Supporting Information

Zinc Ion Coordination Significantly Improved the Transfection Efficiency of Low Molecular Weight Polyethylenimine

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Figures and Tables

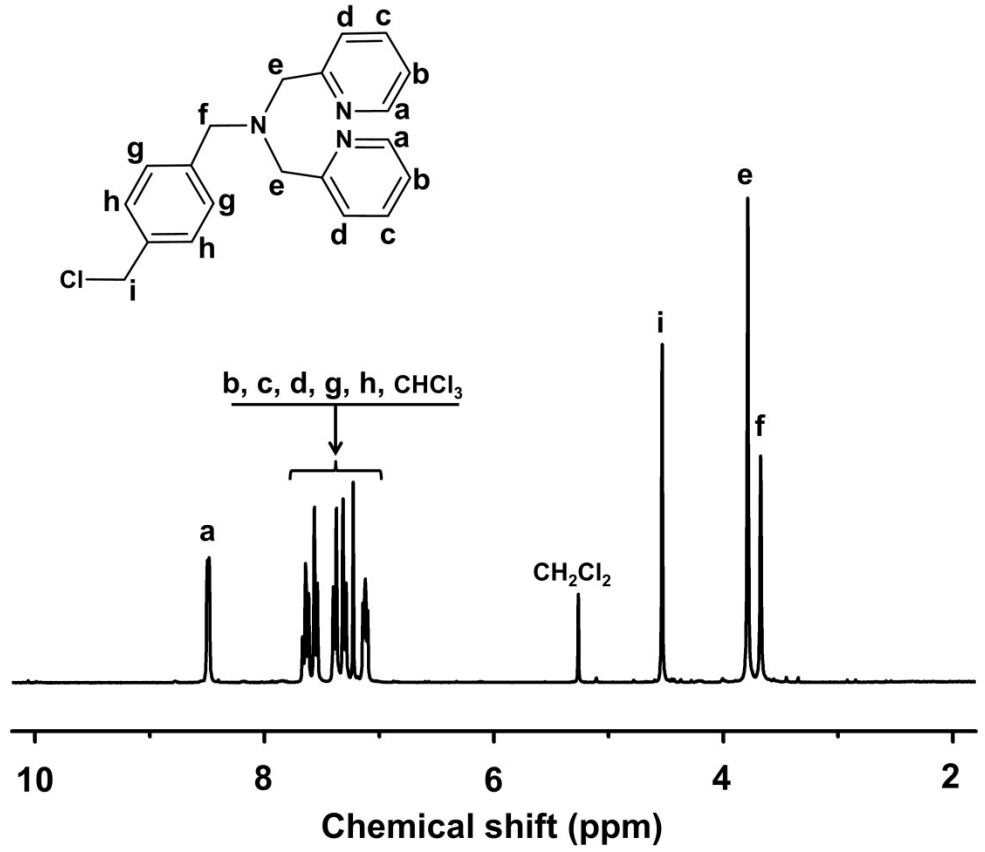


Fig. S1 The ^{1}H NMR of compound 1 in $CDCl_3$.

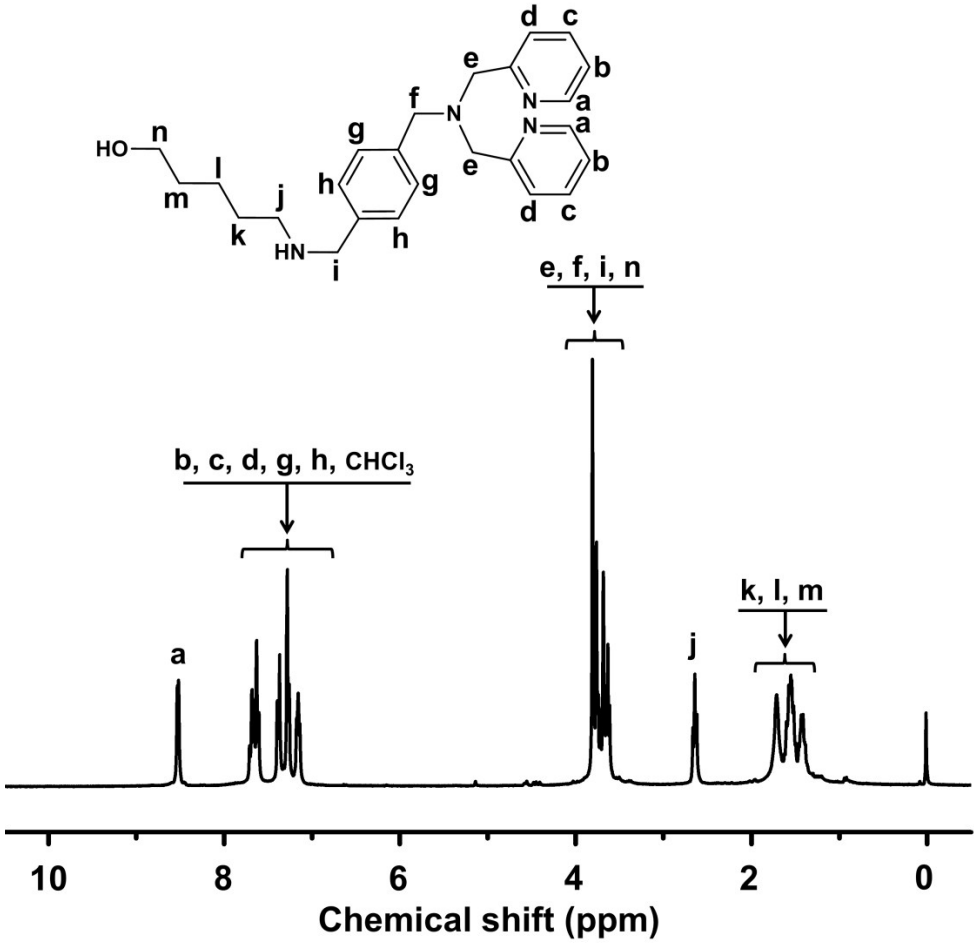


Fig. S2 The ^{1}H NMR of compound 2 in $CDCl_3$.

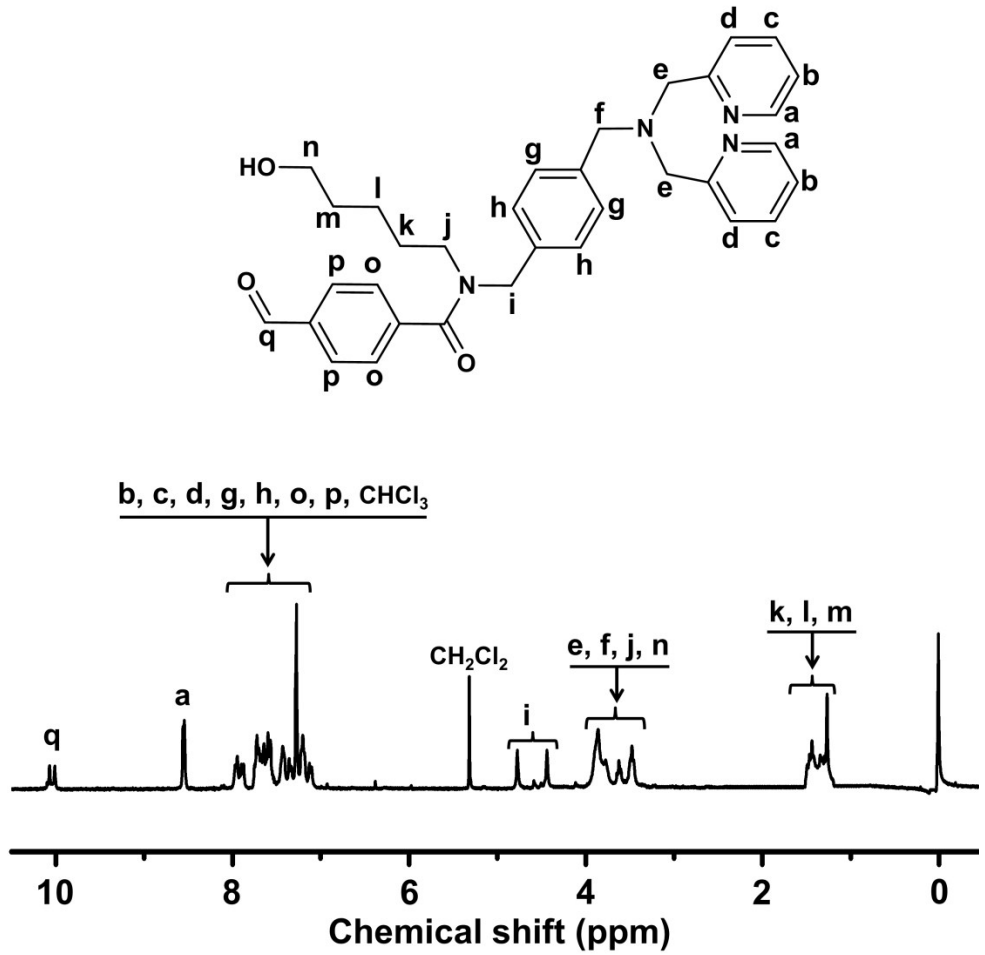


Fig. S3 The ^{1}H NMR of compound 3 in $CDCl_3$.

