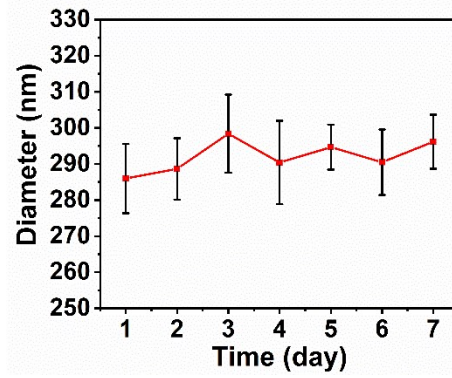


**Supporting Information**

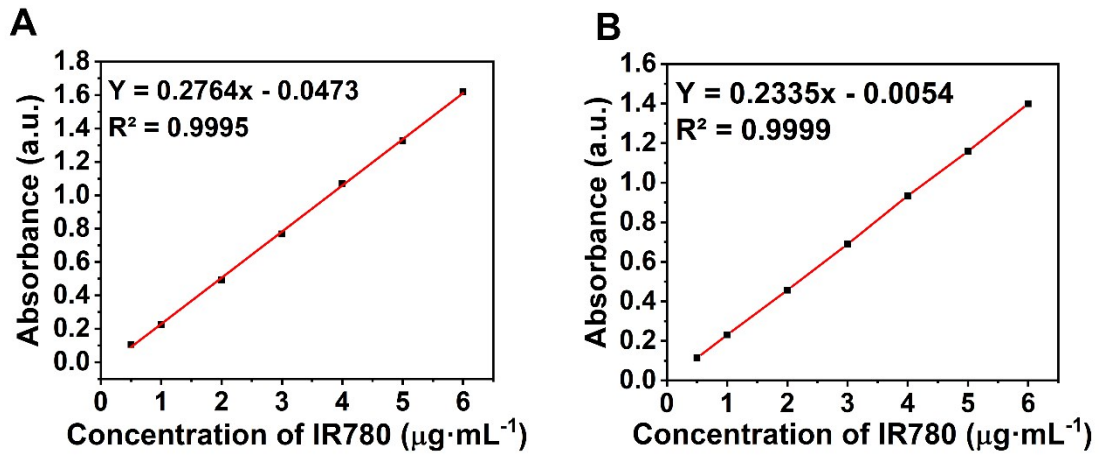
**Mitochondria-Targeted Anticancer Nanoplatfom with Deep  
Penetration for Enhanced Synergistic Sonodynamic and Starvation  
Therapy**

Ruo Zhang<sup>a</sup>, Liang Zhang<sup>a</sup>, Haitao Ran<sup>a</sup>, Pan Li<sup>a</sup>, Ju Huang<sup>a</sup>, Mixiao Tan<sup>a</sup>, Yang Yang<sup>\*a</sup>, Zhigang Wang <sup>\*a</sup>

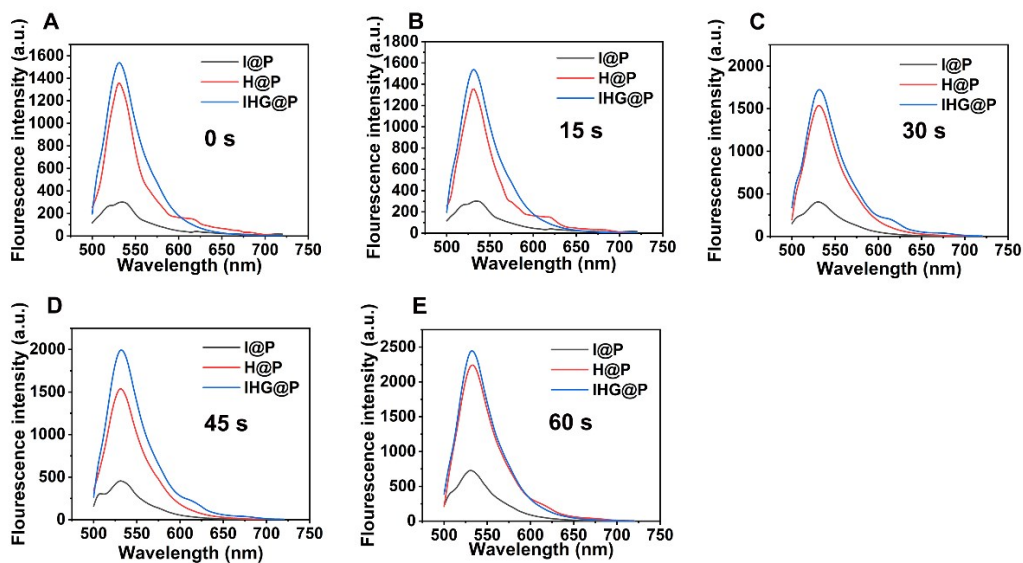
<sup>a</sup> Chongqing Key Laboratory of Ultrasound Molecular Imaging, Institute of Ultrasound Imaging, The Second Affiliated Hospital, Chongqing Medical University, Chongqing 400010, P.R. China.



