Supplementary Materials for

Inhibition of platelet function using liposomal nanoparticles blocks tumor metastasis

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Table S1. Encapsulation efficiency of Ticagrelor into liposome nanoparticles at varying weight ratios of liposome/ticagrelor.

Liposome:Ticagrelor Ratio	**40：5**	**40：10**	**40：15**
Encapsulation efficiency of Ticagrelor (%)	**85.4 ± 1.28**	**81.4 ± 1.11**	**75.8 ± 0.46**

The ratio of 40:5 of liposome to ticagrelor was chosen for the current study as high encapsulation efficiency was observed and the nanoparticles had a narrow size distribution.

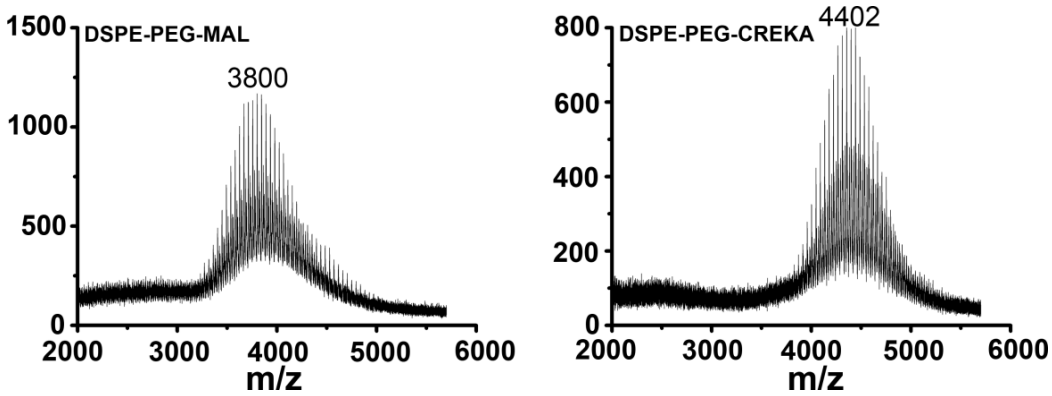

Figure S1. MALDI-TOF-MS examination of DSPE-PEG-CREKA conjugation. The molecular weight of DSPE-PEG increased from 3800 (left) to 4402 (right), indicating the successful conjugation of DSPE-PEG and CREKA peptide.

