

## Supporting Information

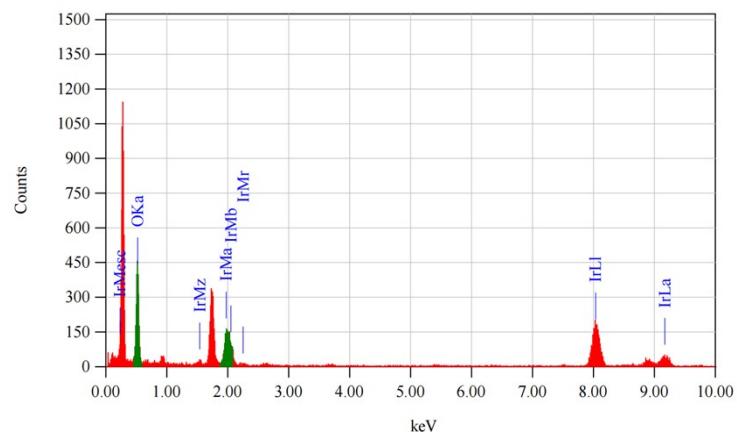
# A Multifunctional Nanocatalytic Ferroptosis Amplifier Based on Glutathione Scavenging and Lipid Peroxidation Amplification for Cancer Therapy

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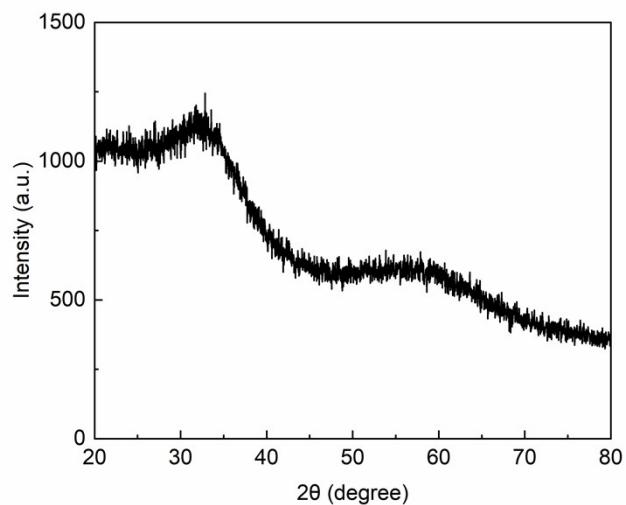
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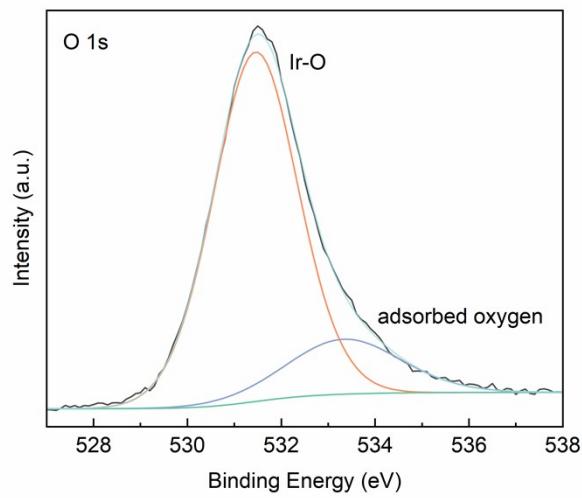
‡ The authors contribute equally to this article.



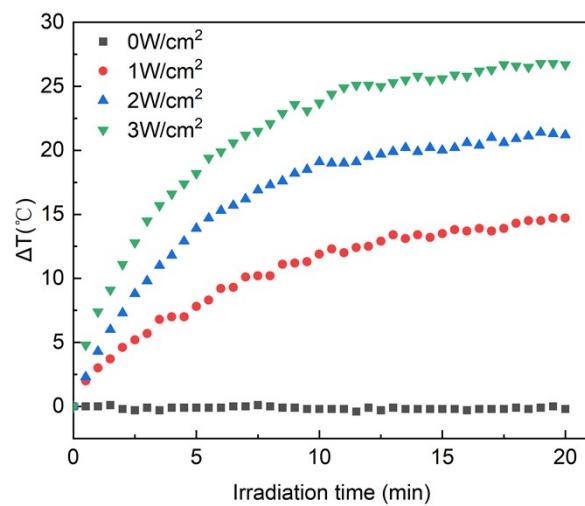
**Fig. S1** EDS of  $\text{IrO}_x$  nanoparticles.



