Supporting information of

Targeting drug delivery and efficient lysosomal escape for chemo-photodynamic cancer therapy by a peptide/DNA nanocomplex

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Synthesis of mPEG-COOH

Polyethylene glycol monomethyl ether-2000 (6 g, 3 mmol) and succinic anhydride (0.6 g, 6 mmol) were dissolved in toluene (20 mL). Then triethylamine (0.2 mL, 1.5 mmol) was added dropwise at room temperature. The reaction was stirred overnight at 60 ℃. Water was added to the mixture, the solution was extracted with DCM. The collected organic phase was washed with hydrochloric acid and saturated NaCl, then dried with anhydrous Na_2SO_4, and finally concentrated by rotary evaporation. The concentrated solution was precipitated with excess diethyl ether for three times to obtain mPEG-COOH, and the precipitate was vacuum-dried. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30 – 4.24 (m, 2H), 3.65 (s, 180H), 3.39 (s, 3H), 2.74 – 2.53 (m, 4H).

Synthesis of mPEG-NH_2

The mPEG-COOH (2 g, 1 mmol), NHS (0.14 g, 1.2 mmol) and EDCI (0.23 g, 1.2 mmol) were dissolved in DCM (5 mL). After stirred at room temperature for 3 h, the mixed solution was added dropwise into the hexamethylenediamine (0.58 g, 5 mmol) solution. The reaction was continued for 24 h, the solution was concentrated by rotary evaporation, and precipitated with excess diethyl ether for three times. The target product mPEG-NH_2 was obtained by filtration and vacuum-dried. ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.10 (dd, J = 5.8, 3.8 Hz, 2H), 3.51 (s, 180H), 3.25 (s, 3H), 3.02 (m, 2H), 2.63 (m, 4H), 2.34 (t, J = 6.9 Hz, 2H), 1.57 – 1.21 (m, 6H).

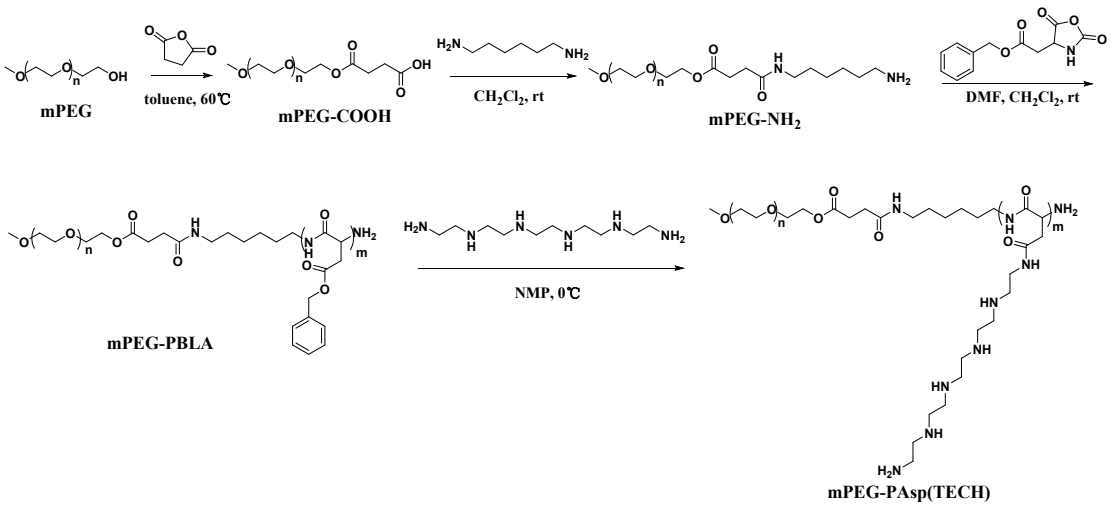
Synthesis of mPEG-PBLA

BLA-NCA (1 g, 4 mmol) was dissolved in DMF (1.5 mL) and diluted with DCM (6 mL). The mPEG-NH_2 (0.2 g, 0.1 mmol) was added to initiate the ring-opening polymerization of NCA. The reaction was stirred at room temperature for two days, the solution was concentrated by rotary evaporation and precipitated in excess diethyl ether for three times. The mixture was filtrated and

vacuum-dried, the target product mPEG-PBLA was obtained. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.53 – 7.97 (m, 50H), 7.47 – 7.02 (m, 256H), 5.24 – 4.85 (m, 100H), 4.76 – 4.31 (m, 50H), 3.51 (s, 180H), 3.25 (s, 3H), 3.05 – 2.54 (m, 108H), 1.42 – 0.97 (m, 6H).