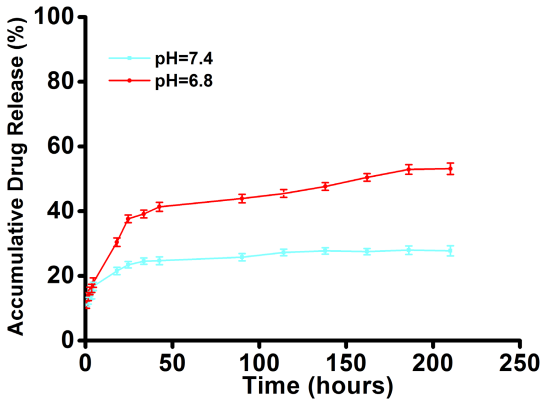

Figure S2: The drug release profiles of CREKA-Lipo-T at two pH conditions

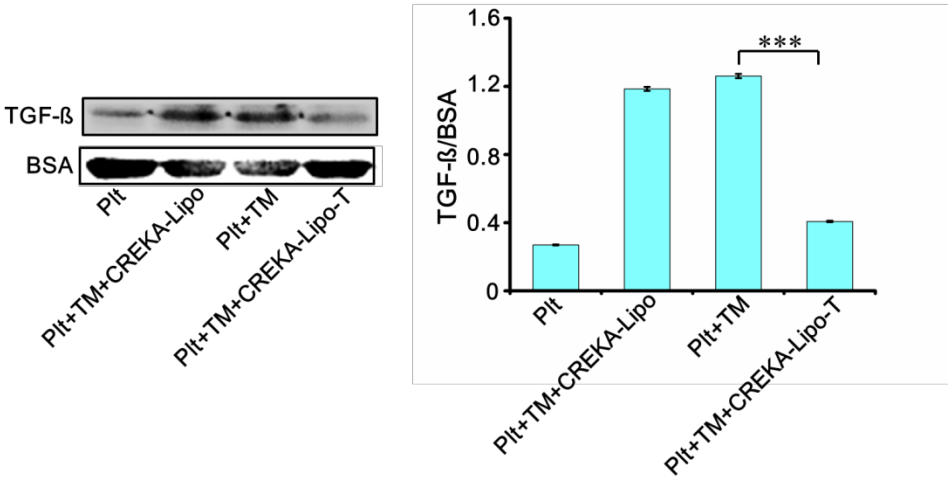

Figure S3. The inhibition of platelet TGF-β secretion by CREKA-Lipo-T. (**A**) Western blot analysis shows that conditioned medium from 4T1 tumor cells can stimulate the secretion of TGF-β from platelets (Plt), and that CREKA-Lipo-T reduced the secretion of TGF-ß about 70%, while the CREKA-Lipo group did not show this effect. (**B**) Quantitative analysis of the data in A (n=3). ***p<0.001. TM: tumor cell conditioned medium, Plt: platelets.

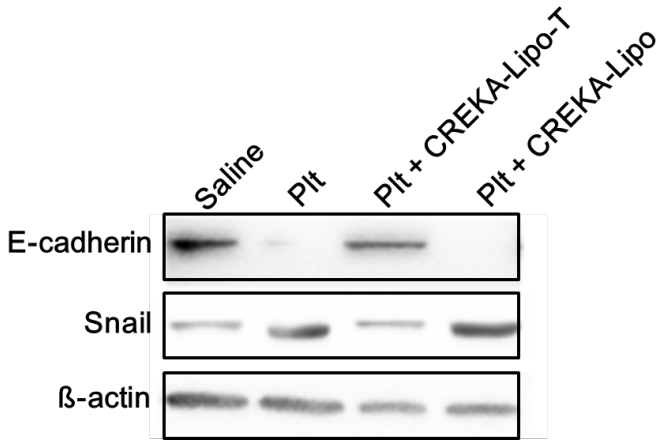

Figure S4. Expression of EMT markers in 4T1 cells following treatment with different drug formulations. Western blotting was used to measure the expression of E-cadherin and Snail in 4T1 cells. Low expression of E-cadherin and high expression of Snail indicate the transition of tumor cells from an epithelial to an invasive mesenchymal phenotype when platelets are present. CREKA-Lipo-T, but not CREKA-Lipo abolished this transition effect. Plt: platelets.

