

# Supporting Information

## **Bioactive phospho-therapy with black phosphorus for *in vivo* tumor suppression**

Shengyong Geng<sup>1,2</sup>, Ting Pan<sup>1</sup>, Wenhua Zhou<sup>1</sup>, Haodong Cui<sup>1</sup>, Lie Wu<sup>1</sup>, Zhibin Li<sup>1</sup>,  
Paul K. Chu<sup>3</sup>, and Xue-Feng Yu<sup>1,4\*</sup>

<sup>1</sup> Materials and Interfaces Center, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

<sup>2</sup> Medical Oncology, Shenzhen People's Hospital, the Second Clinical Medical College of Jinan University, Shenzhen 518055, China

<sup>3</sup> Department of Physics, Department of Materials Science and Engineering, and Department of Biomedical Engineering, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, China

<sup>4</sup> Institute of Environment and Health, Jiangnan University, Wuhan 430056, China

\* Corresponding author: Xue-Feng Yu

Tel: +86-13971313505

Email: [xf.yu@siat.ac.cn](mailto:xf.yu@siat.ac.cn)

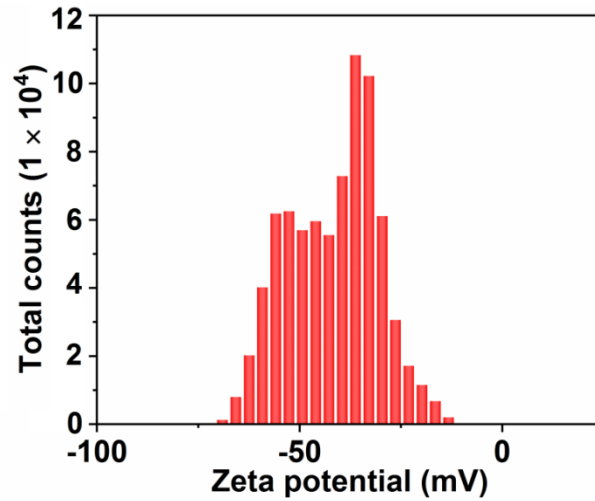


Figure S1. Zeta potentials of BPs.

