

# **Co-delivery of autophagy inhibitor and gemcitabine using a pH-activatable core-shell nanobomb inhibits pancreatic cancer progression and metastasis**

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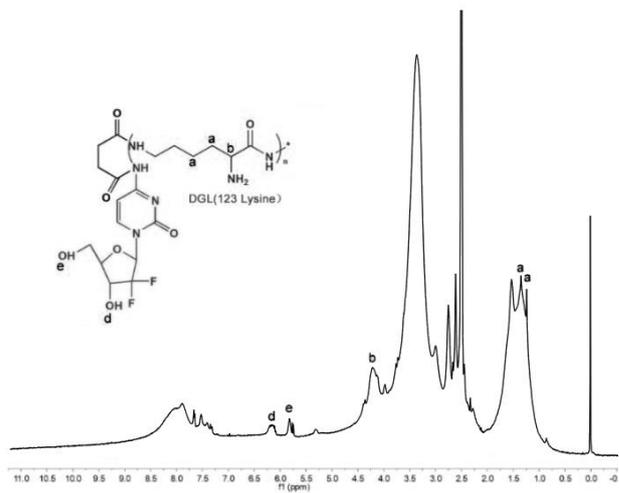


Figure S1. <sup>1</sup>H-NMR confirmation of DGL-GEM.

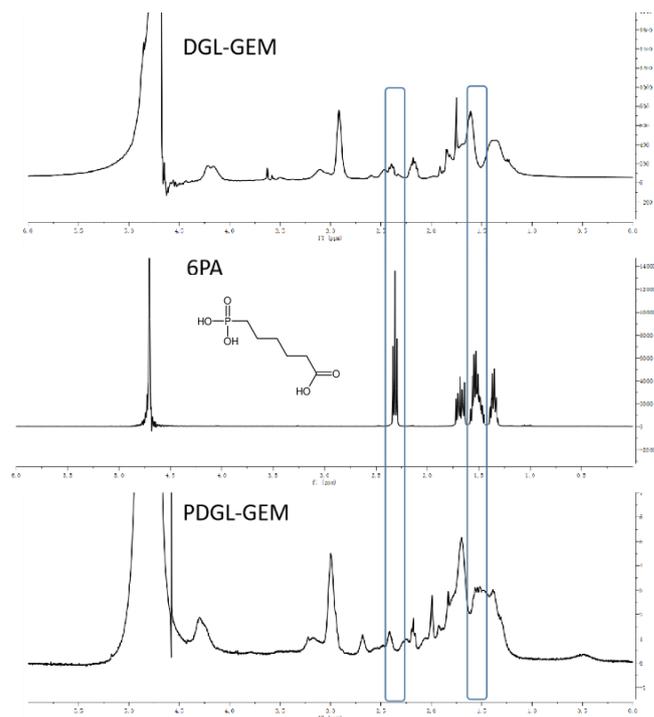


Figure S2. Confirmation of 6PA modified DGL-GEM.

