Supporting Information

Black Phosphorus Assisted Polyionic Micelles with Efficient PTX Loading for Remotely Controlled Release and Synergistic Treatment on Drug-Resistant Tumors

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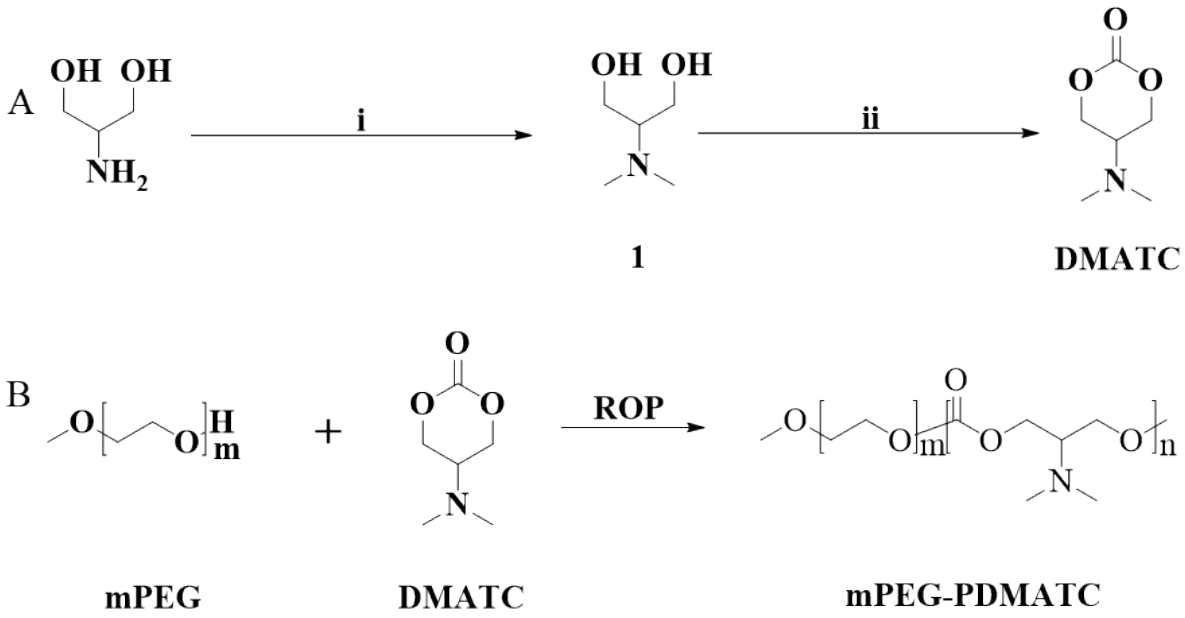
Materials and Methods

Materials: Serinol (98%, Energy Chemical Co., Ltd.), paclitaxel (PTX, 98%, Energy Chemical Co., Ltd.) and 2-(4-amidinophenyl)-6-indolecarbamidine dihydrochloride (DAPI, Beyotime Biotechnology, China) were used as received. Methoxy poly(ethylene glycol) (mPEG-OH, M_n = 5.0 kg/mol, Fluka) was dried by azeotropic distillation from anhydrous toluene. Dichloromethane (DCM) was dried by refluxing over CaH_2 under an argon atmosphere prior to distillation. Small black phosphorus (BP) nanoparticles were prepared according to the previous report.[1] Hela/PTX^R cells were cultured in Dulbecco's modified eagle's medium (DMEM, supplemented with 10% heat inactivated fetal bovine serum, 2 mM glutamine, nonessential amino acids, and sodium pyruvate) at 37 °C in a constant humidity condition with 5% CO_2. The medium and supplements were purchased from Life Technologies (Nanjing, China). The healthy nude mice were purchased from Model Animal Research Center of Nanjing University, Nanjing, China.

Characterization: ^{1}H NMR spectra were measured on a Bruker ECX 400 (Germany), and the chemical shifts were calibrated against residual solvent peaks as the internal standard. Dynamic light scattering (DLS, Anton Paar Litesizer 500) and transmission electron microscopy (TEM, FEI Philips Tecnai 20) were utilized to determine the sizes of the nanoparticles. Fluorescence images were recorded by a fluorescence microscope (IX73, Olympus, Japan). Flow cytometry analysis was performed by using a FACS Calibur (Backman CytoFLEX S). In vivo imaging was performed by using a near-infrared fluorescence imaging system (PE IVIS Lumina III).



Scheme S1 (A) Synthetic route of DMATC monomer: (i) 37% formaldehyde and formic acid, 80 °C, overnight; (ii) triphosgene, room temperature, 18 h. (B) Synthesis of biodegradable mPEG-PDMATC copolymer by ring-opening polymerization in DCM at 50 ºC with the catalyst of zinc bis[bis(trimethylsilyl)amide]).

