Electronic Supplementary Information

Hemin-lipid Assembly as Artemisinin Oral Delivery System for Enhanced Cancer Chemotherapy and Immunotherapy

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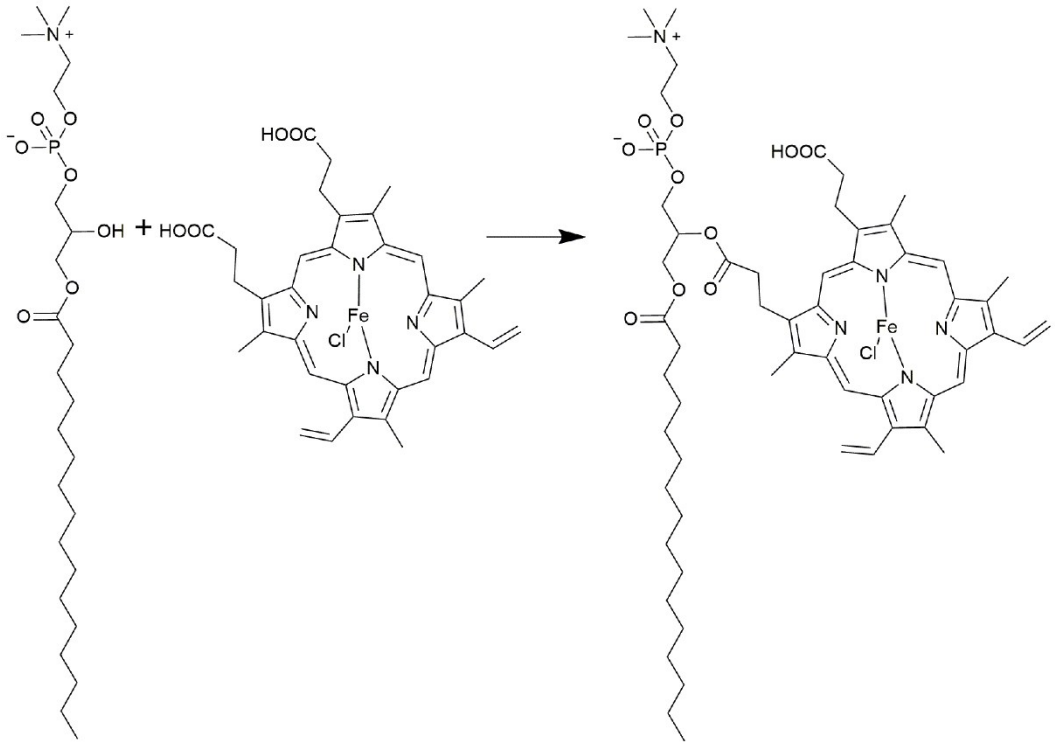

Figure. S1 Schematic for the synthesis of hemin-lipid conjugate.

