Supplementary Information for:

Dual endogenous stimuli-responsive polyplex micelles as smart two-step delivery nanocarriers for deep tumor tissue penetration and combating drug resistance of cisplatin

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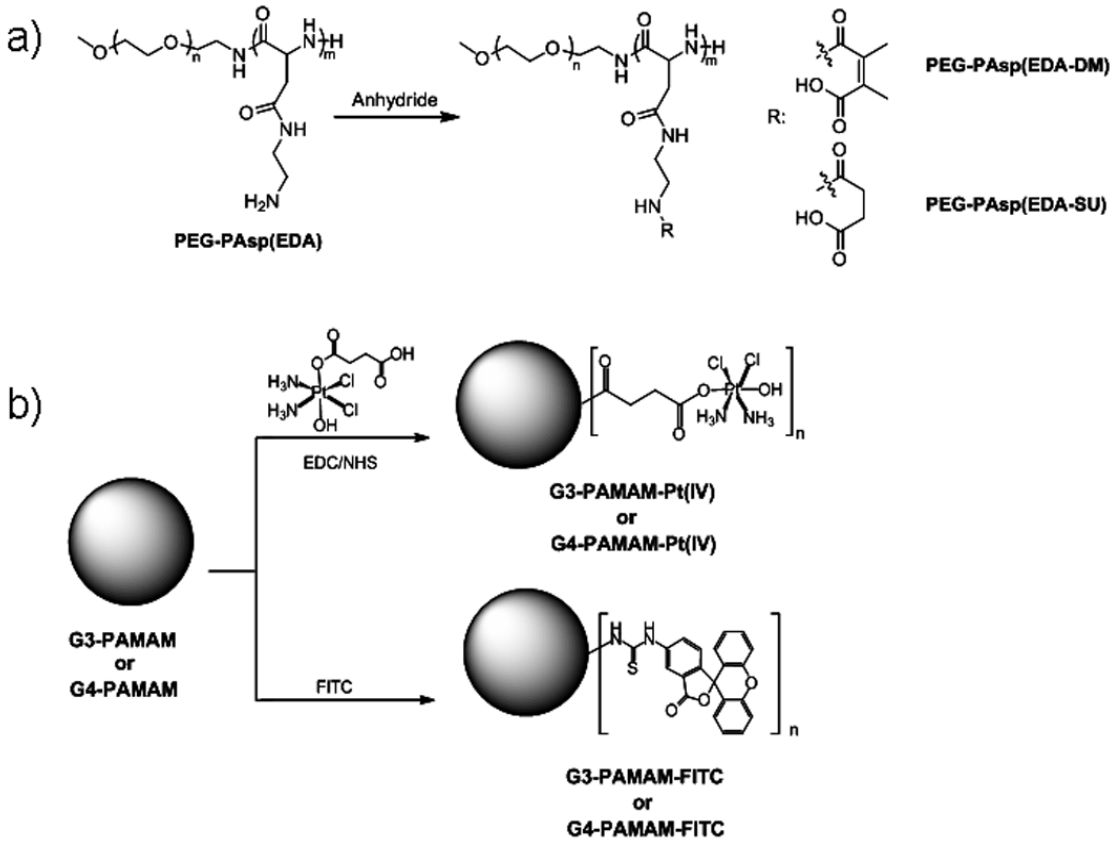

Scheme S1. Synthetic routes for the preparation of (a) block copolymers, PEG-PAsp(EDA-DM) and PEG-PAsp(EDA-SU), and (b) Pt(IV) or FITC-conjugated PAMAM dendrimers.

Table S1. DLS characterization of the polyplex micelles prepared from the complexation between PEG-PAsp(EDA-DM) and PAMAM-Pt(IV).

