Supporting Information to:

Targeting DNA to endoplasmic reticulum efficiently enhances gene delivery and therapy

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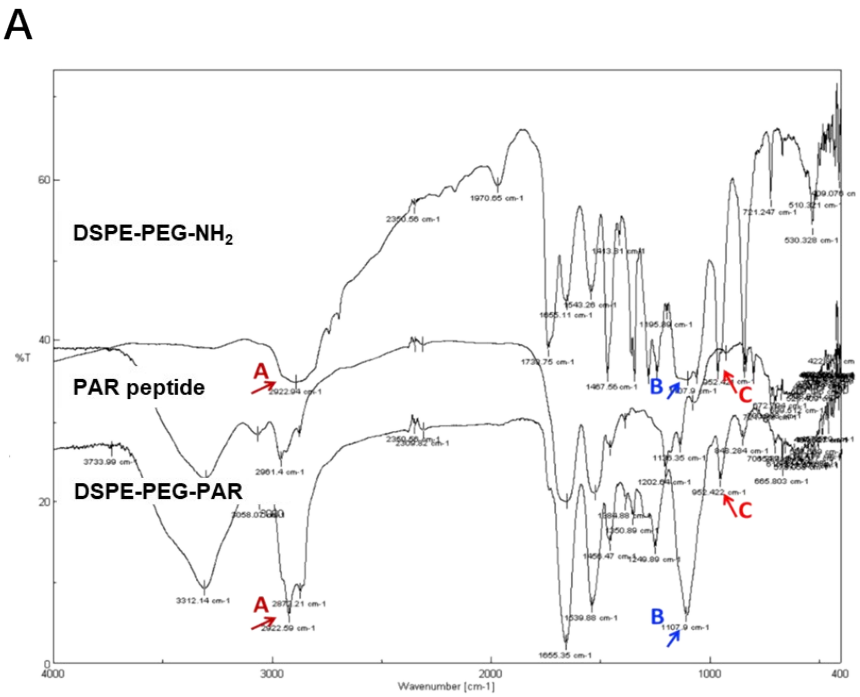

Figure S1: Synthesis and characterization of DSPE-PEG$_{2000}$-PAR. (A) The FT-IR spectrum of DSPE-PEG-NH_2, PAR peptide, and DSPE-PEG$_{2000}$-PAR (A, νC-H=2922.59 cm^{-1}, B, νC-O=1107.9 cm^{-1}, C, ΔC-H (-CH_2-) =952.422 cm^{-1}).

Table S1: Six formulations of cationic liposomes modified with PAR peptide

Lipid(mg)	DOTAP: DOPE					
	2:1		4:1		8:1	
Formula	1	2	3	4	5	6
DOTAP	5.173	5.173	6.208	6.208	6.898	6.208
DOPE	2.587	2.587	1.552	1.552	0.862	1.552
DSPE-PEG	0.06	0.12	0.06	0.12	0.06	0.12
$DSPE\text{-}PEG_{2000}$-PAR	0.18	0.12	0.18	0.12	0.18	0.12