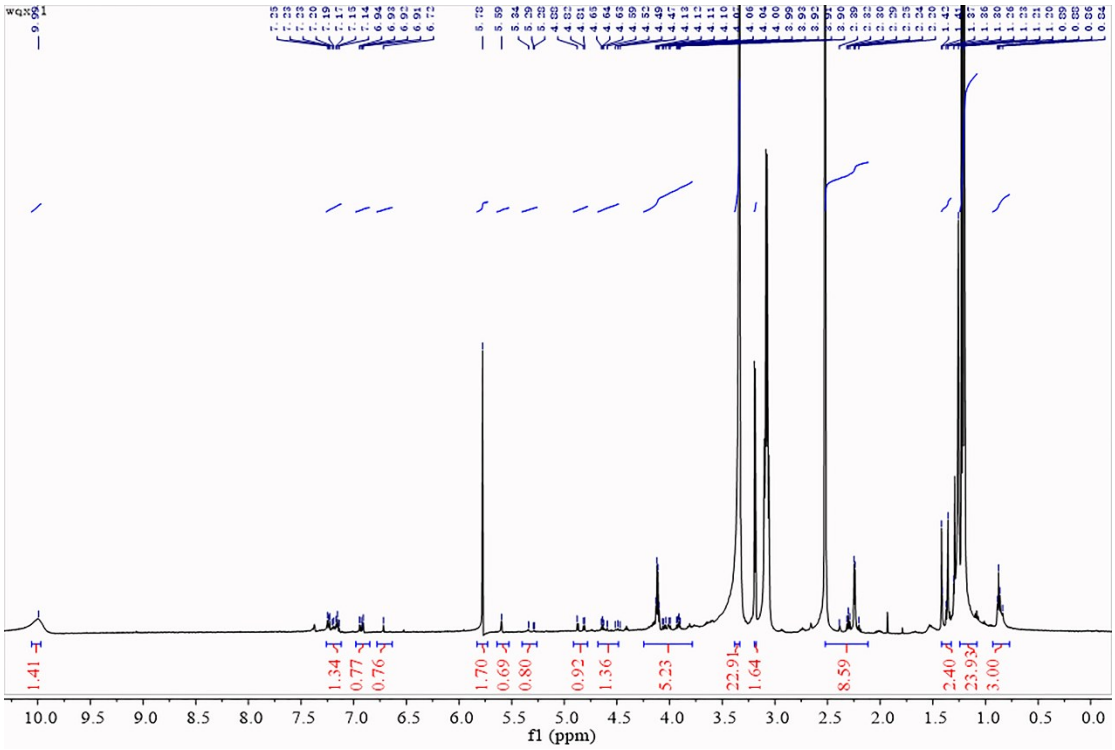

Figure. S2 ^{1}H-NMR spectra of hemin-lipid with a Bruker ACF-300 MHz NMR spectrometer in DMSO-d_6.

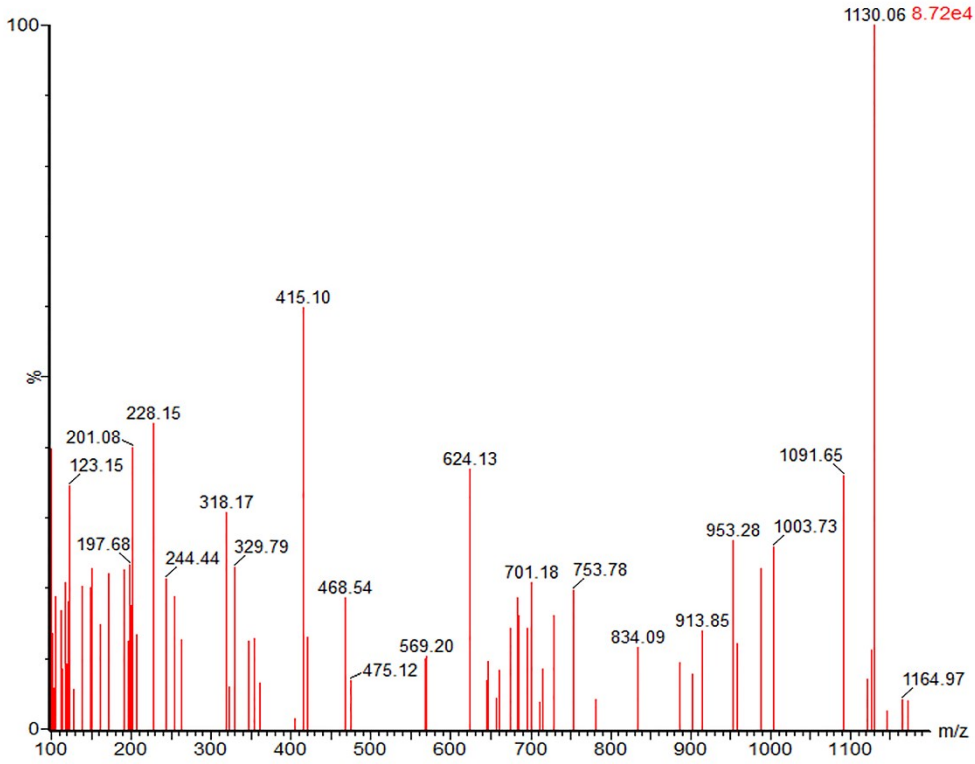

Figure. S3 Mass spectroscopy confirmed the conjugation of hemin to 1-palmitoyl-2-hydroxysn-glycero-3-phosphocholine (16:0 Lyso PC). The Measured m/z of $[M+H]^+$ is 1130.06 and predicted value is 1130.57.

