Supporting Information

Pyropheophorbide A and c(RGDyK) Co-Modified Chitosan-Wrapped Upconversion Nanoparticle for Targeted Near-Infrared Photodynamic Therapy

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Absorption spectra of nanoparticle PEI-UCNP. The absorption spectra of nanoparticle PEI-UCNP in water was obtained using a UV/VIS spectrometer. No characteristic absorption peaks were observed on the absorption spectra of nanoparticle PEI-UCNP (Figure S1).

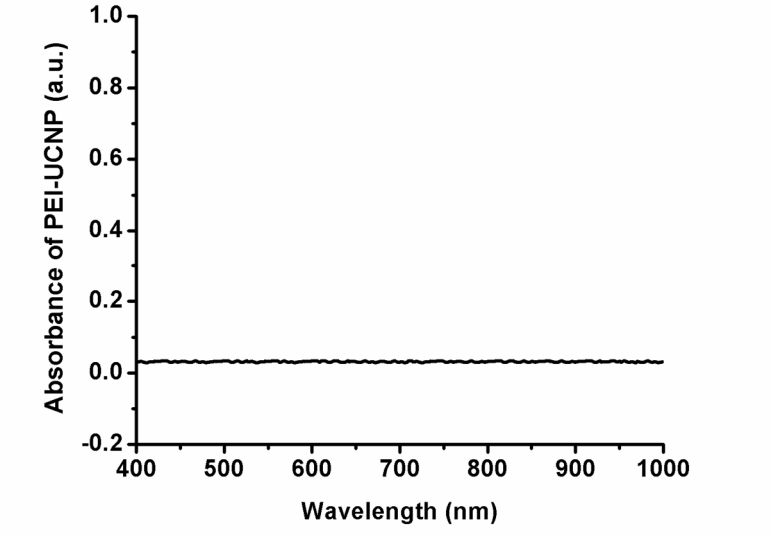

Figure S1: Absorption spectra of nanoparticle PEI-UCNP

Quantitatively measurement of the loading ability of c(RGDyK) and pyropheophorbide a. The chitosan wrapped upconversion nanoplatform OCMC-UCNP has a great potential in carrying biofunctional molecules. The loading level of c(RGDyK) and photosensitizer pyropheophorbide a was measured by

absorbance method, and it was calculated to be about 527:2.8:1 upconversion nanoparticle:pyropheophorbide a:c(RGDyK) by weight basis.

1) To quantitatively measure the loading ability of photosensitizer, pyropheophorbide a (0.25 mg) was dissolved in ethanol (100 mL) to obtain 4.8 μM pyropheophorbide a stock solution. The stock solution was then diluted by ethanol progressively to get samples with different concentrations. The absorption spectra of pyropheophorbide a samples were obtained using a UV/VIS spectrometer (Lambda 35, Perkin-Elmer, USA). The absorbance intensity at 414 nm was correlated with the photosensitizer concentration (μM) to obtain the standard curve: y=0.01＋0.39x (y: absorbance value at 414 nm; x: concentration of pyropheophorbide a) (Figure S2A).

During **Step 2** of **Synthesis of UCNP-Ppa-RGD**, pyropheophorbide a solvent (20 μM, 2 mL) was firstly activated by EDC/NHS for 2 h. Then chitosan wrapped upconversion nanoparticles (5 mg) were added and the mixture was vortexed for 4 h. The suspension was centrifugated at 10,000 rpm for 10 min, then the supernatant was carefully collected. 2 mL of the supernatant was transfered into a cuvette and its pyropheophorbide a concentration was measured by the absorbance value at 414 nm according to the standard carve obtained above. The loading level of pyropheophorbide a was calculated to be about 190:1 upconversion nanoparticle:pyropheophorbide a by weight basis.

2) To quantitatively measure the loading of RGD peptide, 5-aminofluorescein was used instead of c(RGDyK) to quantify the carboxyl groups upon OCMC-UCNP nanoplatform. The method is much similar as described above.

5-aminofluorescein (0.11 mg) was dissolved in deionized water (200 mL) to obtain 1.6 μM 5-aminofluorescein stock solution. It was then diluted by water progressively to get samples with different 5-aminofluorescein concentrations. The absorption spectra of 5-aminofluorescein samples were obtained using a UV/VIS spectrometer. The absorbance intensity at 490 nm was correlated with the 5-aminofluorescein concentration (μM) to obtain the standard curve: y=－0.02＋1.41x (y: absorbance value at 490 nm; x: concentration of 5-aminofluorescein) (Figure S2B).

During **Step 1** of **Synthesis of UCNP-Ppa-RGD**, instead of c(RGDyK), 5-aminofluorescein (2 mg) was dissolved in Na_2CO_3 buffer solution (pH 8.0, 2 mL). Nanoparticles OCMC-UCNP (5 mg) were added into the solution, vortexed at room temperature for 4 h. The suspension was centrifugated at 10,000 rpm for 10 min and the supernatant was carefully collected. 2 mL of the supernatant was transfered into a cuvette, and its 5-aminofluorescein concentration was measured by the absorbance value at 490 nm according to the standard carve. The number of 5-aminofluorescein molecule modified on to nanoparticle is approximately equal to the number of c(RGDyK) upon nanoparticle UCNP-Ppa-RGD. The loading level of c(RGDyK) was calculated to be about 527:1 upconversion nanoparticle:c(RGDyK) by weight basis.

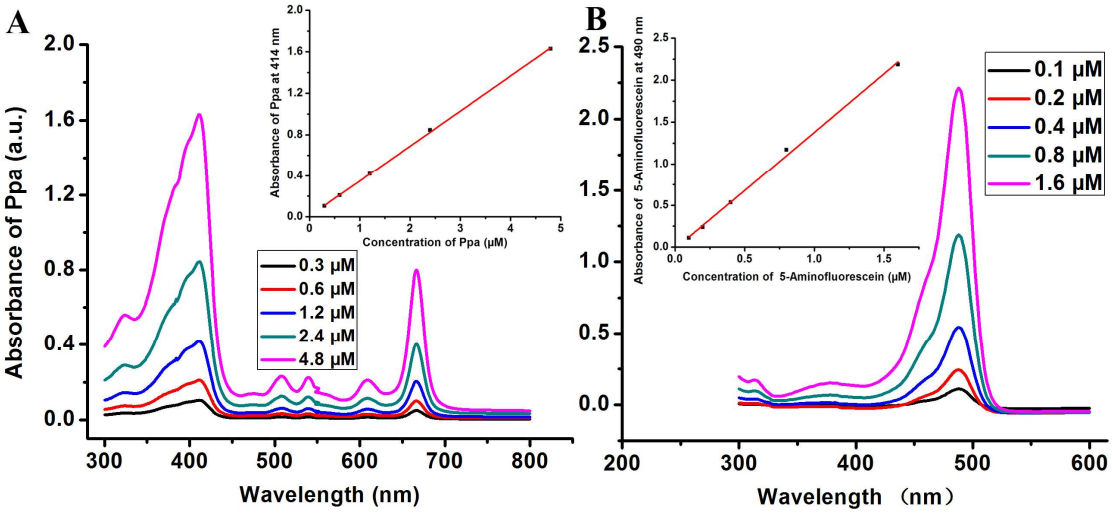

Figure S2. (A) The sbsorption spectra of pyropheophorbide a with different concentrations. Inset: The standard curve for pyropheophorbide a absorbance value at 414 nm. (B) The sbsorption spectra of 5-aminofluorescein with different concentrations. Inset: The standard curve for 5-aminofluorescein absorbance value at 490 nm.