Supporting information

Enhanced nanoparticle accumulation by tumor-acidity-activatable release of sildenafil to induce vasodilation

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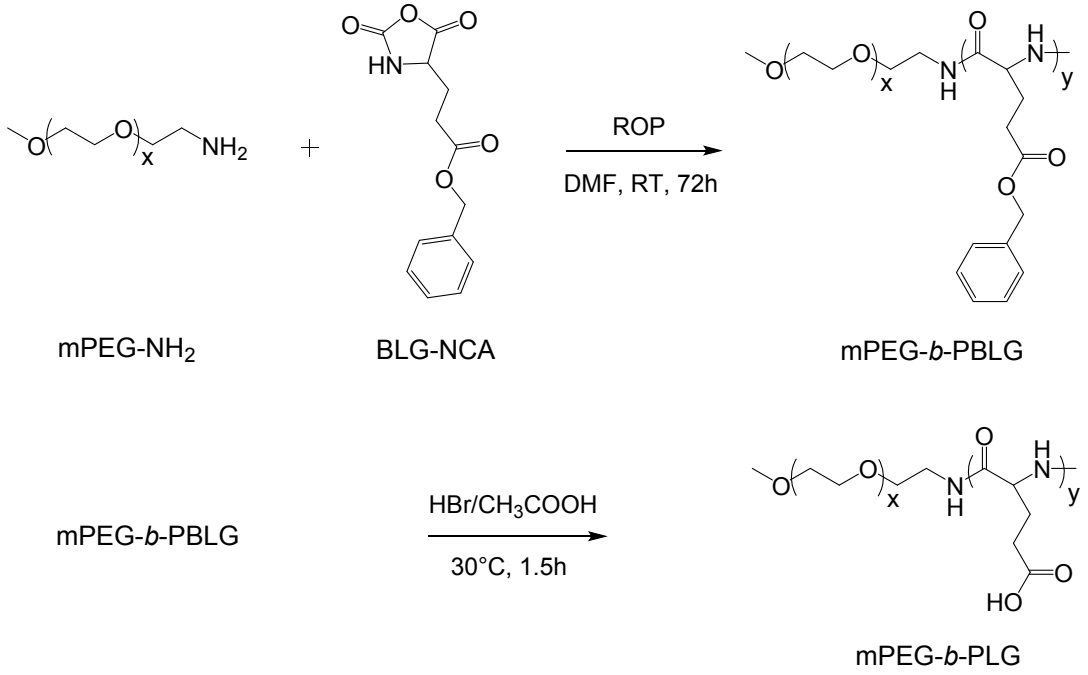

Fig. S1. Synthetic route of mPEG-*b*-PLG.