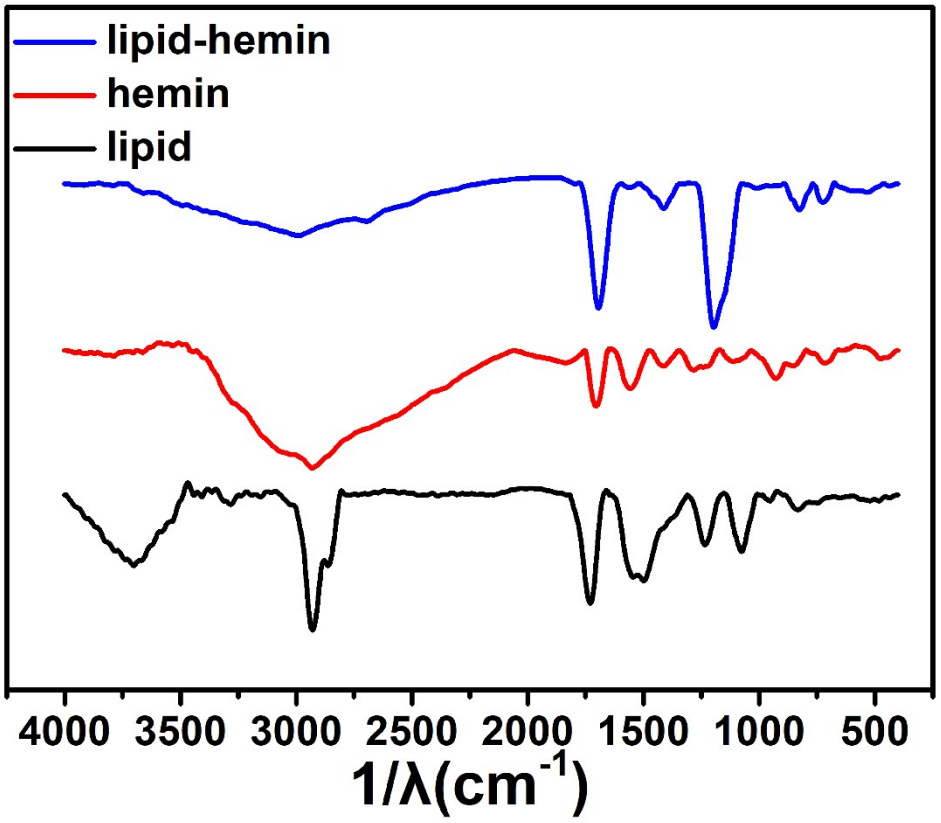

Figure. S4 FT-IR spectra of lipid, hemin and hemin-lipid.

