Supporting Information

Pirfenidone-Loaded Exosomes Derived from Pancreatic Ductal Adenocarcinoma Cells Alleviate Fibrosis of the Premetastatic Niche to Inhibit Liver Metastasis

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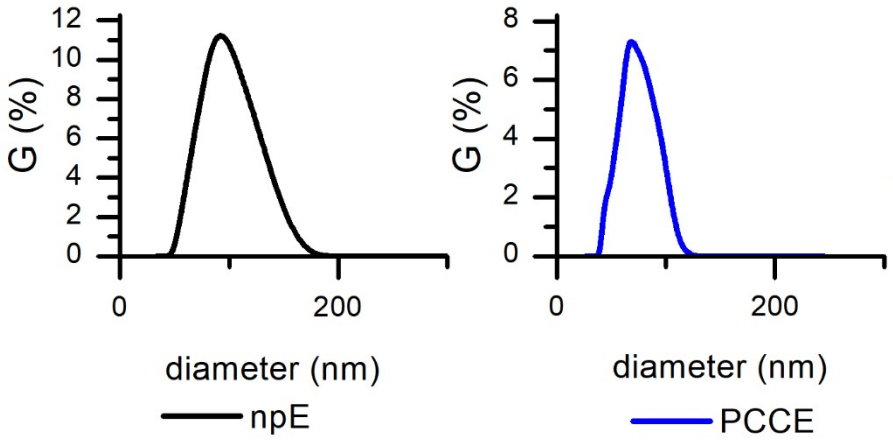

Figure S1. DLS characterization of exosomes. Dynamic light scattering (DLS) measurements of exosomes isolated from supernatant and plasma.

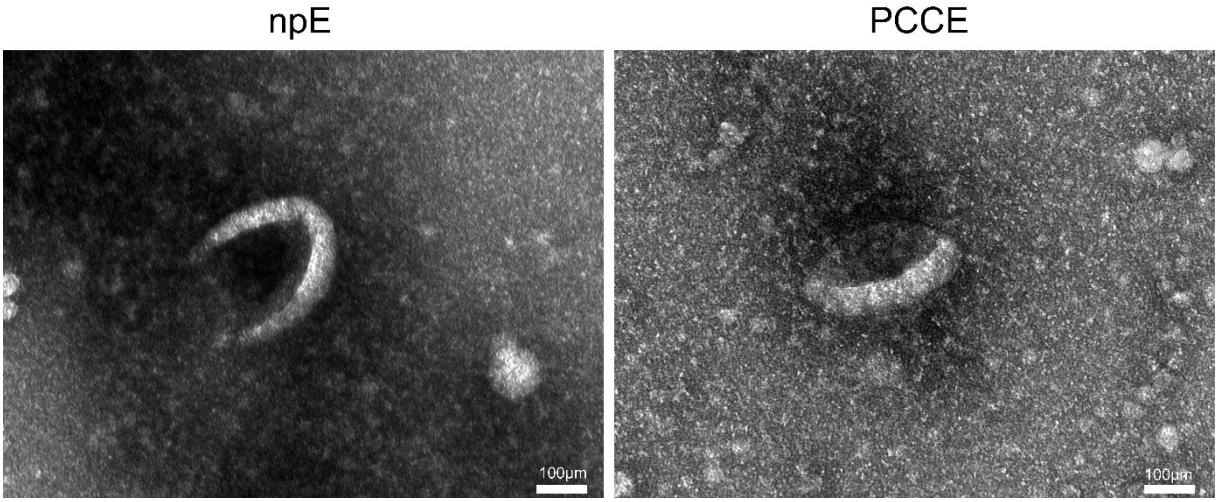

Figure S2. TEM characterization of exosomes. Transmission electron microscopy (TEM) analysis of exosomes isolated from supernatant and plasma.

