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Supporting Information

# Combining PD-L1 Inhibitors with Immunogenic Cell Death Triggered by Chemo-Photothermal therapy *via* a Thermosensitive Liposome System to Stimulate Tumor-specific Immunological Response

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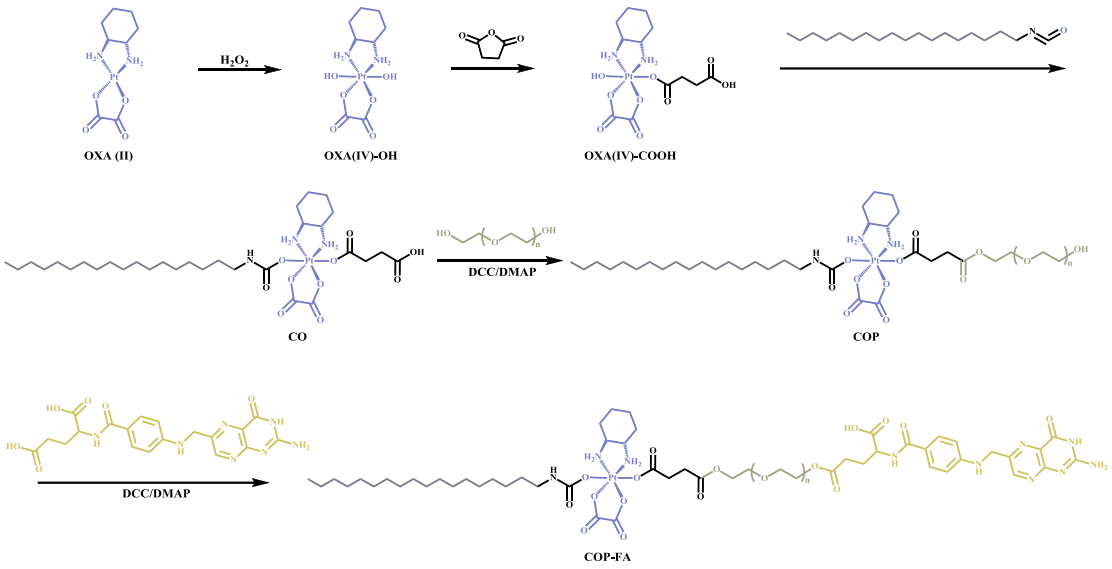



