Supporting information for the article:

"A water-soluble cationic porphyrin showing pH-dependent G-quadruplex recognition specificity and DNA photocleavage activity"

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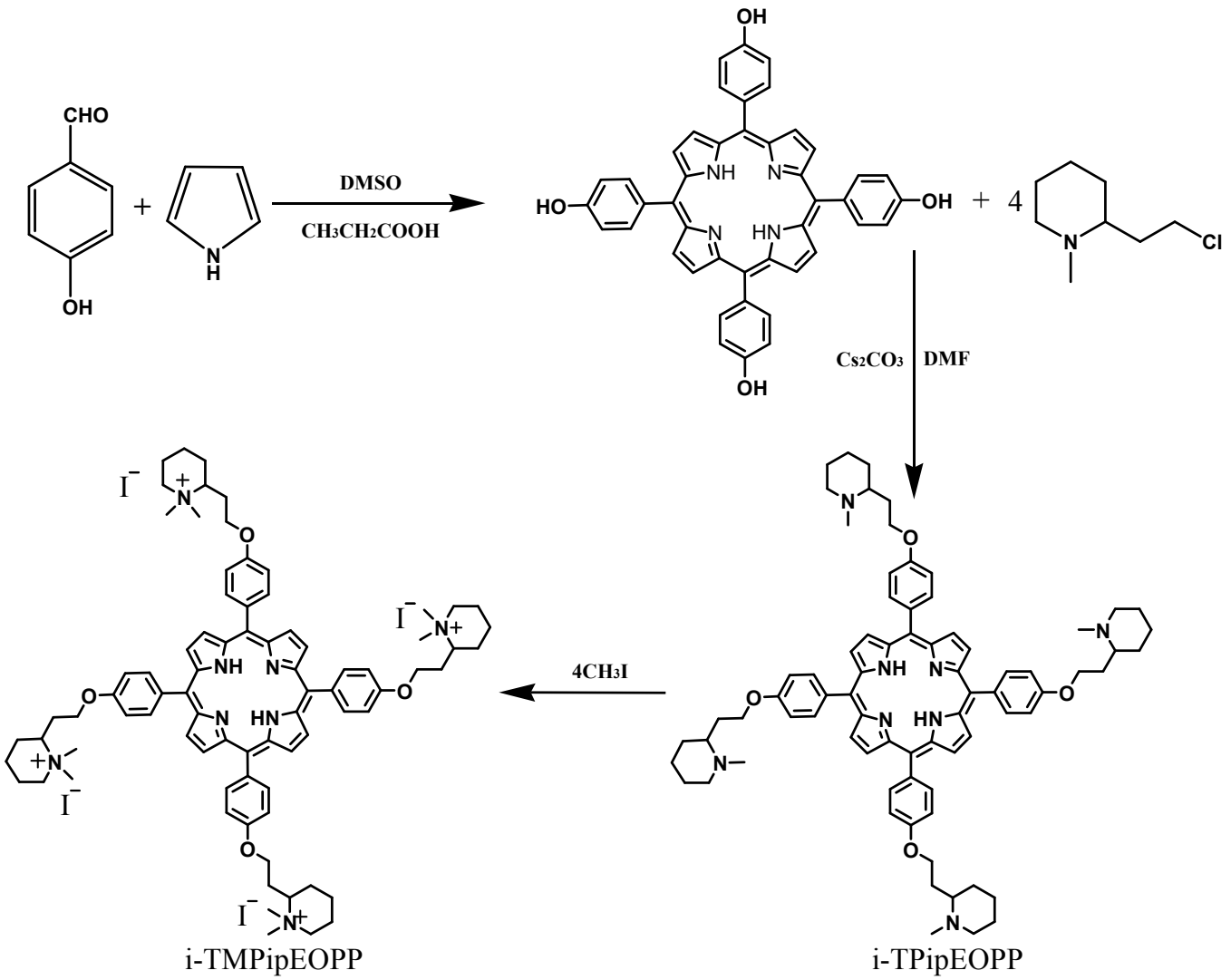
1. Synthesis and characterization of 5,10,15,20-tetra-{4-[2-(N,N-bimethyl-2-piperidinyl) ethoxy]phenyl}porphyrin (*i*-TMPipEOPP).

i-TMPipEOPP was synthesized according to the route shown in Scheme S1. The details are as follows:



Scheme S1. Synthetic route of *i*-TMPipEOPP.