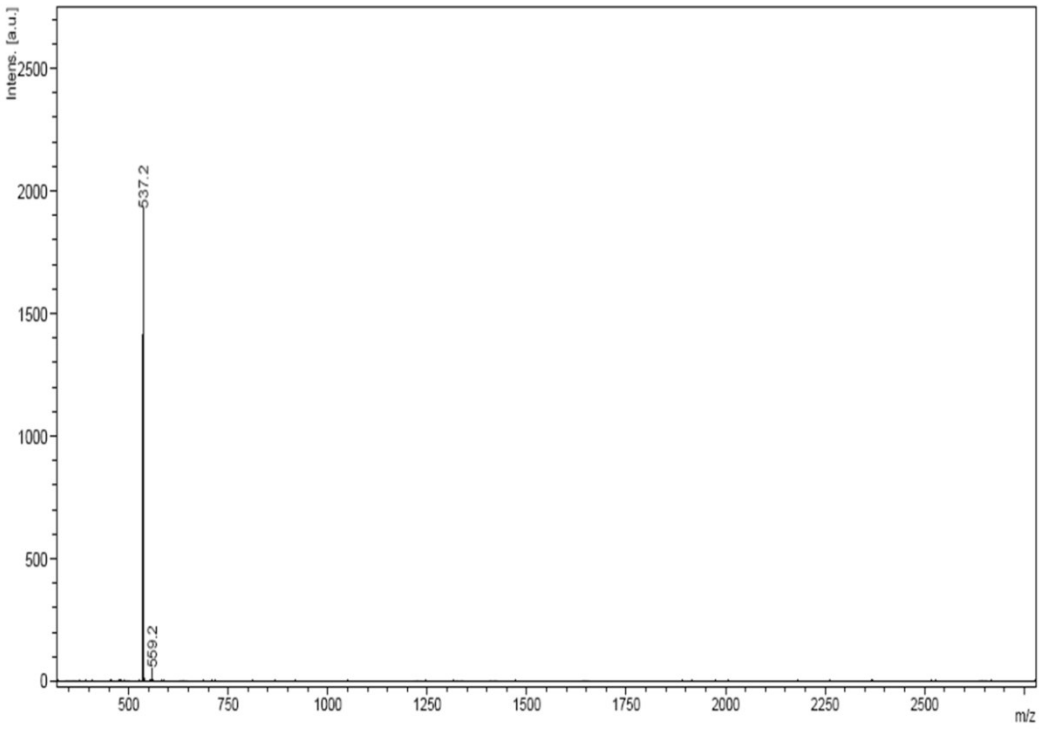


Fig. S4 The mass spectra of compound 3 ESI-H and ESI+Na.

Table S1. The compositions of Zn-DPPAs.

Polymer	Feed ratio [Compound 3]:[PEI1.8k]	Compound 3 mg (mmol)	$Zn(NO_3)_2 \cdot 6H_2O$ mg (mmol)	PEI1.8k mg (mmol)
Zn-DPPA0.5	0.5/1	0.86 (0.0016)	0.48 (0.0016)	5.76 (0.0032)
Zn-DPPA1	1/1	1.07 (0.002)	0.6 (0.002)	3.6 (0.002)
Zn-DPPA2	2/1	1.61 (0.003)	0.9 (0.003)	2.7 (0.0015)
Zn-DPPA4	4/1	2.14 (0.004)	1.2 (0.004)	1.8 (0.001)

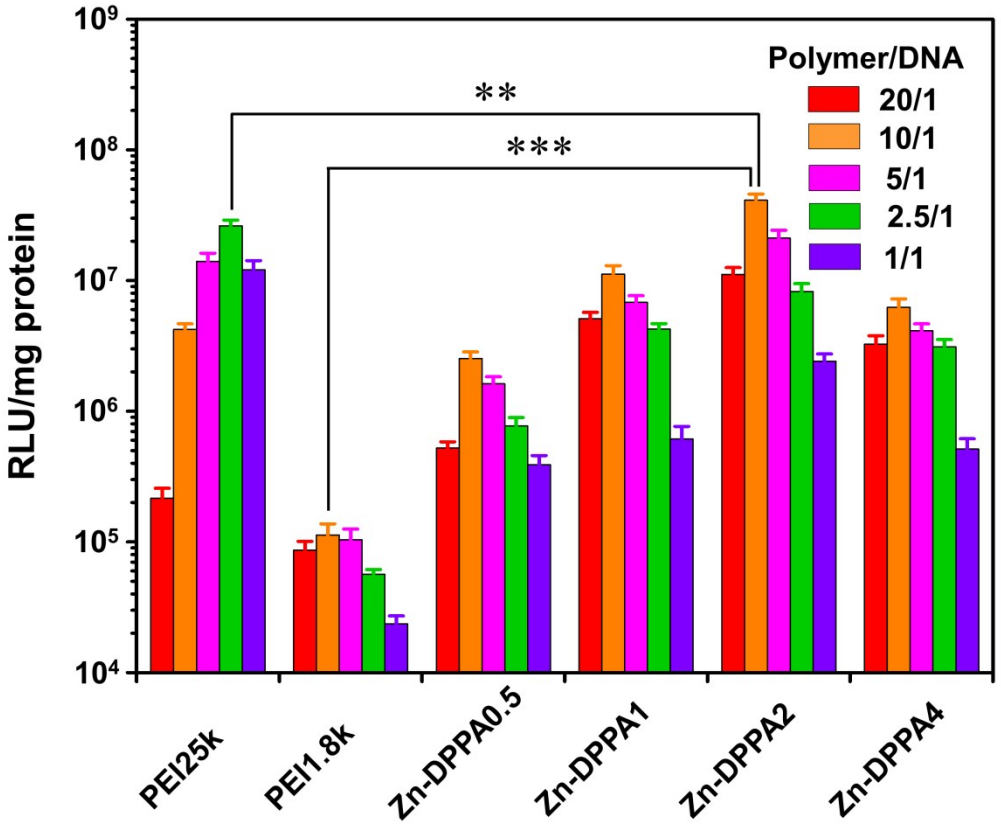


Fig. S5 The DNA transfection of Zn-DPPAs in HeLa cells.

