Targeted tumour theranostics in mice via carbon quantum dots structurally mimicking large amino acids
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Supplementary Methods

Cell culture and materials
Cells except BCSCs were cultured in DMEM or RPMI medium (Invitrogen) supplemented with 10% fetal bovine serum (Invitrogen), 100 units mL\(^{-1}\) penicillin, and 100 μg mL\(^{-1}\) streptomycin (Invitrogen) in a 37 °C incubator containing 5% CO\(_2\). Human BCSCs were enriched and cultured as previously reported \(^1\). All chemicals were purchased from Sigma-Aldrich unless otherwise noted. The antibody against LAT1 was purchased from Novus Biologicals.

Materials and Reagents.
1,4-diaminoanthraquinone (1,4-DAAQ, 90%, Catalogue Number: A19156), 1,5-diaminoanthraquinone (1,5-DAAQ, 97%, Catalogue Number: A18840) were purchased from Alfa. 2,6-diaminoanthraquinone (2,6-DAAQ, 97%, Catalogue Number: D124645-100g) was supplied by Shanghai Aladdin Biochemical Technology Co.,Ltd.. 1,4,5,8-tetraminoanthraquinone (TAAQ, 30%, Catalogue Number: 215643), citric acid (CA, 99.8%, Catalogue Number: 791725), Dichloromethane (99.5%, Catalogue Number: 02575), propidium iodide (PI, 90%, Catalogue Number: 79214), methanol (99.9%, Catalogue Number: 34860) and the cell counting kit-8 (CCK-8, Catalogue Number: C2581-25UL) were purchased from Sigma. The water used throughout all the experiments was purified through a Millipore system (ULUPURE, Chengdu, China). All the BALB/c female mice were purchased from Beijing Laboratory Animal Research Center, and the weight of each mouse was 18-20 g.

Synthesis of LAAM TC-CQDs
0.04 g CA and 0.03 g TAAQ were firstly mixed in 10 mL pure water, and then the solution was transferred into poly(tetrafluoroethylene)-lined autoclaves (25 mL). After heating at 180 °C in oven for 2 hours and cooling down to room temperature naturally, blue suspension was obtained. The crude product was then purified with a silica column chromatography using mixtures of dichloromethane and methanol (10:1) as eluents for three rounds. After removing solvents and further drying under vacuum, the purified LAAM TC-CQDs could be finally obtained in 5 wt% yields.

Synthesis of 1,4-CQDs, 1,5-CQDs, 2,6-CQD, and Phe-CQDs
For synthesis of 1,4-CQDs, 0.04 g CA and 0.03 g 1,4-DAAQ (molar ratio = 3:2) were mixed in 10 mL pure water and transferred into poly(tetrafluoroethylene)-lined autoclaves (25 mL). After heating at 180 °C in an oven for 2 hours and cooling down to room temperature naturally, the resulting crude product was purified with silica column chromatography using mixtures of dichloromethane and methanol (20:1) as eluents. After removing the solvents and further drying under vacuum, 1,4-CQDs were obtained.

1,5-CQDs and 2,6-CQDs were synthesized using the same procedures, except that 1,4-DAAQ was replaced with 1,5-DAAQ and 2,6-DAAQ, respectively.

For synthesis of Phe-CQDs, 0.025 g phenylalanine (Phe) was dissolved in 10 mL ethanol, and was transferred into poly(tetrafluoroethylene)-lined autoclaves (25 mL). After heating at 180
°C in oven for 8 h and cooling down to room temperature naturally, the resulting crude product was purified with silica column chromatography using mixtures of dichloromethane and methanol (50:1) as eluents. After removing solvents and further drying under vacuum, Phe-CQDs were obtained.

**Characterization**

Transmission electron micrographs (TEM) were taken on a JEOL JEM 2100 transmission electron microscope (FEI). Atomic force microscopic (AFM) images were obtained by MultiMode V SPM (VEECO). X-ray diffraction (XRD) patterns were carried out with an X-ray diffraction using Cu-Kα radiation (XRD, PANalytical X’Pert Pro MPD). The Raman spectra were measured using Laser Confocal Micro-Raman Spectroscopy (LabRAM Aramis). X-ray photoelectron spectroscopy (XPS) was performed with an ESCALab 250Xi electron spectrometer from VG Scientific using 300 W Al Kα radiation. UV-vis absorption and fluorescence spectra were recorded on UV-2600 spectrophotometer and a PerkinElmer-LS55 fluorescence spectrometer, respectively. The Fourier transform infrared spectroscopy (FT-IR) were measured using a Nicolet 380 spectograph. The 13C NMR spectra were recorded at 400 MHz on a Bruker Advance III spectrometer in CH3OD, with chemical shift values in parts per million.

**Photothermal effects for LAAM TC-CQDs in aqueous solution**

To evaluate the photothermal effects in aqueous solution, LAAM TC-CQDs aqueous solution at various concentrations (0-10 µg/mL) were exposed to 650 nm laser irradiation (0.5 W/cm²) with the illumination direction from the top to the bottom of the cuvette for 5 min. An equivalent amount of pure water with the same laser irradiation was used as a control. Real-time temperature was recorded every 30 s by an infrared thermal camera.

**Computational methods**

The ground state and the first excited state of one fluorescent unit of CQDs were obtained from theoretical calculation with density function theory (B3LYP/6-31G(d)). The geometric parameters of the ground state were optimized and verified at B3LYP/6-31G(d) leve and the geometric parameters of the first excited state were optimized with TD-B3LYP/6-31G(d).

**Flow cytometry**

MDA-MB-231 SP cells were sorted according to our previously reported methods. Briefly, cells harvested at about 85% confluence were resuspended in RPMI-1640 supplemented with 2% fetal bovine serum (FBS) at a density of 1×10⁶ cells/mL and incubated with Hoechst 33342 at a concentration of 5 µg/mL at 37 °C. After 90 min, the cells were suspended in cold PBS at a concentration of 1×10⁶ cells/mL, filtered through a 40 µm cell strainer to remove cell aggregates, stained with 1 µg/mL propidium iodide (PI), and analyzed and sorted using a FACSDiva (Becton Dickinson, USA). To characterize SP cells, freshly sorted SP cells were suspended in cold PBS and stained with antihuman CD44-FITC and CD24-PE or their appropriate isotype controls on ice for 30 min. The cells were washed 3 times with cold PBS, resuspended in 400 mL of cold PBS, and analyzed by a FACScan flow cytometer (BD, Ann Arbor, MI).
To characterize the interaction between CQDs and cells, selected cells were placed on a 6-well plate and treated with LAAM TC-CQDs at 10 µg/mL. Cells without CQD treatment were used as controls. After 12 h, the cells were washed with fresh medium, trypsinized, resuspended in PBS with 0.5% FBS, and analyzed using a BD FACSCalibur (BD Biosciences, USA). Data were analyzed using FlowJo 7.6.

Confocal laser scanning microscope imaging
To determine cellular uptake, cells were placed on glass chamber slides and treated with CQDs at 10 µg/mL. After 8 h, cells were washed with PBS, fixed with 4% polyformaldehyde for 30 min at room temperature, followed by addition of DAPI for cell nuclei staining. Finally, the slides were washed three times, fixed, sealed with cover glasses, and imaged with excitation/emission: 561/700 using a confocal laser scanning microscopy (Leica TCS-SP8, Germany). To determine the effects of Leu, Phe, Gly or BCH on CQD uptake, HeLa cells were placed and treated with Leu, Phe, Gly or BCH. Four hours later, LAAM TC-CQDs were added to cells. After an additional 8 h, the cells were washed, fixed, and imaged.

PA imaging of LAAM TC-CQDs
LAAM TC-CQDs with different concentrations (0, 2, 4, 6, 8 and 10 µg/mL) were added to agarose tubes (37 ºC) and subjected to scanning using a PA imaging instrument (mode: iTheraMedical Co. MOST inVision 128; excitation wavelength ranged from 640-840 nm with 5 nm interval). PA signal was recorded.

Cellular toxicity tests
Cells were plated into a 96-well plate at a density of 1×10^4 cells per well and treated with LAAM TC-CQDs, TPTC, or TPTC/LAAM TC-CQDs at various concentrations. After 12 h, the cultured medium was removed, and washed with PBS. One hundred microliters of fresh medium containing 10 µL CCK-8 (Sigma) was added to each well. After 2 h incubation at 37 ºC, the absorbance at 450 nm was measured using a microplate reader.

NIR FL imaging of LAAM TC-CQDs in vivo
This project was approved by the Animal Use Committee at Beijing Normal University and Yale IACUC. For establishment of mice bearing HeLa tumors, 2×10^6 HeLa cells were prepared and subcutaneously inoculated into female BALB/c mice. When the tumor volumes reached about ~100 mm^3, LAAM TC-CQDs (5 mg/kg) was intravenously administered into mice. NIR FL images were captured at 1, 2, 4, 6, 8 and 10 h using an animal optical imaging system (IVIS SpectrumCT, PerkinElmer). The same method was used to image mice bearing U87 gliomas (Fig. 5a) or A549/HeLa tumors (Fig. S31, S37), except that the mice were continuously anaesthetized and images were captured at various time points.

PA imaging of LAAM TC-CQDs in vivo
Prior to intravenous injection of LAAM TC-CQDs, pre-contrast data with excitation wavelength from 640 to 840 nm were obtained. Tumor-bearing mice were treated with LAAM TC-CQDs at 5 mg/kg. Post-contrast data were acquired at 2, 4, 6, 8 and 10 h after injection. PA
images were reconstructed using data acquired from all 128 transducers at each view through a modified back-projection algorithm.

**Therapeutic evaluation in tumor-bearing mice**

HeLa cells were subcutaneously inoculated into female BALB/c mice. When the tumor volumes reached ~100 mm$^3$, the mice were intravenously administered with saline, TPTC or TPTC/LAAM TC-CQDs ($n = 5$). Changes in tumor volume and body weight were monitored daily. The volume of the tumor was calculated according to the following formula: $V = D \times d^2/2$ (where $D$ and $d$ is the longest and shortest diameters of tumor, respectively, measured using a vernier caliper). Relative tumor volumes were calculated as $V/V_0$ ($V_0$ is the initial tumor volume when the treatment was started).