Table S1. The DNA oligonucleotides used for the synthesis of TDNs, 3A-TDNs and Cy5-labeled 3A-TDNs.

ssDNA	Sequence (5' – 3')
S1	ACATTCCTAAGTCTGAAACATTACAGCTTGCTACACGAGAAGAGCCGCC ATAGTA
S2	TATCACCAGGCAGTTGACAGTGTAGCAAGCTGTAATAGATGCGAGGGTC CAATAC
S3	TCAACTGCCTGGTGATAAAACGACACTACGTGGGAATCTACTATGGCGG CTCTTC
S4	TTCAGACTTAGGAATGTGCTTCCCACGTAGTGTCGTTTGTATTGGACCCT CGCAT
AS2	GGTGGTGGTGGTTGTGGTGGTGGTGGTTTTTTTTATCACCAGGCAGTTGA CAGTGTAGCAAGCTGTAATAGATGCGAGGGTCCAATAC
AS3	GGTGGTGGTGGTTGTGGTGGTGGTGGTTTTTTTTCAACTGCCTGGTGATA AAACGACACTACGTGGGAATCTACTATGGCGGCTCTTC
AS4	GGTGGTGGTGGTTGTGGTGGTGGTGGTTTTTTTTTCAGACTTAGGAATGT GCTTCCCACGTAGTGTCGTTTGTATTGGACCCTCGCAT
Cy5-S1	Cy5- ACATTCCTAAGTCTGAAACATTACAGCTTGCTACACGAGAAGAGCCGCC ATAGTA



Scheme S1. The synthetic route of mPEG-PAsp(TECH).

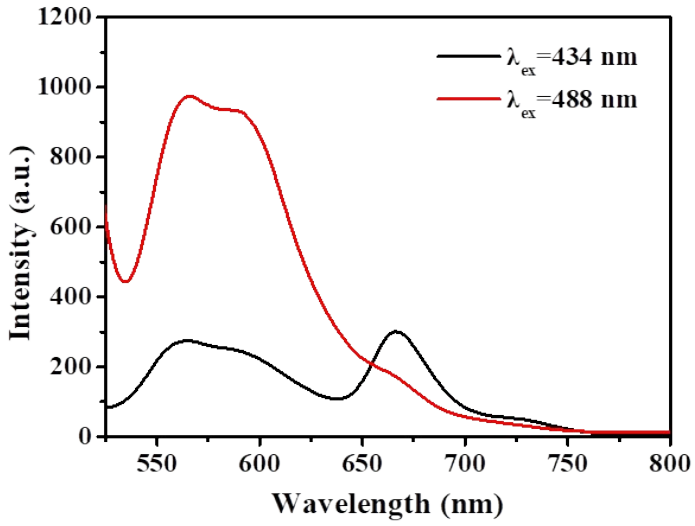


Figure S1. Fluorescence spectroscopy of 3A-TDNs@DT with different excitation wavelength.

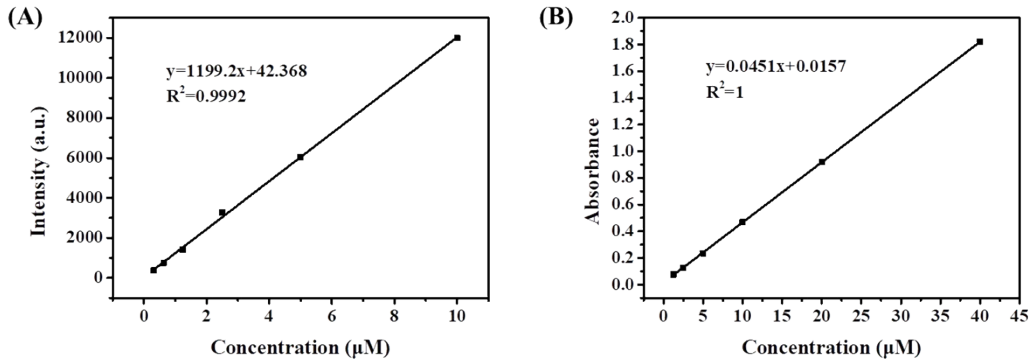


Figure S2. (A) Fluorescence standard curve of DOX. (B) UV-vis absorption standard curve of TMPyP4.