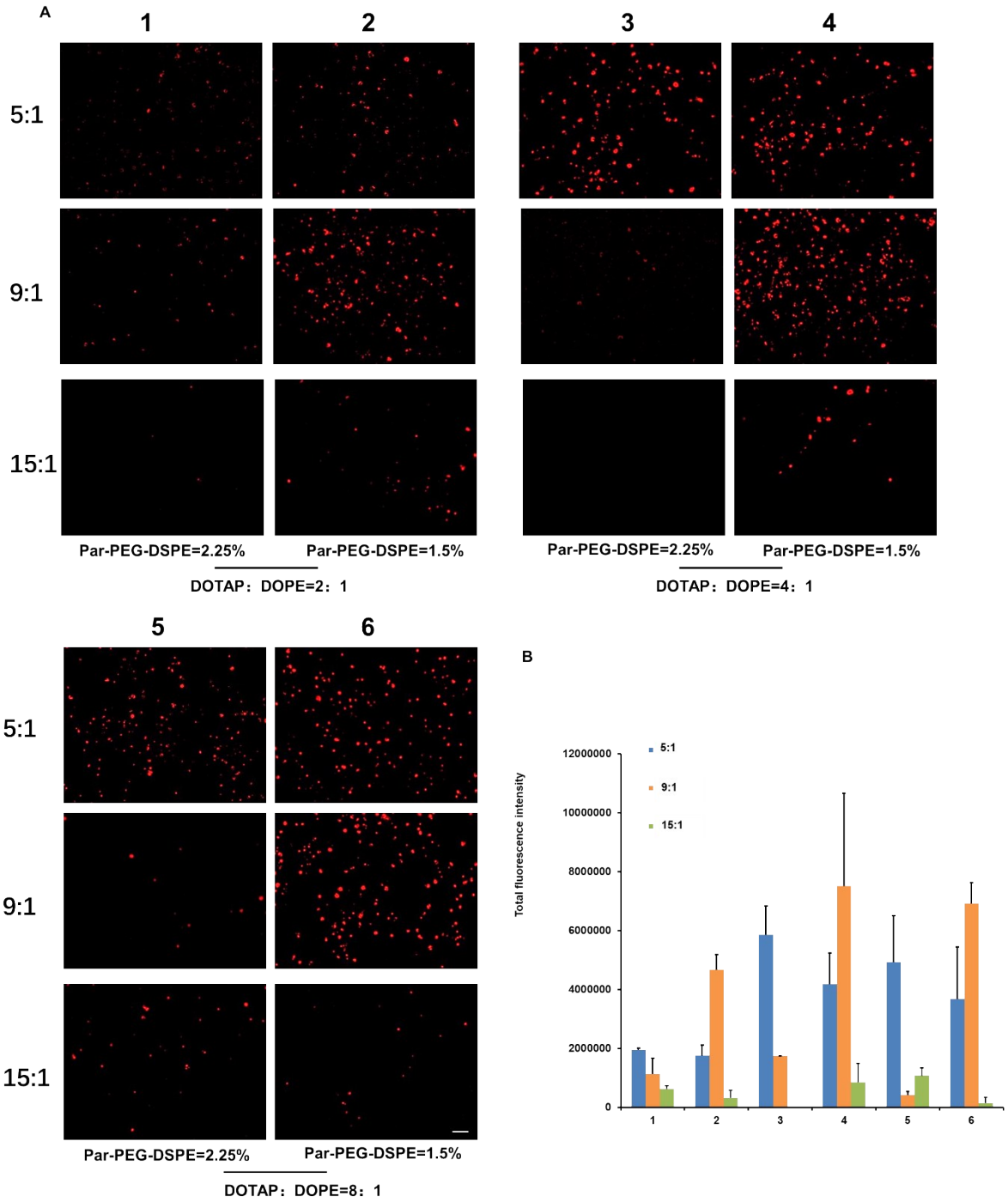

Figure S2: The exploration of the optimal prescriptions for transfection. (A) The cellular uptake efficiency of the different PAR-modified cationic liposome/DNA complexes (5:1, 9:1, 15:1). (B) The total fluorescence intensity of (A) was measured by using ImageJ. Scale bars, 100 μm. All error bars are expressed as ± SD, n = 3.

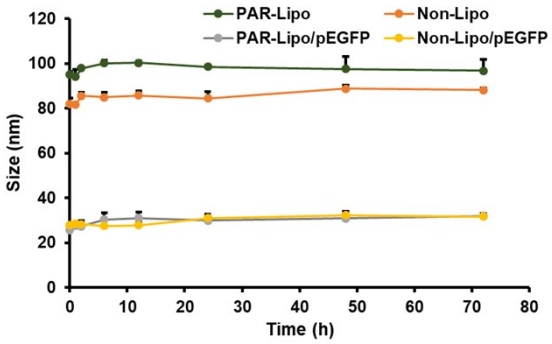

Figure S3: The serum stability of liposomes in PBS + 10% FBS at 37 °C.

