Electronic Supplementary Information (ESI)

Design of zwitterionic polyester based nano-carriers for platinum (IV) prodrug delivery†

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1. Experimental supplement

1.1. Instruments

^{1}H and ^{13}C NMR spectra were measured using Bruker AVANCE AV400 NMR spectrometer. Fourier transform infrared spectroscopy (FT-IR) spectra were recorded on a Nicolet 6700 spectrometer. Electrospray mass spectrometry (ESI-MS) measurements were performed on Liquid chromatography mass spectrometer (Q-TOF, Waters) equipped with an electrospray interface (ESI). The molecular weight and molecular weight distribution were determined by gel permeation chromatography (GPC) on an apparatus with Waters degasser, Waters 1515 Isocratic HPLC pump, and three Styragel HT3 7.5 × 300 mm columns in series with a mobile phase of chloroform (J. T. Baker) pumped at a flow rate of 1.0 mL/min at temperature 35 ^{o}C. The detector is Waters 2414 Refractive Index Detector. Micelle size and polydispersity were determined using dynamic light scattering (DLS) at 25 ^{o}C by a Malvern Zetasizer Nano ZS90 equipped with a 633 nm vertically polarized He–Ne laser using back-scattering detection. The di□raction angle is 90^{o}. Measurements were done in triplicate at 25 ^{o}C. Transmission electron microscopy (TEM) was performed using a JEM-1011 TEM operated at an accelerating voltage of 100 kV. The samples were prepared by dropping 7 μL of 1.25 mg mL^{-1} micelle suspension on the copper grid followed by staining with

phosphotungstic acid (20 mg mL^{-1}). An inductively coupled plasma mass spectrometer (ICP-MS, 7700x, Agilent Technologies, USA) was used to measure platinum loading in the polymer-Pt(IV) conjugates. An inductively coupled plasma mass spectrometer (ICP-MS, Thermo iCAP RQ, Thermo Fisher, USA) was used for quantitative determination of trace levels of platinum in the cell lysis liquid and dialysis samples in drug release experiments. The thermodynamic properties of the polyesters and nanoparticles were measured by Thermo Gravimetric Analyzer (TGA 8000, N_2, PerkinElmer, USA) and Differential Scanning Calorimeter (DSC，Q200 liquid nitrogen，TA instruments，USA). Fluorescence images were captured with Confocal Laser Scanning Biological Microscope FV1000-IX81 (Olympus, Japan), with 405, 488, 635 nm laser as the excitation sources. The quantification of the intracellular uptake of the platinum drug-loaded nanoparticles was determined by using CytoFLEX Flow Cytometry (Beckman Coulter Commercial Enterprise (China) Co, Ltd).

1.2. Cell culture

A2780 cells were grown in RPMI 1640 (Corning) supplemented with 10% fetal bovine serum, 0.03% L-glutamine and 1% penicillin/streptomycin in 5% CO_2 at 37 ^oC. HEK-293 cells were cultured in DMEM (Corning) supplemented with 10% fetal bovine serum, 0.03% L-glutamine and 1% penicillin/streptomycin in 5% CO_2 at 37 ^oC.

2. Supplementary figures

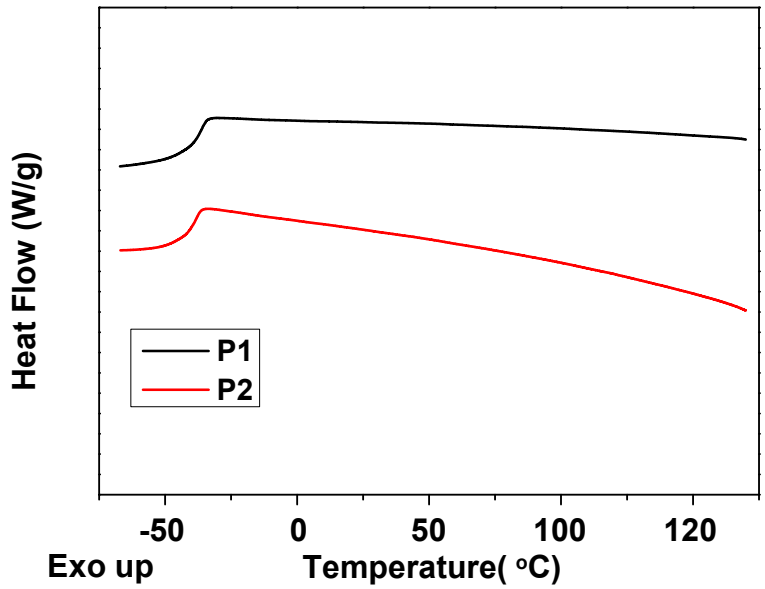
Table S1. Composition and molecular weight of the copolymer P(BF-ran-PEG200F).

