

## Supplementary Material

# New Strategy for Precise Cancer Therapy: Tumor-Specific Delivery of Mitochondria-Targeting Photodynamic Therapy Agent and in situ O<sub>2</sub>-Generation in Hypoxic Tumor

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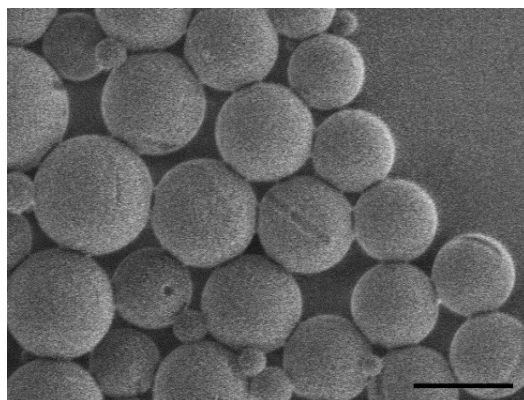
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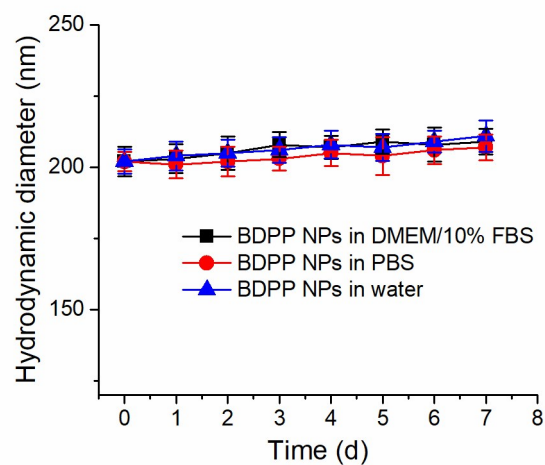
### Supplementary figures

1. **Fig. S1.** SEM micrographs of BDPP NPs. Scale bar: 200 nm.
2. **Fig. S2.** Long-term-stability study of BDPP NPs in DMEM with 10% FBS, PBS or water.
3. **Fig. S3.** Dissolved oxygen changes after the addition of 100  $\mu\text{M}$  H<sub>2</sub>O<sub>2</sub> and 50  $\mu\text{g mL}^{-1}$  BDPP NPs, or 100  $\mu\text{M}$  H<sub>2</sub>O<sub>2</sub> and 50  $\mu\text{g mL}^{-1}$  BDPP NPs (without catalase) into deoxygenated water.
4. **Fig. S4.** Colocalization images of BDPP NPs in U87-MG cells. Cells were incubated with 50  $\mu\text{g mL}^{-1}$  BDPP NPs for 4 h and then incubated with 100 nM LysoTracker Deep Red, MitoTracker Deep Red, ER Tracker Red or Hoechst 33342 for 10 min. Scale bars: 20  $\mu\text{m}$ .
5. **Fig. S5.** Plots of change in fluorescent intensity of 1  $\mu\text{M}$  SOSG ( $\lambda_{\text{ex}} = 488 \text{ nm}$ ,  $\lambda_{\text{em}} = 525 \text{ nm}$ ) vs incubation time measured from BDPP NPs in the presence or absence of 100  $\mu\text{M}$  H<sub>2</sub>O<sub>2</sub>, and the BDPP NPs (without catalase) in the presence of H<sub>2</sub>O<sub>2</sub>. The fluorescent intensity of SOSG was measured after 525-nm irradiation at a power of 100  $\text{mW cm}^{-2}$  for 5 min.
6. **Fig. S6.** Confocal fluorescence images of U87-MG cells with different treatments after 525 nm irradiation: (b) SOSG only; BDPP NPs + SOSG; NAC + BDPP NPs + SOSG; BDPP NPs (without catalase) + SOSG. Scale bar = 20  $\mu\text{m}$ .
7. **Fig. S7.** Confocal fluorescence images showing increased intracellular O<sub>2</sub> level after treated with BDPP NPs. U87-MG cells incubated with 5  $\mu\text{M}$  [Ru(dpp)<sub>3</sub>]Cl<sub>2</sub> for 4 h, followed by incubation with the BDPP NPs for 0 h, 8 h, 16 h and 24 h, respectively. Scale bars: 20  $\mu\text{m}$ .