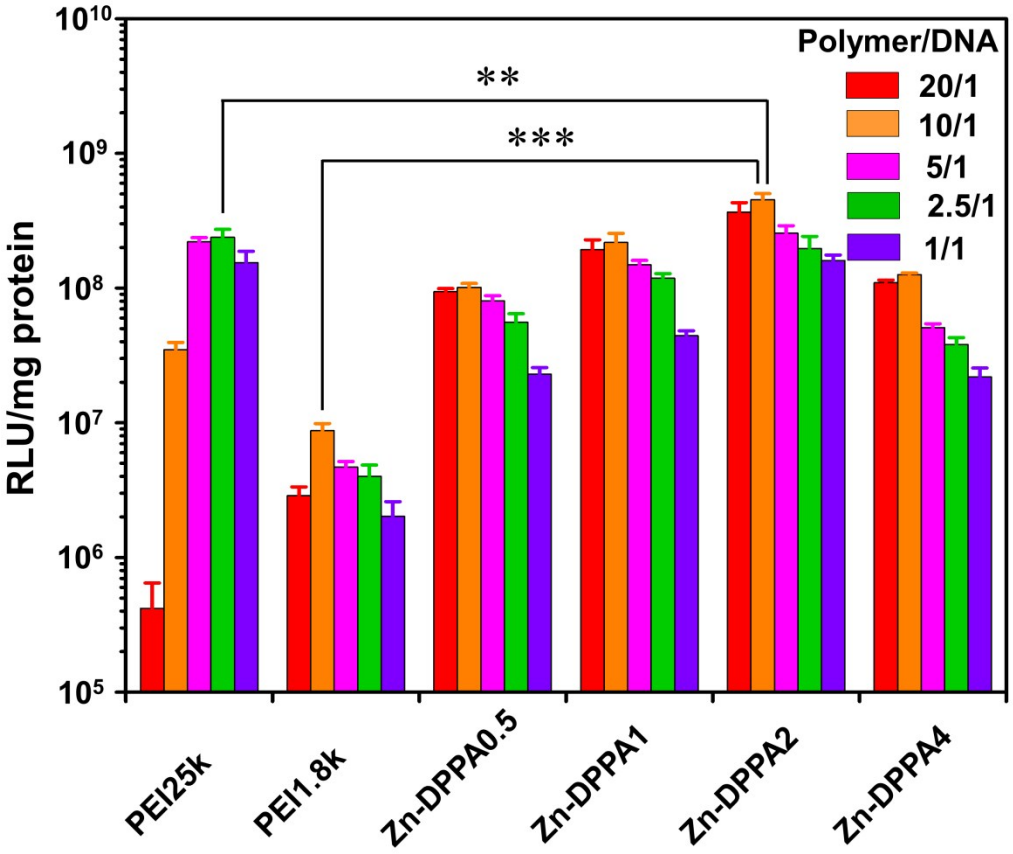


Fig. S6 The DNA transfection of Zn-DPPAs in CHO cells.

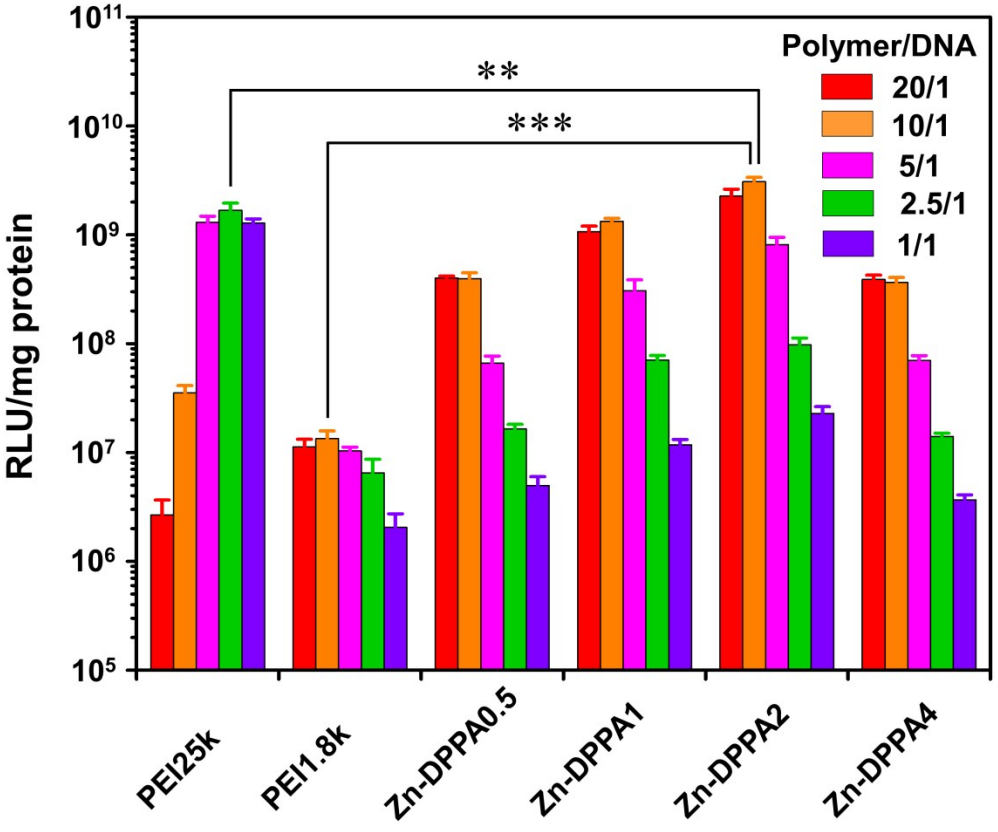


Fig. S7 The DNA transfection of Zn-DPPAs in 293T cells.

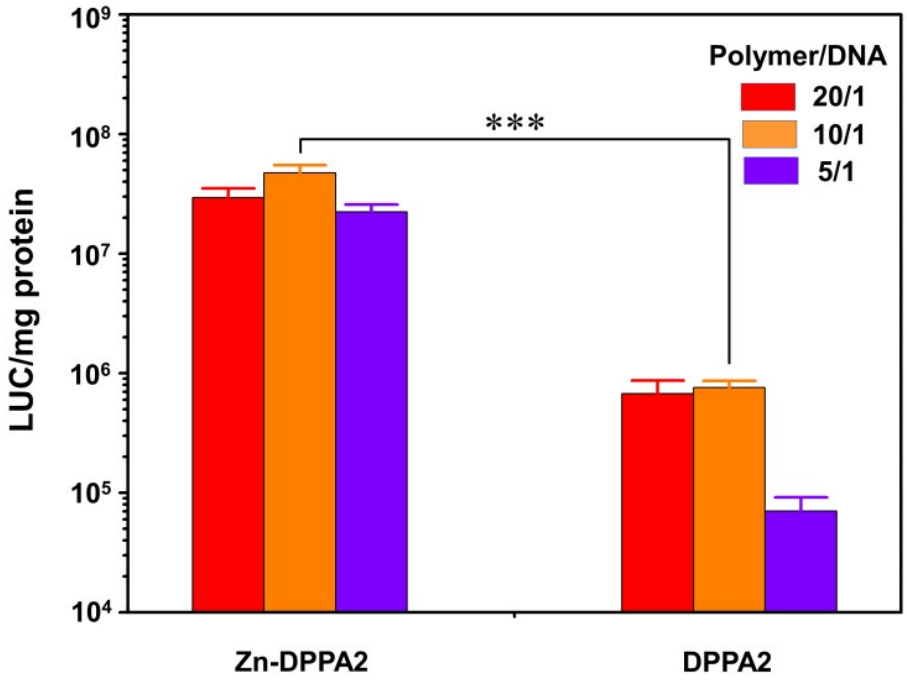


Fig. S8 The DNA transfection of Zn-DPPAs and DPPA2 in MCF-7 cells.

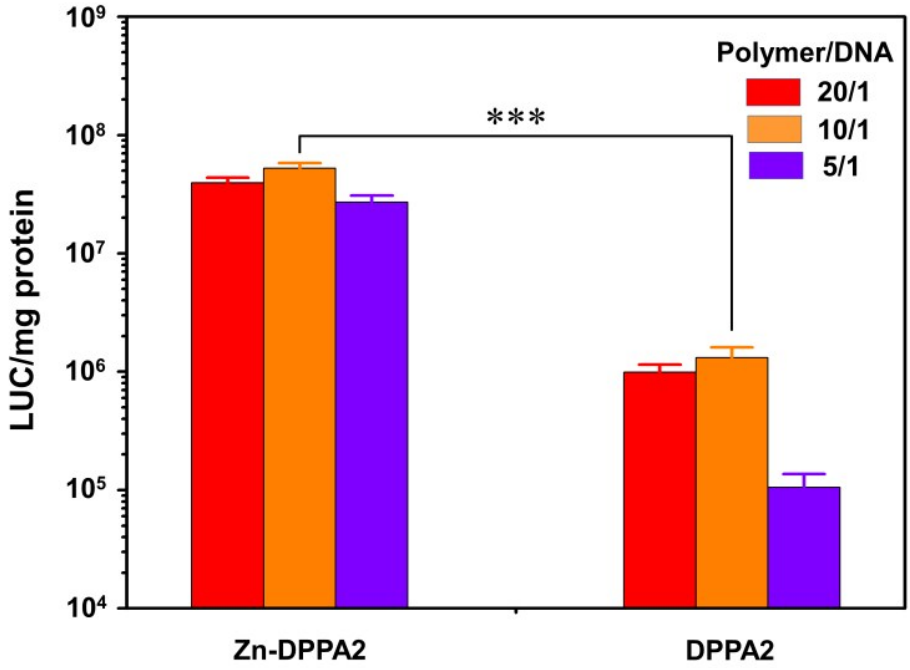


Fig. S9 The DNA transfection of Zn-DPPAs and DPPA2 in HeLa cells.

