Smart Cu(II)-aptamer complexes based gold nanoplatform for tumor micro-environment triggered programmable intracellular prodrug release, photodynamic treatment and aggregation induced photothermal therapy of hepatocellular carcinoma

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Figure S1, (A) The Vis-NIR spectra of Aptamer-SH and Aptamer_{Ce6}-SH; (B) The fluorescence spectra of Aptamer_{Ce6} and Apt_{Ce6} -GNPs.



Figure S2, (A) The fluorescence spectra of Apt_{Ce6} -GNPs in the presence of DTT (10 mM) with different incubation times; (B) The fluorescence spectra of Apt_{Ce6} -GNPs in the absence of DTT (10 mM) with different incubation times; (C) Fluorescence recovery of Apt_{Ce6} -GNPs with or without DTT under different incubation times.



Figure S3, The absorbance of 9, 10-dimethylanthracene (ABDA, 100 μ M) after photodecomposition by ROS generation upon 670 nm laser irradiation at 0.5 W/cm² in the presence of Apt_{Ce6}-GNPs but without incubated with DTT (10 mM) in PBS solution;



Figure S4, Hydrodynamic size distribution of GNPs, Apt_{Ce6}-GNPs and AQ4N-Cu(II)-Apt_{Ce6}-GNPs in water.



Figure S5, The cumulative AQ4N release kinetics of AQ4N-Cu(II)-Apt_{Ce6}-GNPs in PBS buffer (pH 7.4) supplemented with 10% FBS or 10 μ M ssDNA at 37°C (n=3).



Figure S6, (A) Vis-NIR spectra of AQ4N-Cu(II)-Apt_{Ce6}-GNPs in pH 7.4. (B) Vis-NIR spectra of AQ4N-Cu(II)-Apt_{Ce6}-GNPs in pH 4.5.



Figure S7, Hydrodynamic size distribution of AQ4N-Cu(II)-Apt_{Ce6}-GNPs under different pH conditions with (A) or without incubation with 10 mM DTT (B).



Figure S8, Confocal images of HepG2 cells or HeLa cells which were incubated with AQ4N-Cu(II)-Apt_{TAMRA}-GNPs for 4hrs.



Figure S9, Confocal images of HepG2 cells and HeLa cells that received different treatments as indicated: the cells treated with free Ce6 or AQ4N-Cu(II)-Apt_{Ce6}-GNPs without laser irradiation, and none treated cells were taken as control; DCFH-DA was taken as the ROS indicator (scale bar = $50 \mu m$).



Figure S10, Cell viability of LO2 cells treated with different concerntration of AQ4N-Cu(II)-Apt_{Ce6}-GNPs (n = 6).



Figure S11, (C) Cell viability of HepG2 cells treated with Apt_{Ce6}-GNPs or Cu(II)-Apt_{Ce6}-GNPs with or without laser irradiation (670 nm, 0.5 W/cm²) (n = 6), and the statistical analysis was performed with the two-tailed paired Student's T-test, **p<0.01.



Figure S12, (A) Chromatograms of the AQ4N standard (48 μ M); (B)The peak area of various concentration of AQ4N from 2 μ M to 48 μ M at the retention time of 3.297 min.



Figure S13, The average tumor weight of PBS, Ce6, AQ4N-Cu(II)-Apt_{Ce6}-GNPs treated mice when exposed to an 670 nm laser irradiation (0.5 W/cm²) or AQ4N treated mice at the 18 days (n=4), and statistical analysis was performed with the two-tailed paired Student's T-test, *p<0.05, **p<0.01.



Figure S14. The pathological changes of main organs evaluated by H&E staining which were acquired at different time intervals post intravenous injection of AQ4N-Cu(II)-Apt_{Ce6}-GNPs. (Scale bar: 50 μ m). No noticeable pathological changes were observed in these organs.