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Ultrafast Charge-Conversional Nanocarrier for Tumor-Acidity-Activated Targeted Drug Delivery

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Preparation of PEG_{113}-*b*-$PCEA_{50}$-*b*-$PCHMA_{85}$.

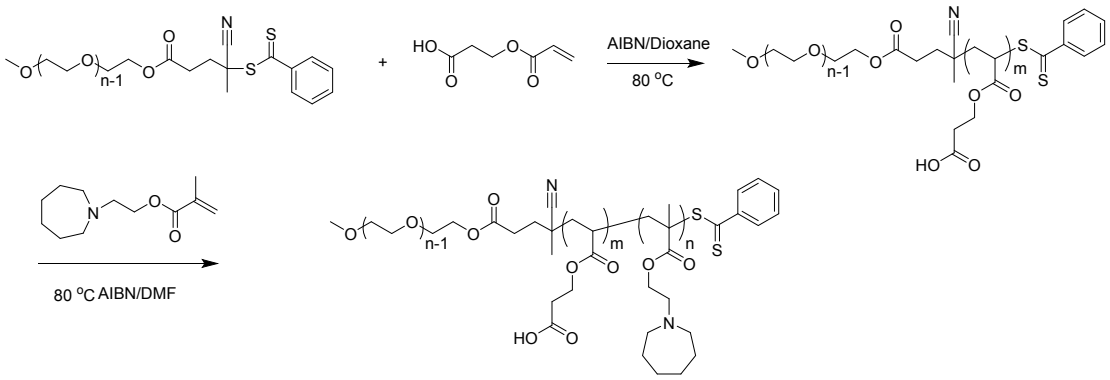
The control materials preparation was similar with PEG_{113}-*b*-$PCEA_{50}$-*b*-$PAEMA_{85}$. Briefly, $mPEG_{113}$-*b*-$PCEA_{50}$ (0.20 g, 1.0 eqv.), CHMA (0.49 g, 140.0 eqv.) and AIBN (1.2 mg, 0.33 eqv.) were dissolved in anhydrous DMF, after stirring at 80 °C for 10 h, the product was precipitated into cold hexane twice and obtained the final product PEG_{113}-*b*-$PCEA_{50}$-*b*-$PCHMA_{85}$. ^{1}H NMR (400 MHz, DMSO-d6, ppm): 4.45-4.05 (m, 270 H), 3.51 (m, 454 H), 2.56 (m, 100 H), 2.21 (m, 51 H), 0.75-2.00 (m, 1650 H).

Preparation of NP3/Pt.

PEG-*b*-PCEA-*b*-PCHMA was dissolved in hot DMF at the concentration of 10 mg/mL, and then 0.5 mL of PEG-*b*-PCEA-*b*-PCHMA solutions were added into 5 mL of hot water dropwise to form nanoparticle by self-assemble. Then the mixture was purified by dialysis in water with a dialysis bag (MWCO = 14,000 Da) to remove DMF. After that, cisplatin was added into the mixture to crosslink the nanoparticle by reacting with carboxyl groups. After 48 h, the shell-crosslinked nanoparticle was purified by dialysis against water with a dialysis bag (MWCO = 14,000 Da) to remove unreacted cisplatin. The platinum content in the NP3/Pt was measured by ICP-MS.

Preparation of rhodamine labeled UCC-NP3/Pt and NP3/Pt.

For the $^{Rho\ B}$UCC-NP3/Pt and $^{Rho\ B}$NP3/Pt preparation, 100 μL of ethanediamine (with the concentration of 2 mg/mL), 100 μL of NHS (with the concentration of 4 mg/mL), and 2 mL of UCC-NP3/Pt or NP3/Pt (with the concentration of 1 mg/mL) were mixed and stirred for 24 h, after that, 10 μL of Rhodamine B isothiocyanate (with the concentration of 1 mg/mL) was added to the solutions and reacted further 4 h, then the mixture was purified by dialysis in water with a dialysis bag (MWCO = 14,000 Da) to remove unconjugated fluorescent probe.