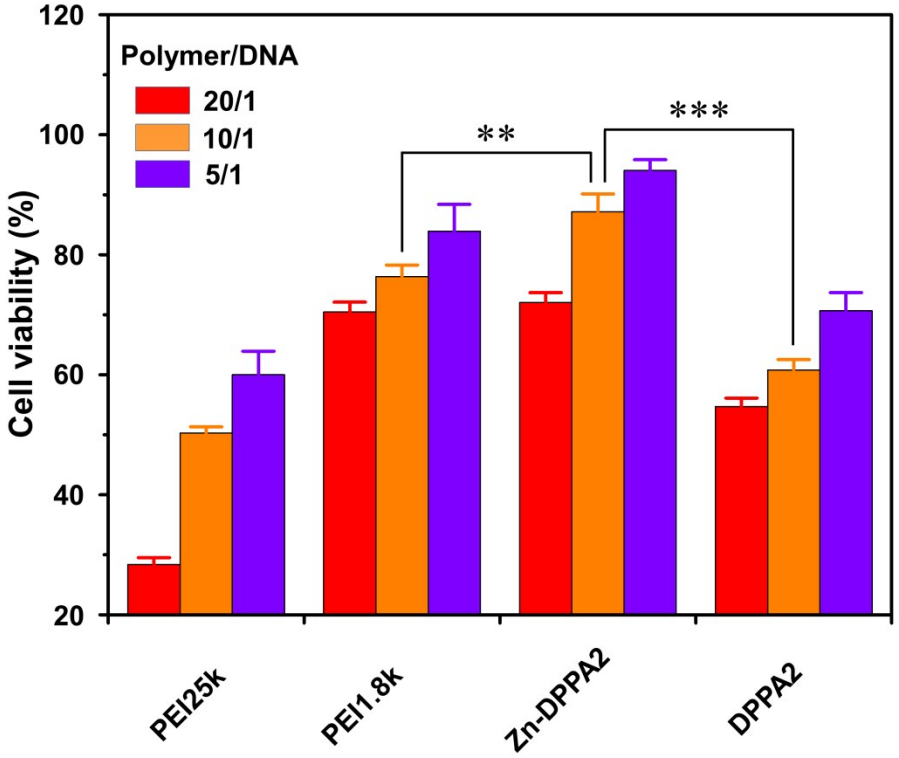


Fig. S10 The cell viability of polymer/DNA complexes in MCF-7 cells.

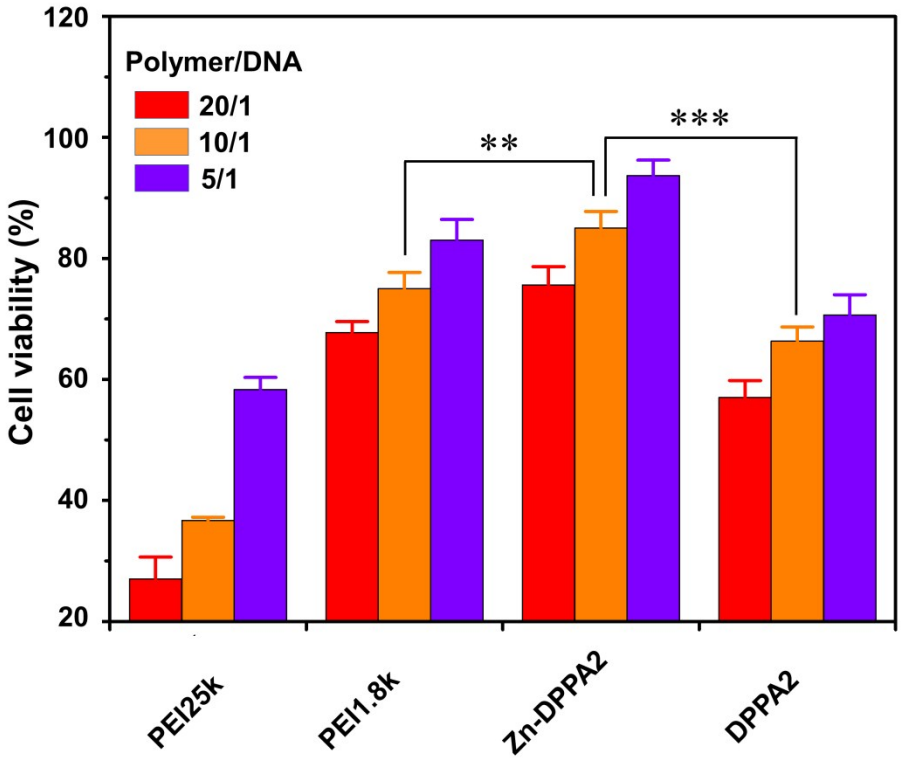


Fig. S11 The cell viability of polymer/DNA complexes in HeLa cells.

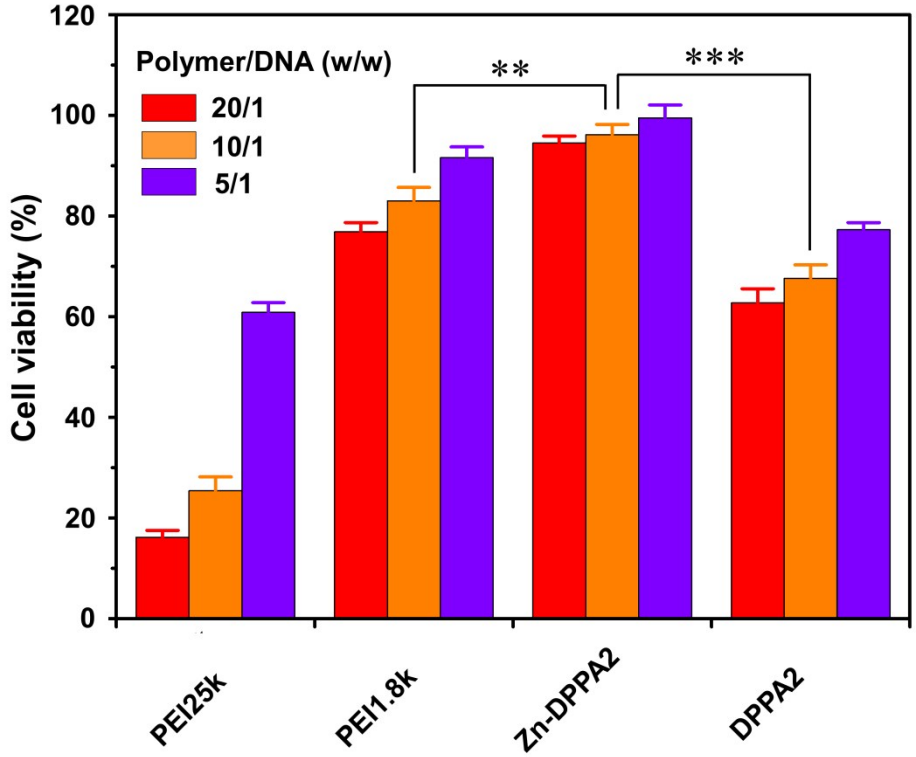


Fig. S12 The cell viability of polymer/DNA complexes in CHO cells.

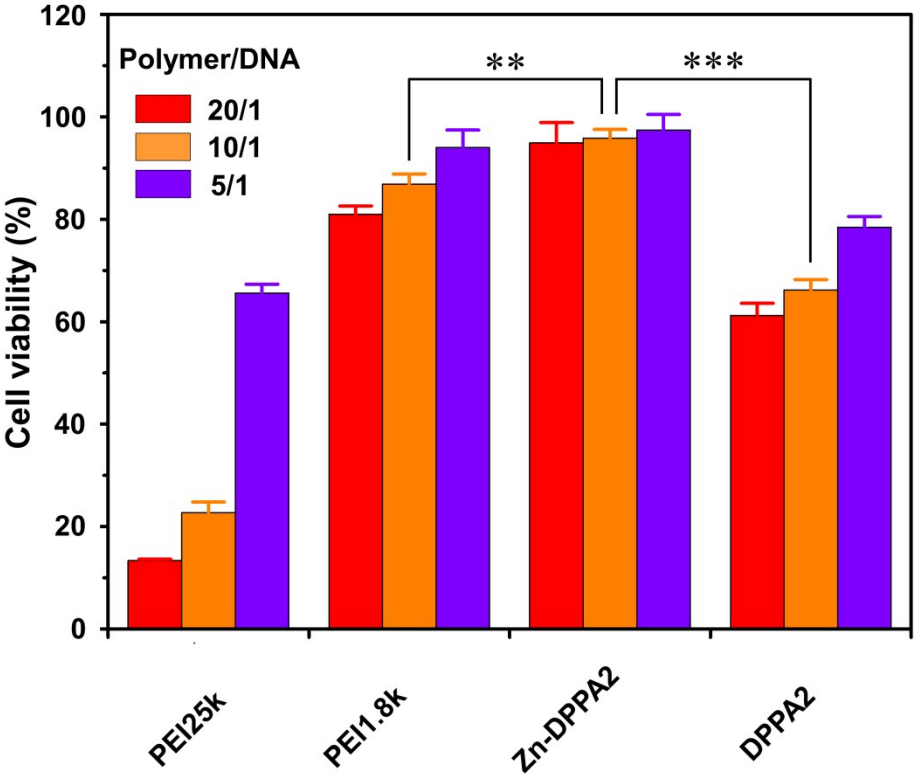


Fig. S13 The cell viability of polymer/DNA complexes in 293T cells.

