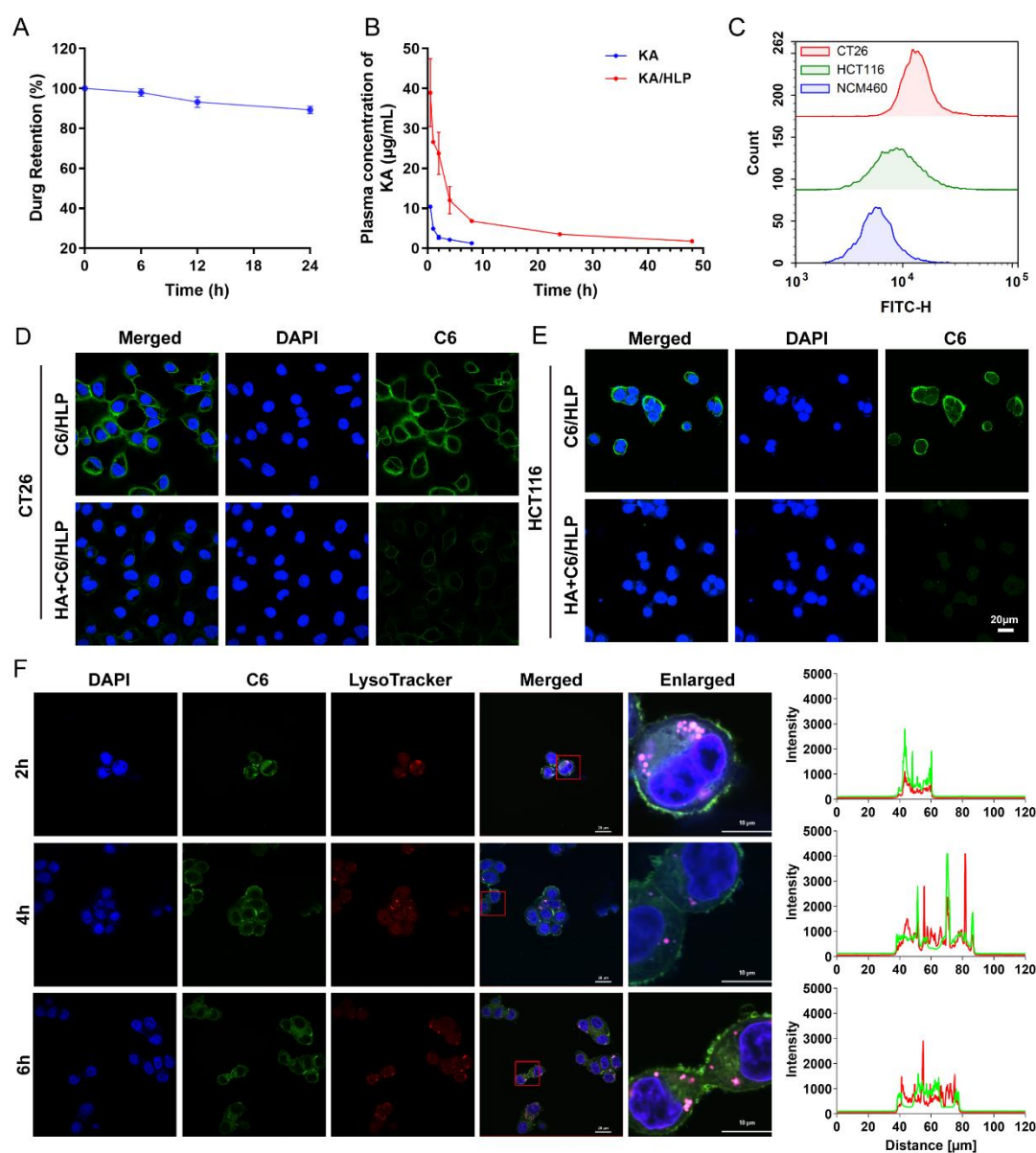
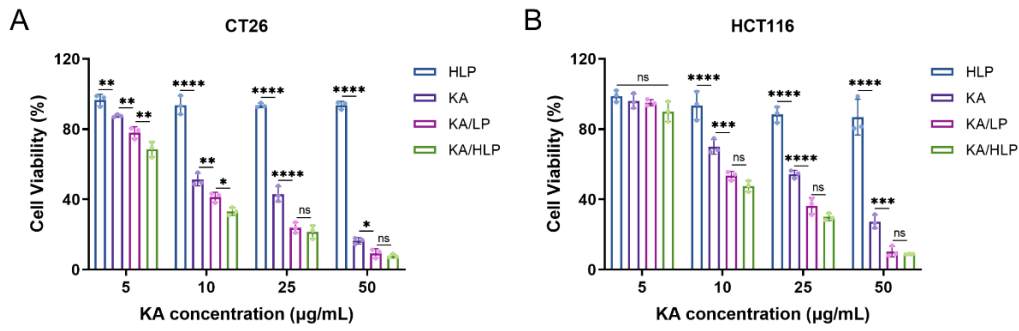
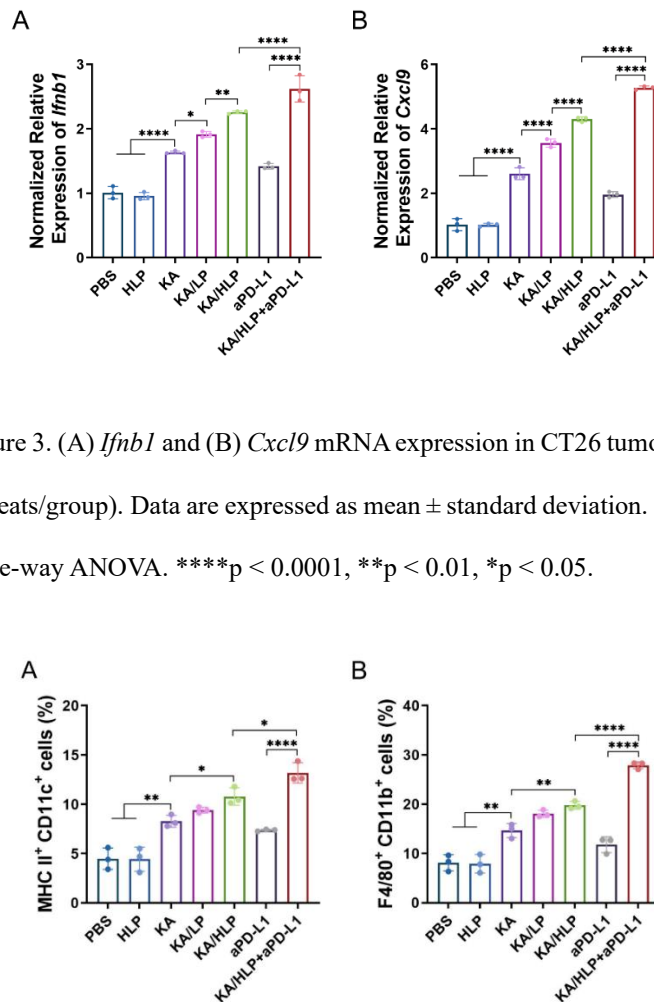




