## **Supporting Information**

## Differential Diagnosis and Precision Therapy of Two Typical Malignant Cutaneous Tumors Leveraging on Their Tumor Microenvironment: A Photomedicine Strategy

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## Author Contributions

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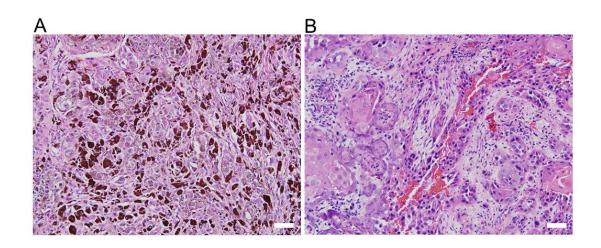


Figure S1. Histopathologic pictures of the two representative skin cancers, MM (A) and cSCC (B). Scale bars =  $50 \ \mu m$ 

Pathology results show that MM tissues are in loose structure with patchy distribution and vascular infiltration, while cSCC cells are clustered compactly as squamous pearls. Moreover, the surface of cSCC is highly cuticularized. These characteristics may cause heterogeneous and a few scattered enhanced signals in PA and MRI mode for XL50 cSCC tumor (**Figure 3 and Figure 4**).

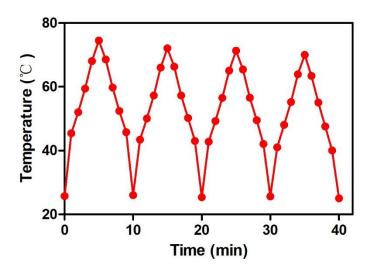


Figure S2. Photothermal stability of iHRANPs under 808 nm laser irradiation (1 W/cm<sup>2</sup>) for 4 cycles.

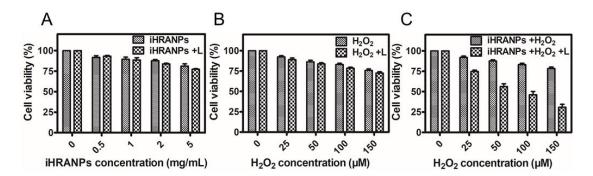


Figure S3. In vitro cytotoxicity and  $H_2O_2$ -dependent PTT effect of iHRANPs on A375. (A) The cell viability after incubation with different concentrations of iHRANPs with and without laser irradiation. (B) The cell viability after incubation with different concentrations of  $H_2O_2$  with and without laser irradiation. (C) The cell viability after incubation with iHRANPs (5 mg/mL) in the presence of different concentrations of  $H_2O_2$  with and without laser irradiation (808 nm,  $1W/cm^2$ , 5 min).

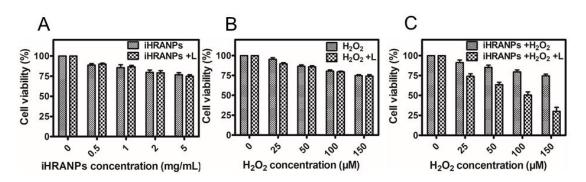


Figure S4. In vitro cytotoxicity and  $H_2O_2$ -dependent PTT effect of iHRANPs on XL50. (A) The cell viability after incubation with different concentrations of iHRANPs with and without laser irradiation. (B) The cell viability after incubation with different concentrations of  $H_2O_2$  with and without laser irradiation. (C) The cell viability after incubation with iHRANPs (5 mg/mL) in the presence of different concentrations of  $H_2O_2$  with and without laser irradiation (808 nm, 1W/cm<sup>2</sup>, 5 min).

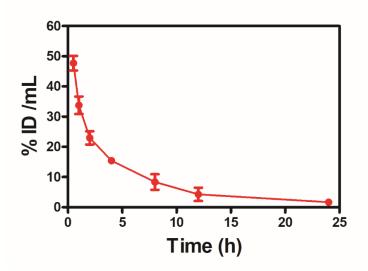


Figure S5. Pharmacokinetics of iHRANPs over a span of 24 h. The blood retention of

iHRANPs was decreased to 1.67  $\pm$  2.08% ID/mL at 24 h post-intravenous injection.