Electronic Supplementary Information (ESI)

Robust Hybrid Nanozyme@Hydrogel Platform as a Biomimetic Cascade Bioreactor for Combination Antitumor Therapy

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1. Experimental

1.1 Calculation of photothermal conversion efficiency

According to the methods of these articles,[1, 2] taking the first heating-cooling process in the photothermal cycle, the photothermal conversion efficiency of hPB@gellan hydrogel using the following formula.

$$\theta = (T_{amb} - T) / (T_{amb} - T_{max})$$

$$\tau_s = (-t) / \ln\theta$$

$$hS = \sum mC_p / \tau_s$$

$$\eta = hS (T_{max} - T_{max,\ water}) / I (1 - 10^{-A})$$

where h is the heat transfer coefficient, S is the surface area of the photothermal test vessel, τ_s is the time constant of the sample, m is the mass of the sample (~ 1.0 g) , and C_p is the specific heat capacity of water (C_p = 4.2 J·mol^{-1}), A is the absorbance at 808 nm of hPB@gellan hydrogel (A = 1.45). The maximum temperature of water is 26 °C under the same illumination conditions. According to the first heating-cooling process in the photothermal cycle, τ_s is obtained by the linear relationship between the the cooling period and natural logarithm of driving force temperature (Fig. S1).

1.2 Enzymatic assay of glucose oxidase (GOD)

The method for the enzyme activity is referred to the enzymatic assay of glucose oxidase according to the Sigma Quality Control Test Procedure. The reaction velocity is determined by an increase in absorbance at 500 nm resulting from the oxidation of *o*-dianisidine through a peroxidase coupled system. The temperature is 35 °C, pH is 5.1.

2. Supplementary Figures

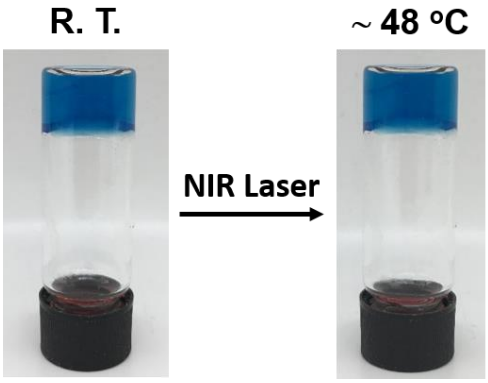

Fig. S1 The images of hPB@gellan hydrogel before and after the NIR laser irradiation (808 nm, 0.5 W cm^{-2}, 5 min).

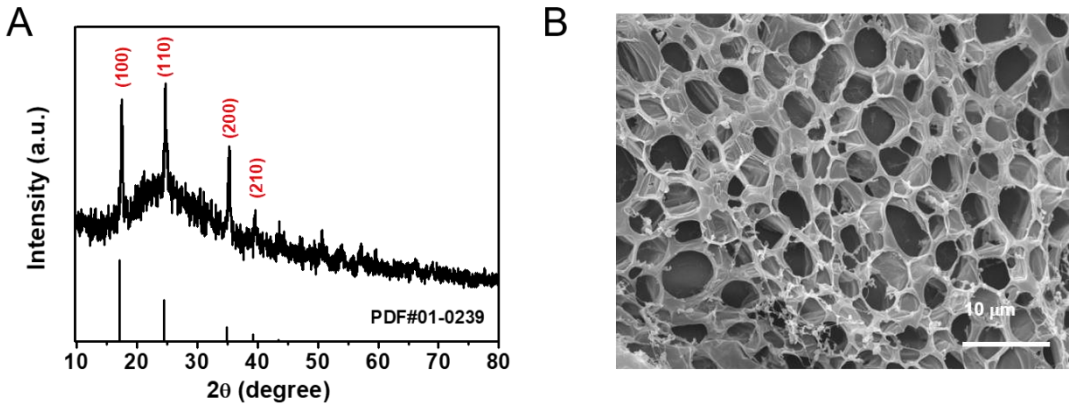

Fig. S2 (A) XRD pattern of PB nanoparticles in the hPB@gellan hydrogel after NIR laser irradiation. (B) SEM of hPB@gellan hydrogel after NIR laser irradiation (808 nm, 0.5 W cm^{-2}, 5 min).

