Theranostic Liposomes with Hypoxia-Activated Prodrug to Effectively Destruct Hypoxic Tumors post Photodynamic Therapy

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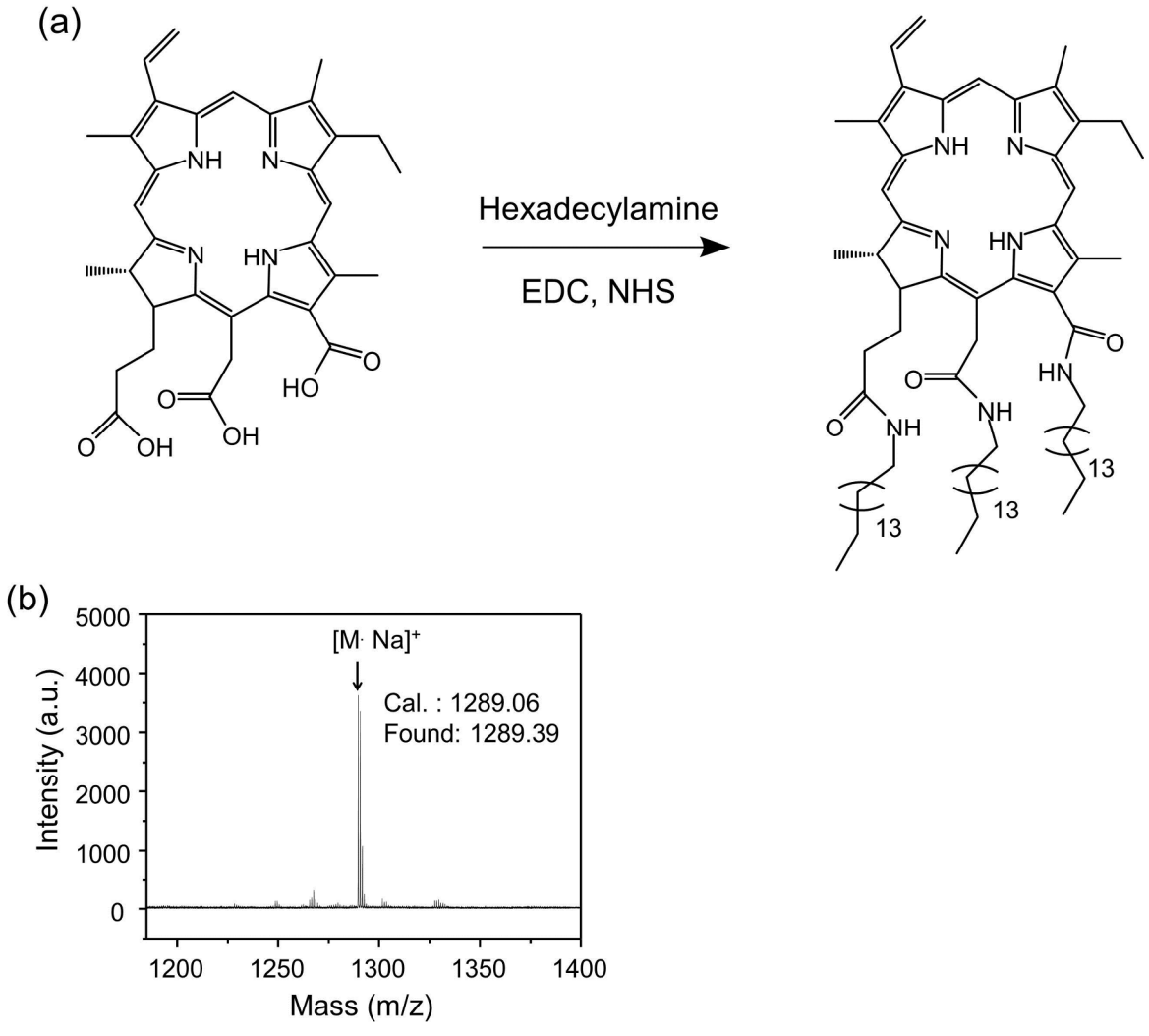


Supporting Figure S1. (a) A scheme showing the synthesis process of hexadecylamine conjugated Ce6 (*h*Ce6). (b) MAIDI-TOF spectrum of as-prepared *h*Ce6.