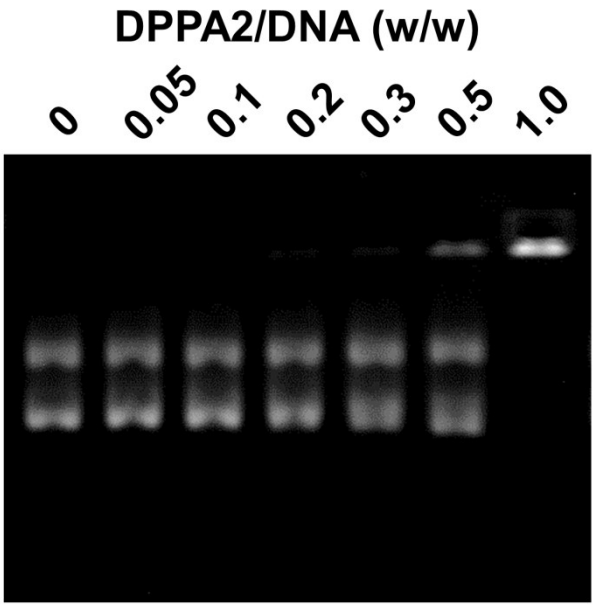


Fig. S14 Gel retardation assay of DPPA2/DNA at various mass ratios.

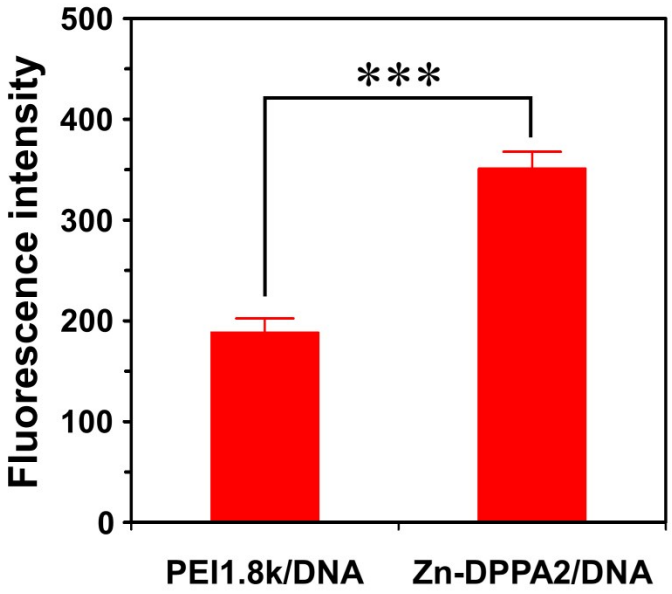


Fig. S15 The flow cytometry of Zn-DPPA2/DNA complexes in HeLa cells, PEI1.8k/DNA complexes were included as control.

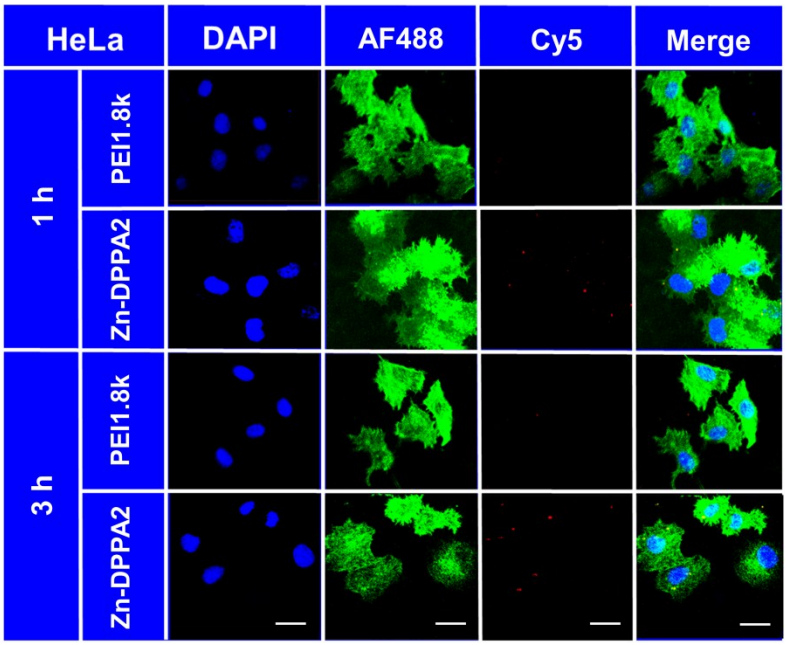


Fig. S16 Representative CLSM images to observe the cellular uptake of Zn-DPPA2/DNA complexes and PEI1.8k/DNA complexes in HeLa cells, scale bar: 20 μm.

Table S2. The thermodynamic parameters of ITC curves by titrating PEI1.8k or Zn-DPPA2 into cardiolipin.

Sample	K_a ($\times 10^5$ M^{-1})	ΔH (kcal mol^{-1})	TΔS (kcal mol^{-1})	No.[a]
PEI1.8k	K=1.02±0.08	ΔH=-15.04±0.04	TΔS=-363.74	1
Zn-DPPA2	K=4.90±0.31	ΔH=7.62±0.12	TΔS=15.38	1

[a]Indicates the number of sequential binding sites, T=25 °C.