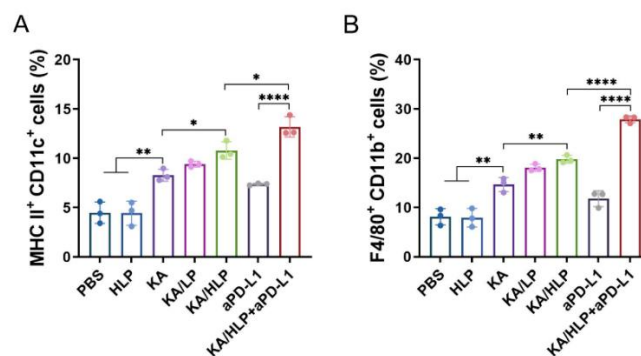
Supplementary Figure 1. (A) KA retention in liposomes incubated in PBS buffer for 24 h (n=3 repeats/group). (B) Pharmacokinetics of free KA and KA/HLP by measuring plasma KA concentration in mice (n=3 repeats/group). (C) Flow cytometry analysis of CD44 protein expression in three cell lines (n=3 repeats/group). (D, E) Cellular uptake of C6/HLP in CT26 and HCT116 cells with or without CD44 blockade (n=3 repeats/group). Blue, DAPI-stained nuclei. Green, C6-labeled HLP. (F) Representative images illustrating lysosomal escape of C6/HLP in HCT116 cells after incubation at 37 °C for 2, 4 and 6 h (n=3 repeats/group). Green, red, and blue fluorescence represent C6, endo/lysosome, and nuclei, respectively.