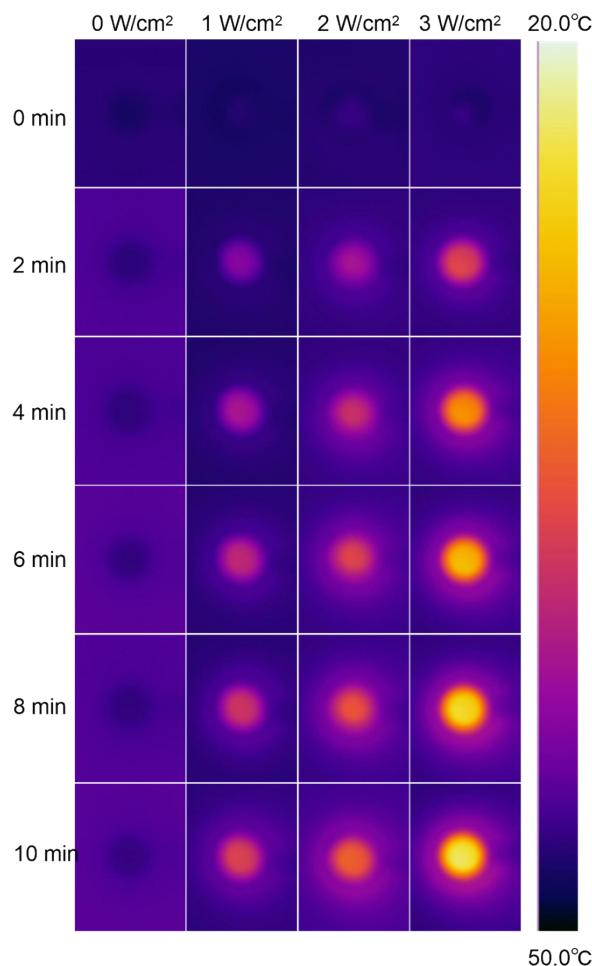
**Fig. S2** XRD spectrum of  $\text{IrO}_x$  nanoparticles.



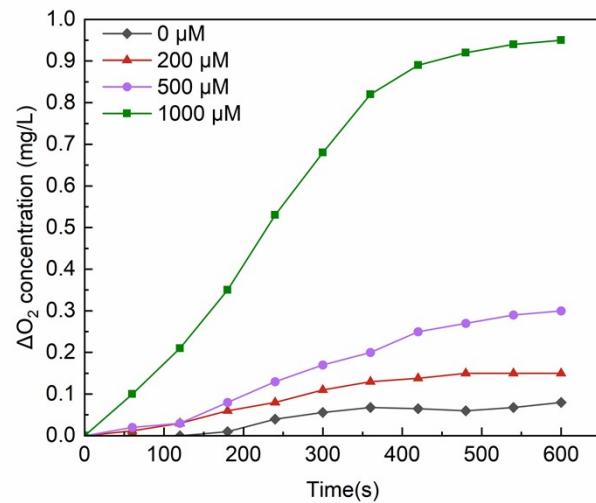
**Fig. S3** O 1s XPS spectrum of the  $\text{IrO}_x$  nanoparticles.