**Toxicity evaluation in mice**

Female BALB/c mice were intravenously administered with TPTC (10 mg/kg, 0.05 mL per mice) or TPTC/LAAM TC-CQDs (10 mg/kg for TPTC, 0.05 mL per mice) ($n = 5$). Mice treated with saline were used as controls. At selected time points, blood samples were collected in heparinized microhematocrit tubes and centrifuged at a speed of 3000 rpm for 10 min. At the end of the study, mice were euthanized. Major organs, including the heart, liver, spleen, kidney and brain were excised, fixed in formalin, and analyzed.

**Evaluation in brain cancer models**

For establishment of mice bearing brain tumors, nude mice were anesthetized and positioned on small animal stereotaxic frames. Fifty-thousand luciferase-expressing U87 cells in 2 μL of PBS were injected into the right striatum 2 mm lateral and 0.5 mm anterior to the bregma and 3.3 mm below the dura using a stereotactic apparatus with a UltraMicroPump (UMP3) (World Precision Instruments, FL). The animals’ weight, grooming, and general health were monitored on a daily basis. Animals were euthanized after either a 15% loss in body weight or when it was humanely necessary due to clinical symptoms.

**Statistical analysis**

All data were collected in triplicate and reported as mean and standard deviation. Comparison of two conditions was evaluated by the unpaired t-test. One-way ANOVA analysis was carried out to determine the statistical significance of treatment related to survival. $p < 0.05$ (*), 0.01 (**), and 0.0001 (****) were considered significant.
Figure S1. Synthesis and separation diagram of LAAM TC-CQDs.

Figure S2. Characterization of fluorescence emission spectra (a) and quantum yield (b) of LAAM TC-CQD dialysates collected at the indicated time points. Fluorescence from small molecular fragment by-products generated form hydrothermal synthesis is often a major concern in CQD synthesis.\textsuperscript{24-28} We found that purification using silica column chromatography for three rounds is the most effective for this specific CQDs and further dialysis, which is useful for purification of some CQDs,\textsuperscript{29} did not provide additional benefits.
Figure S3. The size distribution of LAAM TC-CQDs.

Figure S4. Raman spectrum of the LAAM TC-CQDs.
Figure S5. (a) AFM image of the LAAM TC-CQDs on a Si substrate. (b) Height profile along the lines in (a).

Figure S6. XRD pattern of the LAAM TC-CQDs.

Figure S7. Characterization of the amount of amino acid groups on the edge of each LAAM TC-CQD. (a) UV-vis spectra of Asp, Glu, Met, Phe, Tyr and Gly after ninhydrin reactions. (b) Correlation of glycine concentration and absorbance of glycine after ninhydrin reaction. (c) UV-vis spectra of LAAM TC-CQD solution before and after ninhydrin reaction.
Figure S8. XPS survey spectrum of the LAAM TC-CQDs.

Figure S9. C1s spectra of LAAM TC-CQDs.

Figure S10. N1s spectra of LAAM TC-CQDs.
Figure S11. FT-IR spectra of LAAM TC-CQDs.

Figure S12. $^{13}$C-NMR spectra of LAAM TC-CQDs.
Figure S13. The main geometric parameters (Å) for the optimized ground (a) and excited (b) structures of one FL unit of LAAM TC-CQDs. The optimized electron delocalization molecular orbital (MO) diagrams of LAAM TC-CQDs (c, d) and its band positions (e) obtained from theoretical calculation with density functional theory calculations (B3LYP/6-31G(d,p)).

Figure S14. Characterization of FL emission spectrum of LAAM TC-CQDs. (a) FL emission spectrum of LAAM TC-CQD aqueous solution with various excitation wavelength from 560 to 660 nm.; (b) Full excitation emission map (EMM) of LAAM TC-CQDs.
Figure S15. (a) The photothermal curves of LAAM TC-CQDs at various concentrations (0-10 μg/mL) under 650 nm laser irradiation (0.5 W/cm²) recorded every 30 s. The inset are IR thermal images of LAAM TC-CQDs (0-10 μg/mL) after 650 nm laser irradiation (0.5 W/cm²) for 5 min. Data are presented as means ± s.d. (n=5). (b) The temperature change of LAAM TC-CQDs (10 μg/mL) for five laser on/off cycles (650 nm laser irradiation, 0.5 W/cm²). (c) Photothermal effect of the LAAM TC-CQDs aqueous solution when illuminated with 650 nm laser (0.5 W/cm²). The laser was shut off after irradiation for 5 min. (d) Plot of cooling time versus negative natural logarithm of the temperature driving force obtained from the cooling stage as shown (c). The time constant for heat transfer of the system was determined to be $\tau_s = 83.86$ s.

Given their efficient NIR absorption features, the photothermal performance of LAAM TC-CQDs aqueous solution are investigated. The temperatures of LAAM TC-CQDs aqueous solution at various concentrations (0-10 μg/mL) are monitored under continuous laser irradiation (650 nm, 0.5 W/cm²) with an infrared thermal camera, as displayed in Fig. S12a. No obvious temperature rise is observed in the control sample of pure water, while LAAM TC-CQDs (10 μg/mL) could quickly trigger the increase of temperature and display a concentration-dependent hyperthermia (above 42 °C) during a short photoirradiation (5 min), leading to an irreversible damage to tumor cells. To further study the photothermal stability and transduction efficiency of LAAM TC-CQDs, LAAM TC-CQDs aqueous solution (10 μg/mL, 3 mL) is continuously illuminated by a 650 nm laser (0.5 W/cm²) until it reaches a steady-state temperature, at which point the laser is stopped and the suspension is allowed to cool naturally. The temperature change during the heating-cooling process is monitored for five cycles to derive a heat generation-dissipation curve as shown in Fig. S12b. An almost equal temperature elevation of 25.6 °C occurred during each laser ON/OFF cycle, suggesting that LAAM TC-CQDs possess preferable photothermal stability compared with extensively used organic dyes and inorganic nanomaterials with surface plasmon resonance. The photothermal conversion efficiency ($\eta$) of LAAM TC-CQDs was calculated using the following equation.
\[ \eta = \frac{hS(T_{\text{Max}} - T_{\text{Surr}}) - Q_{\text{dis}}}{I(1 - 10^{-A_{\text{650}}})} \]  

(1)

Where \( h \) is heat transfer coefficient, \( S \) is the surface area of the container, \( T_{\text{Max}} \) is the maximum system temperature, \( T_{\text{Surr}} \) is ambient temperature of the surroundings, \( Q_{\text{dis}} \) is the baseline energy inputted by the sample cell, \( I \) is incident laser power and \( A_{\text{650}} \) is the absorbance of the LAAM TC-CQDs at wavelength of 650 nm. \( (T_{\text{Max}} - T_{\text{Surr}}) \) is 25.6 °C according to Fig. S12c, \( I \) is 0.5 W/cm² and \( A_{\text{650}} \) is 1.4908. \( Q_{\text{dis}} \) expresses heat dissipated from light absorbed by the quartz sample cell itself, and it was measured independently to be 37.2 mW using a quartz cuvette cell containing pure water without LAAM TC-CQDs. Thus, only \( hS \) remains unknown for calculating \( \eta \).

In order to get \( hS \), a dimensionless driving force temperature (\( \theta \)) and a sample system time constant \( \tau_s \) are introduced.

\[ \theta = \frac{T - T_{\text{Surr}}}{T_{\text{Max}} - T_{\text{Surr}}} \]  

(2)

\[ \tau_s = \frac{\sum m_i C_{p,i}}{hS} \]  

(3)

Where \( m \) and \( C_p \) are the mass and heat capacity of water, respectively. When \( \theta \) and \( \tau_s \) are substituted into the following total energy balance equation (4) for the system, Equation (5) is yielded.

\[ \sum m_i C_{p,i} \frac{dT}{dt} = Q_{\text{NC}} + Q_{\text{dis}} - Q_{\text{Surr}} \]  

(4)

Where \( Q_{\text{NC}} \) is the energy inputted by LAAM TC-CQDs, and \( Q_{\text{Surr}} \) is heat conduction away from the system surface by air.

\[ \frac{d\theta}{dt} = \frac{1}{\tau_s} \left[ \frac{Q_{\text{NC}} + Q_{\text{dis}}}{hS(T_{\text{Max}} - T_{\text{Surr}})} - \theta \right] \]  

(5)

At the cooling stage of the aqueous dispersion of the LAAM TC-CQDs, the light source was shut off, and \( Q_{\text{NC}} + Q_{\text{dis}} = 0 \).

\[ dt = -\tau_s \frac{d\theta}{\theta} \]  

(6)

\[ t = -\tau_s \ln \theta \]  

(7)

Therefore, time constant for heat transfer from the system is determined to be \( \tau_s = 83.86 \) s by applying
the linear time data from the cooling period (after 300 s) vs negative natural logarithm of driving force temperature (Fig. S12d). In addition, \( m \) is 0.3 g and \( C_p \) is 4.2 J/g. Thus, according to equation (3), \( hS \) is deduced to be 16.1 mW/°C. Substituting 16.1 mW/°C of \( hS \) into equation (1), the \( \eta \) of LAAM TC-CQDs can be calculated to be 77.4%, which is comparable to that of the previously reported photothermal conversion agents (PTCAs), such as Au bellflowers (74%), Au nanocages (64%), Au nanorods (55%), dopamine-melanin nanospheres (40%), carbon dots (38.5%), CuOSe nanocrystals (25.7%), Cu2xSe nanocrystals (22%), and so on (Supplementary Tab. 3)\textsuperscript{33-15}.

**Figure S16.** Photoacoustic (PA) signal intensities of LAAM TC-CQDs at concentrations ranging from 0 to 10 μg/mL.

**Figure S17.** PA signal intensity and imaging (insert) of LAAM TC-CQDs at concentrations ranging from 2 to 10 μg/mL.
Figure S18. Characterization of side population cells sorted from MDA-MB-231 cells. (a) was from the cells stained with isotype controls; (b) was from the cells stained with anti-human CD44-FITC and CD24-PE antibodies. CSCs cells were analyzed with flow cytometry.

Figure S19. LCSM images of different types of cancer cells co-incubated with LAAM TC-CQDs. The scale bar is 100 μm.
Figure S20. LCSM images of different types of normal cells co-incubated with LAAM TC-CQDs. The scale bar is 100 μm.