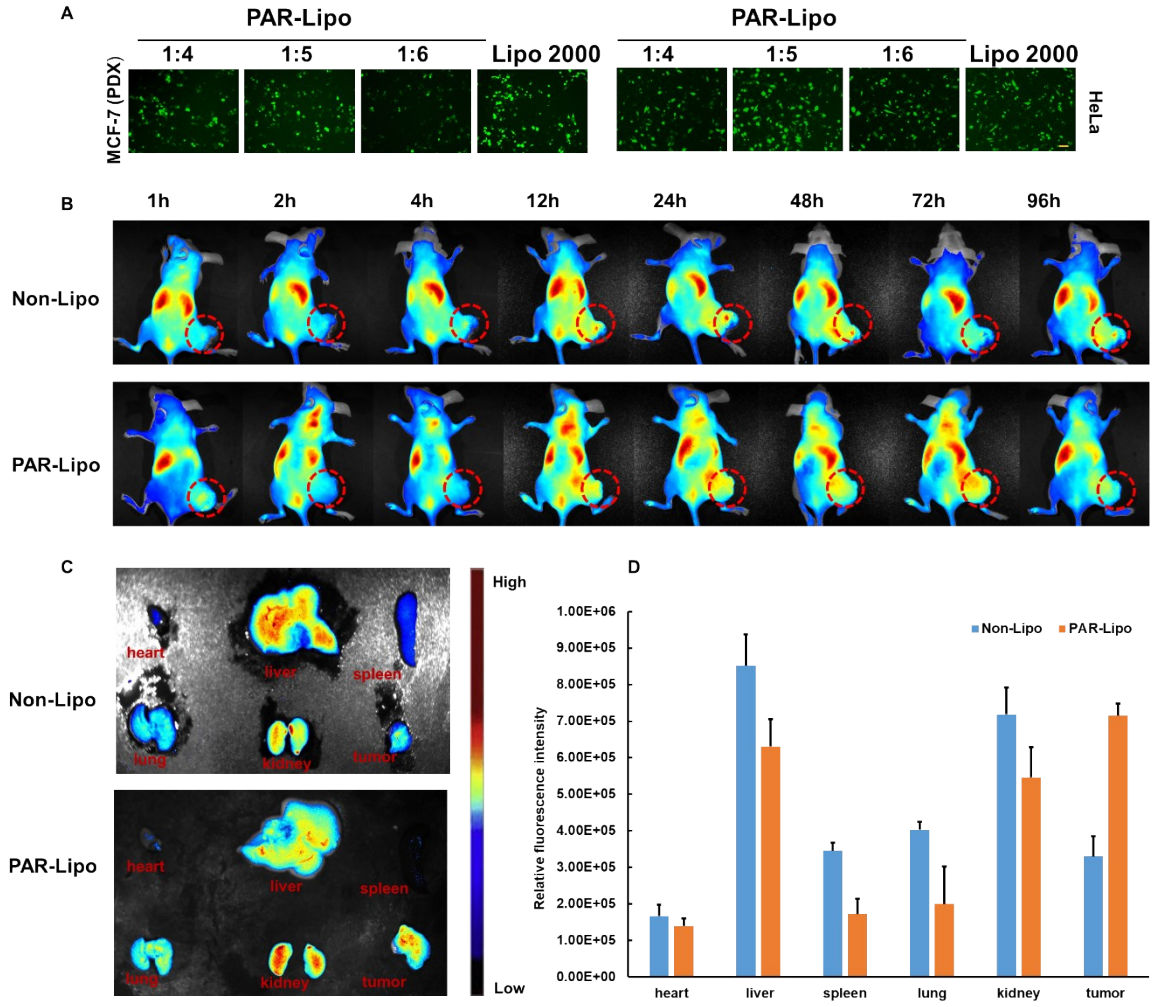

Figure S4: The exploration of the optimal transfection proportion of the PAR-Lipos and the biodistribution observed for the PAR-Lipos and Non-Lipos. (A) Green fluorescence protein expression 24 h after transfection. Scale bars, 100 μm. (B) *In vivo* bioluminescence imaging of MCF-7 (PDX) tumor-bearing mice injected intravenously with DiR-labeled Non-Lipos and PAR-Lipos at different time points. (C) Fluorescent imgaes of DiR-labeled Non-Lipos and PAR-Lipos tissue distribution in MCF-7(PDX) tumor bearing mice at 72 h after injection. (D) Quantification of the ex vivo fluorescence signals of various tissues in (C). All error bars are expressed as ± SD, n = 3.