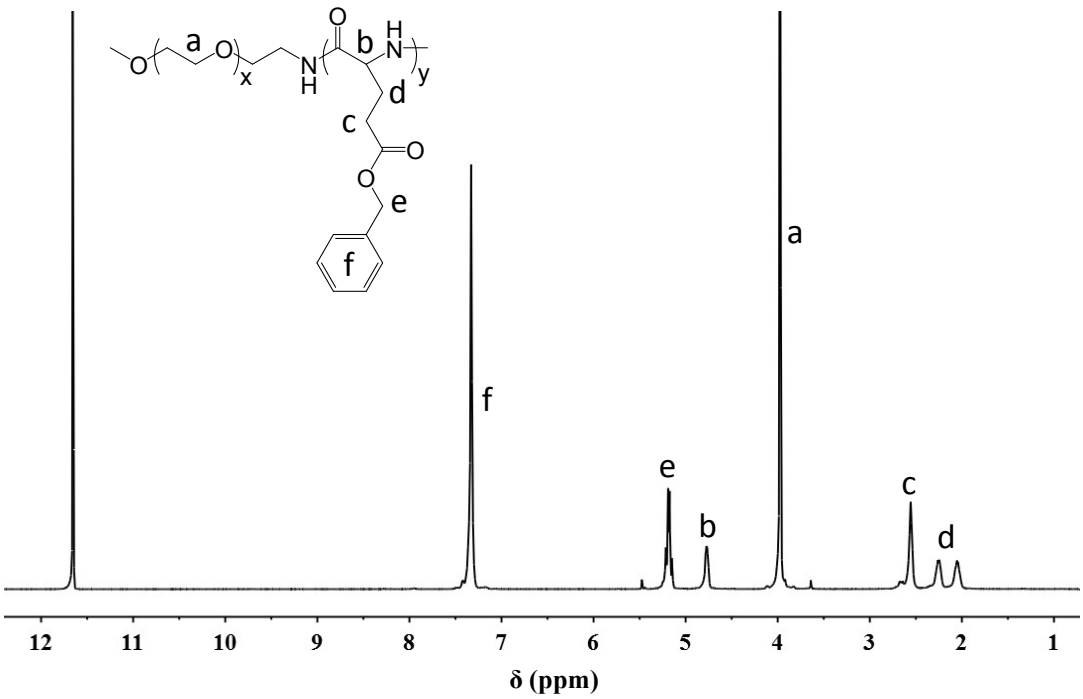

Fig. S2. ^{1}H NMR spectrum of mPEG-*b*-PBLG in CF_3COOD.

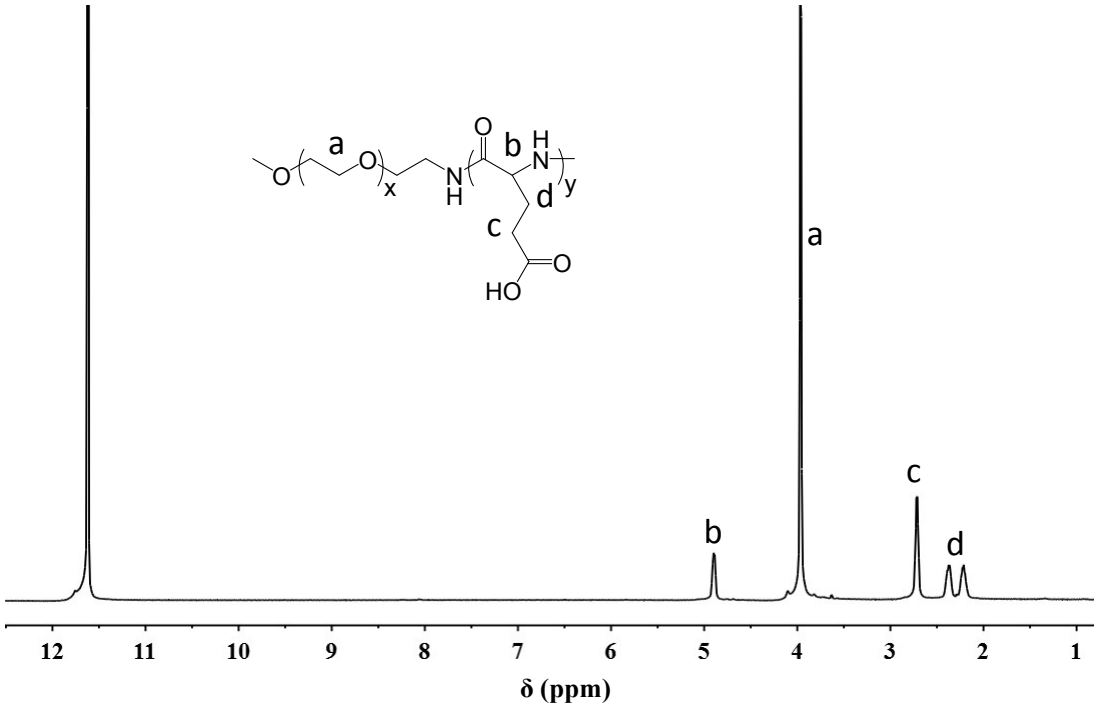

Fig. S3. ^{1}H NMR spectrum of mPEG-*b*-PLG in CF_3COOD.