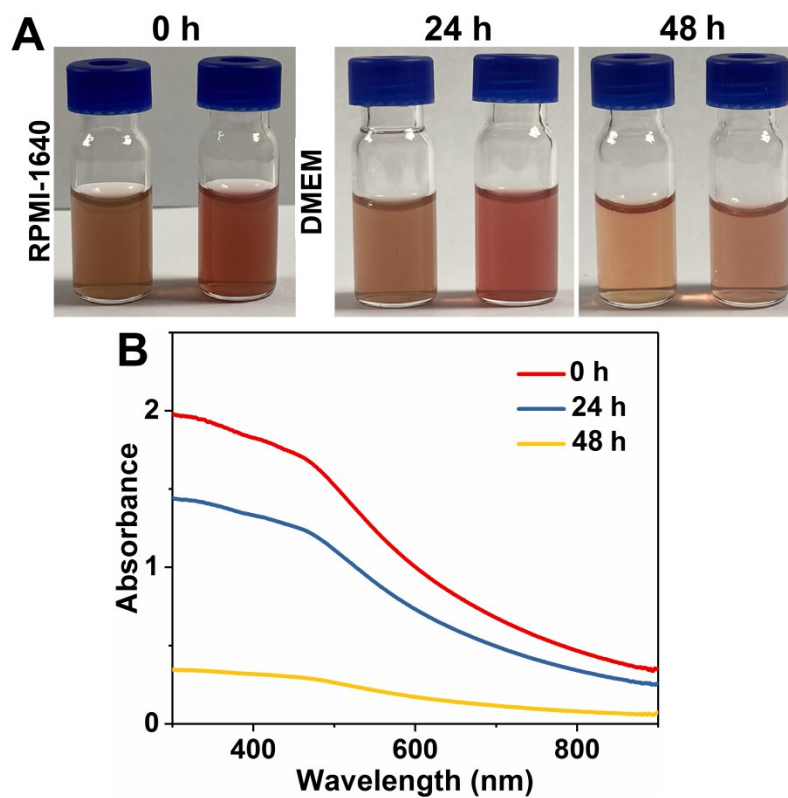
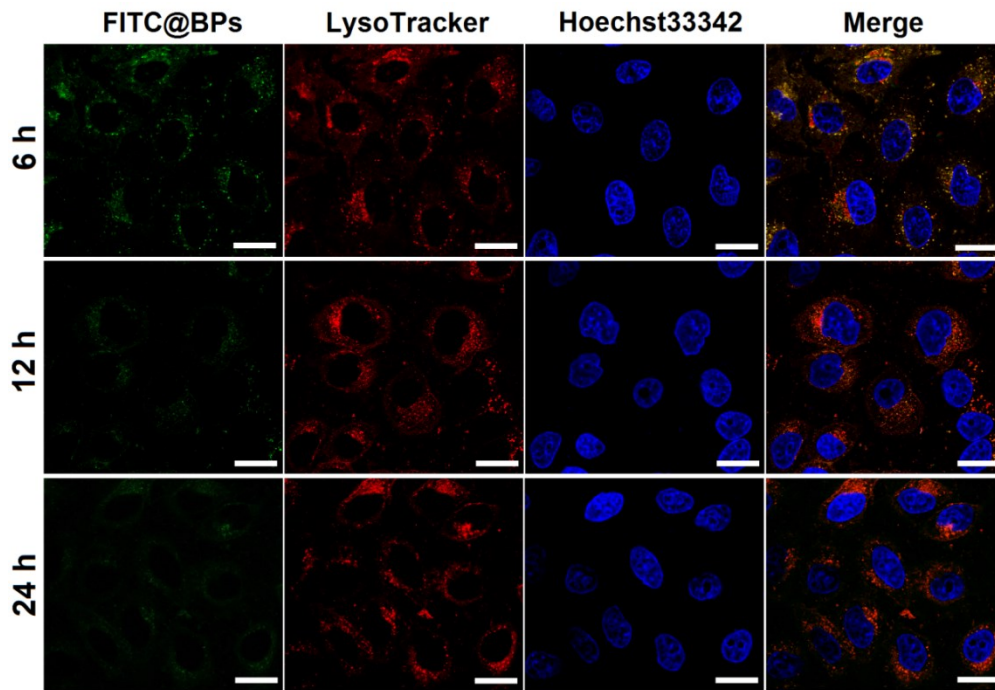
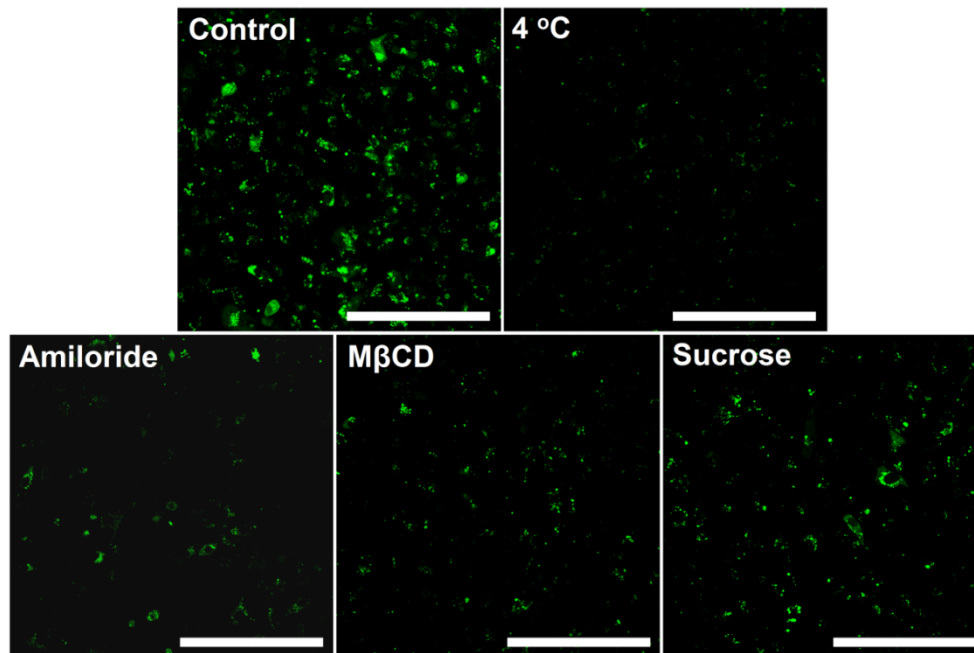