1.1 Synthesis of 5,10,15,20-tetra-(4-hydroxyphenyl)porphyrin.

6.1 g 4-Hydroxybenzaldehyde (0.05 mol) was dissolved in 120 mL propionic acid and 6 mL dimethyl sulfoxide (DMSO) mixed solution, stirred and heated to 128 °C. Under the condition of the dark, the mixture of 3.5 mL (0.05 mol) freshly distilled pyrrole and 10 mL propionic acid was slowly added. The resulted mixture was heated to 141 °C and refluxed over 2 h at this temperature. Then, the mixture filtrated under reduced pressure. The crude product was recrystallized in CH_3CH_2OH, and purified using silica gel columns. CH_3COCH_3 was used to elute the pure product. The purple solid of the product was obtained in 7.27% yield (0.6172g, 0.91 mmol).

1.2 Synthesis of 5,10,15,20-tetra-{4-[2-(N-methyl-2-piperidinyl)ethoxy]phenyl}porphyrin (*i*-TPipEOPP).

0.2035 g 5,10,15,20-tetra-(4-hydroxyphenyl)porphyrin (0.30 mmol), 0.5232 g N-(2-chloroethyl)-methylpiperidine hydrochloride (2.40 mmol) and 1.3032 g Cs_2CO_3 (4.00 mmol) were mixed in dry DMF (50 mL) and stirred at 60 °C

under N_2 atmosphere for 72 h. Then the solvent was evaporated under reduced pressure. The resulted solid was dissolved in 30 mL CH_2Cl_2 and extracted with water. Product that existed in organic layer was purified by silica gel columns. $(C_2H_5)_3N/CH_2Cl_2/CH_3OH$ (v:v:v = 70:30:1) was used to elute the pure prodct. The purple-red solid of the product *i*-TPipEOPP were obtained in 26.6% yield (0.0943 g, 0.08 mmol).

1.3 Synthesis of 5,10,15,20-tetra-{4-[2-(N,N-bimethyl-2-piperidinyl)ethoxy]phenyl} porphyrin, tetraiodide (*i*-TMPipEOPP·4I).

0.0589g *i*-TPipEOPP (0.05 mmol) was dissolved in dry CH_2Cl_2 (35 mL), and stirred at 40 ^oC under N_2 atmosphere. Under the condition of the dark, the mixture of 15 mL CH_3I (0.24 mmol) and 15 mL CH_2Cl_2 was slowly added into the solution. After reaction for 24 h, the reaction mixture was filtered, and the obtained product was washed with CH_2Cl_2. Pure purple-red solid of the product *i*-TMPipEOPP-4I was obtained in 40% yield (0.0349 g, 0.02 mmol).

