Supporting Information

Light-triggered nitric oxide release and targeted fluorescence imaging in tumor cells developed from folic acid-graft-carboxymethyl chitosan nanospheres

Rijun Gui,[a,b] Ajun Wan,[a,b,*] Yalei Zhang,[a] Huili Li,[c,*] and Tingting Zhao[b]

[a] *State Key Laboratory of Pollution Control and Resources Reuse, National Engineering Research Center of Facilities Agriculture, Tongji University, Shanghai 200092, P.R. China. E-mail: wanajun@tongji.edu.cn (A. Wan); Fax: +86 21 54745706. Tel.: +86 21 34201245.*

[b] *Department of Chemistry, School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, Shanghai 200240, P.R. China.*

[c] *School of Pharmacy, Shanghai Jiao Tong University, Shanghai 200240, P.R. China. E-mail: lihl@sjtu.edu.cn (H. Li).*

Part S1 Synthesis of PEI-stabilized CQD

Briefly, 200 mg of glucose was added into 10 mL solution of glycol/water (1/1, v/v) to form clear mixed solution under stirring and ultrasound. The mixed solution was added to a high pressure nitrifying pot, and heated at 180 °C in a constant-temperature drying oven for 3 h to generate bare CQD. Then, 1.0 mL of PEI solution (20%, v/v) was mixed with 10 mL of the bared CQD solution and rapidly stirred for 3 h at 80 °C. Under ultraviolet lamp excitation, strong fluorescence emission of the final reaction solution indicated the formation of PEI modified or stabilized CQD (*i.e.* PEI-CQD, 1 wt.%).

Part S2 Determination of NO concentrations

To determine the NO release from CMC-FA-RBS hybrid nanospheres in aqueous solution (PBS, 10 mM, pH 7.4), the colorimetric Griess reaction was employed to measure nitrite or nitrate content in the PBS of CMC-FA-RBS. The details are available as follows: aliquots of PBS of CMC-FA-RBS (1.0 mg·mL^{-1}, 5 mL) was taken and stirred in a centrifugal tube at 37 °C in a water bath. At appropriate time intervals, the solution was centrifuged for 10 min, and the supernatant (0.5 mL) was extracted, replenished with the PBS and combined with Griess reagent **(I)** (0.1 wt.% of *β*-naphthylethylenediamine dihydrochloride aqueous solution, 1 mL) and **(II)** (1 wt.% of sulfanilamide in 5 wt.% of phosphoric acid aqueous solution, 1 mL). The resultant mixed solution was incubated for 15 min at room temperature, protected from light (*i.e.*, in the dark). A purple/magenta color appeared immediately. The maximum absorbance was recorded (at 540 nm) by using UV-vis spectrophotometer, and the standard curve was determined by measuring sodium nitrite (0-100 μM) in PBS. The total release of NO was calculated according to the following equations:

$R_1 = C_1 \times 0.005$;

$R_2 = C_2 \times 0.005 + C_1 \times 0.001$;

$R_3 = C_3 \times 0.005 + (C_2 + C_1) \times 0.001$;

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$R_n = C_n \times 0.005 + (C_{n-1} + C_{n-2} + \ldots\ldots + C_1) \times 0.001$

where R_n is the release amount of NO measured at each time point, and C_n is the concentration of NO.

Part S3 PL stability of CMC-FA-CQD hybrid nanospheres

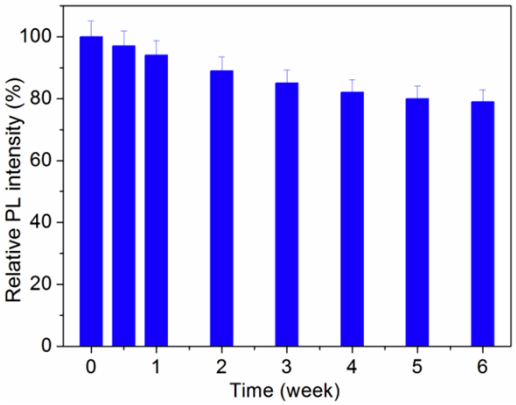

Fig. S1 Relative PL intensity of 1.0 mg·mL^{-1} of CMC-FA-CQD hybrid nanospheres stored in 10 mM of PBS (pH 7.4) for different times at room temperature (~20 °C).

