Supplementary Figure 1. Chemical structure of telodendrimer PEG5k-Por4-CA4.

Supplementary Figure 2. The MALDI-TOF MS of PEG5k-Por4-CA4 telodendrimer.
**Supplementary Figure 3.** $^1$H NMR Characterizations. $^1$H NMR spectra of PEG$_5$K-Por$_4$-CA$_4$ telodendrimer recorded in DMSO-d$_6$ (A) and D$_2$O (B), respectively. The chemical shift of PEG chains (3.5-3.7 ppm), cholic acid (0.5-2.4 ppm) and pyropheophorbide-a (0.9-2.2 ppm) could be observed in the $^1$H NMR spectra of the telodendrimers in DMSO-d$_6$ (A). The characteristic peaks of methyl proton 18, 19, and 21 in cholic acid were seen at 0.58, 0.80 and 0.95 ppm, respectively. The characteristic peaks of methyl proton 8 and 18 in pyropheophorbide-a were observed at 1.8 and 1.9 ppm, respectively. When the NMR spectrum was recorded in D$_2$O, the peaks of cholic acid protons and protons of pyropheophorbide-a in PEG$_5$K-Por$_4$-CA$_4$ were highly suppressed (B), indicating the movements of cholanes and protons of pyropheophorbide-a were highly restricted by the formation of core-shell micellar architecture in the aqueous environment.
Supplementary Figure 4. Particle size and distribution of NPs. The particle size of NPs in the absence (A) and in the presence (B) of 2.5 g/L SDS. The particle size was measured by dynamic light scattering (DLS). NPs were broken down completely upon addition of SDS.

Supplementary Figure 5. TEM image of Cu(II) loaded NPs without staining.
Supplementary Figure 6. The bright field image of the drops of NP solution in the absence and in the presence of SDS.

Supplementary Figure 7. Particle size of NM-POR. The particle size of free pyropheophorbide-a loaded standard PEG^2k-CA₈ nanomicelles^3 (NM-POR) in the absence (A) and in the presence (B) of 2.5 g/L SDS. The particle size was measured by dynamic light scattering (DLS). NM-POR was broken down completely upon addition of SDS.
Supplementary Figure 8. Near-infrared fluorescence imaging of NPs versus NM-POR. Near-infrared fluorescence imaging of NM-POR \(^3\) solution (10 µL) (Upper panel) in the absence and in the presence of SDS with an excitation bandpass filter at 625/20 nm and an emission filter at 700/35 nm in comparison with that of NP solution (Lower panel). The concentration of pyropheophorbide-a was kept at the 0.2 mg/mL for NM-POR, which was equal to the concentration of pyropheophorbide-a in 1.0 mg/mL of NPs. By calculating the ratio of the average fluorescence intensity in SDS to that in PBS, NPs were found to have 10 times more self-quenching than NM-POR with the same concentration of Por.
Supplementary Figure 9. Heat generation of NM-POR. Thermal images of NM-POR solution (10 µL) in the absence and in the presence of SDS was monitored by a thermal camera after irradiation with NIR laser (690 nm) at 1.25 w/cm² for 20 seconds. The concentration of pyropheophorbide-a was kept at the 0.2 mg/mL for NM-POR, which was equal to the concentration of pyropheophorbide-a in 1.0 mg/mL of NPs.
Supplementary Figure 10. Chemical structure of telodendrimer PEG$_{5k}$-Cys$_4$-Por$_4$-CA$_4$.

Supplementary Figure 11. The MALDI-TOF MS of PEG$_{5k}$-Cys$_4$-L$_8$-CA$_8$ telodendrimer.
Supplementary Figure 12. Particle size characterizations of CNPs. The particle size of CNPs in the absence (A) and in the presence of 2.5 g/L SDS (B), 2.5 g/L SDS + 20 mM NAC (C), 2.5 g/L SDS+20 mM GSH (D). The particle size was measured by dynamic light scattering (DLS). We found that upon addition of SDS, NPs were broken down completely (Fig S6). In contrast, the size of the CNPs persisted at 20-30 nm under the same condition. The CNPs formed was dissociated in the present of SDS at around 40 min after adding the endogenous reducing agent glutathione (GSH, 20mM) and exogenous reducing agent N-acetylcysteine (NAC, 20mM).

