General methods and materials. All the reagents and solvents were commercially available and used as received unless otherwise specified purification. ^{1}H NMR spectra were recorded with a AVANCE III HD 400 MHz spectrometer (Bruker) in the indicated solvents at 25 °C. Variable-temperature ^{1}H NMR experiments were carried out with a AVANCE III HD 500 MHz spectrometer (Bruker). Chemical shifts were referenced to the residual solvent peaks. Dynamic light scattering (DLS) experiments were conducted on a Malvern Zetasizer Nano ZS90 using a monochromatic coherent He–Ne laser (633 nm) as the light source and a detector that detected the scattered light at an angle of 90°. Fluorescent measurements were performed on a VARIAN CARY Eclipse Fluorescence Spectrophotometer. Fluorescent microscopic experiments were performed on the Leica DMi8 fluorescent microscope. Flow cytometric experiments were conducted with a Gallios 3L 10C flow cytometry system (Beckman Coulter, USA). Fetal bovine serum (FBS), 1640 Medium, DMEM Medium, MEM Medium were purchased from Thermo Fisher Scientific. Cy5-ssDNA-21 and Cy5-dsDNA-21 were commercials purchased from Shanghai HuaGen Biotech Co., Ltd. Lipo2000 was commercial purchased from Thermo Fisher Scientific Co. Compound **T1** was prepared according to the reported method.[1]

Isothermal titration calorimetry (ITC) experiments (with FOF1 as example): An aqueous solution of **FOF1** (0.05 mM) was placed in the sample cell (350 μL). Then a solution of ssDNA-21bp (0.1 mM) was added in a series of 20 injections (2 μL per injection), the heat evolved was recorded at T = 298.15 K. Computer simulations (curve fitting) were performed by using the Malvern Micro Cal PEAQ ITC. analyze software. Thermodynamic parameters were obtained by using the “one set of binding sites” model.

Cell culture. Hela, MCF-7, A549 and H9C2 cells were obtained from Chinese Academy of Sciences Cell Bank of Type Culture Collection (www.cellbank.org.cn), and incubated in corresponding medium with 10% FBS and 1% penicillin streptomycin at 37 °C in a humidified atmosphere containing 5% CO_2.

In vitro cytotoxicity assay of FOFs. The cytotoxicity of the FOFs against Hela cells was evaluated by the Cell Counting Kit-8 (CCK-8) assay. In brief, Hela cells were seeded in 96-well plates at an appropriate density of 1×10^4 cells per well and then incubated for 24 hours. After adherence, the cells were treated with the FOFs with different concentrations ranging from 0 to 0.12 mg/mL. After 24 hours of incubation, the medium was replaced with fresh complete medium containing CCK-8. Then, after incubating for 1 hours, the absorbance was measured at 450 nm using a microplate reader (Bio-Tek, Synergy H1, USA). The relative cell viability was calculated as: cell viability = (OD450 (samples)/OD450 (control)) × 100%, where OD450 (control) was obtained in the absence of **FOF1-5**, and OD450 (samples) was obtained in the presence of **FOF1-5**. The evaluation with other cells was conducted under similar conditions.

Fluorescence microscopy. For microscopic observations, ana-1 cells (1*106 cells per dish) were seeded in coverglass bottom dishes (35 mm × 35 mm). After culture for 24 hours, the cells were incubated with complete medium containing free Cy5-ssDNA-21, Cy5-ssDNA-21 + **FOF1-4** (Cy5-ssDNA-21 = 2.5 μg/mL; [**FOF1-5**] = 20 μg/mL) at 37 °C for 2 hours. After washing the cells by PBS (1 mL) twice to remove excessive **FOF1-5** and DNA, the cells were fixed with 4% paraformaldehyde solution, then treated with immunostaining permeabilization Buffer with Triton X-100. Cells were stained with 10 μg/mL DAPI for 10 min and 5 μg/mL FITC phalloidin for 30 min at 37 °C, and then washed with PBS (1 mL) three times. The cells were imaged on Leica DMi8 fluorescent microscope.

Flow cytometry assay. Hela, MCF-7, A549 and H9C2 cells were seeded at 5×10^5 cells per well in 12-well plate and further cultured for 24 hours. The culture media were replaced by 1 mL of fresh culture medium. Free Cy5-ssDNA-21, Cy5-dsDNA-21, Cy5-ssDNA-21 + **FOF1-5** or Cy5-dsDNA-21 + **FOF1-5** (Cy5-dsDNA-21 = 2.5 μg/mL; [**FOF1-5**] = 20 μg/mL) were added to the cells, respectively. Following incubating for 2 h, the cells were digested, and then followed by flow cytometry assay in FL6 channel on a Gallios 3L 10C flow cytometry system (Beckman Coulter, USA).

Synthesis of T1. A solution of compounds **1** (0.35 g, 0.50 mmol) and isonicotinaldehyde **2** (0.43 g, 4.0 mmol) in anhydrous DMF (10 mL) was heated to 100 °C for 12 hours and then cooled to room temperature. The precipitate formed was filtered and washed with acetonitrile (20 mL × 3) and dried in vacuo to afford **T1** as a yellowish powder (0.48 g, 86%). ^{1}H NMR (400 MHz, D_2O): δ 8.87 (d, *J* = 6.4 Hz, 8H), 8.11 (d, *J* = 6.4 Hz, 8H), 7.43 (d, *J* = 8.0 Hz, 8H), 7.36 (d, *J* = 8.0 Hz, 8H), 6.19(s, 4H) , 5.76(s, 8H). ^{13}C NMR (400 MHz, D_2O): δ 160.07, 147.49, 144.42, 131.36, 130.69, 128.68, 125.43, 87.33, 63.46. HRMS (ESI): calcd for $C_{53}H_{52}N_4O_8$ $[M-4Br + 4H_2O]^{4-}$: 218.0941. Found: 218.0992.

Synthesis of FOF1. To a solution of compound **T1** (0.11 g, 0.10 mmol) in water (10 mL) was added **L1** (36 mg, 0.20 mmol). The solution was stirred at room temperature for 2 hours to afford the solution of **FOF1**. ^{1}H NMR in D_2O indicated that the reaction was complete in 2 hours and **T1** and **L1** reacted to yield **FOF1** quantitatively.

FOF2-5 were prepared from **T1** and **L2-L5** respectively under the same conditions as described above for **FOF1**.

Reference

1. J. Tian, Y.-D. Ding, T.-Y. Zhou, K.-D. Zhang, X. Zhao, H. Wang, D.-W. Zhang, Y. Liu and Z.-T. Li, *Chem. Eur. J.*, 2014, **20**, 575–584.