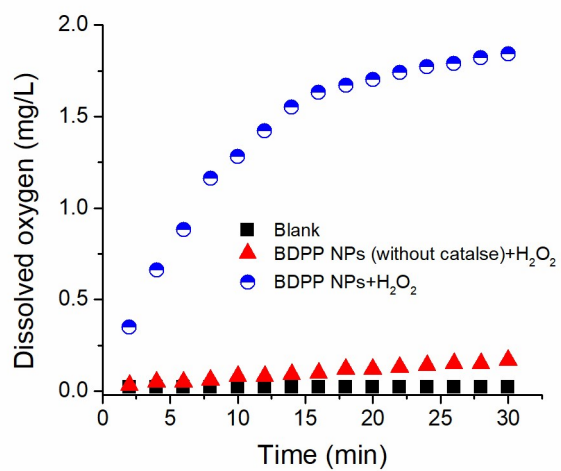
8. **Fig. S8.** Immuno fluorescence staining with HIF-1 $\alpha$  antibodies and corresponding HIF-1 $\alpha$  staining of tumor slides from tumor-bearing mice treated with BDPP NPs or BDPP NPs (without catalase) at a dose of 10 mg kg<sup>-1</sup>.
9. **Fig. S9.** Colocalization images of BDPP in U87-MG cells. Cells were incubated with 50  $\mu$ g mL<sup>-1</sup> BDPP NPs for 4 h and then incubated with 100 nM LysoTracker Blue, MitoTracker Blue, or Hoechst 33342 for 10 min. Scale bars: 20  $\mu$ m.
10. **Fig. S10.** Time-dependent in vivo fluorescence images of subcutaneous U87-MG tumor-bearing mice after i.v. injection of 10 mg kg<sup>-1</sup> BDPP NPs, BDPP NPs (without cRGD), or BDPP NPs with pre-injection of free cRGD. The fluorescence images were acquired using an IVIS Spectrum instrument equipped with 675/30 nm excitation and 720/20 nm emission filters.
11. **Fig. S11.** Representative images of tumour-bearing mice and excised tumor after different treatment at day 13. (a) Saline; (b) BDPP NPs; (c) Laser; (d) BDPP NPs (without catalase)+laser; (e) Free BDPP+laser; (f) BDPP NPs+laser.
12. **Fig. S12.** H&E stained images of tissue sections from different organs of mice after BDPP NPs treatment and the age-matched healthy mice without treatment (control). Scale bars: 100  $\mu$ m.