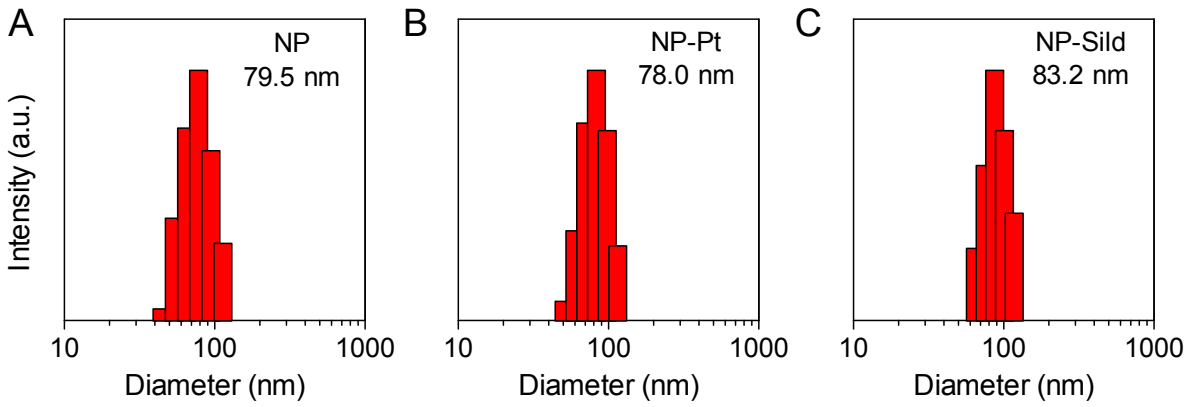

Fig. S4. Particle size of NP (A), NP-Pt (B) and NP-Sild (C) in PBS (pH 7.4) determined by DLS.

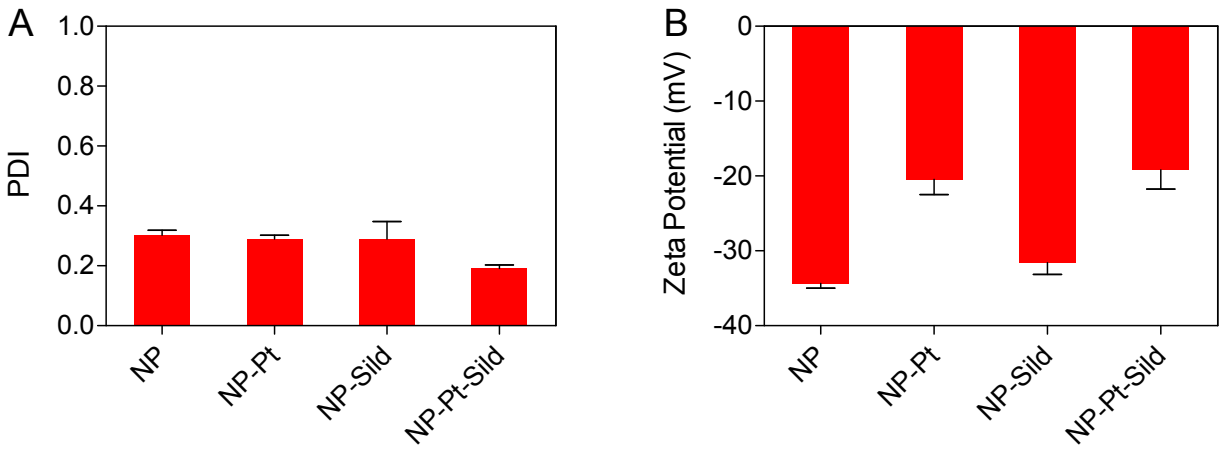

Fig. S5. (A) PDI of NP, NP-Pt, NP-Sild and NP-Pt-Sild in PBS (pH 7.4) determined by DLS. (B) Zeta potential of NP, NP-Pt, NP-Sild and NP-Pt-Sild in PBS (pH 7.4) determined by DLS. Data are shown as mean ± SD (n = 3).

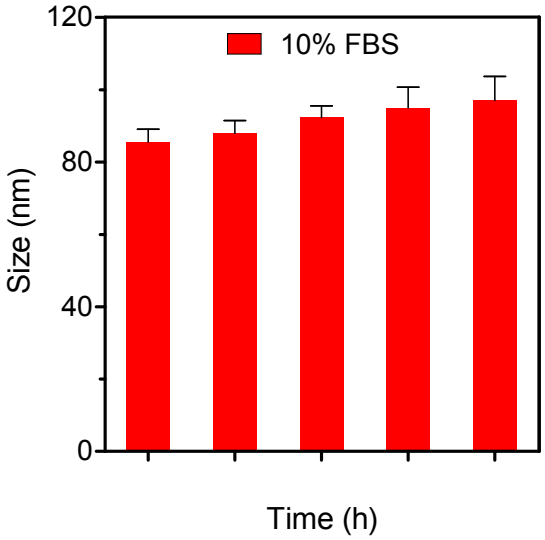

Fig. S6. Particle size of NP-Pt-Sild in PBS (pH 7.4) containing 10% FBS at different times determined by DLS. Data are shown as mean ± SD (n = 3).