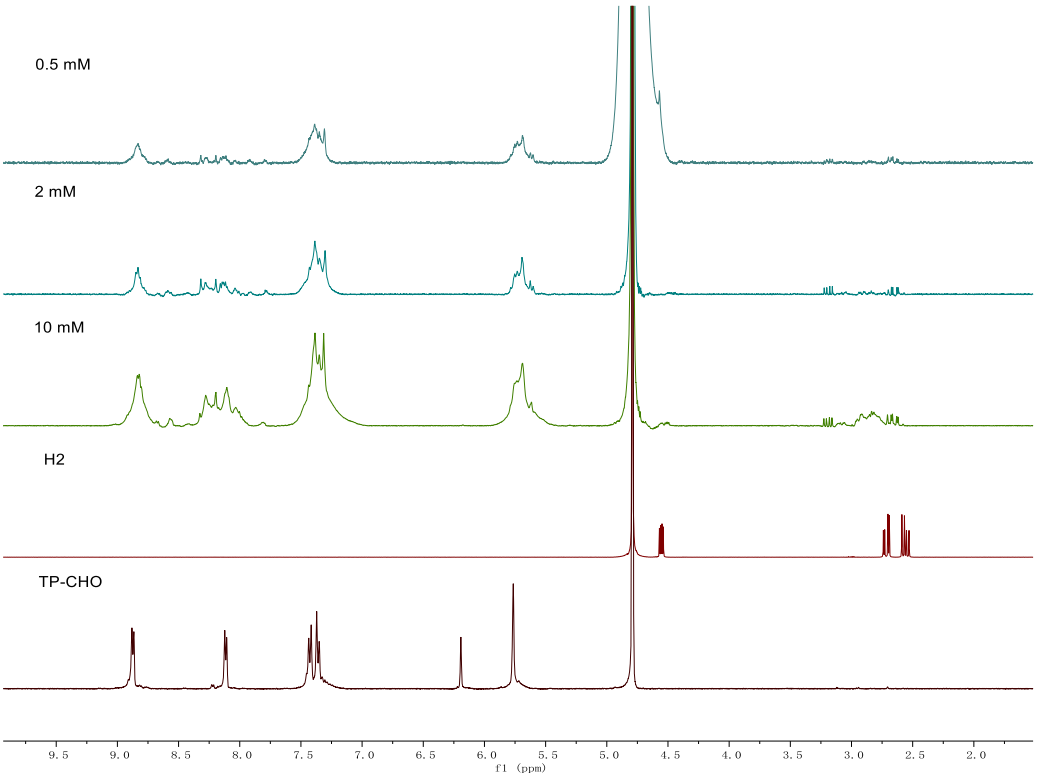

Fig. S1 ^{1}H NMR spectra (400 MHz) of **T1** (10 mM), **L2** (20 mM) and **FOF2** of different concentration, indicated by [**T1**], at 25 °C (400 MHz, D_2O).

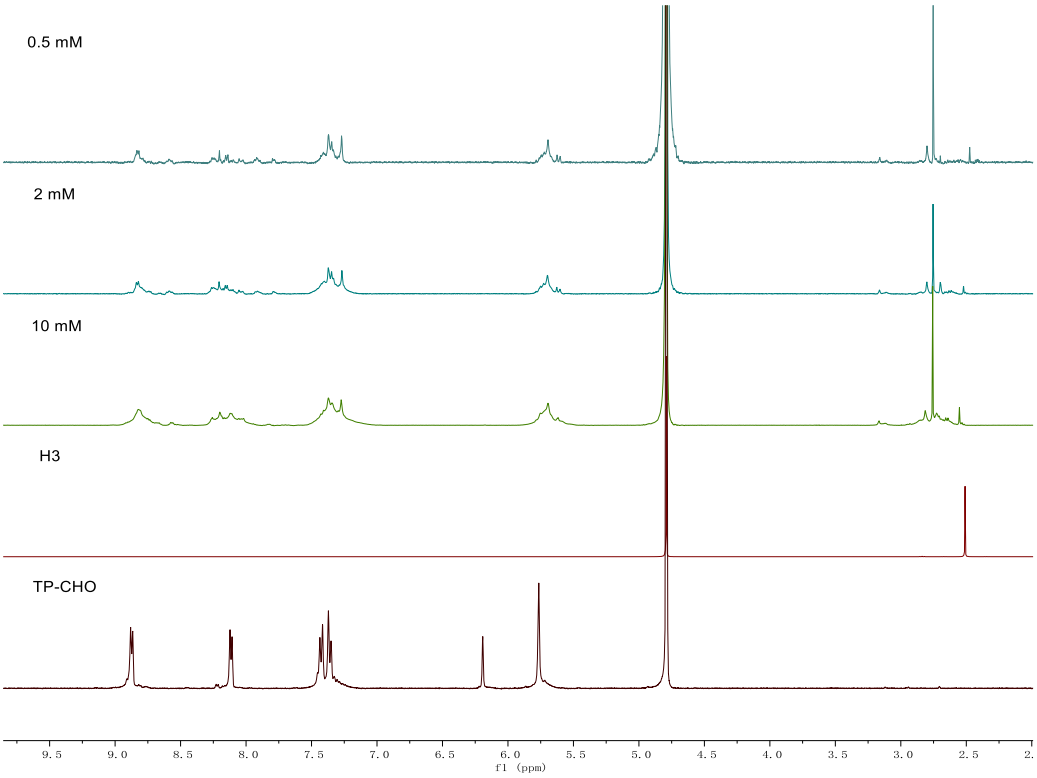

Fig. S2 ^{1}H NMR spectra (400 MHz) of **T1** (10 mM), **L3** (20 mM) and **FOF3** of different concentration, indicated by [**T1**], at 25 °C (400 MHz, D_2O).

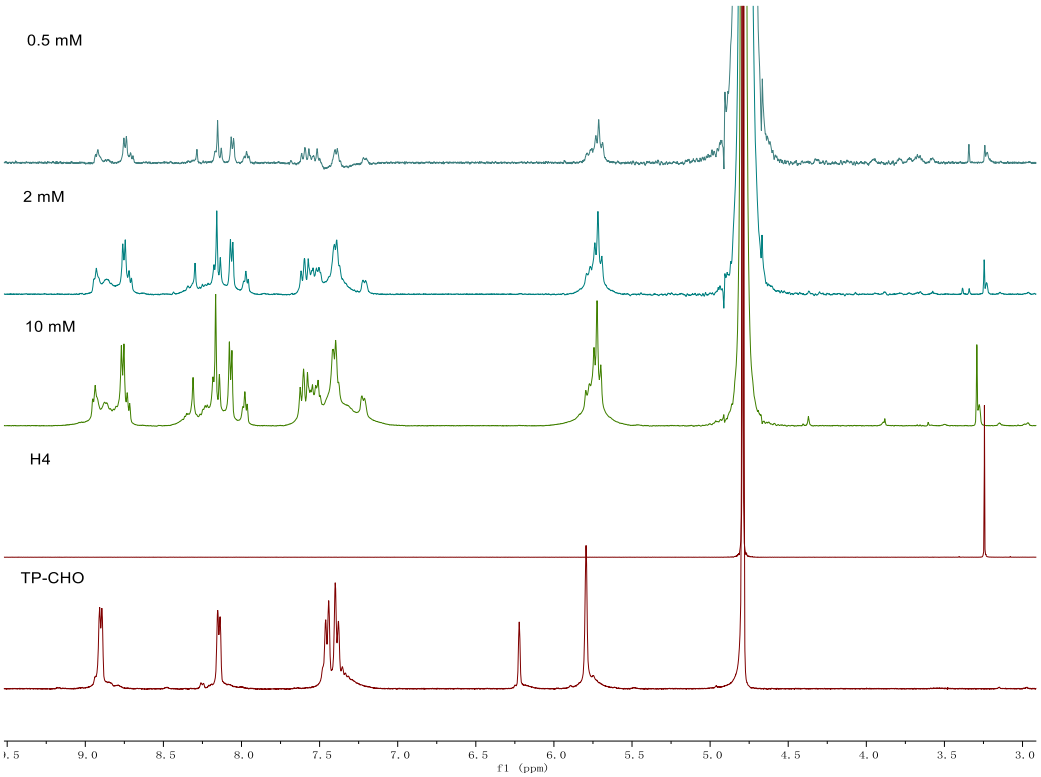

Fig. S3 ^{1}H NMR spectra (400 MHz) of **T1** (10 mM), **L4** (20 mM) and **FOF4** of different concentration, indicated by [**T1**], at 25 °C (400 MHz, D_2O).