1.4 Characterization of *i*-TMPipEOPP

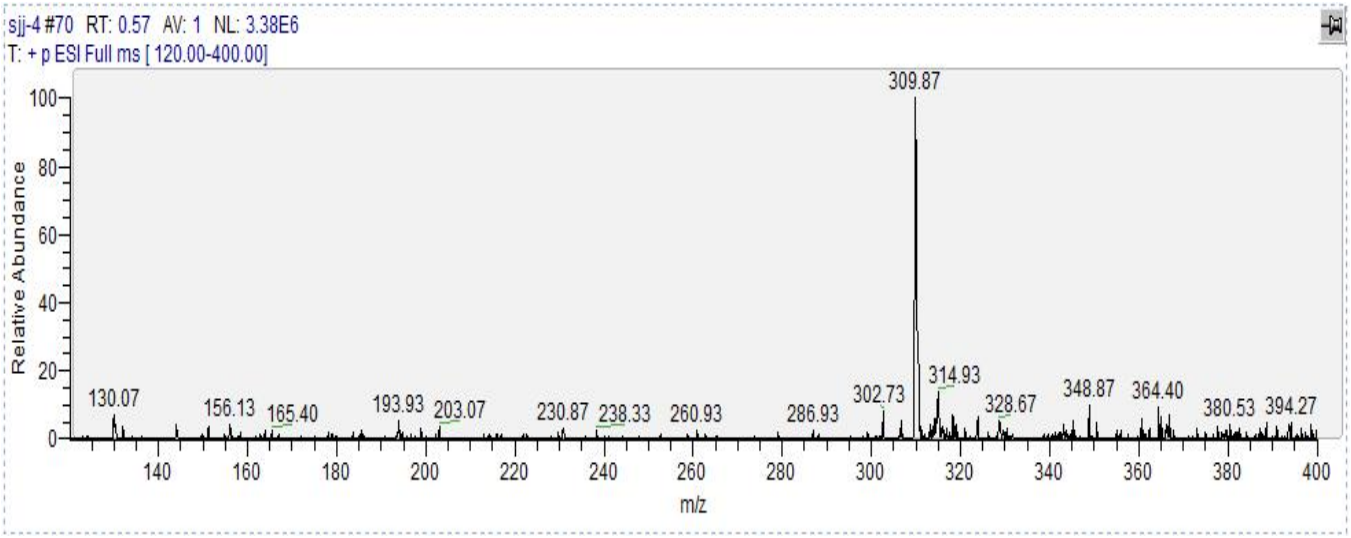


Figure S1. ESI-MS of 5,10,15,20-tetra-{4-[2-(N,N-bimethyl-2-piperidinyl)ethoxy]phenyl}porphyrin (*i*-TMPipEOPP). ESI:m/z: calcd for $[C_{80}H_{102}N_8O_4\text{-}4I]/4$: 309.7; found: 309.9 $[M^+\text{-}4I]/4$.

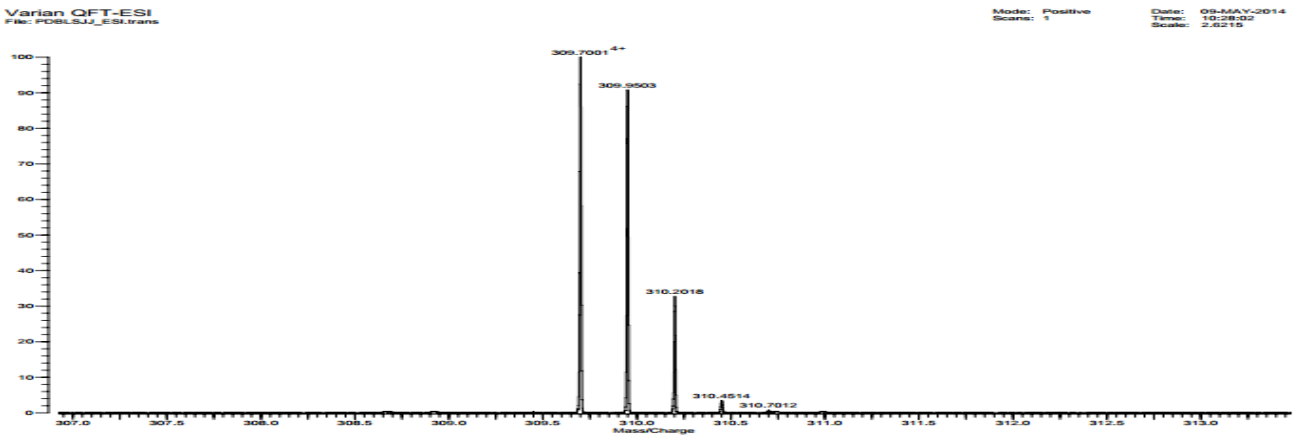


Figure S2. FT-MS of 5,10,15,20-tetra-{4-[2-(N,N-bimethyl-2-piperidinyl)ethoxy]phenyl}porphyrin (*i*-TMPipEOPP). m/z: calcd for $[C_{80}H_{102}N_8O_4\text{-}4I]/4$: 309.7000; found: 309.7001[M].

^{1}H-NMR (300 MHz, [D6]DMSO, 25 ºC, TMS) (Figure S3): δ = 8.83 (s, 8H; β-pyrrole H), 8.12 (d, *J* = 7.8 Hz, 8H; Ph-H), 7.40 (d, *J* = 7.8 Hz, 8H; Ph-H), 4.36 (d, *J* = 17.3 Hz, 8H; OCH_2), 3.68 (t, *J* = 9.8 Hz, 4H; piperidine H), 3.55 (dd, *J* = 19.4, 11.6 Hz, 8H; piperidine H), 3.26 (s, 12H; NCH_3), 3.04 (s, 12H; NCH_3), 2.73–2.62 (m, 4H; piperidine H), 2.18 (d, *J* = 14.6 Hz, 4H; piperidine H), 2.01–1.88 (m, 8H; CH_2), 1.88–1.72 (m, 12H; piperidine H), 1.63–1.52 (m, 4H; piperidine H), -2.90 ppm (s, 2H; pyrrole H).