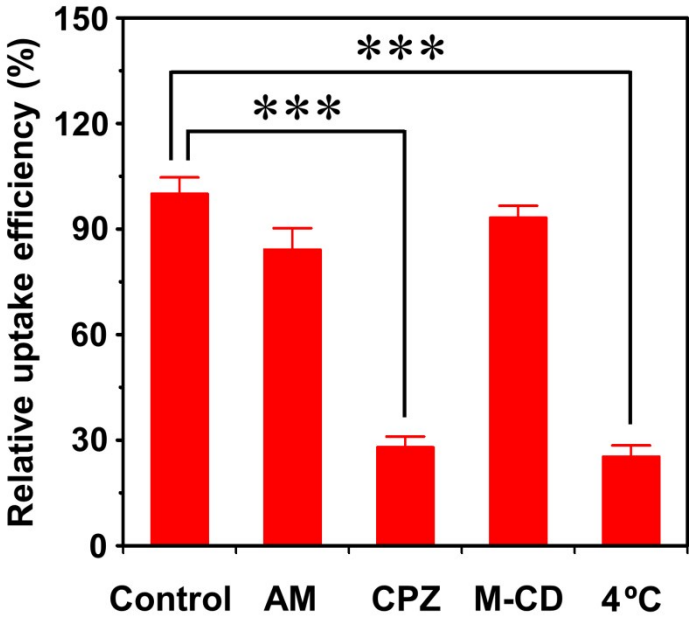
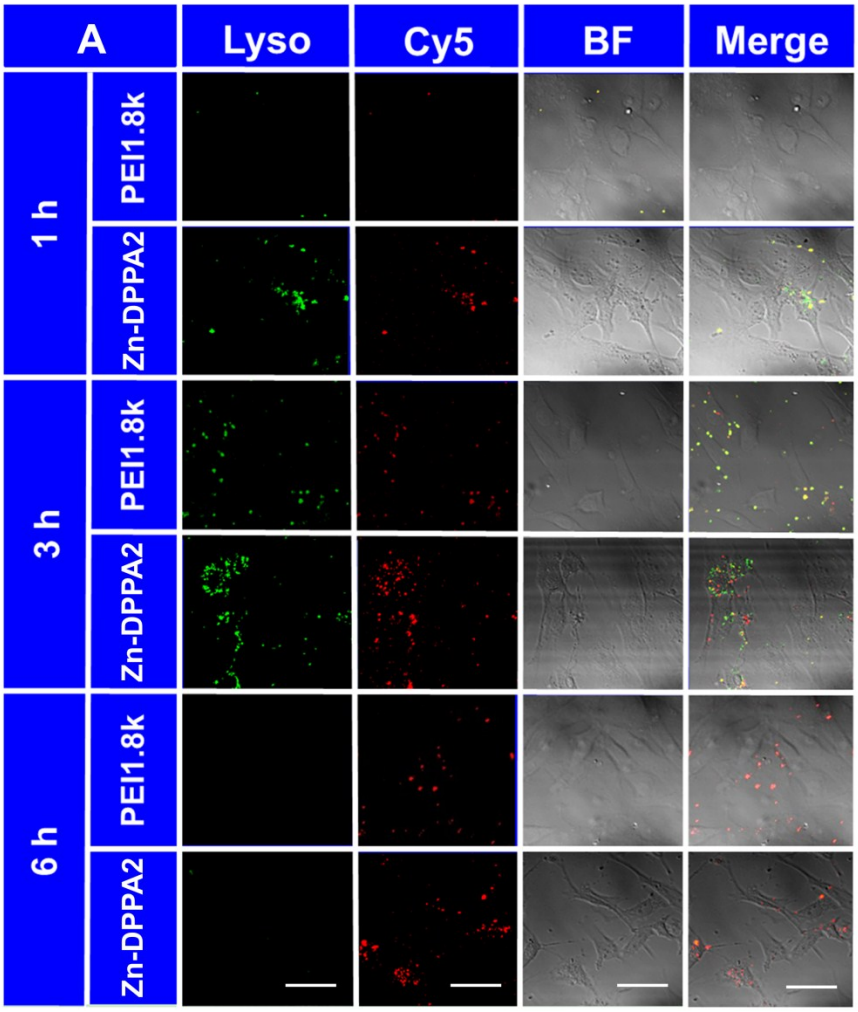


Fig. S17 The cellular uptake of Zn-DPPA2/DNA complexes treated with different inhibitors or at 4 °C in HeLa cells.



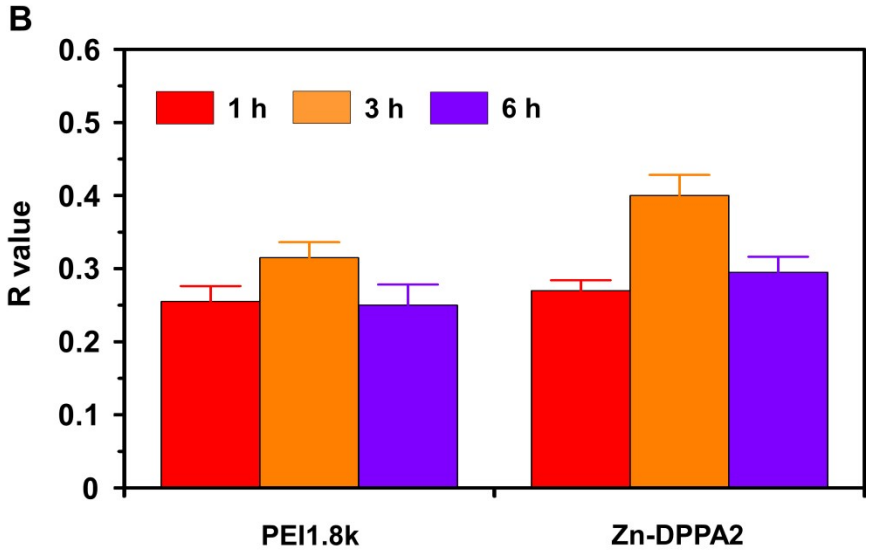


Fig. S18 (A) Representative CLSM images to observe the endosomal escape of Zn-DPPA2/DNA complexes in MCF-7 cells, PEI1.8k/DNA complexes were included as control, scale bar: 50 μm. (B) Correlation coefficient R value acquired from the CLSM images to evaluate endosomal escape behavior.

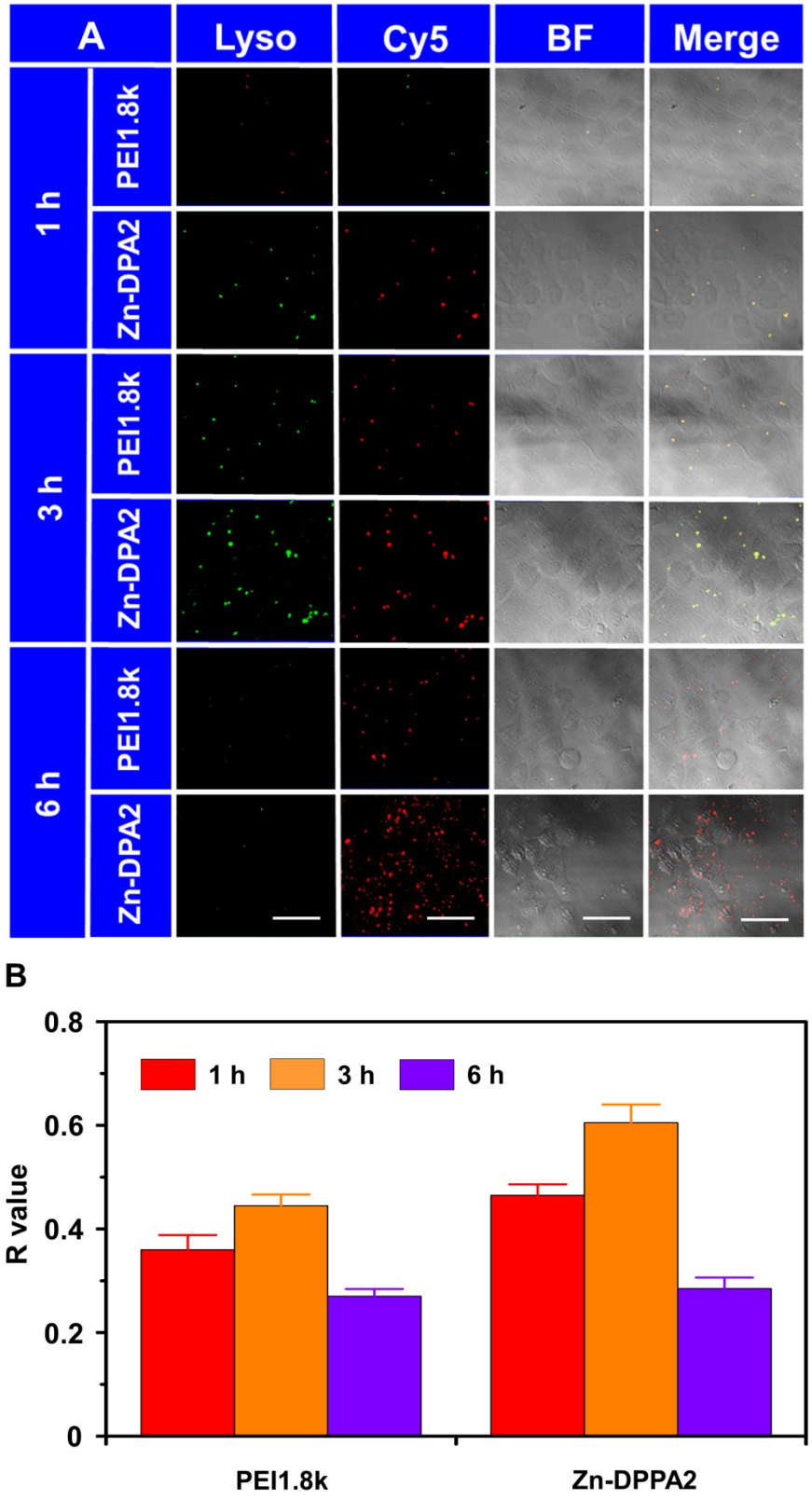


Fig. S19 (A) Representative CLSM images to observe the endosomal escape of Zn-DPPA2/DNA complexes in HeLa cells, PEI1.8k/DNA complexes were included as control, scale bar: 50 μm. (B) Correlation coefficient R value acquired from the CLSM images to evaluate endosomal escape

behavior.