Figure S21. Uptake rates of LAAM TC-CQDs in 21 types of cancer cells obtained by flow cytometric profiles.
Figure S22. Uptake rates of LAAM TC-CQDs in 18 types of normal cells obtained by flow cytometric profiles.

Figure S23. Imaging analyses of LAAM TC-CQDs in representative BCSCs.
Figure S24. Flow cytometry analyses of LAAM TC-CQDs in BCSCs.

Figure S25. LCSM images of HeLa cells treated with LAAM TC-CQDs for different time (1-8 h). The scale bar is 25 μm.
Figure S26. LCSM images of CCC-ESF-1 cells (blue, Hoechst 33342) treated with LAAM TC-CQDs (red). Images were captured from the same slide at the indicated time points. Scale bar: 25 μm.

Figure S27. Semiquantitative biodistribution of LAAM TC-CQDs in tumor-bearing mice determined by the averaged FL intensity of major organs and tumors. Data are presented as means ± s.d. (n=5).
Figure S28. The PA signal intensities at the tumor area for different times. Data are presented as means ± s.d. (n=5).

Figure S29. NIR FL images of mice with subcutaneous tumor xenografts derived from A549 (a), PANC-1 (b), MCF-7 (c) and MD-MBA-231 (d) cells following intravenous injection of LAAM TC-CQDs during 10 h. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr). Images are set on the same scale.
Figure S30. Ex vivo NIR FL imaging of major organs (heart, liver, spleen, lung and kidney) and tumors from nude mice with subcutaneous tumor xenografts derived from A549 (a), PANC-1 (b), MCF-7 (c) and MD-MBA-231 (d) cells after the injection of LAAM TC-CQDs at 8 h post-injection. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr).

Figure S31. Representative NIR FL images of nude mice with A549 tumor (left) and HeLa tumor (right). Following injection of LAAM TC-CQDs, mice were anaesthetized. Images were captured at the indicated time points. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr). Images are set on the same scale.
Figure S32. Ex vivo NIR FL imaging of major organs (heart, liver, spleen, lung and kidney) and tumors from nude mice with hepatic (A549) tumor left and ovarial (HeLa) tumor right after the injection of LAAM TC-CQDs at 8 h post-injection. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr).
Figure S33. LCSM images of HeLa and CCC-ESF-1 cells treated with G-CQDs, Y-CQDs, B-CQDs and B,S-CQDs, respectively. The scale bar is 100 μm. Note: G-CQDs refer to green fluorescent CQDs synthesized by pyrolysis of citric acid; Y-CQDs refer to yellow fluorescent CQDs synthesized by electrolysis of graphite in alkaline condition and reduction of the products with hydrazine at room temperature; B-CQDs refer to boron (B) doped CQDs synthesized by electrolysis of graphite in borax aqueous solution; B,S-CQDs refer to boron (B) and sulfur (S) co-doped CQDs synthesized by electrolyzing graphite rods in sodium p-toluenesulfonate (TsONa) acetonitrile solution.

Figure S34. The uptake rates of G-CQDs, Y-CQDs, B-CQDs and B,S-CQDs in HeLa and CCC-ESF-1 cells. Data are presented as means ± s.d. (n=5).

Figure S35. Three-dimensional reconstruction of G-CQDs distribution in the tumor 8 h after injection.
**Figure S36.** Quantification of G-CQDs in the indicated organs and tumors based on FL intensity 8 h after injection. Representative FL images can be found in our recent publication (Li S. ACS Appl Mater Interfaces. 2017, 9: 22332). Data are presented as means ± s.d. (n=5).

**Figure S37.** Representative NIR FL images of nude mice with A549 tumor (left) and HeLa tumor (right). Following injection of FA-G-CQDs, mice were anaesthetized. Images were captured at the indicated time points. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr). Images are set on the same scale.
**Figure S38.** Ex vivo NIR FL imaging of major organs (heart, liver, spleen, lung and kidney) and tumors after the injection of FA-G-CQDs at 8 h post-injection. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr).

**Figure S39.** FL emission spectrum of LAAM TC-CQDs in the indicated pH (a) or in the presence of amino acids (Asp, Glu, Met, Phe, Tyr and Gly) or MMP-2 (b).
Figure S40. Photostability of LAAM TC-CQDs after long time storage or irradiation. (a) PL spectra of freshly prepared LAAM TC-CQDs solution (black) and LAAM TC-CQDs three months after storage at room temperature (red). (b) Change of ratio of PL intensity of LAAM TC-CQDs after irradiation at the indicated time point ($F$) to that of fresh LAAM TC-CQDs ($F_0$) with time. Data are presented as means ± s.d. (n=5).

Figure S41. Characterization of the impact of 5 hours UV irradiation at 365 nm on fluorescence intensity, surface groups, and cancer-targeting specificity of LAAM TC-CQDs. (a) Fluorescence emission spectra of LAAM TC-CQDs before (black) and after (red) UV irradiation. (b) UV-vis spectra of LAAM TC-CQDs before (black) and after (red) UV irradiation after treatment of ninhydrin. (c) Flow cytometry analysis of uptake of control and UV irradiation-treated LAAM TC-CQDs in HeLa cells and CCC-ESF-1 cells. Data are presented as means ± s.d. (n=5).
Figure S42. Characterization of serum stability of LAAM TC-CQDs. (a,b) Size distributions of fresh LAAM TC-CQDs (a) and LAAM TC-CQDs after incubation in PBS buffer containing 10% FBS for 30 days. (c) Change of ratio of PL intensity of LAAM TC-CQDs after incubation in PBS buffer containing 10% FBS at the indicated time point (F) to that of fresh LAAM TC-CQDs (F0) with time.

![Graph showing cellular uptake rate distribution](image)

- Hela
- A549
- PANC-1
- MCF-7
- MDA-MB-231
- Breast CSCs

Figure S43. The uptake rates of LAAM TC-CQDs (control), LAAM TC-CQDs pretreated with Leu, Phe, Gly or BCH in HeLa, A549, PANC-1, MCF-7, MDA-MB-231 and MDA-MB-231 SP CSCs cells. Data are presented as means ± s.d. (n=3).

![Graph showing uptake rates](image)

Figure S44. Full scans of the blots (a) and the uptake rates of LAAM TC-CQDs in wild type HeLa cells, sgLAT1-1 and sgLAT1-2 HeLa cells, respectively (b). Data are presented as means ± s.d. (n=3).
Figure S45. The relative LAT1 expressions in different types of cells were measured by WB tests.

Figure S46. Characterization of the affinity of binding between LAT1 protein and LAAM TC-CQDs by surface plasmon resonance (SPR) (a) or HeLa cells (b). Data are presented as means ± s.d. (n=3).

Regarding characterization of the binding of LAAM TC-CQDs with LAT1 protein: LAT1 was expressed and extracted according previously reported procedures, and coated to a CM5 chip using an Amine coupling kit (GE Healthcare). Single cycle kinetic experiments were performed without regeneration. The binding was determined by surface plasmon resonance on a BIAcore T100 (GE Healthcare). Regarding characterization of the binding using HeLa cells: The measurement of Km was performed in the presence and absence of inhibitors (BCH). To determine the non-specific binding, cells were pretreated with BCH, a LAT1 inhibitor, at 5 mM, following with LAAM TC-CQD treatment and flow cytometry analysis. The fluorescence intensity was obtained by flow cytometry on a population of 10,000 cells. LAT1-dependent uptake was obtained by subtracting the non-specific binding from the total binding. $K_m$ was obtained by fitting the Michaelis-Menten equation to the data using weighted nonlinear least-squares.
Figure S47. Docking analysis of the binding between LAT1 and LAAM TC-CQDs. (a,b) Docked model of LAT1–4F2hc and LAAM TC-CQDs in different view mode. The docked structures of LAAM TC-CQDs and residues Lys 77, Lys 453, Asn 242, Leu 238 and Trp 452 are shown as sticks. Atoms are colored by type with red and blue corresponding to oxygen and nitrogen. Carbon atoms at different positions are colored in yellow, green and wathet, respectively.

In order to establish the complex model containing both LAT1–4F2hc and substrate LAAM TC-CQDs, LAAM TC-CQDs was first docked into the active site of the crystal structure of LAT1–4F2hc (PDB code: 6IRS) using AutoDock 4.2. The geometry structure of the ligand LAAM TC-CQDs molecule was optimized by density functional theory (DFT) method B3LYP functional with 6–31G(d) basis set. In the docking process, the protein was set to be rigid except the side chain of residues Lys 77, Lys 453, Glu 78, Asn 242, Leu 238 and Trp 452, which were flexible. The ligand LAAM TC-CQDs was set to be rotatable bonds to allow it to better fit in the pocket. A cubic grid having 92 × 88 × 78 grid points and a spacing of 0.736 Å was chosen to ensure complete coverage of the region of interest. Docking simulations were performed using the AutoDock Lamarckian Genetic algorithm. Default docking parameters were applied. All the docking simulations were performed for 100 runs.

Figure S48. Flow cytometry analysis of LAAM TC-CQDs uptake in Hela cells without and with treatment of Genistein (Gen), Chlorpromazine (Chl), or BCH. Data are presented as means ± s.d. (n=3).
Figure S49. Kinetics of LAAM TC-CQD uptake in Hela cells without (black) and with (blue) the presence of BCH. Data are presented as means ± s.d. (n=3).

Figure S50. LCSM imaging (a) and quantification (b) of intracellular and extracellular concentrations of LAAM TC-CQDs after 12 hours incubation. scale bar: 40 μm.

HeLa cells were incubated with 10 μg/mL LAAM TC-CQDs on poly-L-lysine (PLL)-coated coverslips. After 8 h, cells were washed with PBS twice, fixed with 4% polyformaldehyde for 30 min at room temperature. The culture medium was collected. The fluorescence intensity of cells and culture medium were determined using a confocal laser scanning microscopy.
**Figure S51.** Flow cytometry quantification of LAAM TC-CQDs in HeLa cells with the indicated treatment. LAAM TC-CQDs were added to HeLa cells at 10 μg/mL concentration. After 12 hours, the medium containing LAAM TC-CQDs was removed and replaced with medium containing leucine at 10 μg/mL concentration. After additional 2 hours, the cells, together with control untreated cells and cells without treatment of leucine, were collected and subjected to flow cytometry analysis. Data are presented as means ± s.d. (n=5).