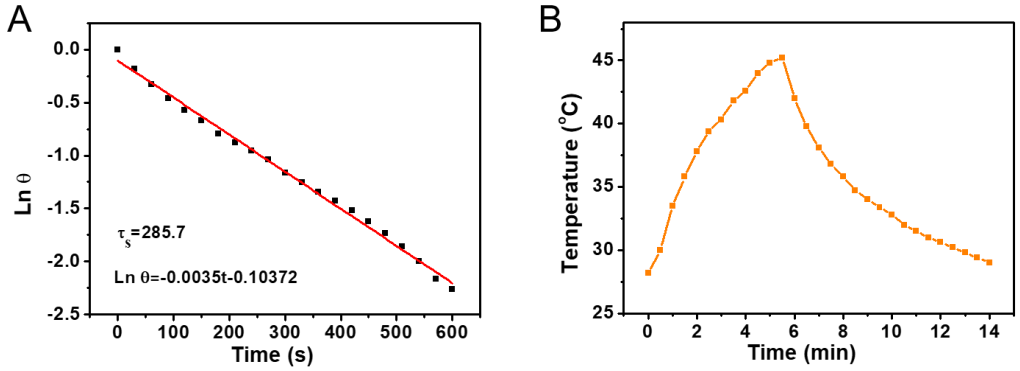

Fig. S3 Calculation of photothermal conversion efficiency using the first photothermal cycle of hPB@gellan hydrogel (A and B).

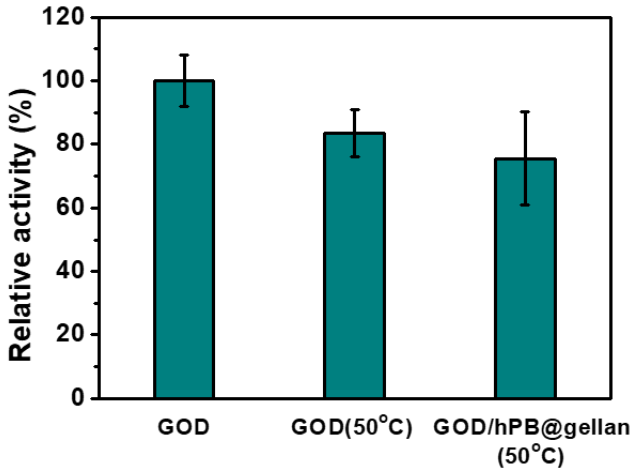

Fig. S4 The relative enzyme activity of GOD/hPB@gellan hydrogel samples (n = 6).

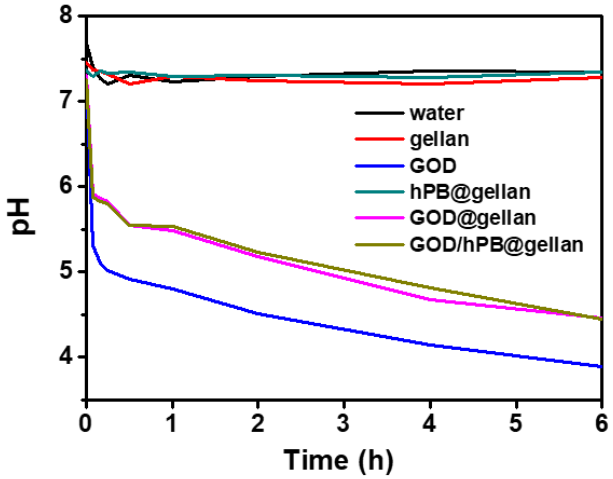

Fig. S5 The pH curves of different samples in the glucose consumption by the GOD-containing samples (glucose: 2 mg mL^{-1}).

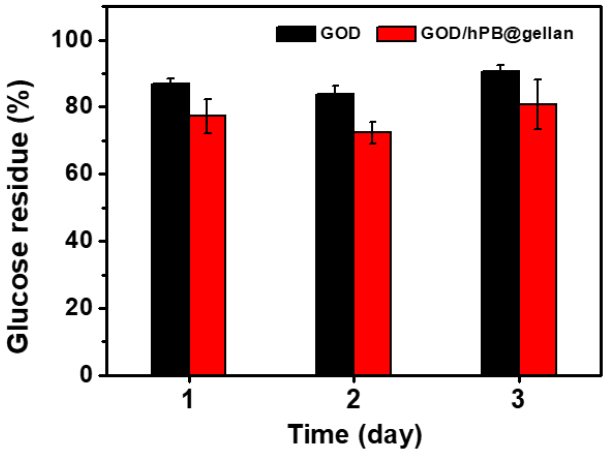

Fig. S6 The glucose residue (%) in the catalytic reaction at 24 h. GOD and GOD/hPB@gellan hydrogel were first incubated at 37 °C for different time.