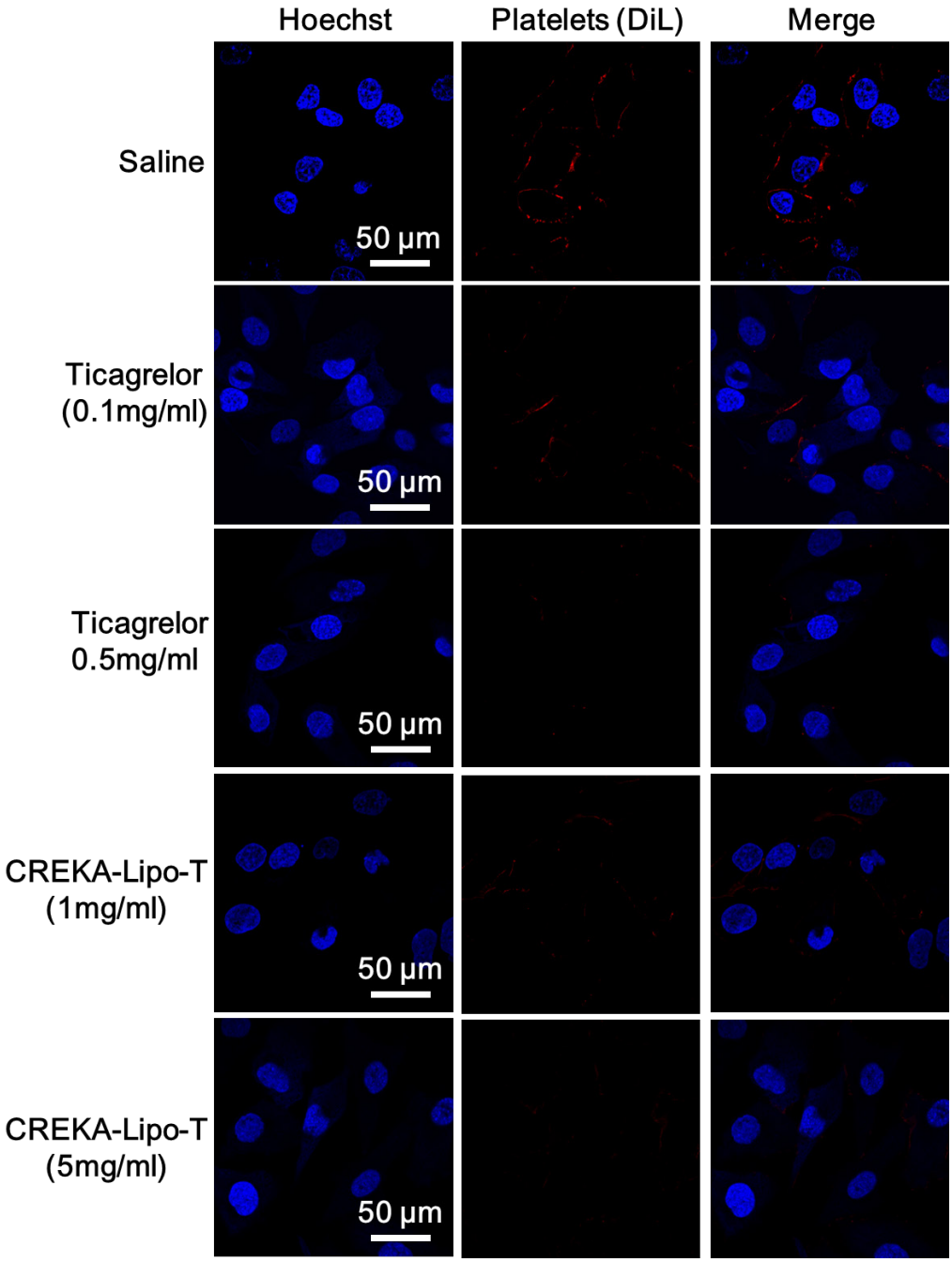

Figure S5. Ticagrelor and CREKA-Lipo-T impedes the interaction between 4T1 tumor cells and platelets with dose dependent feature. Platelets (red) were labelled with the fluorescent dye DiL and tumor cell nuclei (blue) were stained with Hoechst 33342.

Figure S6. Gross morphology of the lungs of mice bearing 4T1 tumors treated with different drug formulations. Fewer metastatic foci were observed on the surface of the lungs from CREKA-Lipo-T treated mice compared to the other experimental groups.

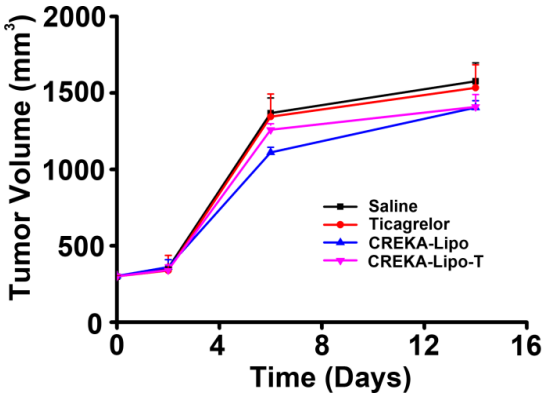

Figure S7. *In vivo* effects of different drug formulations on primary 4T1 tumor size. No significant differences were observed between the different groups after treatment with Saline, Ticagrelor, CREKA-Lipo and CREKA-Lipo-T.

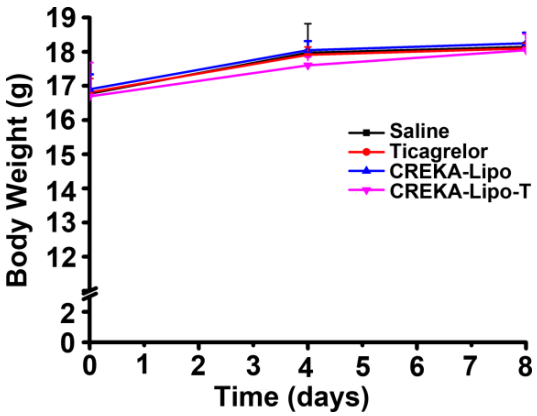

Figure S8. Body weight of mice treated with different drug formulations. No apparent changes of body weight were observed in wild-type BALB/c mice after treatment with saline, ticagrelor, CREKA-Lipo or CREKA-Lipo-T, three times every two days (n = 5).