**Scheme S1.** Synthesis of AOP-FA.

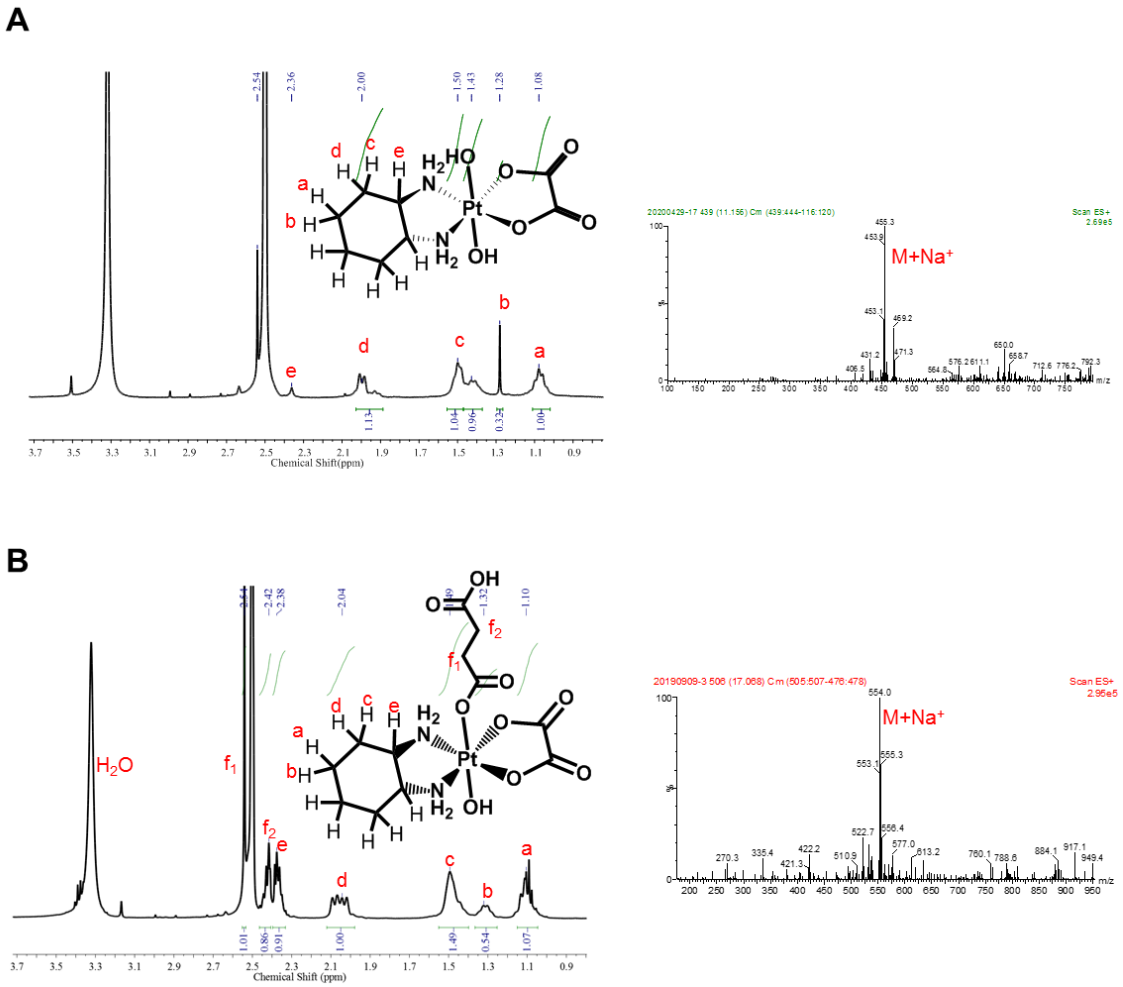



**Figure S1.** $^1$H NMR and ESI-MS spectra of (A) oxidized OXA and (B) mono-carboxylated OXA.

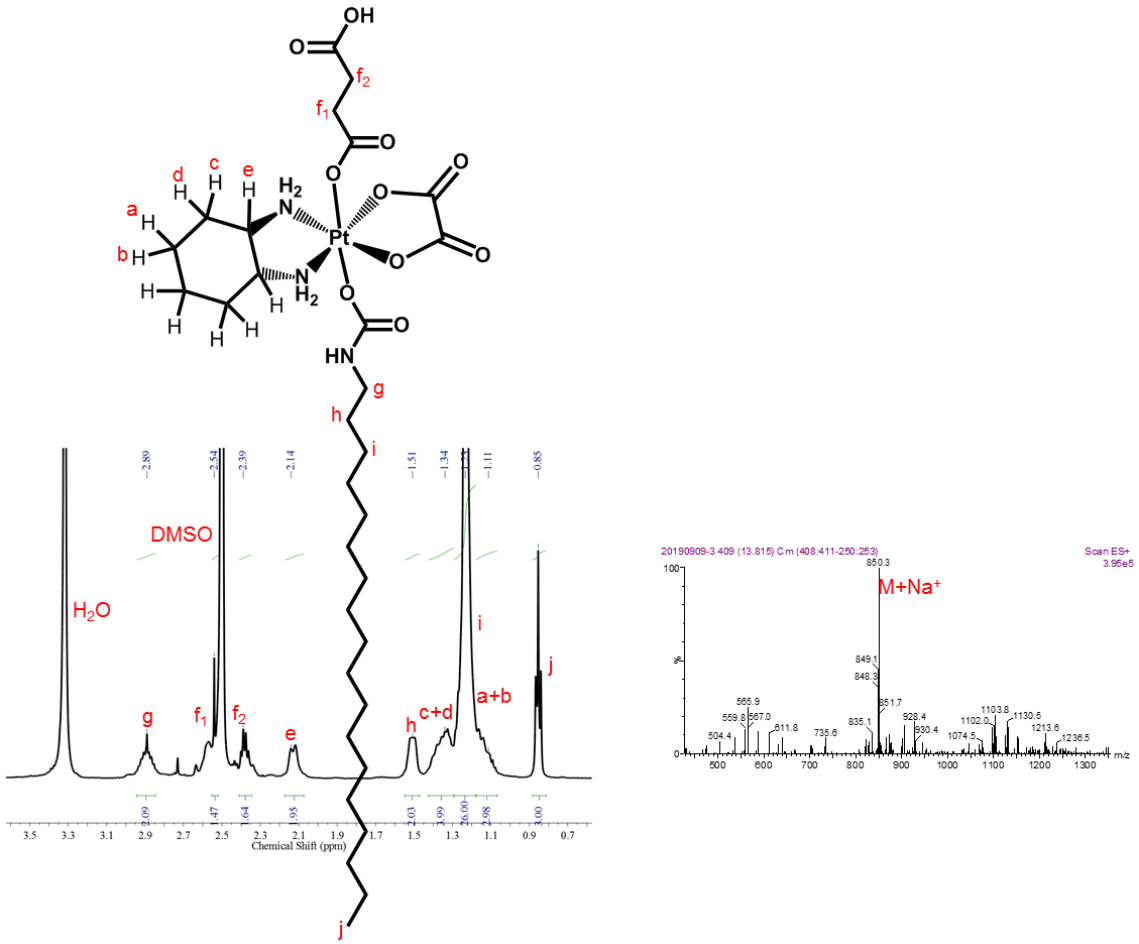



**Figure S2.** $^{1}$H NMR and ESI-MS spectra of Carboxylated lipophilic OXA prodrug (LO).