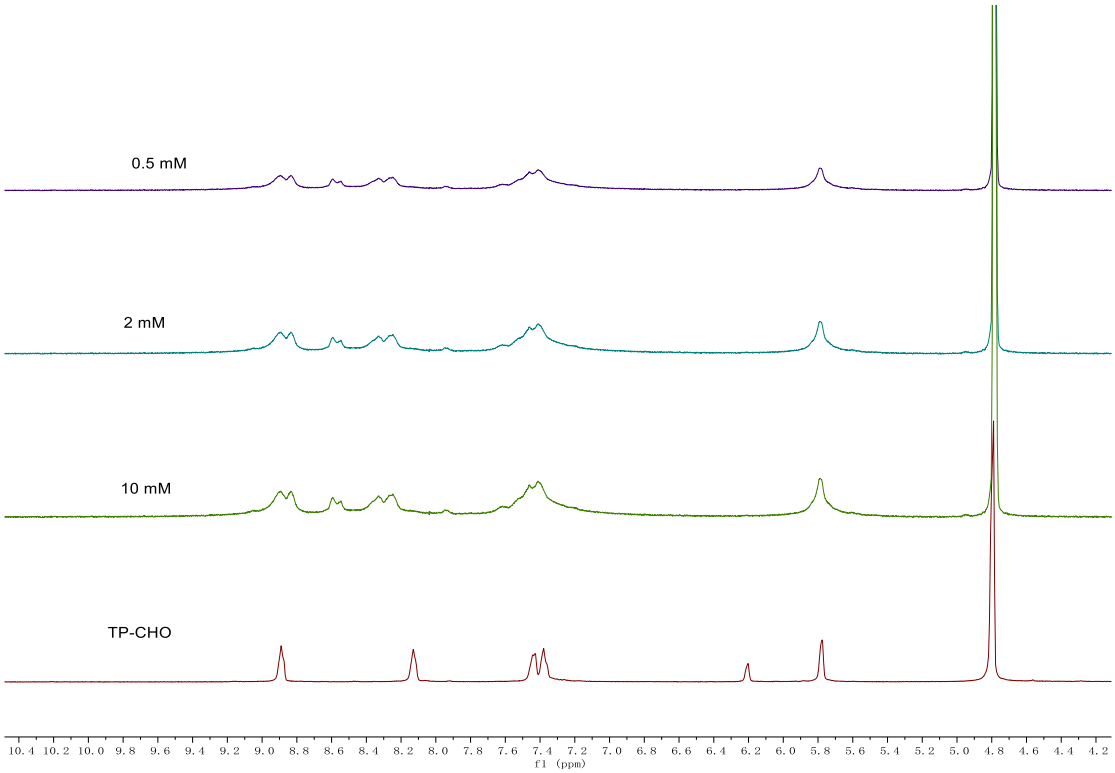

Fig. S4 ^{1}H NMR spectra (400 MHz) of **T1** (10 mM), **L5** (20 mM) and **FOF5** of different concentration, indicated by [**T1**], at 25 °C (400 MHz, D_2O).

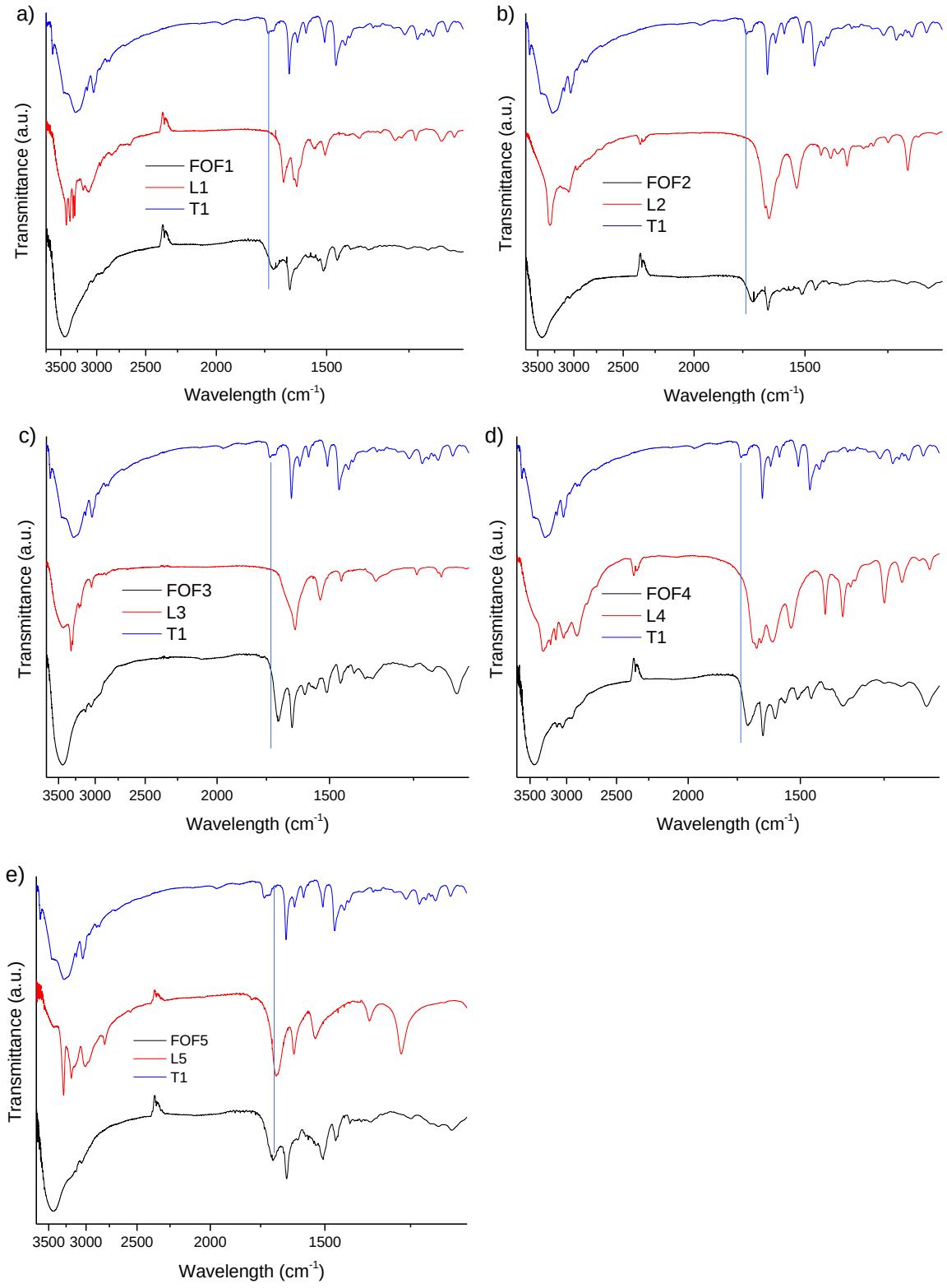

Fig. S5 IR spectra of a) **FOF1**, **L1** and **T1**, b) **FOF2**, **L2** and **T1**, c) **FOF3**, **L3** and **T1**, d) **FOF4**, **L4** and **T1**, and e) **FOF5**, **L5** and **T1** (KBr tabletting).

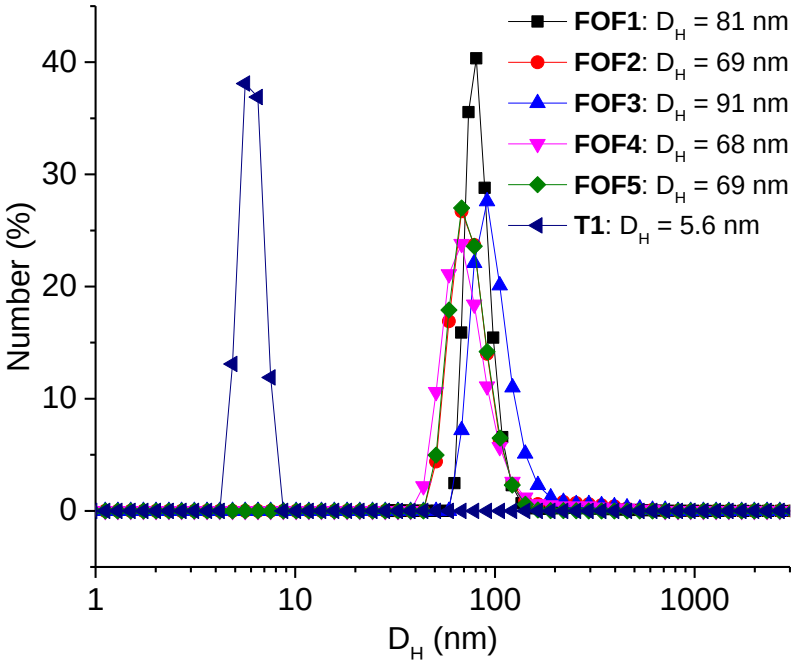

Fig. S6 DLS profile of **FOF1-5** ([**T1**] = 0.1 mM) and **T1** (0.1 mM) in water at 25 °C. The solutions were left to stand for 24 h before being measured.