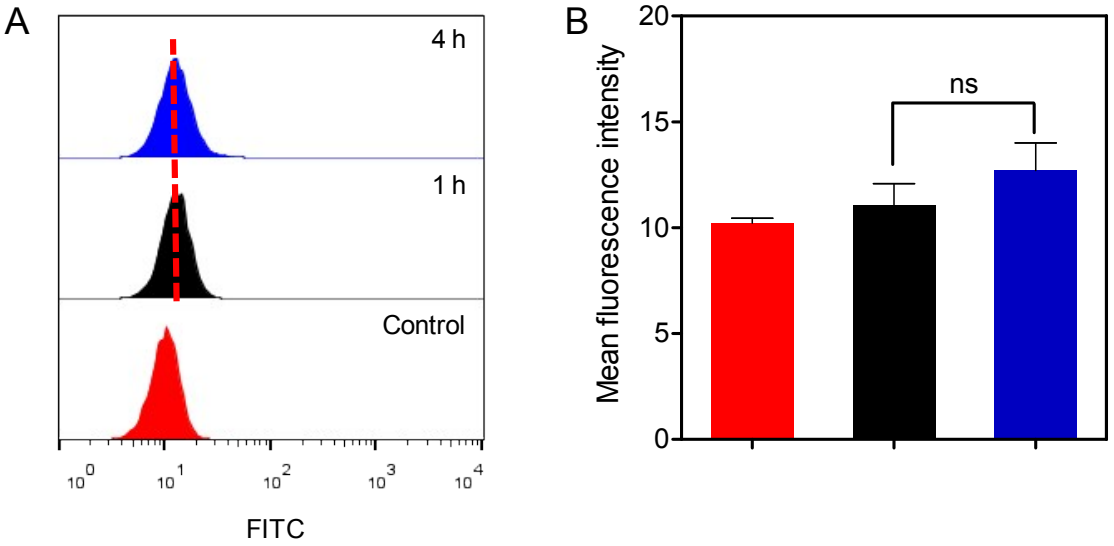

Fig. S7. (A) Cellular internalization of NP-Pt-FITC incubated with B16F10 cells for 1 h or 4 h at 37 °C determined by flow cytometry. (B) Mean fluorescence intensities of B16F10 cells treated as described in (A) determined by flow cytometry. ns: no significant difference. Data are shown as mean ± SD (n = 3).