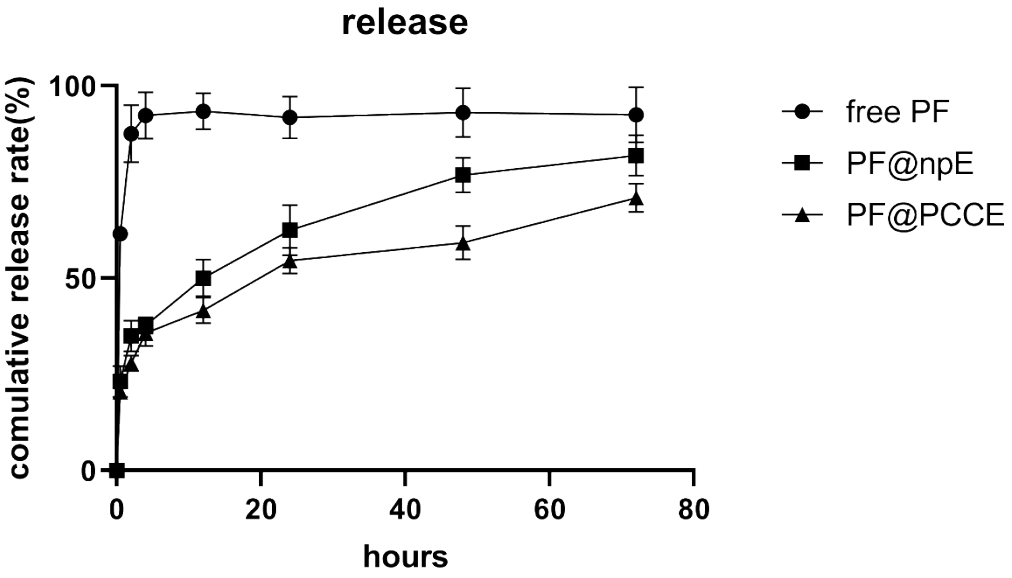

Figure S3. Release test of free PF, PF@npE and PF@PCCE. The concentration ratio of free drug to total drug in the 3 systems over 72 h.

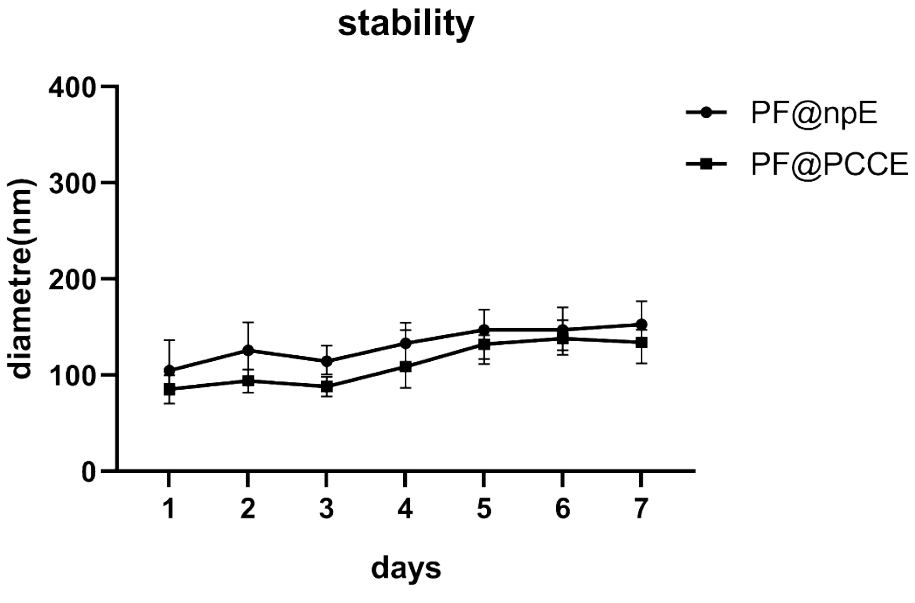

Figure S4. Stability test of PF@npE and PF@PCCE. Diametre change of two types of exosome vehicles over 1 week examined by DLS.