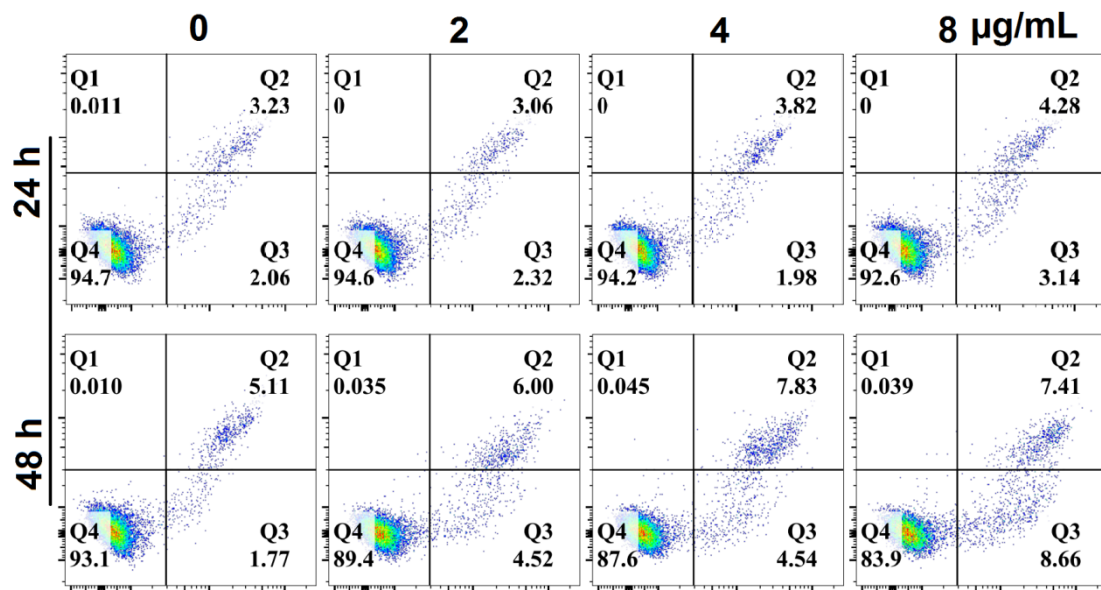
Figure S2. Stability evaluation of BPs: (A) Photographs and (B) Absorption spectra of the cell culture medium (RPMI-1640 and DMEM) containing 10% serum and 20  $\mu\text{g/mL}$  of BPs.



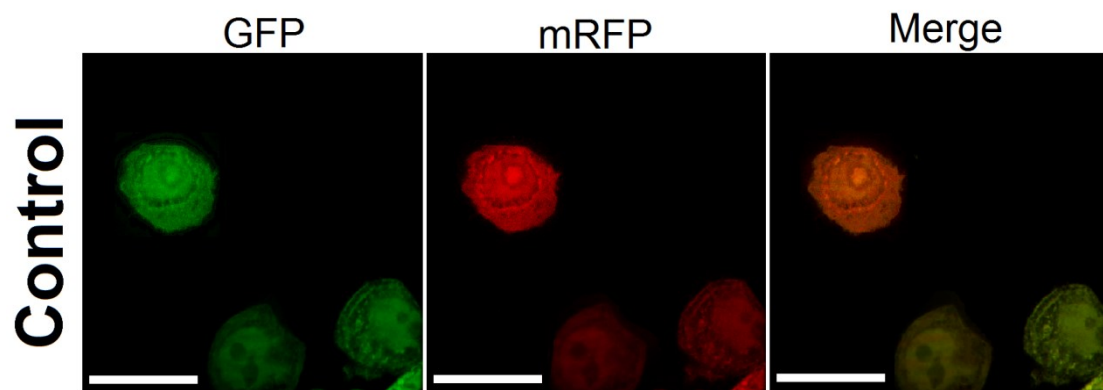
**Figure S3.** Confocal fluorescence images of QSG-7701 cells treated with BPs (4  $\mu\text{g}/\text{mL}$ ) for different time intervals. The green and red fluorescence images show FITC and LysoTracker Red DND-99, respectively. The scale bar is 20  $\mu\text{m}$ .



