Supporting Information

for

Octopod PtCu Nanoframe for Dual-Modal Imaging-Guided Synergistic Photothermal Radiotherapy

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List of Contents

| Figure S1. TEM images of OPCNs along with synthesis steps | S3 |
|---|-----------|
| Figure S2. SEM images of the as-synthesized OPCNs | S4 |
| Figure S3. Particle size distribution of the as-synthesized OPCNs | S5 |
| Figure S4. HAADF-STEM images of OPCNs from different perspectives | S6 |
| Figure S5. XPS spectra of the as-prepared OPCNs | \$7 |
| Figure S6. FTIR spectra of OPCNs-PEG-FA | S8 |
| Figure S7. Zeta potentials of the as-synthesized nanoparticles | S9 |
| Figure S8. Stability, dispersion and thermogenesis capacity of OPCNs- | PEG-FA in |
| different solutions | S10 |
| Figure S9. Targeting uptake of the OPCNs-PEG-FA | S11 |
| Figure S10. Cell endocytosis mechanism assay | S12 |
| Figure S11. The predicted isobologram for combined treatment | S13 |
| Figure S12. Cell death analysis by flow cytometry analysis | S14 |
| Table S1. Pharmacokinetic study of the OPCNs-PEG-FA | S15 |
| Table S2. Hemocompatibility study of the OPCNs-PEG-FA in vivo | S16 |

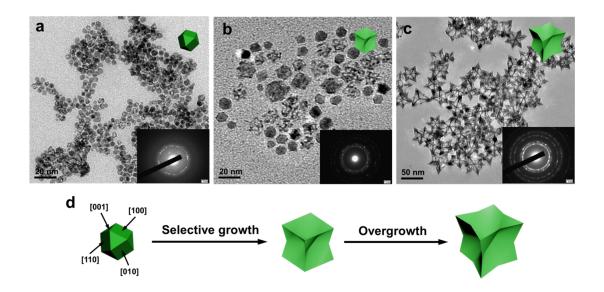


Figure S1. TEM images obtained at different times during the fabrication of octopod PtCu nanoframes: (a) 1 h, (b) 6 h and (c) 48 h, respectively. The inset images exhibit the diffraction rings of nanoframes at different steps; and (d) schematic preparation of OPCNs of the major steps during synthesis process.

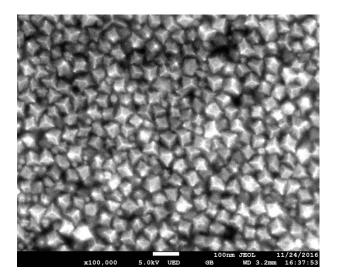


Figure S2. Representative SEM image of the as-synthesized OCPNs. Scale bar: 100 nm.

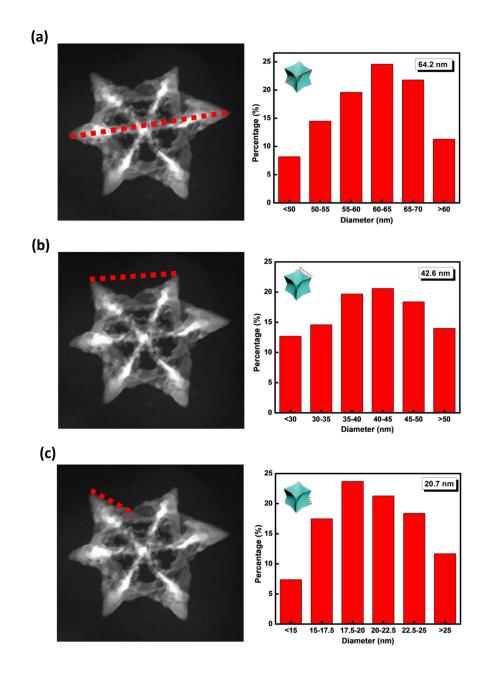


Figure S3. Particle size distributions of the as-synthesized OPCNs: (a) diagonal length;(b) edge breadth; and (c) eight symmetric feet length, respectively.

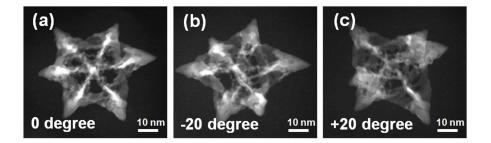


Figure S4. Angle dependent HAADF-STEM images of the OPCNs from different perspectives with concave octopod feature: (a) original position; (b) -20 degree at X-axis; and (c) +20 degree at X-axis.