Supplementary Figure 2. (A, B) Cell viability of CT26 and HCT116 cells after different formulations treatment at 48 h (n=3 repeats/group). Data are expressed as mean $\pm$ standard deviation. Statistical analysis was performed using two-way ANOVA. ****p < 0.0001, ***p < 0.001, **p < 0.01, *p < 0.05.

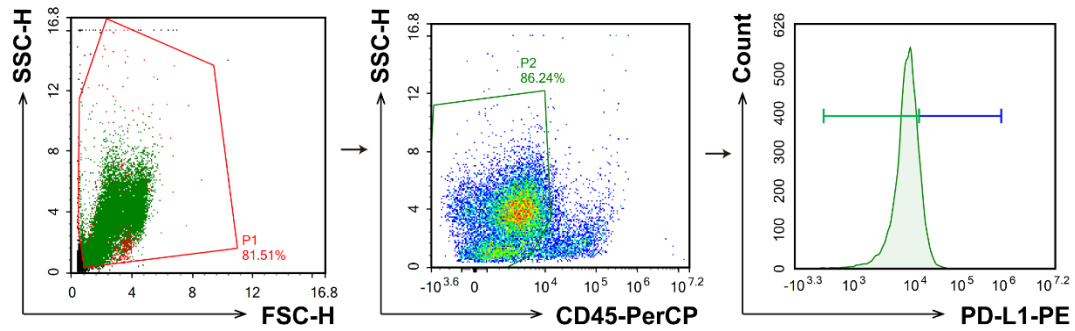


Supplementary Figure 3. (A) *Ifnb1* and (B) *Cxcl9* mRNA expression in CT26 tumor tissues after different treatments (n=3 repeats/group). Data are expressed as mean $\pm$ standard deviation. Statistical analysis was performed using one-way ANOVA. ****p < 0.0001, **p < 0.01, *p < 0.05.



Supplementary Figure 4. (A) MHC II⁺ CD11c⁺ and (B) F4/80⁺ CD11b⁺ cells quantitative results. Data are expressed as mean $\pm$ standard deviation. Statistical analysis was performed using one-way ANOVA.

**** $p < 0.0001$, ** $p < 0.01$, * $p < 0.05$.



Supplementary Figure 5. Gating strategy of the flow cytometry analyses for PD-L1 in tumors of mice after different treatments.

Supplementary Table 1. Characterization of the different KA/HLP formulations.