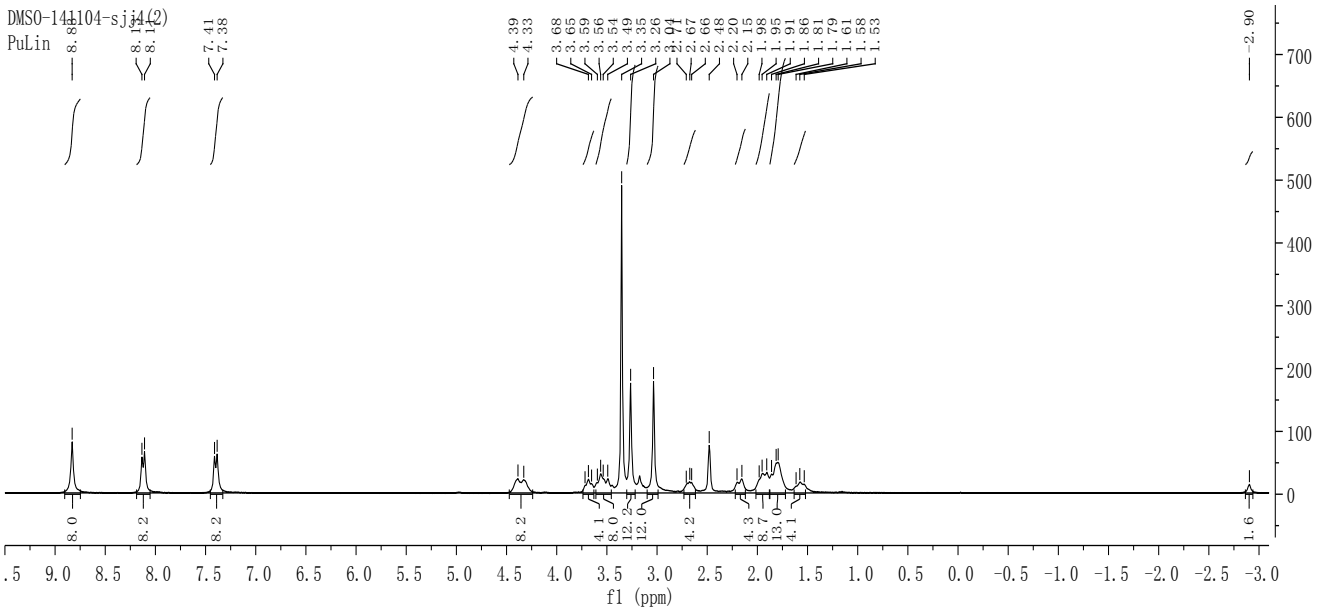


Figure S3. ^{1}H-NMR of 5,10,15,20-tetra-{4-[2-(N,N-bimethyl-2-piperidinyl)ethoxy]phenyl}porphyrin (*i*-TMPipEOPP). The NMR spectra were recorded on Mercury Vx-300 spectrometer. Chemical shifts in the ^{1}H NMR spectra are reported in ppm relative to the residual hydrogen atoms in the deuterated solvents: d = 2.50 and 3.40 ppm for [D_6]DMSO.