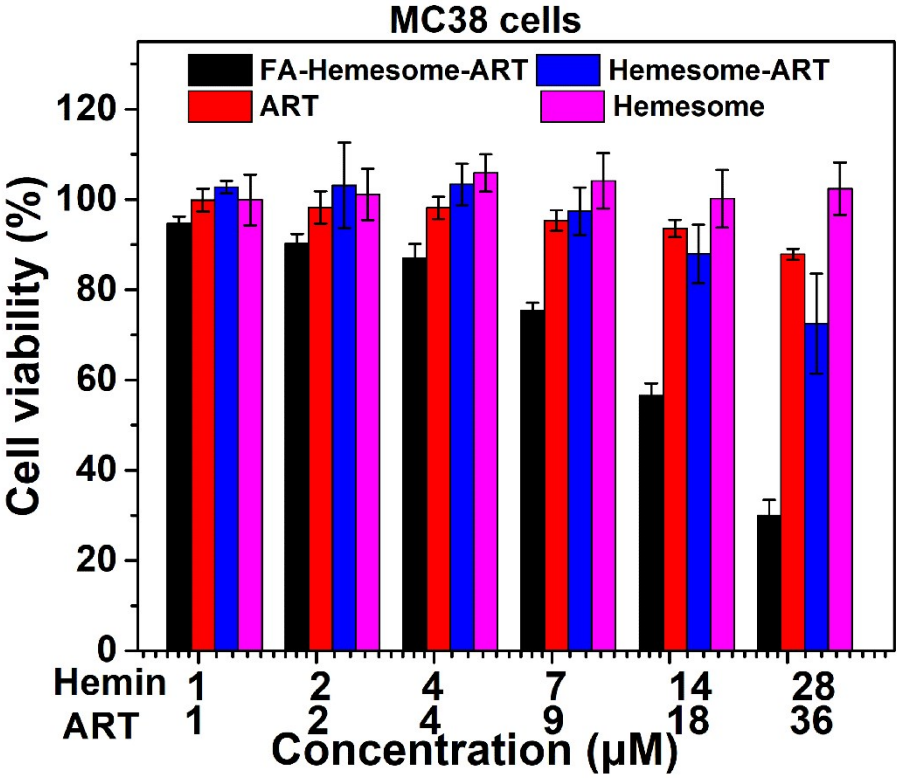

Figure. S5 Cytotoxicity of MC38 cells treated with ART, Hemesome, Hemesome-ART, FA-Hemesome-ART in vitro. Data represent mean ± SD (n = 3).

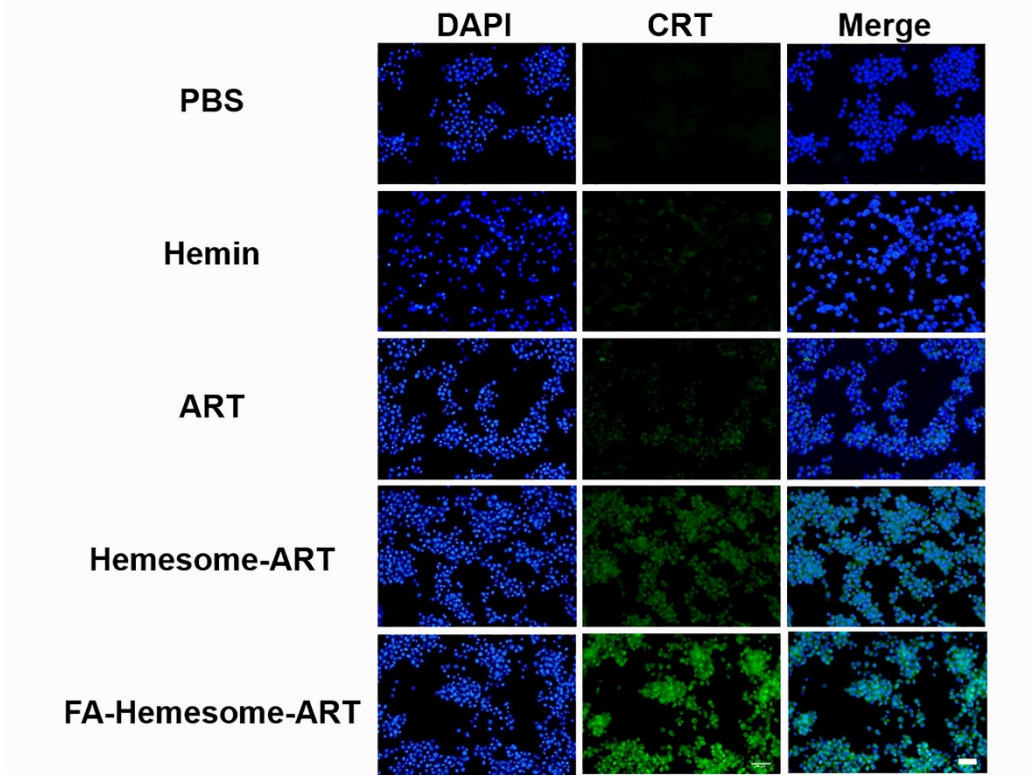

Figure. S6 CRT expression on the MC38 cell surface after different treatments. Scale bar: 100 μm.