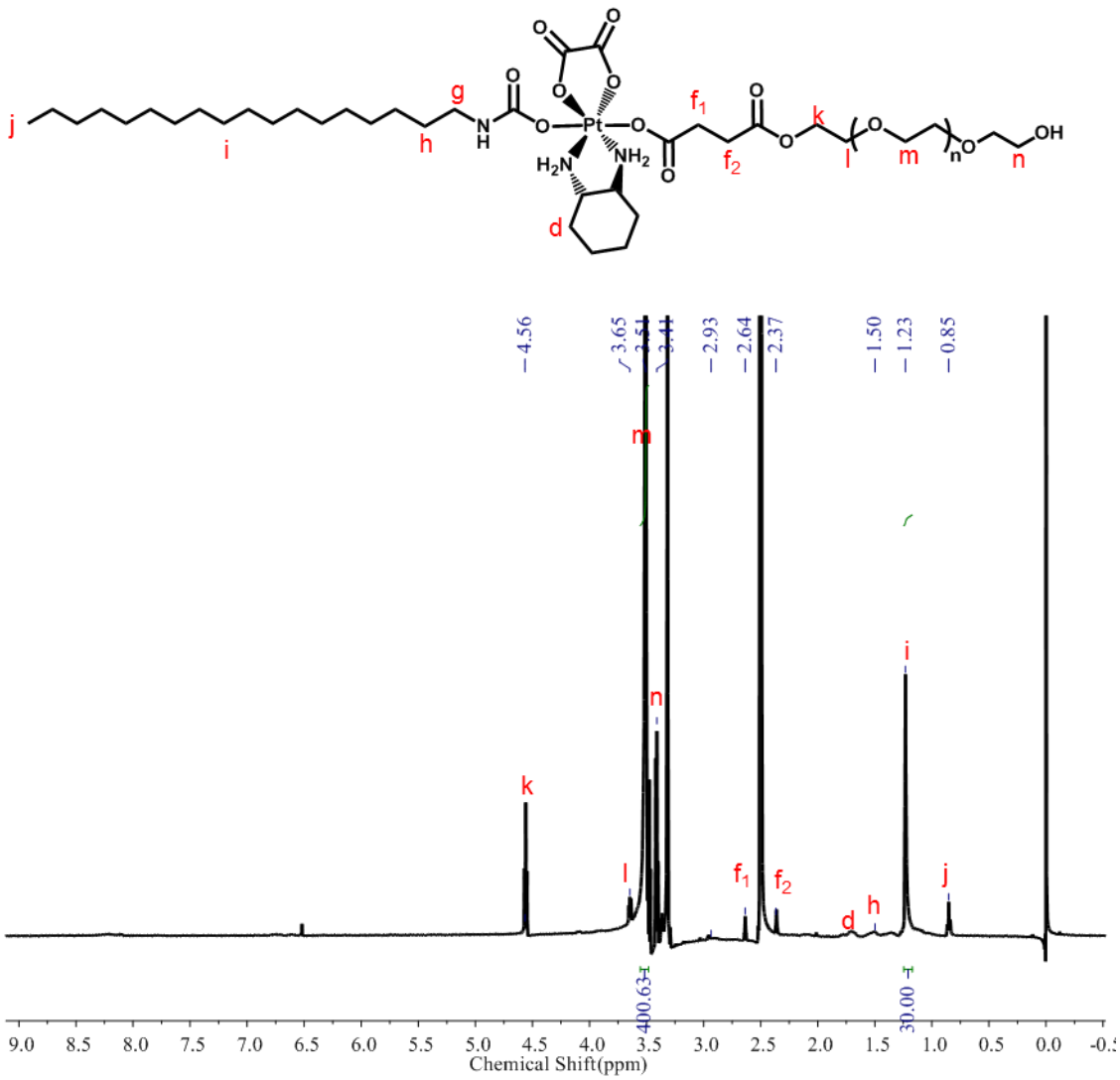
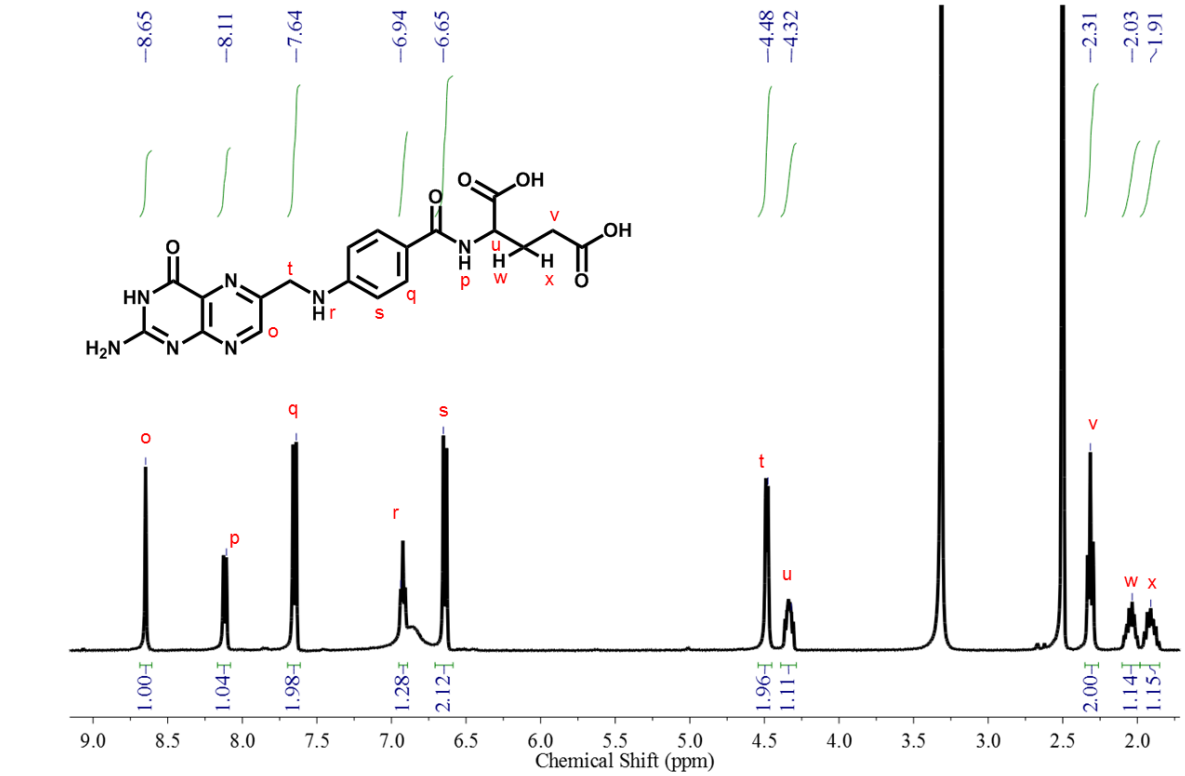



**Figure S3.** $^{1}$H NMR spectra of PEG modified amphipathic carboxylated oxaliplatin prodrug (AOP).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6.94
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4.32