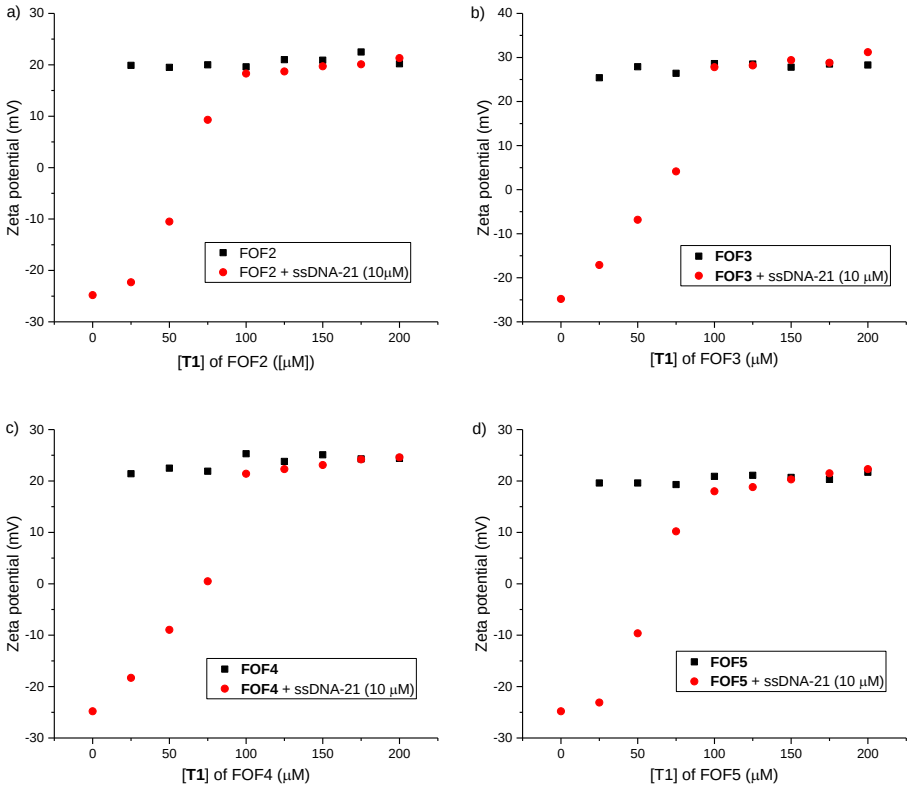

Fig. S7 ζ Potential of the solution of ssDNA-21 (10 μM) in the absence and presence of a) **FOF2**, b) **FOF3**, c) **FOF4** and d) **FOF5** of incremental concentration, which was related to [**T1**], in water at 25 °C.

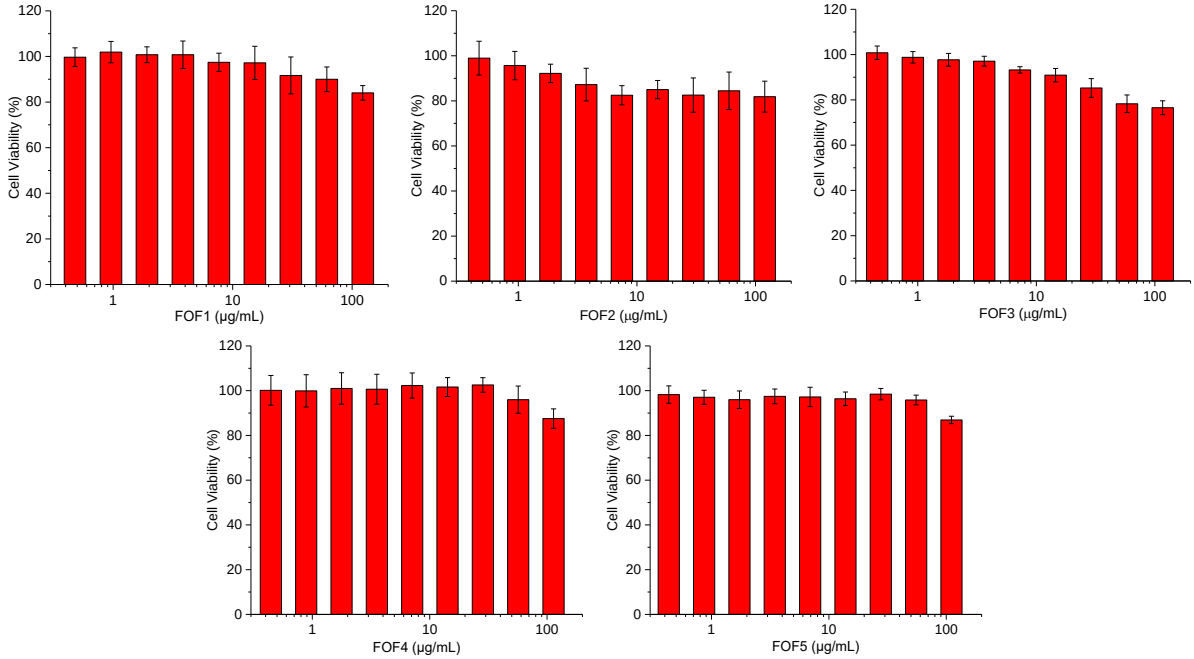

Fig. S8 Cell viability values (%) of a) H9C2, b) Hela, c) MCF-7 and d) a549 cell lines evaluated by CCK-8 proliferation tests versus the incubation concentration of **FOF1-5**. The cells (~2×10^4 per well) were incubated with the FOFs at 37 °C for 24 h. Error bars represent the s.d. of uncertainty for each point.

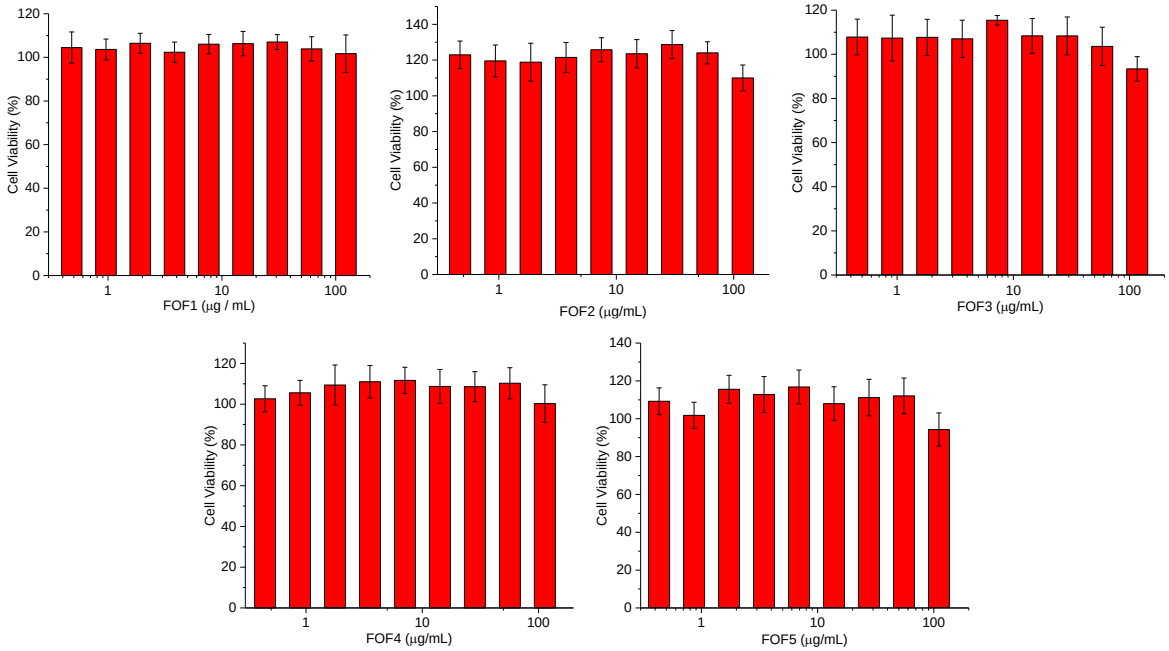

Fig. S9 Cell viability values (%) of Hela cell line evaluated by CCK-8 proliferation tests versus the incubation concentration of **FOF1-5**. The cells (~2×10^4 per well) were incubated with the FOFs at 37 °C for 24 h. Error bars represent the s.d. of uncertainty for each point.