2. Effects of different DNAs on the UV-vis absorption spectrum of *i*-TMPipEOPP

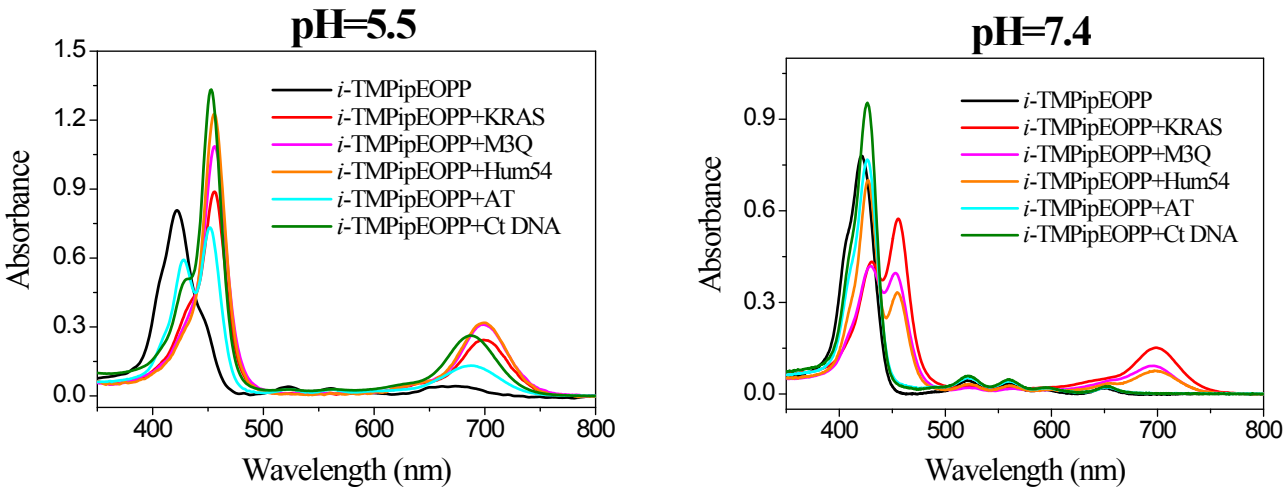
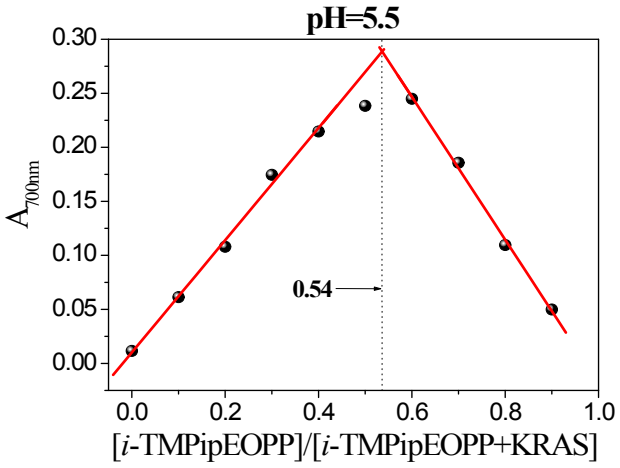
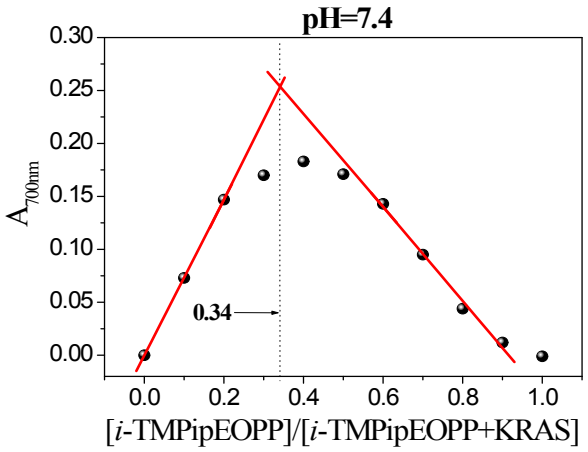
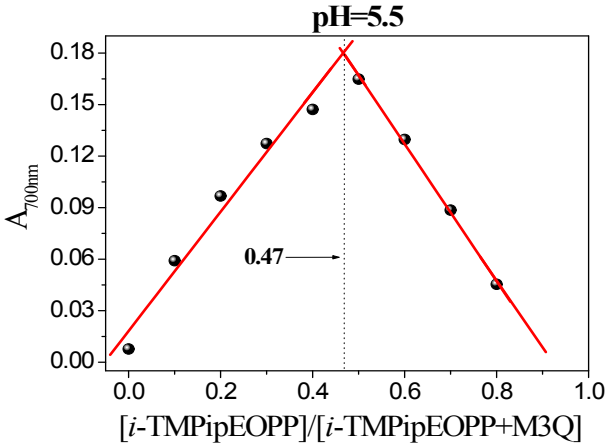


