Supporting Information

Dynamic split G-quadruplex programmed reversible nanodevice

Yanyan Yu,[a] Yao Zhou,[a] Min Zhu,[a] Gaoxing Su,*[a] Haohua Deng,[b] Wei Chen*[b] and Huaping Peng*[b]

[a] School of pharmacy, Nantong University, Nantong 226001, Jiangsu Province, China

[b] School of pharmacy, Fujian Medical University, Fuzhou 350004, Fujian Province, China

* Corresponding author. Tel: +86 591 22862016, fax: +86 591 22862016.

E-mail address: sugaoxing@ntu.edu.cn (G.X. Su); chenandhu@163.com (W. Chen); phpfjmu@126.com (H.P. Peng)

EXPERIMENTAL SECTION

Materials and Reagents.

All oligonucleotides were synthesized and purified with HPLC by Sangon Biotech (Shanghai, China), and the sequences were shown in Table S1. Sequences of the DNA (Table S1) were designed with the help of the Integrated DNA Technologies. Tris (hydroxyl methyl) amino methane (Tris), potassium chloride, and ThT was purchased from Aladdin Reagent Corporation (Shanghai, China). Tris-acetic acid-magnesium (1×TAMg) buffer (45 mM Tris-acetic acid and 7.6 mM magnesium acetate, pH 8.0) was used for all self-assembled reactions. All reagents from commercial suppliers were used without further purification. Stock solutions of ThT (400 μM) were prepared in H_2O, stored in the dark at −20℃, and diluted before use with 1×TAMg buffer.

Apparatus.

Oligonucleotide quantification was done with an UV1800PC spectrophotometer (Shanghai, China). Fluorescence spectra were recorded on a RF-5301PC (Shimadzu) spectrofluorophotometer. All DNA samples were annealed on an Applied Biosystems 96-well thermocycler. DNA bands were imaged and analyzed using a Syngene gel imaging system under UV light.

Preparation of the DNA nanodevice.

Equivalent of three component strands L1, L2, G4-1 and G4-2 were mixed at a concentration of 1 μM in one pot in a Tris-acetic acid-magnesium (TAMg) buffer and annealed from 95 ℃ to 4 ℃. The resulting samples were then analyzed with 8 %

native polyacrylamide gel electrophoresis (PAGE). The electrophoresis was conducted in 1 × TBE buffer (89 mM Tris, 89 mM boric acid, 2 mM EDTA, pH 8.0) and a constant voltage of 100 V was used for 1.5 hour. The gels were stained with 4S Red prior to imaging.

Fluorometric assays.

Firstly, the annealed device (100 μL) was mixed with 10 μL KCl (500 mM) and 1 μL ThT (400 μM). The final concentration of ThT was 3.6 μM. The resulting samples were incubated for an hour at room temperature before the ThT fluorescence emission spectra were recorded from 450 to 600 nm at an excitation wavelength of 405 nm in a 100 μL quartz cuvette. All experiments were repeated at least three times.

Circular Dichroism Measurements

CD spectra of the DNA strands (4 μM) were measured on a Chirascan CD Spectrometer (Applied Photophysics Ltd, UK). The wavelength was varied from 205 nm to 330 nm at 100 nm min^{-1}. The samples were measured with a square quartz cell with a 0.1 cm path length in the TAMg buffer at room temperature.

Cell Culture and Lysis Preparation

Human cervical carcinoma cells (HeLa) and human breast cancer cells (MCF-7) were cultured in DMEM and RPMI 1640 medium, respectively. The mediums were supplemented with 10% fetal calf serum, 100 U mL^{-1} penicillin, and 100 μg mL^{-1} streptomycin. All cells were cultured at 37°C in a 5% CO_2 incubator. Exosomes were harvested from MCF-7 cells according to the literature[1, 2] by differential centrifugation method.

Table S1 Oligonucleotides used in this work.

Name	Sequence 5'→3'
G4-a	AACGAGACTGTGGGTGGG
G4-b	GGGTGGGTCGTCACTCCA
let-7a	UGAGGUAGUAGGUUGUAUAGUU
let-7b	UGAGGUAGUAGGUUGUGUGGUU
Random	CAUAACUUCAUAAUCCUUAACA
L1-8	TGGAGTGACGTGAGGTAGCAGTCTCGTT
L1-10	TGGAGTGACGTGAGGTAGTACAGTCTCGTT
L1-12	TGGAGTGACGTGAGGTAGTAGGCAGTCTCGTT
L1-14	TGGAGTGACGTGAGGTAGTAGGTTCAGTCTCGTT
L1-16	TGGAGTGACGTGAGGTAGTAGGTTGTCAGTCTCGTT
L1-18	TGGAGTGACGTGAGGTAGTAGGTTGTATCAGTCTCGTT
L1-20	TGGAGTGACGTGAGGTAGTAGGTTGTATAGCAGTCTCGTT
L2	AACTATACAACCTACTACCTCA