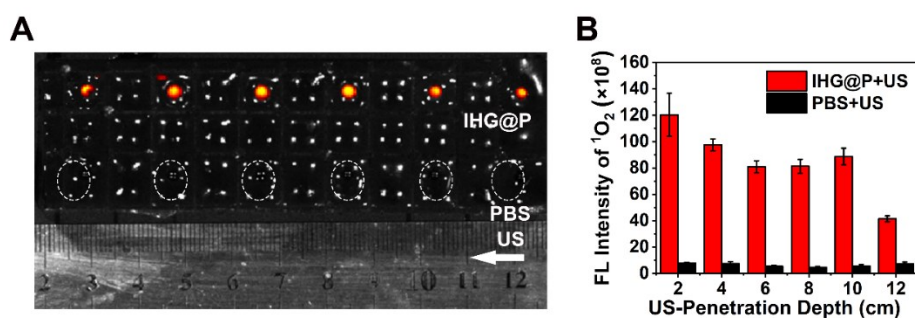
**Figure S1.** The size changes of IHG@P NPs in fetal blood serum within seven days.



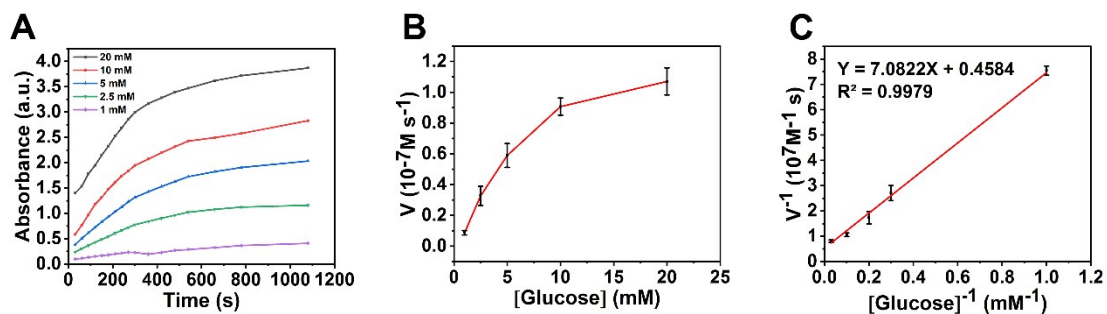
**Figure S2.** The relative absorbance of (A) IR780 and (B)HMME.



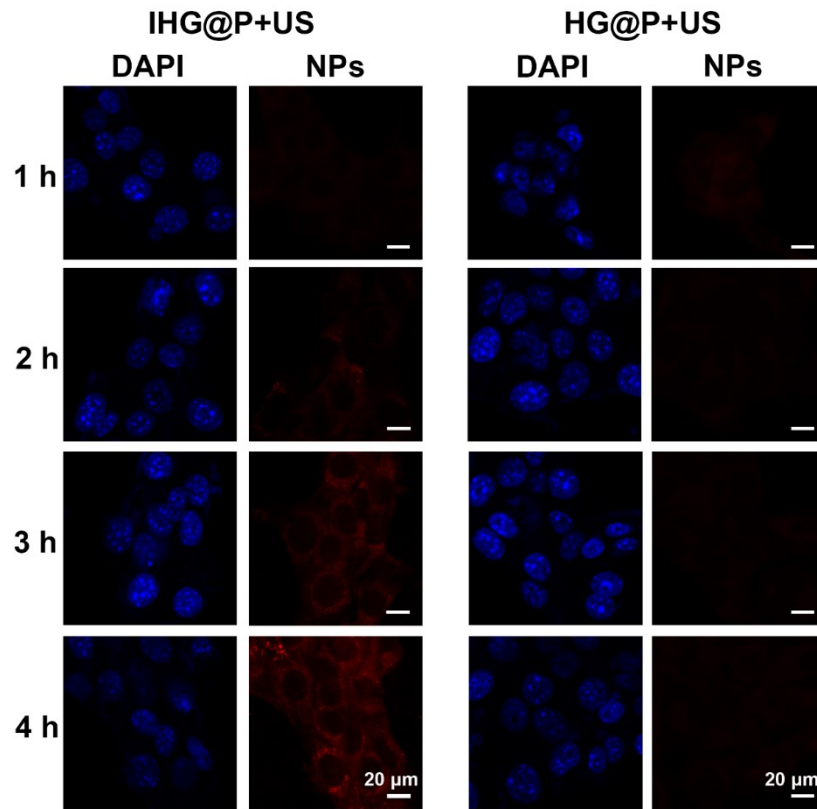
**Figure S3.** ROS generation of I@P NPs, H@P NPs and IHG@P NPs as irradiated for different time duration (A: 0 s, B: 15 s, C: 30 s, D: 45 s, and E: 60 s). The concentration of NPs is  $50 \mu\text{g}\cdot\text{mL}^{-1}$ .