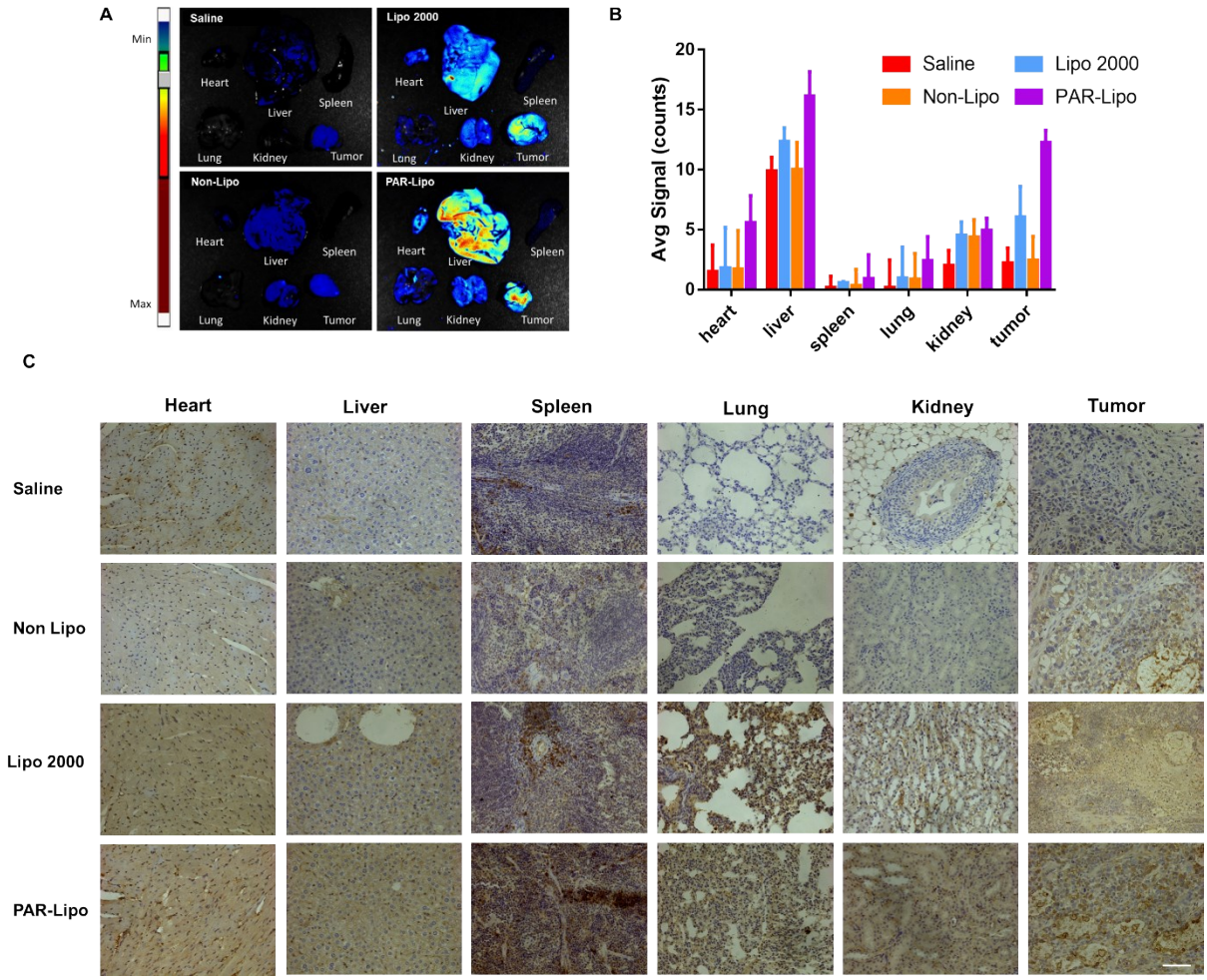

Figure S5: In *vivo* gene transfection efficiency mediated by various complexes. (A) GFP expression in MCF-7 (PDX) tumor-bearing mice after intravenous injection with Lipo 2000/pEGFP, Non-Lipo/pEGFP or PAR-Lipo/pEGFP complexes. (B) Results from the quantitative analysis of fluorescence intensity in (A). (C) Immunohistochemical staining of GFP after transfection *in vivo*. Scale bars, 100 μm. All error bars are expressed as ± SD, n = 5.