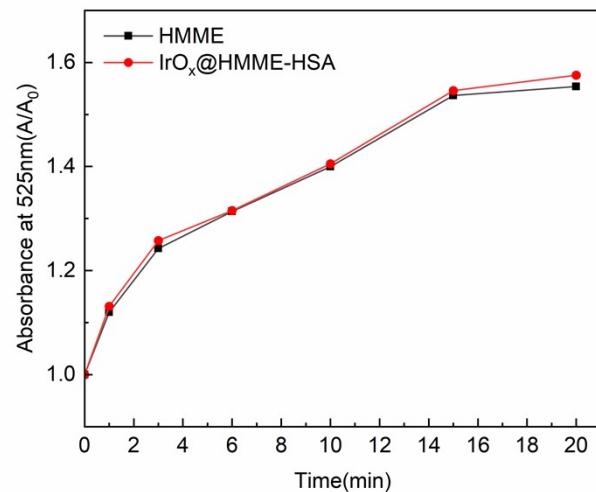
**Fig. S4** The curve shows the temperature change of  $\text{IrO}_x@\text{HMME-HSA}$  aqueous solutions with a concentration of  $100\mu\text{g}/\text{mL}$  over 20 min irradiation of different power densities (0, 1, 2, and 3  $\text{W}/\text{cm}^2$ ).



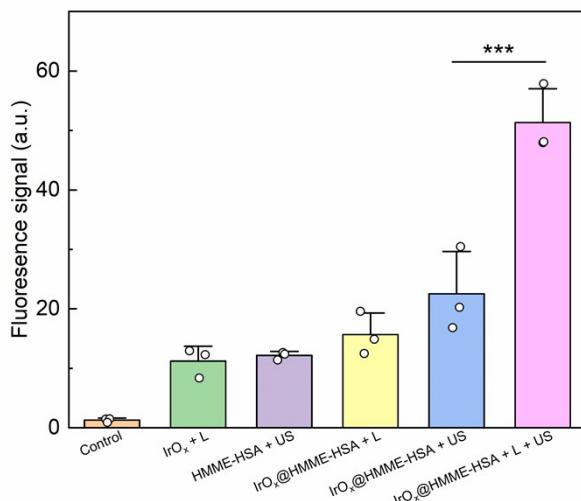
**Fig. S5** Thermal image of the  $\text{IrO}_x@\text{HMME-HSA}$  aqueous solution under laser irradiation of different power densities (0, 1, 2, and 3  $\text{W}/\text{cm}^2$ ).



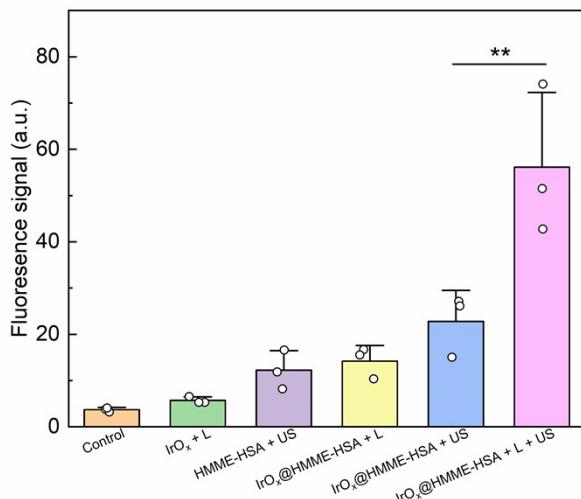
**Fig. S6** The curves show the  $\text{O}_2$  production of  $\text{IrO}_x@\text{HMME-HSA}$  solutions at different concentrations of  $\text{H}_2\text{O}_2$  (0, 200, 500, 1000  $\mu\text{M}$ ).



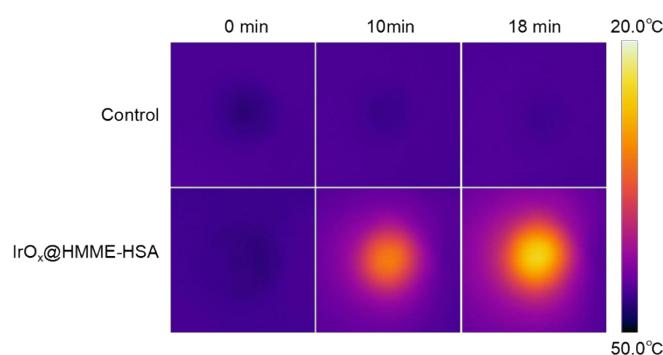
**Fig. S7** Time-dependent generation of singlet oxygen ( ${}^1\text{O}_2$ ) detected using SOSG as a probe. The fluorescence intensity of the reaction product at 525 nm ( $\text{A}/\text{A}_0$ ) was monitored over time for HMME and  $\text{IrO}_x@\text{HMME-HSA}$ .



