Electronic Supplementary Material (ESI) for Biomaterials Science.

Supplementary information

A versatile polyion complex can intelligently response tumor microenvironment to eliminate tumor stem cells for enhanced lung cancer targeted therapy

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Synthesis procedure

Synthesis of PEI-SS-PLA copolymer

Redox-responsive copolymer PEI-SS-PLA has been synthesized successfully by our group. The details were according to the reference.[1]

Synthesis of CDI-PEG-CDI copolymer

CDI-PEG-CDI was synthesized as Fig.S1. NH_2-PEG-NH_2 was placed into a conical flask and dissolved with anhydrous tetrahydrofuran (THF). Meanwhile, CDI was also dissolved using THF. CDI solution was added into the flask dropwise (molar ratio of PEG derivate and CDI was 1:10) under 40℃ for 2 h. Thereafter, THF was removed and the product was added into cold diethyl ether. The precipitate was collected and the product was obtained.

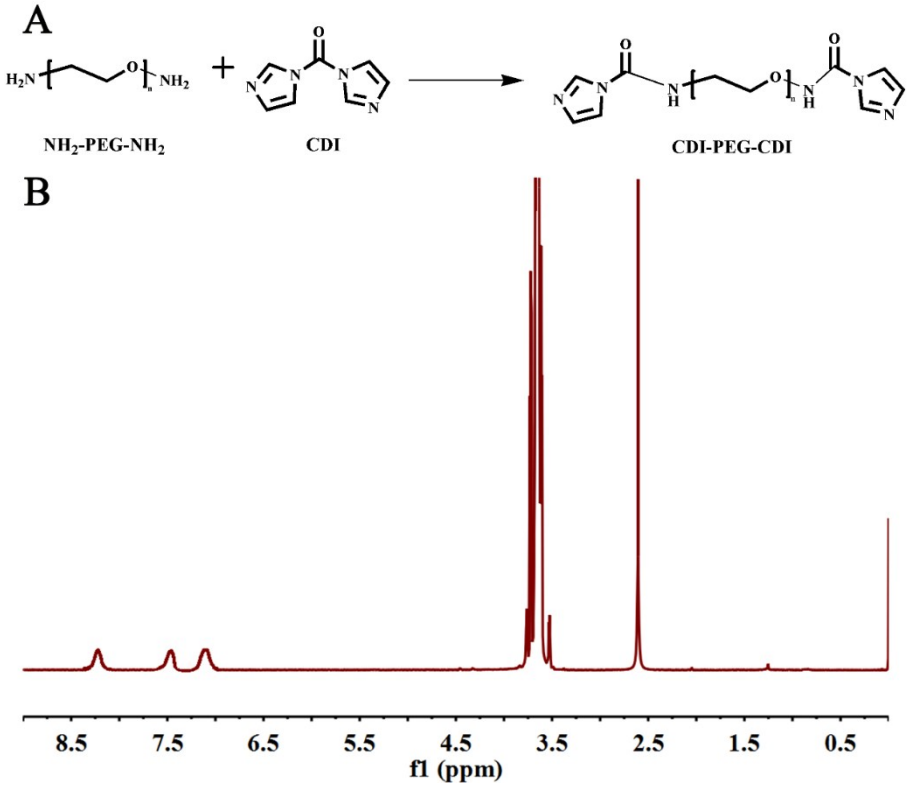

Fig.S1: synthesis pathway (A) and typical ^{1}H-NMR spectrum (B) of CDI-PEG-CDI.

As shown in Fig.S1, the peaks of δ 8.23 ppm, δ 7.45 ppm and δ 7.09 ppm corresponding to the protons of imidazole ring of CDI. Peaks groups of 3.48~3.82 ppm corresponding to the protons of PEG.

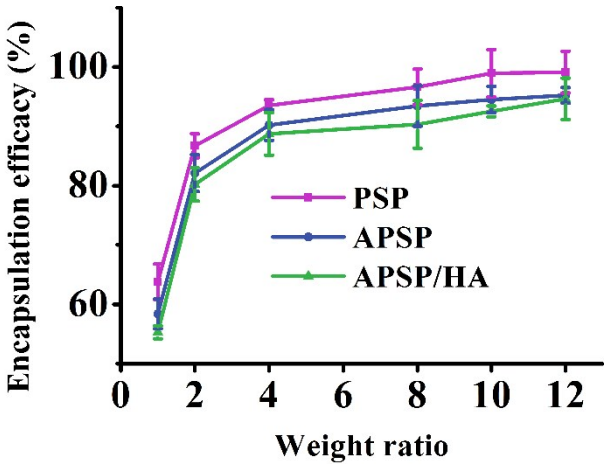

Fig.S2: encapsulation efficacy variation of different formulations as the variation of weight ratio (copolymer: miRNA, *w/w*).