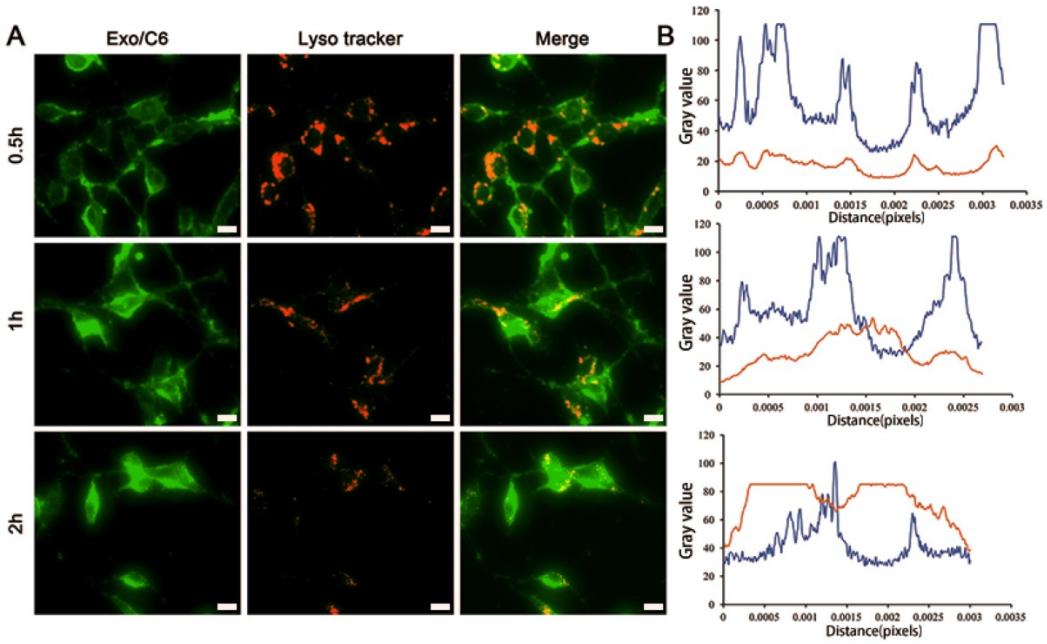

Figure S5. Evaluation of endosomal escape capacity of PCCE on HSC cells.
Endosome/lysosome in HSC was stained by LysoTracker red. The bar is 20 μm. B) Line-scan profiles of PCCE and LysoTracker red after 0.5h, 1 h, and 2h of incubation. The level of the overlapped blue line and orange line is negatively correlated to endosomal escape of PCCE.

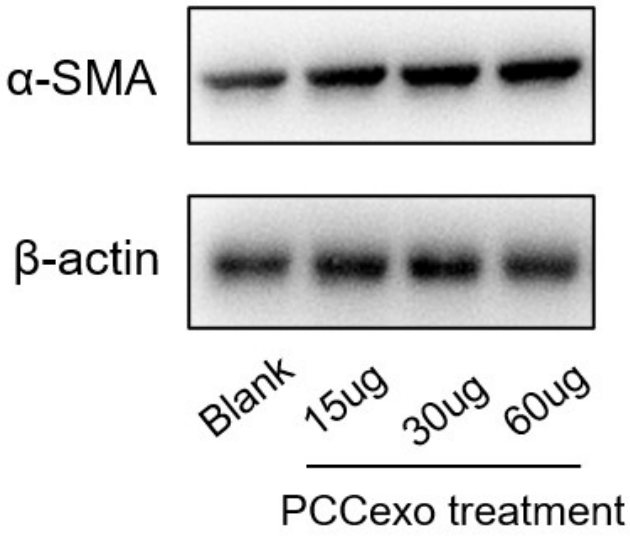

Figure S6. Lx2 activation induced by exosomes derived from pancreatic cancer cells.
Western blot of α-SMA of Lx2 treated by exosomes derived from pancreatic cells.

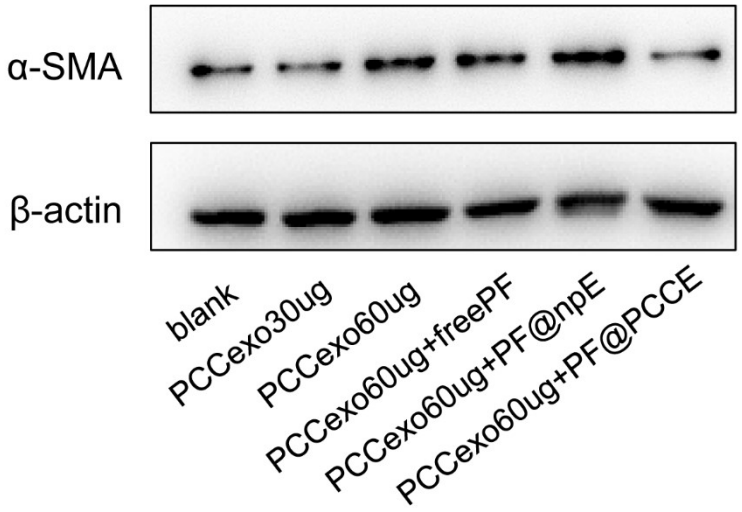

Figure S7. Anti-fibrotic effects of PF@PCCE on Lx2. Western blot of α-SMA of Lx2 treated by exosomes derived from pancreatic cells and PF with different loading vehicles.