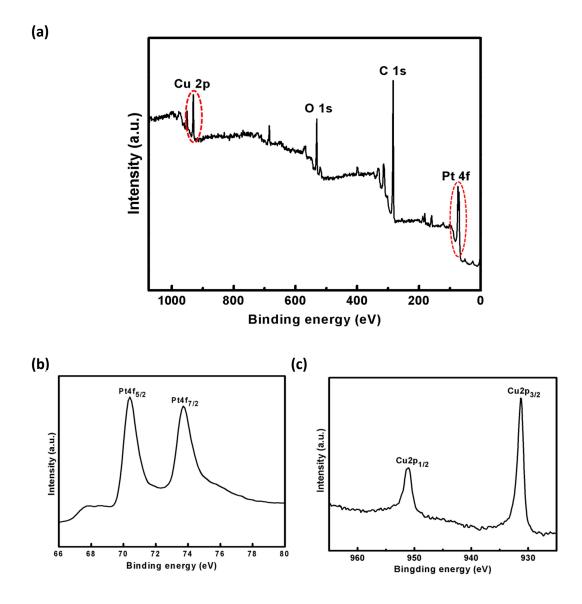


Figure S5. XPS spectra of the as-prepared PtCu nanoframes: (a) OPCNs; (b) Pt 4f; and

(c) Cu 2p bands.

S7

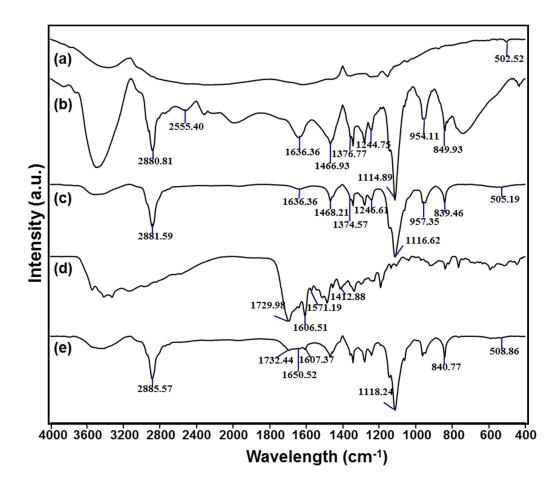


Figure S6. FTIR spectra of nanoparticles at major steps during the synthesis process of OPCNs-PEG-FA: (a) OPCNs; (b) Pure SH-PEG-NH₂; (c) OPCNs-PEG; (d) Pure FA; and (e) OPCNs-PEG-FA, respectively.

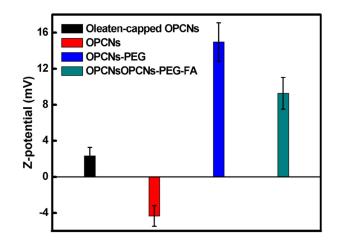


Figure S7. Zeta potentials of the as-synthesized nanoparticles at different steps during the fabrication process (n = 5).

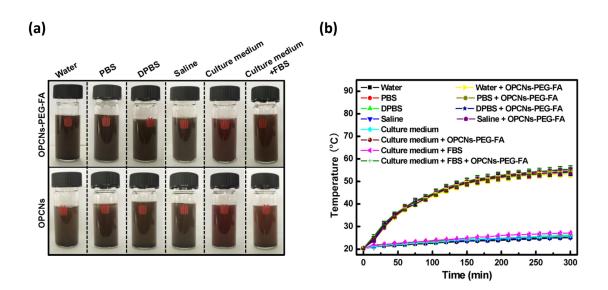


Figure S8. (a) The stability and dispersion of OPCNs nanoparticles in different solutions after 24 h; and (b) thermogenesis capacity of OPCNs-PEG-FA (200 μ g/mL) irradiated with NIR laser (808 nm, 2.4 W/cm², 5 min) in different solutions.

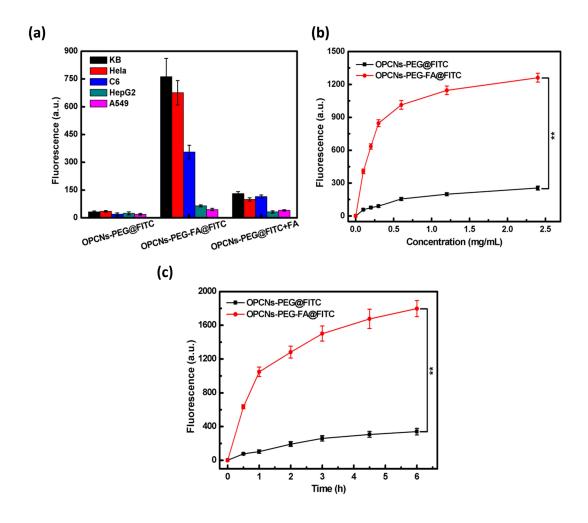


Figure S9. Targeting uptake assay: (a) folic acid-receptor (FR) mediated targeting capacity of OPCNs-PEG-FA evaluated with FR positive (KB, Hela, C6) and negative (HepG2, A549) cancer cells; (b) concentration dependence of OPCNs-PEG-FA@FITC nanoparticles uptake by Hela cells (incubation time: 1 h); and (c) time dependence of OPCNs-PEG-FA@FITC (200 μ g/mL) uptake by Hela cells. ** p<0.01 (n = 3).