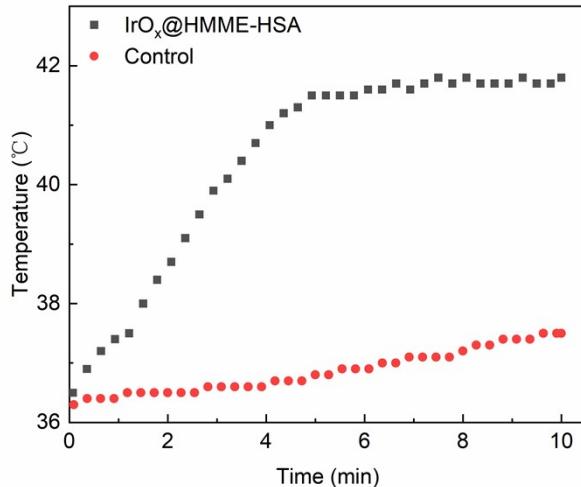
**Fig. S8** Semi-quantitative analysis of ROS-related fluorescence intensity in Fig. S3C by Image J software. Data are presented as the mean  $\pm$  SD ( $n = 3$ ). Significant differences were assessed using t test ( $***p < 0.001$ ).



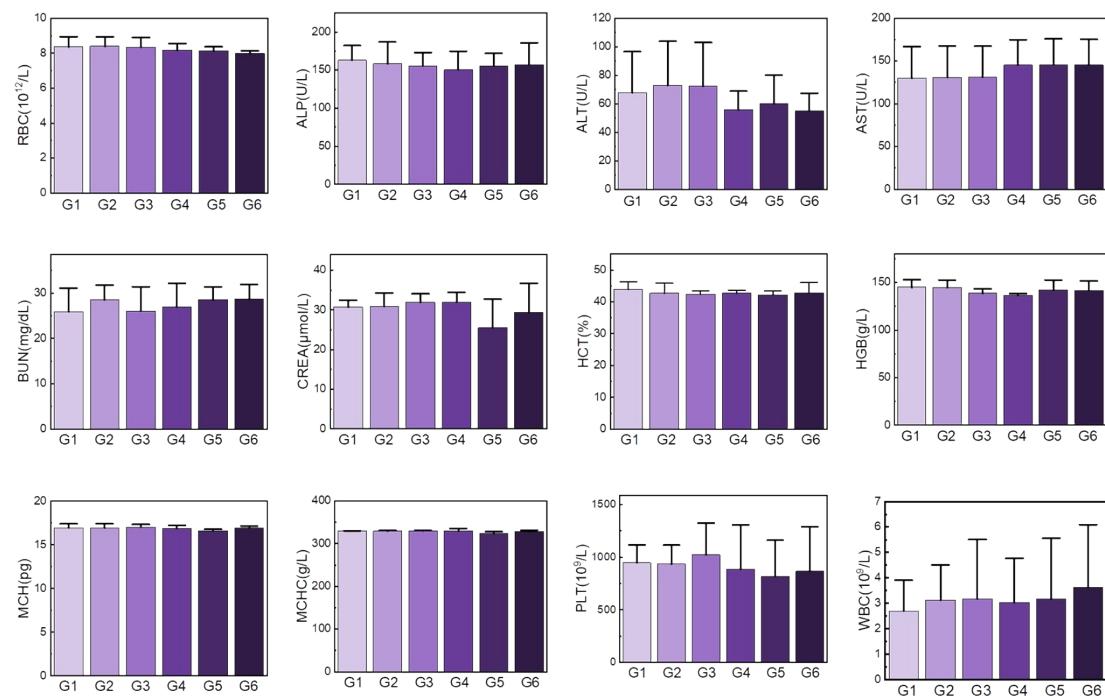
**Fig. S9** Semi-quantitative analysis of LPO fluorescence intensity. Data are represented as mean  $\pm$  SD ( $n = 3$ ; \*\* $p < 0.01$  ).