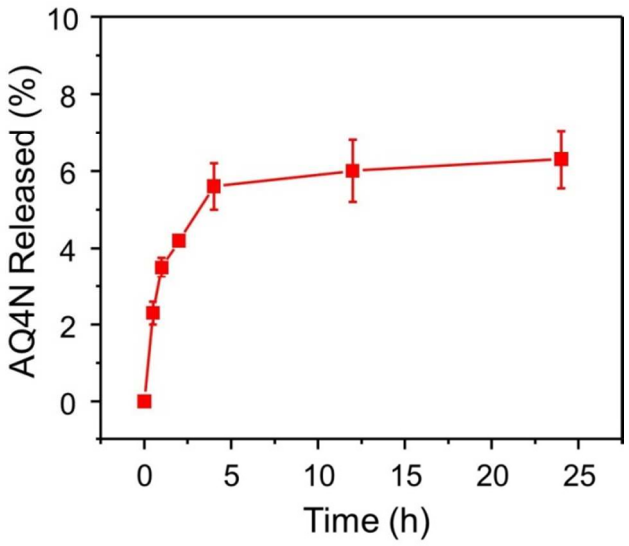


Figure S2. AQ4N release profile from AQ4N-hCe6-liposome in PBS (10 mM, pH7.4). AQ4N-*h*Ce6-liposome (1 mL) in a dialysis tube with a molecular weight cut-off (MWCO) of 3.5 kDa was suspended in a glass vial containing 10 mL PBS (pH 7.4) at 37 ^{o}C. The released AQ4N was determined by its characteristic absorbance at 610 nm.

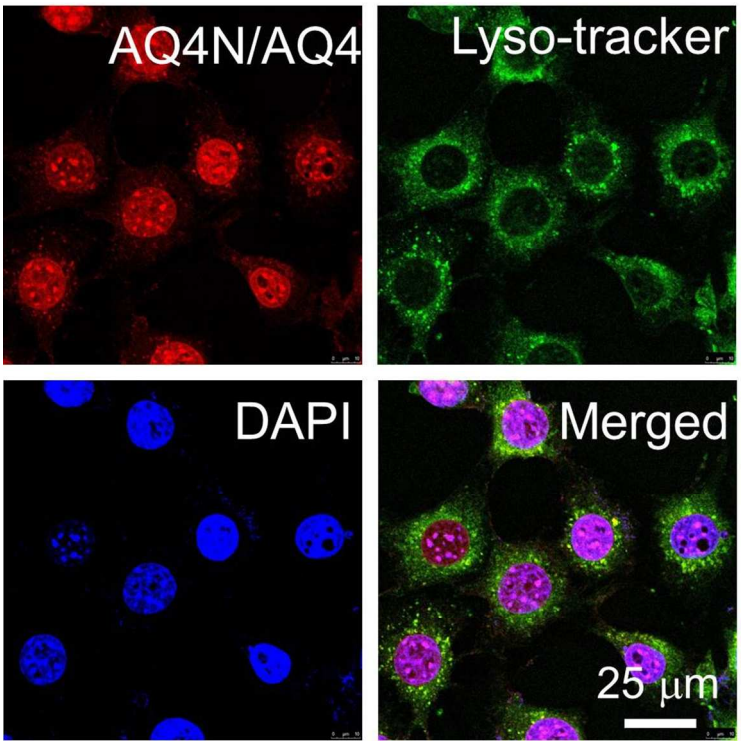
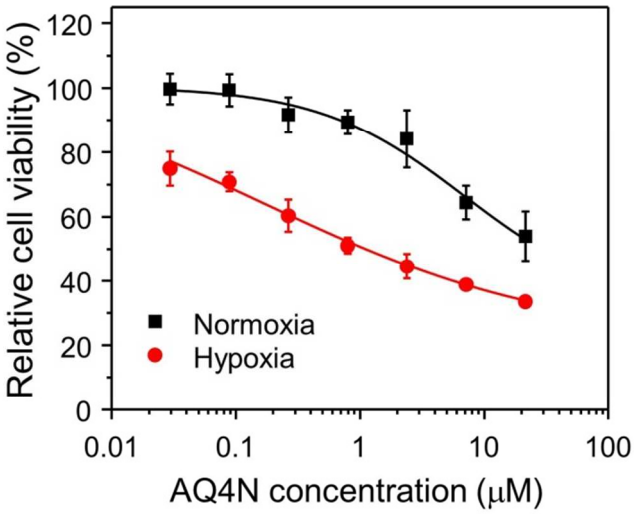


Figure S3. Intracellular distribution profile of AQ4N / AQ4 in 4T1 cells after being incubated with AQ4N-liposome under hypoxic condition for 12 h.