**Figure S52.** UV-vis absorption spectra of (a) LAAM TC-CQDs, TPTC and TPTC/LAAM TC-CQDs, (b) LAAM TC-CQDs, DOX and DOX/LAAM TC-CQDs, and (c) LAAM TC-CQDs, HCPT and HCPT/LAAM TC-CQDs aqueous solution.

**Figure S53.** The FL emission spectrum of TPTC.
Figure S54. Mean FL intensities of TPTC and TPTC/LAAM TC-CQDs in the nuclei were calculated using Image-Pro Plus 6.0 software. Data are presented as means ± s.d. (n=5).

Figure S55. A representative image of TPTC/liposomes. Liposomes were synthesized according to the standard extrusion method as previously reported\textsuperscript{22,23}. 
Figure S56. NIR FL images of nude mice with bearing HeLa tumors right after the intravenous injection of TPTC or TPTC/LAAM TC-CQDs during 10 h. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr).

Figure S57. Ex vivo NIR FL imaging of major organs (heart, liver, spleen, lung and kidney) and tumors from nude mice bearing HeLa tumors after the intravenous injection of TPTC or TPTC/LAAM TC-CQDs at 8 h post-injection. Colour bar is displayed with intensities reported in units of radiance (p/sec/cm²/sr).
Figure S58. (a) Representative images of tumor-bearing mice receiving the indicated treatments. (b) Representative images of tumors obtained from mice receiving the indicated treatments at day 15 after treatment.

Figure S59. Characterization of LAAM TC-CQDs in HeLa (a,b) and A549 (c,d) mouse xenografts. (a, c) Tumor growth curves for individual HeLa tumor- (a) or A549 tumor- (c) bearing mice in the indicated treatment group. (b, d) Kaplan-Meier survival curves for mice bearing intracranial HeLa (b) or A549 (d) tumours received the indicated treatments.

Figure S60. Change of body weight with time in mice bearing intracranial HeLa (a) or A549 (b) tumours received the indicated treatments. Data are presented as means ± s.d. (n=5).
Figure S61. Histological evaluation of major organs from mice treated with saline, TPTC or TPTC/LAAM TC-CQDs. Each organ was sliced for H&E staining. The scale bar is 200 μm.
Figure S62. The complete blood panel data from healthy control and treated mice, including WBC (a), RBC (b), HGB (c), HCT (d), MCV (e), MCH (f), MCHC (g), PLT (h), RDW (i), PDW (j), MPV (k) and PCT (l). All the parameters of blood analysis fell well in the normal range. No significant difference in all blood test data was noticed between control and treated groups. Error bars were based on five mice per group. Data are presented as means ± s.d. (n=5).

Figure S63. Serum biochemical parameters measurements. (a) Three indicators including ALT, AST and ALP for hepatic function, and another two, UREA (b) and CREA (c) for renal function were evaluated via blood samples from healthy control and treated mice. Data are presented as means ± s.d. (n=5).
Figure S64. Characterization of metabolism of LAAM TC-CQDs after intravenous administration. (a) Correlation of LAAM TC-CQD concentration with its fluorescence intensity (excited at 600 nm). (b,c) Quantification of LAAM TC-CQDs in urine (b) and feces (c) with time after intravenous injecting at 5 mg/kg. Control mice received treatment of saline. Data are presented as means ± s.d. (n=3).

Figure S65. Characterization of TPTC/LAAM TC-CQDs in U87 brain tumor-bearing mice. (a) Schematic diagram of in vitro BBB model. (b) Changes in serum concentration of TPTC, when delivered in form of free drug or with TPTC/LAAM TC-CQDs, with time. Data are expressed as percentage of total injected dose (% ID). (c) Change of body weight with time in mice received the indicated treatments. Data are presented as means ± s.d. (n=5).
Figure S66. Preparation of NH$_2$ null LAAM TC-CQDs and COOH null LAAM TC-CQDs.

Figure S67. FL emission spectra of NH$_2$ null LAAM TC-CQDs (a) and COOH null LAAM TC-CQDs (b). (c) The normalized FL emission spectra of LAAM TC-CQDs ($\lambda_{ex} = 600$ nm), NH$_2$ null LAAM TC-CQDs ($\lambda_{ex} = 580$ nm) and COOH null LAAM TC-CQDs ($\lambda_{ex} = 600$ nm), respectively.
Figure S68. The FT-IR spectra of NH$_2$ null LAAM TC-CQDs (a) and COOH null LAAM TC-CQDs (b).

Figure S69. The uptake of LAAM TC-CQDs, NH$_2$ null LAAM TC-CQDs and COOH null LAAM TC-CQDs in HeLa and CCC-ESF-1 cells obtained by flow cytometric profiles.
Figure S70. Preparation of (a) 1,4-CQDs, (b) 1,5-CQDs and (c) 2,6-CQDs by hydrothermal treatment of CA and 1,4-DAAQ, 1,5-DAAQ or 2,6-DAAQ, respectively.

Figure S71. TEM image of 1,4-CQDs (a), 1,5-CQDs (b) and 2,6-CQDs (c). The scale bar is 10 nm. AFM image of 1,4-CQDs (d), 1,5-CQDs (e) and 2,6-CQDs (f) on a Si substrate. The insets in Figure S59d-e are height profiles along the lines.

Figure S72. Raman (a), XRD (b) and FT-IR spectra of 1,4-CQDs, 1,5-CQDs and 2,6-CQDs.
Figure S73. XPS survey (a), C1s (b, c, d) and N1s (e, f, g) spectra of 1,4-CQDs, 1,5-CQDs and 2,6-CQDs.

Figure S74. (a) UV-vis absorption and FL spectra of 1,4-CQDs (b), 1,5-CQDs (c) and 2,6-CQDs (d), respectively.
**Figure S75.** The optimized electron delocalization molecular orbital (MO) diagrams of one FL unit of (a) 1,4-CQDs, (b) 1,5-CQDs and (c) 2,6-CQDs obtained from theoretical calculation with density functional theory calculations (B3LYP/6-31G(d,p)).

**Figure S76.** The uptake of LAAM TC-CQDs, 1,4-CQDs, 1,5-CQDs and 2,6-CQDs in HeLa and CCC-ESF-1 cells obtained by flow cytometric profiles.

**Figure S77.** (a) Preparation of Phe-CQDs via solvothermal method by using Phe and ethanol as precursor.

**Figure S78.** The TEM (a) and HRTEM (b) image of Phe-CQDs.
Figure S79. FT-IR (a), XPS survey (b), C1s (c), N1s (c), and O1s (e) spectra of Phe-CQDs.

Figure S80. The UV-vis absorption (a) and FL emission (b) spectra of Phe-CQDs.
Figure S81. The uptake of LAAM TC-CQDs and Phe-CQDs in HeLa and CCC-ESF-1 cells obtained by flow cytometric profiles.
Table S1. Optimized cartesian coordinates (Å) of the FL unit for ground state and excited state.

