

## Supplementary Information

### Active targeting nano-scale bubbles enhanced ultrasound cavitation chemotherapy in Y<sub>1</sub> receptor-overexpressed breast cancer

Xuechen Qian <sup>a, c, †</sup>, Yinjie Wang <sup>b, d, †</sup>, Youfeng Xu <sup>a, c, †</sup>, Ling Ma <sup>a</sup>, Nianyu Xue <sup>a</sup>, Zhenqi Jiang <sup>b, d</sup>, Yi Cao <sup>b, d</sup>, Ozioma Udochukwu Akakuru <sup>b, d</sup>, Juan Li <sup>b, \*</sup>, Shengmin Zhang <sup>a, c, \*</sup>, Aiguo Wu <sup>b, \*</sup>

a. Department of Ultrasound, Ningbo First Hospital, Ningbo 315010, China.

b. Cixi Institute of Biomedical Engineering, CAS Key Laboratory of Magnetic Materials and Devices, Zhejiang Engineering Research Center for Biomedical Materials, Ningbo Institute of Materials Technology and Engineering, Chinese Academy of Sciences, Ningbo 315201, China.

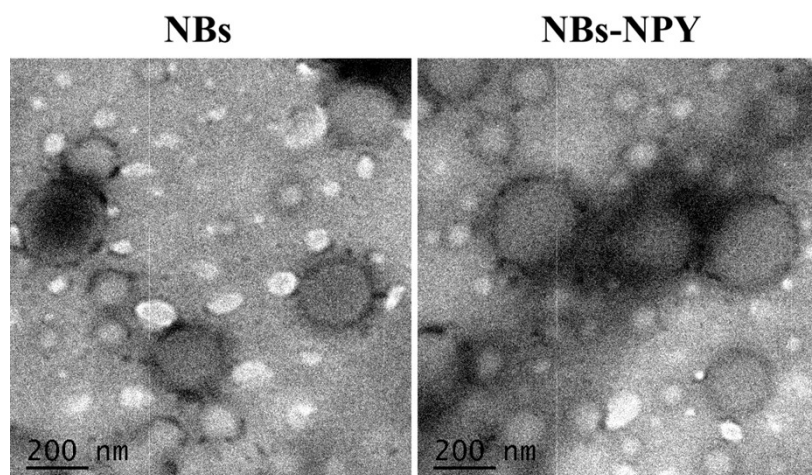
c. Medical School of Ningbo University, Ningbo 315211, China.

d. University of Chinese Academy of Sciences, Beijing 100049, China.

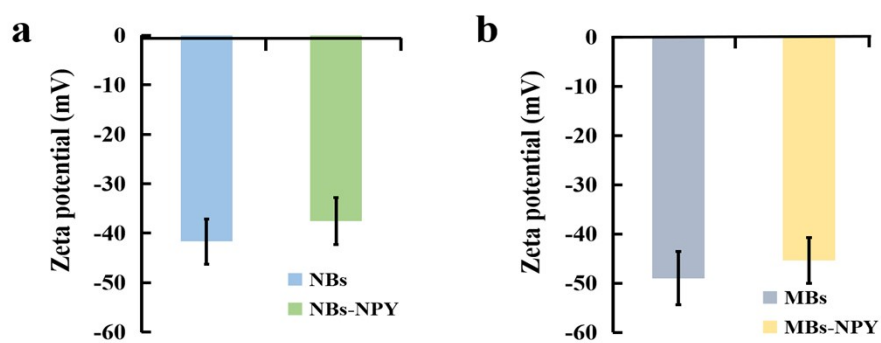
† These authors contributed equally to this work.

\*Corresponding author.