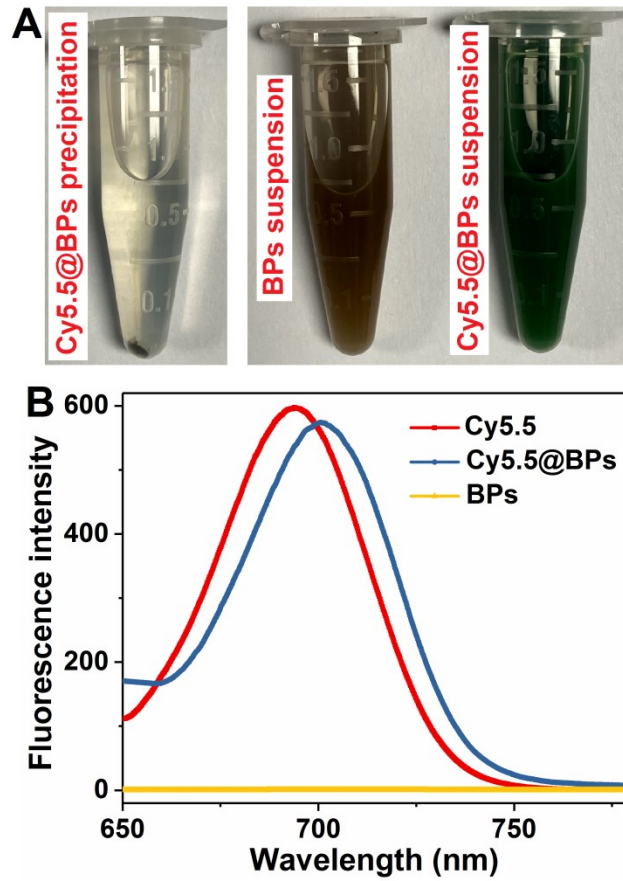
**Figure S4.** Confocal fluorescence images of HepG2 cells after treatment at low temperature (4 °C) with different endocytosis inhibitors. The scale bar is 100  $\mu\text{m}$ .



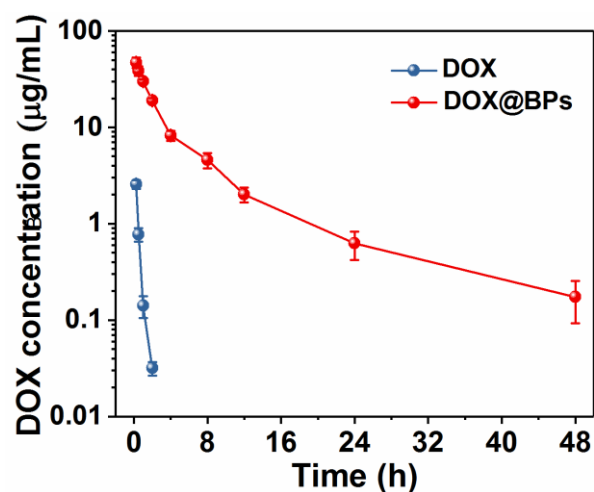
**Figure S5.** Apoptosis assay of QSG-7701 cells by Annexin V/PI staining after treatment with different concentrations of BPs for 24 or 48 h.



**Figure S6.** Confocal fluorescent images of mRFP-GFP-LC3-transfected HepG2 cells without treatment with BPs for 48 h (Scale bar = 20 µm).



**Figure S7.** Characterization of Cy5.5-labeled BPs: (A) Photographs of the BPs and Cy5.5-labeled BPs; (B) Fluorescence spectra of Cy5.5 and Cy5.5-labeled BPs (Excitation wavelength = 675 nm). No fluorescence can be observed from the BPs without Cy5.5 labeling.

