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Supporting Information

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Light-regulated DNA release and nuclear delivery using photolabile gold nanoparticles

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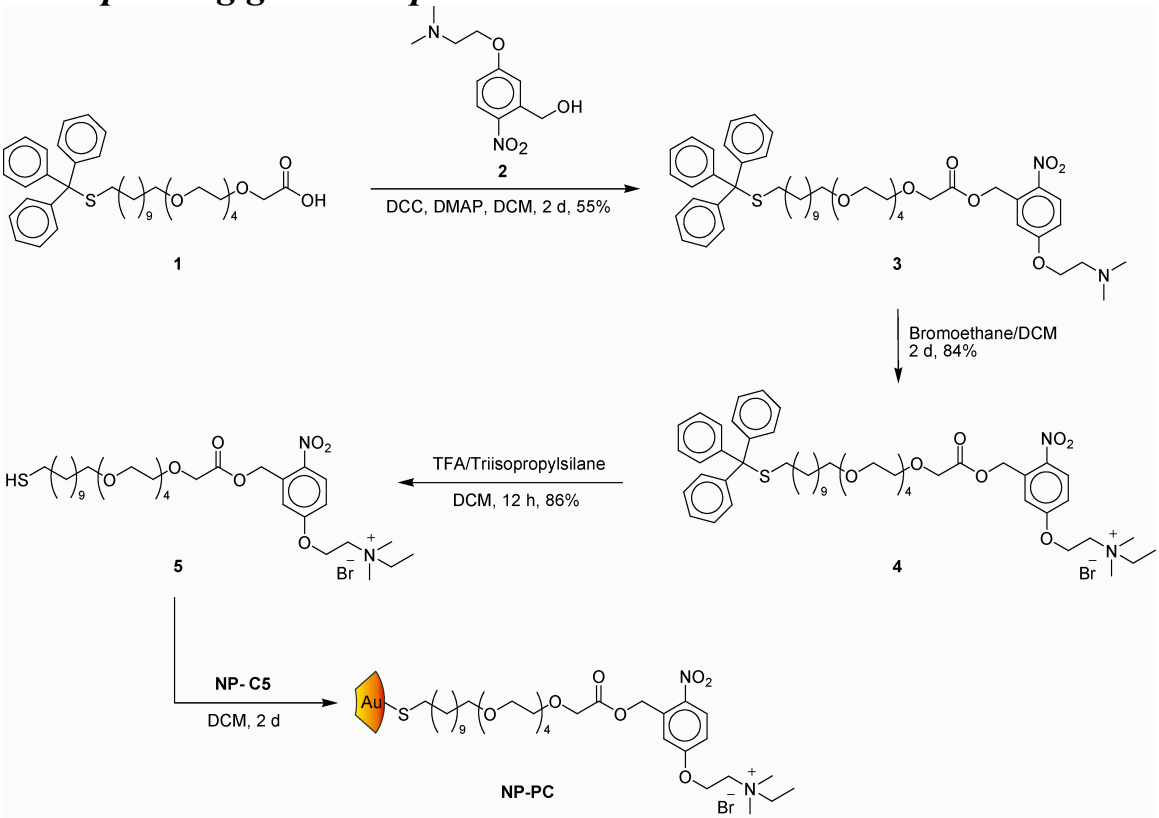
Synthesis of the photocleavable ligand and construction of the corresponding gold nanoparticle



Scheme S1. Synthesis of the photocleavable ligand and fabrication of the corresponding gold nanoparticle.