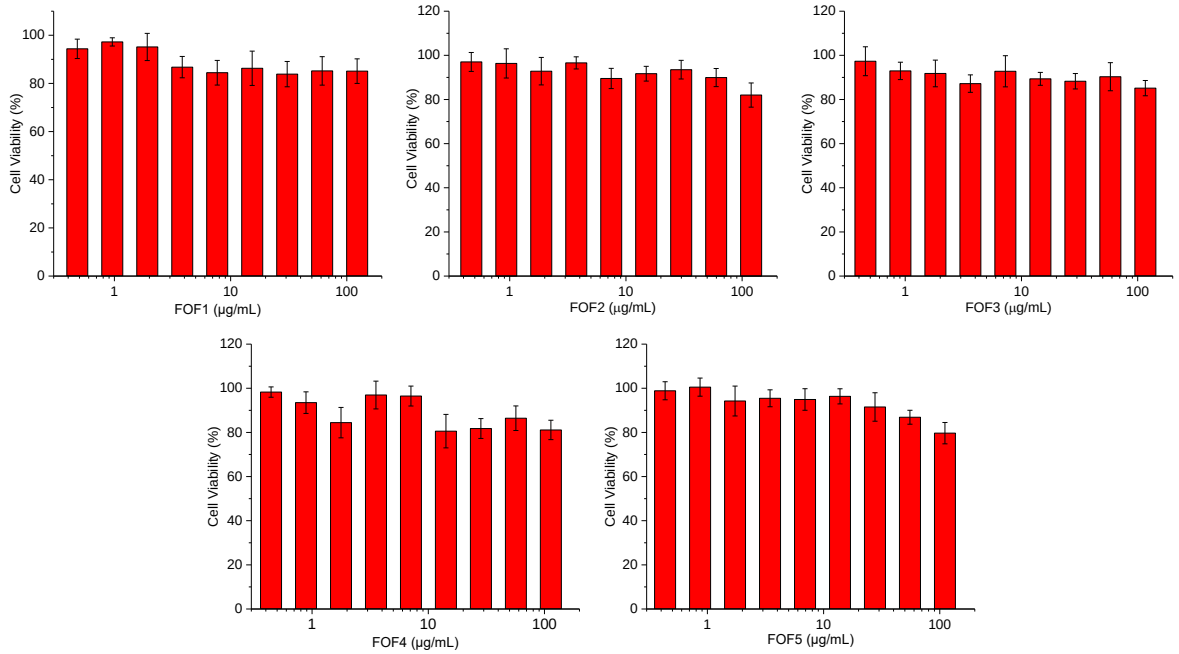

Fig. S10 Cell viability values (%) of MCF-7 cell line evaluated by CCK-8 proliferation tests versus the incubation concentration of **FOF1-5**. The cells (~2 × 10^4 per well) were incubated with the FOFs at 37 °C for 24 h. Error bars represent the s.d. of uncertainty for each point.

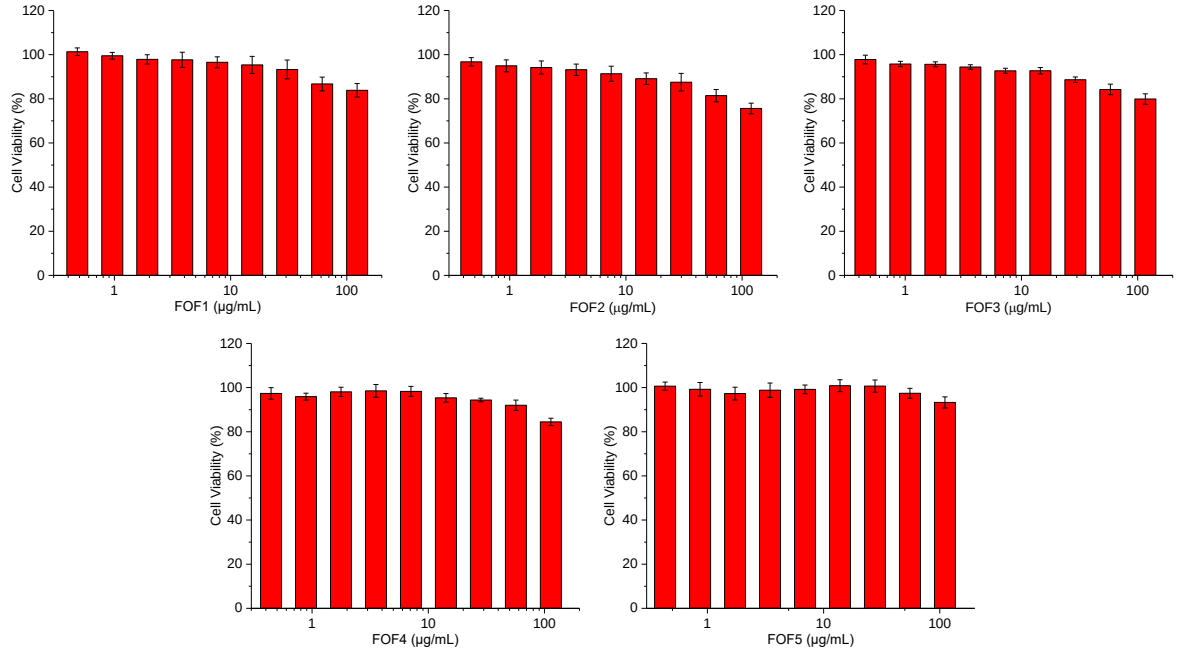

Fig. S11 Cell viability values (%) of a549 cell line evaluated by CCK-8 proliferation tests versus the incubation concentration of **FOF1-5**. The cells (~2 × 10^4 per well) were incubated with the FOFs at 37 °C for 24 h. Error bars represent the s.d. of uncertainty for each point.