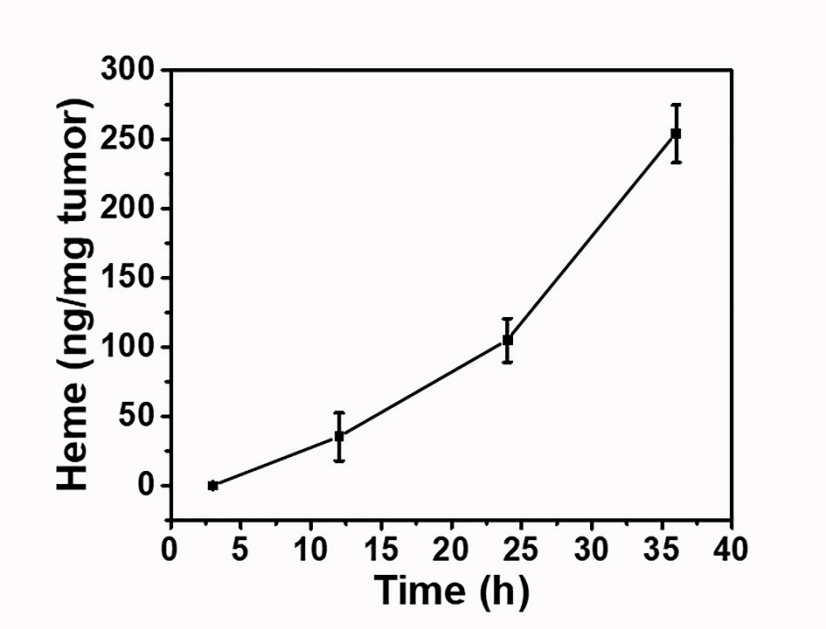

Figure. S7 The content of heme in the tumor after oral administration of FA-Hemesome-ART at different time-point: 3, 12, 24 and 36 h.

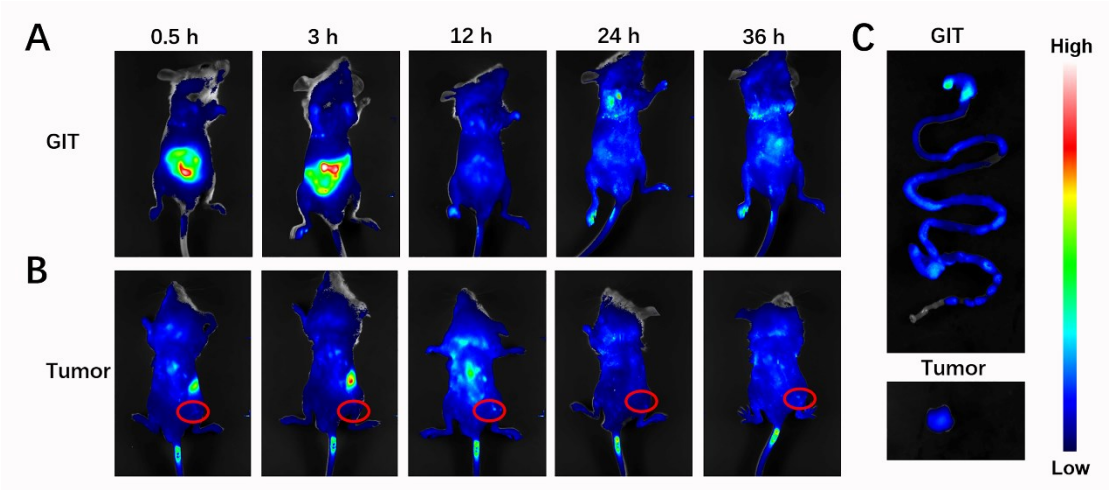

Figure. S8 Fluorescence images of 4T1 tumors bearing mice after oral administration of PpIX at different time-point.