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2.03
1.91
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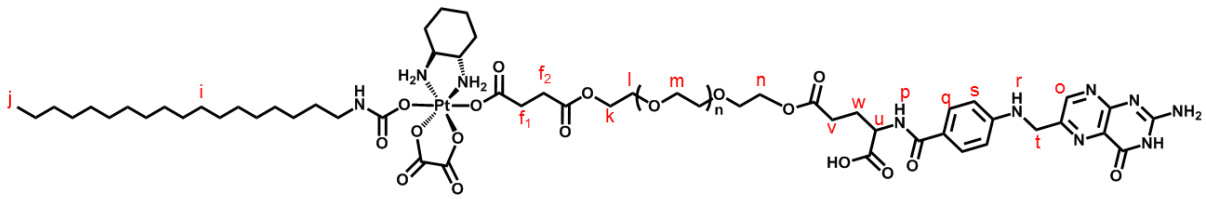
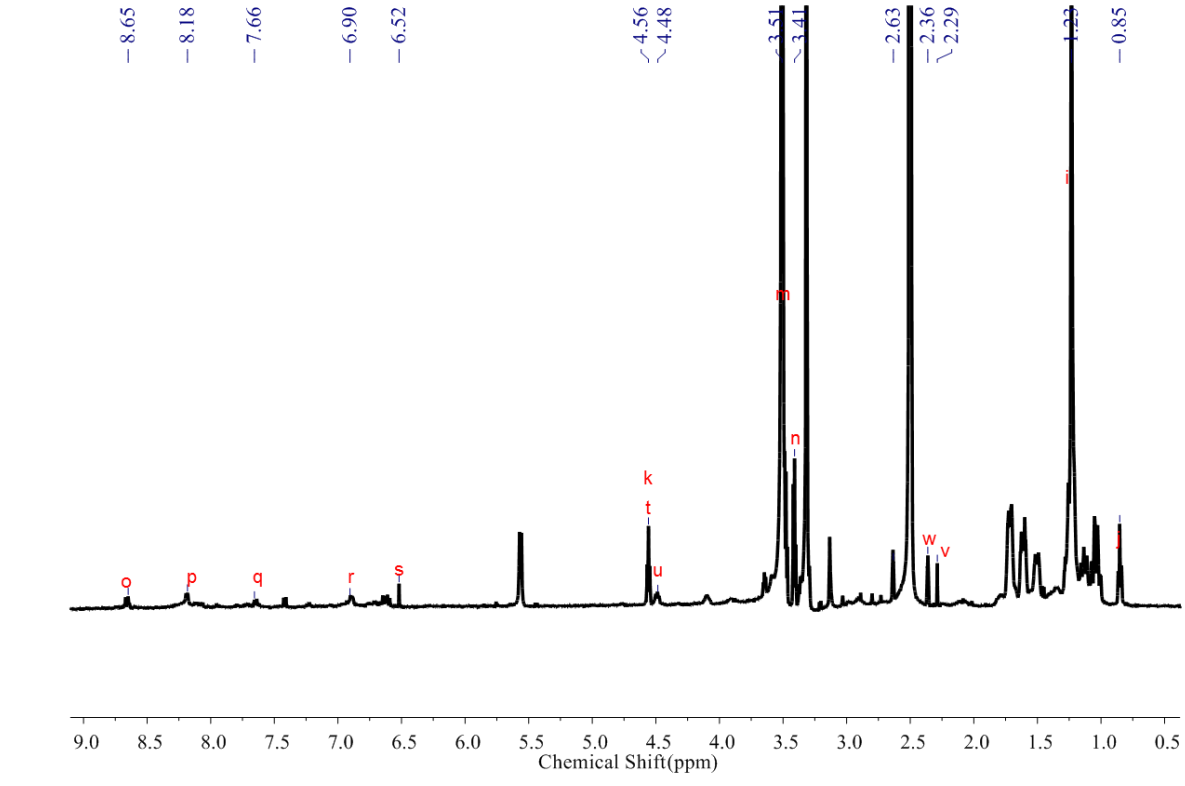
1.28
2.12
1.96
1.11
2.00
1.14
1.15
Chemical Shift (ppm)