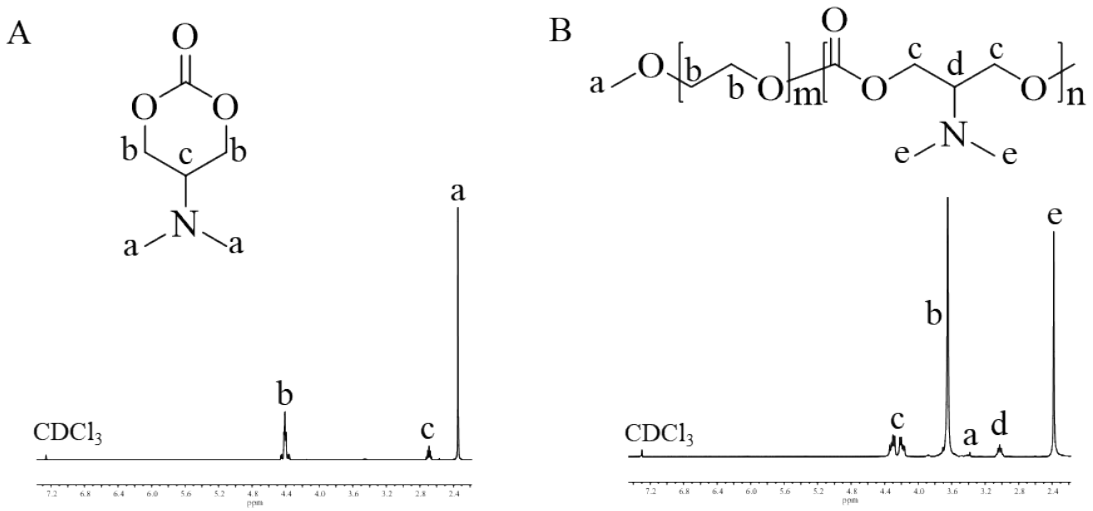


Fig. S1 ^{1}H NMR spectra (300 MHz, $CDCl_3$) of DMATC monomer (A), and mPEG-PDMATC copolymer (B).

Table S1 Characteristics of PD-M@PTX and PD-M@BP/PTX nanosystems at different PTX feed ratios determined by HPLC and DLS.

Nanosystems [a]	DLC (wt%)		DLE [b] (%)	Size [c] (nm)	PDI [c]
	Theory	Determined [b]			
PD-M@PTX	1%	0.93%	96.70%	149.6	0.23
	2%	1.28%	61.34%	137.5	0.17
	5%	1.29%	25.80%	141.9	0.23
PD-M@BP/PTX	1%	0.95%	95.10%	124.1	0.16
	5%	4.95%	96.90%	125.7	0.11
	10%	9.94%	97.80%	146.2	0.19
	12%	10.05%	94.10%	162.4	0.22

[a] The concentration of PD-M micelles was set at 1.0 mg/mL; [b] Drug loading content (DLC) and drug loading efficiency (DLE) were determined by HPLC; [c] Determined by DLS.

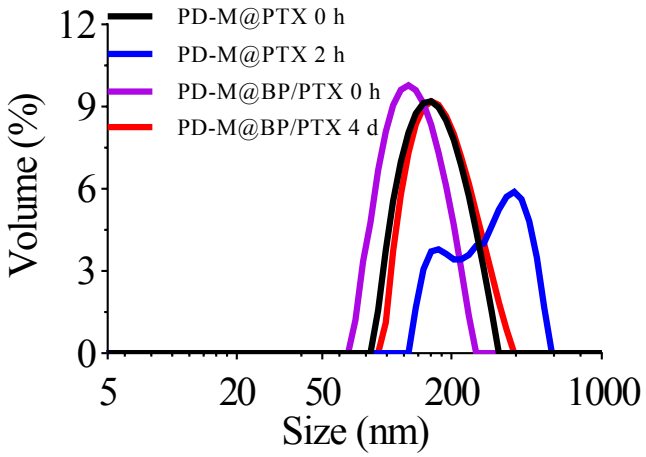


Fig. S2 Stability of PD-M@PTX and PT-M@BP/PTX micelles incubated in PBS at 37 ºC.

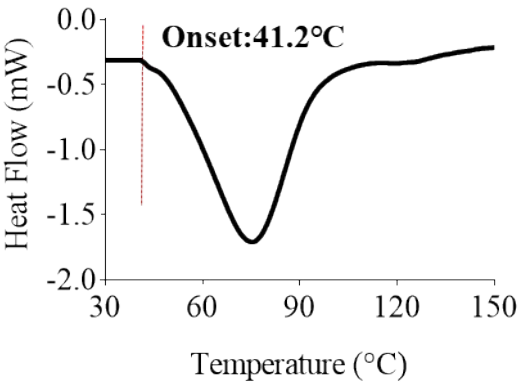


Fig. S3 DSC curve of mPEG-PDMATC copolymer with the onset melting temperature at 41.2 ℃.