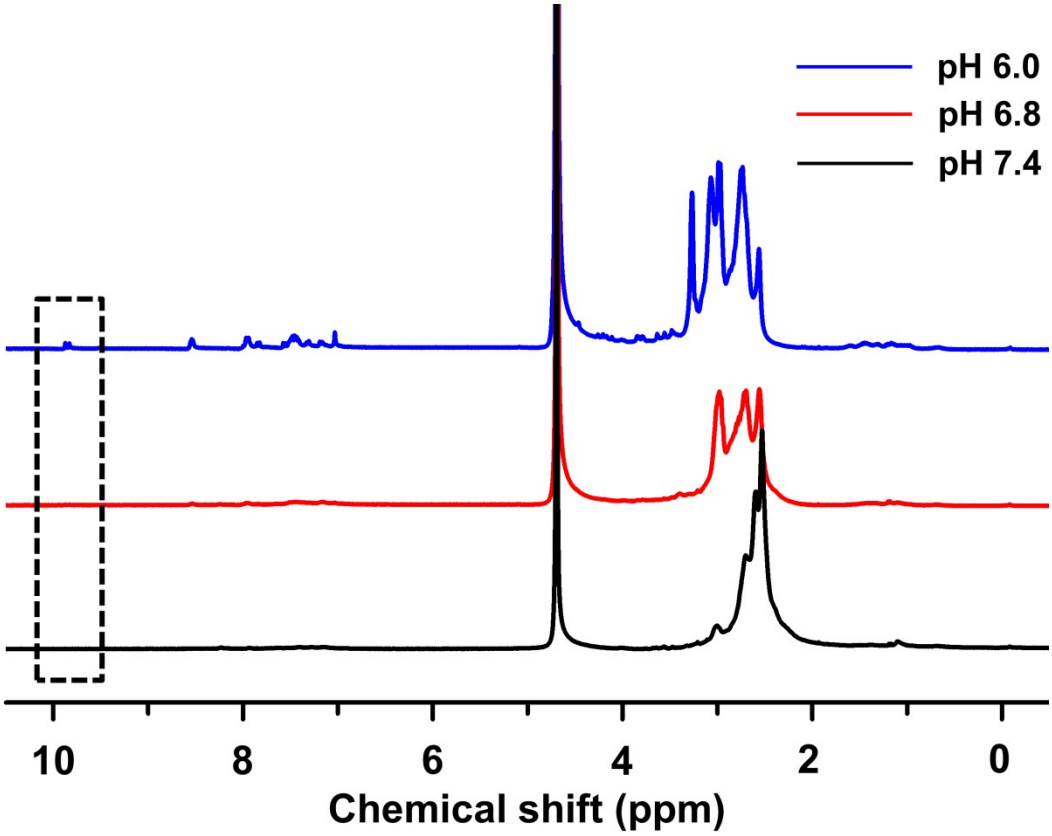


Fig. S20 The ^{1}H NMR of Zn-DPPA2 at different pH values.

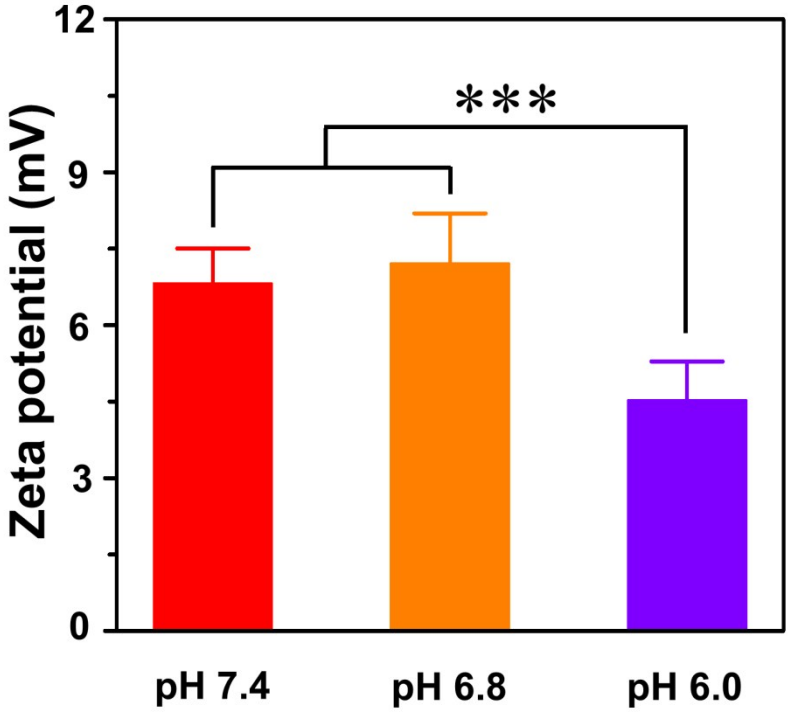


Fig. S21 Zeta potential of Zn-DPPA2/DNA complexes at different pH values.

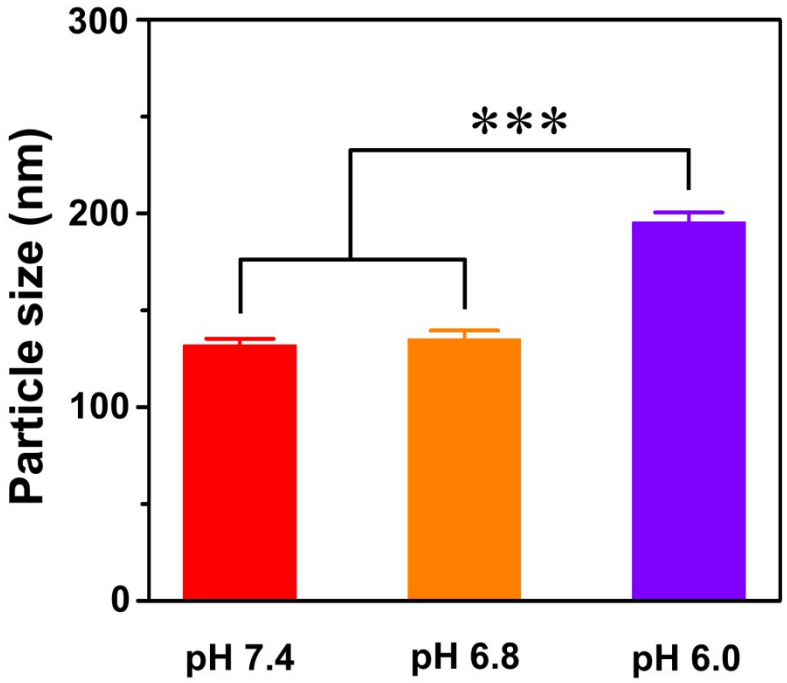


Fig. S22 Particle size of Zn-DPPA2/DNA complexes at different pH values.

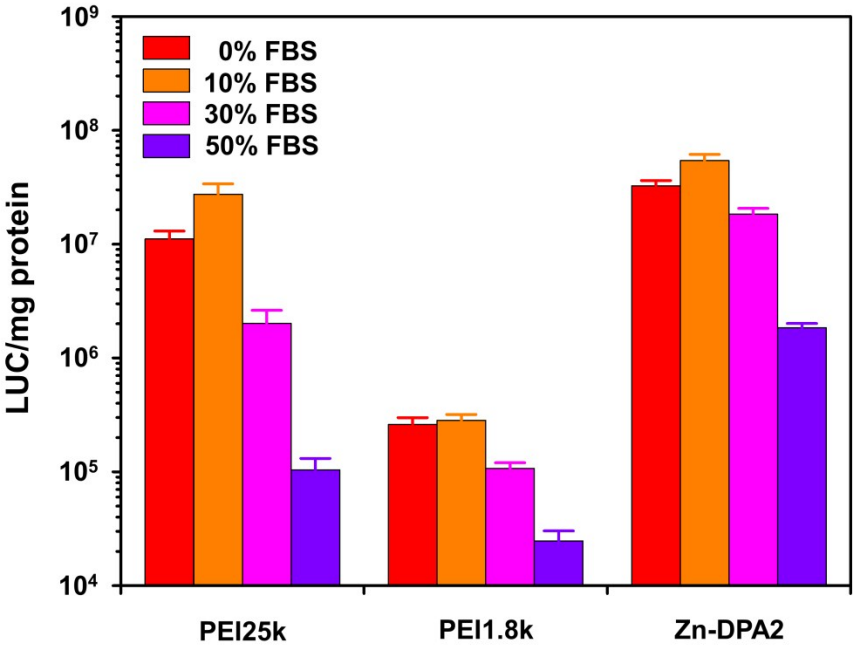


Fig. S23 The transfection efficiency of Zn-DPPA2/DNA complexes at different percentages of FBS in HeLa cells, PEI25k/DNA complexes and PEI1.8k/DNA complexes were included as control.