| Species | Cartesian coordinates |
|---------|-----------------------|
|         |                      | Ground state |
|         |                      | C            | -2.764883000 | 0.834352000 | -0.192789000 |
|         |                      | C            | -3.524862000 | 2.024114000 | -0.611560000 |
|         |                      | N            | -2.795185000 | 3.203204000 | -0.716309000 |
|         |                      | C            | -1.443244000 | 3.315502000 | -0.546818000 |
|         |                      | C            | -0.705703000 | 2.140280000 | -0.407935000 |
|         |                      | C            | -1.374222000 | 0.849602000 | -0.344996000 |
|         |                      | C            | -0.503083000 | -0.334604000 | -0.441505000 |
|         |                      | C            | -0.964823000 | -1.593053000 | -0.850744000 |
|         |                      | N            | -4.435073000 | 0.475433000 | 1.515857000 |
|         |                      | C            | -3.643771000 | -0.246351000 | 0.488761000 |
|         |                      | C            | 0.704029000  | 2.253794000 | -0.214384000 |
|         |                      | C            | 1.485176000  | 1.102994000 | -0.075788000 |
|         |                      | C            | 0.897790900  | -0.199868000 | -0.216694000 |
|         |                      | C            | -0.806906000 | 4.595263000 | -0.520000000 |
|         |                      | C            | 0.539384000  | 4.699491000 | -0.312365000 |
|         |                      | C            | 1.355558000  | 3.531184000 | -0.132299000 |
|         |                      | C            | 1.760430000  | -1.315492000 | -0.242612000 |
|         |                      | C            | 1.240699000  | -2.586030000 | -0.581203000 |
|         |                      | C            | -0.112937000 | -2.692483000 | -0.912315000 |
|         |                      | N            | 2.664121000  | 3.679891000 | 0.115455000 |
|         |                      | C            | 3.424159000  | 2.561545000 | 0.263820000 |
|         |                      | C            | 2.867532000  | 1.240616000 | 0.139644000 |
|         |                      | C            | 3.686704000  | 0.089266000 | 0.244490000 |
|         |                      | N            | 3.114950000  | -1.181344000 | 0.020996000 |
|         |                      | O            | -4.728171000 | 2.057800000 | -0.905187000 |
|         |                      | C            | -2.818500000 | -1.276894000 | 1.298608000 |
|         |                      | O            | -2.064374000 | -0.968841000 | 2.200127000 |
|         |                      | O            | -3.123401000 | -2.558243000 | 1.014396000 |
|         |                      | C            | -4.610119000 | -0.903767000 | -0.528908000 |
|         |                      | C            | -5.641988000 | -1.867416000 | 0.030445000 |
|         |                      | O            | -6.115409000 | -1.827976000 | 1.149656000 |
|         |                      | O            | -6.107453000 | -2.794918000 | -0.833167000 |
|         |                      | C            | 4.806960000  | 2.664647000 | 0.547191000 |
|         |                      | C            | 5.577756000  | 1.525411000 | 0.699077000 |
|         |                      | C            | 5.033925000  | 0.232369000 | 0.556057000 |
|         |                      | N            | 5.813173000  | -0.928569000 | 0.745103000 |
|         |                      | C            | 5.304465000  | -2.132671000 | 0.280878000 |
|         |                      | C            | 4.017952000  | -2.305362000 | -0.081603000 |
|         |                      | C            | 3.485256000  | -3.584946000 | -0.582955000 |
|         |                      | N            | 2.089904000  | -3.673081000 | -0.628934000 |
|         |                      | C            | 4.241810000  | -4.638608000 | -0.952924000 |
|         |                      | H            | -3.348599000 | 4.019865000 | -0.949647000 |
|       |       |       |       |
|-------|-------|-------|-------|
| H     | -1.989139000 | -1.723031000 | -1.166741000 |
| H     | -3.806913000  | 0.715190000   | 2.279626000  |
| H     | -5.137793000  | -0.167313000  | 1.880125000  |
| H     | -1.415727000  | 5.484842000   | -0.650519000 |
| H     | 1.024318000   | 5.669022000   | -0.270585000 |
| H     | -0.498757000  | -3.653171000  | -1.240063000 |
| H     | -2.628107000  | -3.121116000  | 1.635510100  |
| H     | -4.036520000  | -1.397551000  | -1.316577000 |
| H     | -5.156435000  | -0.077644000  | -0.997561000 |
| H     | -5.657760000  | -2.734083000  | -1.689846000 |
| H     | 5.246458000   | 3.650833000   | 0.647271000  |
| H     | 6.635524000   | 1.615332000   | 0.929953000  |
| H     | 6.816584000   | -0.817973000  | 0.711202000  |
| H     | 6.004102000   | -2.955371000  | 0.248117000  |
| H     | 1.709493000   | -4.533072000  | -0.998899000 |
| H     | 3.777949000   | -5.567247000  | -1.266632000 |
| H     | 5.321743000   | -4.601546000  | -0.945665000 |
| Excited state C | -2.788355000 | 0.818576000 | -0.219107000 |
| C     | -3.538408000  | 1.991830000   | -0.633312000 |
| N     | -2.797996000  | 3.175923000   | -0.798556000 |
| C     | -1.454194000  | 3.305119000   | -0.559065000 |
| C     | -0.717210000  | 2.137481000   | -0.378081000 |
| C     | -1.365736000  | 0.832137000   | -0.354764000 |
| C     | -0.490392000  | -0.333510000  | -0.496711000 |
| C     | -0.924838000  | -1.592907000  | -0.940951000 |
| N     | -4.406769000  | 0.450758000   | 1.566267000  |
| C     | -3.650140000  | -0.251536000  | 0.495671000  |
| C     | 0.678046000   | 2.266159000   | -0.159215000 |
| C     | 1.474728000   | 1.108985000   | -0.048396000 |
| C     | 0.909285000   | -0.204857000  | -0.256821000 |
| C     | -0.830299000  | 4.594473000   | -0.498667000 |
| C     | 0.507275000   | 4.710340000   | -0.245407000 |
| C     | 1.317827000   | 3.535616000   | -0.062075000 |
| C     | 1.773291000   | -1.309112000  | -0.317469000 |
| C     | 1.270650000   | -2.593389000  | -0.645387000 |
| C     | -0.076140000  | -2.700426000  | -0.992138000 |
| N     | 2.637056000   | 3.676427000   | 0.202274000  |
| C     | 3.394228000   | 2.566941000   | 0.321401000  |
| C     | 2.846244000   | 1.246870000   | 0.161931000  |
| C     | 3.686565000   | 0.104711000   | 0.202229000  |
| N     | 3.151626000   | -1.172766000  | -0.067138000 |
| O     | -4.761884000  | 2.066235000   | -0.865137000 |
| C     | -2.805275000  | -1.306635000  | 1.248843000  |
| O     | -2.047982000  | -1.035317000  | 2.160214000  |
|       | X-Coordinate  | Y-Coordinate  | Z-Coordinate  |
|-------|--------------|--------------|--------------|
|  O    | -3.07625200  | -2.58108900  | 0.89643500   |
|  C    | -4.65930300  | -0.89043100  | -0.49200200  |
|  C    | -5.67488400  | -1.85706300  | 0.08617000   |
|  O    | -6.04832100  | -1.89715300  | 1.24269700   |
|  O    | -6.24599200  | -2.70237000  | -0.80200900  |
|  C    | 4.79088600   | 2.68138800   | 0.59863000   |
|  C    | 5.59209500   | 1.56197700   | 0.68173000   |
|  C    | 5.06230000   | 0.27080200   | 0.47489100   |
|  N    | 5.85052800   | -0.85696300  | 0.52157500   |
|  C    | 5.34223700   | -2.09185500  | 0.24376600   |
|  C    | 4.01572600   | -2.27903300  | -0.08856900  |
|  C    | 3.49892400   | -3.60131300  | -0.47906400  |
|  N    | 2.11422900   | -3.68121800  | -0.63701900  |
|  C    | 4.27029400   | -4.69152500  | -0.67500800  |
|  H    | -3.35811600  | 3.98785500   | -1.02597700  |
|  H    | -1.94665800  | -1.72171400  | -1.27208600  |
|  H    | -3.73432900  | 0.72666300   | 2.27874500   |
|  H    | -5.04340500  | -0.22256800  | 1.99268100   |
|  H    | -1.44415400  | 5.47871600   | -0.64387600  |
|  H    | 0.98708600   | 5.68089700   | -0.17954600  |
|  H    | -0.46462200  | -3.66240500  | -1.31220500  |
|  H    | -2.55528900  | -3.15937500  | 1.48111400   |
|  H    | -4.11812500  | -1.37881900  | -1.30694400  |
|  H    | -5.21146500  | -0.04977200  | -0.92869200  |
|  H    | -5.87141500  | -2.57976100  | -1.68771400  |
|  H    | 5.20710200   | 3.67307400   | 0.73528100   |
|  H    | 6.65234300   | 1.65961500   | 0.89350300   |
|  H    | 6.83240500   | -0.76872000  | 0.74591700   |
|  H    | 6.03572200   | -2.91550900  | 0.29245500   |
|  H    | 1.73944000   | -4.56720500  | -0.94501200  |
|  H    | 3.81820400   | -5.63928800  | -0.94371800  |
|  H    | 5.34584800   | -4.66814500  | -0.58166000  |
Table S2. Absolute FL quantum yield of LAAM TC-CQDs in different solvents.

| Solvent  | water | methanol | ethanol | DMF  | formamide | DMSO |
|----------|-------|----------|---------|------|-----------|------|
| QY       | 6.8%  | 7.2%     | 8.2%    | 10.7%| 9.4%      | 10.5%|
Table S3. Examples of experimentally determined photothermal conversion efficiencies ($\eta$) for different PTCAs, listed from highest to lowest.

| PTT agents                          | Laser                                      | Photothermal conversion efficiency ($\eta$) | Reference |
|-------------------------------------|--------------------------------------------|--------------------------------------------|-----------|
| Au bellflowers                      | 1 W/cm$^2$, 808 nm                        | 74.0%                                      | s3        |
| Au nanocages                        | 0.4 W/cm$^2$, 808 nm                      | 64.0%                                      | s4        |
| Au nanomatryoshkas                  | Continuous-wave (CW) laser, 2 W/cm$^2$, 810 nm | 63.0%                                      | s5        |
| Au/Au$_2$S nanoshells               | 815 nm                                    | 59.0%                                      | s6        |
| Nanoporous Au disks                 | CW laser, 0.1 W/mm$^2$, 700-900 nm        | 56.0%                                      | s7        |
| Au nanorods                         | 815 nm                                    | 55.0%                                      | s6        |
| Au nanobipyramids                   | CW laser, 809 nm                          | 51.0%                                      | s8        |
| Au nanorods                         | 2 W/cm$^2$, 808 nm                        | 50.0%                                      | s9        |
| Dopamine-melanin nanospheres        | 2 W/cm$^2$, 808 nm                        | 40.0%                                      | s10       |
| Au nanoshells                       | CW laser, 2 W/cm$^2$, 810 nm              | 39.0%                                      | s5        |
| Red-emissive carbon dots            | 2 W/cm$^2$, 671 nm                        | 38.5%                                      | s11       |
| Au vesicles                         | 1 W/cm$^2$, 808 nm                        | 37.0%                                      | s12       |
| Au/SiO$_2$ nanoshells               | 815 nm                                    | 30.0%                                      | s6        |
| Au hexapods                         | 0.4 W/cm$^2$, 808 nm                      | 30.0%                                      | s4        |
| Plate-like Cu$_9$S$_5$ nanocrystals | 0.51 W/cm$^2$, 980 nm                     | 25.7%                                      | s13       |
| Au nanoshells                       | 2 W/cm$^2$, 808 nm                        | 25.0%                                      | s9        |
| Au nanorods                         | 0.51 W/cm$^2$, 980 nm                     | 23.7%                                      | s13       |
| Au nanorods                         | 0.4 W/cm$^2$, 808 nm                      | 22.0%                                      | s4        |
| Cu$_2$Se NCs                        | 2 W/cm$^2$, 800 nm                        | 22.0%                                      | s4        |
| Commercial Au nanorods              | 2 W/cm$^2$, 800 nm                        | 21.0%                                      | s14       |
| Fe$_3$O$_4$@Cu$_2$S NCs             | 2 W/cm$^2$, 980 nm                        | 16.0%                                      | s15       |
| Commercial Au nanoshells            | 2 W/cm$^2$, 800 nm                        | 13.0%                                      | s14       |
| Cancer cells | Origin | Uptake (%) | Normal cells | Origin | Uptake (%) |
|--------------|--------|------------|--------------|--------|------------|
| HeLa         | Human cervical cancer cells | 99.6 | CCC-ESF-1 | Human embryonic skin fibroblasts | 10.0 |
| A549         | Human lung carcinoma cells | 99.8 | HUVEC | Human umbilical vein endothelial cells | 15.1 |
| PANC-1       | Human pancreatic carcinoma cells | 99.9 | CDD-1095SK | Human skin fibroblasts | 4.2 |
| MCF 7        | Human breast adenocarcinoma cells | 99.7 | HL-7702 | Human hepatic cells | 13.0 |
| MDA-MB-231   | Human breast adenocarcinoma cells | 99.8 | RWPE-1 | Human prostate epithelial cells | 17.7 |
| MKN-45       | Human gastric adenocarcinoma cells | 99.8 | HaCaT | Human keratinocyte cells | 26.5 |
| A498         | Human renal carcinoma cells | 99.7 | Hs578Bst | Human breast epithelial cells | 12.0 |
| HepG2        | Human hepatocellular carcinoma cells | 99.9 | MCF 10A | Human mammary epithelial cell | 29.5 |
| HTB-9        | Human bladder carcinoma cells | 99.8 | BEAS-2B | Human bronchial epithelial cells | 6.0 |
| EC109        | Human esophageal carcinoma cells | 99.8 | MRC-5 | Human lung fibroblasts | 28.0 |
| PC-3         | Human prostate adenocarcinoma cells | 99.7 | WISH | Human amniotic cells | 14.3 |
| SF126        | Human glioblastoma cells | 99.8 | HKC | Human renal tubular epithelial cells | 1.7 |
| SK-MEL-1     | Human melanoma cells | 99.8 | 1301 | Human T lymphocytes | 12.0 |
| NCI-H1975    | Human lung adenocarcinoma cells | 99.8 | HLF-a | Human lung fibroblasts-a | 23.0 |
| T84          | Human colonic carcinoma cells | 99.6 | CCC-HEK-1 | Human embryonic kidney diploid cells | 9.4 |
| CAL-27       | Human oral carcinoma cells | 99.8 | CCC-HPE-2 | Human embryonic pancreatic cells | 4.6 |
| SH-SY5Y      | Human neuroblastoma cells | 99.9 | CCC-HIE-2 | Human embryonic intestinal mucosa cells | 12.3 |
| Hep-2        | Human laryngeal carcinoma cells | 99.7 | HBMSC | Human bone marrow stromal stem cells | 2.7 |
| H460         | Human lung carcinoma cells | 99.7 |        |        |            |
| Jurkat       | Human leukemic T-cell lymphoblast cells | 99.8 |        |        |            |
| Cell Line          | Cell Type                              | Percentage |
|-------------------|----------------------------------------|------------|
| MDA-MB-231 SP cells | Side population cells isolated from MDA-MB-231 | 99.9       |
| 4T1               | Mouse mammary carcinoma cells           | 100.0      |
| GL261             | Mouse glioma cells                     | 100.0      |
| U87               | Human glioblastoma cells               | 100.0      |
| CT26              | Mouse colon carcinoma cells             | 100.0      |
| MDA-MB-435        | Human melanoma cells                   | 100.0      |
| HCT116            | Human colorectal carcinoma cells        | 100.0      |
| DU145             | Human prostate cancer cells             | 100.0      |
| GBM-1             | Human glioblastoma cancer stem cells   | 95.0       |
| GBM-6             | Human glioblastoma cancer stem cells   | 100.0      |
| GBM-12            | Human glioblastoma cancer stem cells   | 100.0      |
| GBM-15            | Human glioblastoma cancer stem cells   | 100.0      |
| PS16              | Human glioblastoma cancer stem cells   | 100.0      |
| PS30              | Human glioblastoma cancer stem cells   | 100.0      |
| GS5               | Human glioblastoma cancer stem cells   | 100.0      |
| PS24              | Human glioblastoma cancer stem cells   | 100.0      |
| PS11              | Human glioblastoma cancer stem cells   | 100.0      |
| GBM4              | Human glioblastoma cancer stem cells   | 100.0      |
| GBM5              | Human glioblastoma cancer stem cells   | 100.0      |
| GBM7              | Human glioblastoma cancer stem cells   | 99.0       |
Table S5. The relative LAT1 expression and uptake of LAAM TC-CQDs in various types of cancer cells and normal cells for test. (Note: the relative LAT1 expressions in different types of cells were measured by WB tests from Figure S40 and the uptake of LAAM TC-CQDs were obtained from Figure S18 and 19).