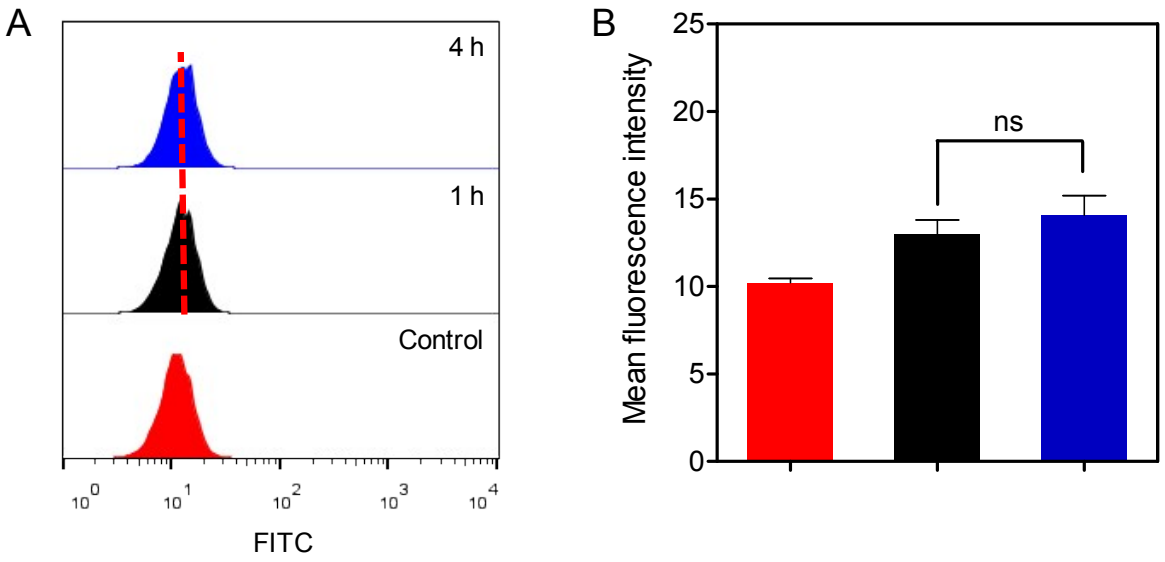

Fig. S8. (A) Cellular internalization of NP-Sild-FITC incubated with B16F10 cells for 1 h or 4 h at 37 °C determined by flow cytometry. (B) Mean fluorescence intensities of B16F10 cells treated as described in (A) determined by flow cytometry. ns: no significant difference. Data are shown as mean ± SD (n = 3).

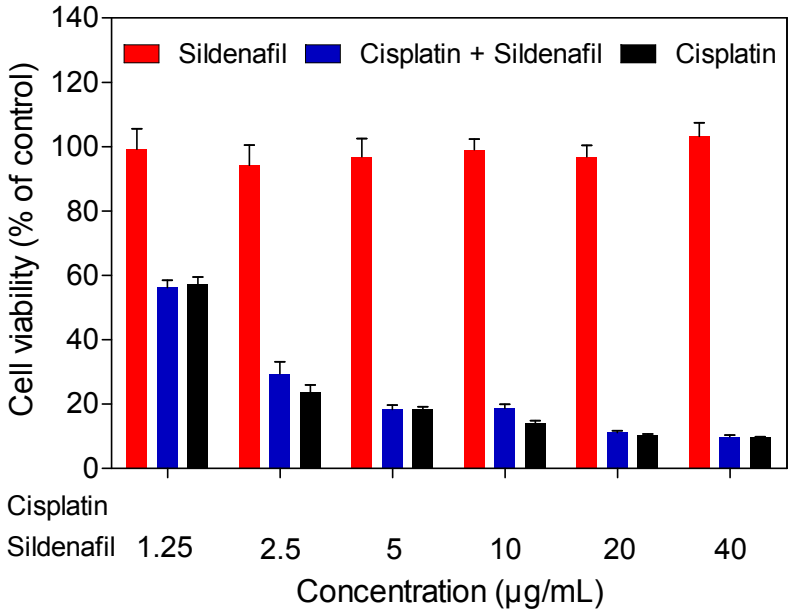

Fig. S9. *In vitro* cytotoxicity of sildenafil, the mixture of cisplatin and sildenafil, and cisplatin against B16F10 cells as determined by MTT assay. Cells were incubated with the indicated agents for 72 h at 37 °C. Data are shown as mean ± SD (n = 3).