**Fig. S1.** SEM micrographs of BDPP NPs. Scale bar: 200 nm.

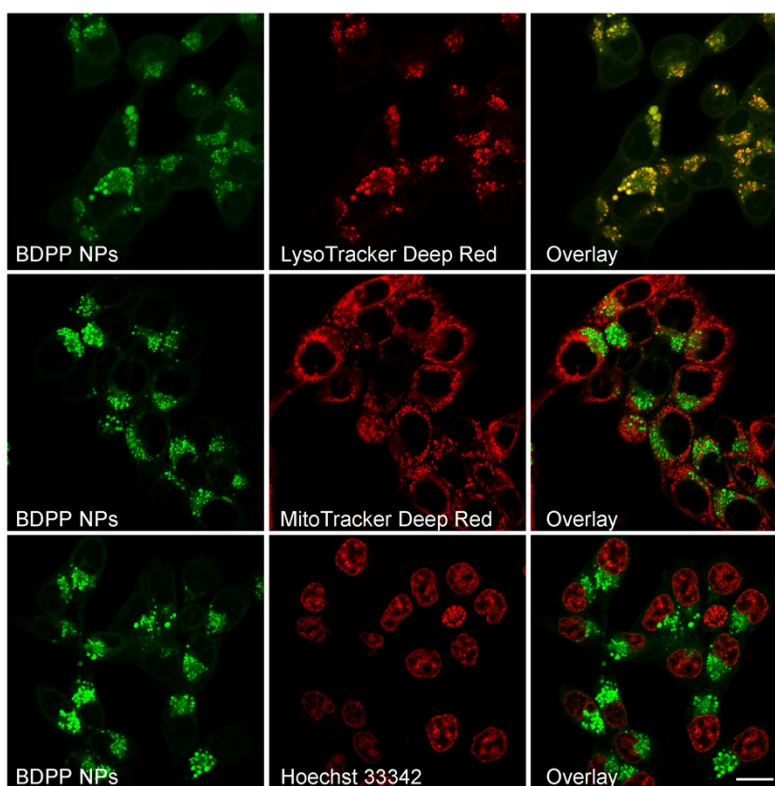


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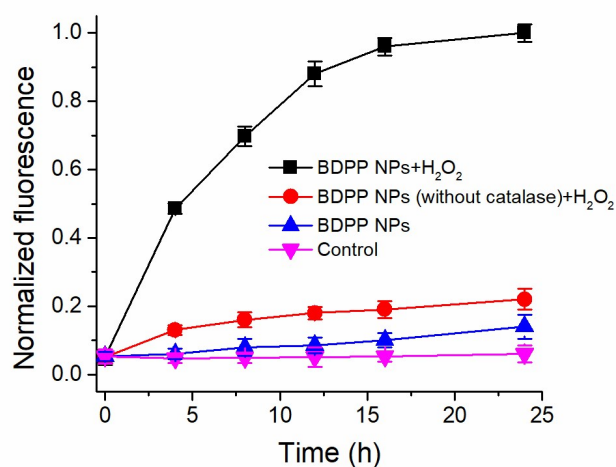


**Fig. S3.** Dissolved oxygen changes after the addition of 100  $\mu\text{M}$  H<sub>2</sub>O<sub>2</sub> and 50  $\mu\text{g mL}^{-1}$  BDPP

NPs, or 100  $\mu\text{M}$   $\text{H}_2\text{O}_2$  and 50  $\mu\text{g mL}^{-1}$  BDPP NPs (without catalase) into deoxygenated water.