| Cancer cells       | Relative LAT1 expression (LAT1/GAPDH) | Uptake     | Normal cells | Relative LAT1 expression (LAT1/GAPDH) | Uptake     |
|--------------------|--------------------------------------|------------|--------------|--------------------------------------|------------|
| HeLa               | 0.88                                 | 36779.4    | CCC-ESF-1    | 0.12                                 | 2592.7     |
| A549               | 0.89                                 | 37930.2    | HUVEC        | 0.20                                 | 3638.3     |
| PANC-1             | 0.85                                 | 34354.9    | CCD-1095SK    | 0.06                                 | 1795.6     |
| MCF-7              | 0.87                                 | 36402.8    | HL-7702      | 0.17                                 | 3021.1     |
| MDA-MB-231         | 0.83                                 | 33323.2    | RWPE-1       | 0.22                                 | 4159.3     |
| MKN-45             | 0.52                                 | 18149.9    | HaCaT        | 0.25                                 | 4896.3     |
| A498               | 0.73                                 | 29750.3    | Hs578Bst     | 0.13                                 | 2601.5     |
| HepG2              | 0.68                                 | 24932.2    | MCF 10A      | 0.29                                 | 5361.4     |
| HTB-9              | 0.64                                 | 23637.1    | BEAS-2B      | 0.09                                 | 2197.1     |
| EC109              | 0.72                                 | 25988.0    | MRC-5        | 0.26                                 | 5167.4     |
| PC-3               | 0.77                                 | 31056.1    | WISH         | 0.03                                 | 3420.1     |
| SF126              | 0.91                                 | 38389.6    | HKC          | 0.14                                 | 1003.7     |
| SK-MEL-1           | 0.75                                 | 28992.0    | 1301         | 0.14                                 | 2683.8     |
| NCI-H1975          | 0.90                                 | 37807.0    | HLF-a        | 0.23                                 | 4250.0     |
| T84                | 0.84                                 | 34429.7    | CCC-HEK-1    | 0.11                                 | 2353.0     |
| CAL-27             | 0.67                                 | 24041.8    | CCC-HPE-2    | 0.08                                 | 2016.2     |
| SH-SY5Y            | 0.85                                 | 35323.2    | CCC-HIE-2    | 0.16                                 | 2987.7     |
| Hep-2              | 0.61                                 | 20411.8    | HBMSCs       | 0.05                                 | 1413.5     |
| H460               | 0.79                                 | 33210.4    |              |                                      |            |
| Jurkat             | 0.68                                 | 23434.0    |              |                                      |            |
| Breast CSCs        | 0.86                                 | 35216.9    |              |                                      |            |
Table S6. Optimized cartesian coordinates (Å) of one FL unit of 1,4-CQDs, 1,5-CQDs and 2,6-CQDs for ground state and excited state.