Supporting Figure S4. Relative cell viability of 4T1 cells treated with free AQ4N under normoxic or hypoxic conditions. Error bars were based triplicated measurements.

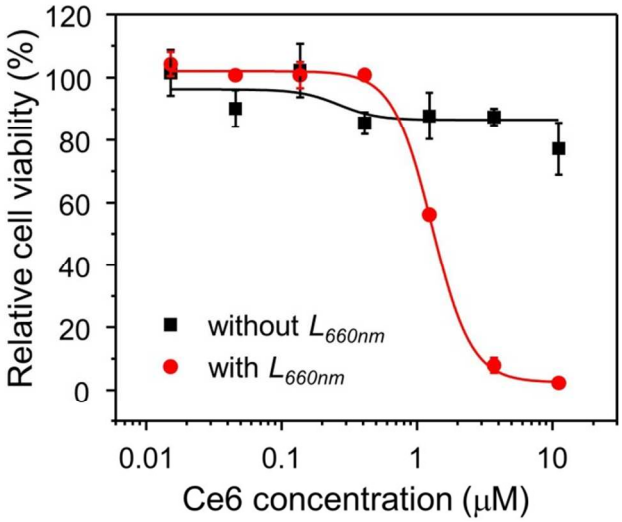
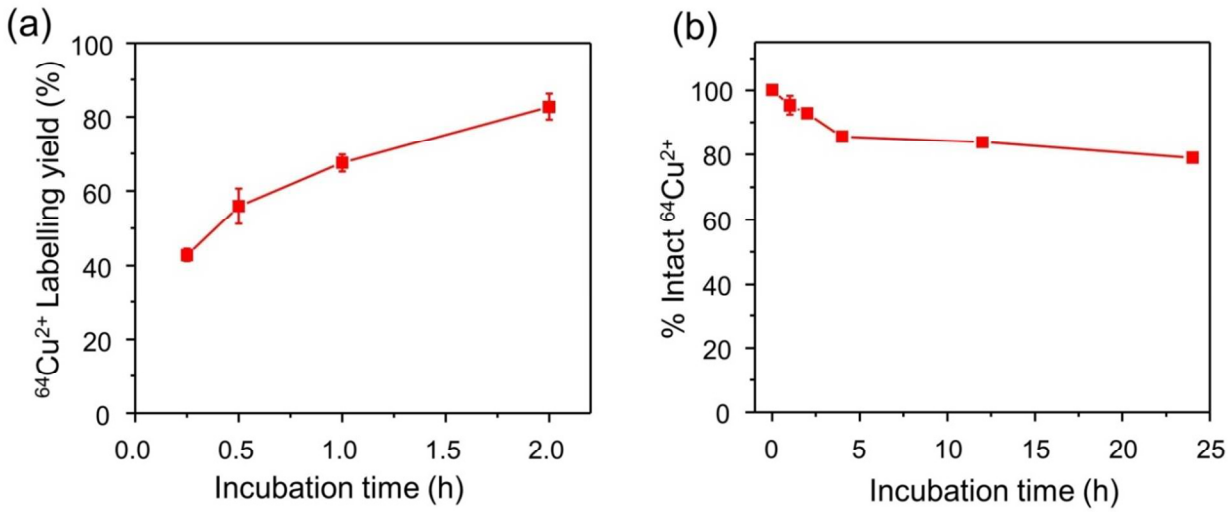


Figure S5. Cytotoxicity of *h*Ce6-liposome to 4T1 cells in the presence or absence of 660-nm LED light irradiation recorded by the standard MTT assay. The error bars were based on triplicated measurements.



Supporting Figure S6. (a) Quantified labeling yields of $^{64}Cu^{2+}$ on AQ4N-*h*Ce6-liposome after incubation for different periods of time. (b) Radiolabeling stability test of ^{64}Cu labeling on AQ4N-*h*Ce6-liposome after incubation in mouse serum at 37 °C for different periods of time. Error bars were based on standard deviations (SD) of three samples at each time point.