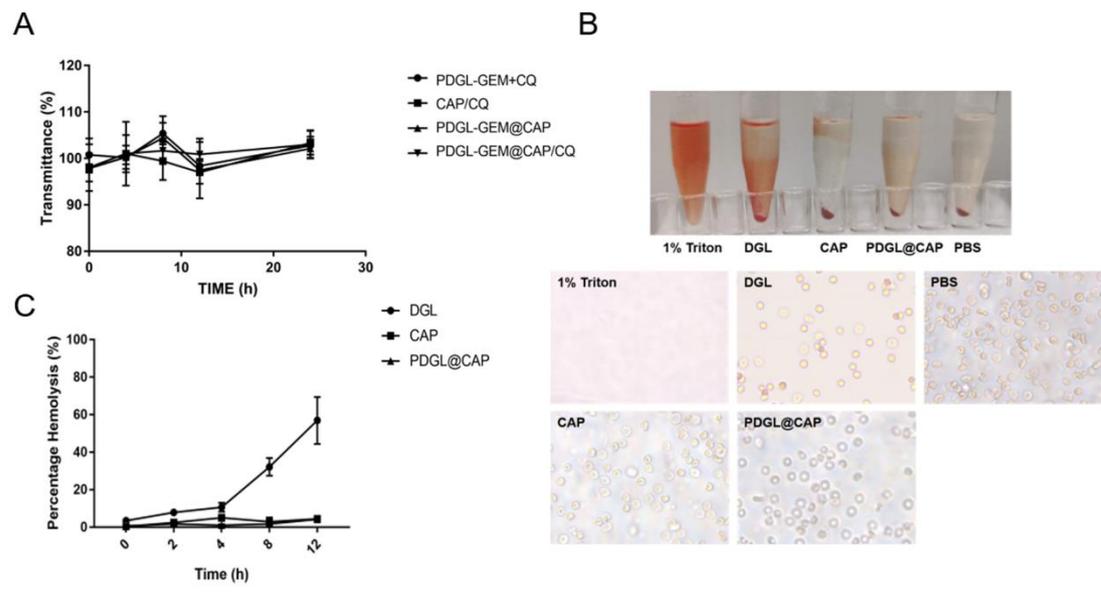


Figure S3 (A) The variations of transmittances of different nanoparticles in 50% FBS (n = 3, mean ± SD). (B) Image of red blood cells incubated with DGL, CAP and PDGL@CAP for 12 h. (C) Time-related hemolysis rates of DGL, CAP and PDGL@CAP for 12 h (n = 3, mean ± SD).

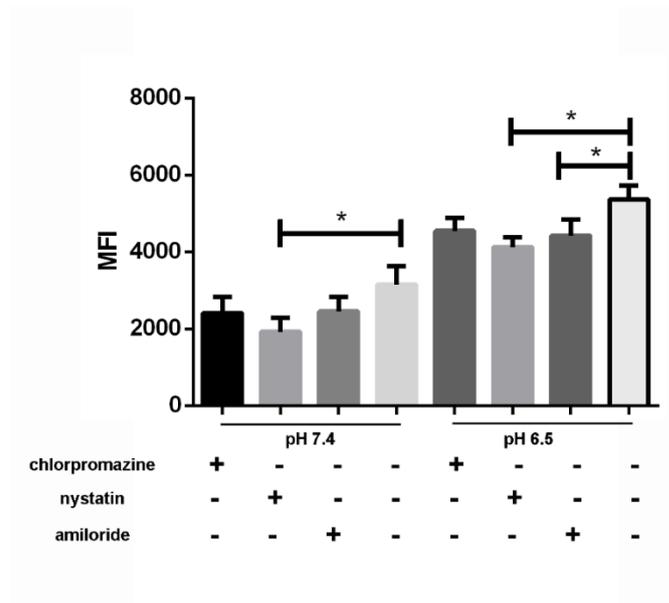


Figure S4. The cellular uptake mechanism of PDGL@CAP (mean  $\pm$  SD, n = 3. \*p < 0.05).

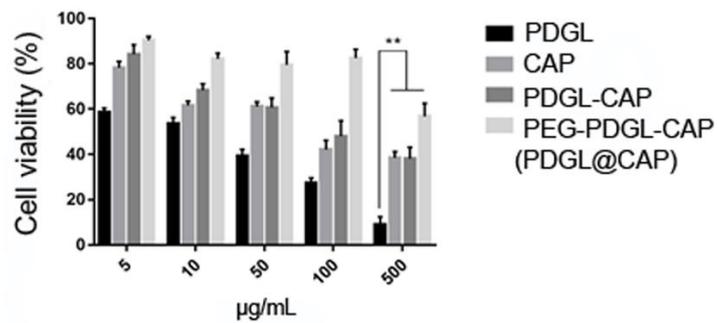


Figure S5. Cell viability of the PDGL, CAP, PDGL@CAP and pegylated PDGL@CAP on NIH3T3 cells (mean  $\pm$  SD, n=5, \*\*p < 0.01)

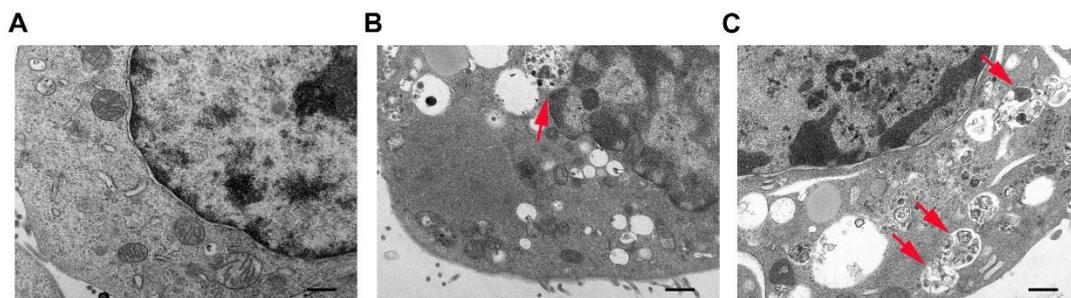


Figure S6. The TEM of Pan 02 cells after treatment with (A) HEPES, (B) PDGL-GEM@CAP/CQ at pH 7.4 and (C) PDGL-GEM@CAP/CQ at pH 6.5. Scale bar = 500 nm.