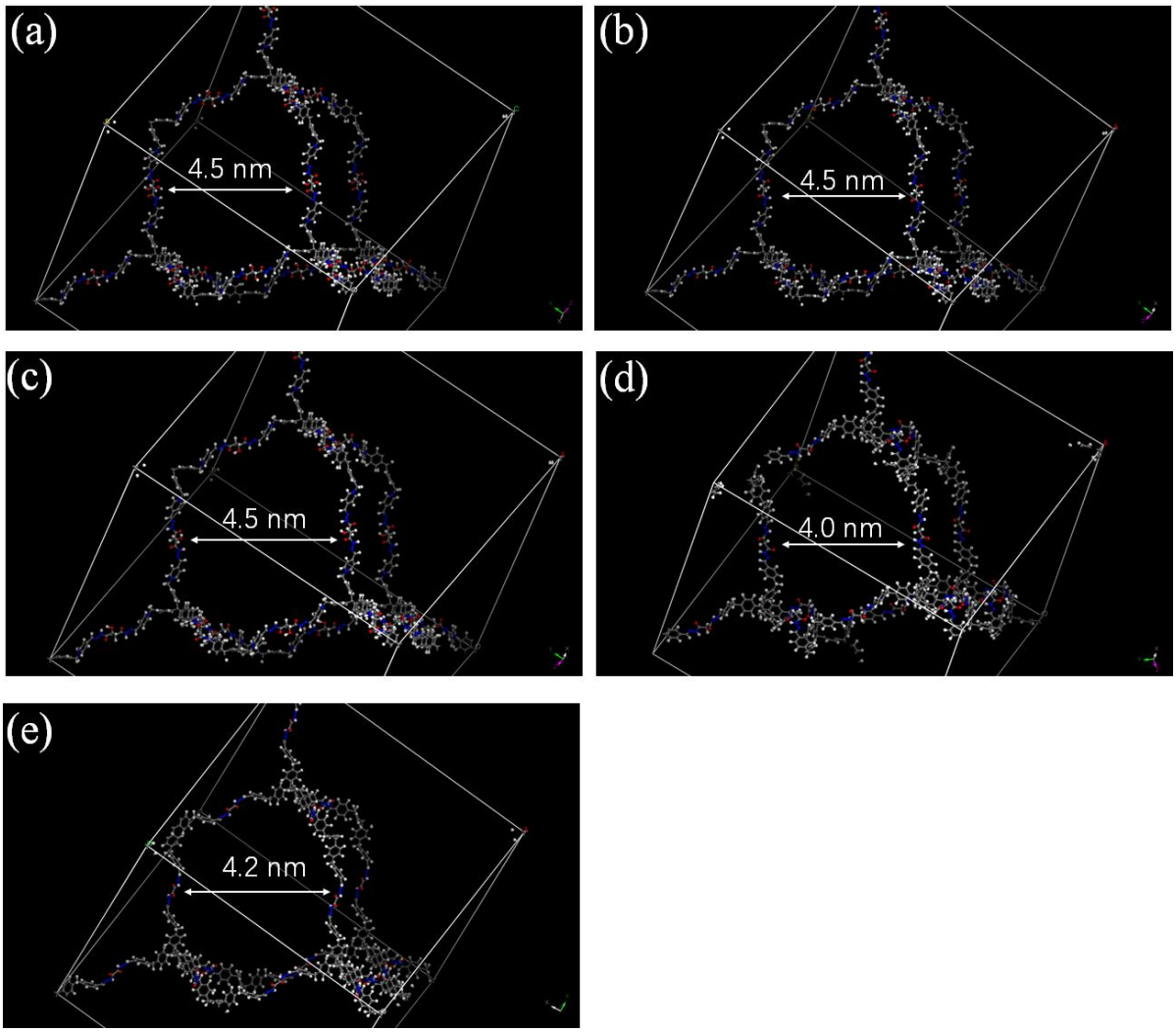

Fig. 12 Molecular modelling of the diamondoid unit of **FOF1-5** with the linkers adopting extended conformations.

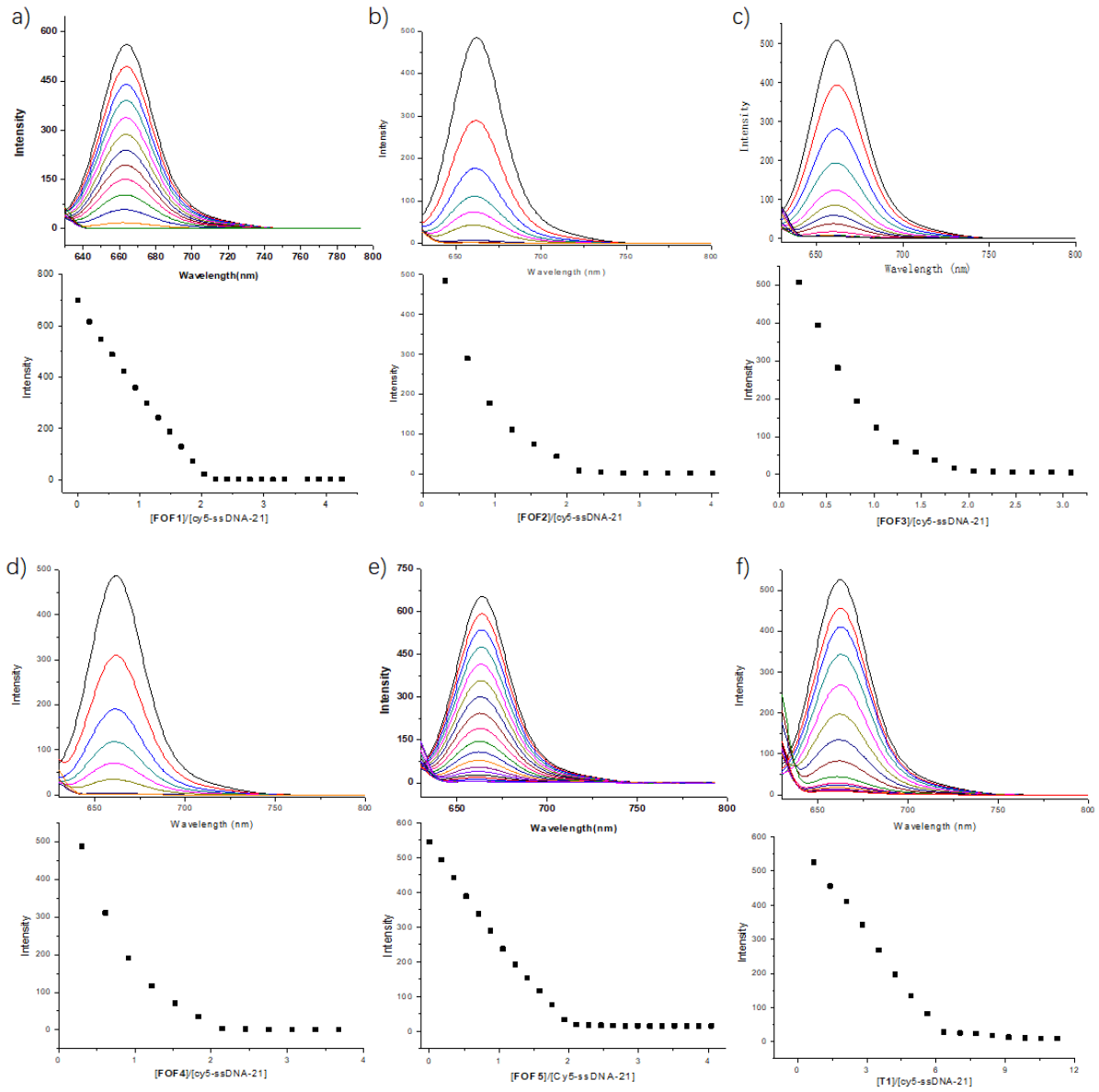

Fig. S13 Fluorescence spectra of Cy5-ssDNA-21 (0.5 μM) with the addition of incremental amount of a) **FOF1**, b) **FOF2**, c) **FOF3**, d) **FOF4**, e) **FOF5** and f) **T1** in water at 25 °C. The concentration of the frameworks was related to [**T1**].

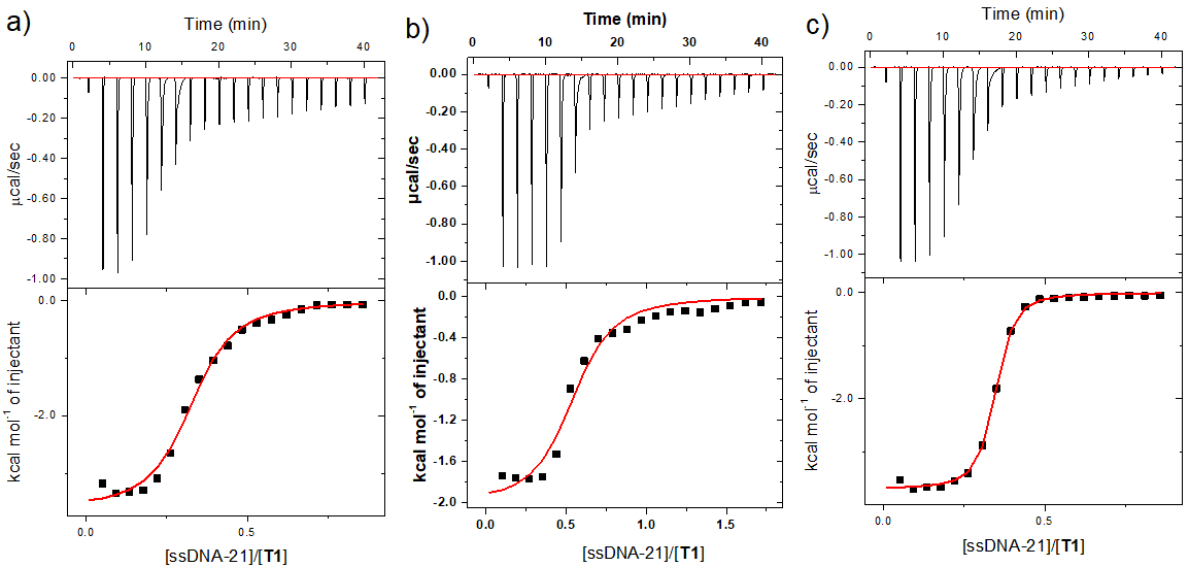

Fig. S14 Isothermal titration thermogram recorded by adding the solution of ssDNA-21 (0.1 mM) into the solution of a) **FOF3**, b) **FOF4** and b) **FOF5** ([**T1**] = 50 µM) in water at 25 °C. The injection volume of the DNA was 2 µL.