Part S4 light-triggered NO release from CMC-FA-RBS nanospheres

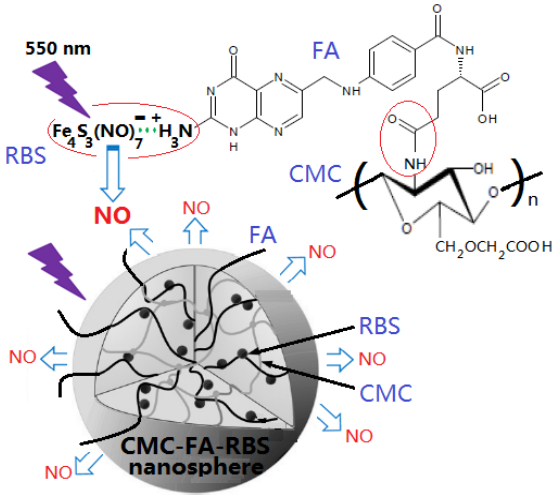

Fig. S2 Schematic illustration of the chemistry structure, spherical model and light-triggered NO release of the designed CMC-FA-RBS hybrid nanosphere system.

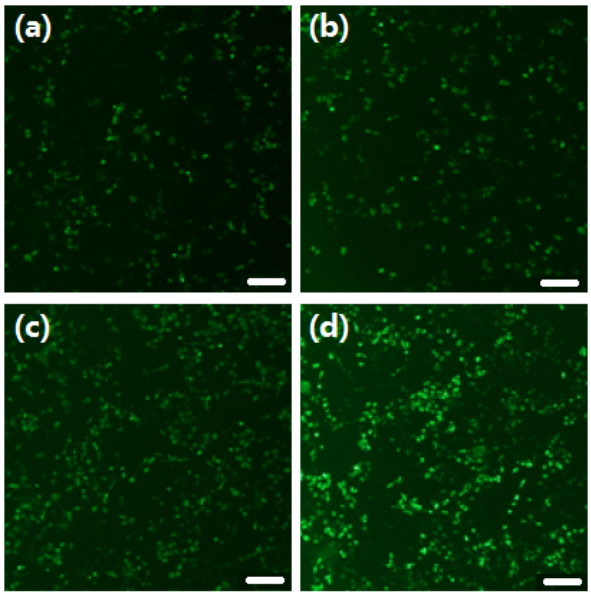

Fig. S3 Fluorescence imaging of (a) L02, (b) A549, (c) HepG2, and (d) HeLa cells after 24 h incubation with the CMC-FA-CQD hybrid nanospheres (1 mg·mL^{-1}), excited at 440 nm. The scale bar is 100 μm.

Part S5 Florescence imaging from CMC-FA-CQD nanospheres

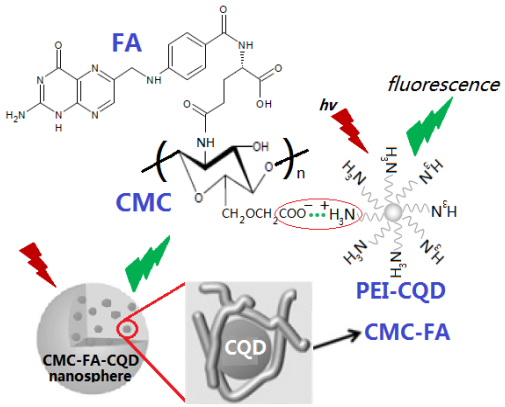

Fig. S4 Schematic illustration of the chemistry structure, spherical model and fluorescence emission of the designed CMC-FA-CQD hybrid nanosphere system.