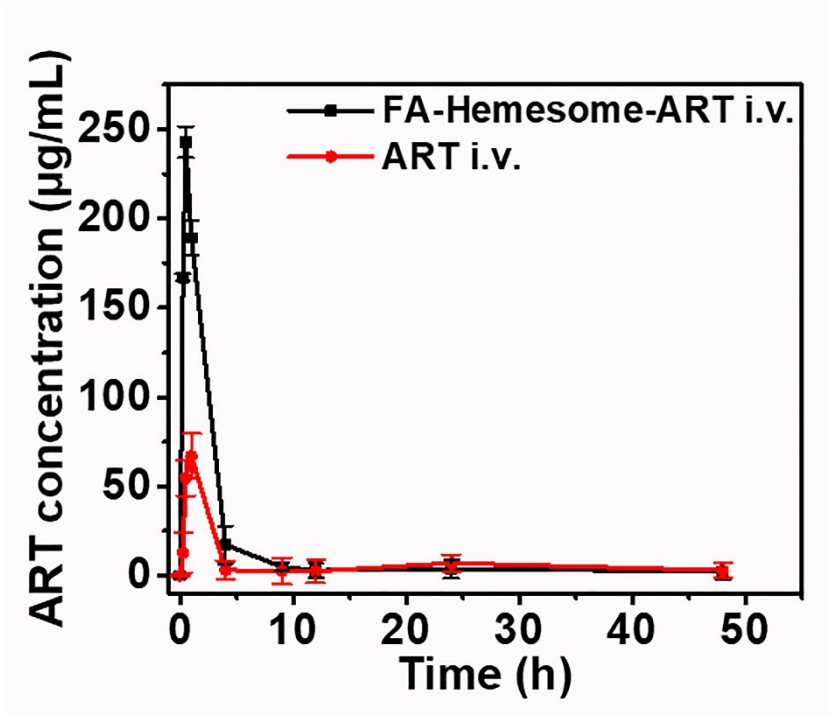

Figure. S9 Plasma concentration-time profiles of ART and FA-Hemesome-ART NPs in mice by intravenous injection.