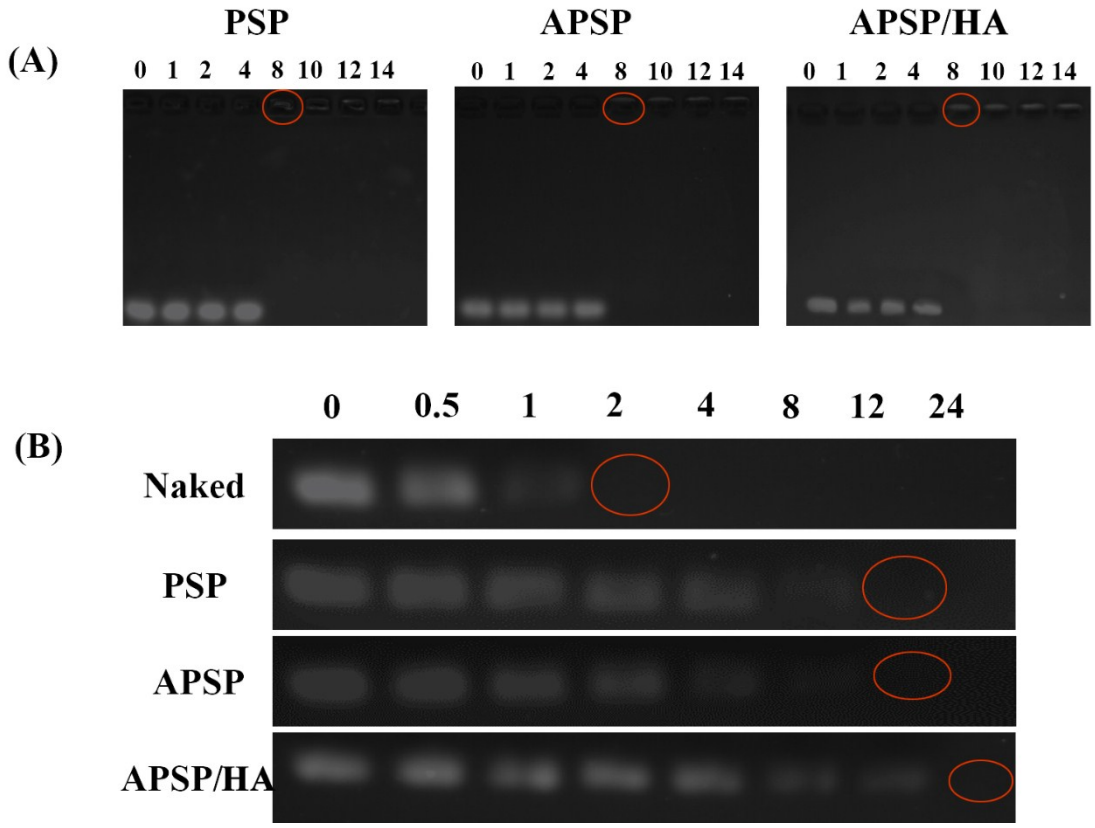

Fig.S3: (A) Agarose gel electrophoresis assay. Binding capability of different formulations with different weight ratios; (B) serum stability of different formulations at different time point.

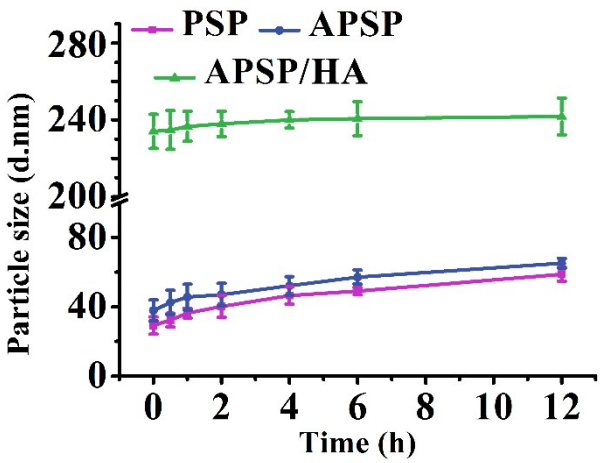

Fig.S4: *in vitro* serum stability of different formulations at 37℃.(n=3)

