Supporting Information for

# A Therapeutic Sheep in Metastatic Wolf's Clothing: Trojan Horse Approach for Cancer Brain Metastases Treatment

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## **Supplementary Figures**



**Fig. S1** Flow cytometry spectra of MDA-MB-231/Br after being treated with free DOX, DOX-PLGA, and DOX-PLGA@CM. Cells were analyzed after being incubated with different treatments for 3 h



**Fig. S2** Flow cytometry spectra of MDA-MB-231 after being treated with free DOX, DOX-PLGA, and DOX-PLGA@CM. Cells were analyzed after being incubated with different treatments for 3



**Fig. S3** Characterization of cell membrane proteins from different cell lines by SDS-PAGE. Then red arrow indicates the cell special protein, and blue arrow indicates the common protein but different abundance.



**Fig. S4** Cell viability of NIH3T3 cells after the treatments with various concentrations of DOX-PLGA@CM, DOX-PLGA and Free DOX for 24 h measured by the MTT assay



**Fig. S5** The flow cytometry spectra of NIH3T3 cells after being treated with free DOX, DOX-PLGA, and DOX-PLGA@CM. Cells were analyzed after being incubated with different treatments for 3 h



**Fig. S6** Establishment of brain metastases of breast cancer model. (**a**) Ex vivo bioluminescence imaging of stably luciferase expressed MDA-MB-231/Br cells. (**b**) Linear correlation between the bioluminescence signal intensity and the number of MDA-MB-231/Br using IVIS Spectrum system. (**c**) Photograph of intracardiac injection of MDA-MB-231/Br to BALB/c nu mouse. In vivo bioluminescence imaging of mice 30 min (**d**) and three weeks (**e**) after the intracardiac injection of MDA-MB-231/Br cells. (**f**) Ex vivo bioluminescence imaging of mice at three weeks after intracardiac injection of MDA-MB-231/Br cells



Fig. S7 Body weight change of brain metastases bearing mice in different groups during the treatment



Fig. S8 H&E staining of the major organs (heart, liver, spleen, and kidney) of the mice in different treatment groups