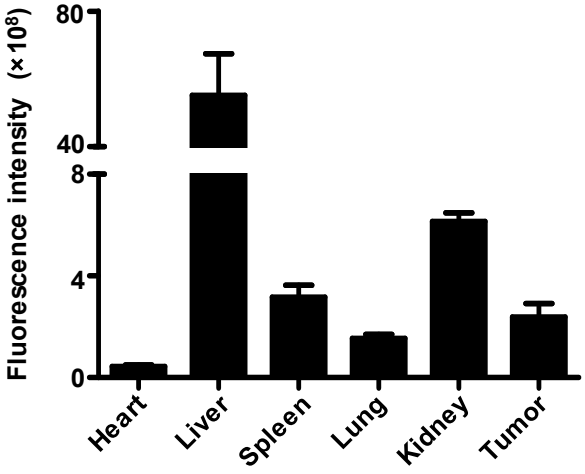


Fig. S5 Statistical analysis of *ex vivo* biodistribution of NPs (labelled with Cy7.5) in mice bearing 4T1 xenografts post 24 h of injection (IVIS, Spectrum CT, PerkinElmer, E_x/E_m=780 nm/810 nm).

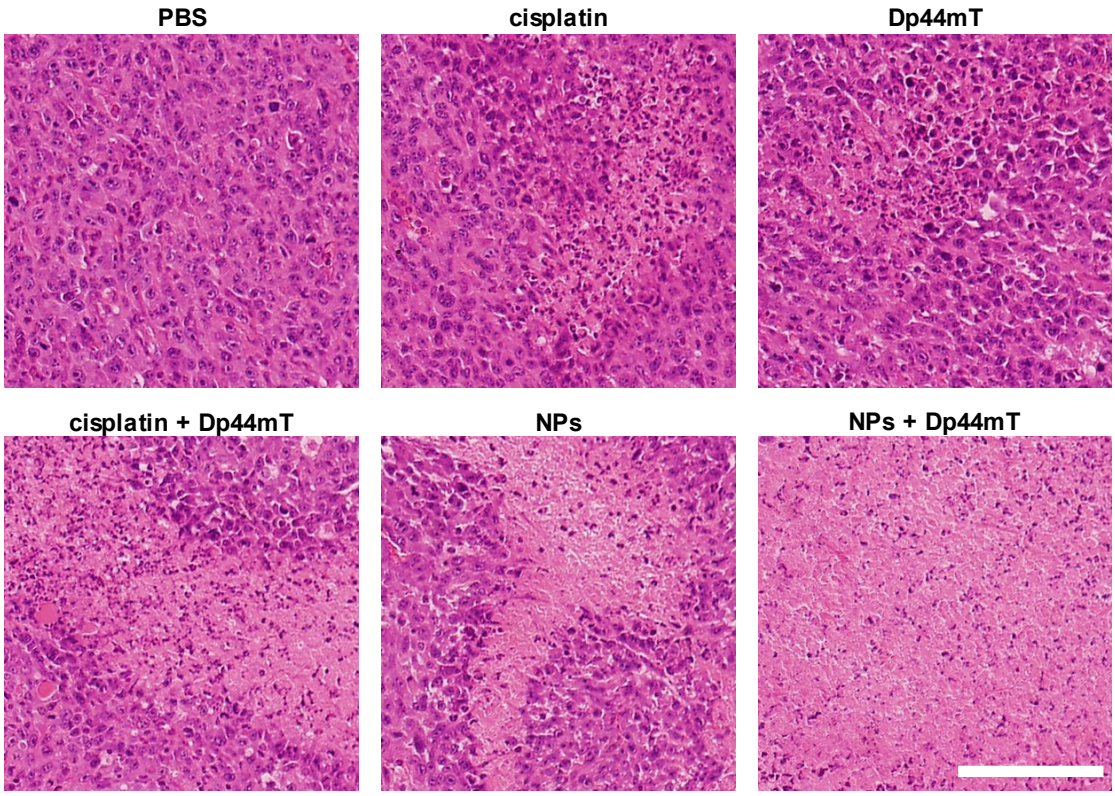


Fig. S6 H&E staining images of tumor sections from mice bearing 4T1 xenografts with different treatments: PBS; Cisplatin (2.5 mg Pt/kg body weight); Dp44mT; Cisplatin (2.5 mg Pt/ kg body weight) + Dp44mT (3 mg/kg body weight); NPs (2.5 mg Pt/kg body weight); NPs (2.5 mg Pt/ kg body weight) + Dp44mT (3 mg/kg body weight). Scale bar: 100 μm.

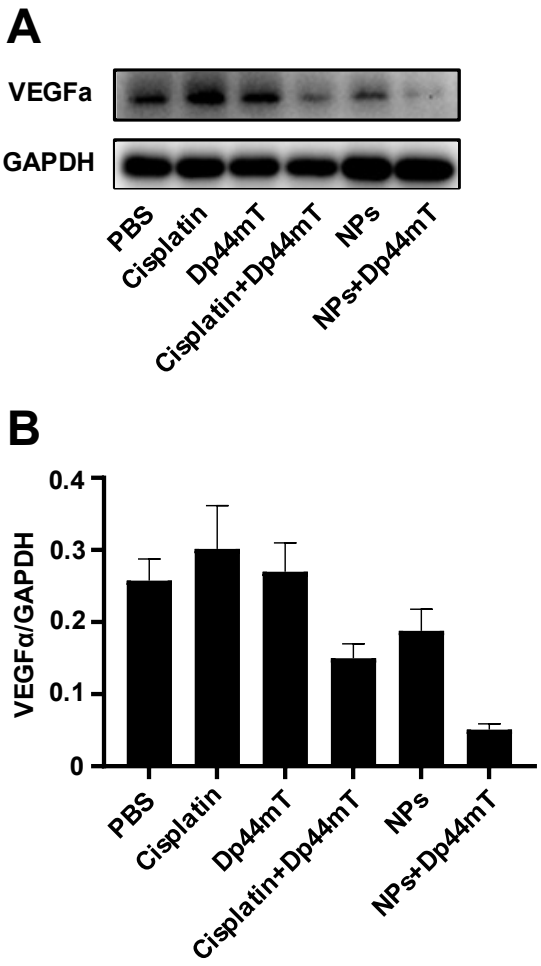


Fig. S7 Expression level (A) and its statistical analysis (B) of VEGFα in tumors of mice bearing 4T1 xenografts with different drug formulations: PBS; Cisplatin (2.5 mg Pt/kg body weight); Dp44mT; Cisplatin (2.5 mg Pt/kg body weight) + Dp44mT (3 mg/kg body weight); NPs (2.5 mg Pt/kg body weight); NPs (2.5 mg Pt/kg body weight) + Dp44mT (3 mg/kg body weight).