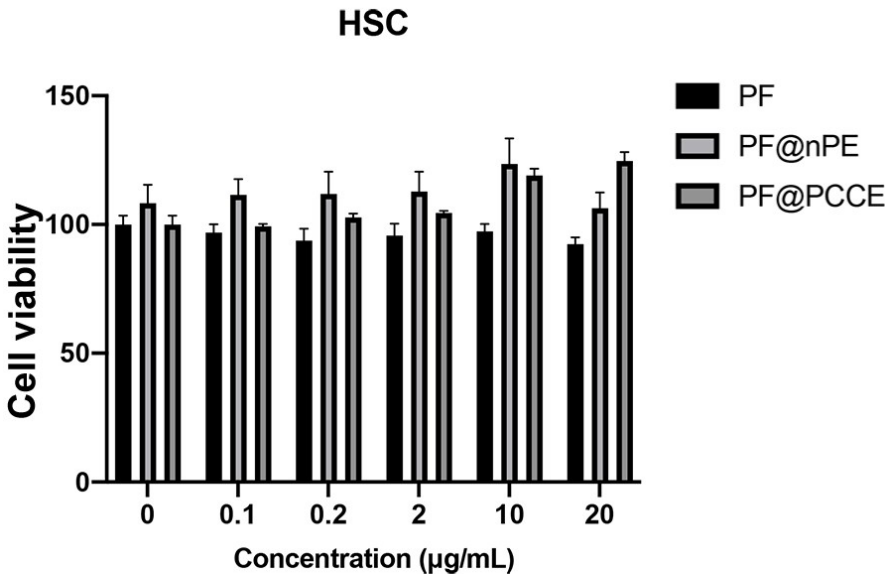

Figure S8. Cell viability of Lx2 after treated by PF, PF@npE, and PF@PCCE. CCK8 test for the evaluation of proliferation of HSC treated by PF, PF@npE, PF@PCCE at different concentration for 48h.

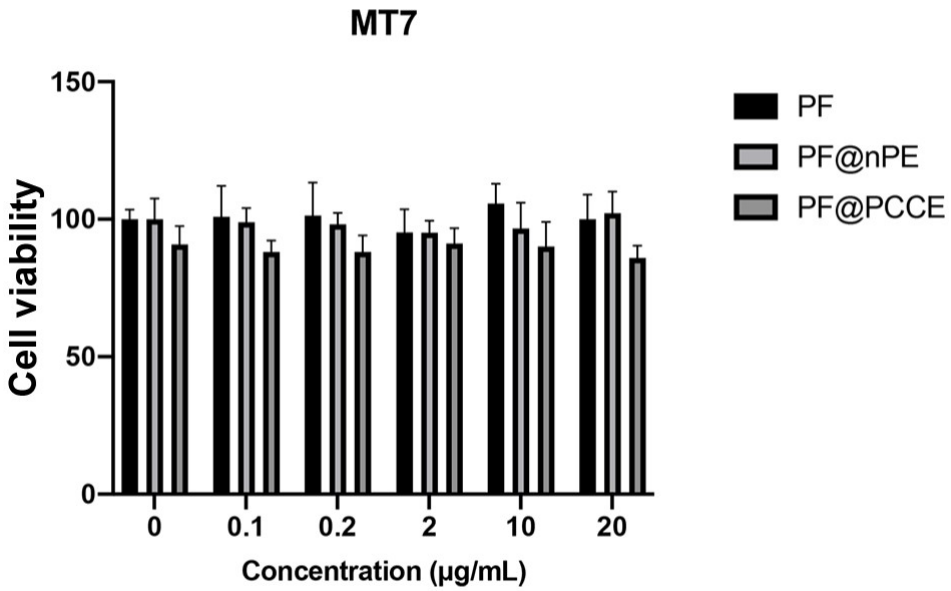

Figure S9. Cell viability of mT7 after treated by PF, PF@npE, and PF@PCCE. CCK8 test for the evaluation of proliferation of mT7 treated by PF, PF@npE, PF@PCCE at different concentration for 48h.