BF/PEG molar ratio in feed	The time of transesterification reaction/h	The BF/EGF ratio in copolymer [a]	M_n ×10^{-4} (g/mol) [b]	M_w ×10^{-4} (g/mol) [b]	PDI (M_w/M_n) [b]	Name
1: 1.05	7	38.0: 62.0	2.31	3.43	1.48	P1
1: 1.05	9	33.0: 67.0	2.28	5.40	2.37	P2

[a] Calculated by NMR spectra.

[b] Detected by GPC.

A



B

The ratio of chain segment (BF/EGF)	T_g / °C
38.0 : 62.0	-36.31
33.0 : 67.0	-38.30

Figure S1. A) DSC heating scans of the copolymers for T_g analysis. B) The glass transition temperatures of the copolymers show in the table.

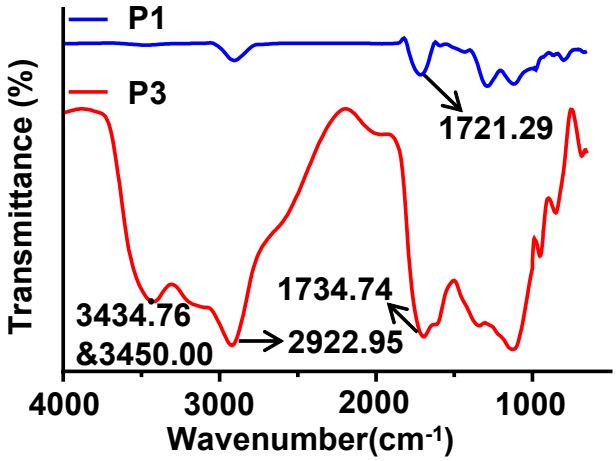


Figure S2. FT-IR spectrum of the zwitterionic copolyester P3.

A

Sample	d_{DLS}/nm	PDI [a]
P3	118.7	0.522
P4	51.32	0.686

B

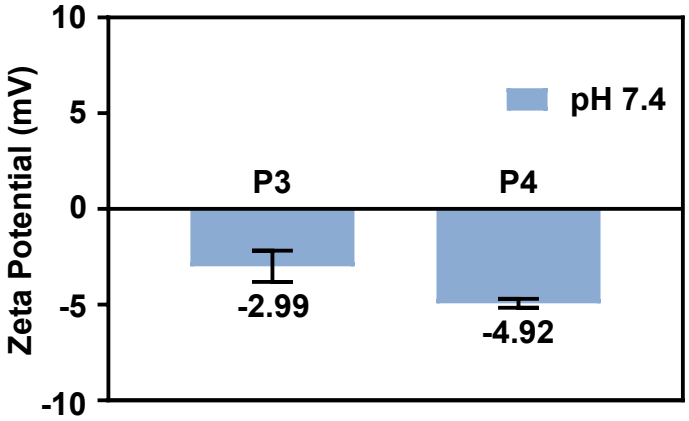


Figure S3. A) The size data ([a] These data show the systems are medium dispersion of particle size) and B) zeta potential values of P3/P4 in PBS buffer solution at pH 7.4. The average values and their standard deviations, from nine measurements, are shown.