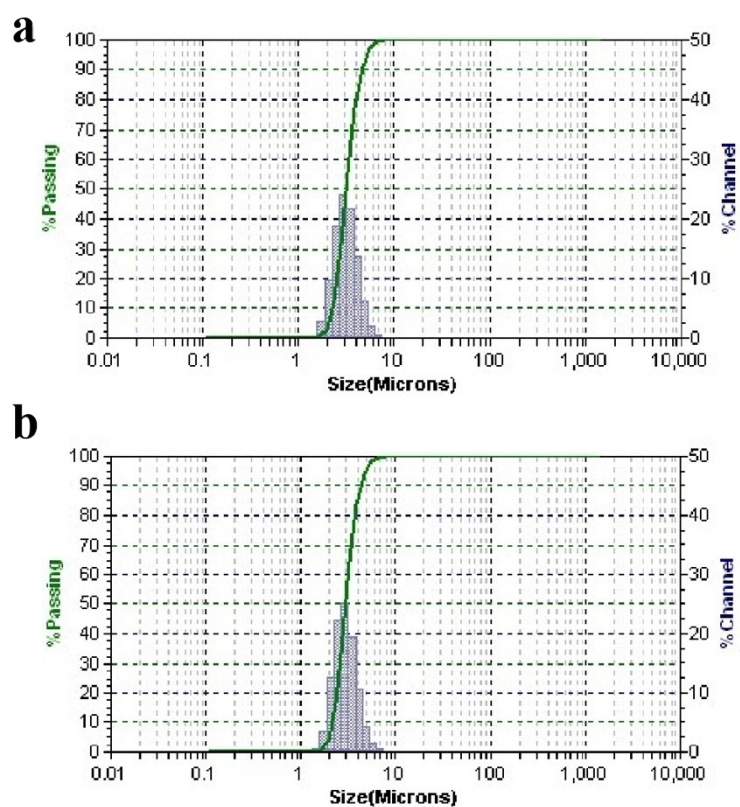
E-mail: aiguo@nimte.ac.cn, 1261142692@qq.com, lij@nimte.ac.cn



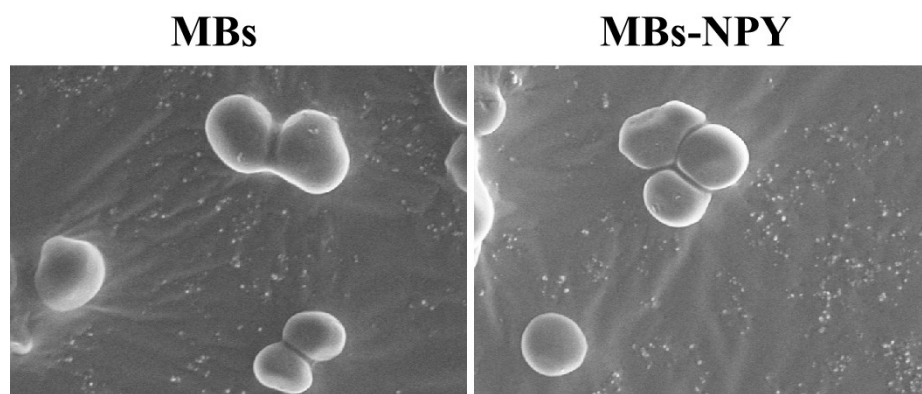
**Fig. S1.** TEM images of NBs and NBs-NPY at pH=5.5. (15000 $\times$ ).



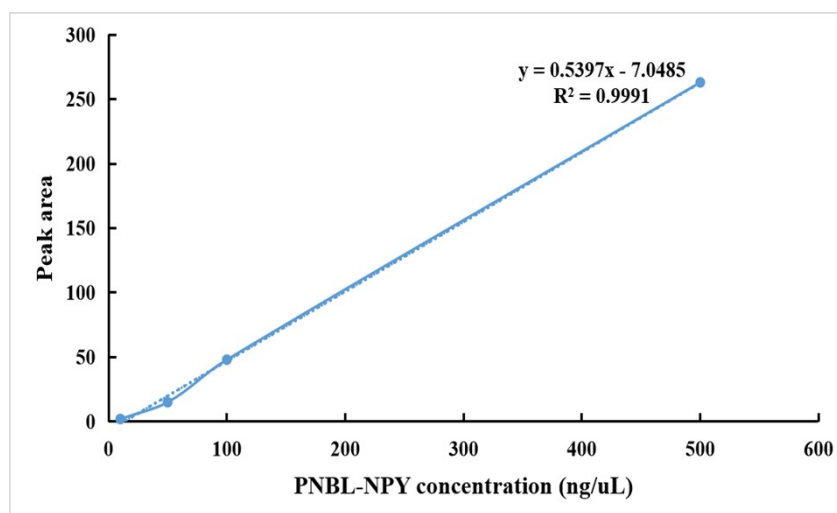
**Fig. S2.** (a, b) Zeta potential of NBs, NBs-NPY and MBs, MBs-NPY in PBS by dynamic light scattering (DLS) using a particle size-zeta potential analyzer, respectively.