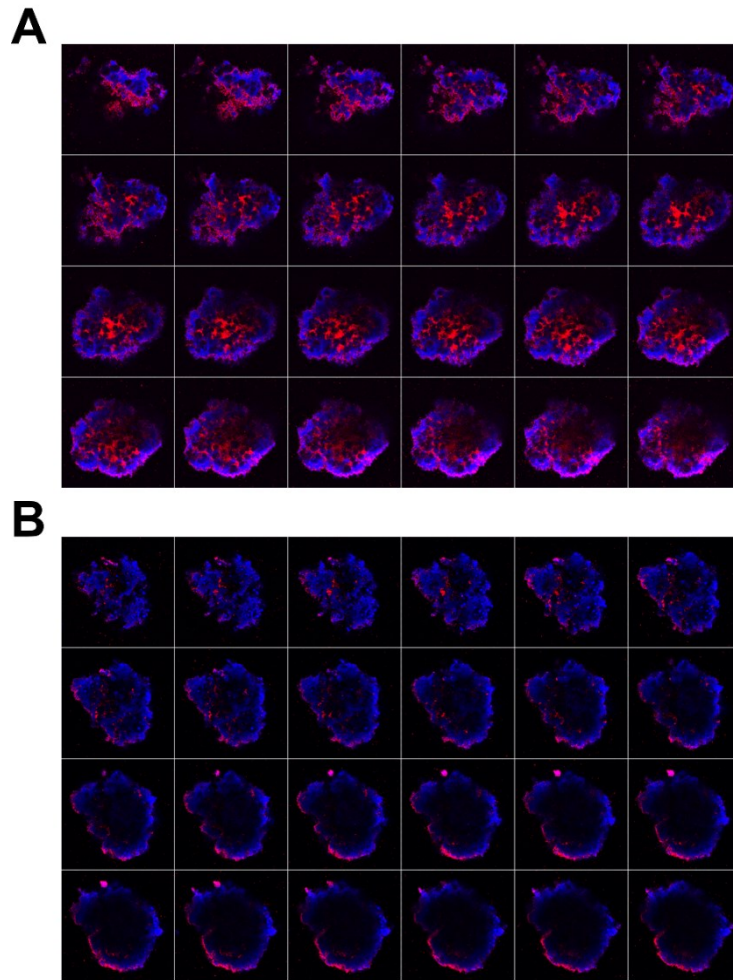
**Figure S4.** The FL image of IHG@P NPs and PBS suspension containing SOSG in different depth upon US irradiation.