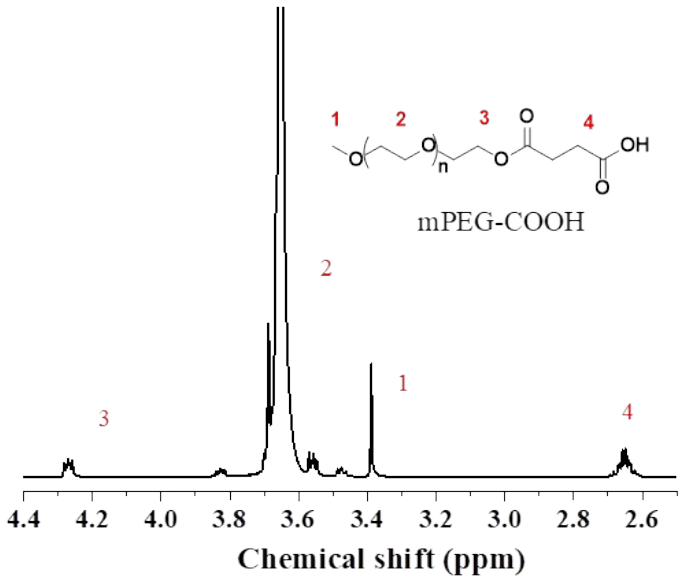


Figure S3. ^{1}H NMR spectrum of mPEG-COOH in $CDCl_3$.

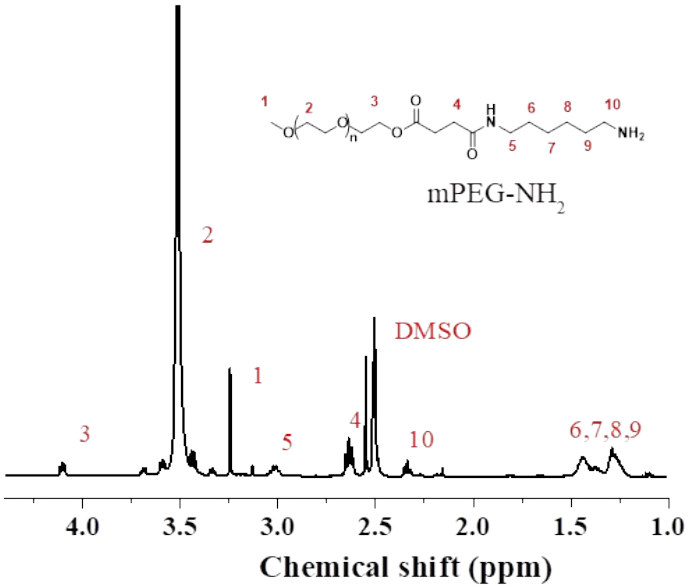


Figure S4. ^{1}H NMR spectrum of mPEG-NH_2 in DMSO-d_6.

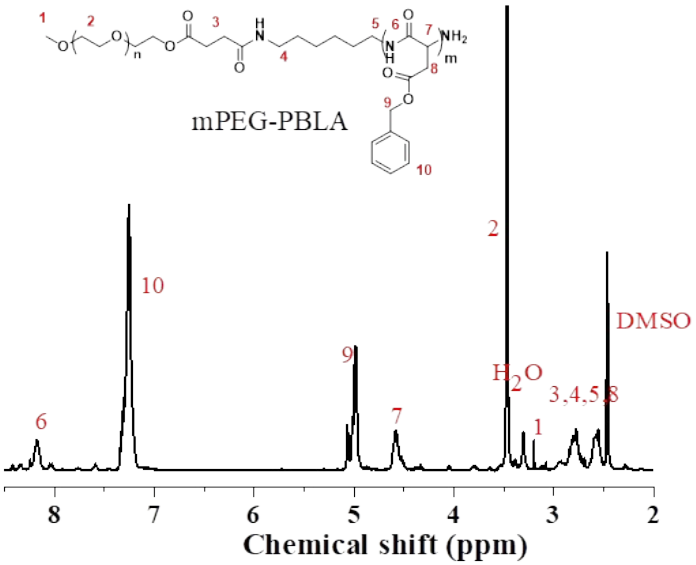


Figure S5. ^{1}H NMR spectrum of mPEG-PBLA in DMSO-d_6.