Scheme S1. Synthetic routes of PEG-*b*-PCEA-*b*-PAEMA.

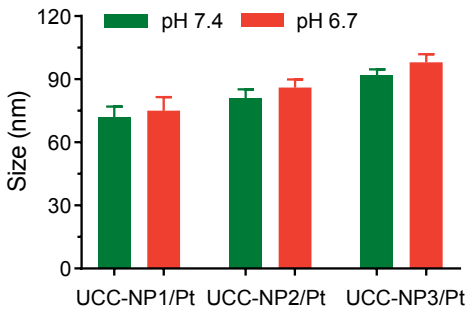


Figure S1. The sizes of UCC-NP1/Pt, UCC-NP2/Pt and UCC-NP3/Pt after incubated in PB buffer with pH 7.4 and 6.7.

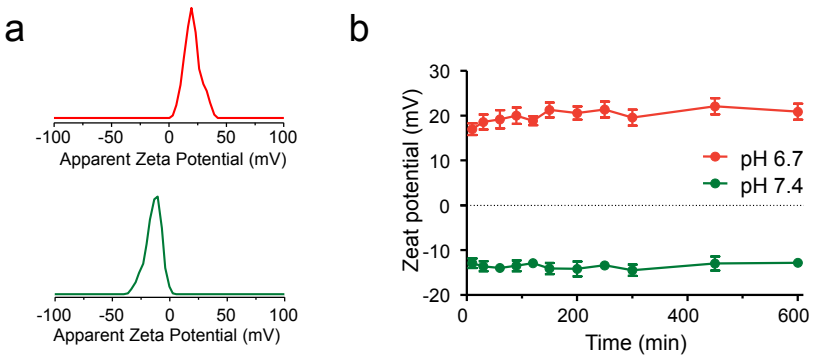


Figure S2. (a) The surface charge of UCC-NP3/Pt at pH 7.4 (green) and pH 6.7 (red), (b) zeta potential of UCC-NP3/Pt after incubated at PB buffer with pH 6.7 and pH 7.4.