Polyplex micelles	Diameter / nm	μ_2/Γ^2
PEG_{273}-$PAsp(EDA\text{-}DM)_{68}$/G3-PAMAM-Pt(IV)	140.2	0.212
PEG_{273}-$PAsp(EDA\text{-}DM)_{68}$/G4-PAMAM-Pt(IV)	165.7	0.173
PEG_{454}-$PAsp(EDA\text{-}DM)_{96}$/G3-PAMAM-Pt(IV)	142.3	0.091
PEG_{454}-$PAsp(EDA\text{-}DM)_{96}$/G4-PAMAM-Pt(IV)	222.5	0.092

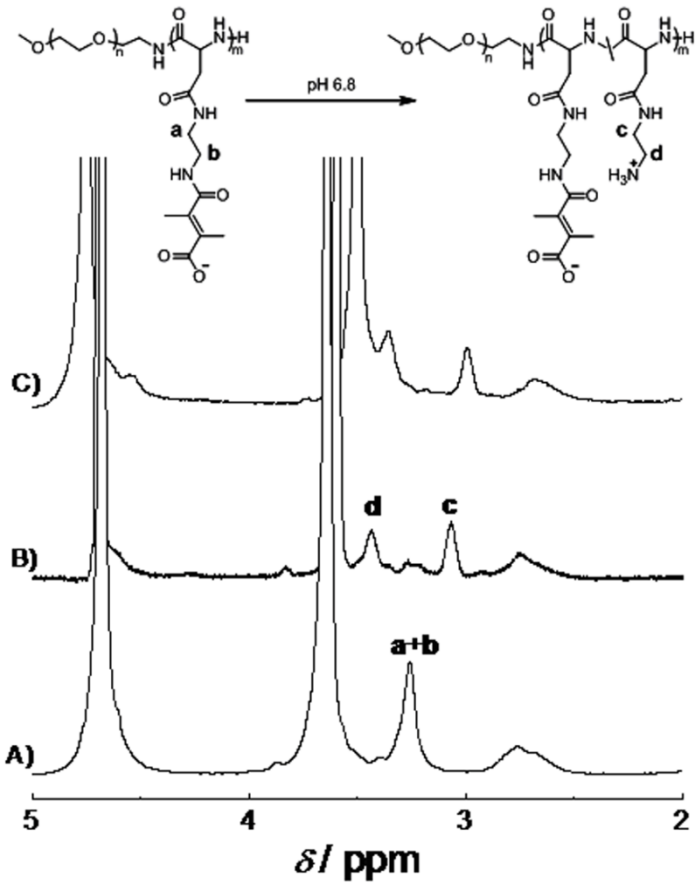

Fig. S1. ^{1}H NMR spectra recorded for PEG-PAsp(EDA-DM) block copolymer in D_2O at pH 6.8 after incubation for varying times (A: 0 min, B: 60 min, and C: 120 min).

