Supplementary Information

Systemic siRNA Delivery to Tumors by Cell-Penetrating α-Helical Polypeptide-Based Metastable Nanoparticles

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Table S1. Sequences of EGFR siRNA and siRNA with scrambled sequence (sc).

	Sequence
siRNA sense (EGFR)	5'-CCAUAAAUGCUACGAAUAUtt-3'
siRNA anti-sense (EGFR)	5'-AUAUUCGUAGCAUUUAUGGag-3'
siRNA sense (sc)	5'- UAACGACGCGACGACGUAAtt -3'
siRNA anti-sense (sc)	5'- UUACGUCGUCGCGUCGUUAtt-3'

Table S2. Sizes of PVBLG-8/PLG complexes at different weight ratios.[a]

PVBLG-8/PLG ratio (w/w)	Charge ratio (positive/negative)	Size (nm)	PDI
10/1	10/1.5	87.7	0.168
10/2	10/3	93.6	0.118
10/5	10/7.5	173.3	0.220
10/10	10/15	373.7	0.288
10/20	10/30	507.4	0.213

[a] PVBLG-8/siRNA weight ratio was maintained constant at 10:0.5.

Table S3. Primer sequences for EGFR and GAPDH.

	Sequence
EGFR F	5'- GCG TCT CTT GCC GGA ATG T -3'
EGFR R	5'- CTT GGC TCA CCC TCC AGA AG -3'
GAPDH F	5'- ATT CCA CCC ATG GCA AAT TC -3'
GAPDH R	5'- TGG GAT TTC CAT TGA TGA CAA G -3'

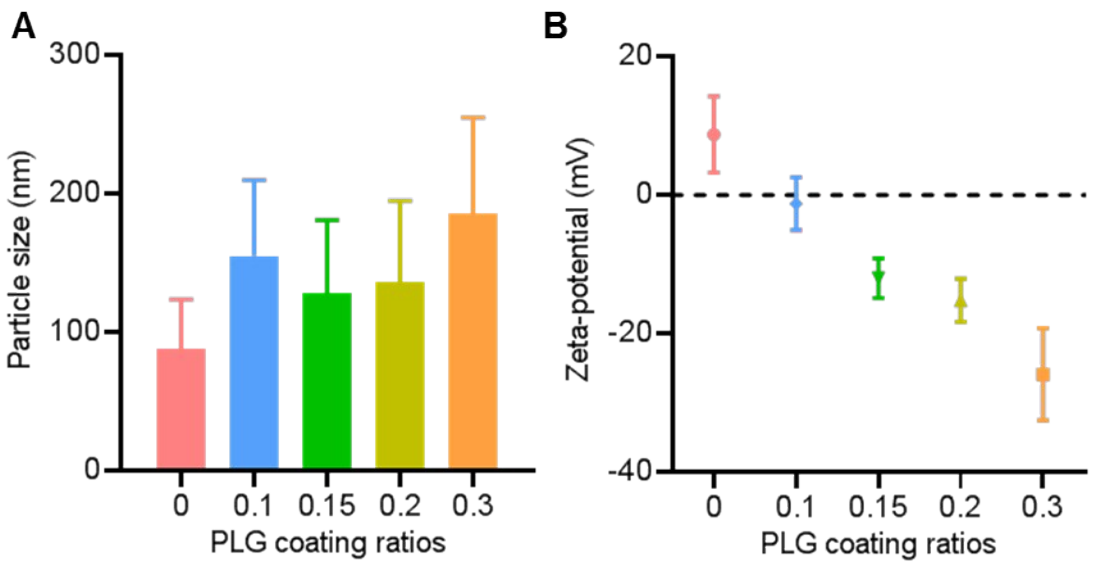

Fig. S1 (A) Particle size and (B) zeta potential of PSP NPs with different PLG coating ratios (PLG coating/PVBLG-8 weight ratios).

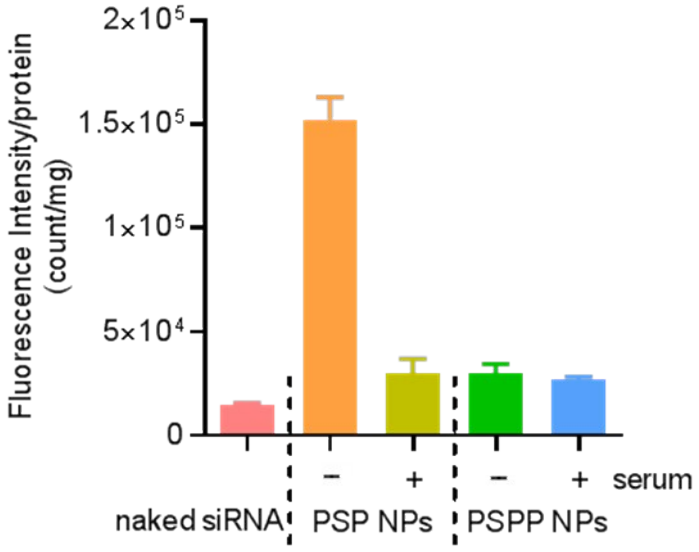

Fig. S2 Fluorescence intensity of Cy3-siRNA in HEK-293 cells following treatment with naked siRNA, PSP NPs, or PSPP NPs at pH 7.4 in the presence of absence of 10% FBS (n = 4).