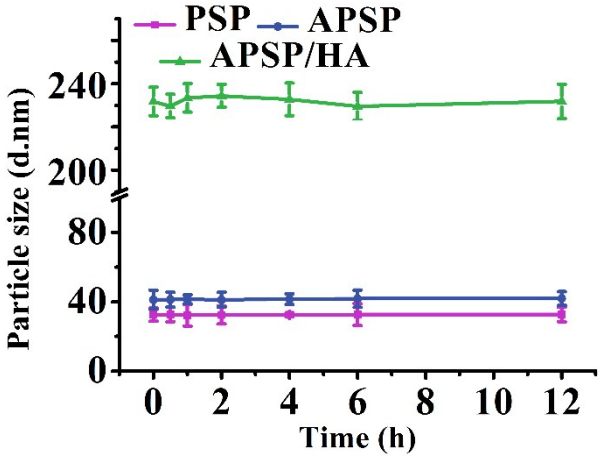

Fig.S5: *in vitro* PBS stability of different formulations at 37℃.(n=3)

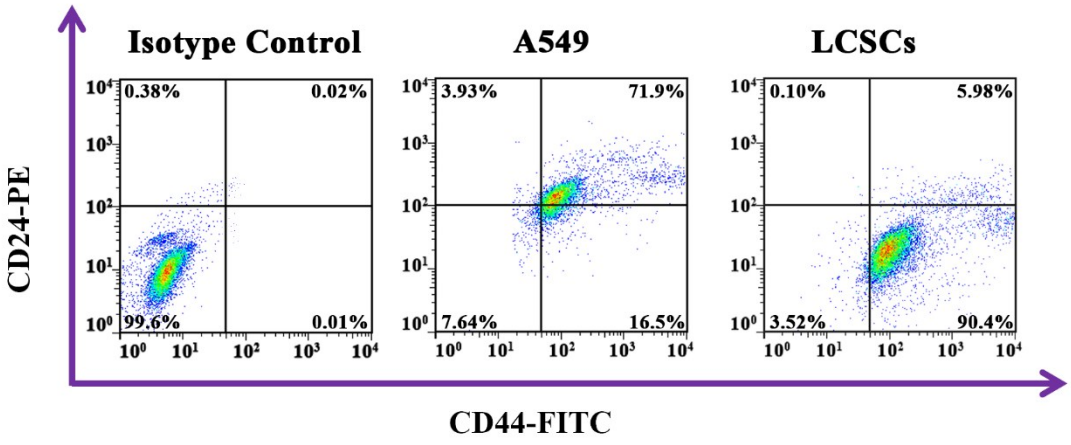

Fig.S6: $CD44^{+}/CD24^{-}$ cell subpopulation analysis against A549 and LCSCs cell line.

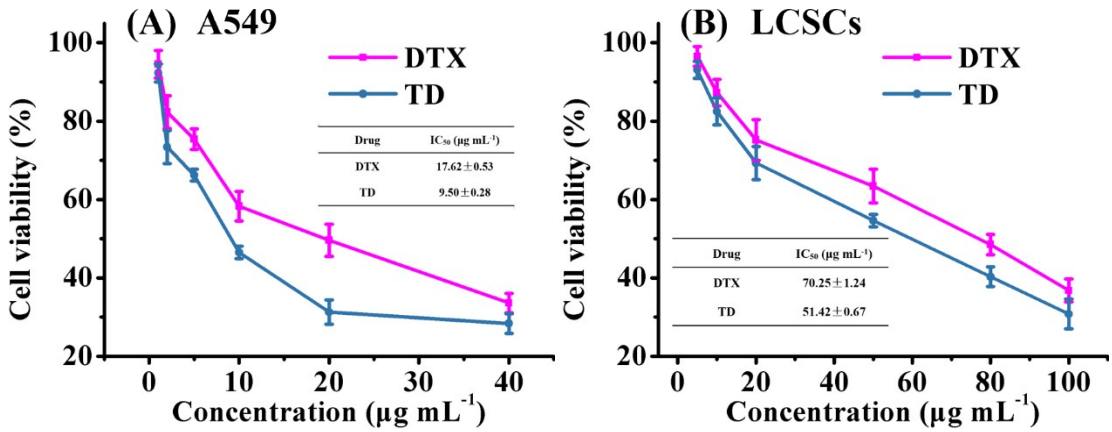

Fig.S7: *in vitro* cytotoxicity DTX and TD against A549 and LCSCs cell lines. (n=3)

