## **Suppotring Information**

## Synergistic Combination Chemotherapy of Carrier-free Celastrol and Doxorubicin Nanocrystals for Overcoming

Yating Xiao<sup>1, 2, §</sup>, Jing Liu<sup>1, 3, §</sup>, Mengyu Guo<sup>1</sup>, Huige Zhou<sup>1</sup>, Jun Jin<sup>1</sup>, Jiaming Liu<sup>1</sup>, Ying Liu<sup>1</sup>, Zhanjun Zhang<sup>2, \*</sup>, Chunying Chen<sup>1, 4,\*</sup>.

<sup>1</sup> CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety & CAS Center for Excellent in Nanoscience, National Center for Nanoscience and Technology of China, University of Chinese Academy of Sciences, Beijing 100190, China

<sup>2</sup> School of Chemical Sciences, University of Chinese Academy of Sciences, Beijing 100049, China

<sup>3</sup> The college of Life Sciences, Northwest University, Xi'an 710069, Shaanxi, China

<sup>4</sup> College of Materials Science and Optoelectronic Technology, University of Chinese Academy of Sciences, Beijing 101408, China

§These authors contributed equally.

## **Corresponding Authors**

\*E-mail: zhangzj@ucas.edu.cn

\*E-mail: chenchy@nanoctr.cn (C.C.).



Figure S1. TEM images of (A) free CST and (B) carrier-free CST/DOX NPs nanostructure.

**Table S1.** Size distribution, zeta potential and polydispersity index (PDI) of free CST nanostructure and carrier-free CST/DOX NPs.

	Zeta-average	Zeta-potential	PDI
CST NPs	113.8 nm	-7.6 mV	0.086
CST/DOX NPs	125.7 nm	23.8 mV	0.119



**Figure S2.** Different molar ratios of DOX to CST. (A) TEM images of CST/DOX NPs assembled from different molar ratios of DOX to CST (1:1, 1:2, 1:4 and 1:6). (B) Fluorescence spectra of DOX and CST/DOX NPs in aqueous solution.  $\lambda_{ex}$  (DOX) = 475 nm.



**Figure S3.** FITR spectra of CST, DOX, CST/DOX NPs. (A) FTIR spectra of CST, DOX and CST/DOX NPs. (B) Patrtial FTIR of CST, DOX and CST/DOX NPs in



range of 825 to 2125 cm<sup>-1</sup>

Figure S4. UV spectra of CST, DOX, CST/DOX NPs



Figure S5. Stability of CST/DOX NPs in water containing 1%, 5% and 10% FBS respectively.



Figure S6. The level of ROS in MCF-7 and MCF-7/ADR cells measured by flow



**Figure S7.** Confocal images of MCF-7/ADR cells after incubation with free DOX and CST/DOX NPs. BF, bright field images.



Figure S8. The level of P-gp expression in MCF-7 and MCF-7/ADR cells.