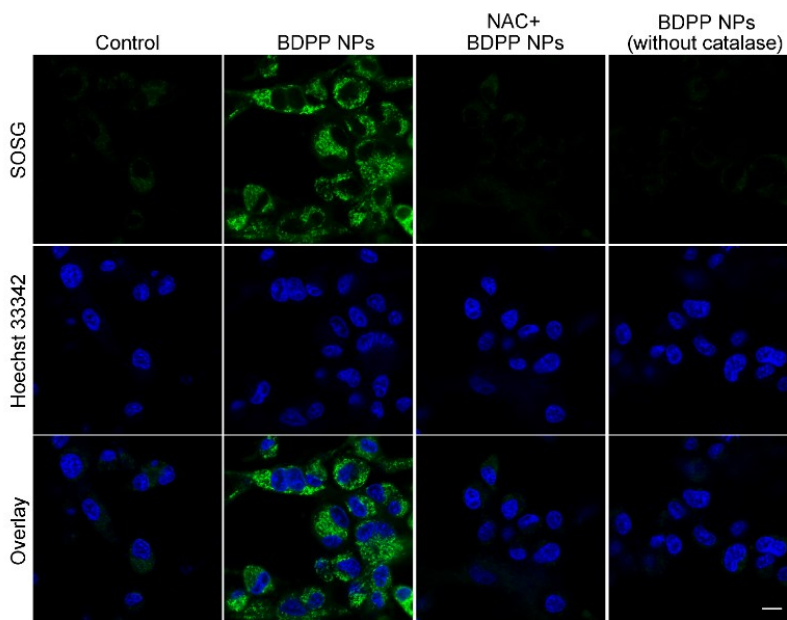


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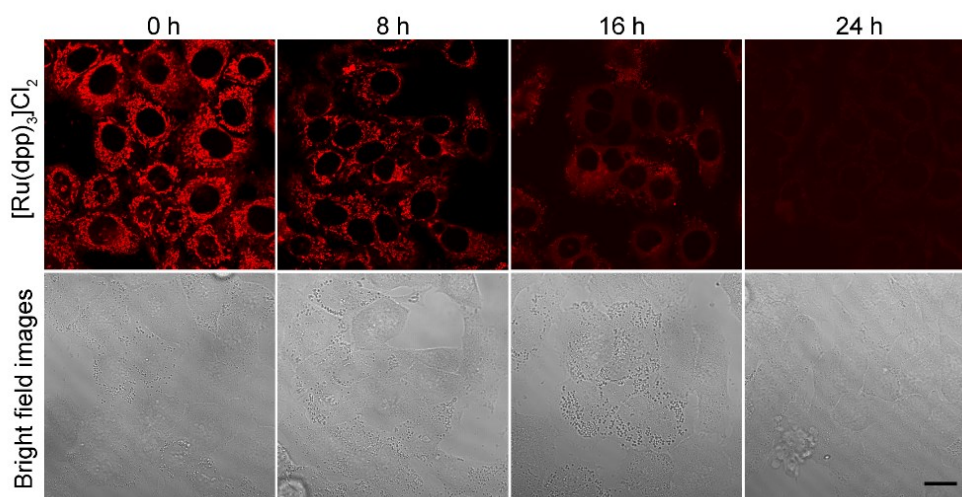


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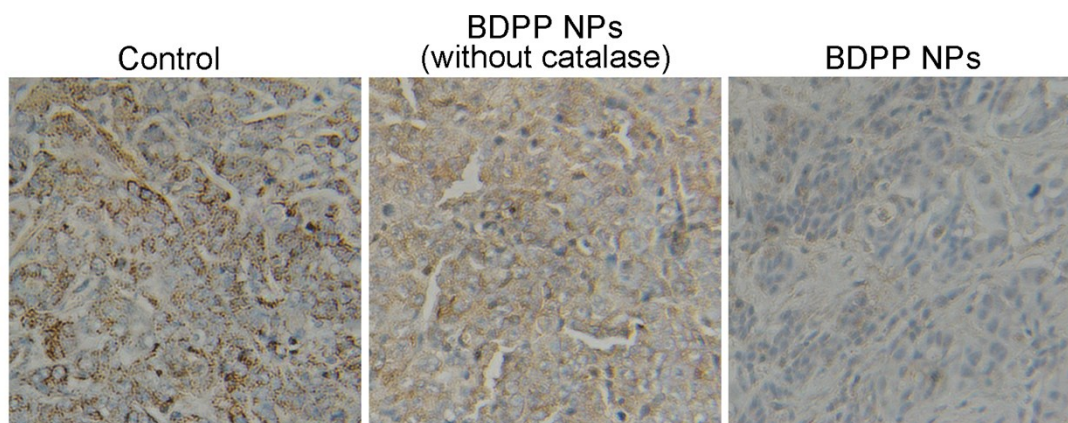


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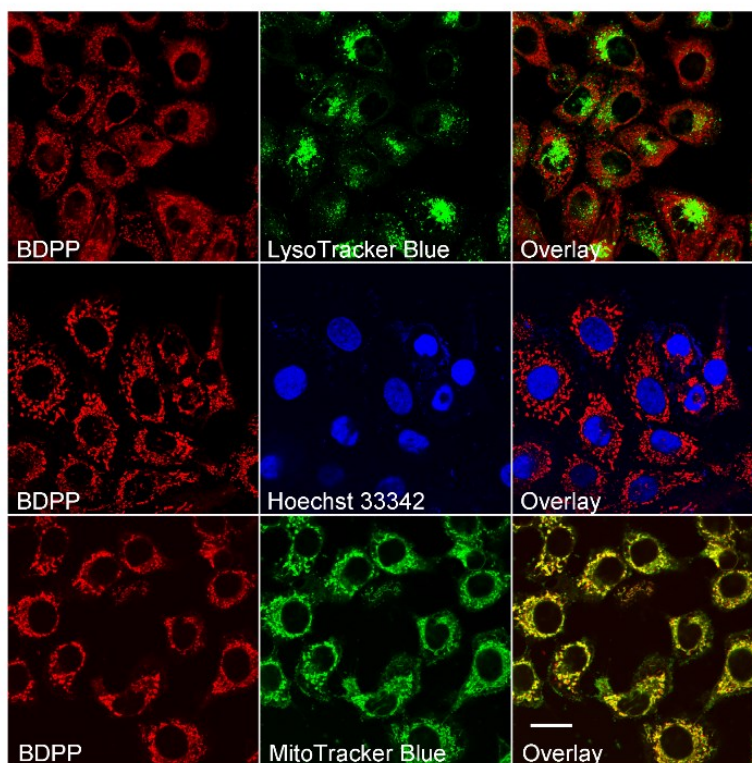