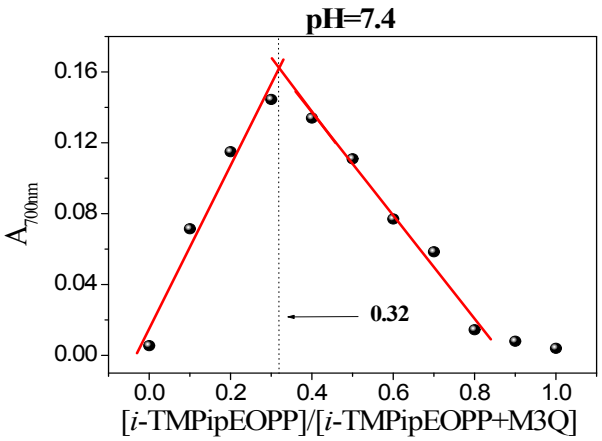
Figure S4. UV-vis absorption spectrum of *i*-TMPipEOPP in the absence or presence of monomeric G-quadruplex (KRAS, M3Q), multimeric G-quadruplex (Hum54) or duplex DNA (AT, Ct DNA) under acidic and neutral conditions. [*i*-TMPipEOPP] = 5 μM; [KRAS] = [M3Q] = [AT] = 20 μM; [Hum54] = 10 μM; [Ct DNA] = 400 μM (base concentration).

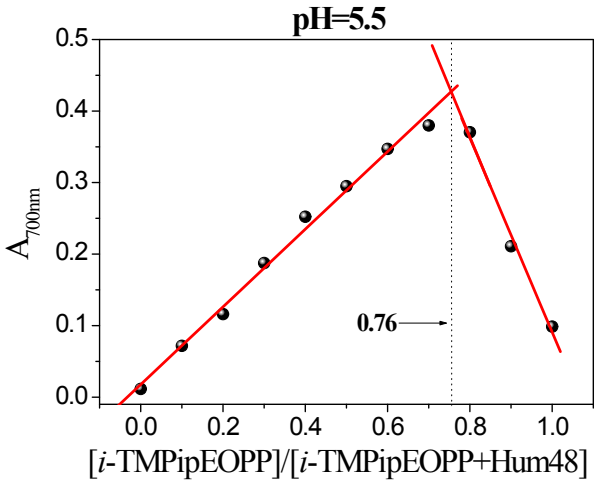
3. Job plot analysis for the interactions between *i*-TMPipEOPP and different DNAs