KA: HLP	1:26	1:17	1:13
EE (%)	96.57±1.84	81.34±0.89	65.41±1.92
DL (%)	3.49±0.01	4.33±0.05	4.56±0.13

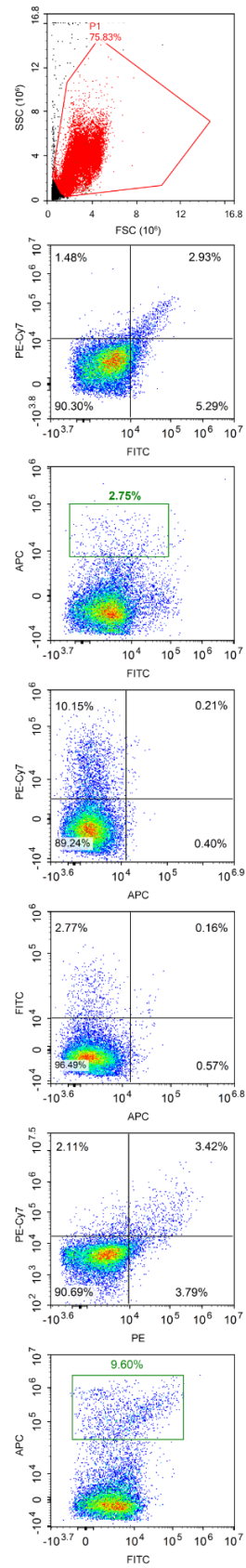
Supplementary Table 2. The primer sequences of genes in RT-qPCR experiment.

Gene	Forward sequence	Reverse sequence
Mouse-Ifnb1	TCGAACAAAAGACGAGGCGA (5' -3')	CCTTCCTCTGCTCTGACACG (5' -3')
Mouse-Cxcl9	GGGACCACAGACTATTCCCC (5' -3')	GCCAATGCCTGGTGTGTAAC (5' -3')
Mouse-ND-1	CCGAGCATCTTATCCACGCT (5' -3')	ATGGTGGTACTCCCGCTGTA (5' -3')
Human-Nd-1	TACGGACGAACAGACGCAAA (5' -3')	TGGAATGCTGGTTGGTGGAA (5' -3')
Mouse-Gapdh	TCTCTGCTCCTCCCTGTTCC (5' -3')	TACGGCCAAATCCGTTTACA (5' -3')
Human-GAPDH	CTCTGCTCCTCCTGTTTCGAC (5' -3')	GACTCCGACCTTCACCTTCC (5' -3')

The gating strategy for flow cytometry

These figures present supporting data for the mechanistic model described in Figures 6 and 7 of the main

text.