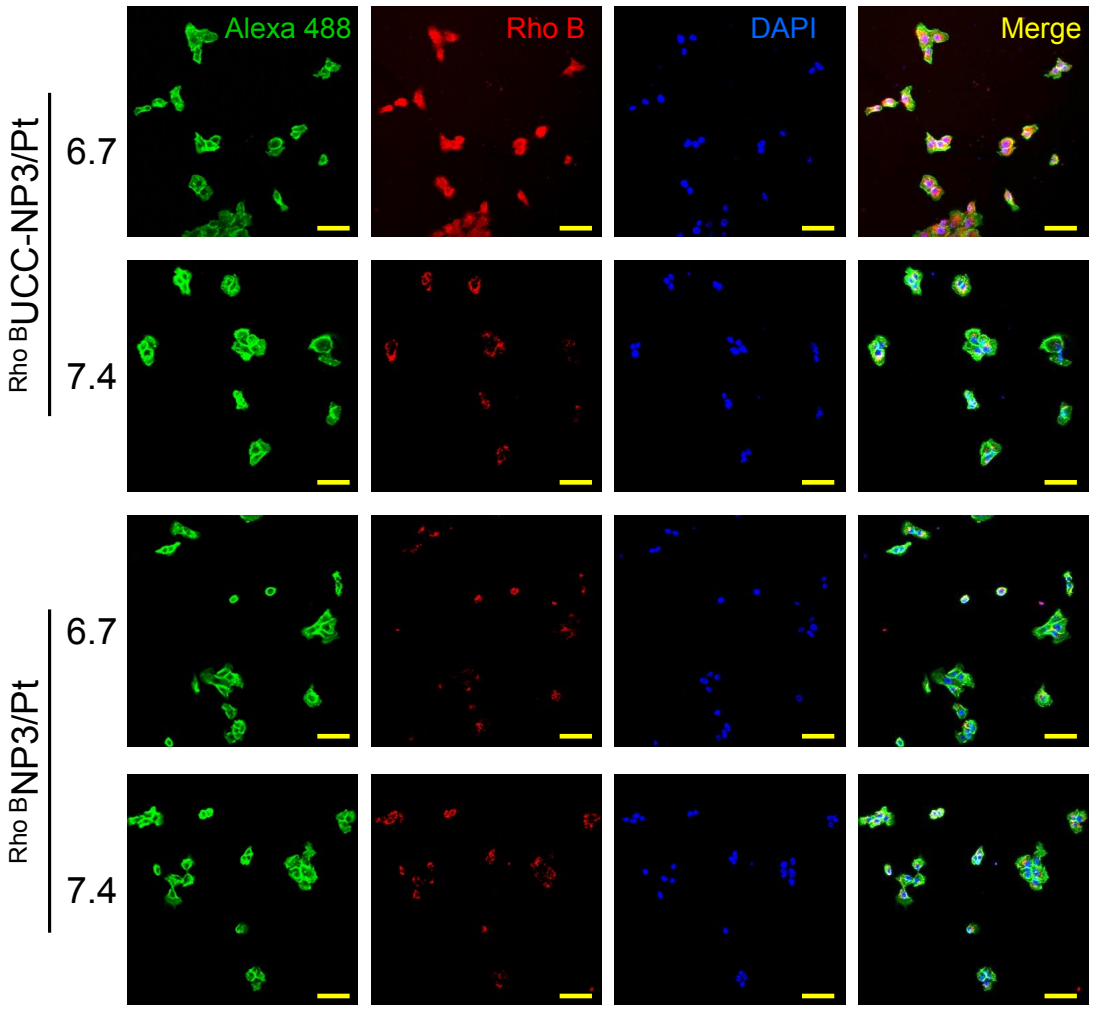


Figure S3. The images of A549R cells incubated with rhodamine B labeled shell-crosslinked nanoparticle ($^{Rho\ B}$UCC-NP3/Pt and $^{Rho\ B}$NP3/Pt) in DMEM medium at pH 6.7 and pH 7.4. The Cytoskeletal F-actin and nuclei of the cells were stained with Alexa Fluor 488 phalloidin (green) and 4', 6-diamidino-2-phenylindole (DAPI; blue), respectively. Scale bar = 50 μm.

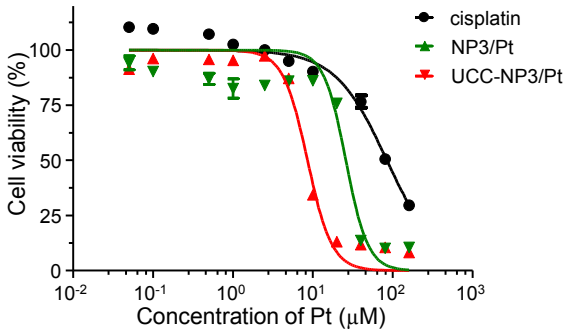


Figure S4. The cell viability of SGC-7901R cells after various treatments at pH 6.7 for 24 h.

	UCC-NP3/Pt	NP3/Pt
Size	92±2.8 nm	90±5.5 nm
Zeta potential	-14.3±2.1 mV	-14.8±3.3 mV
Drug content	18.7±1.6 %	19.3±2.2 %

Table S1. The size, zeta potential and Pt drug content of UCC-NP3/Pt and NP3/Pt.

	A549R	SGC-7901R
Cisplatin	43.74 μM	84.94 μM
NP3/Pt	8.56 μM	26.00 μM
UCC-NP3/Pt	1.75 μM	8.61 μM

Table S2. The IC50 values of A549R and SGC-7901R cells after treated with cisplatin, NP3/Pt and UCC-NP3/Pt.