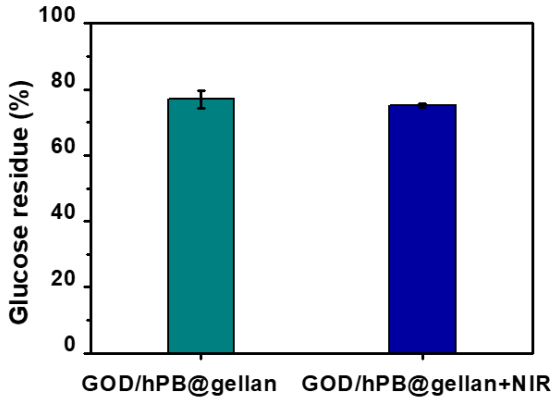

Fig. S7 The glucose residue (%) in the catalytic reaction at 24 h by GOD/hPB@gellan hydrogel before and after NIR irradiation (NIR: 808 nm, 0.5 W cm^{-2}, 5 min; Glucose: 2 mg mL^{-1}).

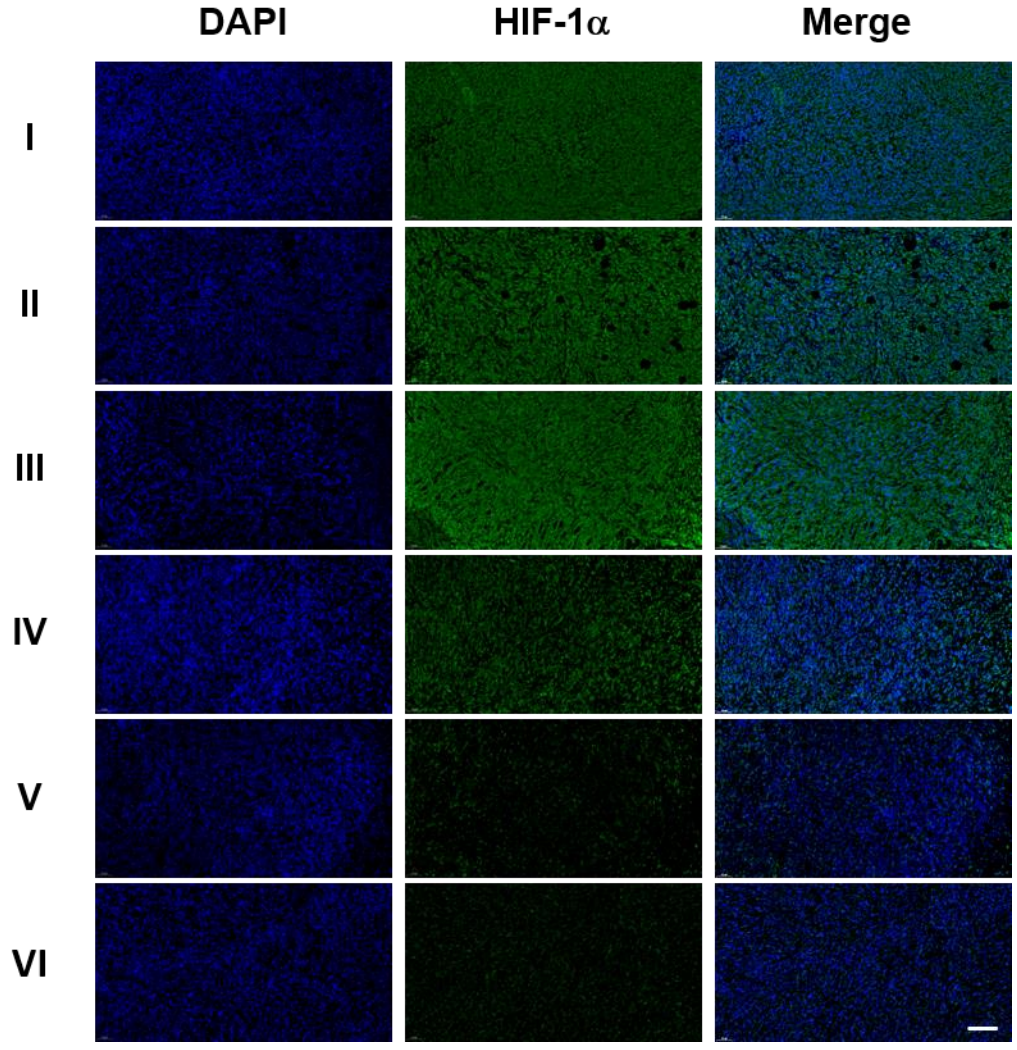

Fig. S8 Representative immunofluorescence staining of HIF-1α (green) and DAPI (blue) on 4T1-Luc tumor slices collected at 24 h after different treatments (I: PBS; II: GOD; III: GOD@gellan; IV: GOD/hPB@gellan; V: hPB@gellan + NIR; VI: GOD/hPB@gellan + NIR. The scale bar: 100 μm).