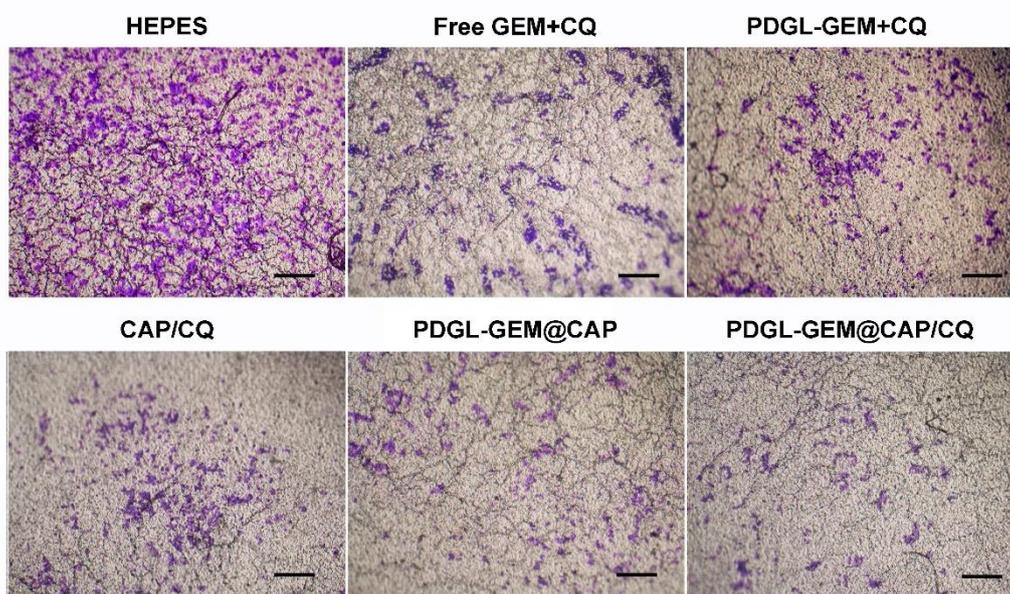


Figure S7. The image of invasion of Pan 02 cells after treatment with different formulation. Scale bar = 100  $\mu\text{m}$ .

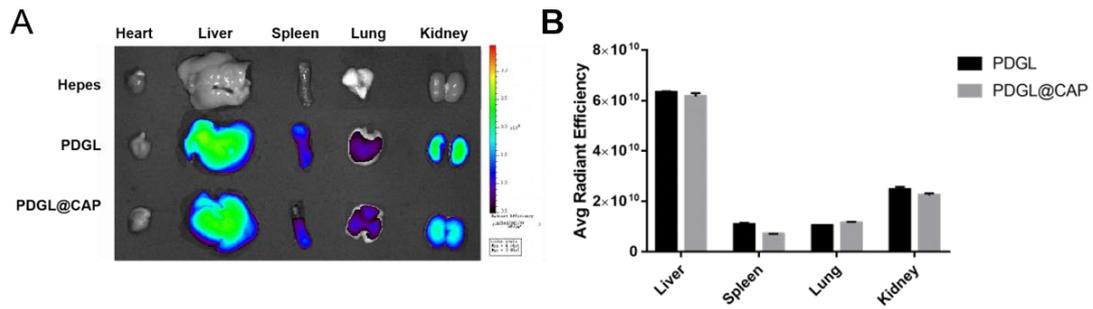


Figure S8. (A) The fluorescence image of ex vivo organs. (B) The semi-quantification results of ex vivo fluorescence in major organs ( $n = 3$ , mean  $\pm$  SD).