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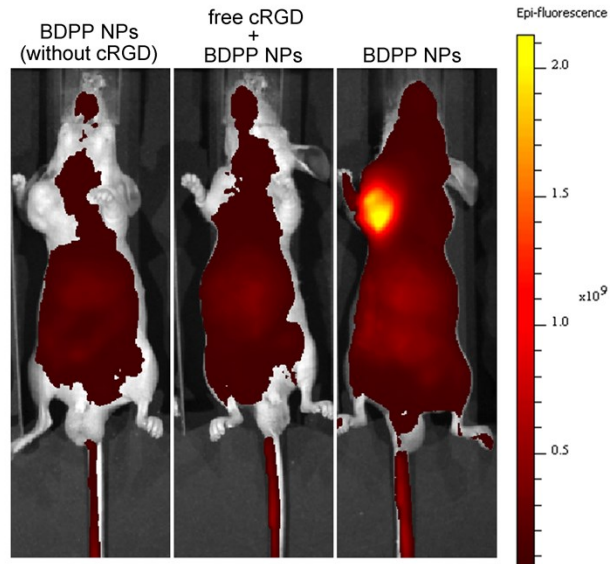
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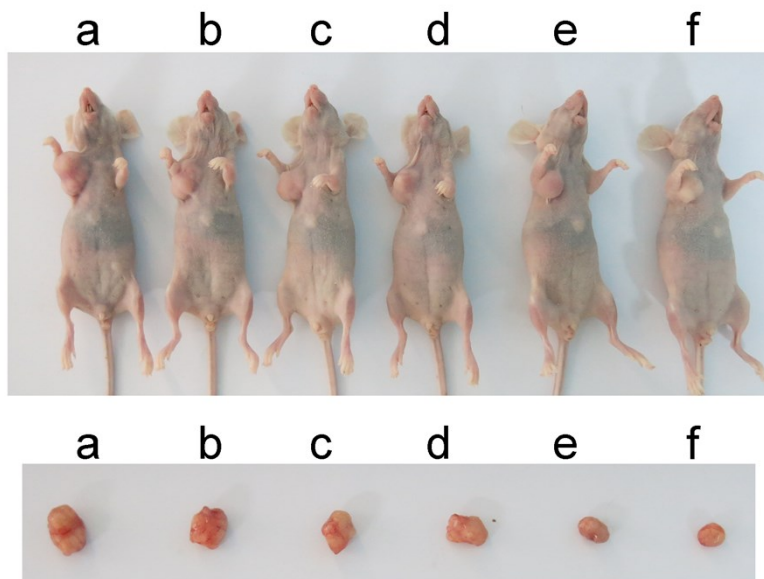
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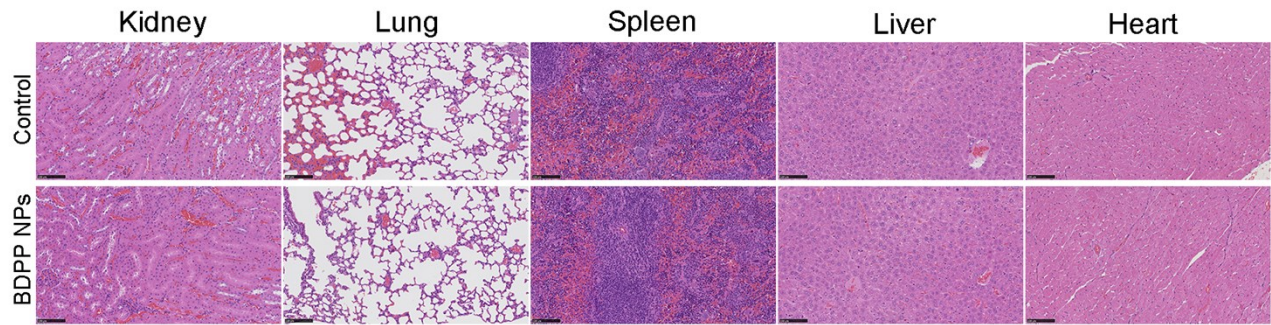
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