Supporting information

of

An MMP-2 responsive liposome integrating anti-fibrosis and chemotherapeutic drugs for enhanced drug perfusion and efficacy in pancreatic cancer

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Supporting Tables and Figures

Table S1. Characterization of LRC and LC NPs and drug-loaded LRC

Groups	Particles size (nm)	Zeta potential (mV)	Polydispersity
LRC	68.2±3.7	-27.6±0.3	0.29
LC	65.8±2.9	-28.5±0.4	0.31
LRC-GEM	71.3±2.1	-28.7±0.2	0.28
LC-GEM	67.5±3.1	-29.2±0.4	0.29
LRC-PFD	70.8±2.5	-28.6±0.2	0.30
LRC-GEM-PFD	71.5±4.2	-30.8±0.5	0.28

All results were determined by DLS. Nanoparticles were prepared by dissolving in PBS (pH 7.4) at a concentration of 0.2 mg/mL of LRC or LC. Results are mean ± S.D. (n=3).

Table S2. Encapsulation efficiencies of LRC and LC with different mass of PFD or GEM added (the mass of LRC and LC used was 1.0 mg)

	PFD added (μg)	10	20	50	100	200	500
LRC-PFD	**PFD encapsulated (μg)**	9.8	19.2	42.2	74.6	88.7	88.2
	Encapsulation efficiency (%)	98	96	84.4	74.6	44.4	17.6
	GEM added (μg)	50	100	200	500	1000	2000
LRC-GEM	**GEM encapsulated (μg)**	25.2	42.3	80.2	147.6	146.5	146.2
	Encapsulation efficiency (%)	50.4	42.3	40.1	29.5	14.7	7.3
LC-GEM	**GEM encapsulated (μg)**	24.3	43.8	81.6	145.2	145.9	144.3
	Encapsulation efficiency (%)	48.6	43.8	40.8	29.0	14.6	7.2

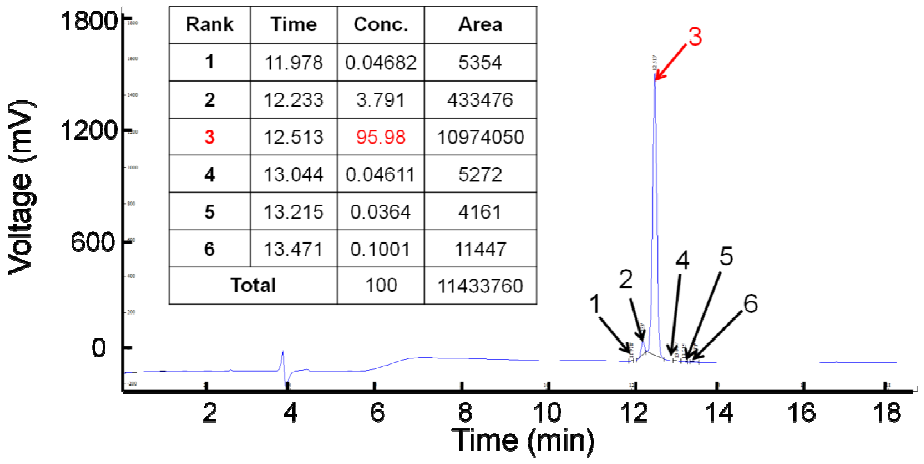

Figure S1. The purity of the MMP-2 responsive peptide. The purity of the peptide was 95.98%.