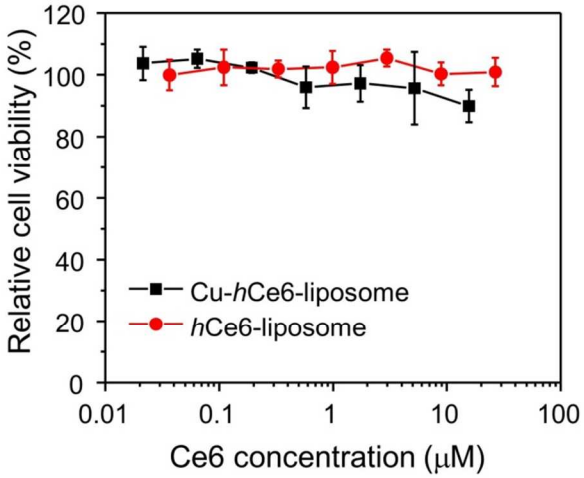
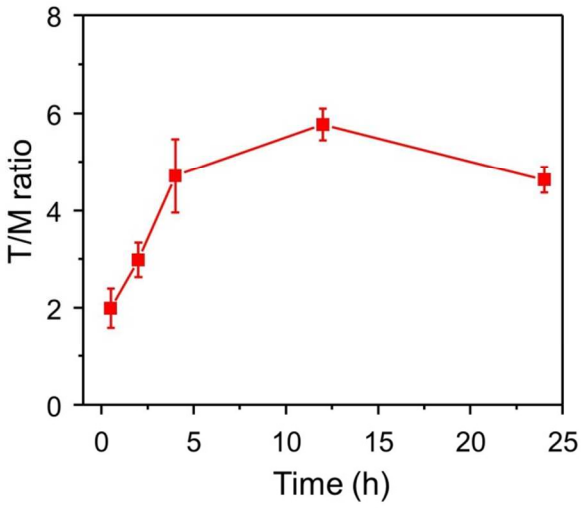
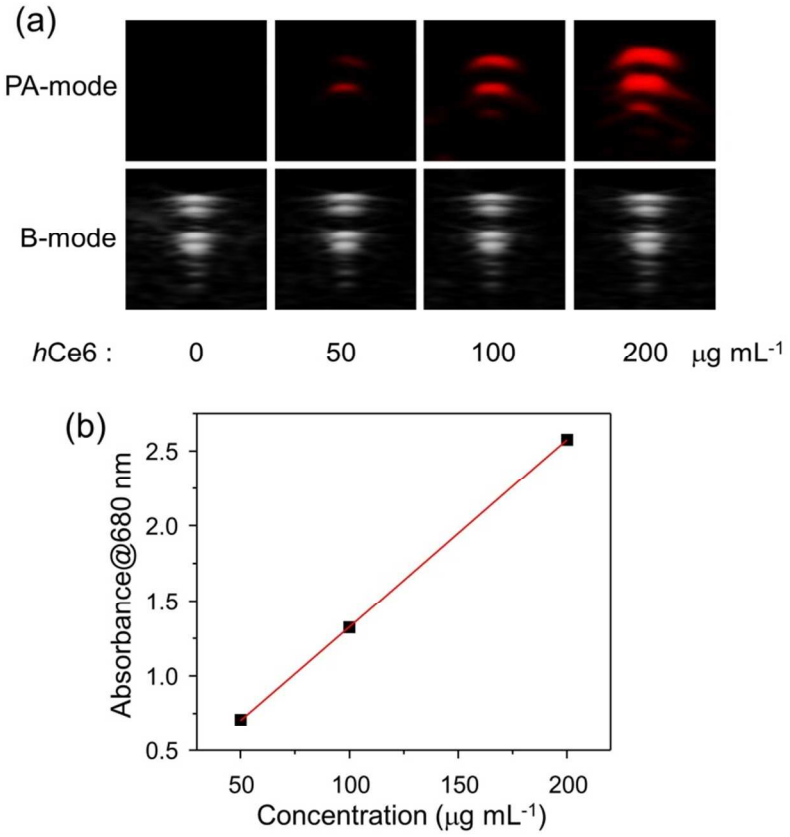


Figure S7. Cytotoxicity of Cu-*h*Ce6-liposome to 4T1 cells recorded by the standard MTT assay



Supporting Figure S8. The tumor/muscle (T/M) ratios at various time points p.i. based on quantification analysis shown in Figure 4b.



Supporting Figure S9. (a) PA imaging of AQ4N-*h*Ce6-liposome at indicated *h*Ce6 concentrations under the Visualsonic Vevo® 2100 LAZER system (680 nm, 21 MHz). (b) Linear correlation of the absorbance of AQ4N-*h*Ce6-liposome at 680 nm against its corresponding concentrations.