Supplementary Figure 13. Stability of CNP-DOX. Continuous particle size measurements of DOX-loaded CNPs (CNP-DOX) in the presence of 50% percent (v/v) of human plasma.
Supplementary Figure 14. GSH level dependent NIRF signal of CNPs in cells. The GSH level (upper) and NIRF signal from dissociated CNPs (lower) in three cell lines SKOV3 (human ovarian cancer cells), PC3m (human prostate cancer cells) and MB49 (mouse bladder cancer cells) quantitatively measured by flow cytometry. Intracellular GSH levels were evaluated by staining ThiolTracker™ Violet (Life technologies) for 30 minutes. Cells were treated with 10 µg/mL CNPs for 20 minutes and then harvested immediately for flow cytometry analysis without fixing. Results present as mean ± SD.
Supplementary Figure 15. Dark photo-toxicity of CNPs, NM-POR and free pyropheophorbide-a (Por). Cytotoxicity of SKOV3 ovarian cancer cells after 2 hrs exposure to CNPs, NM-POR and free Por followed by additional 22 hrs incubation under dark condition. Results present as mean ± SD.
**Supplementary Figure 16. Fluorescence quenching of CNPs in blood.** Representative NIR fluorescence signal of blood drops drawn from xenograft tumor bearing mice 1 min post-injection of CNPs (Por dose: 5 mg/kg) in the absence and in the presence of SDS and GSH (10 mM).

**Supplementary Figure 17. Intracellular delivery of CNPs.** NIR fluorescence images of SKOV3 xenograft tumor in nude mice at 24 and 48 hrs after injection of CNPs. Tumors were harvested and 10 µm thick of cryo-sections were made. Nucleus was stained by Hoechst 33342. Images were acquired by Deltavision deconvolution microscope (scale bar = 30 µm).
**Supplementary Figure 18.** Histopathological imaging of metastatic lesions in the lung. Histopathological imaging confirming the metastatic lesions (arrows) in lungs of breast cancers from the transgenic mice (FVB/n Tg(MMTV-PyVmT). (H&E stain, 40X and insertion 400X).

**Supplementary Figure 19.** $^{64}$Cu labeling. Instant thin-layer chromatography trace of $^{64}$Cu-NPs (left panel) and Gd-$^{64}$Cu-NPs (right panel) post-centrifuge filtration. The radiochemical yields (RYC) is above 96.5% while the radiochemical purity is above 97%. ITLC Method: Biodex strips developed in 90 mM EDTA/0.9% NaCl (aq), imaged on Bioscan plate reader.
**Supplementary Figure 20. Fluorescence signal of CNPs and NM-POR in blood.** (a) The absorbance of CNPs and NM-POR (both contain 0.5 mg/mL of Por) in 10x DMSO. (b) NIR fluorescence signal and (c) quantitative fluorescence of blood drops drawn from nude mice bearing implanted tumor xenografts 1 min post-injection of CNPs and NM-POR (Por dose: 5 mg/kg). Images were analyzed as the average signal in the region of interest (ROI). Results present as mean ± SD. *** p<0.001, t-test.
Supplementary Figure 21. Hemolytic activity of CNPs and NM-POR in blood. *Ex vivo* hemolytic activity from nude mice bearing implanted tumor xenografts. Two microliter of blood collected from mice with CNPs (a&b) and NM-POR (c&d) injection for 1 min was diluted into 100µl of PBS followed by light exposure for 0, 60, and 300 seconds. (Por dose: 5 mg/kg) after light exposure. Light dose: 0.1 W cm⁻², 4 hrs later, blood cells were spun down and hemolysis was observed in the samples from NM-POR treated mice (a&c). Cytospin samples from 300 sec samples were further made for cell morphology evaluation (b&d) (Hema3® stain, 100X oil). In contrast to the normal blood cell morphology found in the CNPs samples (b), both RBCs and WBCs were massively destructed in the NM-POR samples (d) after light exposure, which likely due to ROS related oxidative damage to the blood cells.
Supplementary Figure 22. ROS production of CNPs in tumor cryo-section. *Ex vivo* ROS production in SKOV3 xenograft mouse model. Mice bearing SKOV3 xenograft tumors were injected with PBS or CNP at the dose of 2.5 mg/kg. After 24 hrs, tumors were collected and 10 µm cryo-section of the tumor tissue was prepared on slides. Both samples were incubated with DCF-DA for detection of ROS and Hoechst 33342 for 30 minutes for staining nuclei, respectively. Slides were treated with laser for 2 min and visualized under Olympus fluorescence microscope. Tumor slice from CNP treated group produced higher ROS (green) after light exposure comparing to PBS control tumor.
Supplementary Figure 23. ROS production of CNPs in tumor tissue. White light (left) images, NIRF images (middle) and ROS production (right) of SKOV3 xenograft bearing mice 24 hrs after treatment with PBS and CNPs. ROS production was further confirmed by SOSG at the tumor site with light exposure after treatment with CNPs but not PBS group measured by using SOSG as an indicator. SKOV3 xenograft bearing mice were treated with PBS or CNPs (2.5mg/kg) for 24 hrs. 25 µl of SOSG working solution were intra-tumor injected at one spot designed for light exposure. After 3 minutes of light treatment, mice were sacrificed and the tumor was harvested and slice along with the light treatment area. The green fluorescence from SOSG was imaged by Kodak imaging station.