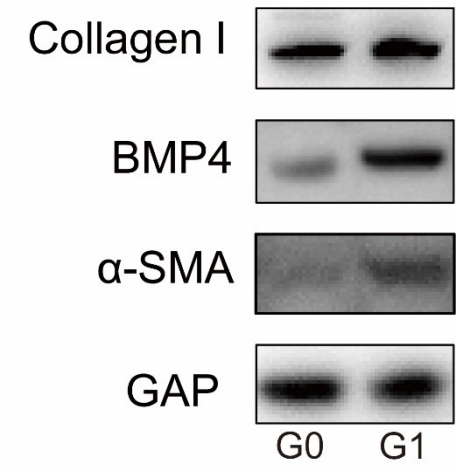

Figure S10. Western blot results of G0 and G1. The expression of Collagen I, BMP4 and α-SMA in the liver of G0 and G1 groups.

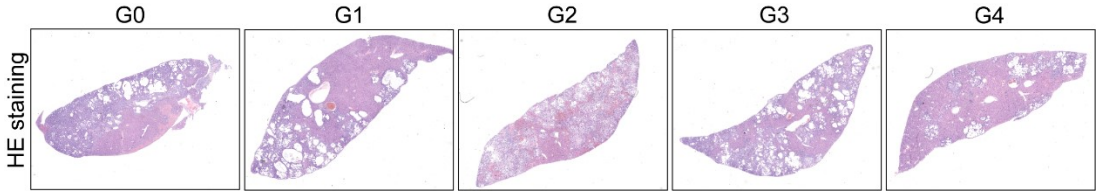

Figure S11. Representative full scan of liver metastasis.

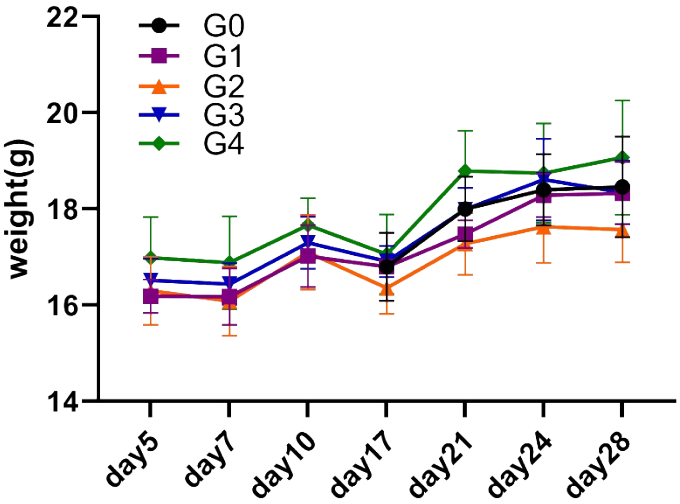

Figure S12. The body weight of mice throughout the study.