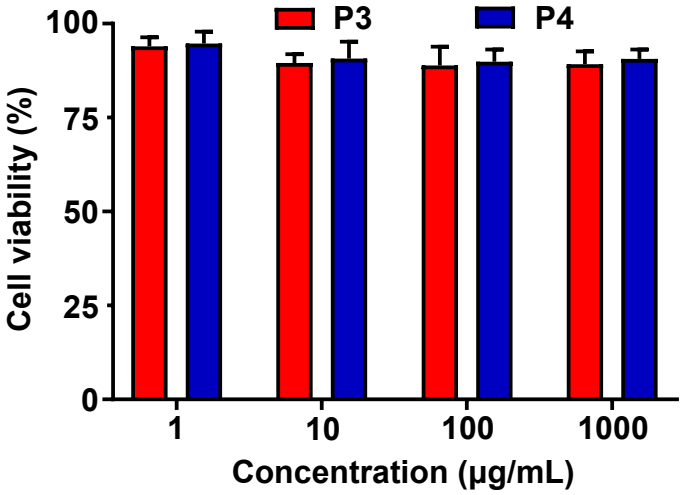
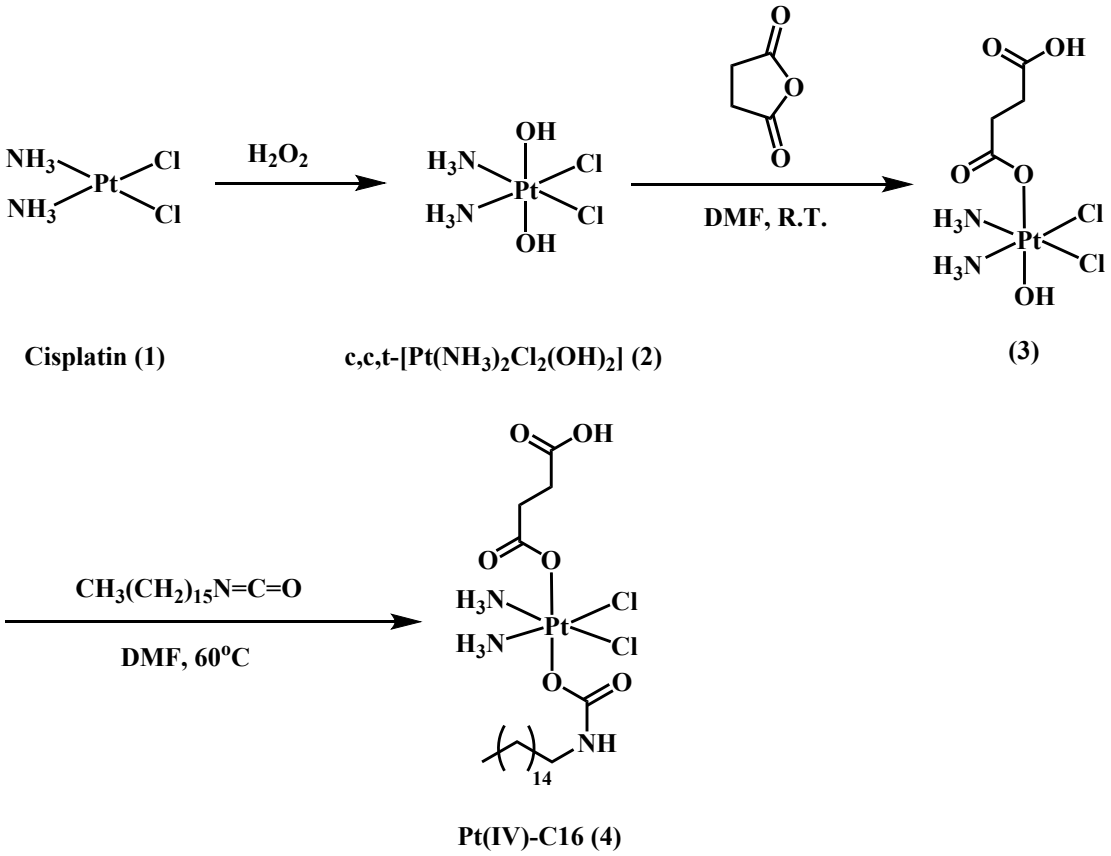