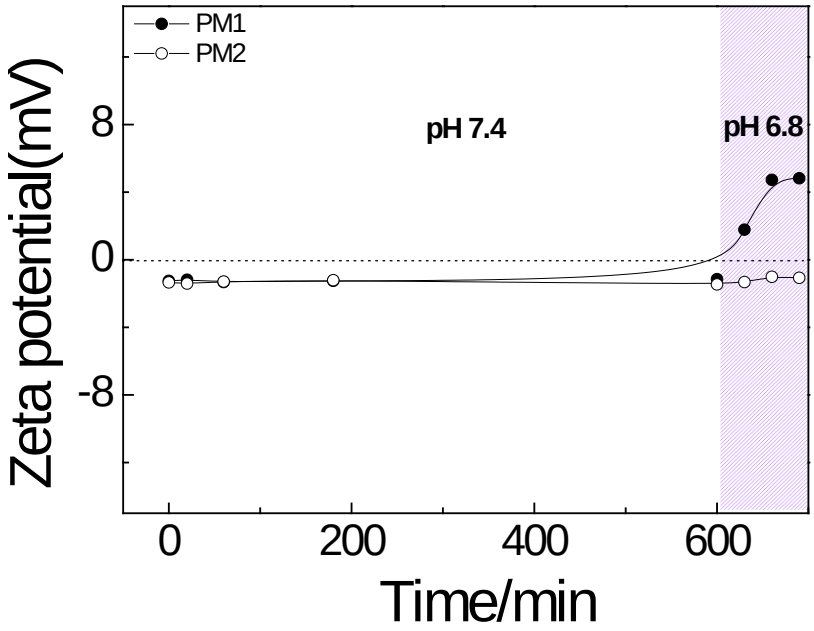

Fig. S2. Time-dependent ξ-potential of **PM1** and **PM2** at pH 6.8 or pH 7.4 in 10 mM PBS buffer.

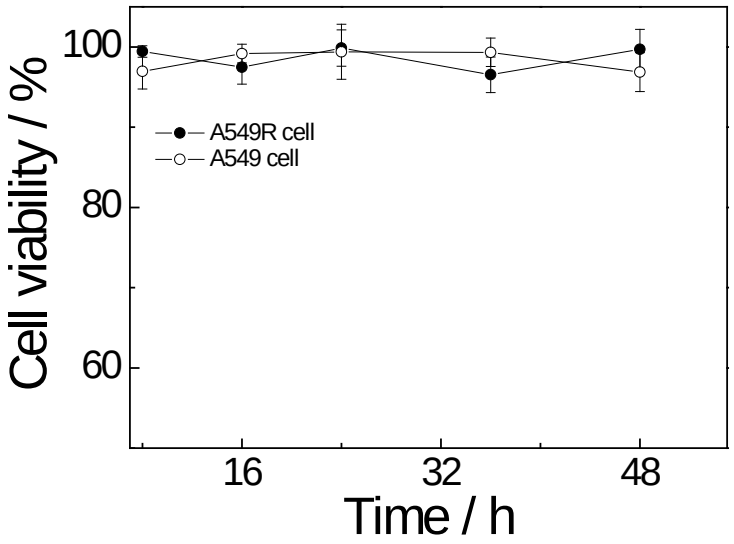

Fig. S3. Cell viability of A549R (closed circles) and A549 cells (open circles) cultured in the medium at pH 6.8 (mean ± SEM, n = 4).

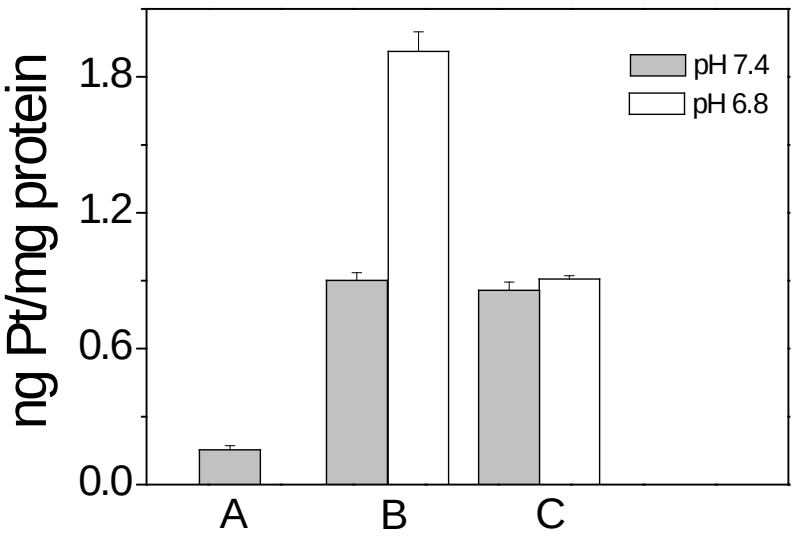

Fig. S4. The cellular uptake of platinum against A549R cells after incubation with cispaltin (A), **PM1** (B) and **PM2** (C) for 3 hours at pH 7.4 or pH 6.8. The total amount of cellular protein was determined from a BCA Protein Assay to normalize Pt content in cells by ICP-MS (mean ± SEM, n = 4).