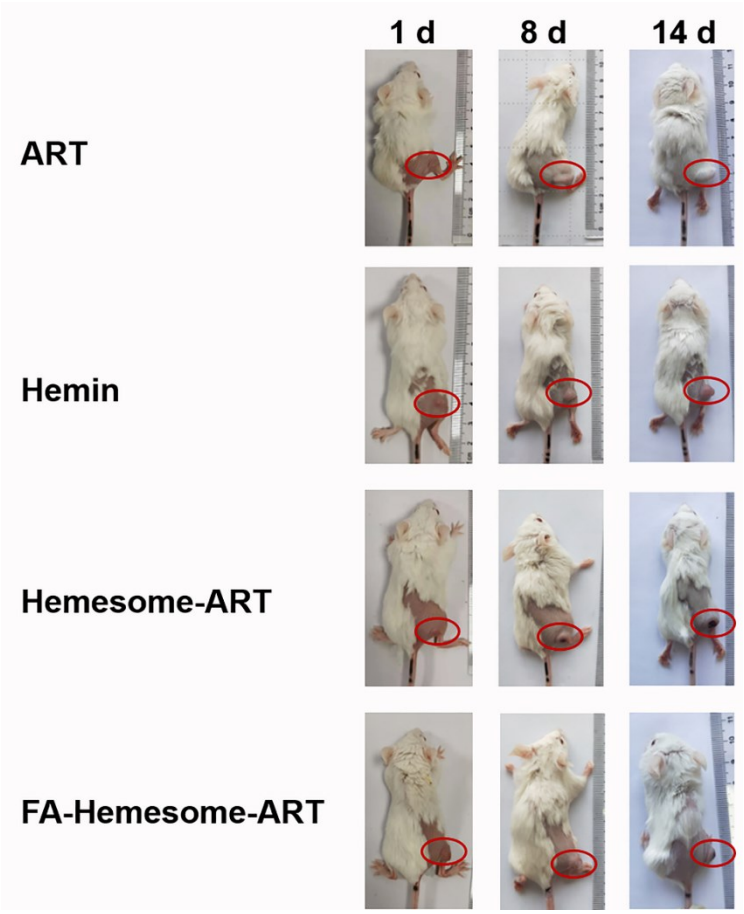

Figure. S10 The images of 4T1 tumor-bearing mice on the 1, 8, 14 day during the different groups by oral administration.

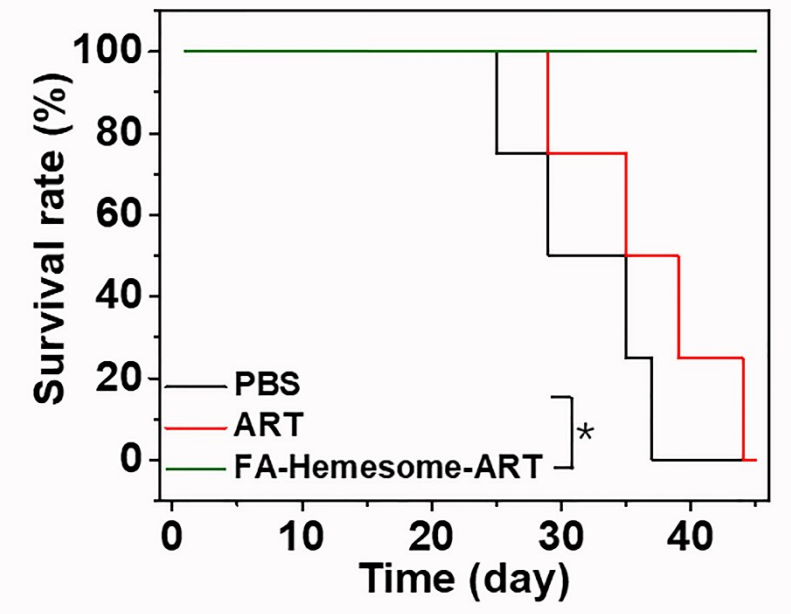

Figure. S11 Survival rate of mice in different groups in 4T1 tumors bearing mice after oral administration (n = 4). *P value < 0.05 by student's two-tailed t test.