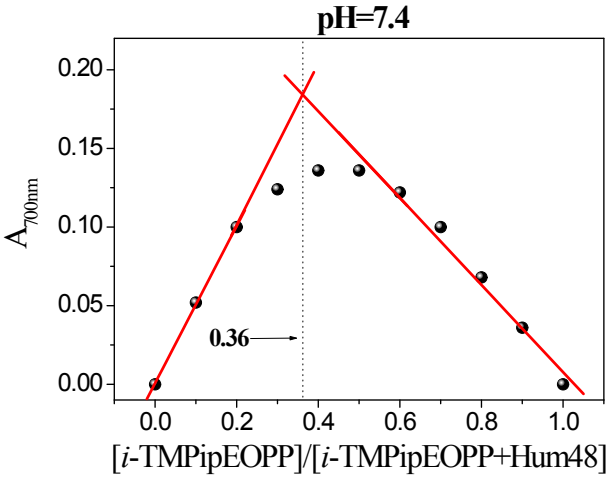












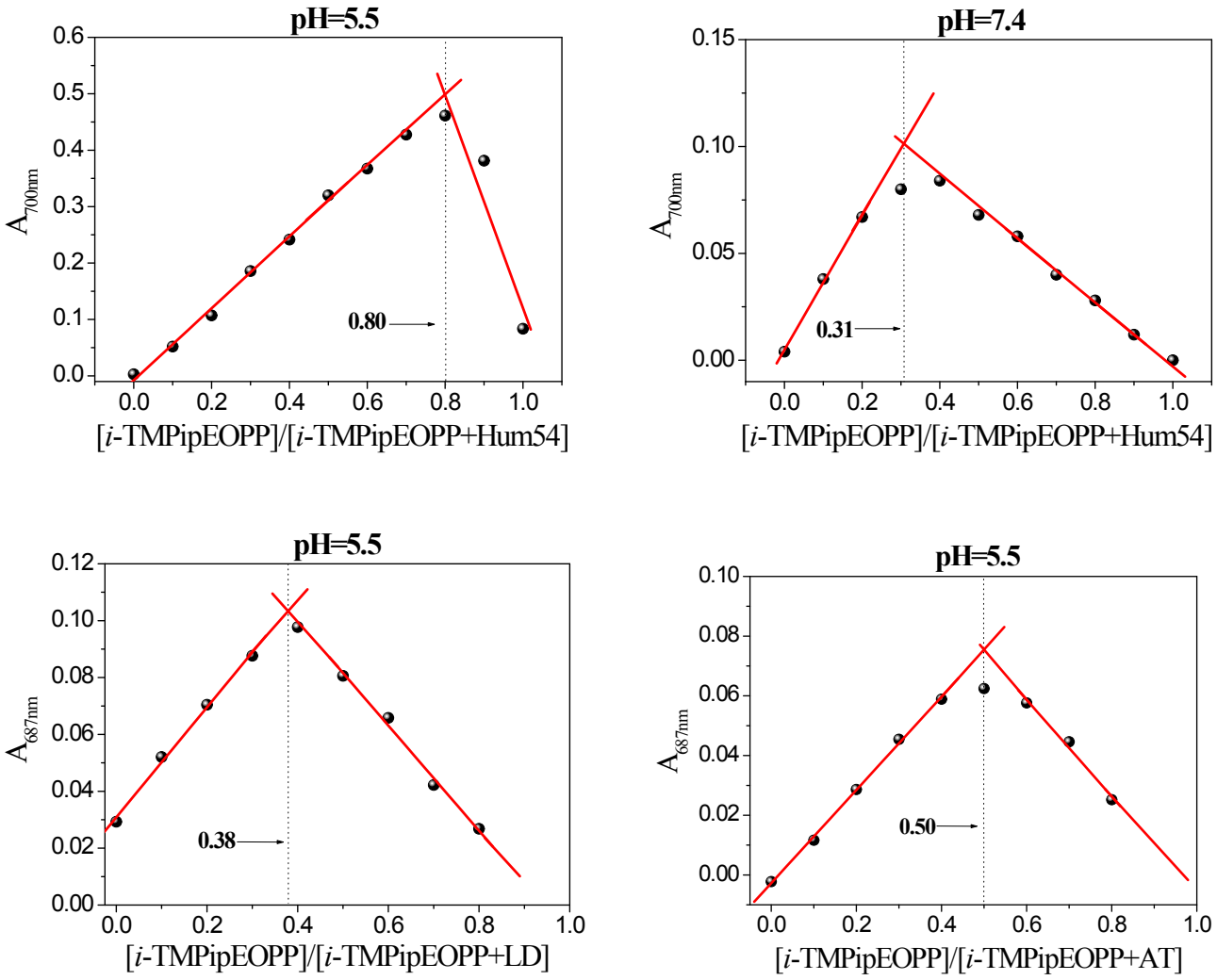
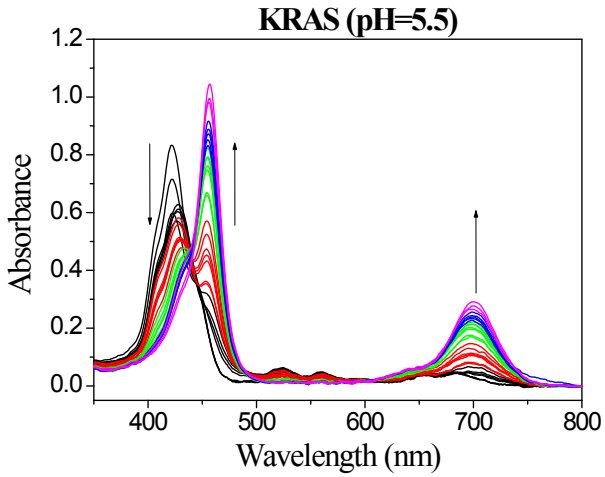
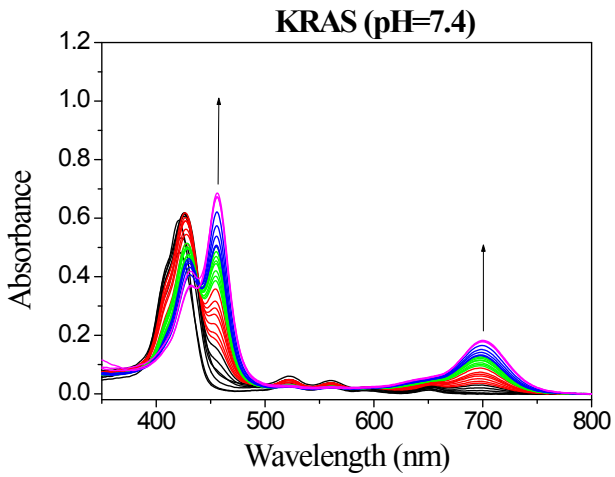
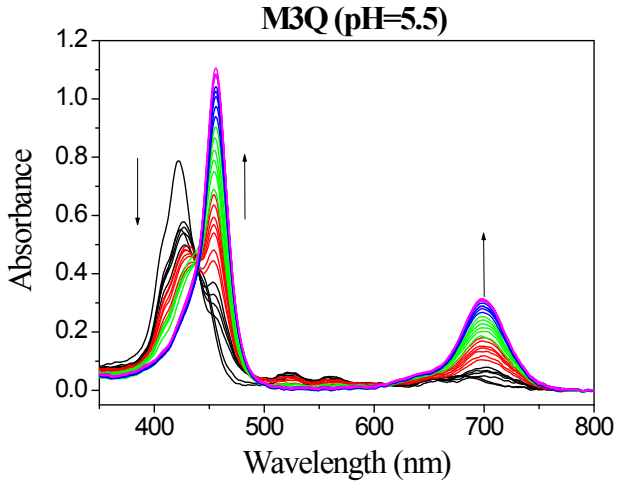