Compound **2**
5-Hydroxy-2-nitrobenzyl alcohol (0.85 g, 5 mmol), 2-(dimethylamino)ethyl chloride hydrochloride (0.86 g, 6 mmol) and sodium hydroxide (0.44 g, 11 mmol) were suspended in a mixture of toluene (50 mL) and ethanol (10 mL). The reaction was heated to reflux and stirred for 48 h. After cooling to room temperature, the dark solution was poured into water (300 mL). The organic layer was isolated and the water phase was washed with toluene. The organic layers were combined and washed successively with sodium bicarbonate solution, water and brine. The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness. The sample was dissolved in a minimum amount of dichloromethane, and a large amount of hexane was added. Long needles were formed after standing at room temperature overnight. Yield 840 mg (70%).
^{1}H NMR ($CDCl_3$, TMS): δ 8.14 (d, J = 9.1 Hz, 1H), 7.31 (d, J = 2.8 Hz, 1H), 6.87 (dd, J = 9.1, 2.8 Hz, 1H), 4.99 (s, 2H), 4.16 (t, J = 5.6 Hz, 2H), 2.77 (t, J = 5.6 Hz, 2H), 2.36 (s, 6H).

Compound **3**
Trityl protected thioalkyl carboxylic acid **1** (1.36 g, 2 mmol) [1] was dissolved in dry dichloromethane (DCM, 30 mL) that was placed in an ice-bath. Dicyclohexylcarbodiimide (DCC, 530 mg, 2 mmol) and 4-dimethylaminopyridine

[1] B. T. Houseman, M. Mrksich, *J. Org. Chem.* **1998**, *63*, 7552-7555.

(DMAP, 100 mg) were then added and the solution was stirred at 0 °C for about 10 min. Subsequently, compound **2** (480 mg, 2 mmol) was added. The reaction mixture was allowed to reach room temperature automatically and stirred for 2 days. The precipitate formed was removed by filtration and the filtrate was concentrated. The residue was charged on silica gel column with DCM/methanol (95:5) as eluent. Yield 1.0 g (55%).
^{1}H NMR ($CDCl_3$, TMS): δ 8.20 (d, J = 9.1 Hz, 1H), 7.40 (m, 6H), 7.28 (m, 6H), 7.20 (m, 3H), 7.08 (d, J = 2.5 Hz, 1H), 6.93 (dd, J = 9.1, 2.5 Hz, 1H), 5.61 (s, 2H), 4.29 (s, 2H), 4.14 (t, J = 5.4 Hz, 2H), 3.77 (m, 2H), 3.71 (m, 2H), 3.65 (m, 10H), 3.57 (m, 2H), 3.43 (t, J = 6.7 Hz, 2H), 2.76 (t, J = 5.4 Hz, 2H), 2.35 (s, 6H), 2.13 (t, J = 7.2 Hz, 2H), 1.56 (m, 2H), 1.38 (m, 2H), 1.22 (m, 14H).

Compound **4**
Compound **3** (820 mg, 0.9 mmol) was dissolved in dry DCM (30 mL) and bromoethane (3 mL, 40 mmol) was added subsequently. The mixture was stirred at room temperature under dark for 2 days. Then, the solvent and the excess bromoethane were removed under a reduced pressure. The residue was washed thoroughly with diethyl ether. After drying under high vacuum, 765 mg product was obtained, yield 84%.
^{1}H NMR ($CDCl_3$, TMS): δ 8.20 (d, J = 9.1 Hz, 1H), 7.40 (m, 6H), 7.27 (m, 6 H), 7.20 (m, 3H), 7.16 (d, J = 2.8 Hz, 1H), 7.09 (dd, J = 9.1, 2.8 Hz, 1H), 5.60 (s, 2H), 4.75 (t, J = 4.2 Hz, 2H), 4.33 (s, 2H), 4.31 (t, J = 4.2 Hz, 2H), 3.81 (q, J = 7.4 Hz, 2H), 3.77 (m, 2H), 3.70 (m, 2H), 3.63 (m, 10H), 3.55 (m, 2H), 3.47 (s, 6H), 3.42 (t, J = 6.9 Hz, 2H), 2.13 (t, J = 7.3 Hz, 2H), 1.55 (m, 2H), 1.50 (t, J = 7.4 Hz, 3H), 1.38 (m, 2H), 1.22 (m, 14H).
MS (ESI): *m*/*z* 930.5 $[M-1]^+$ (calcd for $C_{53}H_{75}N_2O_{10}S^+$ 931.5).

