Supporting Information

Explore the *in vivo* fates of RGD and PEG modified PEI/DNA nanoparticles by optical imaging and optoacoustic imaging

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1. Gel retardation assay

Gel retardation assay was performed to confirm the *p*DNA complexation ability of PEI, PP1.5 and PPR1.5. The results were shown in Fig. S1: The naked *p*DNA was used as a control. Compare with the control, the bands of DNA in all three groups decreased with increasing N/P ratios. The DNA was completely retarded at the weight ratio of 0.2 by PEI/DNA complex because of its high positive charges on the surface of PEI. The DNA could be released from the complex at the same ratio 0.2 in the PP1.5 groups and PPR1.5 groups, which indicated that the amount of charge in PEI was higher than PP1.5 and PPR1.5.

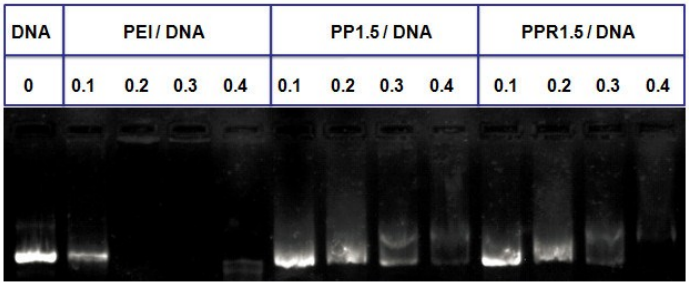

Fig. S1 Gel retardation assay of PEI/*p*DNA, PP1.5/*p*DNA and PPR1.5/*p*DNA. Lane 1, *p*DNA; lanes 2-13, PEI/*p*DNA, PP1.5/*p*DNA and PPR1.5/*p*DNA at weight ratios of 0.1:1, 0.2:1, 0.3:1 and 0.4:1, respectively.

2. ζ-potential and size measurement

The DLS data of PEI-25k, PP1.5 and PPR1.5 were measured using a particle analyzer. As shown in Fig. S2 (A), Fig. S2 (B) and Fig. S2 (C), the PP1.5 and the PPR1.5 had an average size of 140 nm with a narrow distribution which might be an optimal size for the tumor targeting. The particle sizes and the zeta potentials of PEI/*p*DNA, PP1.5/*p*DNA and PPR1.5/*p*DNA complexes at different transfection ratios were measured. The diameter and the surface charge density are two important factors that can influence tumor targeting effect *in vivo*. As shown in Fig. S2 (D) and Fig. S2 (E), the particle sizes of all the three groups exhibited no more than 140 nm, which will be expected to target to tumor through the EPR effect. The zeta potential of the PP1.5 and PPR1.5 groups decreased remarkably to 5.1±2.3 mV, which is expected to have a better long-term efficiency *in vivo*.