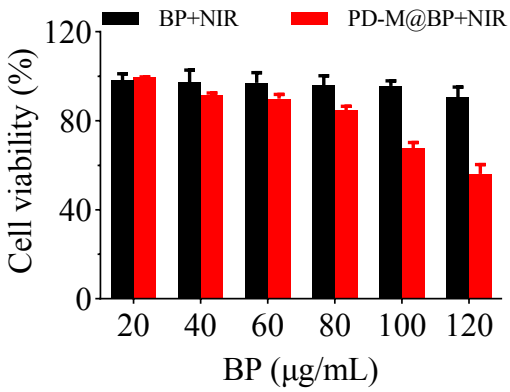


Fig. S4 Cell viability of Hela/PTX^{R} cells with treatment of BP+NIR and PD-M@BP+NIR at different BP concentrations for 24 h determined by MTT assay (NIR irradiation conditions: 10 min, 2.0 W/cm^2).

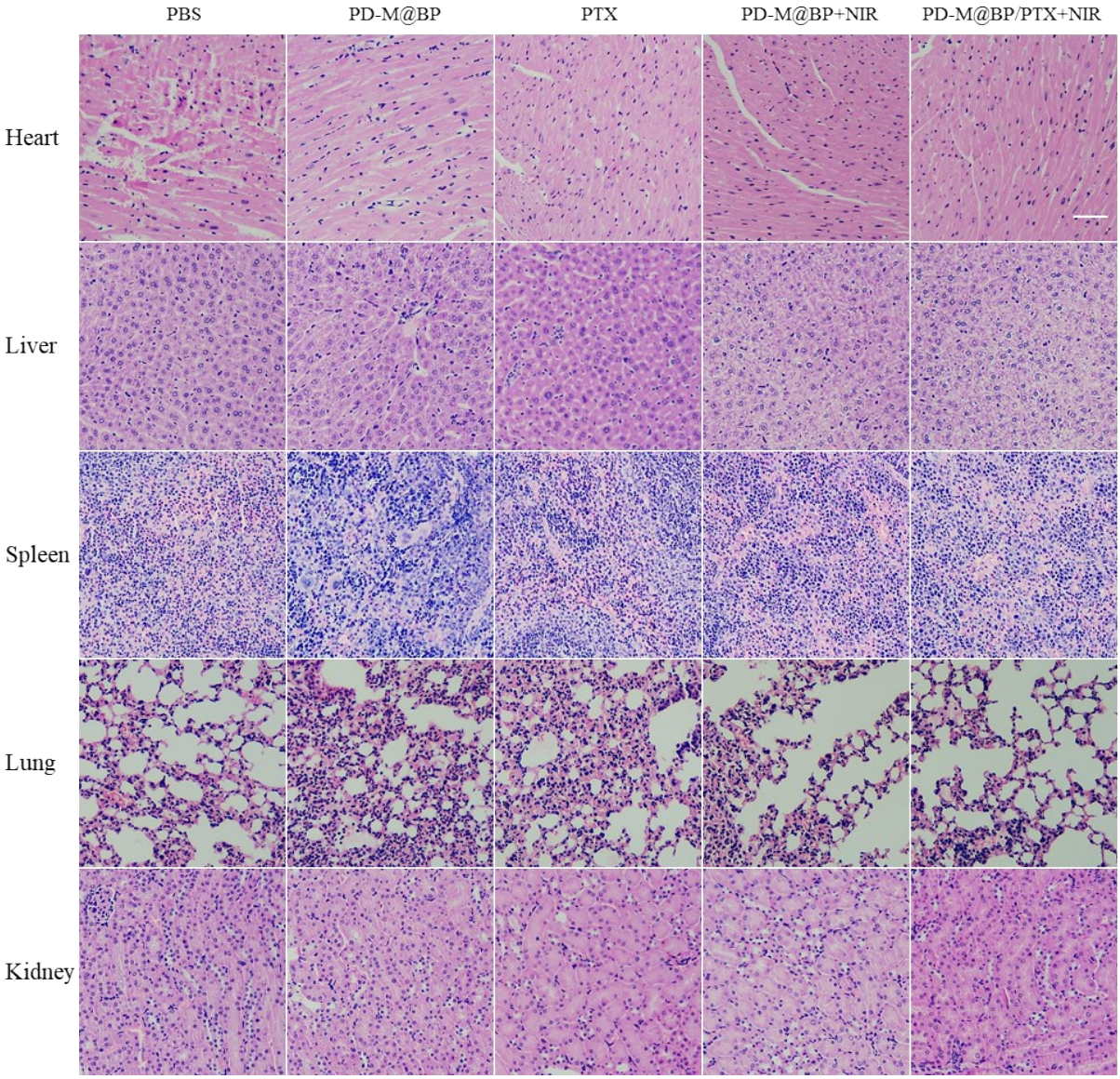


Fig. S5 Histopathological (H&E staining) analysis on normal tissues including heart, liver, spleen, lung, kidney isolated from Hela/PTX^{R} tumor-bearing nude mice with different treatments for 16 days (scale bars: 100 μm).

References

1. Y. Wang, Y. Liu, J. F. Zhang, J.J. Wu, H. Xu, X.W. Wen, X. Zhang, C.S. Tiwary, W. Yang, R. Vajtai, Y. Zhang, N. Chopra, I.N. Odeh, Y.C. Wu and P.M. Ajayan, *Sci. Adv.*, 2017, **3**, e1701500.