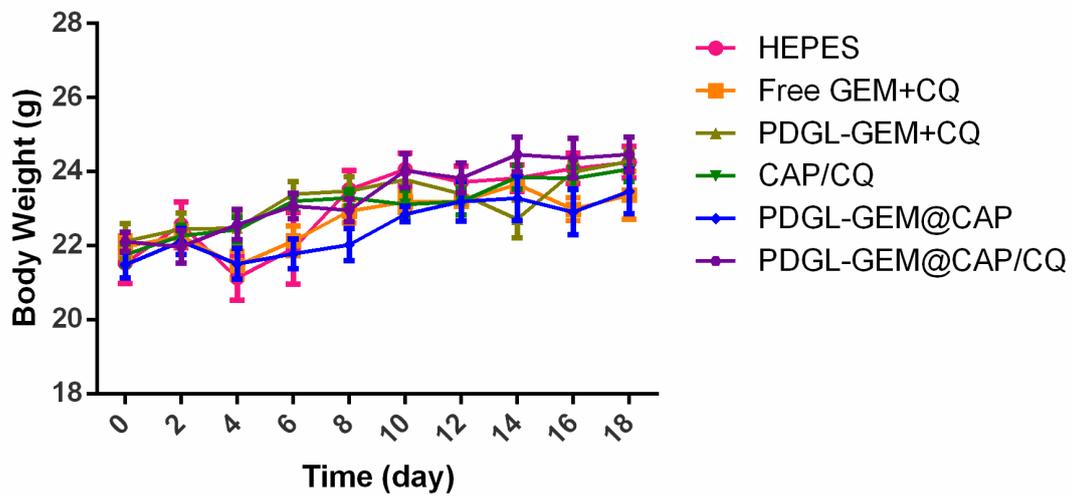


Figure S9. The body weight variation of xenograft Pan 02 tumor-bearing mice ( $n = 7$ , mean  $\pm$  SD).

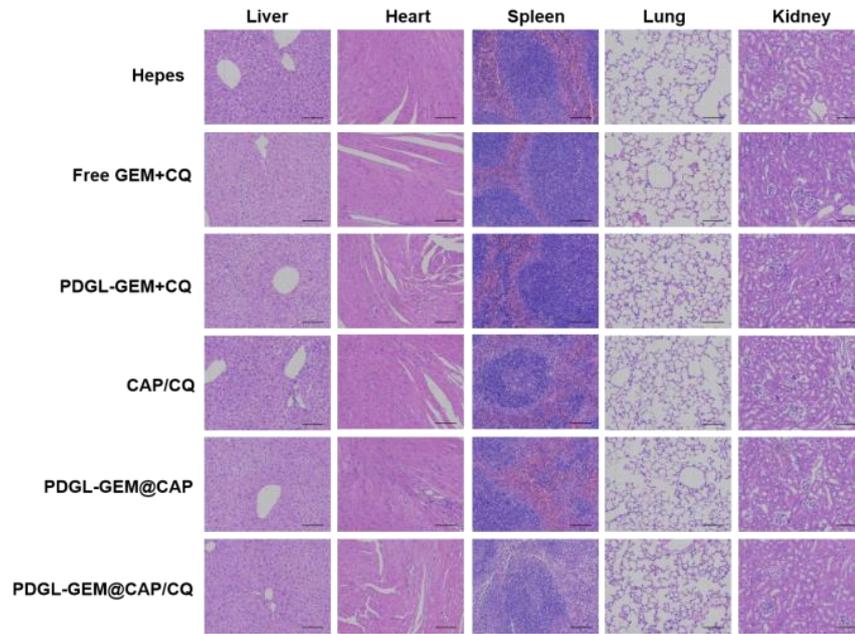


Figure S10. The H&E staining of major organ sections of xenograft Pan 02-bearing mice. Scale bar: 100  $\mu$ m.

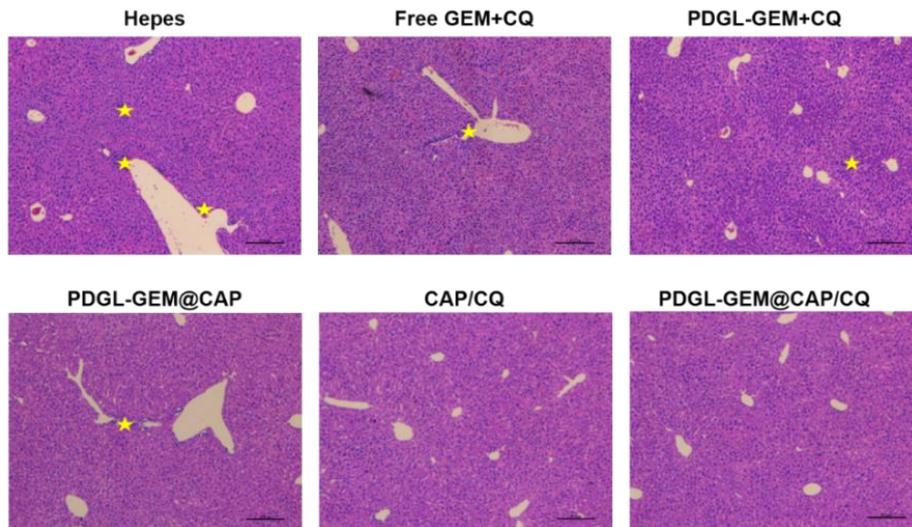


Figure S11. Representative images of liver from each group with H&E staining. Scale bar = 100 μm. Yellow stars indicate the micro metastasis.