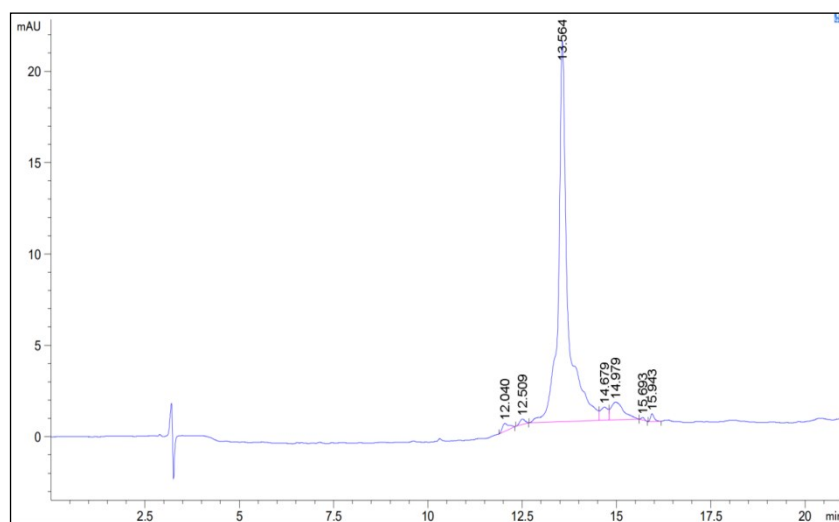
**Fig. S3.** (a, b) Size distributions of MBs and MBs-NPY in PBS by dry-wet laser particle size analyzer, respectively.



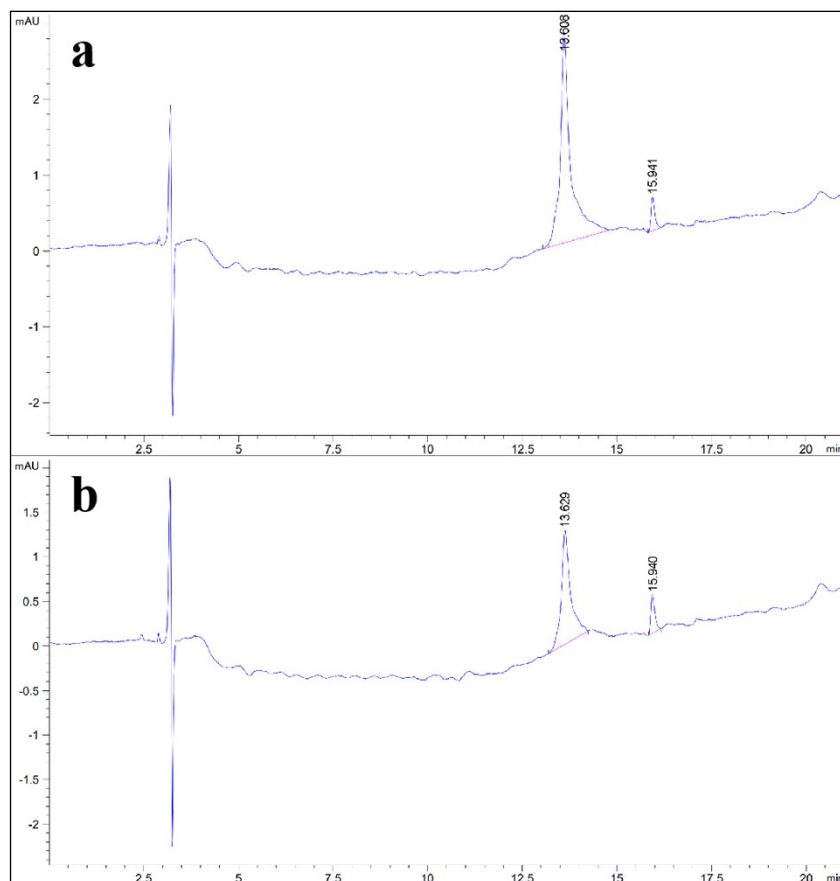
**Fig. S4.** SEM images of MBs and MBs-NPY at pH=5.5. (5000 $\times$ ).