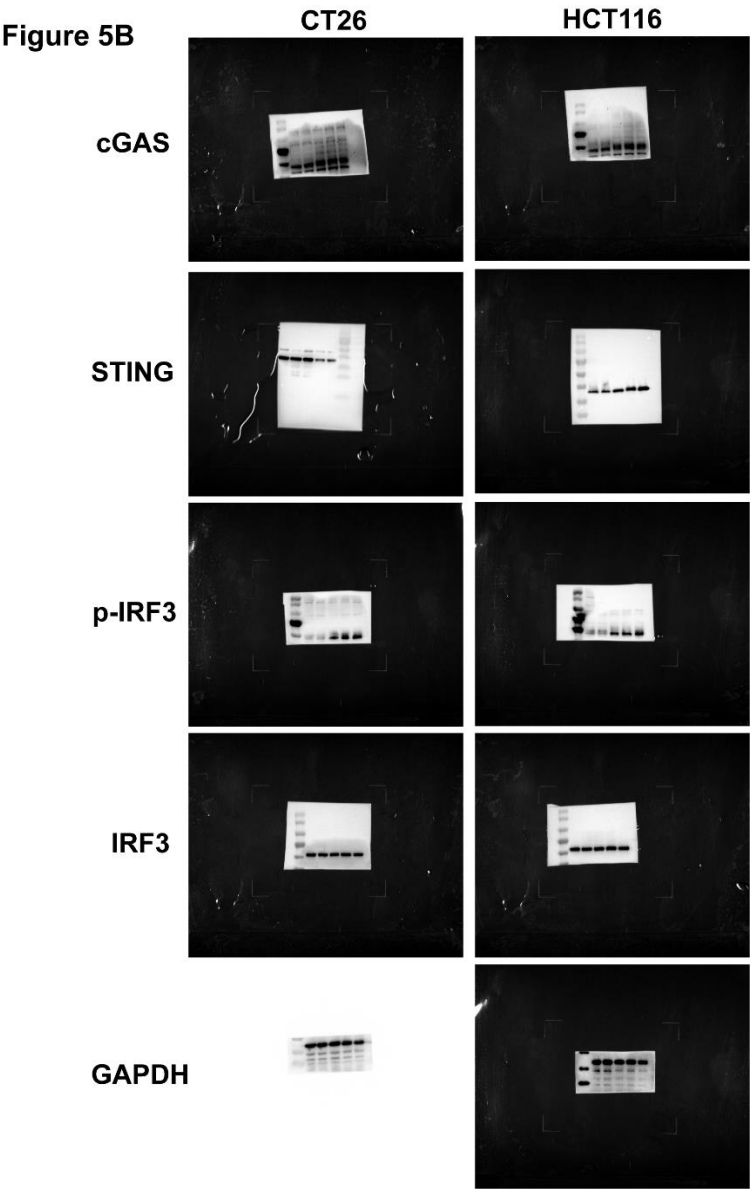


Figure 5E

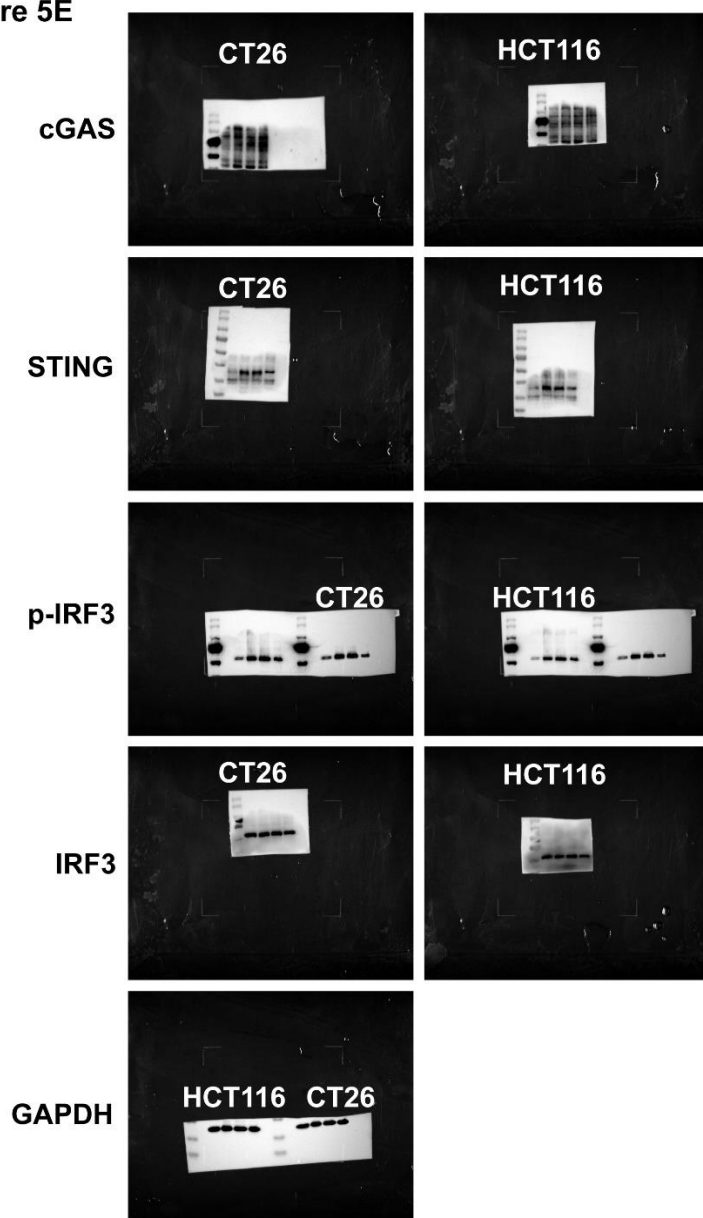


Figure 8C