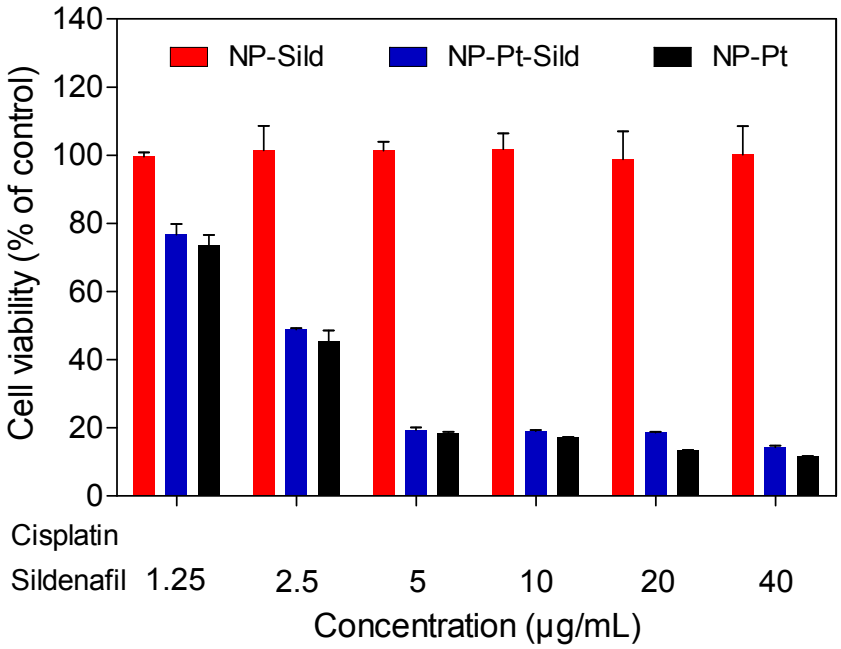

Fig. S10. *In vitro* cytotoxicity of NP-Sild, NP-Pt-Sild and NP-Pt against B16F10 cells as determined by MTT assay. Cells were incubated with the indicated agents for 72 h at 37 °C. Data are shown as mean ± SD (n = 3).

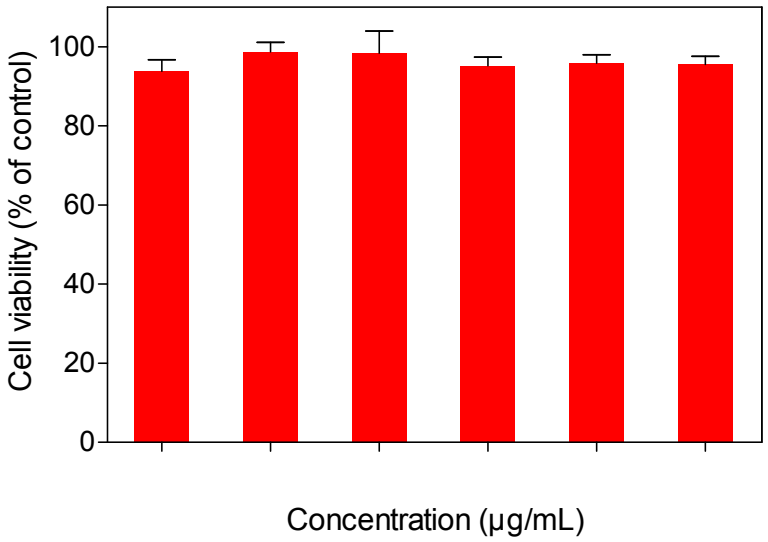

Fig. S11. *In vitro* cytotoxicity of NP against B16F10 cells as determined by MTT assay. Cells were incubated with NP for 72 h at 37 °C. Data are shown as mean ± SD (n = 3).

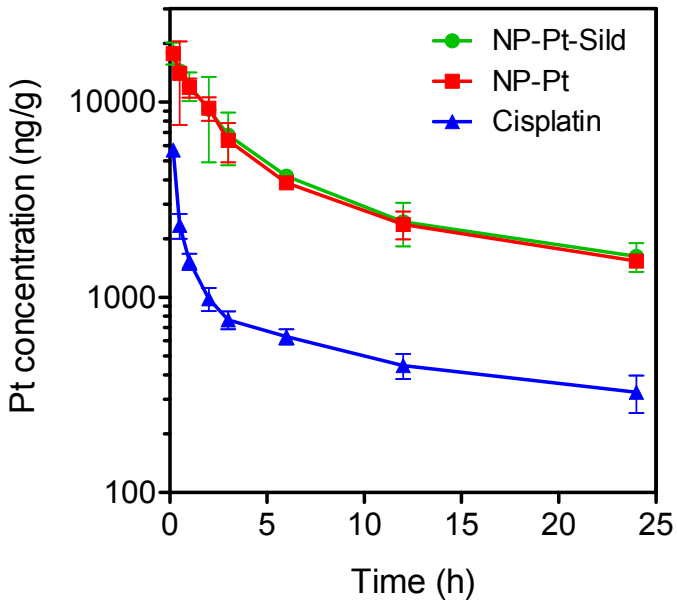

Fig. S12. Pharmacokinetics of cisplatin delivered by free cisplatin solution, NP-Pt and NP-Pt-Sild following intravenous injection.

