

Electronic Supplementary Information

**Coadministration of chemotherapy and PI3K/Akt pathway treatment with
acidity/CathB enzyme multistage responsive nanocarrier for
inhibiting metastasis of breast cancer**

Tiantian Zuo¹, Jing Li¹, Jun Zhang¹, Liang Sun¹, Xiao Liang¹, Jie Yang¹, and Qi Shen¹✉

¹ School of Pharmacy, Shanghai Jiao Tong University, 800 Dongchuan Road,

Shanghai 200240, China

✉Corresponding Author: Qi Shen, E-mail addresses: qshen@sjtu.edu.cn, Fax: +86-21-

34204049

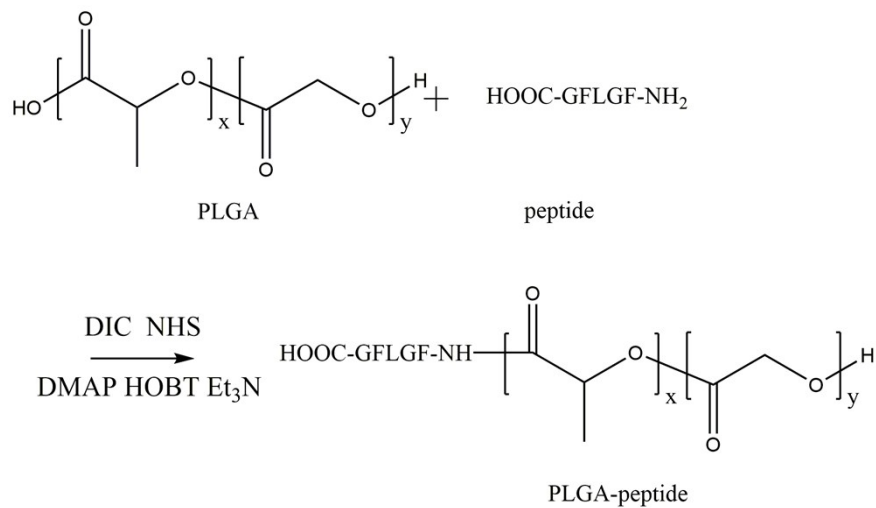


Figure S1 Synthesis of PLGA-peptide

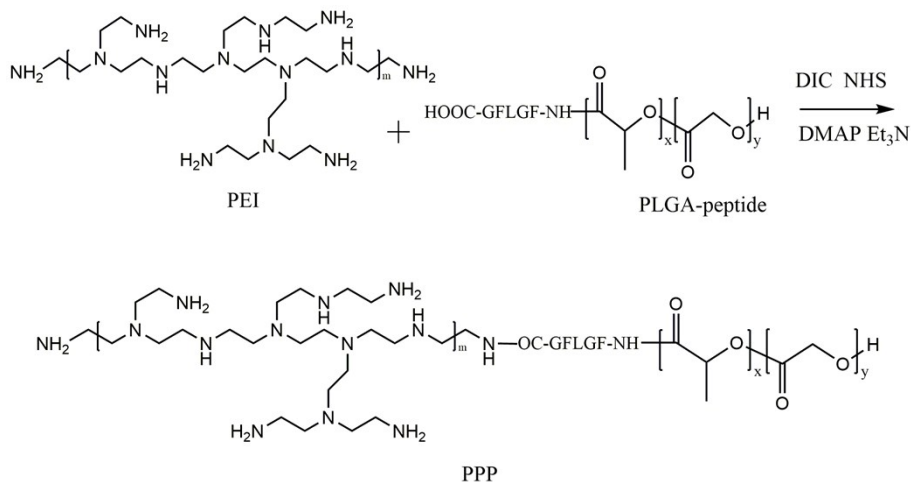


Figure S2 Synthesis of PPP-peptide-PEI

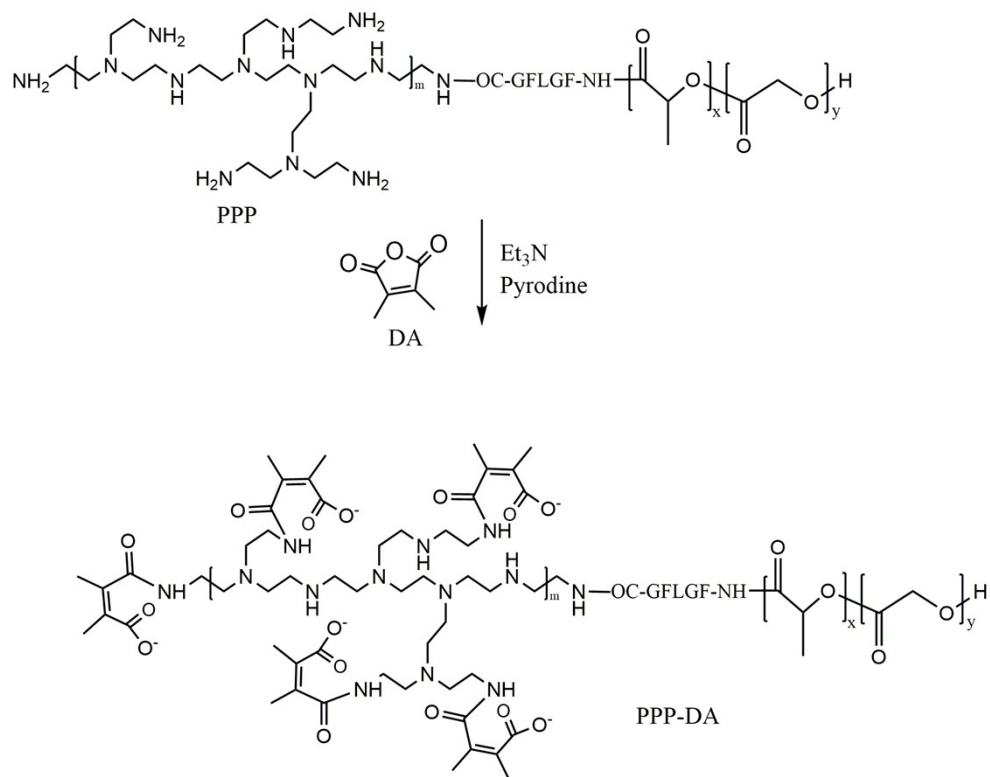


Figure S3. Synthesis of PPP-DA

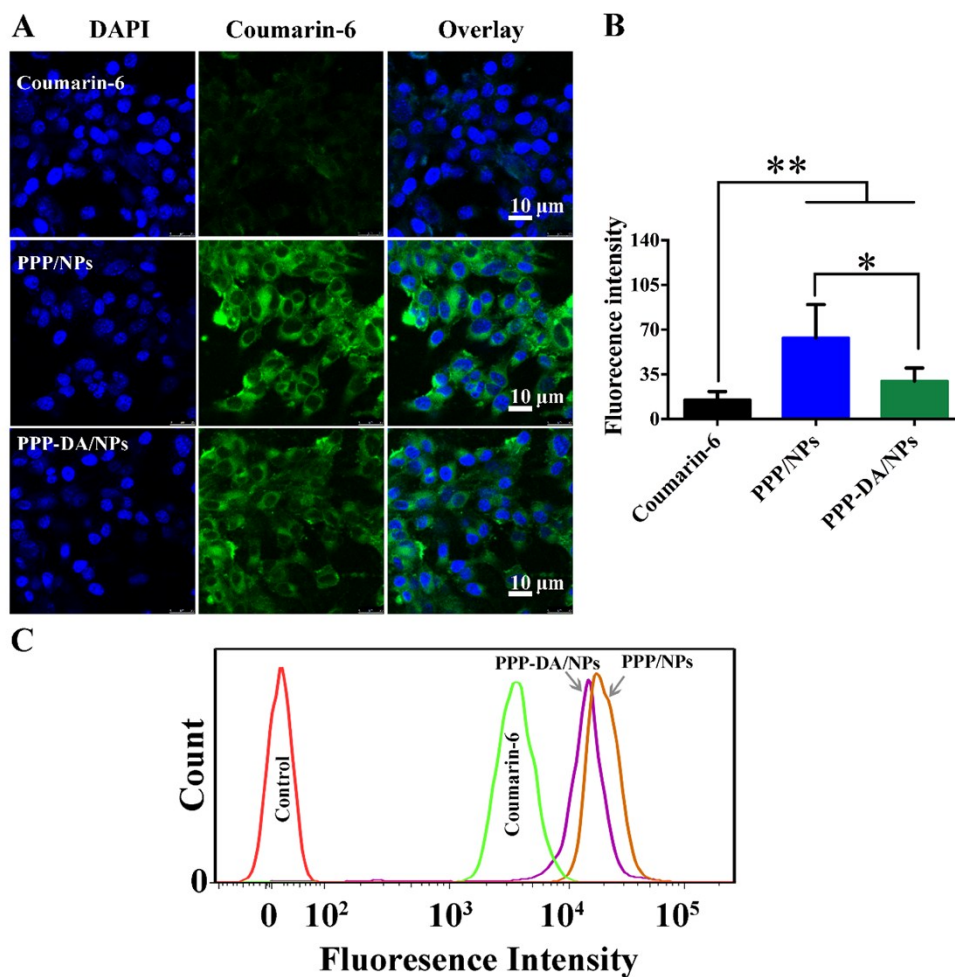


Figure S4. CLSM images (A) and fluorescence quantitative analysis (B) of 4T1 cells after incubation with coumarin-6, PPP/NPs and PPP-DA/NPs for 4 h, in columns from left to right correspond to DAPI (blue), Coumarin-6 (green) and overlay of DAPI and coumarin-6, respectively. (C) Flow cytometry results of 4T1 cells treated with free coumarin-6, PPP/NPs and PPP-DA/NPs (coumarin-6 concentration 2 $\mu\text{g}/\text{mL}$) for 4 h. * $P < 0.05$, ** $P < 0.01$.

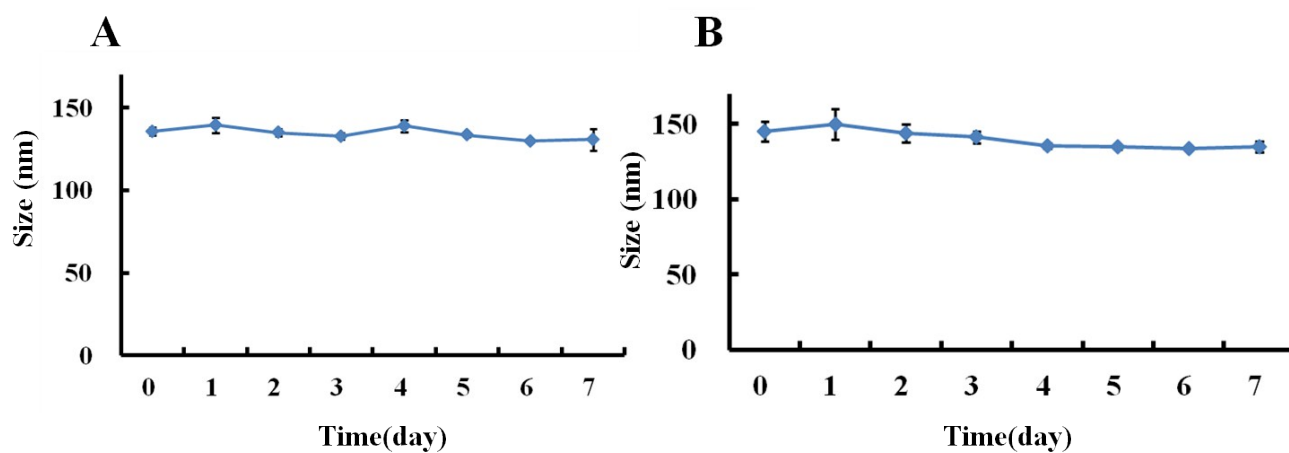


Figure S5. The hydrodynamic diameter of PPP-DA/NPs during incubation in the (A) PBS(0.05M, pH 7.4, 4°C) and (B) RPMI-1640 cell culture medium (pH 7.4, 37°C) supplemented with 10% fetal calf serum for 7days.