| Species | Cartesian coordinates |
|---------|------------------------|
| **1,4-CQDs** | **Ground state** |
| C | 2.64417000 | 0.793691000 | -0.266490000 |
| C | 3.40416000 | 2.002334000 | -0.589448000 |
| C | 2.669177000 | 3.278897000 | -0.945151000 |
| C | 1.226567000 | 3.313785000 | -0.559133000 |
| C | 0.548572000 | 2.111293000 | -0.425828000 |
| C | 1.264486000 | 0.820505000 | -0.487228000 |
| C | 0.424828000 | -0.354435000 | -0.755181000 |
| C | 0.931391000 | -1.483481000 | -1.420222000 |
| N | 4.370709000 | 0.234977000 | 1.455209000 |
| C | 3.524361000 | -0.319044000 | 0.369268000 |
| C | -0.852082000 | 2.124029000 | -0.108199000 |
| C | -1.586270000 | 0.928961000 | -0.048403000 |
| C | -0.961864000 | -0.316272000 | -0.435332000 |
| C | 0.554017000 | 4.548593000 | -0.354060000 |
| C | -0.766501000 | 4.582854000 | 0.011612000 |
| C | -1.517624000 | 3.375614000 | 0.153190000 |
| C | -1.758689000 | -1.466728000 | -0.596833000 |
| C | -1.213278000 | -2.625091000 | -1.207924000 |
| C | 0.116403000 | -2.588100000 | -1.644181000 |
| C | -2.861622000 | 3.376147000 | 0.534872000 |
| C | -3.607470000 | 2.183539000 | 0.619618000 |
| C | -2.960048000 | 0.943171000 | 0.278664000 |
| C | -3.708372000 | -0.267804000 | 0.265770000 |
| N | -3.088430000 | -1.459624000 | -0.186037000 |
| O | 4.645414000 | 1.997396000 | -0.647636000 |
| C | -4.973759000 | 2.146771000 | 1.001426000 |
| C | -5.656586000 | 0.950654000 | 1.035308000 |
| C | -5.038130000 | -0.264719000 | 0.668627000 |
| N | -5.762734000 | -1.483423000 | 0.734415000 |
| C | -5.220528000 | -2.571167000 | 0.046221000 |
| C | -3.939222000 | -2.605504000 | -0.380871000 |
| C | -3.358363000 | -3.756103000 | -1.020160000 |
| C | -2.066999000 | -3.780650000 | -1.414355000 |
| C | 4.506903000 | -0.908643000 | -0.689630000 |
| O | 4.161292000 | -1.252972000 | -1.803694000 |
| O | 5.767203000 | -1.023794000 | -0.270850000 |
| C | 2.720956000 | -1.023794000 | 1.041146000 |
| C | 3.602016000 | -2.389282000 | 1.877260000 |
| O | 4.477018000 | -3.082094000 | 1.404282000 |
| O | 3.350675000 | -2.453788000 | 3.202747000 |
| H | 2.757718000 | 3.389954000 | -2.037710000 |
|  | H | 3.228946000 | 4.118746000 | -0.522341000 |
|  | H | 1.954530000 | -1.478481000 | -1.778865000 |
|  | H | 4.747615000 | 1.135697000 | 1.171757000 |
|  | H | 3.836426000 | 0.370506000 | 2.308799000 |
|  | H | 1.112172000 | 5.473117000 | -0.470341000 |
|  | H | -1.262214000 | 5.531560000 | 0.196151000 |
|  | H | 0.513074000 | -3.453037000 | -2.168839000 |
|  | H | -3.348323000 | 4.319640000 | 0.766105000 |
|  | H | -5.476291000 | 3.071317000 | 1.266897000 |
|  | H | -6.699508000 | 0.925813000 | 1.338758000 |
|  | H | -6.767802000 | -1.387404000 | 0.666267000 |
|  | H | -5.868855000 | -3.425385000 | -0.096469000 |
|  | H | -4.007188000 | -4.613130000 | -1.168917000 |
|  | H | -1.646817000 | -4.655171000 | -1.898634000 |
|  | H | 5.754520000 | -0.715170000 | 0.663502000 |
|  | H | 2.250944000 | -2.105870000 | 0.295034000 |
|  | H | 1.917412000 | -1.027570000 | 1.637207000 |
|  | H | 2.610058000 | -1.880762000 | 3.451179000 |
| Excited state | C | -0.394560000 | 4.502287000 | 0.057048000 |
|  | C | -1.265363000 | 3.367964000 | 0.061342000 |
|  | C | -1.759088000 | -1.523931000 | -0.147711000 |
|  | C | -1.180863000 | -2.831461000 | -0.252301000 |
|  | C | 0.216846000 | -2.954287000 | -0.331042000 |
|  | C | -2.656460000 | 3.486666000 | 0.131329000 |
|  | C | -3.510010000 | 2.353628000 | 0.124978000 |
|  | C | -2.916291000 | 1.048807000 | 0.036880000 |
|  | C | -3.736584000 | -0.106620000 | 0.019869000 |
|  | N | -3.145026000 | -1.384009000 | -0.073852000 |
|  | O | 4.872498000 | 1.436376000 | -0.517417000 |
|  | C | -4.919928000 | 2.445800000 | 0.198944000 |
|  | C | -5.707629000 | 1.302060000 | 0.185010000 |
|  | C | -5.135026000 | 0.030032000 | 0.095701000 |
|  | N | -5.931510000 | -1.130418000 | 0.078749000 |
|  | C | -5.364992000 | -2.356234000 | -0.016644000 |
|  | C | -4.003020000 | -2.531445000 | -0.094727000 |
|  | C | -3.402843000 | -3.808385000 | -0.196884000 |
|  | C | -2.045142000 | -3.968128000 | -0.274656000 |
|  | C | 4.248465000 | -1.085539000 | -1.627821000 |
|  | O | 5.196956000 | -1.835257000 | -1.699139000 |
|  | O | 3.780520000 | -0.466068000 | -2.719654000 |
|  | C | 4.364359000 | -1.164336000 | 0.874090000 |
|  | C | 3.713791000 | -1.183342000 | 2.242045000 |
|  | O | 2.545290000 | -0.979121000 | 2.484651000 |
|  | O | 4.561618000 | -1.452766000 | 3.264759000 |
| 1,5-CQDs | Ground state |
| --- | --- |
| **H** | 3.518540000 | 3.326102000 | 0.852887000 |
| **H** | 3.515191000 | 3.625144000 | -0.862058000 |
| **H** | 2.782827000 | -2.922883000 | -0.401525000 |
| **H** | 1.610582000 | 5.225794000 | -0.008933000 |
| **H** | -0.830461000 | 5.495831000 | 0.108082000 |
| **H** | 0.646955000 | -3.947957000 | -0.411890000 |
| **H** | -3.102912000 | 4.475393000 | 0.190271000 |
| **H** | -5.386662000 | 3.422981000 | 0.267156000 |
| **H** | -6.789163000 | 1.384996000 | 0.243173000 |
| **H** | -6.935084000 | -1.040914000 | 0.129505000 |
| **H** | -6.026788000 | -3.211296000 | -0.030670000 |
| **H** | -4.065699000 | -4.666875000 | -0.212541000 |
| **H** | -1.699615000 | -4.958079000 | -0.353900000 |
| **H** | 3.067272000 | 0.144414000 | -2.454085000 |
| **H** | 5.129309000 | -0.381410000 | 0.850349000 |
| **H** | 4.884141000 | -2.114365000 | 0.707002000 |
| **H** | 5.466571000 | -1.587511000 | 2.942407000 |
| **C** | 2.853633000 | 0.673559500 | -0.281693000 |
| **C** | 3.679242000 | 1.834650000 | -0.612134000 |
| **C** | 3.025108000 | 3.168637000 | -0.917546000 |
| **C** | 1.595546000 | 3.289923000 | -0.505127000 |
| **C** | 0.847407000 | 2.122578000 | -0.386273000 |
| **C** | 1.470017000 | 0.784652000 | -0.473158000 |
| **C** | 0.545499000 | -0.328737000 | -0.727121000 |
| **C** | 0.963873000 | -1.530462000 | -1.372487000 |
| **N** | 4.590110000 | 0.005265000 | 1.393456000 |
| **C** | 3.673806000 | -0.492834000 | 0.338225000 |
| **C** | -0.540396000 | 2.230148000 | -0.073288000 |
| **C** | -1.358066000 | 1.090231000 | -0.035900000 |
| **C** | -0.828223000 | -0.188044000 | -0.436960000 |
| **C** | 0.998241000 | 4.553135000 | -0.275241000 |
| **C** | -0.325367000 | 4.665451000 | 0.086214000 |
| **C** | -1.140075000 | 3.505370000 | 0.197496000 |
| **C** | -1.727748000 | -1.285422000 | -0.594366000 |
| **C** | -1.254311000 | -2.516285000 | -1.131188000 |
| **C** | 0.099989000 | -2.583320000 | -1.563424000 |
| **N** | -2.441412000 | 3.647194000 | 0.550079000 |
| **C** | -3.211376000 | 2.552560000 | 0.590430000 |
| **C** | -2.719040000 | 1.243299000 | 0.266836000 |
| **C** | -3.586004000 | 0.128223000 | 0.221752000 |
| **C** | -3.103746000 | -1.153222000 | -0.226322000 |
| **O** | 4.915768000 | 1.750817000 | -0.710383000 |
| **C** | -4.601554000 | 2.668009000 | 0.936739000 |
| **C** | -5.430794000 | 1.580054000 | 0.918884000 |
|   |   |   |   |   |
|---|---|---|---|---|
| C | -4.936935000 | 0.288403000 | 0.540810000 |
| N | -5.763936000 | -0.791128000 | 0.472004000 |
| C | -5.392135000 | -2.095739000 | 0.083521000 |
| C | -3.980075000 | -2.245609000 | -0.332933000 |
| C | -3.478714000 | -3.464453000 | -0.852707000 |
| C | -2.165117000 | -3.595692000 | -1.251073000 |
| C | -6.315799000 | -3.081307000 | 0.113188000 |
| C | -3.647376000 | -2.557566000 | 1.854212000 |
| O | 4.440434000 | -3.321477000 | 1.347646000 |
| O | 3.452889000 | -2.594386000 | 3.189869000 |
| H | 3.095157000 | 3.303783000 | -2.008467000 |
| H | 3.648350000 | 3.957850000 | -0.486571000 |
| H | 1.982939000 | -1.595437000 | -1.739367000 |
| H | 5.024402000 | 0.873012000 | 1.089767000 |
| H | 4.091978000 | 0.187337000 | 2.260230000 |
| H | 1.610178000 | 5.444719000 | -0.374897000 |
| H | -0.777123000 | 5.631454000 | 0.285715000 |
| H | 0.447130000 | -3.484555000 | -2.059661000 |
| H | -4.979572000 | 3.649952000 | 1.200596000 |
| H | -6.480812000 | 1.686656000 | 1.174366000 |
| H | -6.735053000 | -0.658229000 | 0.722096000 |
| H | -4.143732000 | -4.313778000 | -0.959218000 |
| H | -1.815700000 | -4.536950000 | -1.664332000 |
| H | -6.076718000 | -4.095693000 | -0.171008000 |
| H | -7.333676000 | -2.881513000 | 0.429552000 |
| H | 5.879571000 | -1.049180000 | 0.570477000 |
| H | 2.258397000 | -2.174493000 | 0.329695000 |
| H | 2.069875000 | -1.063891000 | 1.675167000 |
| H | 2.774682000 | -1.960809000 | 3.467922000 |