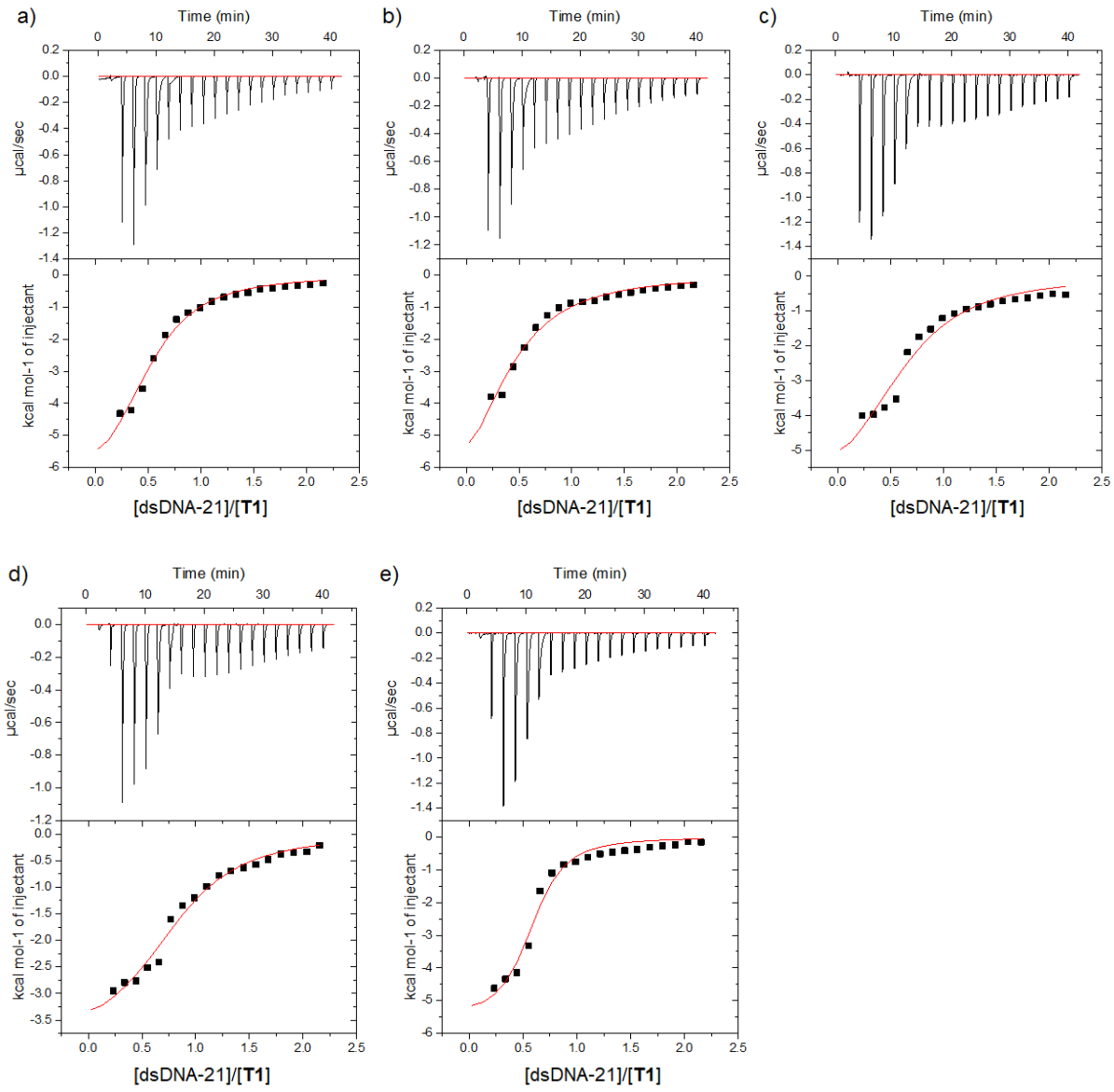

Fig. S15 Isothermal titration thermogram recorded by adding the solution of dsDNA-21 (0.1 mM) into the solution of a) **FOF1**, b) **FOF2**, c) **FOF3**, d) **FOF4** and e) **FOF5** ([**T1**] = 50 µM) in water at 25 °C. The injection volume of the DNA was 2 µL.

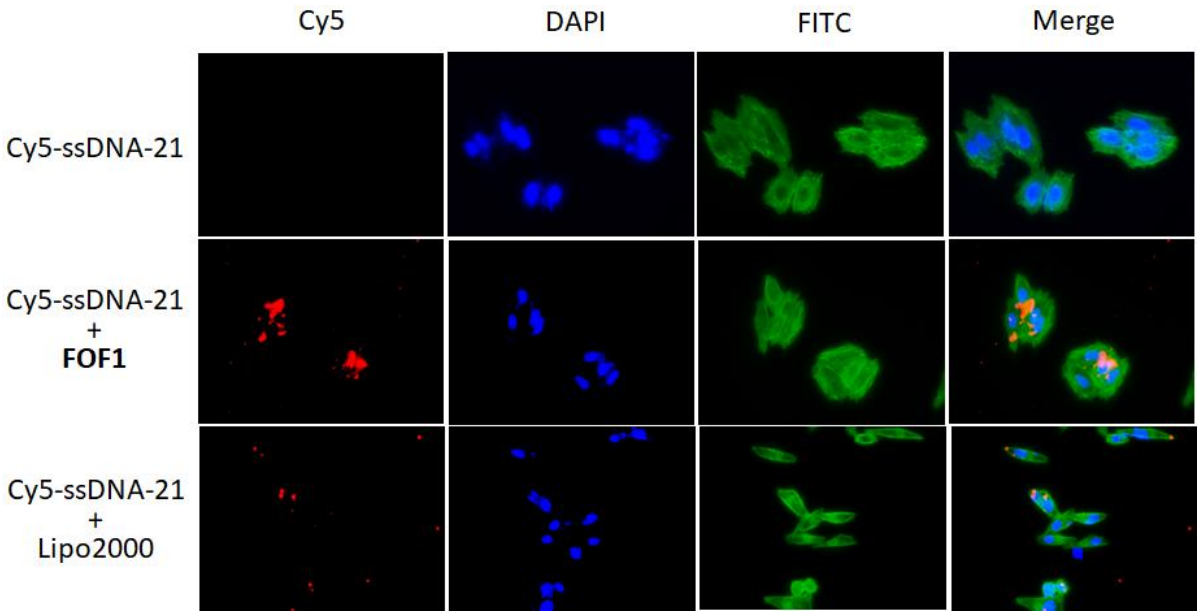

Fig. S16 Florence microscopic image of Cy5-sDNA-21, Cy5-sDNA-21 + **FOF1** and Cy5-sDNA-21 + lipo2000 of A549 cancer cells ([Cy5-sDNA-21] = 2.5 μg/mL, [**FOF1**] = 20.0 μg/mL). Cy5-sDNA-21 showed red fluorescence. Nuclei was stained with DAPI (blue) and cytoskeleton was stained with FITC- phalloidin (green).