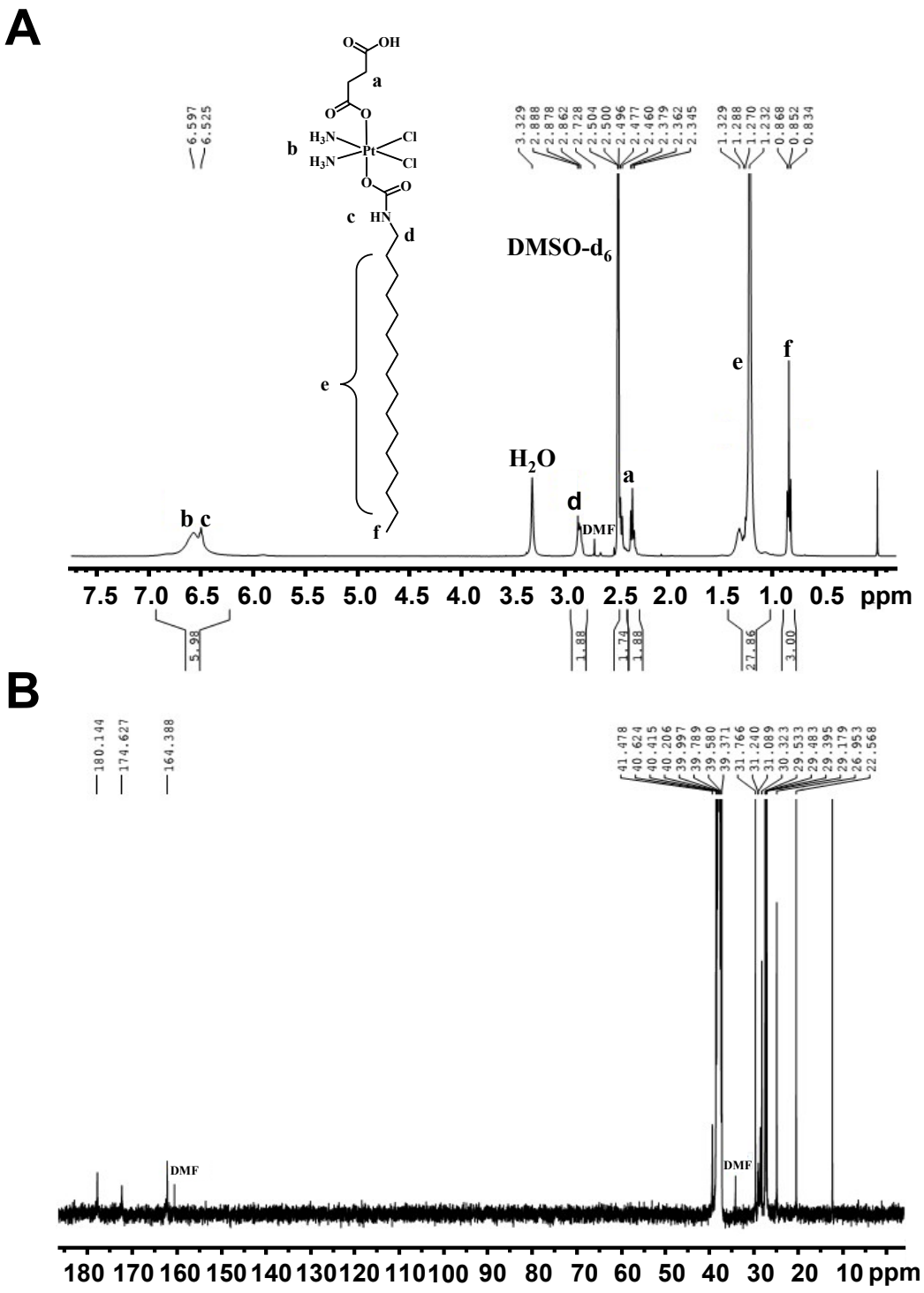


