Electronic Supplementary Information

An upconversion nanoplatform with extracellular pH-driven tumor-targeting ability for improved photodynamic therapy

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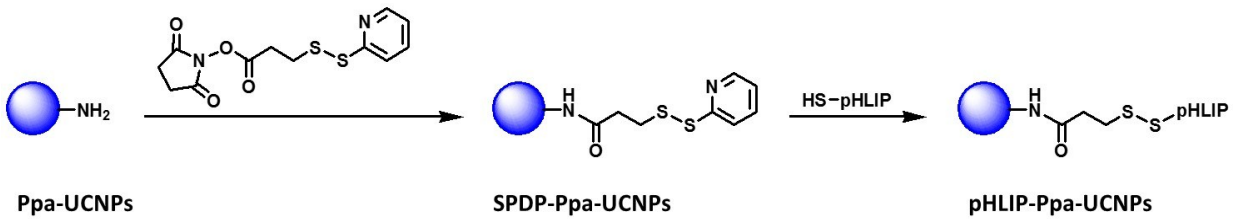
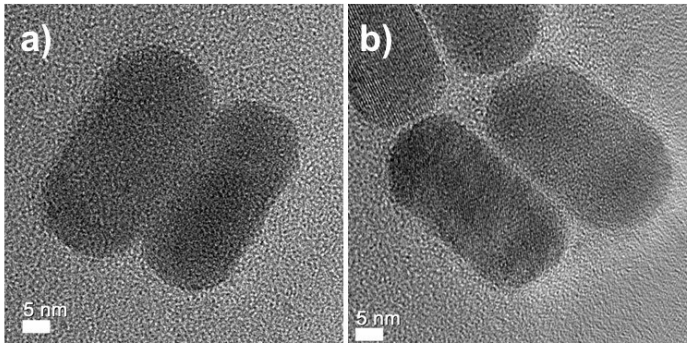
Supplementary Table S1. The number hydrodynamic size (d. nm) of pHLIP-Ppa-UCNPs in Milli-Q water, PBS buffer (pH 7.4), 0.9% NaCl solution, and FBS measured at time 0 and 24 h later.

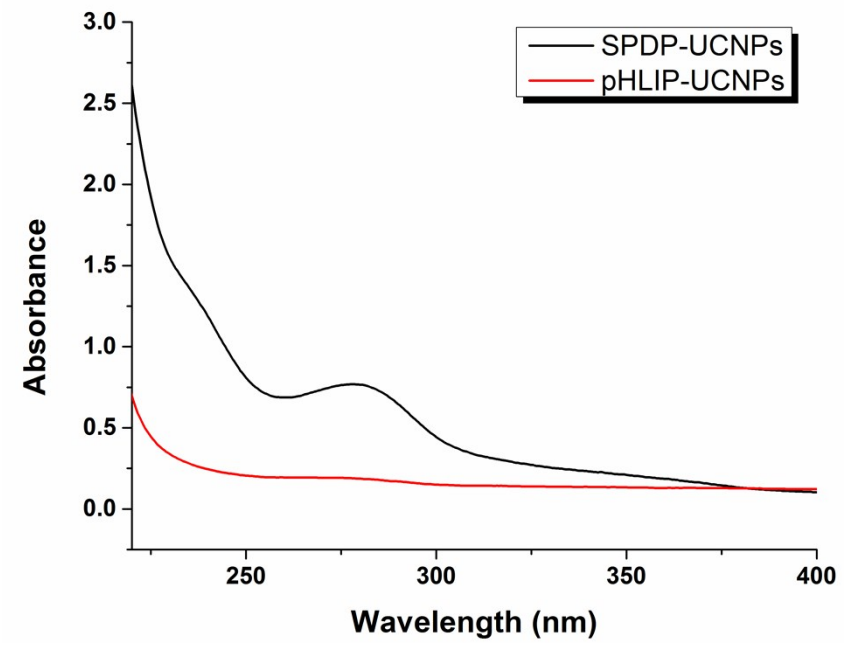
pHLIP-Ppa-UCNP dispersed in different conditions	Number hydrodynamic size (d. nm)	
	0 h	24 h later
Milli-Q water	45.4 ± 8.7	49.2 ± 11.6
PBS buffer (pH 7.4)	52.1 ± 10.6	58.6 ± 6.1
0.9% NaCl solution	67.9 ± 9.8	71.6 ± 9.5
FBS	149.6 ± 16.4	149.7 ± 17.2