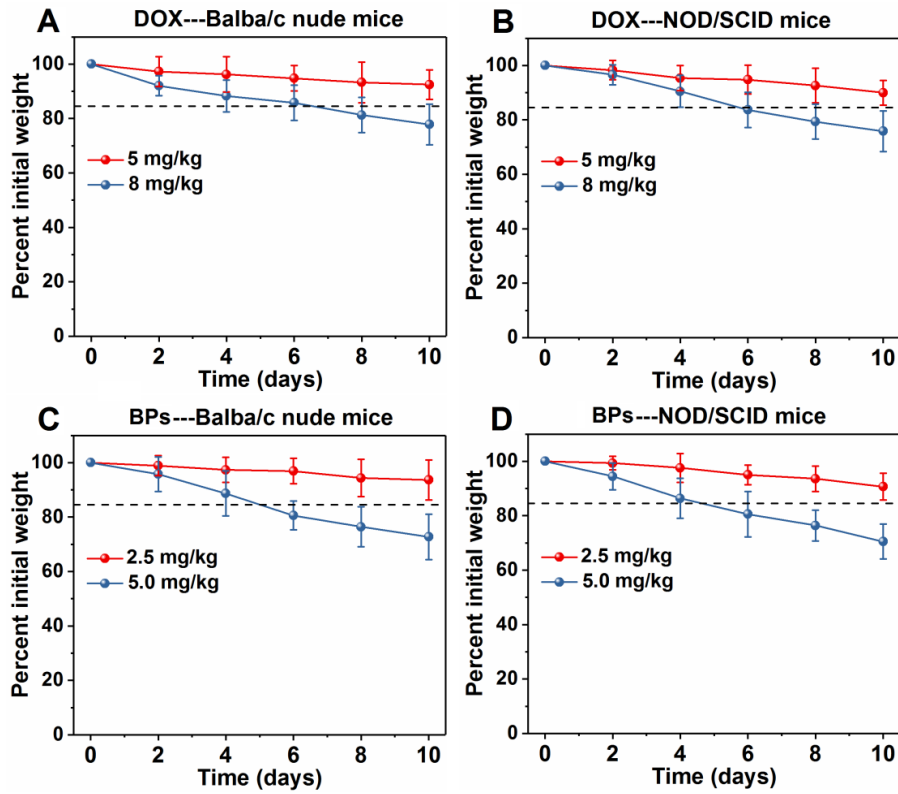


**Figure S8.** Plasma concentration of DOX after a single intravenous injection of free DOX and DOX-labeled BPs (5 mg/kg, n = 3).

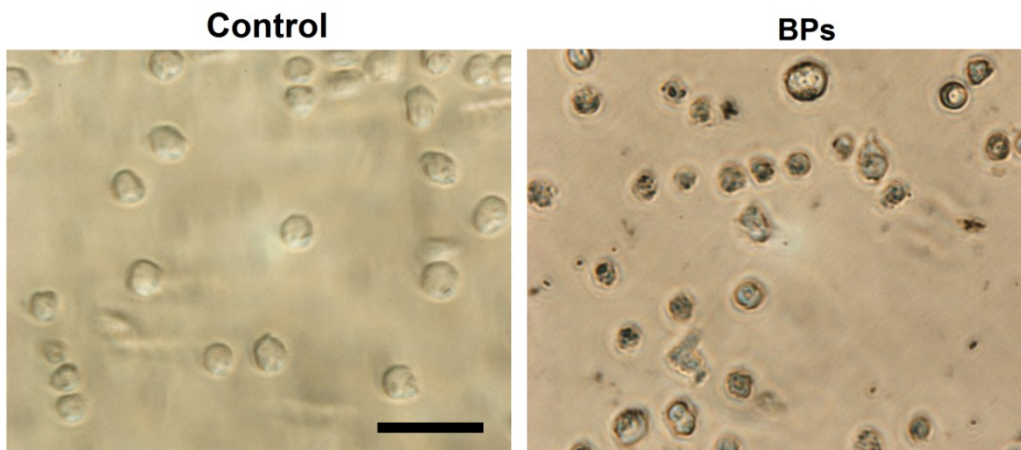
**Table S1.** Pharmacokinetic parameters of free DOX and DOX-labeled BPs (n = 3).

Parameters	$AUC_{0-t}$ (h·µg/mL)	$C_{max}$ (µg/mL)	$Lz$ (1/h)	$MRT_{0-t}$ (h)	$CL$ (mL/h)
Free DOX	0.64 ± 0.1	2.57 ± 0.54	1.82 ± 0.23	0.60 ± 0.08	1856.6 ± 89.5
DOX@BPs	204.6 ± 15.4	47.11 ± 5.63	0.18 ± 0.04	4.36 ± 0.49	5.34 ± 0.97

$AUC_{0-t}$ , total area under the blood concentration versus time curve;  $C_{max}$ , maximum plasma concentration;  $Lz$ , elimination rate constant;  $MRT_{0-t}$ , mean residence time;  $CL$ , total body clearance.



**Figure S9.** Average mouse weights versus time. The data are presented as the percentage of the initial weights for Balb/c nude mice and NOD/SCID mice treated with DOX (A, B) or BPs (C, D) and  $n = 3$  for each treatment group.



**Figure S10.** Optical microscopy images of HL-60 cells without/with incubation with BPs (32  $\mu\text{g}/\text{mL}$ ) for 24 h (Scale bar = 50  $\mu\text{m}$ ).