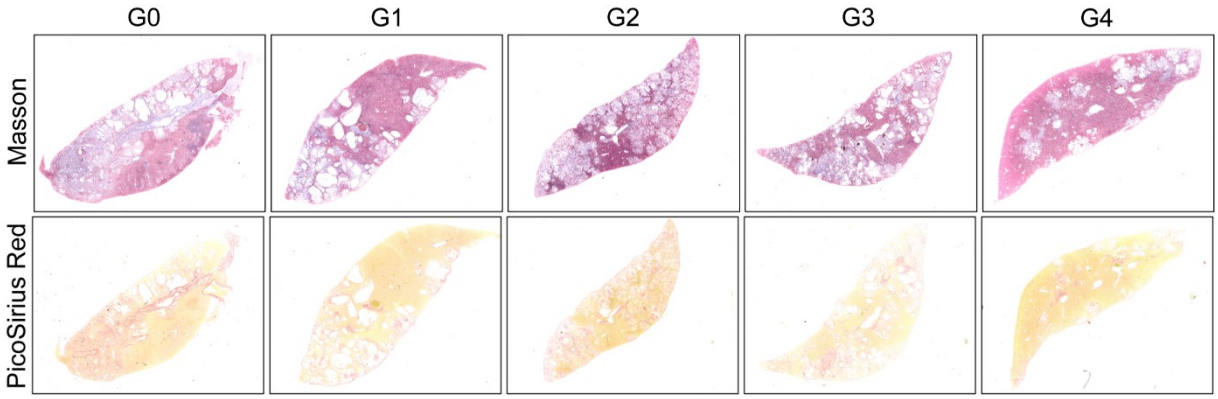

Figure S13. Representative full scan of Masson and picosirius red staining.

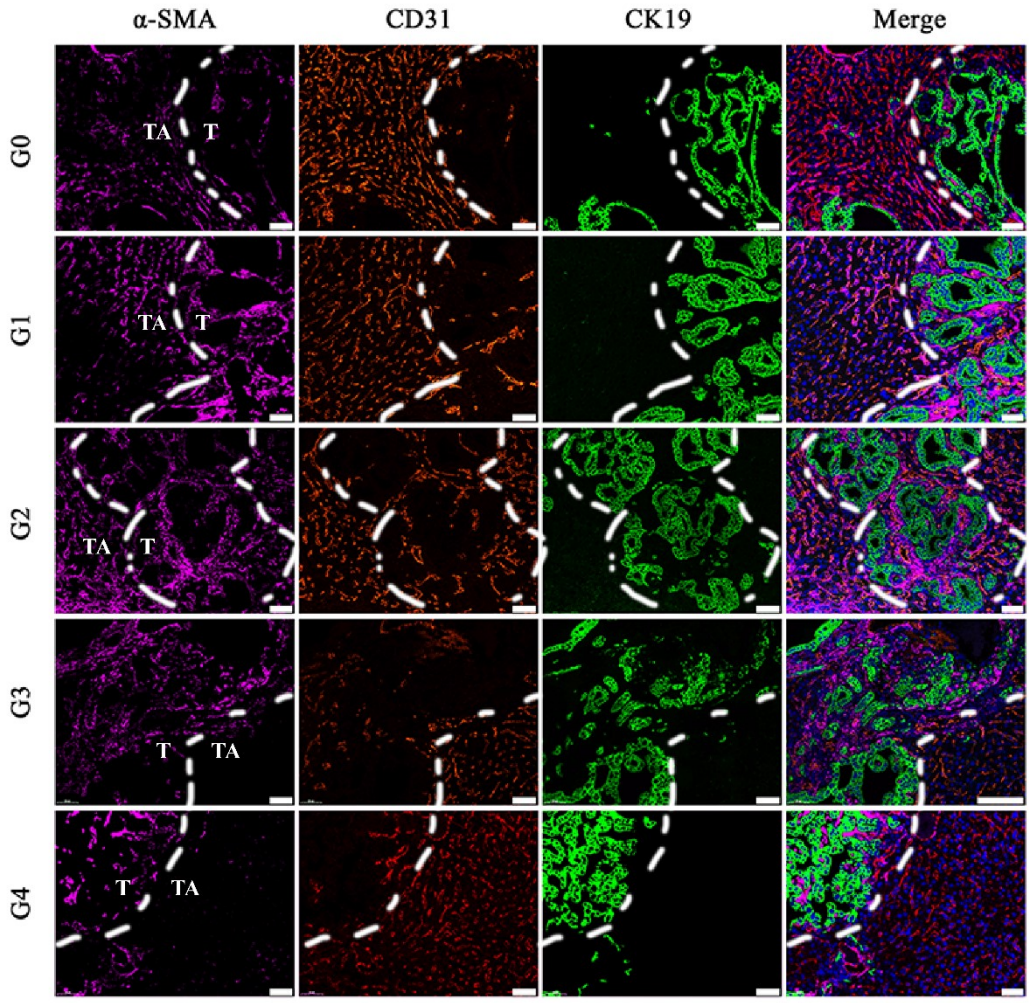

Figure S14. Immunofluorescence staining of mice liver tissues. Green, CK19; pink, α-SMA; blue, DAPI; red, CD31. Dotted lines mark the borders between tumor (T) and tumor adjacent (TA) areas.