Compound **5**
Compound **4** (750 mg, 0.74 mmol) was dissolved in DCM (30 mL) and trifluoroacetic acid (TFA, 2 mL) and triisopropylsilane (1.5 mL) was added successively. The mixture was stirred at room temperature under dark for 12 h. The solvent was removed under a reduced pressure. The residue was washed with diethyl ether (50 mL × 4). After drying under high vacuum, 490 mg pale yellow oil was obtained, yield 86%.
^{1}H NMR ($CDCl_3$, TMS): δ 8.20 (d, J = 8.20 Hz, 1H), 7.15 (d, J = 2.8 Hz, 1H), 7.09 (dd, J = 9.1, 2.8 Hz, 1H), 5.59 (s, 2H), 4.74 (t, J = 4.3 Hz, 2H), 4.33 (s, 2H), 4.26 (t, J = 4.3 Hz, 2H), 3.80 (q, J = 7.4 Hz, 2H), 3.75 (m, 2H), 3.71 (m, 2H), 3.63 (m, 10H), 3.56 (m, 2H), 3.45 (s, 6H), 3.43 (t, J = 6.9 Hz, 2H), 2.52 (q, J = 7.2 Hz, 2H), 1.60 (m, 4H), 1.50 (t, J = 7.4 Hz, 3H), 1.26 (m, 14H).
MS (ESI): *m*/*z* 688.7 $[M-1]^+$ (calcd for $C_{34}H_{61}N_2O_{10}S^+$ 689.4).

Construction of photocleavable gold nanoparticle (**NP-PC**)
The photocleavable gold nanoparticle was prepared by Murray place-exchange reaction[2] of 1-pentanethiol protected 2 nm gold nanoparticle (**NP-C5**) [3] with thiolate ligand **5**. Briefly, **NP-C5** (d ~ 2 nm, 40 mg) were dissolved in DCM (10 mL) and ligand **5** (200 mg) in DCM (5 mL) was added subsequently. The mixture was stirred

[2] M. J. Hostetler, A. C. Templeton, R. W. Murray, *Langmuir* **1999**, *15*, 3782-3789.
[3] M. Brust, M. Walker, D. Bethell, D. J. Schiffrin, R. Whyman, *J. Chem. Soc., Chem. Commun.* **1994**, 801-802.

at room temperature for 2~3 days. The precipitates formed were collected by centrifugation and washed thoroughly with DCM to remove free ligands. The dark solid was dried under high vacuum to remove the solvent. Nanoparticle **NP-PC** is highly soluble in water and stable in solution for several months. The ^{1}H NMR spectrum of **NP-PC** is shown in Figure S1. From literature,[4] it is estimated that *ca.* 100 ligands are anchored on each gold nanoparticle.