**Excited state**

|   |   |   |   |   |
|---|---|---|---|---|
| C | 2.949590000 | 0.314269000 | -0.290861000 |
| C | 3.909301000 | 1.377595000 | -0.304343000 |
| C | 3.421533000 | 2.820726000 | -0.315376000 |
| C | 1.945627000 | 3.029105000 | -0.140694000 |
| C | 1.065109000 | 1.926907000 | -0.147321000 |
| C | 1.563150000 | 0.568085000 | -0.235871000 |
| C | 0.627395000 | -0.506912000 | -0.253866000 |
| C | 1.093310000 | -1.855397000 | -0.372166000 |
| N | 2.437061000 | -2.085705000 | -0.484311000 |
| C | 3.507710000 | -1.103040000 | -0.276932000 |
| C | -0.332102000 | 2.149645000 | -0.040093000 |
| Element | X      | Y      | Z      |
|---------|--------|--------|--------|
| C       | -1.239998000 | 1.066473000 | -0.056571000 |
| C       | -0.769216000  | -0.269593000 | -0.170835000 |
| C       | 1.418717000   | 4.334502000  | 0.001498000  |
| C       | 0.065427000   | 4.571312000  | 0.109812000  |
| C       | -0.870630000  | 3.488090000  | 0.085239000  |
| C       | -1.707365000  | -1.343838000 | -0.198284000 |
| C       | -1.227200000  | -2.678954000 | -0.318372000 |
| C       | 0.181075000   | -2.906437000 | -0.405525000 |
| N       | -2.181843000  | 3.748714000  | 0.085239000  |
| C       | -3.057796000  | 2.694924000  | 0.154097000  |
| C       | -2.623063000  | 1.338153000  | 0.037119000  |
| C       | -0.879630000  | -0.870630000 | 0.085239000  |
| O       | 5.141183000   | 1.167074000  | -0.349111000 |
| C       | -4.450206000  | 2.932972000  | 0.244269000  |
| C       | -5.365560000  | 1.883771000  | 0.218870000  |
| C       | -4.920962000  | 0.551857000  | 0.103022000  |
| N       | -5.811628000  | -0.516226000 | 0.074191000  |
| C       | -5.475057000  | -1.853381000 | -0.039924000 |
| C       | -4.030268000  | -2.146896000 | -0.135511000 |
| C       | -3.538979000  | -3.460882000 | -0.255011000 |
| C       | -2.174644000  | -3.725055000 | -0.344419000 |
| C       | -6.472638000  | -2.792586000 | -0.056736000 |
| C       | 4.464393000   | -1.325892000 | -1.497409000 |
| O       | 5.402978000   | -2.092787000 | -1.478006000 |
| O       | 4.105366000   | -0.717743000 | -2.639544000 |
| C       | 4.324413000   | -1.429230000 | 0.996663000  |
| C       | 3.547178000   | -1.415319000 | 2.296135000  |
| O       | 2.369374000   | -1.165934000 | 2.427200000  |
| O       | 4.280437000   | -1.716181000 | 3.396435000  |
| H       | 3.989439000   | 3.372976000  | 0.445895000  |
| H       | 3.751391000   | 3.254990000  | -1.272490000 |
| H       | 2.735882000   | -3.052076000 | -0.495685000 |
| H       | 2.110033000   | 5.172806000  | 0.016690900  |
| H       | -0.324705000  | 5.578531000  | 0.211422000  |
| H       | 0.540861000   | -3.927091000 | -0.497623000 |
| H       | -4.794634000  | 3.957498000  | 0.333099000  |
| H       | -6.428971000  | 2.091860000  | 0.287453000  |
| H       | -6.798129000  | -0.299779000 | 0.143097000  |
| H       | -4.227542000  | -4.297409000 | -0.279034000 |
| H       | -1.833014000  | -4.751340000 | -0.435295000 |
| H       | -6.259390000  | -3.847238000 | -0.142075000 |
| H       | -7.512302000  | -2.496064000 | 0.016477000  |
| H       | 3.363244000   | -0.112942000 | -2.454569000 |
| 2,6-CQDs | Ground state |
|----------|--------------|
| C        | 2.728354000  | 0.512805000  | -0.317929000 |
| C        | 3.541203000  | 1.687153000  | -0.417668000 |
| C        | 2.868498000  | 3.046558000  | -0.490160000 |
| C        | 1.380006000  | 3.081833000  | -0.294322000 |
| C        | 0.647714000  | 1.883762000  | -0.224612000 |
| C        | 1.319049000  | 0.592140000  | -0.257083000 |
| C        | 0.515450000  | -0.591319000 | -0.237045000 |
| C        | 1.184481000  | -1.890175000 | -0.307539000 |
| C        | 2.541980000  | -1.989714000 | -0.272251000 |
| C        | 3.482095000  | -0.809799000 | -0.191560000 |
| C        | -0.769625000 | 1.965784000  | -0.098535000 |
| C        | -1.543434000 | 0.775591000  | -0.066404000 |
| C        | -0.889453000 | -0.503626000 | -0.153551000 |
| C        | 0.744200000  | 4.322535000  | -0.199698000 |
| C        | -0.635438000 | 4.440540000  | -0.040001000 |
| C        | -1.433327000 | 3.239263000  | -0.013909000 |
| C        | -1.676450000 | -1.694066000 | -0.142442000 |
| C        | -1.029226000 | -2.989114000 | -0.276306000 |
| C        | 0.343961000  | -3.085759000 | -0.397666000 |
| C        | -2.834049000 | 3.283481000  | 0.082173000  |
| C        | -3.605507000 | 2.122576000  | 0.113211000  |
| C        | -2.951740000 | 0.848600000  | 0.037267000  |
| C        | -3.735416000 | -0.335316000 | 0.057020000  |
| C        | -3.069160000 | -1.599754000 | -0.040494000 |
| O        | 4.790765000  | 1.645731000  | -0.483724000 |
| C        | -5.033034000 | 2.162714000  | 0.213096000  |
| C        | -5.776095000 | 1.016030000  | 0.237712000  |
| C        | -5.144965000 | -0.263649000 | 0.156817000  |
| C        | -5.881044000 | -1.478770000 | 0.167222000  |
| C        | -5.227818000 | -2.672402000 | 0.069670000  |
| N        | -3.862996000 | -2.750730000 | -0.037516000 |
| C        | -3.246802000 | -4.008777000 | -0.150996000 |
| C        | -1.911775000 | -4.131783000 | -0.270711000 |
| N        | -1.219674000 | 5.680089000  | 0.031297000  |
| N        | 0.993520000  | -4.311161000 | -0.535020000 |
| C        | 4.438800000  | -1.000475000 | -1.403470000 |
| O        | 5.472305000  | -1.639935000 | -1.372600000 |
| O        | 3.982524000  | -0.521419000 | -2.578810000 |
| C        | 4.373832000  | -0.897114000 | 1.079677000  |
| C        | 3.648774000  | -0.863477000 | 2.407062000  |
| O        | 2.469925000  | -0.659618000 | 2.593440000  |
| Atom | X    | Y    | Z    | Energetics |
|------|------|------|------|------------|
| O    | 4.449628000 | -1.071601000 | 3.488624000 |
| H    | 3.365979000  | 3.707816000  | 0.229733000 |
| H    | 3.109883000  | 3.472776000  | -1.474846000 |
| H    | 3.027330000  | -2.959320000 | -0.244748000 |
| H    | 1.346442000  | 5.226652000  | -0.236432000 |
| H    | -3.354768000 | 4.234799000  | 0.113066000 |
| H    | 5.520852000  | 3.131452000  | 0.271372000 |
| H    | 6.857670000  | 1.058876000  | 0.315249000 |
| H    | 6.961224000  | -1.470729000 | 0.246748000 |
| H    | 5.745368000  | -3.622951000 | 0.067528000 |
| H    | 3.924702000  | -4.850919000 | 0.132450000 |
| H    | 1.522117000  | 5.140632000  | 0.336025000 |
| H    | 2.101037000  | -4.256265000 | 1.087181000 |
| H    | 0.415045000  | -5.068054000 | 0.873948000 |
| H    | 3.177211000  | -0.001751000 | 2.386980000 |
| H    | 5.089411000  | -0.068133000 | 1.063695000 |
| H    | 4.966605000  | -1.817311000 | 1.031368000 |
| H    | 5.365887000  | -1.221176000 | 3.208557000 |

| Atom | X    | Y    | Z    | Energetics |
|------|------|------|------|------------|
| C    | 2.722476000 | 0.515985000 | -0.277185000 |
| C    | 3.549629000 | 1.689494000 | -0.388364000 |
| C    | 2.902436000 | 3.053762000 | -0.279209000 |
| C    | 1.404271000 | 3.100718000 | -0.191375000 |
| C    | 0.653014000 | 1.898657000 | -0.159773000 |
| C    | 1.321225000 | 0.606147000 | -0.205225000 |
| C    | 0.508632000 | -0.585859000 | -0.204840000 |
| C    | 1.153305000 | -1.886215000 | -0.292034000 |
| C    | 2.526233000 | -1.982325000 | -0.255873000 |
| C    | 3.458085000 | -0.810492000 | -0.231767000 |
| C    | -0.762095000 | 1.974981000 | -0.081580000 |
| C    | -1.543568000 | 0.782883000 | -0.062541000 |
| C    | -1.897173000 | -0.503165000 | -0.127645000 |
| C    | 0.771176000 | 4.334581000 | -0.122205000 |
| C    | -0.622333000 | 4.443288000 | -0.013980000 |
| C    | -1.428033000 | 3.248883000 | -0.019528000 |
| C    | -1.670306000 | -1.698708000 | -0.102581000 |
| C    | -1.060286000 | -2.998491000 | -0.205145000 |
| C    | 0.336670000 | -3.074751000 | -0.388140000 |
| C    | -2.831186000 | 3.298657000 | 0.027952000 |
| C    | -3.613319000 | 2.121609000 | 0.056722000 |
| C    | -2.960472000 | 0.858285000 | 0.014606000 |
| C    | -3.747900000 | -0.334319000 | 0.045260000 |
| C    | -3.097267000 | -1.599468000 | -0.007088000 |
|   | X      | Y      | Z      |
|---|--------|--------|--------|
| O | 4.784101000 | 1.621925000 | -0.564529000 |
| C | -5.039077000 | 2.171742000 | 0.127493000 |
| C | -5.798321000 | 1.033760000 | 0.164142000 |
| C | -5.163498000 | -0.249062000 | 0.124087000 |
| C | -5.891418000 | -1.462769000 | 0.158172000 |
| C | -5.239715000 | -2.662719000 | 0.110754000 |
| N | -3.868675000 | -2.751734000 | 0.027344000 |
| C | -3.272323000 | -0.012866000 | -0.017054000 |
| C | -1.893510000 | -4.139995000 | -0.139582000 |
| N | -1.212960000 | 5.684386000 | 0.044936000 |
| N | 0.940373000 | -4.296392000 | -0.565540000 |
| C | 4.333665000 | -1.001448000 | -1.516554000 |
| O | 5.354851000 | -1.654990000 | -1.549320000 |
| O | 3.817076000 | -0.497087000 | -2.652351000 |
| C | 4.435601000 | -0.923886000 | 0.974038000 |
| C | 3.787182000 | -0.915101000 | 2.342008000 |
| O | 2.605609000 | -0.804182000 | 2.582811000 |
| O | 4.656961000 | -1.040458000 | 3.377672000 |
| H | 3.334612000 | 3.533738000 | 0.610260000 |
| H | 3.253844000 | 3.661884000 | -1.122144000 |
| H | 3.009799000 | -2.951744000 | -0.202796000 |
| H | 1.369142000 | 5.242291000 | -0.131631000 |
| H | -3.351777000 | 4.249944000 | 0.020296000 |
| H | -5.519196000 | 3.146331000 | 0.156870000 |
| H | -6.880441000 | 1.081966000 | 0.222501000 |
| H | -6.973377000 | -1.456086000 | 0.220711000 |
| H | -5.759406000 | -3.611193000 | 0.134083000 |
| H | -3.953416000 | -4.847576000 | 0.046786000 |
| H | -1.491917000 | -5.142857000 | -0.137114000 |
| H | -2.099345000 | 5.761036000 | 0.523470000 |
| H | -0.596269000 | 6.461326000 | 0.240026000 |
| H | 1.826023000 | -4.279011000 | -1.082440000 |
| H | 0.339838000 | -5.029118000 | -0.947945000 |
| H | 3.034273000 | 0.038179000 | -2.425388000 |
| H | 5.148807000 | -0.095311000 | 0.916928000 |
| H | 5.018774000 | -1.844762000 | 0.868717000 |
| H | 5.568334000 | -1.125283000 | 3.056515000 |
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