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6.52
4.56
4.48
3.51
3.41
2.63
2.36
2.29
1.22
0.85
Chemical Shift(ppm)

**Figure S4.** (A) $^{1}$H NMR spectra of FA. (B) $^{1}$H NMR spectra of FA modified amphipathic oxaliplatin prodrug (AOP-FA).

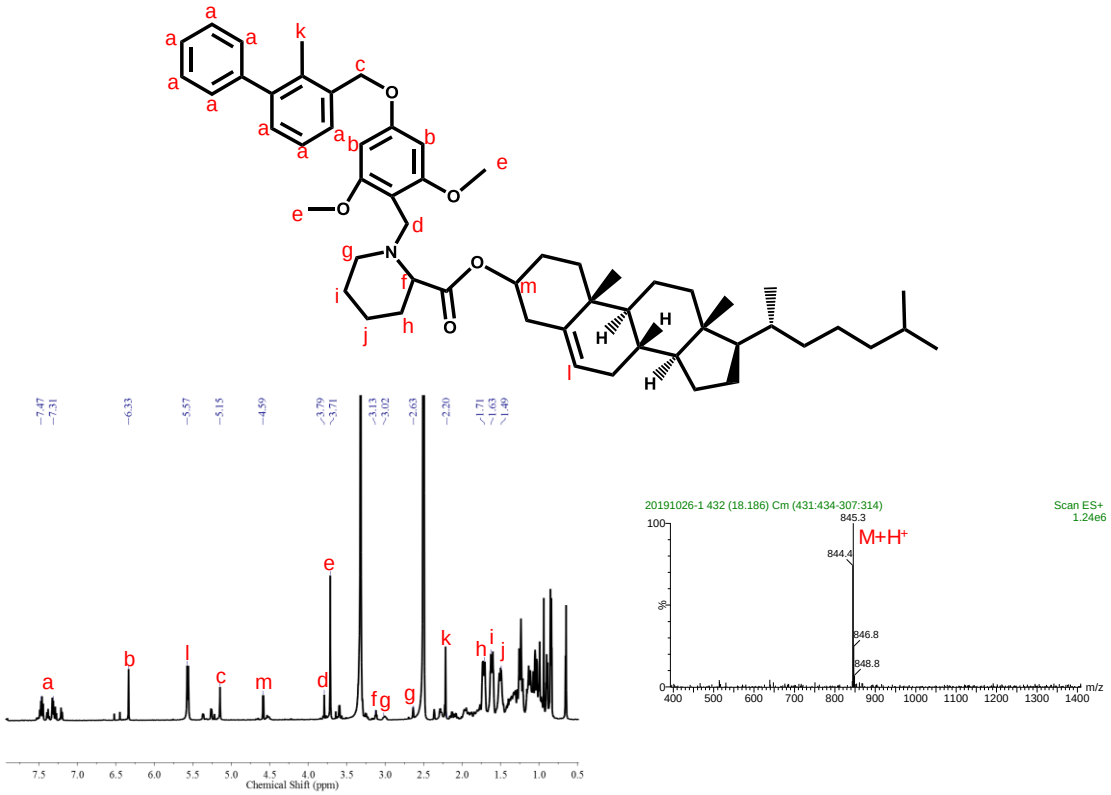



**Figure S5.** $^{1}$H NMR and ESI-MS spectra of Cholesterol conjugated BMS-1 (Chol-BMS).

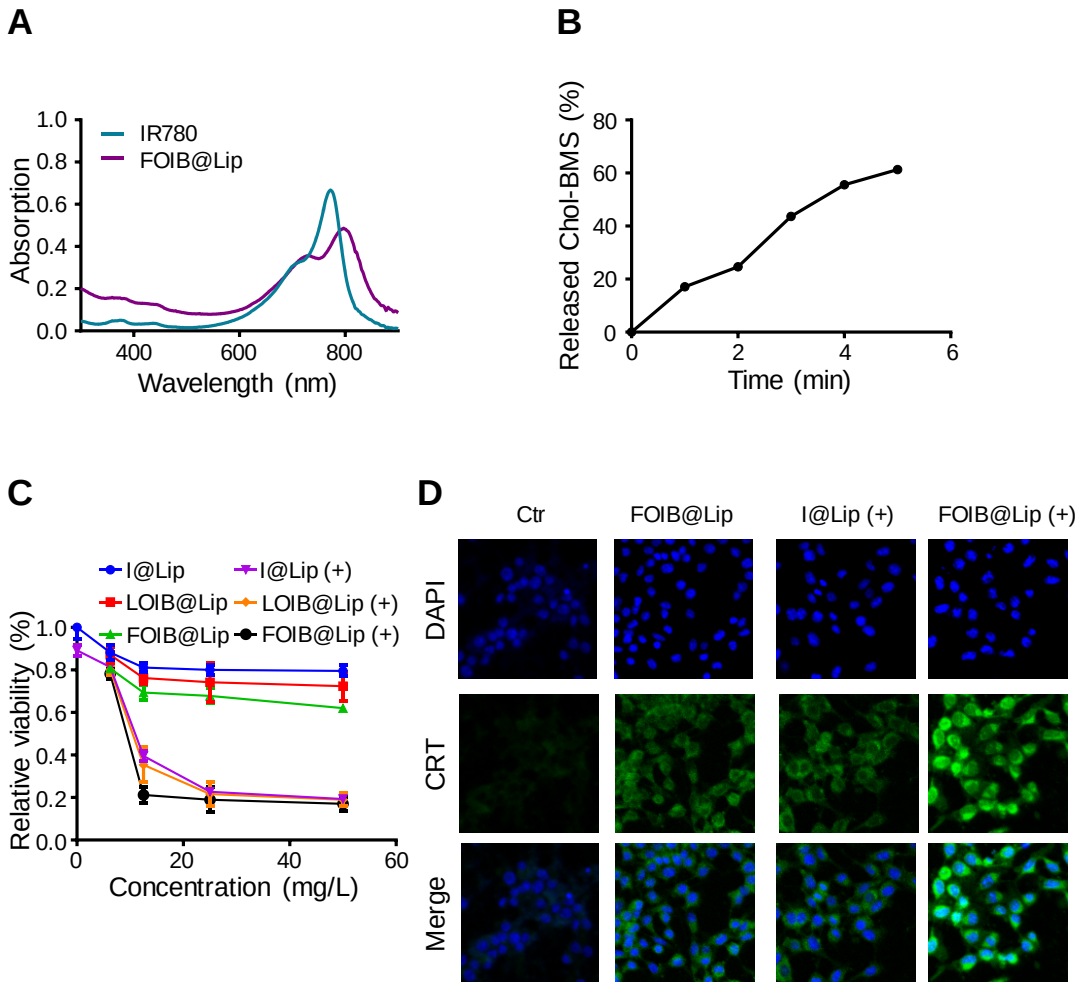



**Figure S6.** (A) The UV-vis of IR780 and FOIB@Lip. (B) Controllable drug release of Chol-BMS at different laser time analyzed by HPLC. (C) Cell viability of different treatment. (D) CLSMs images of CRT stained-CT26 cells treated with FOIB@Lip, I@Lip (+), and FOIB@Lip (+).

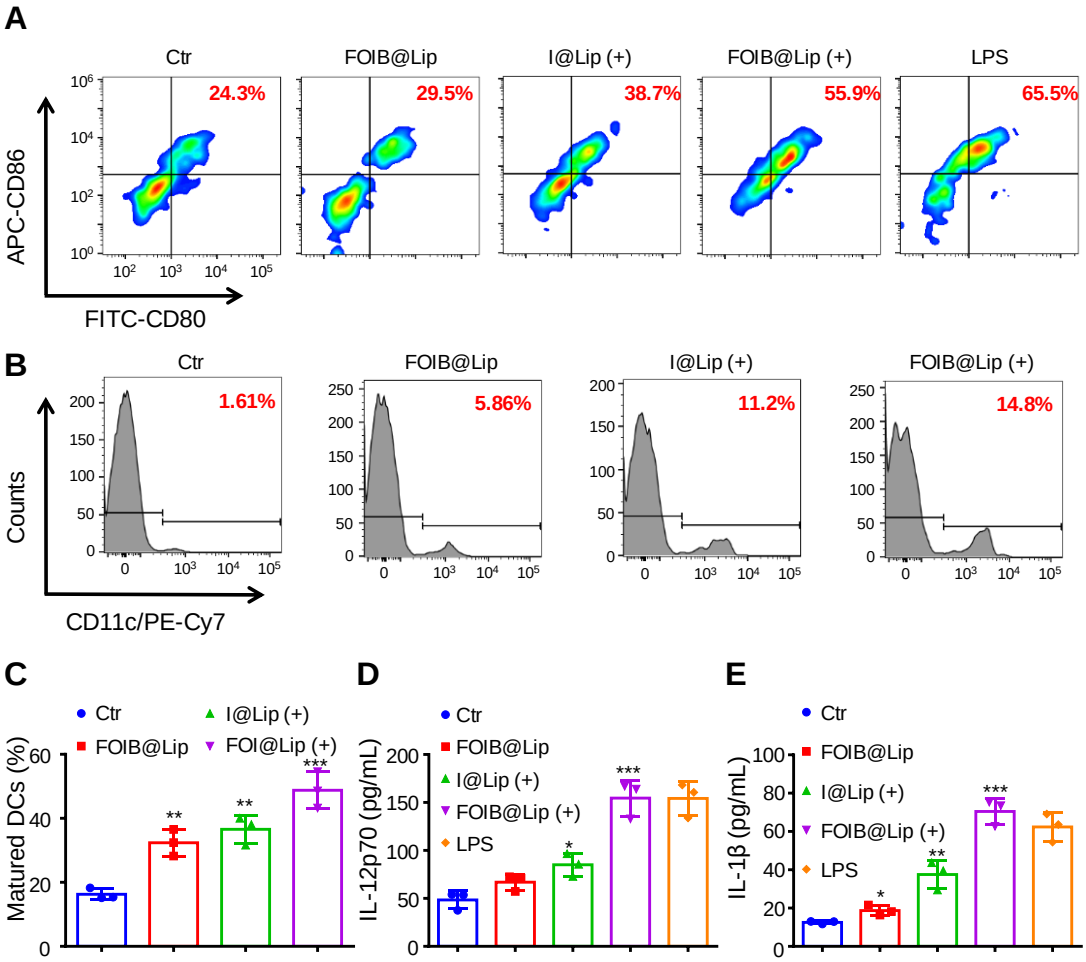



**Figure S7. Immunostimulatory effects of FOIB@Lip based PTT.** (A) Representative FACS plots showing percentage of $CD80^+CD86^+$ mature BMDCs upon the treatment with FOIB@Lip, I@Lip (+), FOIB@Lip (+) in the transwell system. (B) Representative Flow cytometry histogram showing percentage of $CD11c^+$ DC cells in TDLN. (C) Percentage of mature DC cells ($CD80^+CD86^+$) gated by $CD11c^+$ DC cells in TDLN. (D-E) Secretion of IL-12p70 and IL-1β by BMDCs treated with FOIB@Lip, I@Lip (+), FOIB@Lip (+) or LPS (positive control). Data are presented as the mean ± SEM. The (+) refers to laser irradiation 808 nm, 0.8 W/cm$^2$, 5 min. ***P < 0.001 from control by t-test.