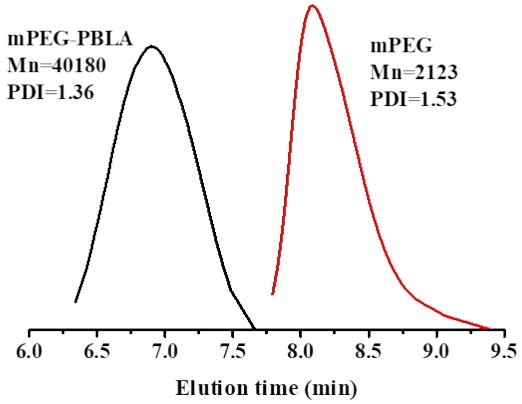


Figure S6. GPC traces of mPEG and mPEG-PBLA.

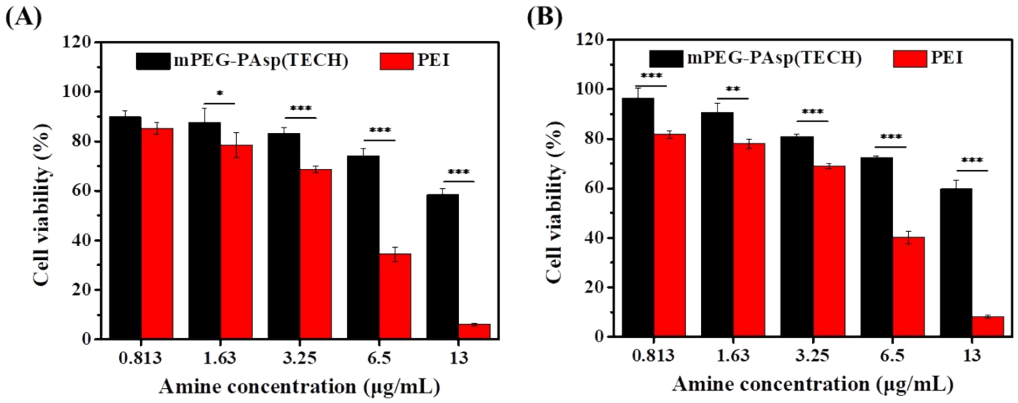


Figure S7. The cytotoxicity of mPEG-PAsp(TECH) and PEI against HeLa (A) and 3T3 (B) cells at different amine concentrations. The results were expressed as mean ± SD ($n = 5$, *$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

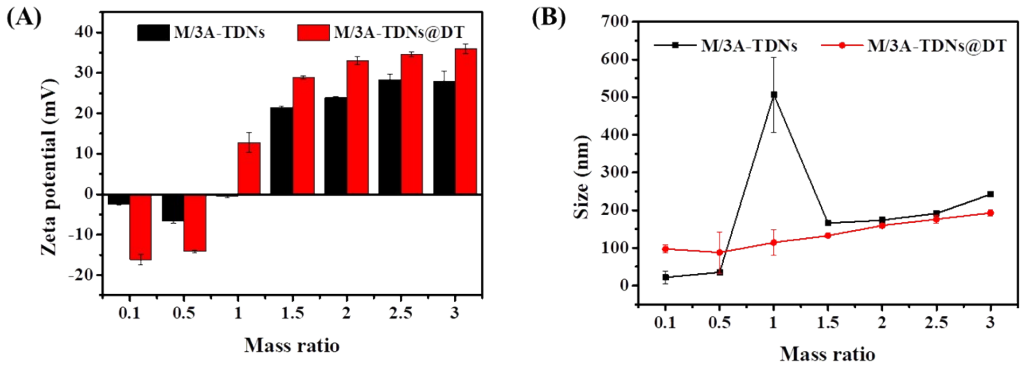


Figure S8. The zeta potentials (A) and particle sizes (B) of M/3A-TDNs and M/3A-TDNs@DT with different feeding mass ratios. The results were expressed as mean ± SD (n = 3).

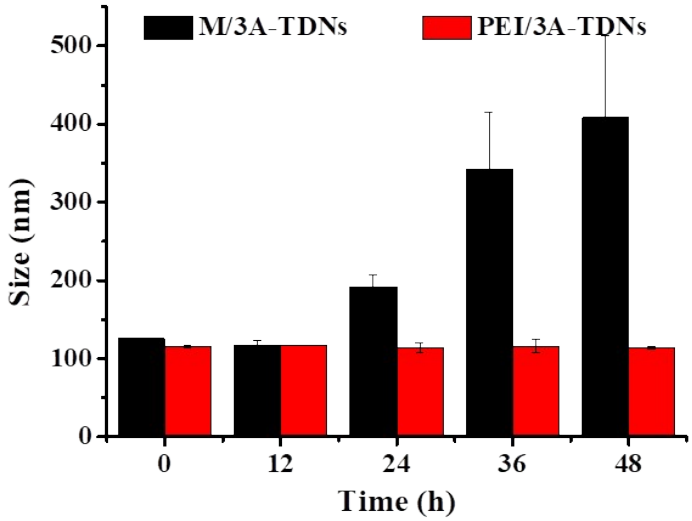


Figure S9. The particle sizes of M/3A-TDNs and PEI/3A-TDNs (mass ratio = 2) after different degradation times. The results were expressed as mean ± SD (n = 3).