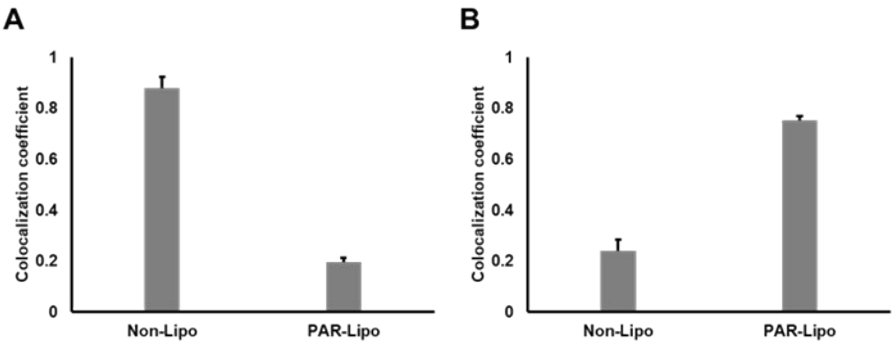

Figure S6: Intracellular fluorescence colocalization of liposomes in ER and lysosomes. (A) The Pearson correlation coefficient (PCC) of liposomes and lysosomes in Figure 5B was evaluated by using ImageJ. (B) The PCC of liposomes and ER in Figure 5C was evaluated by ImageJ. All error bars are expressed as ± SD, n = 3.

