Supporting Information

Lipid-Coated Cisplatin Nanoparticles Induce Neighboring Effect and Exhibit Enhanced Anticancer Efficacy

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Preparations of DiI labeled LPC NPs. DiI labeled LPC NPs were prepared in a method similar to the preparation of LPC NPs. Briefly, a mixture containing 1.0 mL of LPC NPs core, 50 μL of 20 mM DOTAP, 50 μL of 20 mM Cholesterol, 50 μL of 10 mM DSPE–PEG-2000 or DSPE–PEG–AA and 50 μL 1 mM DiI were combined. After evaporating the chloroform, the residual lipids were dispersed in 1.0 mL of d-H_2O.

Cell Toxicity Assay. A375M cells were seeded in 96-well plates at a density of 2000 cells/well and incubated in 10% FBS of DMEM containing 100 U/mL penicillin and 100 mg/mL streptomycin for 20 h. Then, the medium was removed and replaced by Opti-MEM containing CDDP or LPC NPs. Forty-eight hours later, a CellTiter 96 AQueous One Solution

Cell Proliferation Assay (Promega, Madison, WI) kit containing the tetrazolium compound MTS was used to assay cell viability according to the manufacturer's protocols. The IC_{50} values were calculated using Graphpad Prism 5 (Graphpad Software Inc.)

Cellular Uptake. A375M cells ($2x10^5$) were seeded in 35 mm, glass-bottom dishes (MatTek Corporation, MA) 20 h before the experiments began. The cells were treated with LPC NPs labeled with NBD-PE at a concentration of 100 μM Pt at 37 °C for 4 h. The cells were washed twice with PBS. The nucleus was stained with Hoechest 33342 (Sigma, St Louis, MO), and lysosomes were stained by lysotracker red (Invitrogen, Carlsbad, CA). Then, the sample was observed using an Olympus FV 1000-MPE microscope (Olympus, Japan).

***In Vitro* Drug Release in 50% FBS.** A suspension of LPC NPs containing 200 μg Pt in 50% FBS was incubated at 37°C on a shaker at 300 rpm. During different time points, the corresponding samples were centrifuged at 16, 000g for 20 min and the platinum drug released into the supernatant liquid was measured.

Cellular Release of Pt drug and Its Cell Toxicity. A375M cells were seeded in 24-well plates at a density of 3×10^4 cells per well and incubated for 20 h in 10% FBS of DMEM containing 100 U/mL penicillin, and 100 mg/mL streptomycin. The medium was then removed and replaced by 100 μM of Opti-MEM containing CDDP or LPC NPs. All transfections were performed in triplicate. After incubation for 4 h at 37°C in a 5% CO_2, humidified atmosphere, the medium was aspirated. Cells were then washed and lysed in order to determine their uptake of NPs. The amount of Pt in cells was measured using ICP-MS. For the study of cellular release of Pt drug from cells, the medium was collected and replaced

with fresh, completed medium at different time points. The intact NPs and free drug released into the medium were separated by centrifugation at 16,000g for 20 min. The amount of Pt in the supernatant and pellets was measured using ICP-MS. To evaluate the toxicity of released drugs, the medium was transferred and incubated with untreated cells. Forty-eight hours later, a CellTiter 96 AQueous One Solution Cell Proliferation Assay (Promega, Madison, WI) kit containing the tetrazolium compound MTS was used to assay cell viability according to the manufacturer's protocols.

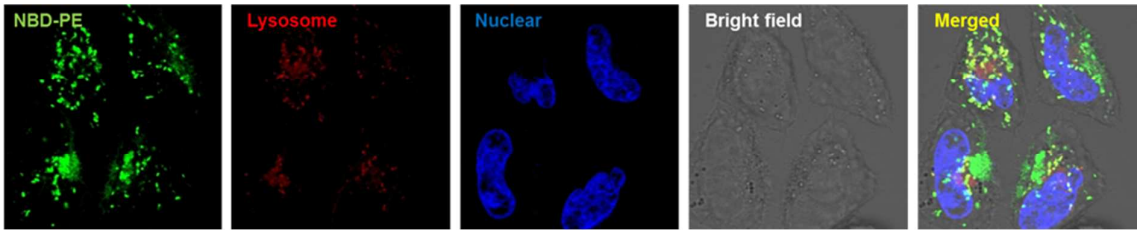

Figure S1. *In vitro* cell uptake of LPC NPs imaged using confocal microscopy. LPC NPs were labeled with NBD-PE lipid (green). Lysosome (red) and nucleus (blue) were stained by Lysotracker-Red and Hoechst 33342, separately.

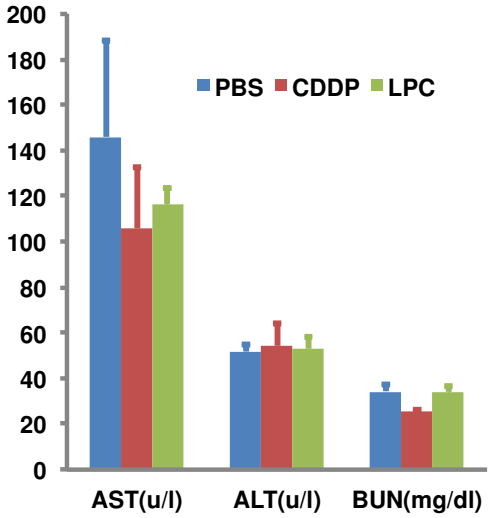

Figure S2. Kidney and liver function parameters, AST (aspartate aminotransferase), ALT (alanine aminotransferase) and BUN (blood urea nitrogen).

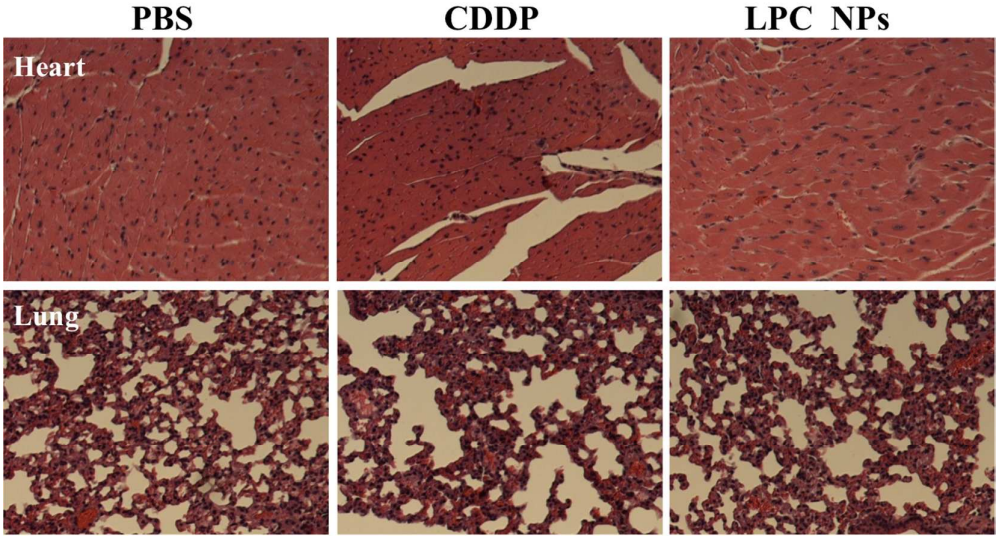

Figure S3. H&E staining of heart and lung from mice which received four doses of treatment (1 mg/kg each).