**Fig. S10** Time-course thermal images of the change in solution temperature culture dishes containing PC-3 cells subjected to laser irradiation.

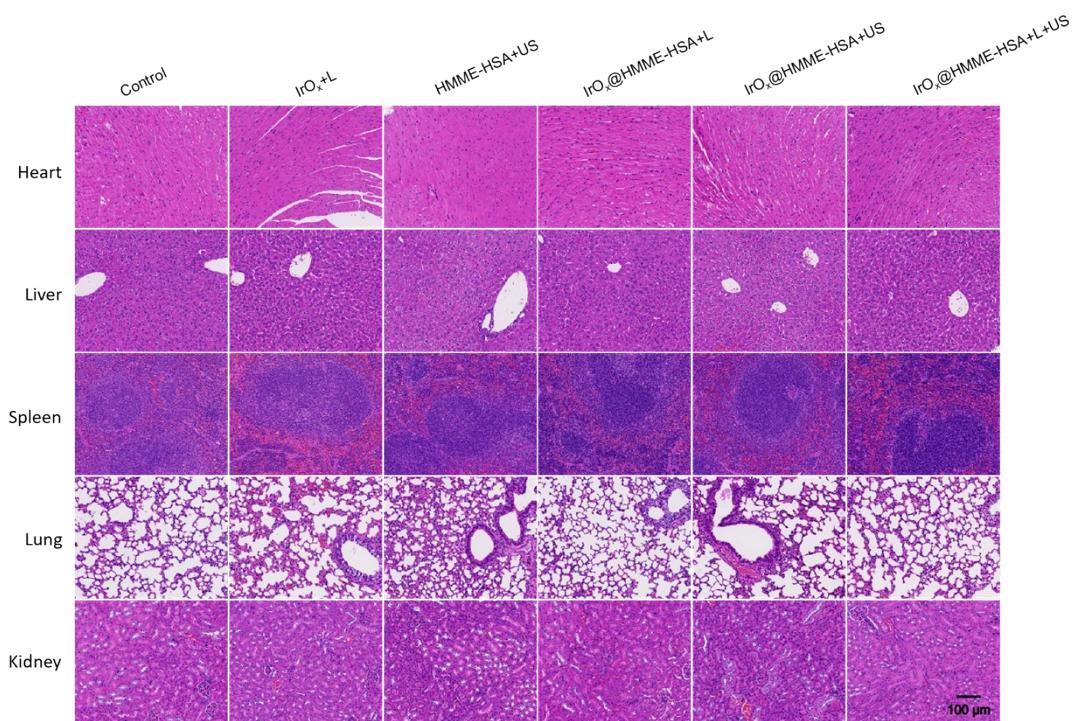


**Fig. S11** Curves shows the temperature change in the body surface of the nude mice under laser irradiation, as recorded using a thermal infrared camera.