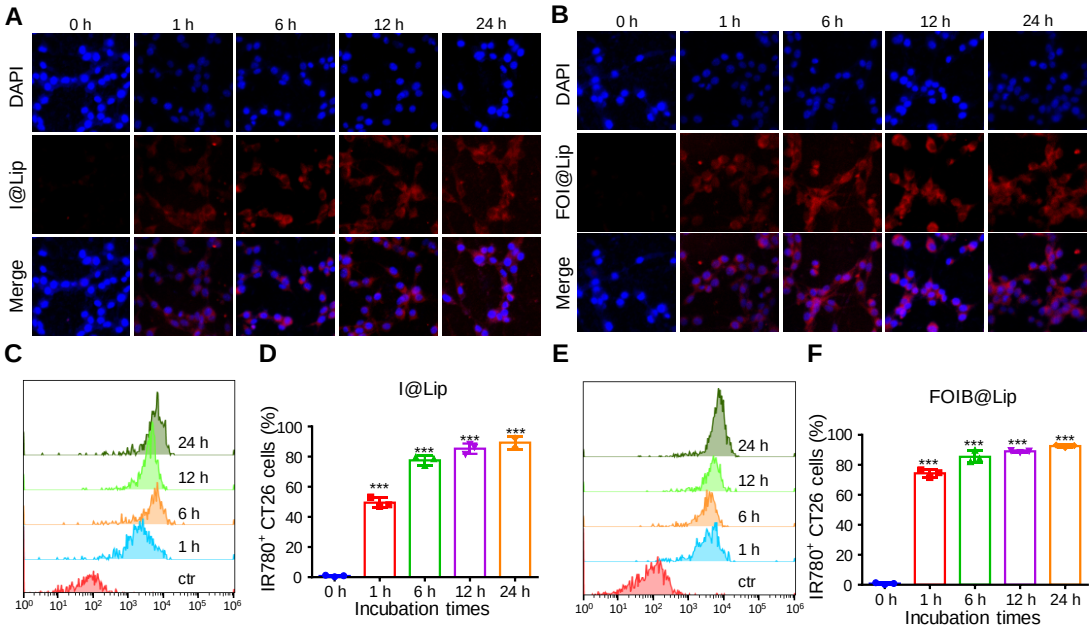



**Figure S8. Endocytosis of I@Lip and FOIB@Lip.** (A-B) CLSMs images of IR-780$^{+}$CT26 cells after incubated with (A) I@Lip and (B) FOIB@Lip. (C-F) Analysis of IR-780$^{+}$ CT26 cells after incubated with (C, D) I@Lip and (E, F) FOIB@Lip using flowsight.

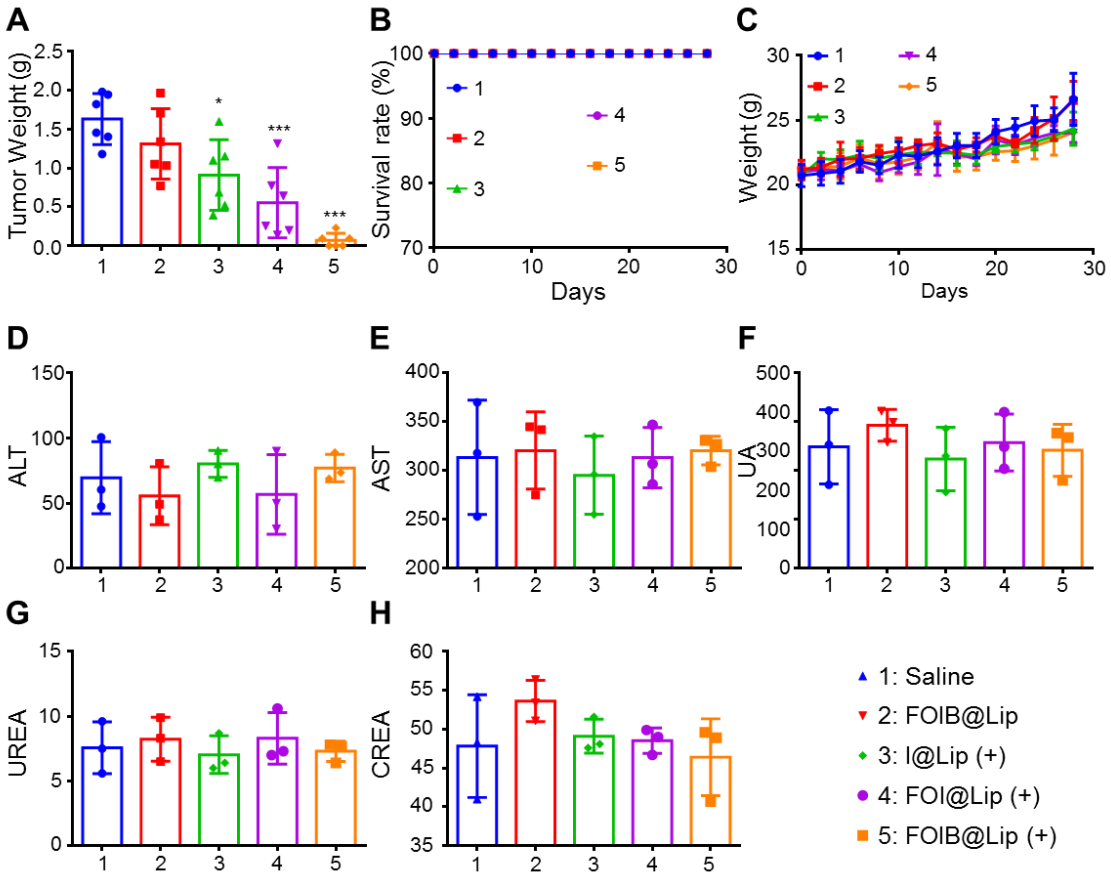
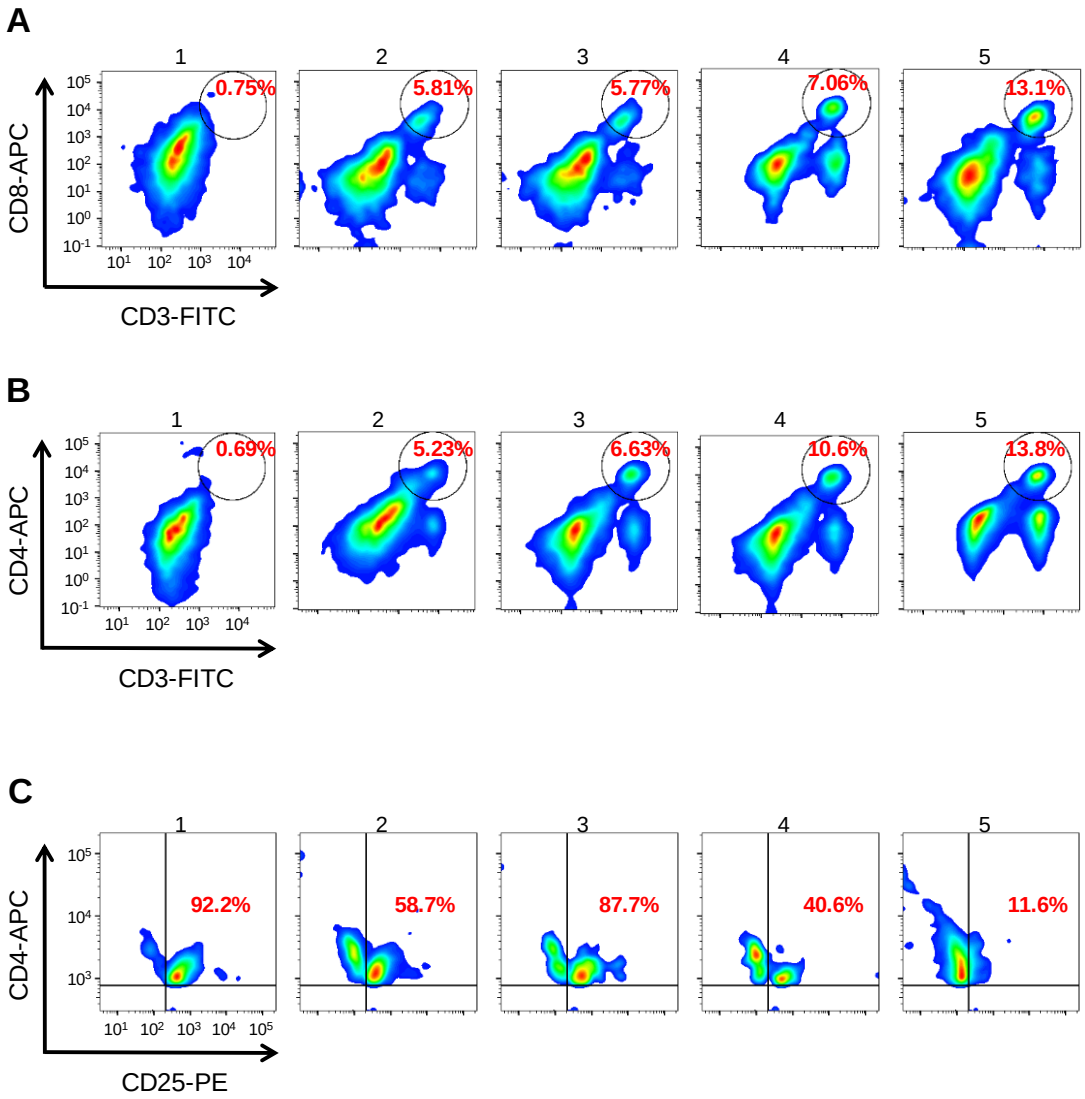