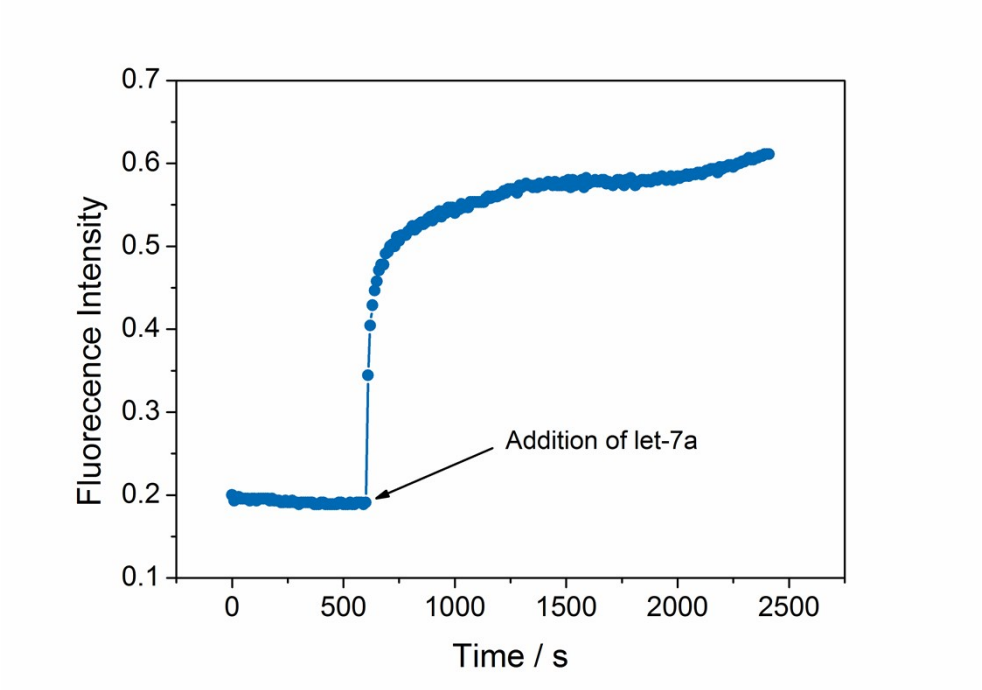

Fig. S1. Time-signal curve for switch with spacer 14 and after addition of let-7a at the interval of 10 s. The reaction system was 1 × TAMg buffer with 50 mM KCl and 4 μM ThT. Then 0.5 μL let-7a (100 μM) was added to the nanodevice sample and fluorescence spectra were recorded every 10 minutes in a 100 μL quartz cuvette.

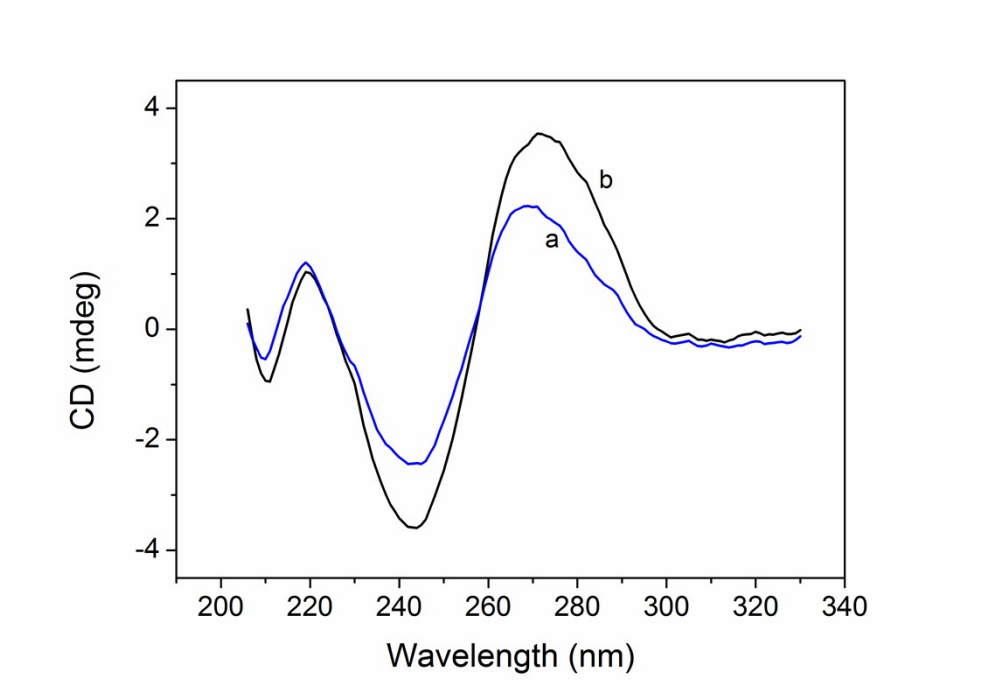

Fig. S2. CD spectra of the switches at OFF (a) and ON (b) state. The higher peak around 260 nm at ON state proves that more G4 has been formed.

References

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2. J. Pablo Tosar, F. Gambaro, J. Sanguinetti, B. Bonilla, K. W. Witwer and A. Cayota, *Nucleic Acids Res.*, 2015, **43**, 5601-5616.