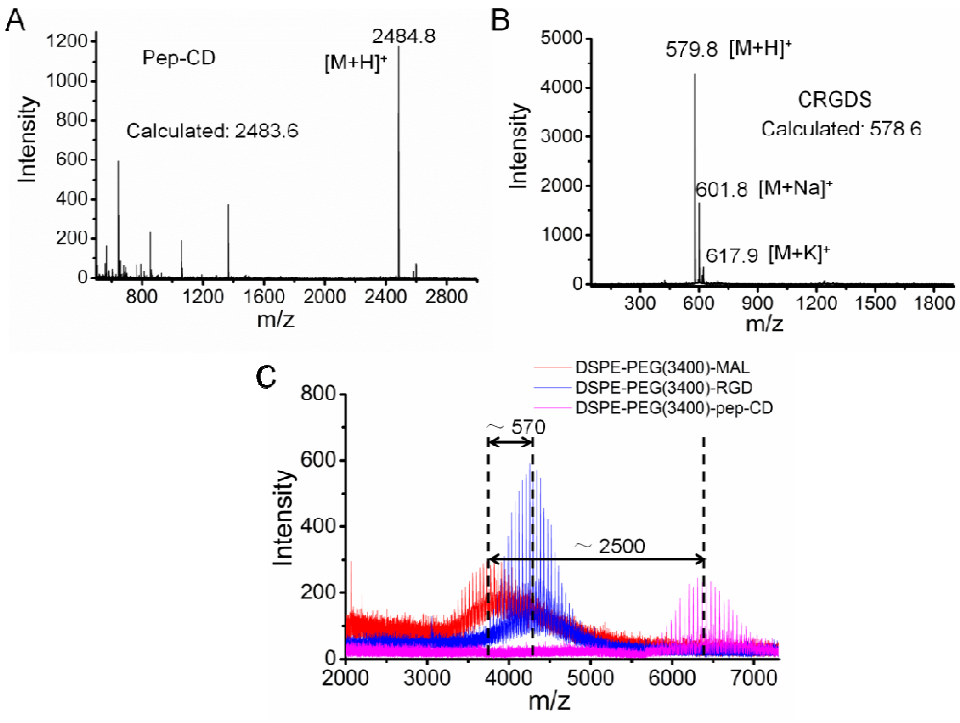

Figure S2. The molecular mass of the pep-CD (A), RGD peptide (CRGDS) (B), DSPE-PEG(3400)-pep-CD and DSPE-PEG(3400)-RGD (C) detected by

MALDI-TOF MS.

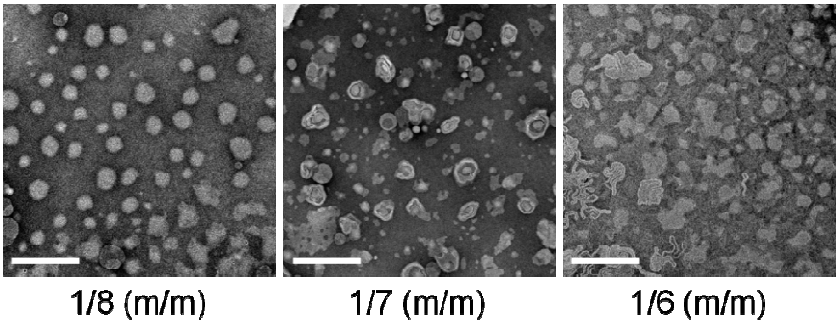

Figure S3. The morphology changes with the increasing the ratio of DSPE-PEG(2000)-pep-CD. The system can not form a regular morphology when the DSPE-PEG(2000)-pep-CD beyond the 1/8 (m/m) ratio. The scale bar is 200 nm.

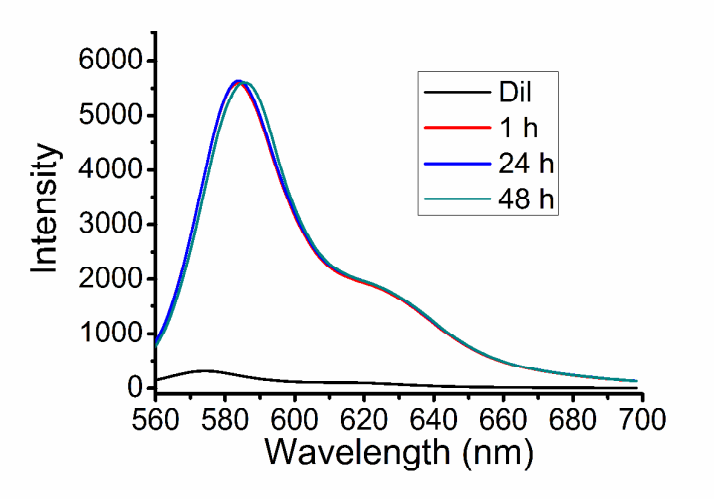

Figure S4. Stability of LRC nanostructure in vitro.