**Fig. S5.** The standard curve of PNBL-NPY by HPLC. The PNBL-NPY concentration was varied from 10 to 500 ng/ $\mu$ L.

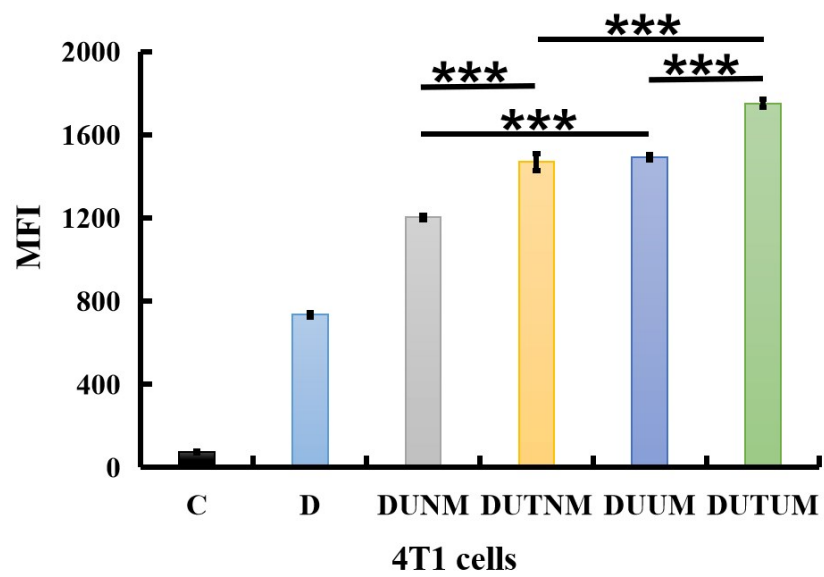


**Fig. S6.** HPLC images of PNBL-NPY before conjugation.

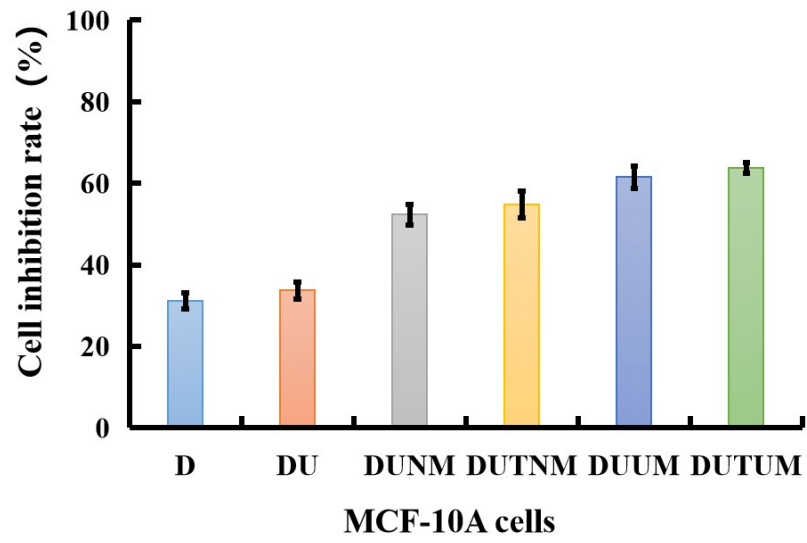


**Fig. S7.** HPLC images of PNBL-NPY after conjugated to MBs or NBs. (a) PNBL-NPY after conjugated to MBs;(b) PNBL-NPY after conjugated to NBs.





**Fig. S8.** The fluorescence intensity of DOX in 4T1 cells. Mean  $\pm$  SD (n = 3), \*\*\*p < 0.001.



**Fig. S9.** Cell inhibition of different bubbles combined with DOX on MCF-10A cells under ultrasound. Mean  $\pm$  SD (n = 4).