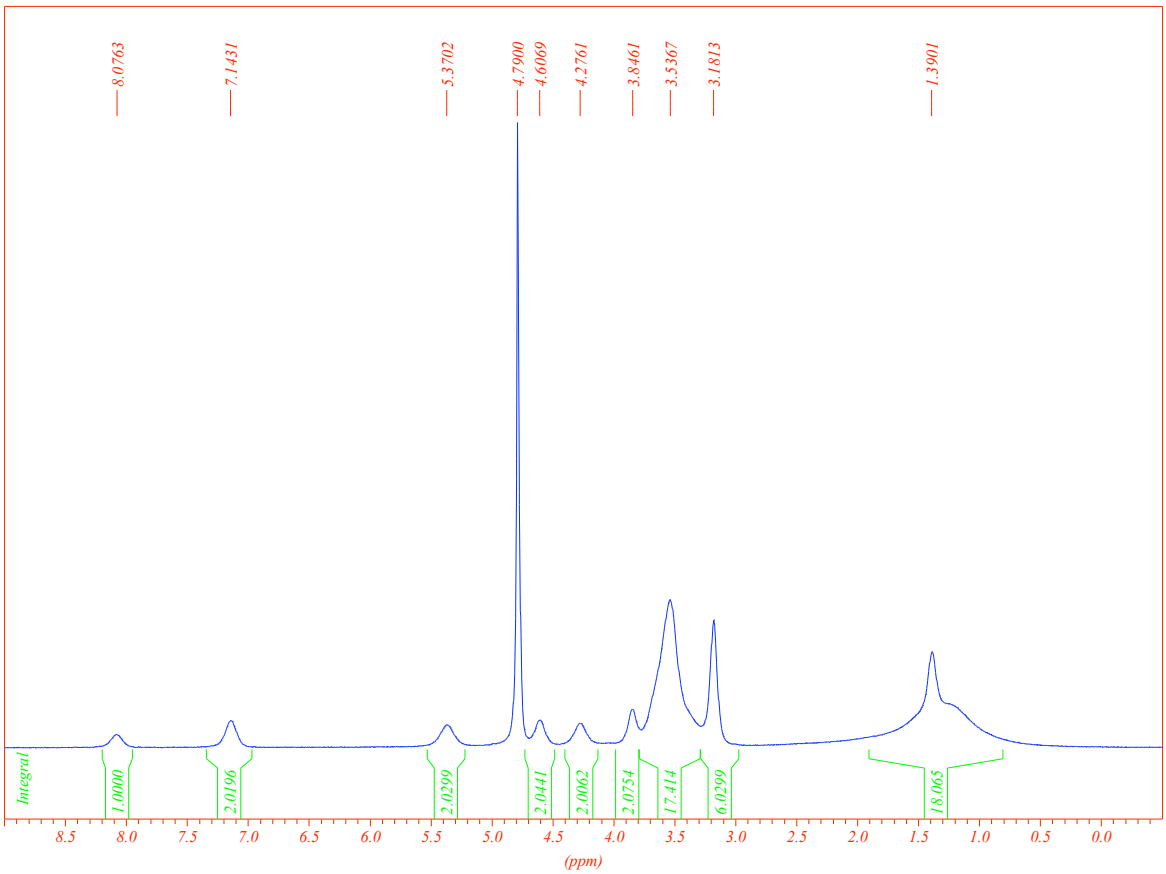


Figure S1. 400 MHz ^{1}H NMR spectrum of **NP-PC** in D_2O.

[4] M. J. Hostetler, J. E. Wingate, C.-J. Zhong, J. E. Harris, R. W. Vachet, M. R. Clark, J. D. Londono, S. J. Green, J. J. Stokes, G. D. Wignall, G. L. Glish, M. D. Porter, N. D. Evans, R. W. Murray, *Langmuir* **1998**, *14*, 17-30.