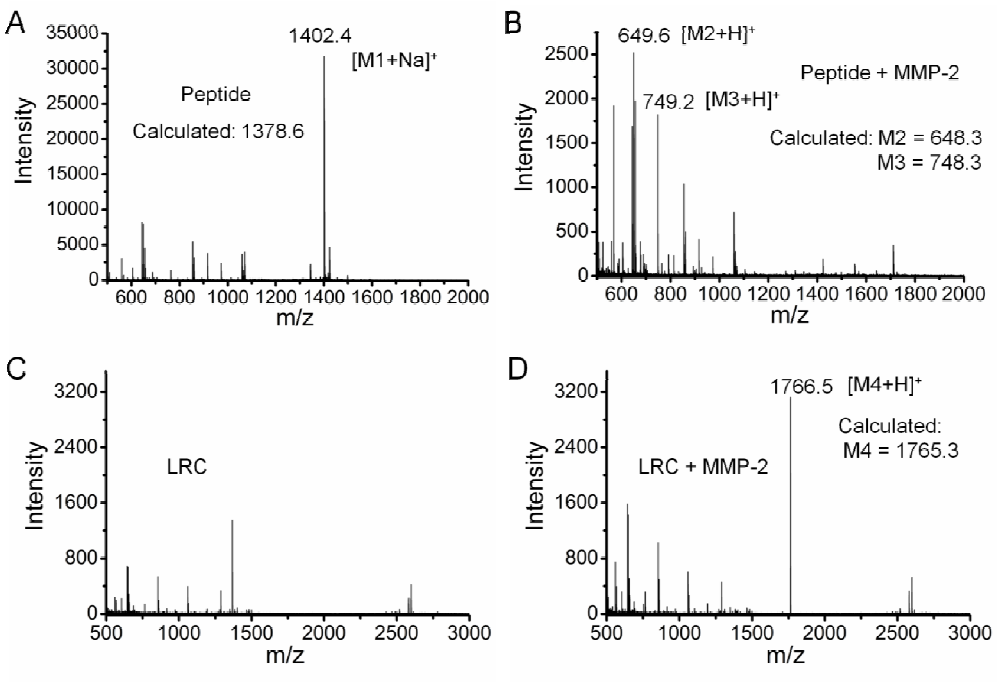

Figure S5. The responsiveness of peptide (A, B) and LRC (C, D) detected by MALDI-TOF MS.

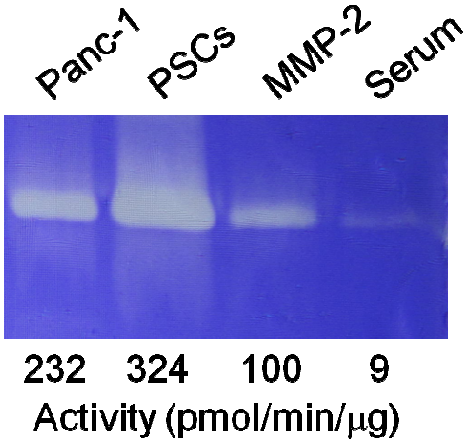

Figure S6. The activity of MMP-2 expressed in cells determined by gelatin zymography assay. Purified MMP-2 was used as positive control.

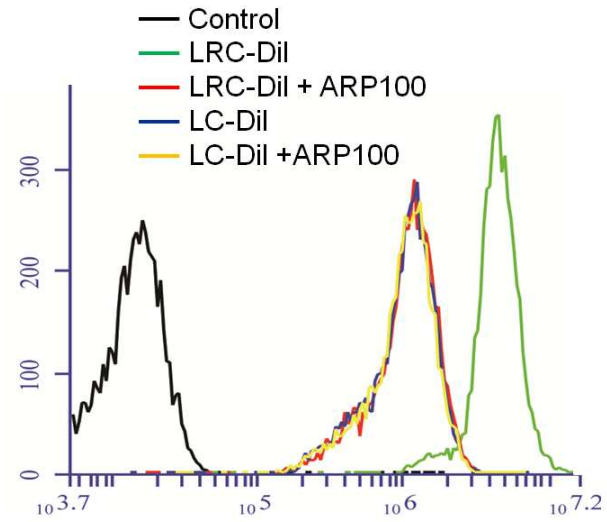

Figure S7. Flow cytometry detection of the cell uptake of LRC-Dil and LC-Dil in vitro