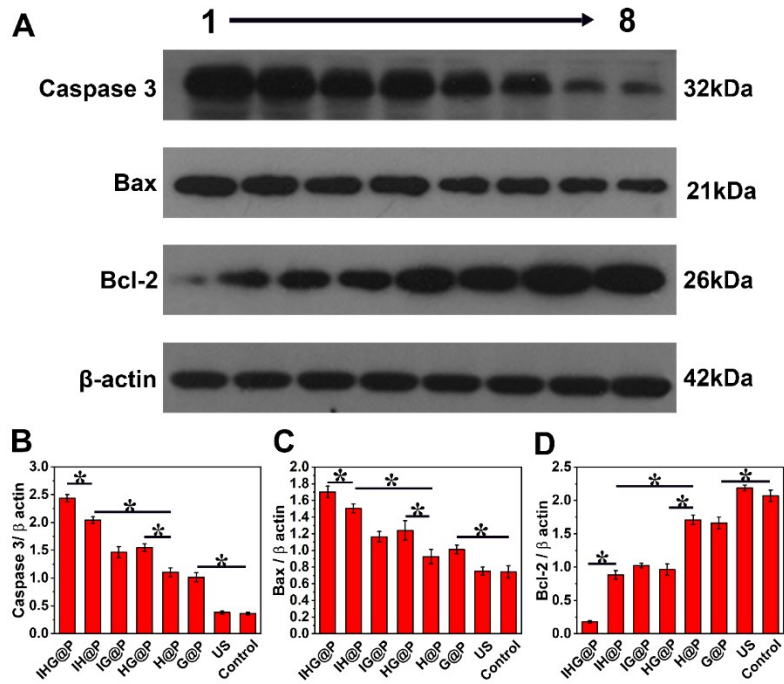
**Figure S5.** (A) Time-dependent absorbance of IHG@P NPs with addition of different concentrations of glucose (1mM, 2.5mM, 5mM, 10mM, 20mM). (B) Michaelis-Menten equation and (C) Lineweaver-Burk fitting of IHG@P NPs.



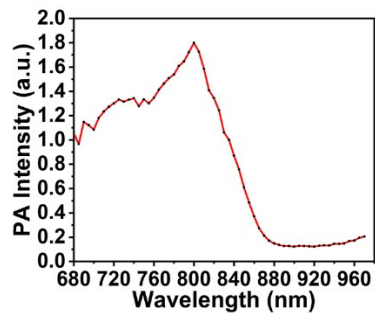
**Figure S6.** CLSM images of cellular uptake of IHG@P and HG@P NPs (scar bar = 20 $\mu$ m).



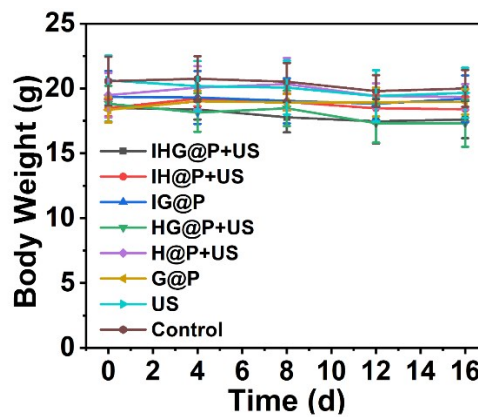
**Figure S7.** Tomography images of 3D spheroid models co-incubated with (A) IHG@P and (B) HG@P NPs.



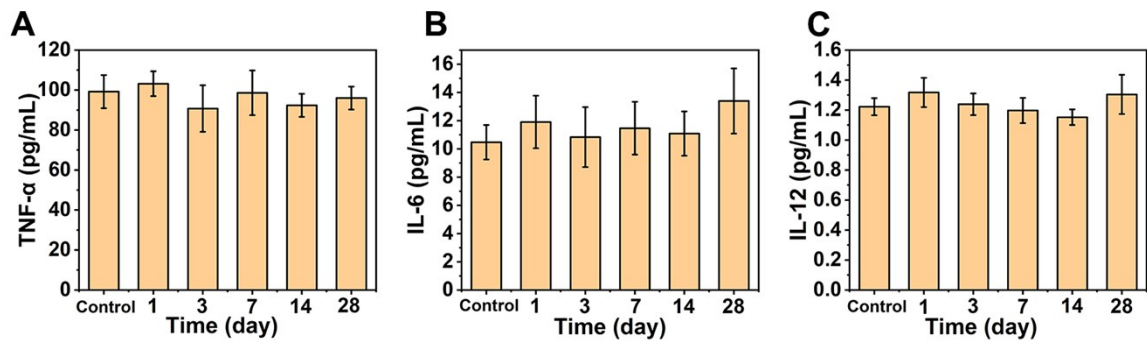
**Figure S8.** The expression levels of Caspase-3, Bax, and Bcl-2 determined by Western blot in 4T1 cells ( $\beta$ -actin is the loading control). From 1 to 8 was IHG@P+US, IH@P+US, IG@P, HG@P+US, H@P+US, G@P, US only, Control group, respectively.



**Figure S9.** Full PA spectrum of IHG@P NPs (from 680nm-970nm).



**Figure S10.** The changes of body weight of mice during therapeutic process (n = 5) (\*P<0.05).



**Figure S11.** Biosafety assay of IHG@P NPs. Assay of pro-inflammation cytokines (A) TNF- $\alpha$  (B) IL-6 and (C) IL-12 after intravenous injection of IHG@P NPs (n = 5).