Figure S4. *In vitro* cytotoxicity study of the polymer P3 and P4 on A2780 cells for 48 h determined by MTT assay.



Scheme S1. The synthesis of the platinum prodrug Pt(IV)-C16.


A
B
DMSO-d6
H2O
DMF
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

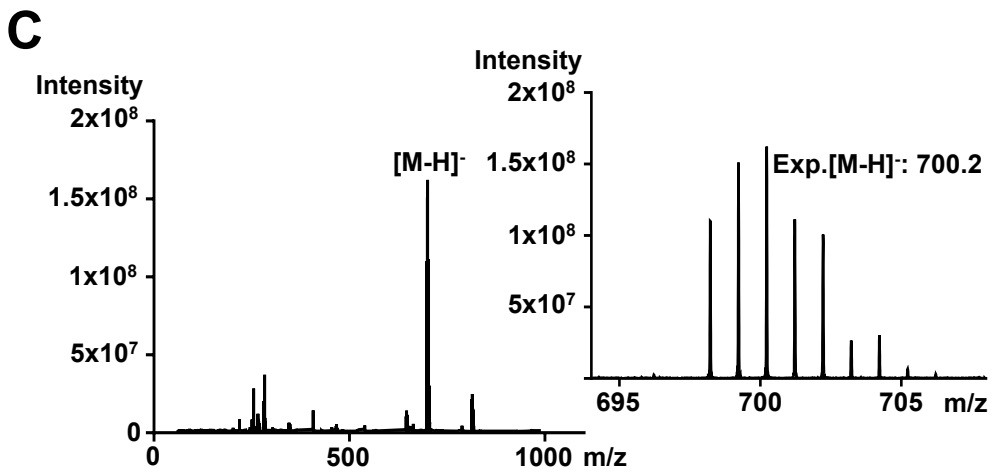


Figure S5. The characterization of the synthesized prodrug Pt(IV)-C16. A) The ^{1}H-NMR spectrum. B) The ^{13}C-NMR spectrum. C) The ESI-MS spectrum.

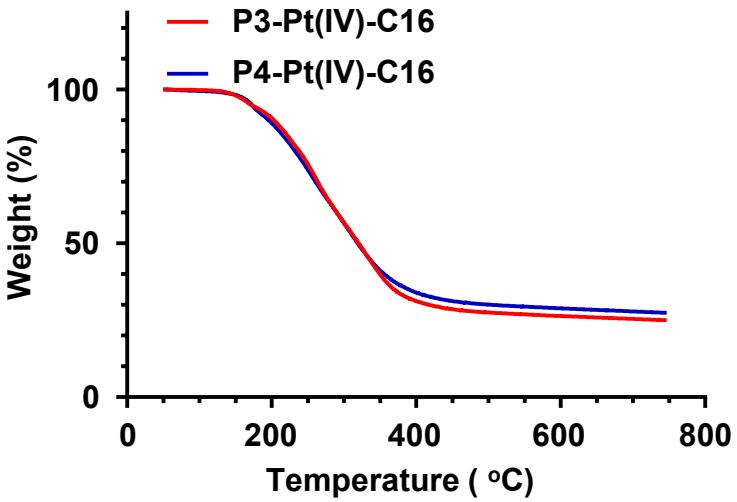


Figure S6. The thermostable curves of the lyophilized P3/P4-Pt(IV)-C16 nanoparticles analyzed by thermal gravimetric analyzer.

Table S2. The drug loading capacity of P3/P4-Pt(IV)-C16 detected by ICP-MS.

Sample	195 Pt [He] Concentration [ng/mL]	The Graft Ratio by EDC/NHS Reaction [%]
P3-Pt(IV)-C16	4.52	15.26
P4-Pt(IV)-C16	6.96	28.03