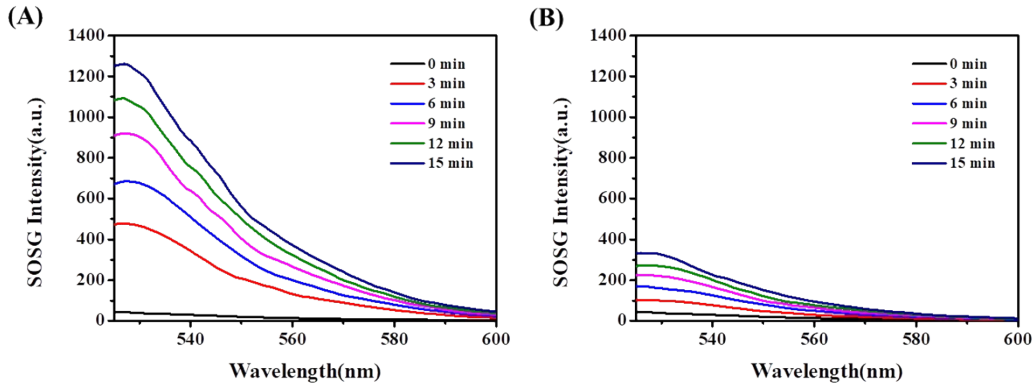


Figure S10. The fluorescence spectroscopy of SOSG in 3A-TDNs@DT (A) and M/3A-TDNs@DT (B) under different illumination times.

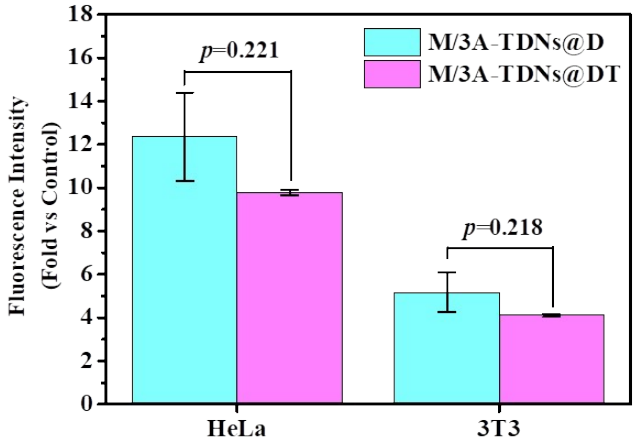


Figure S11. The cellular uptake of M/3A-TDNs@D and M/3A-TDNs@DT by HeLa and 3T3 cells. The flow cytometry results were expressed as mean ± SD (n = 3).

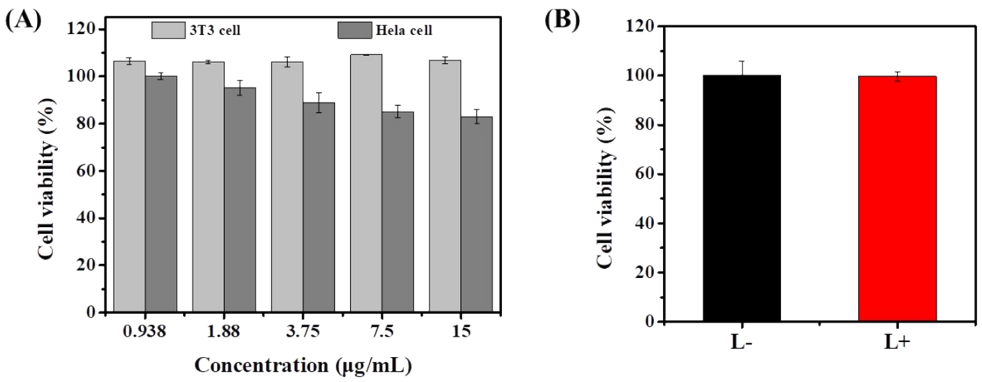


Figure S12. (A) Cytotoxicity of M/3A-TDNs against 3T3 and HeLa cells. (B) Cell viability of HeLa cells after treatment with light irradiation for 40 min. The results were expressed as mean ± SD (n = 5).