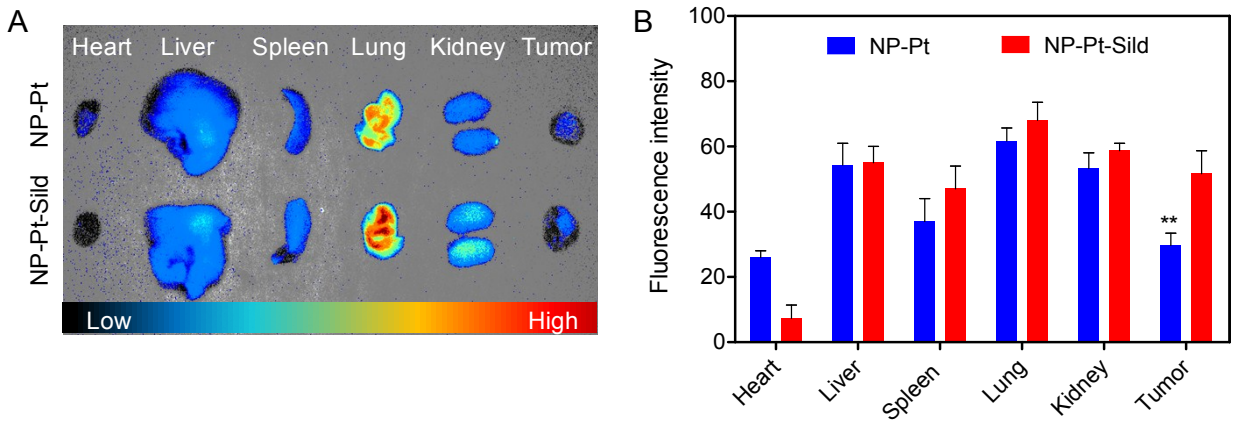

Fig. S13. (A) *Ex vivo* fluorescence imaging of the excised tumors and major organs of NP-Pt-Cy5 and NP-Pt-Sild-Cy5 treated B16F10 tumor-bearing mice at 24 h post-injection. (B) Biodistribution of the corresponding nanoparticles in the tumors and major organs of NP-Pt-Cy5 and NP-Pt-Sild-Cy5 treated B16F10 tumor-bearing mice at 24 h post-injection. *: compared with NP-Pt-Sild. **$p < 0.01$. Data are shown as mean ± SD (n = 3).

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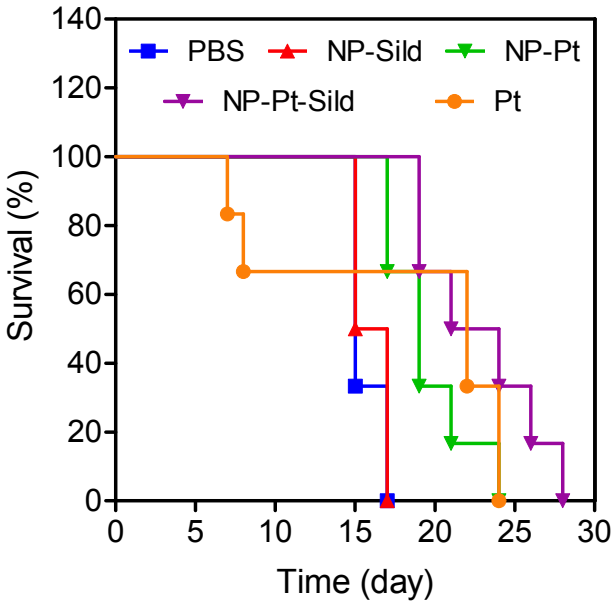

Fig. S14. Survival rates of the B16F10 tumor-bearing mice after intravenous injection of PBS, NP-Sild, NP-Pt, Pt and NP-Pt-Sild on day 0, 2, 7 and 9 (4 mg kg^{-1} cisplatin, 2 mg kg^{-1} sildenafil) within the observation period of 28 d.