Supplementary Figure 24. ROS production of CNPs in tumor cryo-section. Ex vivo ROS production in transgenic mice measured by using SOSG as an indicator. Mice were injected with PBS or CNPs at the dose of 2.5 mg/kg. After 24 hrs, tumors were collected and 10 µm cryo-section of the tumor tissue was prepared on slides. Both samples were incubated with SOSG for detection of ROS and Hoechst 33342 for 30 minutes for staining nuclei, respectively. Slides were treated with laser for 2 min and visualized under Olympus fluorescence microscope. Tumor slice from CNP treated group produced higher ROS (green) after light exposure comparing to PBS control tumor. (10X)
Supplementary Figure 25. Caspase3 reactivity and DNA damage of CNP-mediated phototherapy. Caspase3 reactivity and DNA damage in mammary tumor tissue after CNP mediated PDT/PTT. Transgenic mice treated with PBS (control) or CNPs followed by Light treatment at 24 hrs post-injection. DOX dose: 2.5 mg/kg, CNP dose: 25 mg/kg (equivalent to 5 mg/kg of Por), light dose: 1.25 W cm⁻² for 2 min. Tumors were harvested another 24 hrs later and fixed in formalin. Four micron thick of tissue slides were used to perform IHC for cleaved caspase3. DNA damage was detected using TUNEL (TdT-mediated dUTP Nick-end labeling) detection Kit (GenScript, Piscataway, NJ) per manufactory manual. Antibody reactivity of cleaved caspase3 (Cell signaling) was detected by immunochemistry.
Supplementary Figure 26. Body weight change. Body weight change of mice bearing SKOV3 ovarian cancer xenograft (n=8) treated with CNPs and CNP-DOX at day 0, 4 and 8 (black arrow) followed by exposure to laser light (690 nm) on day 1, and 9 (red arrow). PBS and NM-DOX were injected for comparison. DOX dose: 2.5 mg/kg, NP dose: 25 mg/kg (equivalent to 5 mg/kg of Por), light dose: 0.25 W cm\(^{-2}\) for 2 min. Results present as mean ± SD.
Supplementary Table 1. Complete blood count (CBC) and Serum chemistry. CBC and Serum chemistry mice bearing SKOV3 ovarian cancer xenograft (n=8, Results present as mean ± SD.) treated with CNPs at day 0, 4 and 8 followed by exposure to laser light (690 nm) on day 1 and 9. NP dose: 25 mg/kg (equivalent to 5 mg/kg of Por), light dose: 0.25 W cm$^{-2}$ for 2 min. * $p< 0.05$ (t-test) compared to PBS control.

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**Supplementary References**