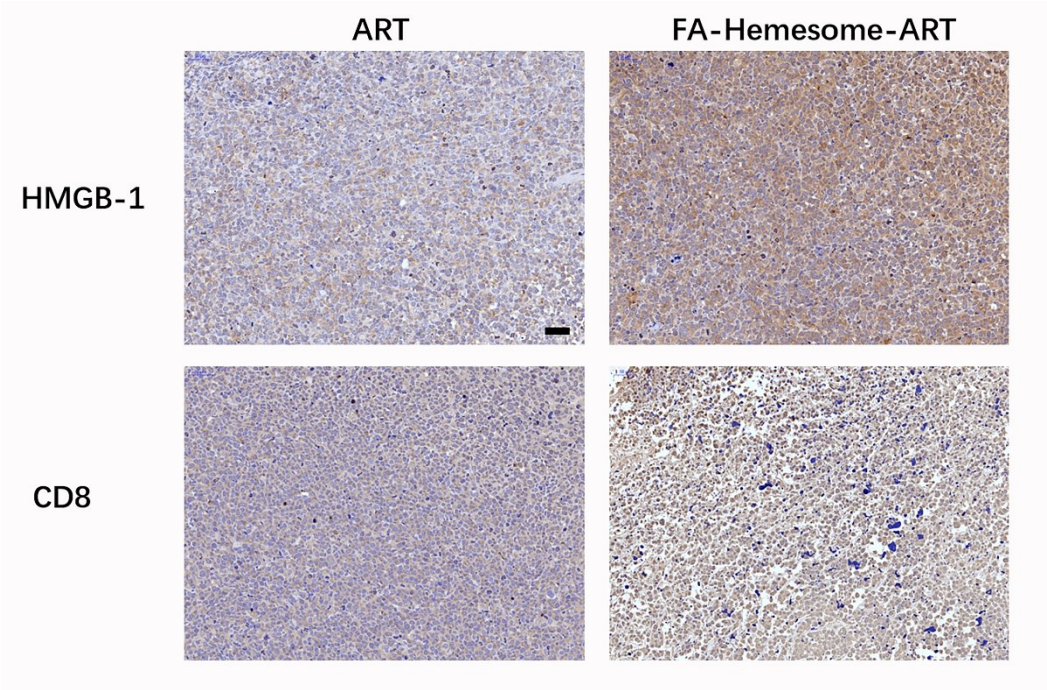

Figure. S12 The *in situ* secretion of HMGB-1 and the infiltration of $CD8^+$ T cells in the tumor were observed by immunohistochemistry. Scale bar: 50 μm.

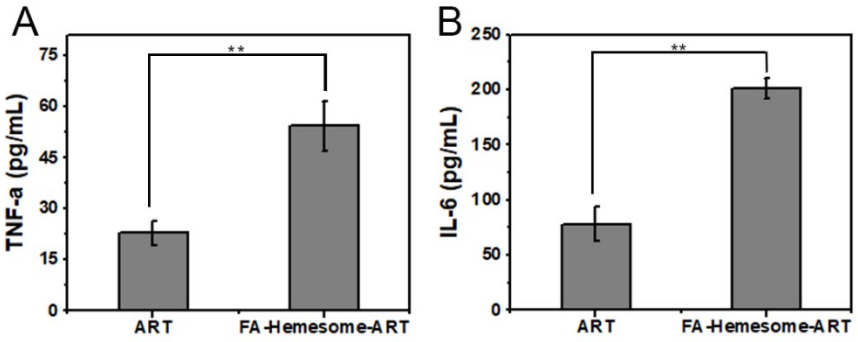

Figure. S13 The intratumoral secretion of (A) TNF-α and (B) IL-6 in the MC38 tumor bearing C57Bl/6 mice receiving oral treatments of ART and FA-Hemesome-ART NPs, respectively (n = 3). **P value < 0.01 by student's two-tailed t test.

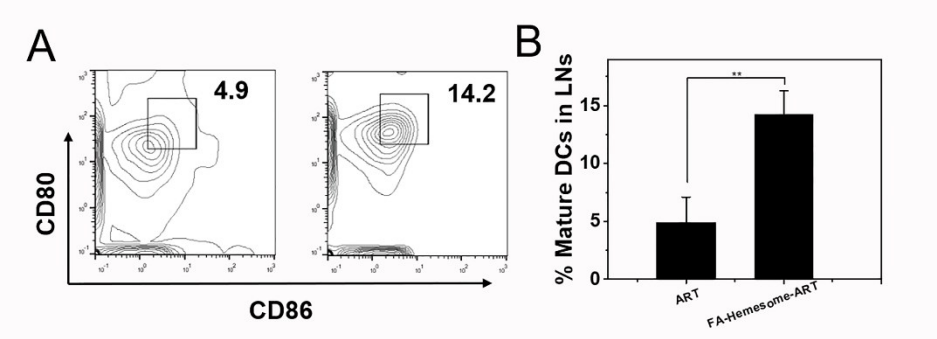

Figure 14 DCs maturation induced by ICD for assessment by flow cytometry after staining with $CD11c^+$, $CD80^+$, and $CD86^+$ on MC38 tumor-bearing mice (gated on $CD11^+$ DCs) (n = 3). **P value < 0.01 by student's two-tailed t test.