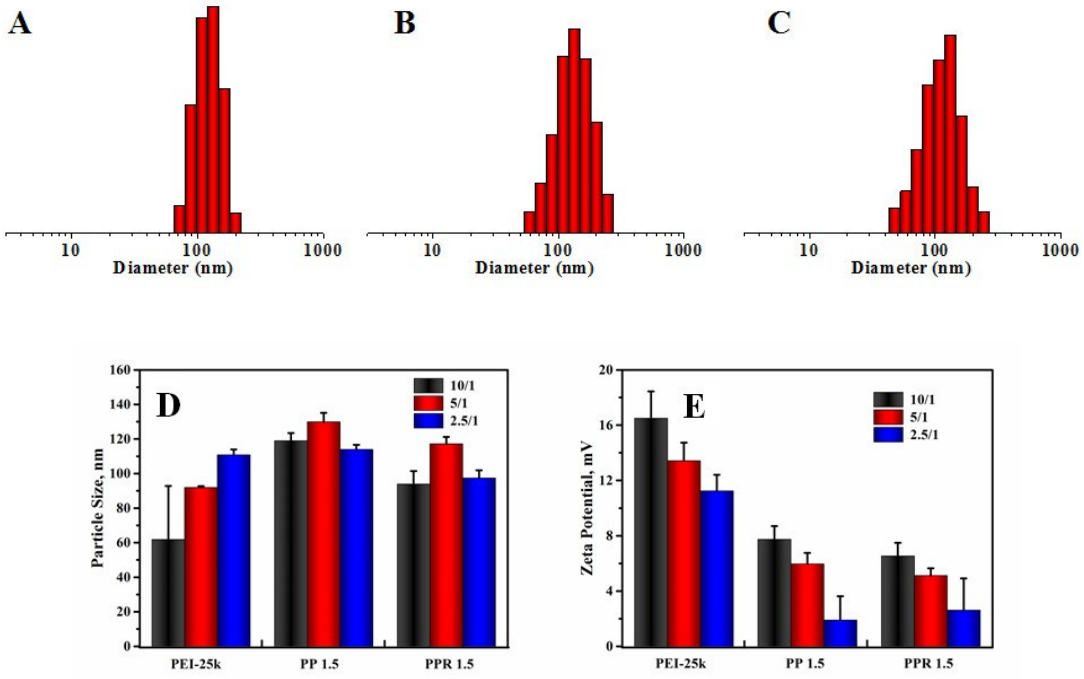

Fig. S2 The DLS data of PEI-25k, PP1.5 and PPR1.5. The particle size (D) and zeta potential (E) of PEI-25k/*p*DNA, PP1.5/*p*DNA and PPR1.5/*p*DNA at different transfection ratio. Data are shown as mean ± SD (n=5).

3. Optoacoustic imaging analysis

In order to further evaluate the tumor accumulation effect, the 3D-optoacoustic tomography systems were used to analyze the targeted distribution of the complexes in tumor tissue of PEI-25k, PP1.5, and PPR1.5 after administration for 72 h. As shown in Fig. S3 (A) and Fig. S3 (B), only the PPR1.5 group shows the obvious signal differences were noticed in the tumor section between the HeLa and EMT-6 tumors compare with the other groups. The PPR1.5 in HeLa tumor showed the strongest signals in the tumor region, while the non-RGD binding receptor EMT-6 tumor showed a weak signal.

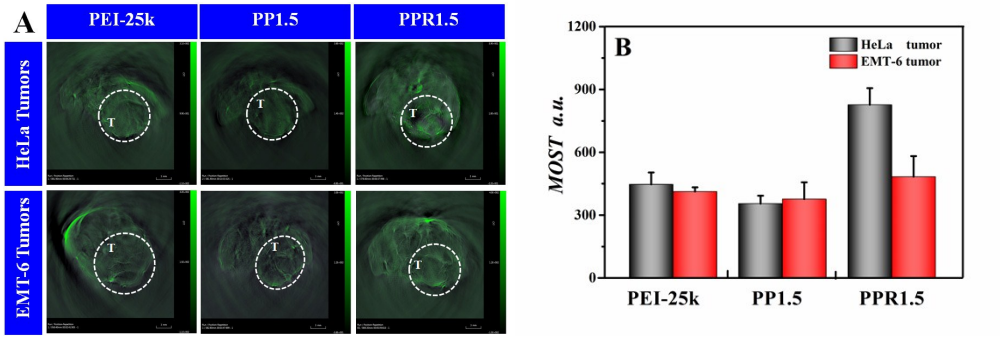

Fig. S3 MSOT images of HeLa tumor-bearing mice and EMT-6 tumor-bearing mice at 72 h following injection of PEI-25k/DNA-Cy7 (5/1), PP1.5/DNA-Cy7 (5/1) and PPR1.5/DNA-Cy7 (5/1) complexes respectively. The tumor regions (A) and Quantitative analysis results (B) of complexes accumulate in tumor at 72 h following injection. Data are shown as mean ± SD (n=5).