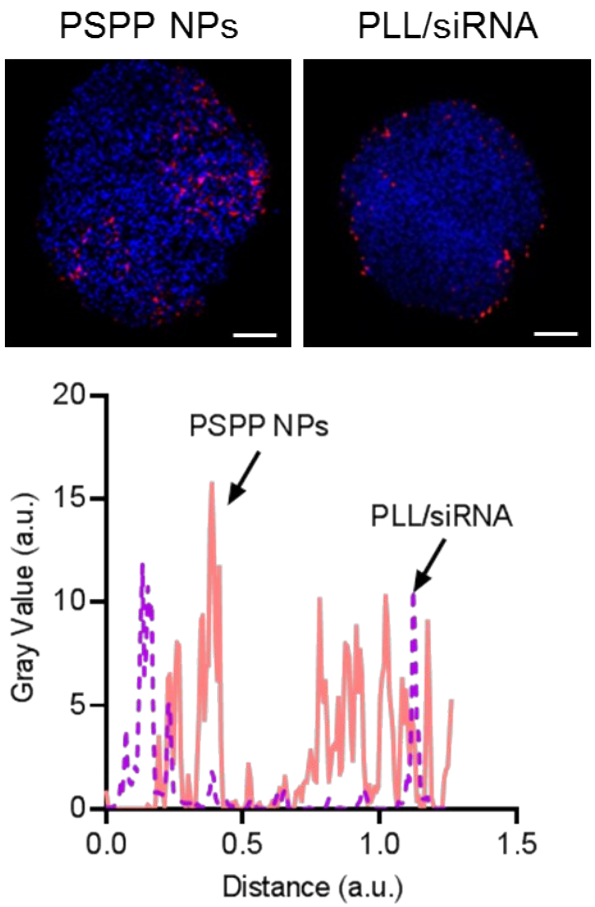

Fig. S3 Cy3-siRNA signal distribution within the tumor spheroids treated with PLL/siRNA NPs or PSPP NPs (at pH 6.5) for 4 h. Representative images were used for Image J analysis.

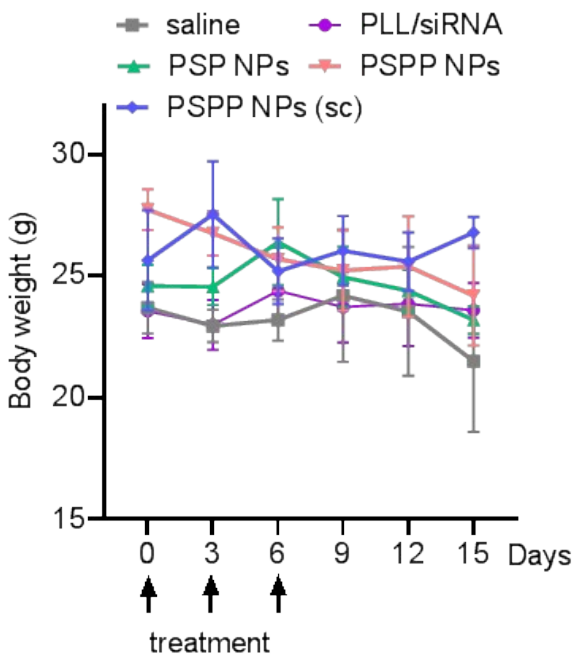

Fig. S4 Body weight changes of mice during the 15-day observation period. Different NPs or saline were injected on Day 0, 3, and 6 (n = 6).

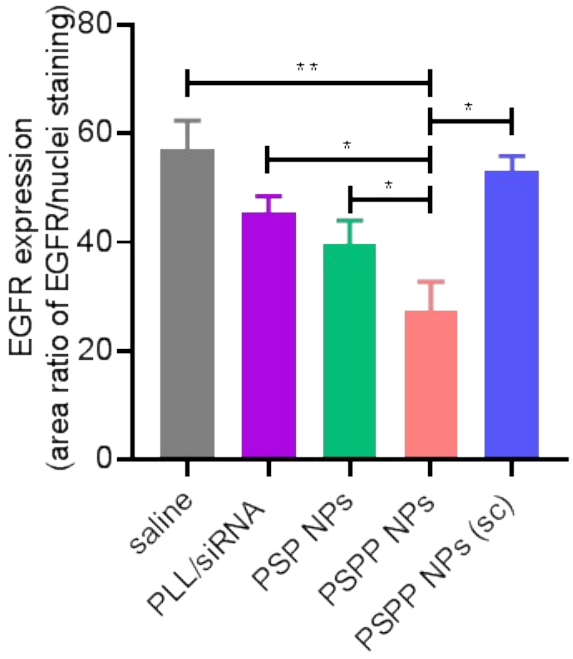

Fig. S5 Quantitative evaluation of EGFR immunostaining in tumor sections with different NPs treatments. (n=3, $*$ $p < 0.05$; $**$ $p < 0.005$; $***$ $p < 0.001$)