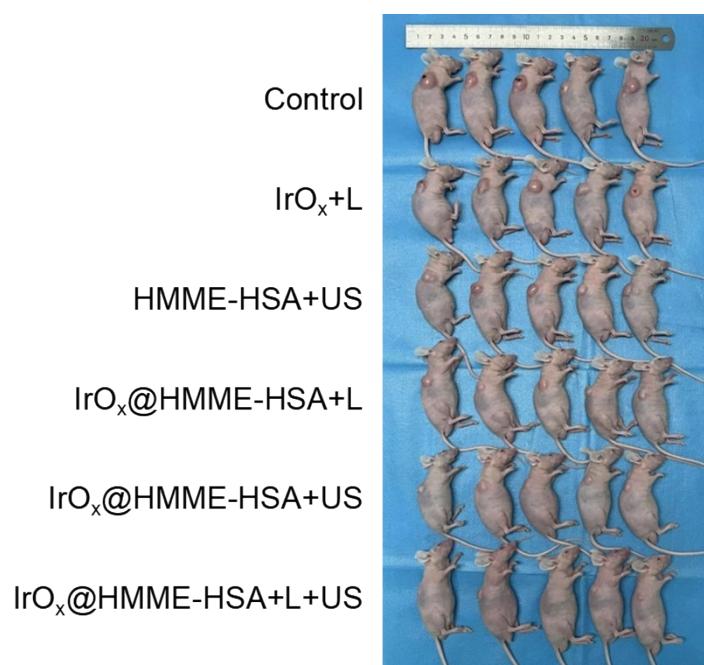


**Fig. S12** Hematological tests, such as regular blood indicators(WBC, PLT, RBC, HCT, MCH, MCHC, HGB,) and functions of liver and kidney (ALT, AST, ALP, CREA, BUN) of different groups (G1: Control, G2: IrO<sub>x</sub> + L, G3: HMME-HSA + US, G4: IrO<sub>x</sub>@HMME-HSA + L, G5: IrO<sub>x</sub>@HMME-HSA + US, G6: IrO<sub>x</sub>@HMME-HSA + L + US).

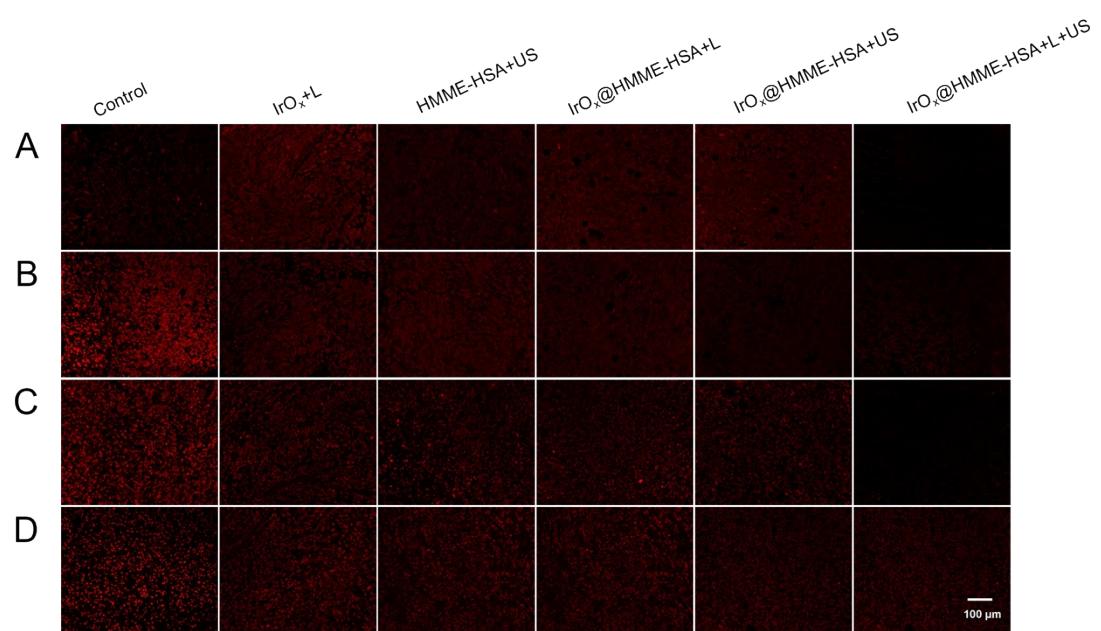
+ L + US ) on day 21 after various treatments. The date are expressed as means  $\pm$  SD (n = 3) (\*\*p < 0.001, \*\*p < 0.01, and \*p < 0.05).



**Fig. S13** Images of H&E-stained sections of the heart, liver, spleen, lung and kidney from mice in each treatment group , scale bar = 100  $\mu$ m.



**Fig. S14** Representative images of tumor-bearing nude mice of different groups.



**Fig. S15** Fluorescence images of tumor slices after HSP70 (A), SLC7A11 (B), GCLM (C), and HIF-1 $\alpha$  (D) immunofluorescence staining ,scale bar = 100  $\mu\text{m}$ .