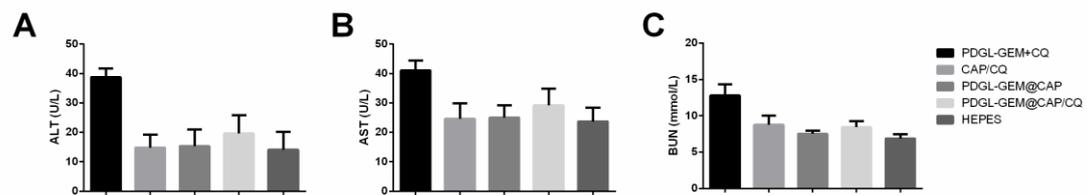


Figure S12. The (A) ALT, (B) AST and (C) BUN level in serum of different formulation treated mice (mean ± SD, n = 3).

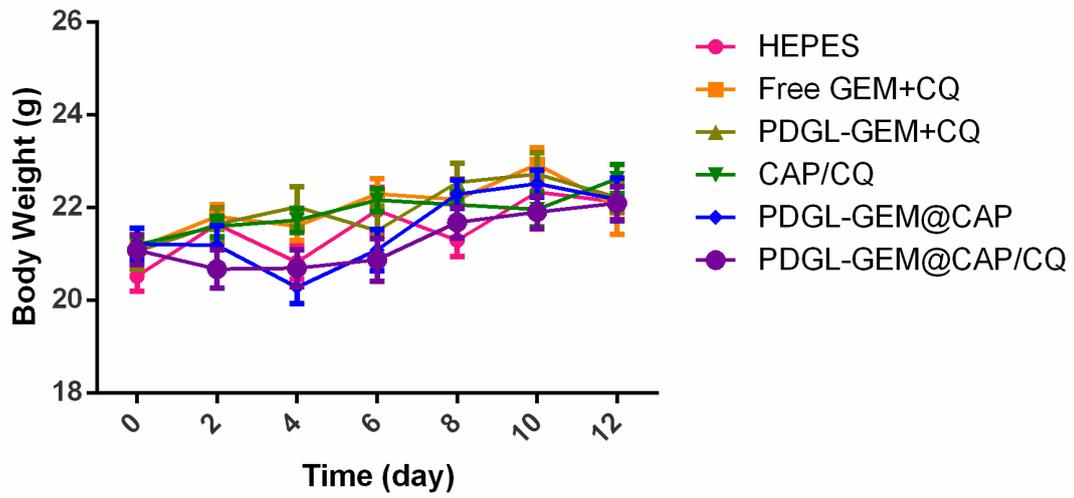


Figure S13. The body weight variation of orthotopic Pan 02 tumor-bearing mice (n = 7, mean  $\pm$  SD).

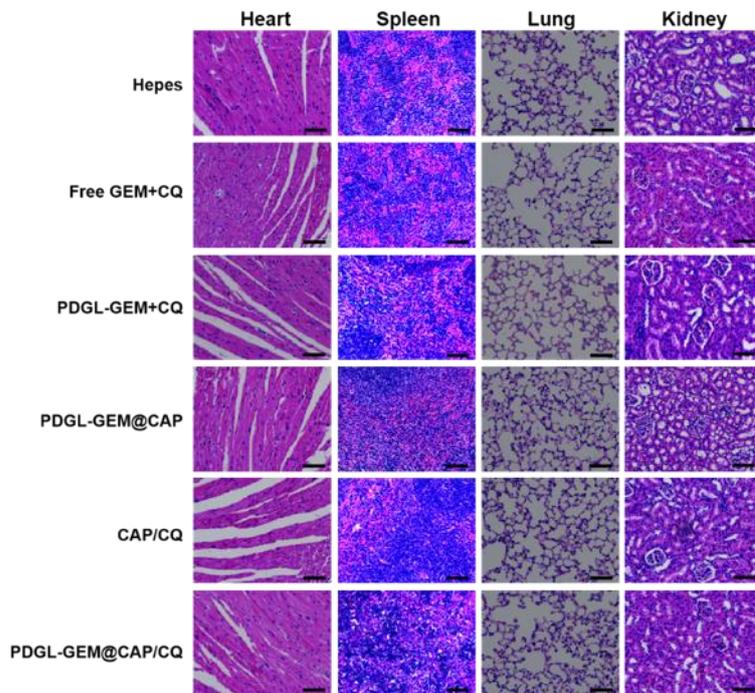


Figure S14. The H&E staining of major organ sections of orthotopic Pan 02-bearing mice. Scale bar = 100  $\mu$ m.