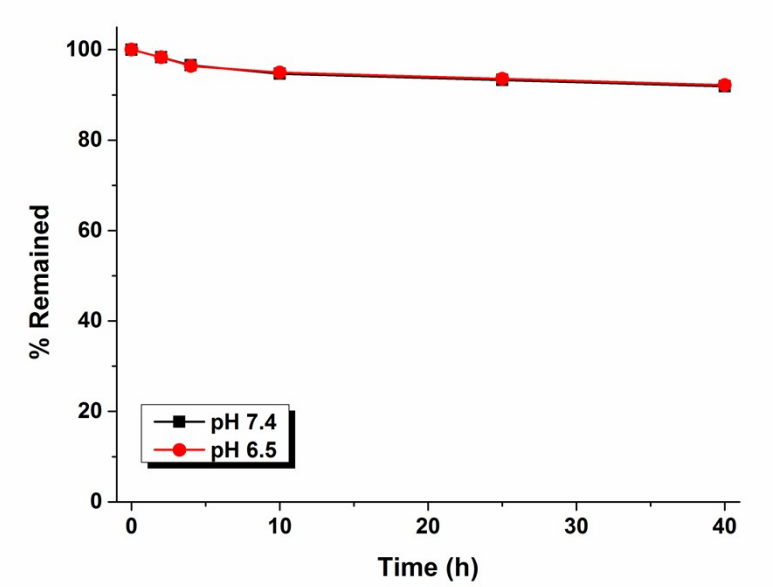
Supplementary Scheme S1. pHLIP modification of functionalized UCNPs with amino groups.



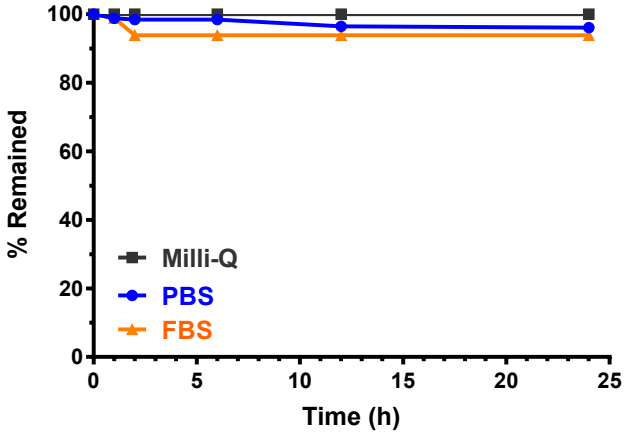
Supplementary Figure S1. High Resolution Transmission Electron Microscopy (HRTEM) of a) NH_2-UCNPs, and b) pHLIP-Ppa-UCNPs. All scale bars are 5 nm.



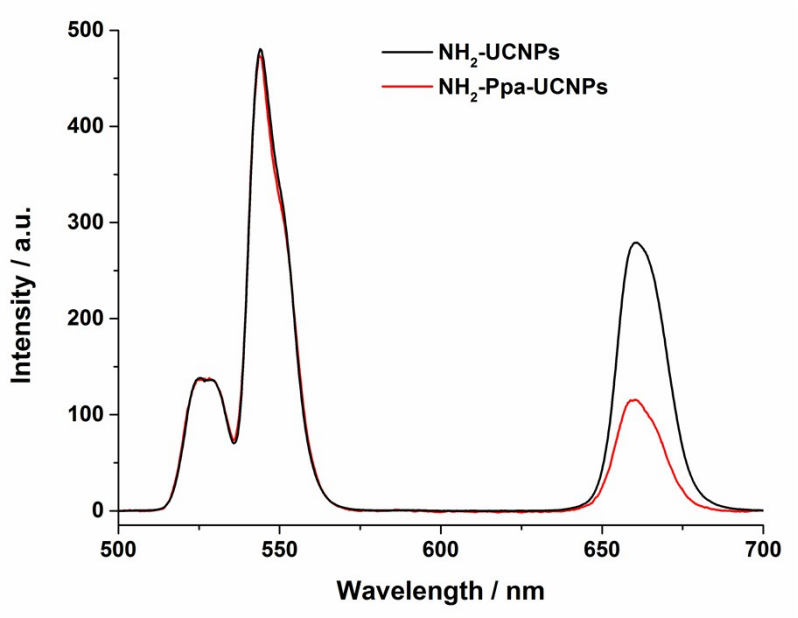
Supplementary Figure S2. UV-Vis spectra for SPDP-UCNPs and pHLIP-UCNPs without loading of Ppa.



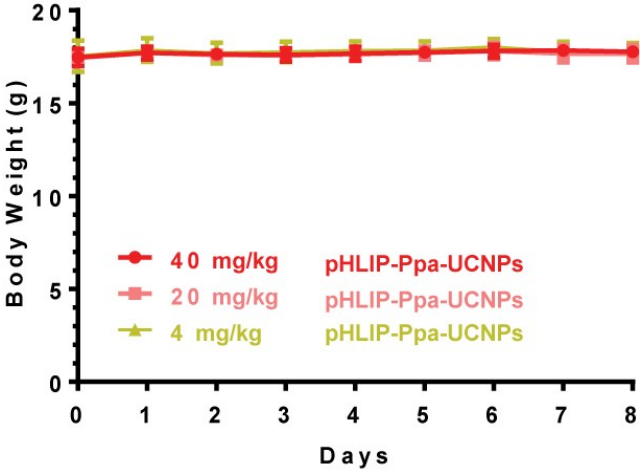
Supplementary Figure S3. Release of Ppa from pHLIP-Ppa-UCNPs at PBS buffer at different pH values (6.5 or 7.4) at 37 °C on different time points.