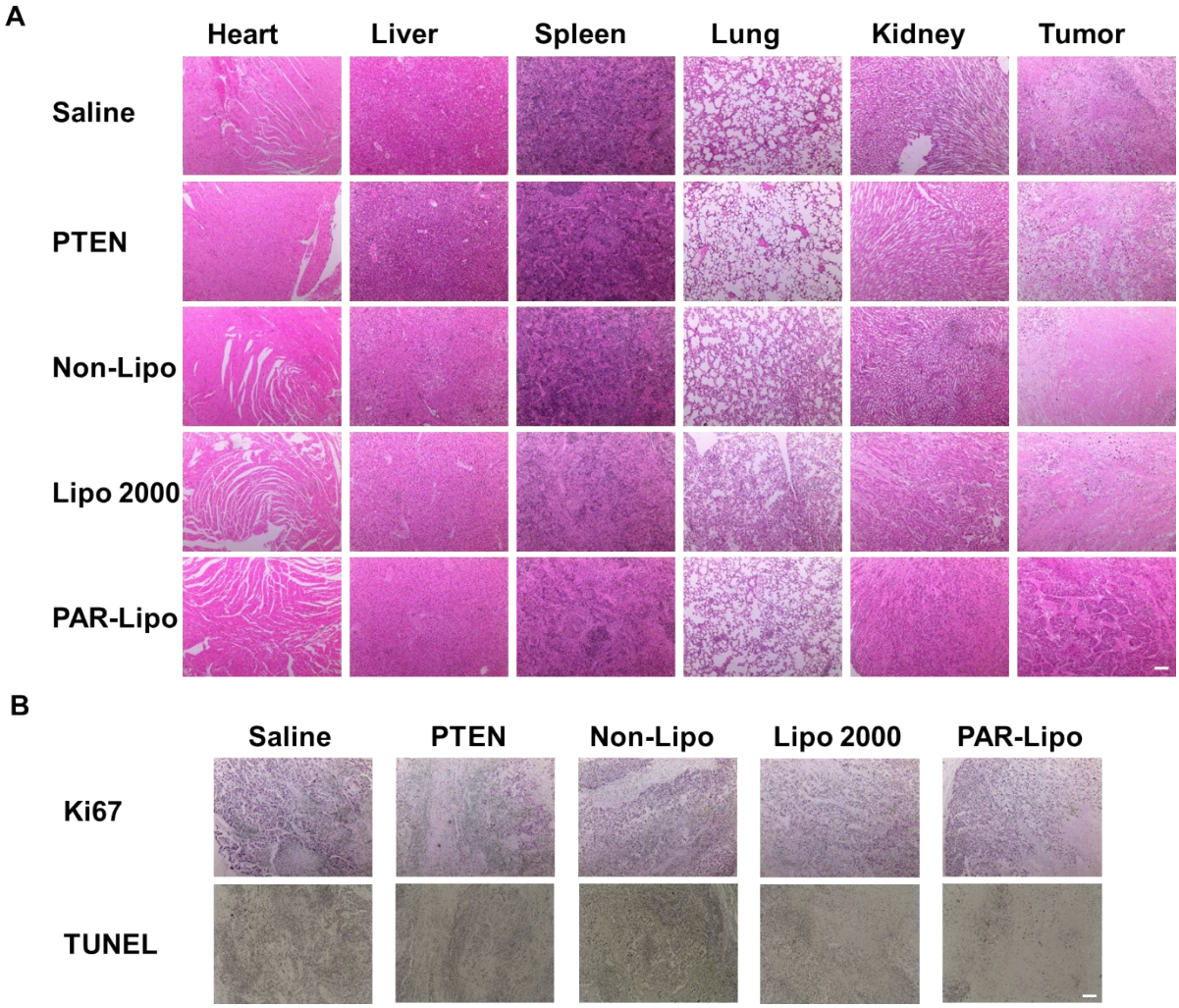

Figure S7: The safety profile of the liposomes transfected with pPTEN in the MCF-7 (PDX) tumor. (A) Results of H&E staining on the heart, liver, spleen, lung and kidney slices from the four groups of mice. Scale bars, 100 μm. (B) Results from the Ki67 and TUNEL staining of tumor tissues. Scale bars, 100 μm.

No. (Formula)	Day 1		Day 3		Day 8	
	Size(d.nm)	PDI	Size(d.nm)	PDI	Size(d.nm)	PDI
1	126.0±6.5	0.219±0.027	60.0±17.3	0.285±0.076	164.0±43.0	0.399±0.193
2	44.6±10.0	0.354±0.033	46.8±4.1	0.523±0.123	50.0±23.2	0.339±0.018
3	61.8±22.6	0.373±0.014	40.7±15.9	0.449±0.003	63.1±23.6	0.315±0.063
4	49.1±17.9	0.398±0.009	32.1±0.5	0.444±0.066	46.5±33.3	0.338±0.0266
5	61.0±14.2	0.368±0.048	30.2±7.7	0.412±0.027	61.7±13.4	0.425±0.048
6	91.6±3.2	0.235±0.030	79.3±5.0	0.255±0.142	68.5±2.8.	0.350±0.067

Table S2: The stability of liposomes stored at 4°C and the particle size were determined