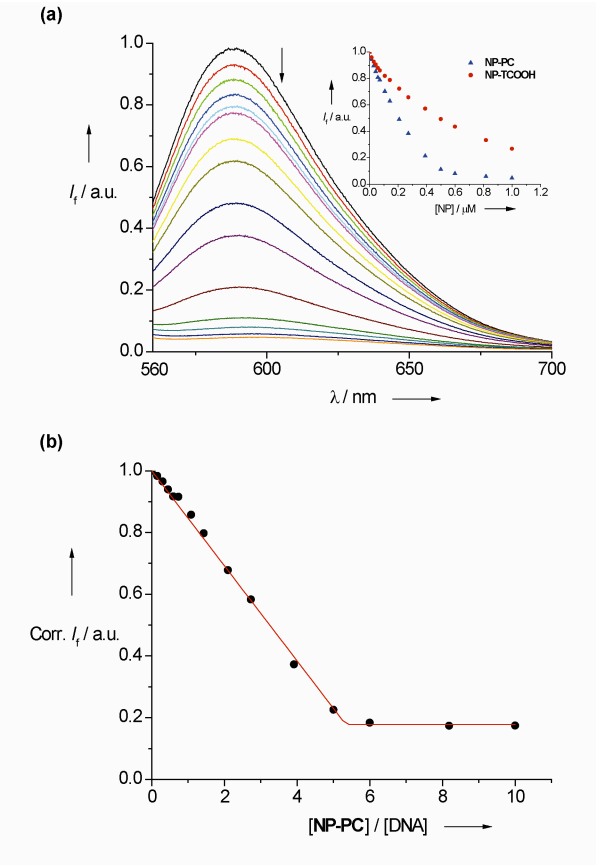


Figure S2. (a) Fluorescence titration of 37mer DNA (100 nM) and **EtBr** (1 μM) with **NP-PC** in PBS. (Inset) The fluorescence intensity of **EtBr**/DNA at 589 nm in the presence of **NP-PC** or **NP-TCOOH**. (b) Titration curve of 37mer DNA (100 nM) and **EtBr** (1 μM) with **NP-PC** in PBS. The fluorescence intensity was calibrated with **NP-TCOOH** as standard at 589 nm.

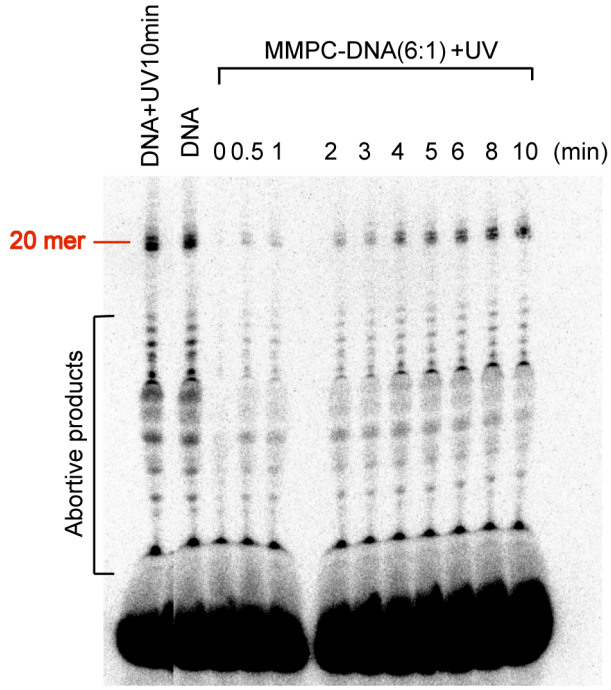


Figure S3. Polyacrylamide gel in T7 RNA polymerase assay

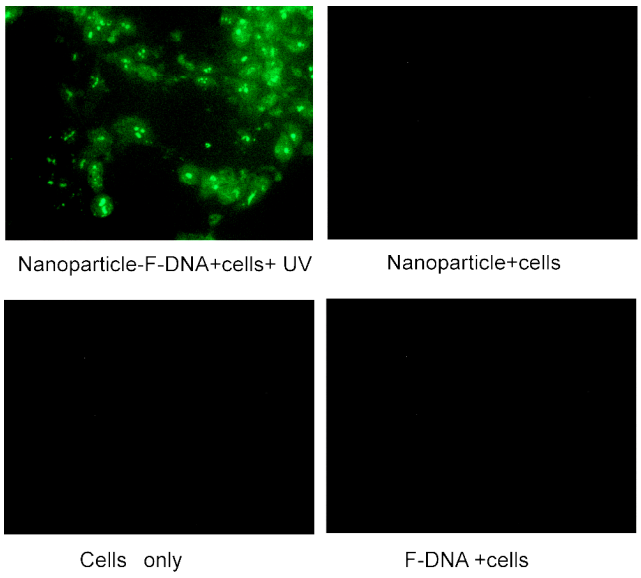


Figure S4. Fluorescence microscope images in the control experiments on the 96 well plates.