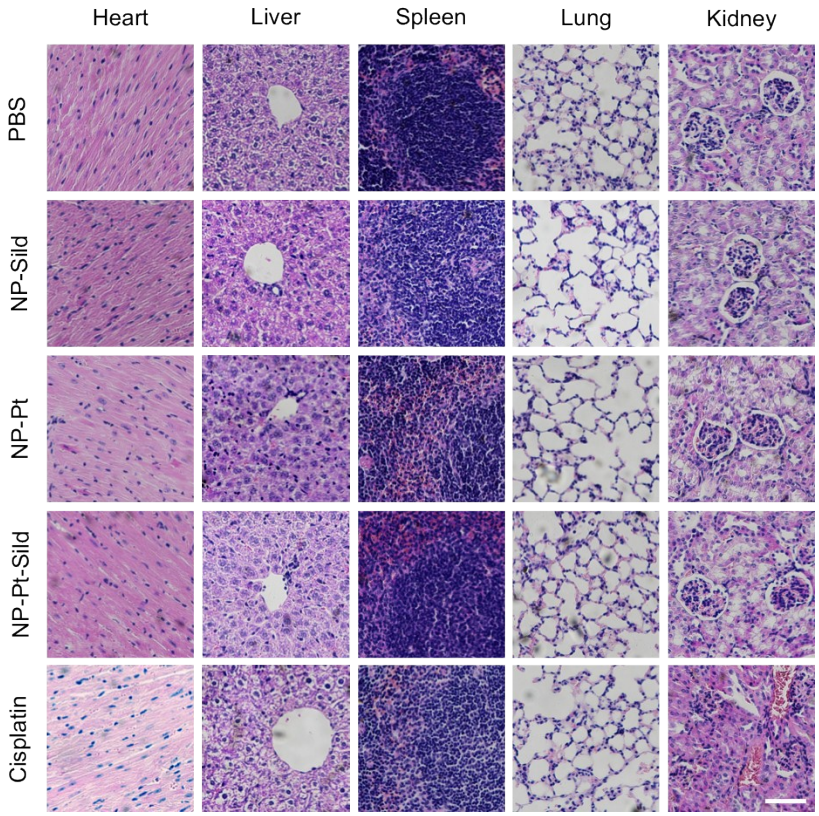

Fig. S15. H&E staining of major organs from the B16F10 tumor-bearing mice at the end of treatment. Scale bar = 100 μm.

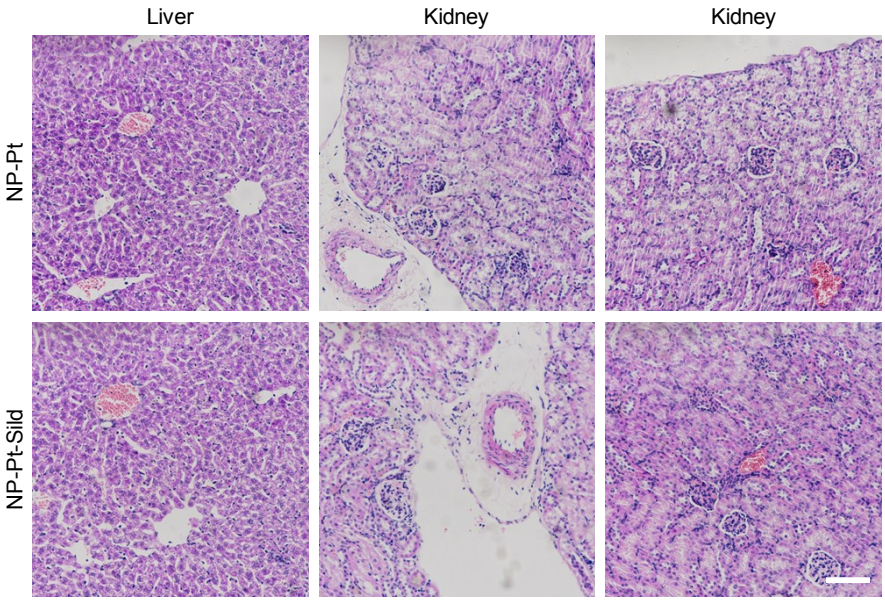

Fig. S16. H&E staining of livers and kidneys from the B16F10 tumor-bearing mice at the end of treatment. Scale bar = 100 μm.