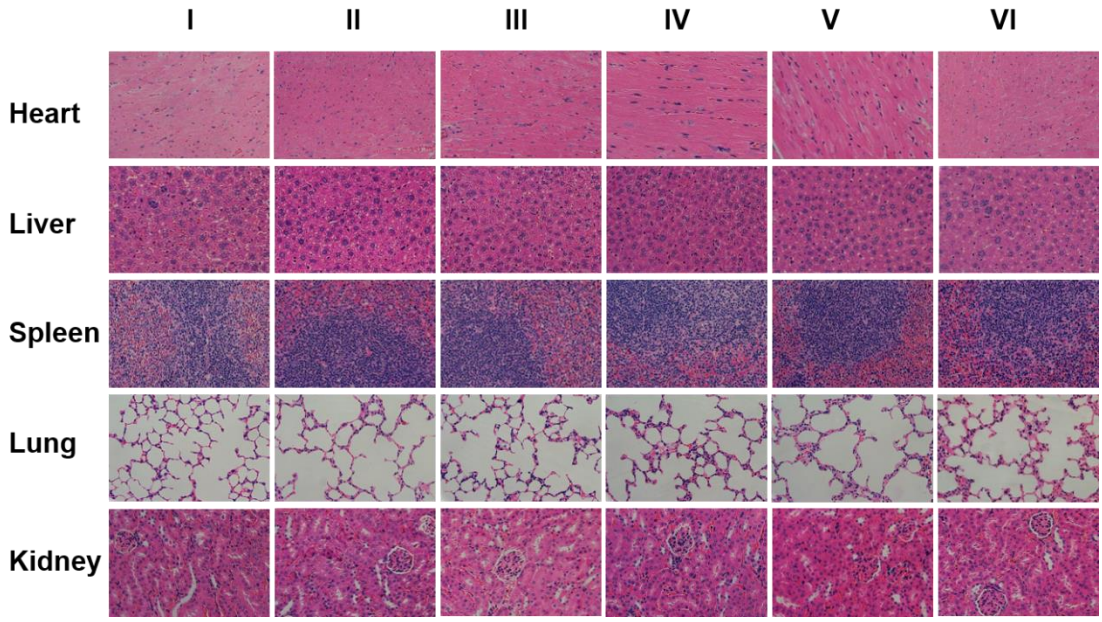

Fig. S9 H&E staining of major organs (heart, liver, spleen, lung, and kidney) in tumor-bearing mice 22 days after treatment with the formula (I: PBS; II: GOD; III: GOD@gellan; IV: GOD/hPB@gellan; V: hPB@gellan + NIR; VI: GOD/hPB@gellan + NIR).

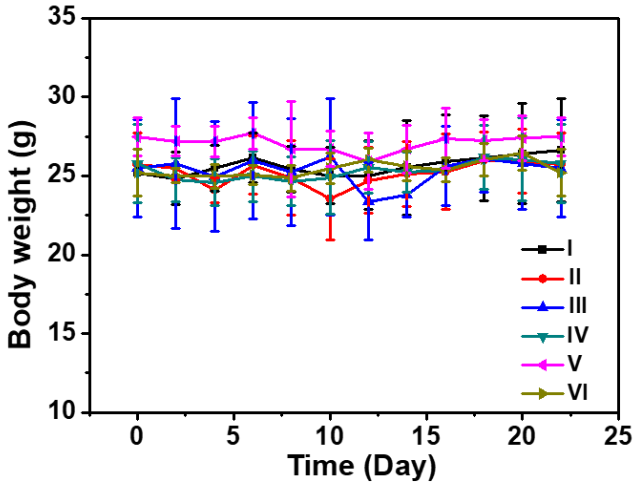

Fig. S10 The body weight of mice during treatment (I: PBS; II: GOD; III: GOD@gellan; IV: GOD/hPB@gellan; V: hPB@gellan + NIR; VI: GOD/hPB@gellan + NIR).

References

1 Q. Tian, F. Jiang, R. Zou, Q. Liu, Z. Chen, M. Zhu, S. Yang, J. Wang, J. Wang and J. Hu, *ACS Nano*, 2011, **5**, 9761-9771.

2 C. Sun, L. Wen, J. Zeng, Y. Wang, Q. Sun, L. Deng, C. Zhao and Z. Li, *Biomaterials*, 2016, **91**, 81-89.