**Figure S9. Remote memory model of FOIB@Lip based PTT.** (A) Tumor weight of different groups of mice after various treatments indicated. (B) survival rate of different groups of mice after various treatments indicated. (C) Weight of different groups of mice after various treatments indicated at a remote memory model. (D-H) Alterations of ALT, AST, CREA, UA and UREA of BALB/c mice bearing CT26 model after treatment.




1: Saline 2: FOIB@Lip 3: I@Lip (+) 4: FOI@Lip (+) 5: FOIB@Lip (+)

**Figure S10. T cells in the secondary tumors of indicated groups: 1: Saline. 2: FOIB@Lip. 3: I@Lip (+). 4: FOI@Lip (+). 5: FOIB@Lip (+).** (A) Representative FACS plots of CD3, CD8 expression to evaluate the infiltrated $CD8^+$ T cells. (B) Representative FACS plots of CD3, CD4 expression to evaluate the infiltrated $CD4^+$ T cells. (C) Representative FACS plots of CD25 expression gated by ($CD3^+CD4^+$) cells to evaluate the Treg in the tumor microenvironment. The (+) refers to laser irradiation 808 nm, 0.8 W/$cm^2$, 5 min.

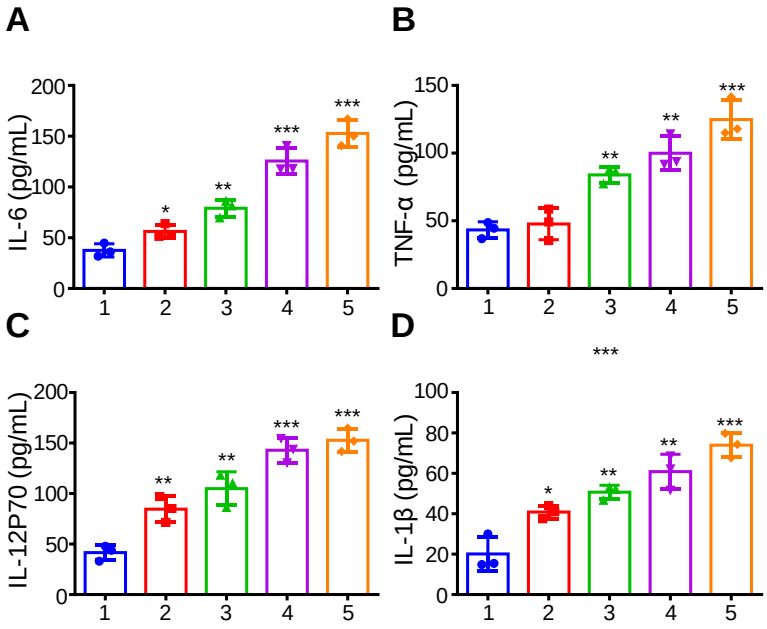



**Figure S11. Remote memory model of FOIB@Lip based PTT.** Cytokine levels in serum from mice isolated at Day 28 post FOIB@Lip based PTT. Data are presented as the mean ± SEM. The (+) refers to laser irradiation 808 nm, 0.8 W/cm$^2$, 5 min. ***P < 0.001 from control by t-test.