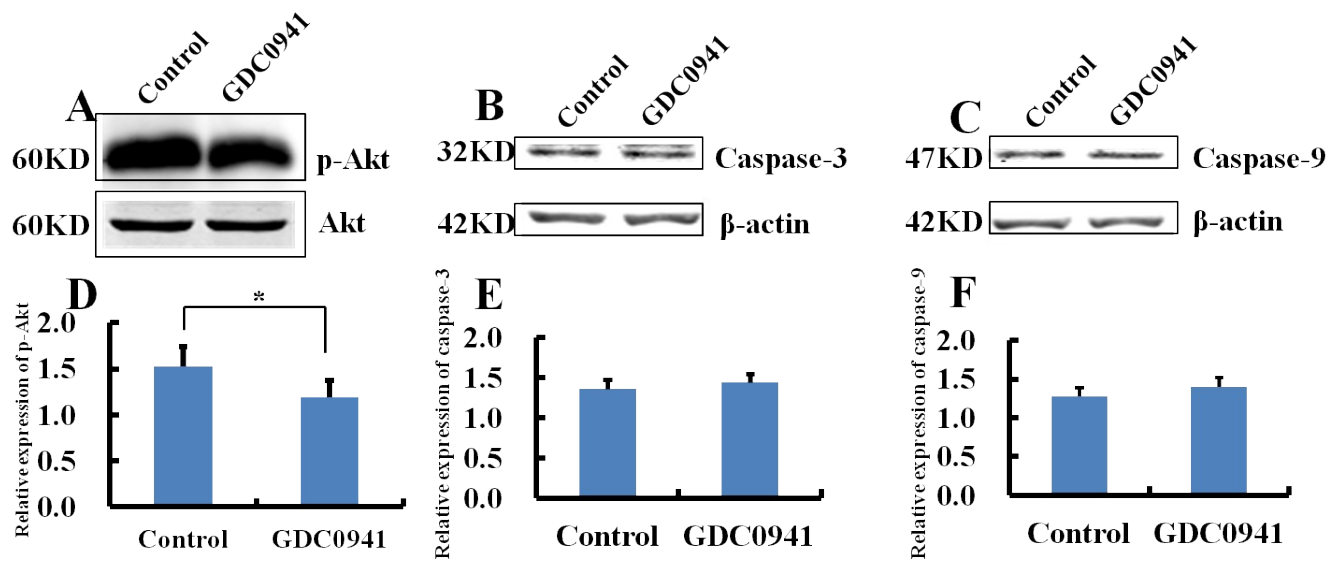


Figure S6. The antitumor mechanistic studies were confirmed by western blotting analysis. Cropped gels images (A, B) and semi-quantitative analysis (C-F) were performed to examine the effect of GDC0941 alone on the expression of p-Akt, Caspase-3/9 protein in 4T1 tumor cells.

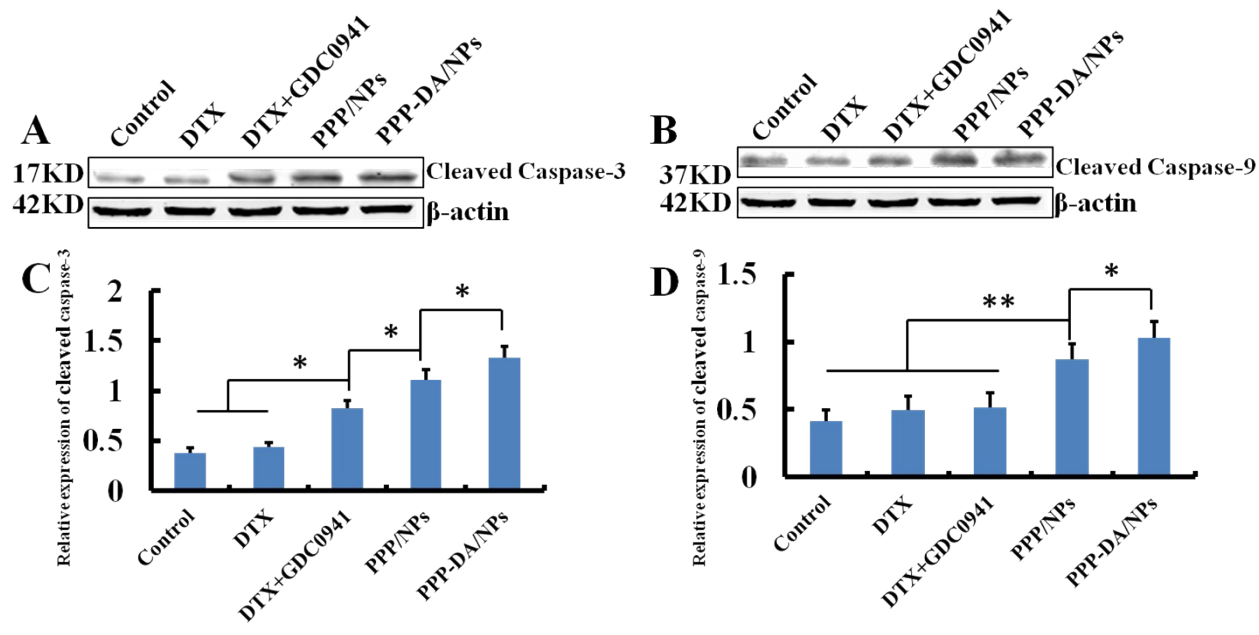


Figure S7. The antitumor mechanistic studies were confirmed by western blotting analysis. Cropped gels images (A, B) and semi-quantitative analysis (C, D) were performed to examine the expression of cleaved caspase-3/9 in 4T1 tumor cells. The sample were extracted from tumor cells treated with saline, DTX, DTX+GDC0941, PPP/NPs and PPP-DA/NPs. * $P < 0.05$, ** $P < 0.01$.