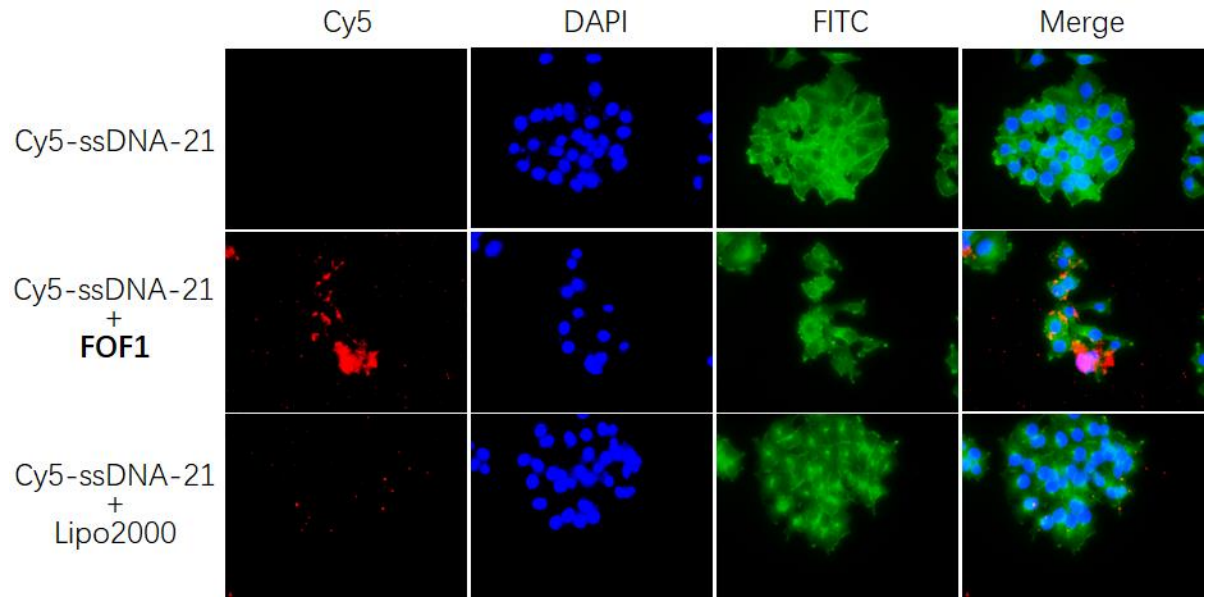

Fig. S17 Florence microscopic image of Cy5-sDNA-21, Cy5-sDNA-21 + **FOF1** and Cy5-sDNA-21 + lipo2000 of MCF-7 cancer cells ([Cy5-sDNA-21] = 2.5 μg/mL, [**FOF1**] = 20.0 μg/mL). Cy5-sDNA-21 showed red fluorescence. Nuclei was stained with DAPI (blue) and cytoskeleton was stained with FITC- phalloidin (green).

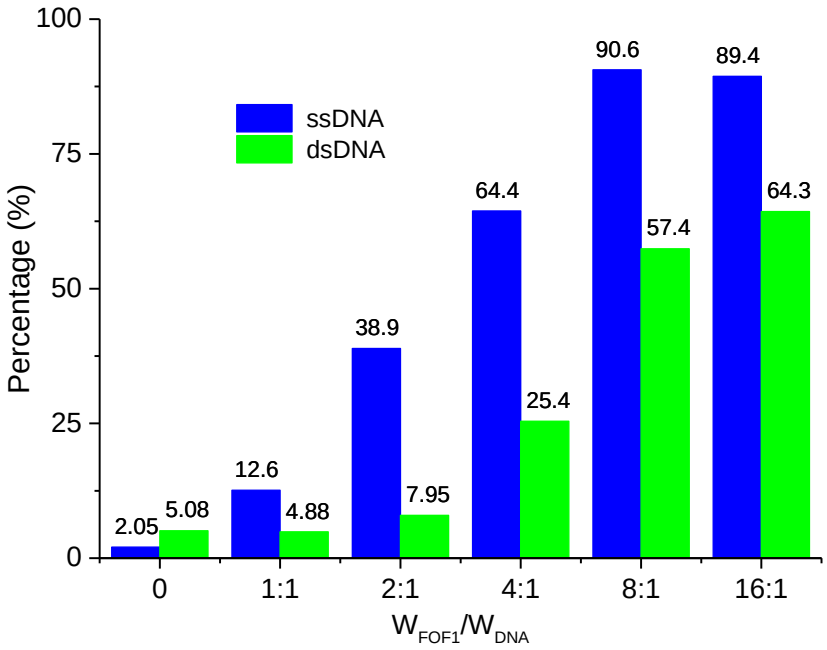

Fig. S18 Delivery (internalization) of Cy5-ssDNA-21 (2.5 μg/mL) and Cy5-dsDNA-21 (5.0 μg/mL) into H9C2 cells by **SOF1** of increasing amount after incubation in complete DMEM medium for 2 h.

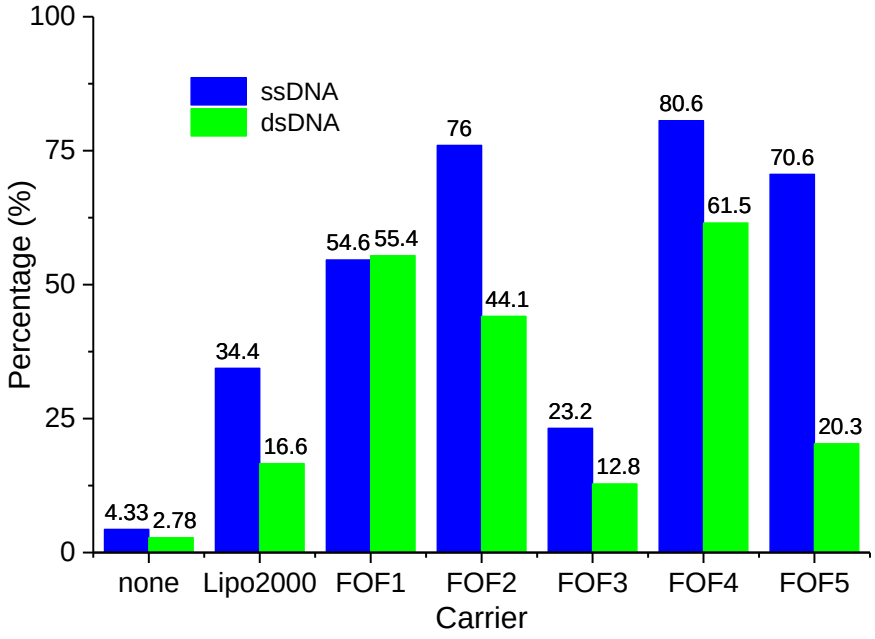

Fig. S19 Delivery (internalization) of Cy5-ssDNA-21 (2.5 μg/mL) and Cy5-dsDNA-21 (2.5 μg/mL) into A549 cells by **FOF1-5** (20 μg/mL for ssDNA and 40 μg/mL for dsDNA) and Lipo2000 (20 μg/mL for ssDNA and 40 μg/mL for dsDNA) after incubation in complete RPMI-1640 medium for 2 h.

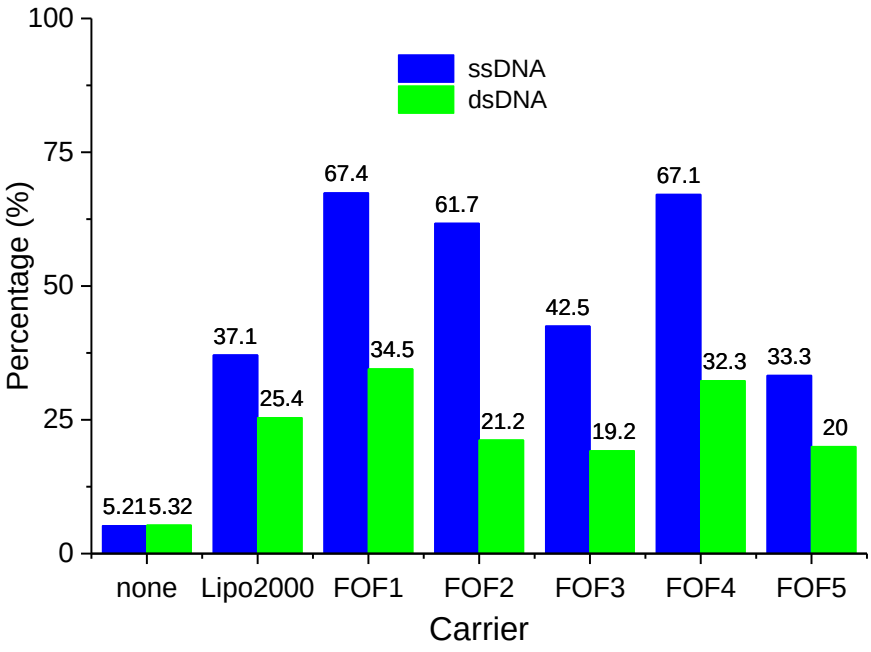

Fig. S20 Delivery (internalization) of Cy5-ssDNA-21 (2.5 μg/mL) and Cy5-dsDNA-21 (2.5 μg/mL) into MCF-7 cells by **FOF1-5** (20 μg/mL for ssDNA and 40 μg/mL for dsDNA) and Lipo2000 (20 μg/mL for ssDNA and 40 μg/mL for dsDNA) after incubation in complete DMEM medium for 2 h.