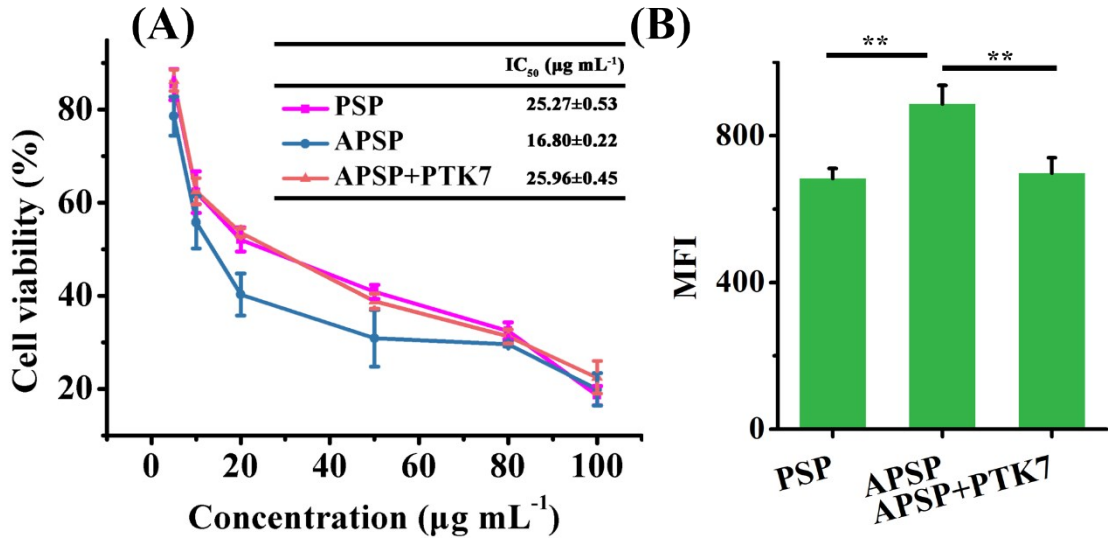

Fig.S8: competitive cytotoxicity (A) and cellular uptake (B) assay of APSP with/without PTK7 antibody.

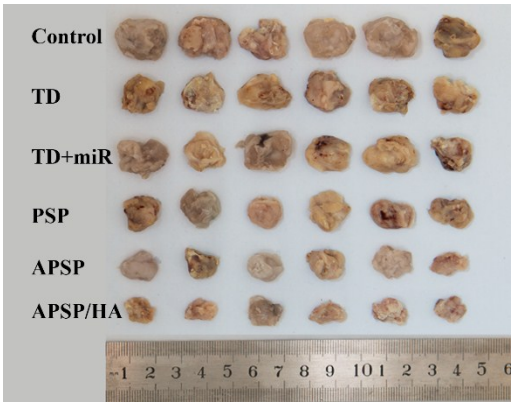

Fig.S9: tumor images of different drug-treated groups after 18 days post administrations. (n=6)

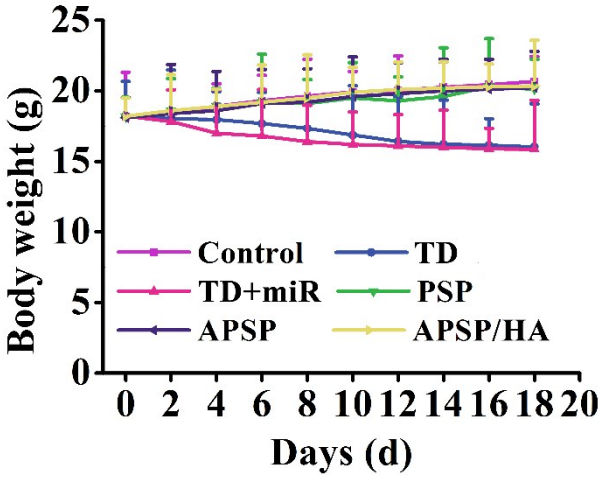

Fig.S10: Body weight changes of different formulations. (n=6)

(1) Sun, X.; Zhang, J.; Yang, C.; Huang, Z.; Shi, M.; Pan, S.; Hu, H.; Qiao, M.; Chen, D.; Zhao, X. Dual-Responsive Size-Shrinking Nanocluster with Hierarchal Disassemble Capability for Improved Tumor Penetration and Therapeutical Efficacy. *ACS Applied Materials & Interfaces* **2019**, DOI: 10.1021/acsami.8b21580.