Supplementary Figure S4. Release of Ppa from pHLIP-Ppa-UCNPs in Milli-Q water, PBS buffer (pH 7.4), and FBS at 37 °C on different time points.

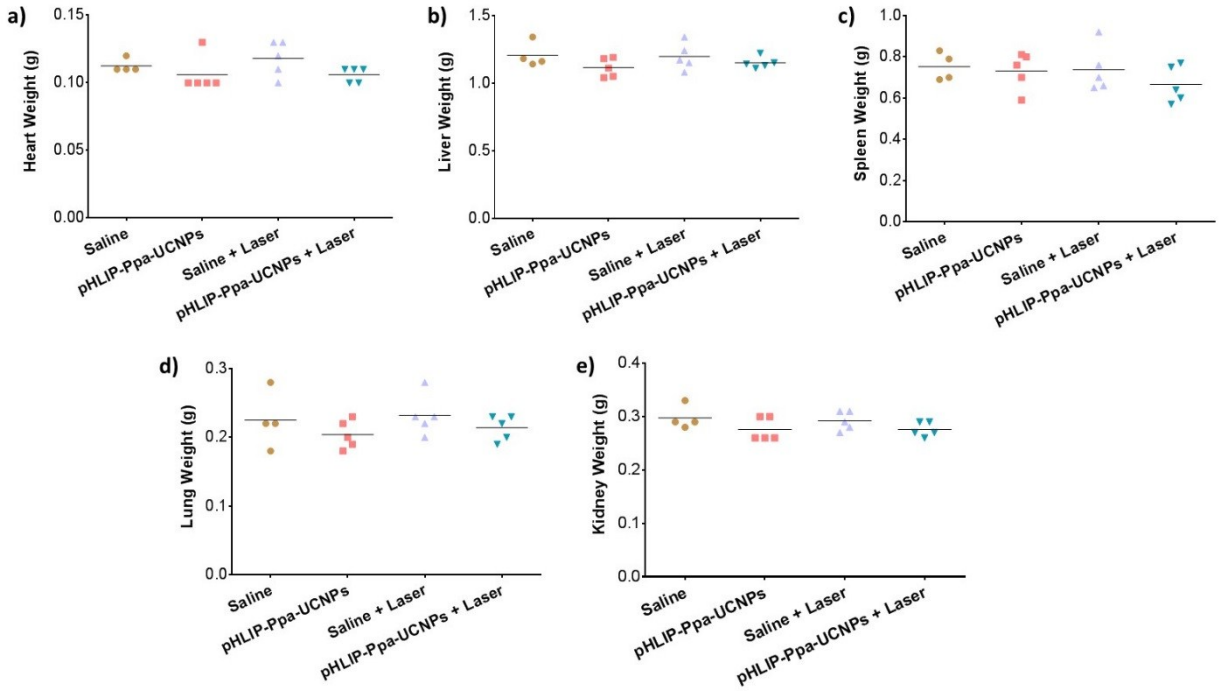


Supplementary Figure S5. Photoluminescence of before (NH_2-UCNPs) and after (NH_2-Ppa-UCNPs) loading of Ppa under 808 nm excitation.

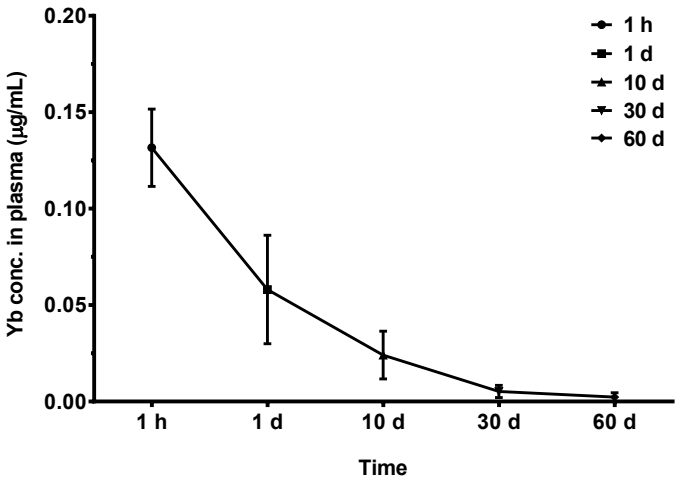


Supplementary Figure S6. The change of body weight in indicated doses of pHLIP-Ppa-UCNPs for MTD test (*s.c.* injection, *single* dose). Mean ± SD; n = 3.

Supplementary Figure S7. The corresponding images of digital photos of mice from different groups after PDT treatment.



Supplementary Figure S8. Weight of major organs a) heart, b) liver, c) spleen, d) lung, and e) kidney, respectively, in each group of saline, pHLIP-Ppa-UCNPs, saline + laser, pHLIP-Ppa-UCNPs + laser.



Supplementary Figure S9. The Yb concentration curve in plasma at each time point after injection (*i.v.*, single dose). Mean ± SD, n = 4.