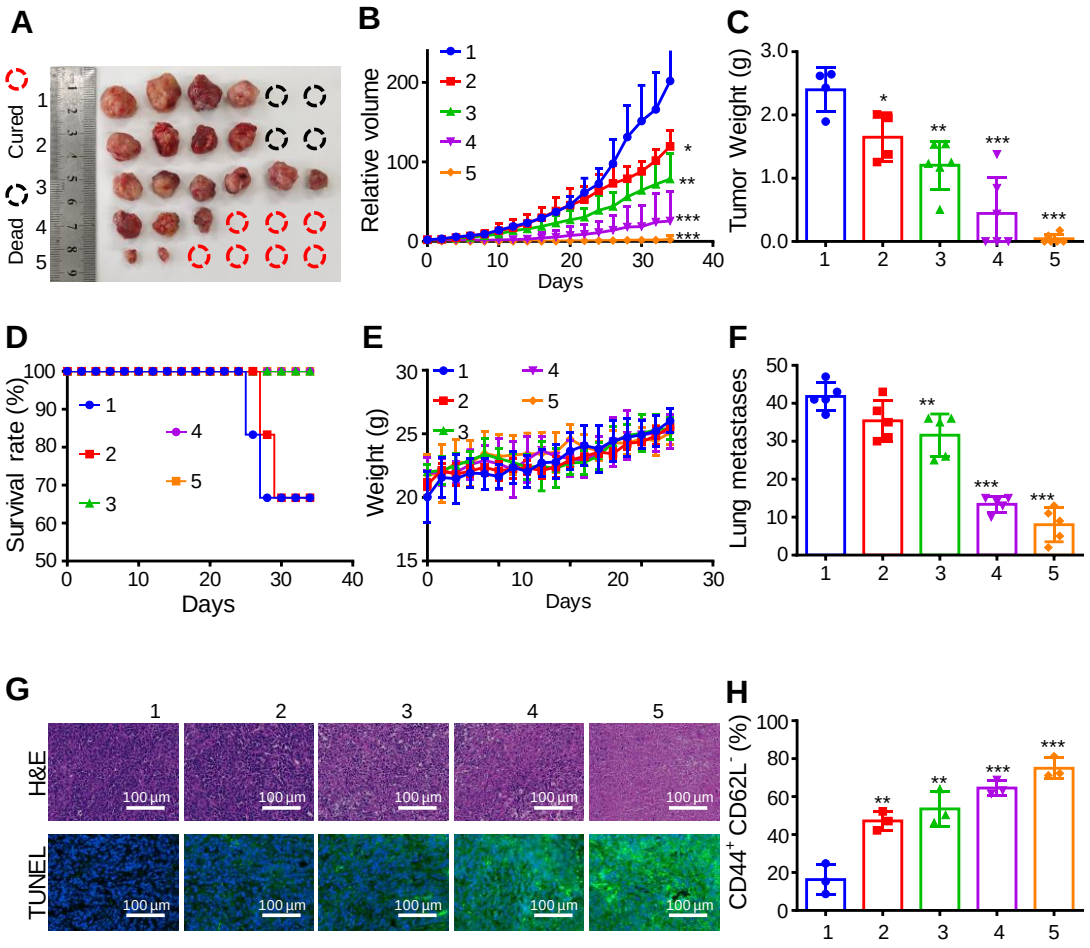



**Figure S12.** ***In vivo*** **efficacy memory evaluation of FOIB@Lip based PTT to prevent tumor recurrence and lung metastasis.** (A) Photographs of excised tumors after 36 d of various treatments. (B) Tumor growth curves of different groups of mice after various treatments indicated (6 mice per group). (C) Tumor weight of different groups of mice after various treatments indicated. (D) Survival rate of different groups of mice after various treatments indicated. (E) Weight of different groups of mice after various treatments indicated at a memory model. (F) Number of metastatic nodules in the lungs. (G) Representative images of H&E stained sections and TUNEL stained tumor sections in the indicated groups (scale bar = 100 μm). (H) Qualification of $T_{EM}$ cells ($CD3^+CD8^+CD44^+CD62L^-$). Data are presented as the mean ± SEM. The (+) refers to laser irradiation 808 nm, 0.8 W/cm$^2$, 5 min. *P < 0.05, **P < 0.01 and ***P < 0.001 from control by t-test.

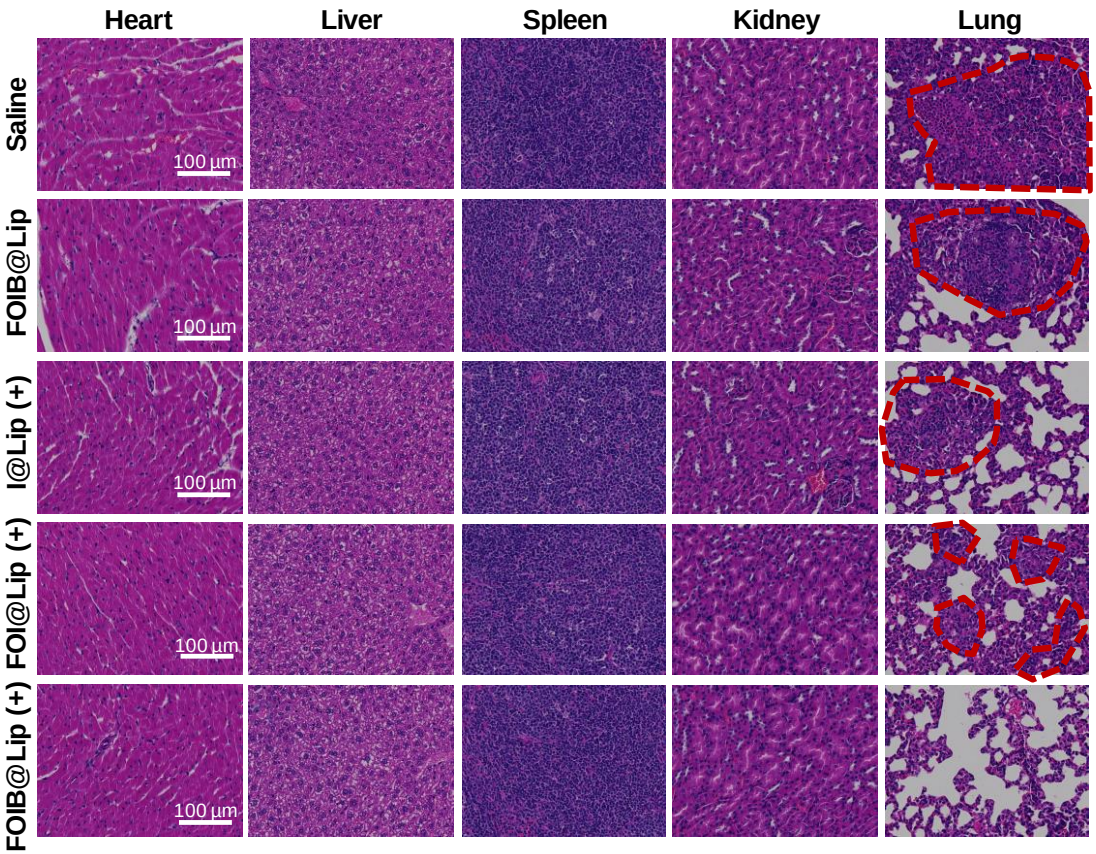



**Figure S13.** Histological analysis of tissues with H&E after different treatments. Circled part in lungs were metastatic tumor cells.