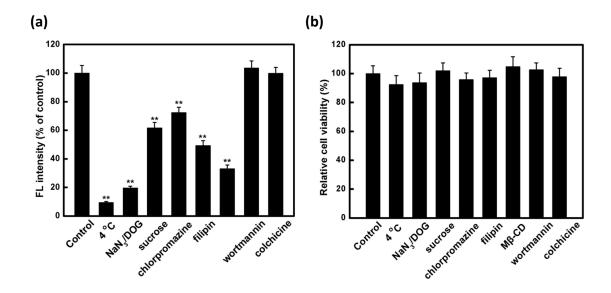


Figure S10. Cell endocytosis mechanism assay: (a) relative uptake percentages of OPCNs-PEG-FA after treatment with different uptake inhibitors; (b) relative cells viability when incubating with corresponding different uptake inhibitors. Data are presented as means \pm SD, p<0.01 (n=3).

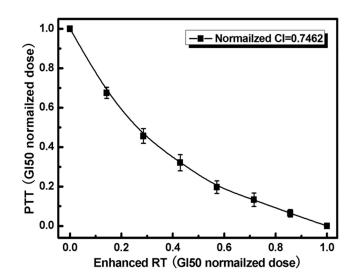


Figure S11. The predicted isobologram for combination enhanced radiotherapy and photothermal therapy.

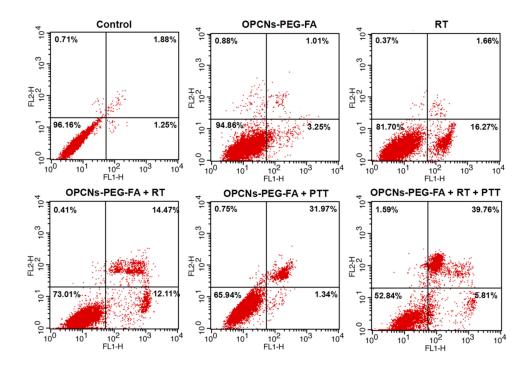


Figure S12. Cell death assay of HepG2 cells after synergic photothermal radiotherapy

by flow cytometry.

| Parameters | OPCNs | OPCNs-PEG-FA |
|---------------------------|--------------------|--------------------|
| C _{max} (mg/L) | 20.620 ± 3.690 | 21.587 ± 3.025 |
| A (mg/L) | 17.639 ± 1.780 | 14.764 ± 3.533 |
| α (1/h) | 0.125 ± 0.014 | 0.178 ± 0.022 |
| B (mg/L) | 3.590 ± 0.630 | 2.448 ± 0.890 |
| β (1/h) | 0.007 ± 0.003 | 0.011 ± 0.005 |
| $AUC_{0-\infty}$ (mg/L/h) | 141.230 ± 27.554** | 367.620 ± 43.264** |
| T _{1/2} (h) | 1.859 ± 0.478** | 3.223 ± 0.674** |
| MRT (h) | 0.976 ± 1.641** | 2.357 ± 3.504** |
| CL (L/kg/h) | 2.18 ± 0.530** | 1.271 ± 3.110** |

Table S1. The main pharmacokinetic parameters of the as-synthesized nanoparticles (n = 5).

Table S2. Hemolytic ratio (HR), Prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT) of the as-synthesized nanoparticles (n = 5).

| Materials | HR(%) | PT(s) | APTT(s) | TT(s) |
|--------------|-------------|------------|------------|------------|
| Control | 2.92± 0.46 | 11.3 ± 2.3 | 32.4 ± 3.8 | 14.5 ± 2.5 |
| OPCNs | 4.02 ± 0.64 | 13.7 ± 1.6 | 34.7 ± 4.6 | 15.6 ± 1.1 |
| OPCNs-PEG | 2.18 ± 0.53 | 11.8 ± 3.1 | 33.1 ± 4.1 | 13.6 ± 3.1 |
| OPCNs-PEG-FA | 3.38 ± 0.99 | 12.4 ± 2.8 | 33.8 ± 3.5 | 14.7 ± 2.4 |