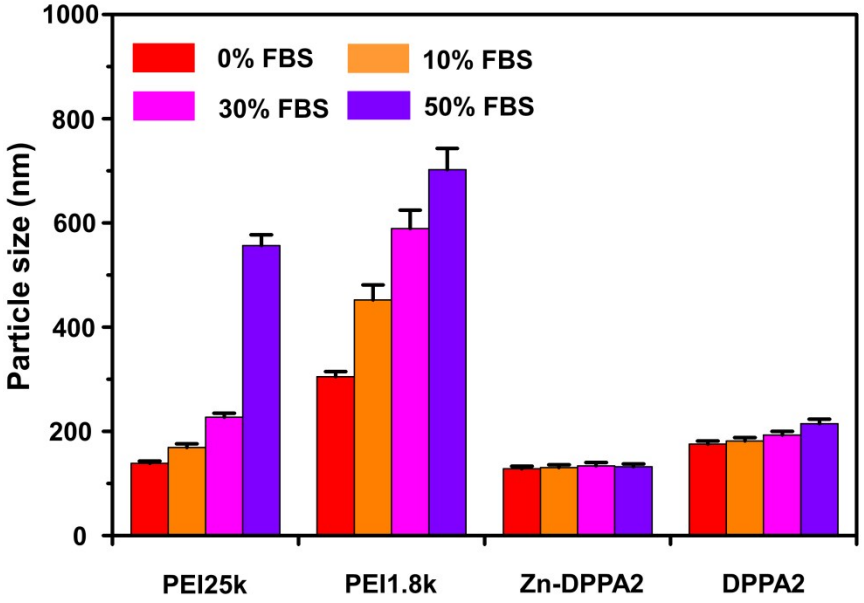


Fig. S24 Particle size stability of Zn-DPPA2/DNA complexes (w/w=10/1) at different FBS contents. PEI25k/DNA (w/w=2.5/1), PEI.18k/DNA (w/w=10/1), and DPP2/DNA (w/w=10/1) were included as control.

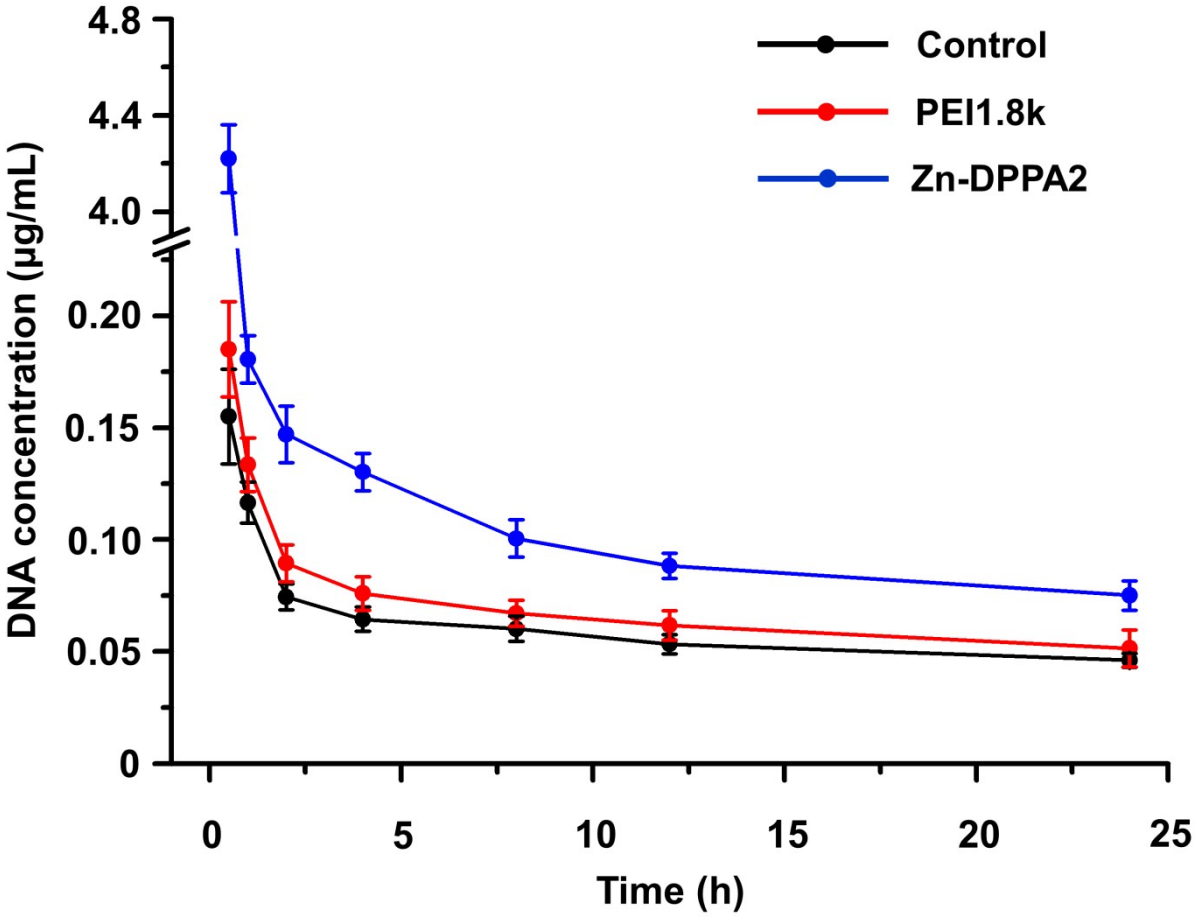


Fig. S25 DNA concentrations in blood versus time after intravenous injection of Cy5-DNA,

PEI1.8k/Cy5-DNA, and Zn-DPPA2/Cy5-DNA complexes, respectively.

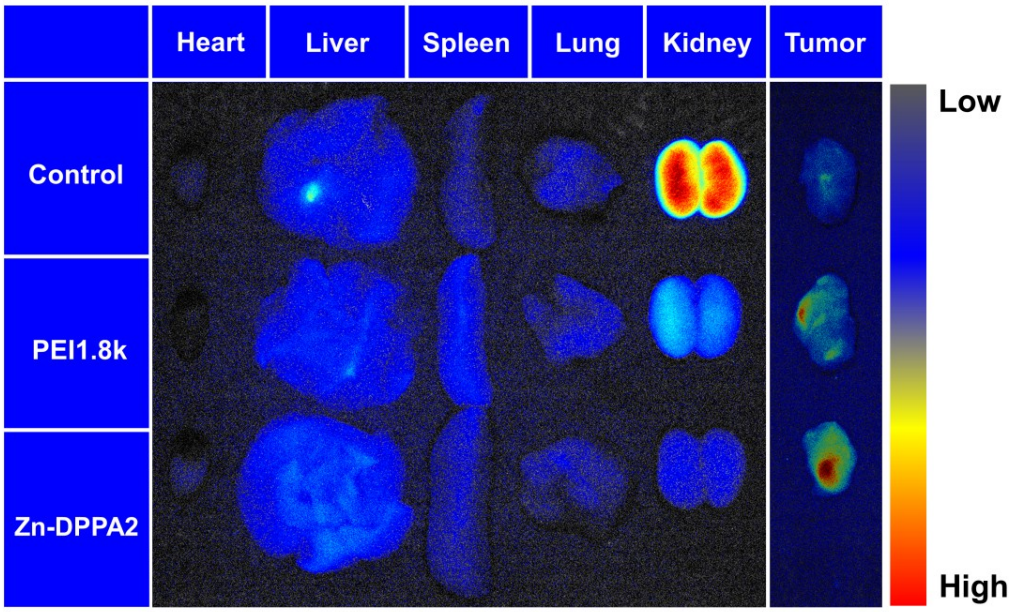


Fig. S26 The representative images of distribution of Zn-DPPA2/DNA complexes in main organs (heart, liver, spleen, lung, kidney) and tumor after intravenously injecting Zn-DPPA2/DNA complexes. PEI1.8k/DNA and DNA were included as control.