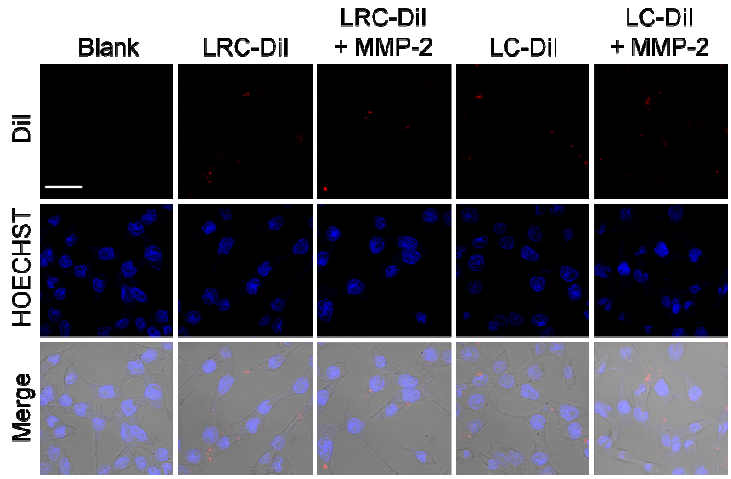

Figure S8. The COS7 cell uptake of Dil labeled LRC and LC with or without MMP-2. The red: Dil; blue: HOECHST. The scale bar, 50 μm.

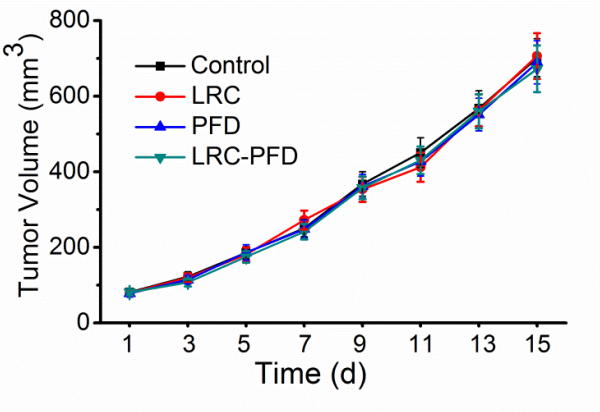

Figure S9. The tumor growth curves of PSCs/Panc-1 co-implanted pancreatic tumor treated by different PFD formulations. PFD dose: 10 mg/kg. The volume of tumors in each group did not exhibited significant differences with others.

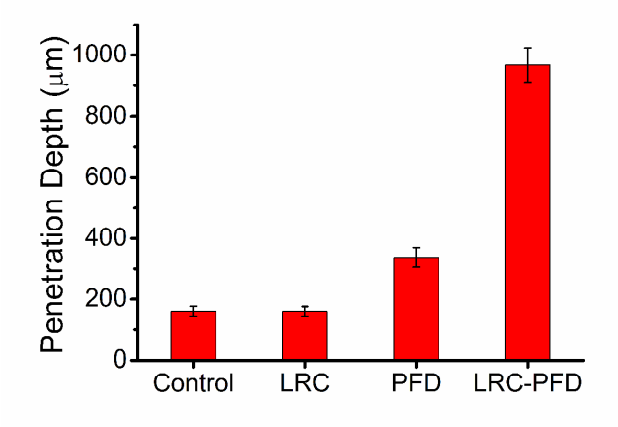

Figure S10. The penetration depths of Rhd in different formulations' treated groups.

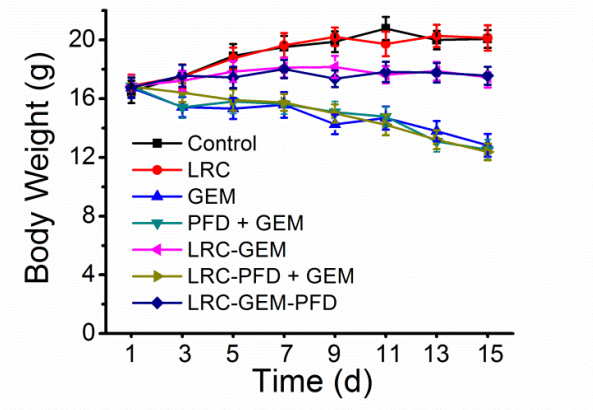

Figure S11. The body weight changes of PSCs/Panc-1 pancreatic tumor bearing mice during different GEM formulations' treatment. GEM dose: 20 mg/kg.