

Supporting Information

Experimental Sections

Reagents and Apparatus

Folic acid (FA) and folate receptor (FR) were purchased from Boisynthesis LTD. (Beijing, China), their stock solutions were prepared in phosphate buffer solution (PBS, pH 7.4) and stored at -20 °C for later use. Exonuclease III (Exo III) was obtained from Sangon Inc. (Shanghai, China). Quinaldine red (QR, the structure was shown in Fig.S1) was purchased from Sigma (St. Louis, MO). Double-distilled water was used throughout the whole process. All other chemicals were of analytical reagent grade and used without further purifying. 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and N - hydroxy succinimide (NHS) were achieved from Sangon Inc. (Shanghai, China).

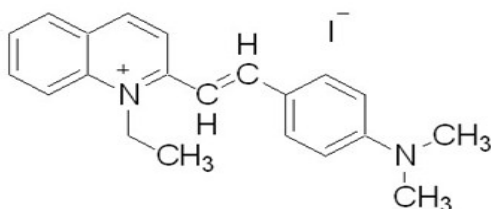


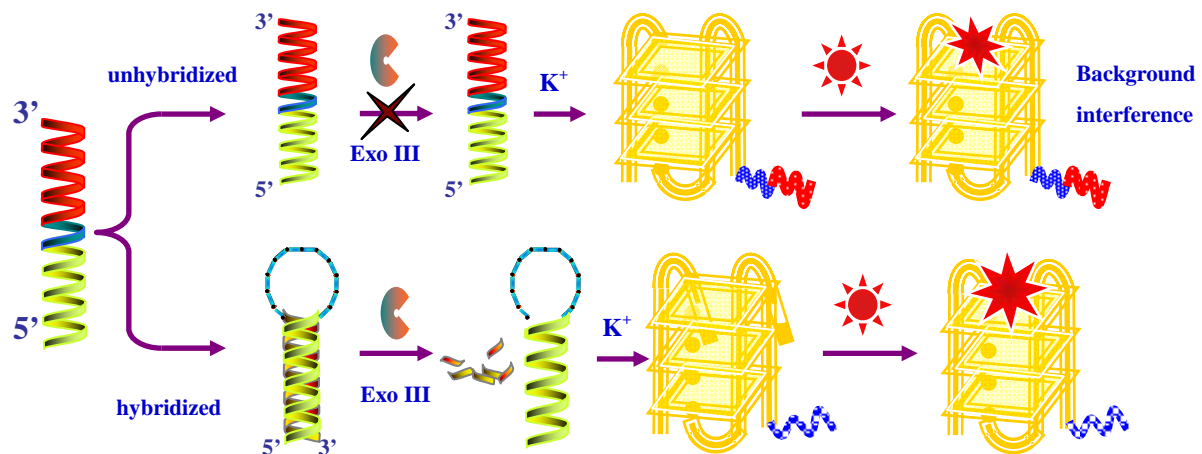
Fig.S1 Chemical structure of Quinaldine red

The DNA sequences used herein were synthesized and purified by Sangon Inc. (Shanghai, China), they were dissolved in Tris-HCl (pH 7.4) buffer solution and stored at 4 °C for later use. The amino-modified guanine-rich single-strand oligomer is a 55-mer oligonucleotide with the -NH₂ label at the 3' end as the following sequences: 5'-AGGG (TTAGGG)₃-CAGAAGGATAA-(CCCTAA)₃CCCT-NH₂-3' (G₅₅).

21 Cary Eclipse Fluorescence Spectrophotometer used for the measurements was from
22 American Varian Corporation. The apparatus parameters were set as follows: $\lambda_{\text{ex}}= 558$
23 nm (slit 5 nm), $\lambda_{\text{em}}= 610-750$ nm (slit 5 nm).

24 **Preparation of the fluorescence biosensor**

25 Firstly, the amino-modified guanine-rich single-strand oligomer (10 $\mu\text{mol/L}$) was
26 hybridized with magnesium ion (100 mmol/L) at 37 °C for 2 h in dark, forming a
27 stem-loop secondary DNA structure (see Fig.1A). Subsequently, we incubated the
28 hairpin DNA with the folic acid solution (50 $\mu\text{mol/L}$) in the presence of the
29 cross-linking agent, which was mixed by 10 μL EDC (1 mmol/L) and 10 μL NHS (5
30 mmol/L), shaping the DNA-3'-small molecule chimeras. The solution was then
31 dialyzed against phosphate buffer solution (PBS, pH 7.4) using a dialysis membrane
32 with molecular weight cutoff of 1000 Da to remove superabundant unreacted folic
33 acid in process. The dialysis process lasted 3 days in dark place and renovated the
34 fresh PBS every 4 h.¹ Afterwards, we joined a series of varying concentrations of
35 folate receptor into the mixture dialyzed entirely for sufficiently incubating at 37 °C
36 for 1 h in dark. Ultimately, through acceding respectively to 500 U/ml ExoIII, the preceding
37 mixture solutions were hydrolyzed absolutely about 2 h in the enzymolysis. Before
38 conducting the fluorescence testing, the solution mingled with potassium ion (100
39 mmol/L) and quinaldine red (10 $\mu\text{mol/L}$). The fluorescent signals of the mixture were
40 promptly represented with fluorescence spectrophotometer.



41

42 Fig.S2 Schematic diagram about the interference from the incomplete hybridization

43 **Reference**

- 44 1. Z. Wu, Z. Zhen, J. H. Jiang, G. L. Shen and R. Q. Yu, *J. Am. Chem. Soc.*, 2009,
45 **131**, 12325–12332.