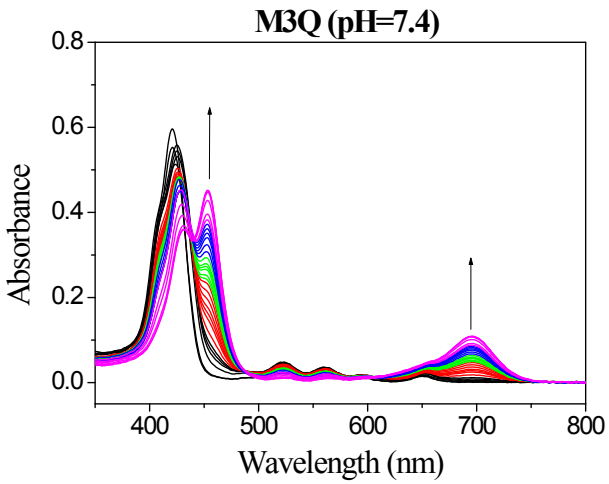
Figure S5. Job plot analysis of the interactions between *i*-TMPipEOPP and different DNAs under acidic and neutral conditions. [*i*-TMPipEOPP] + [DNA] = 10 μM.

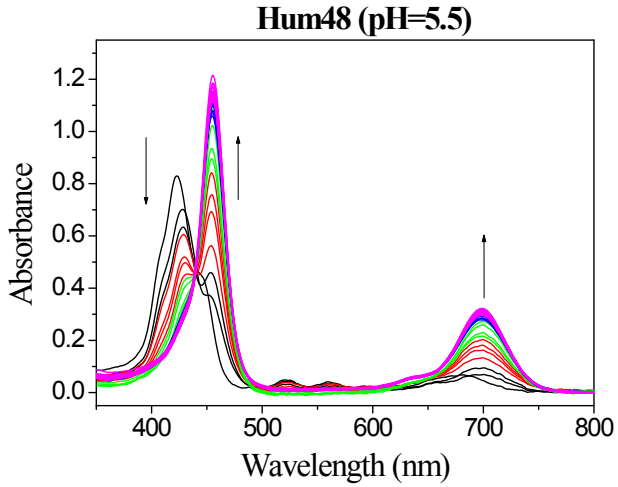
4. Uv-vis absorption titration spectra of *i*-TMPipEOPP by different DNAs

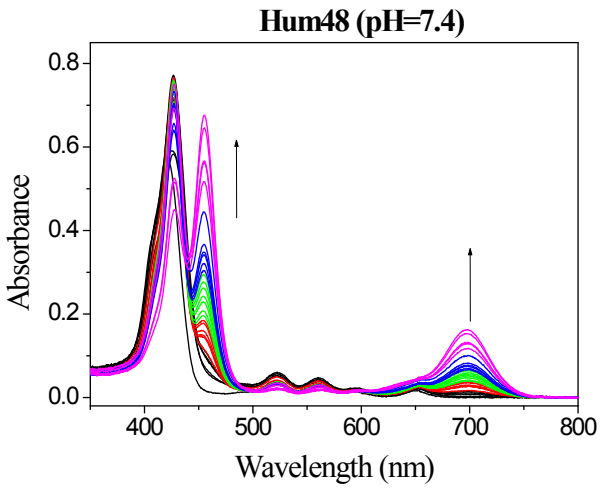












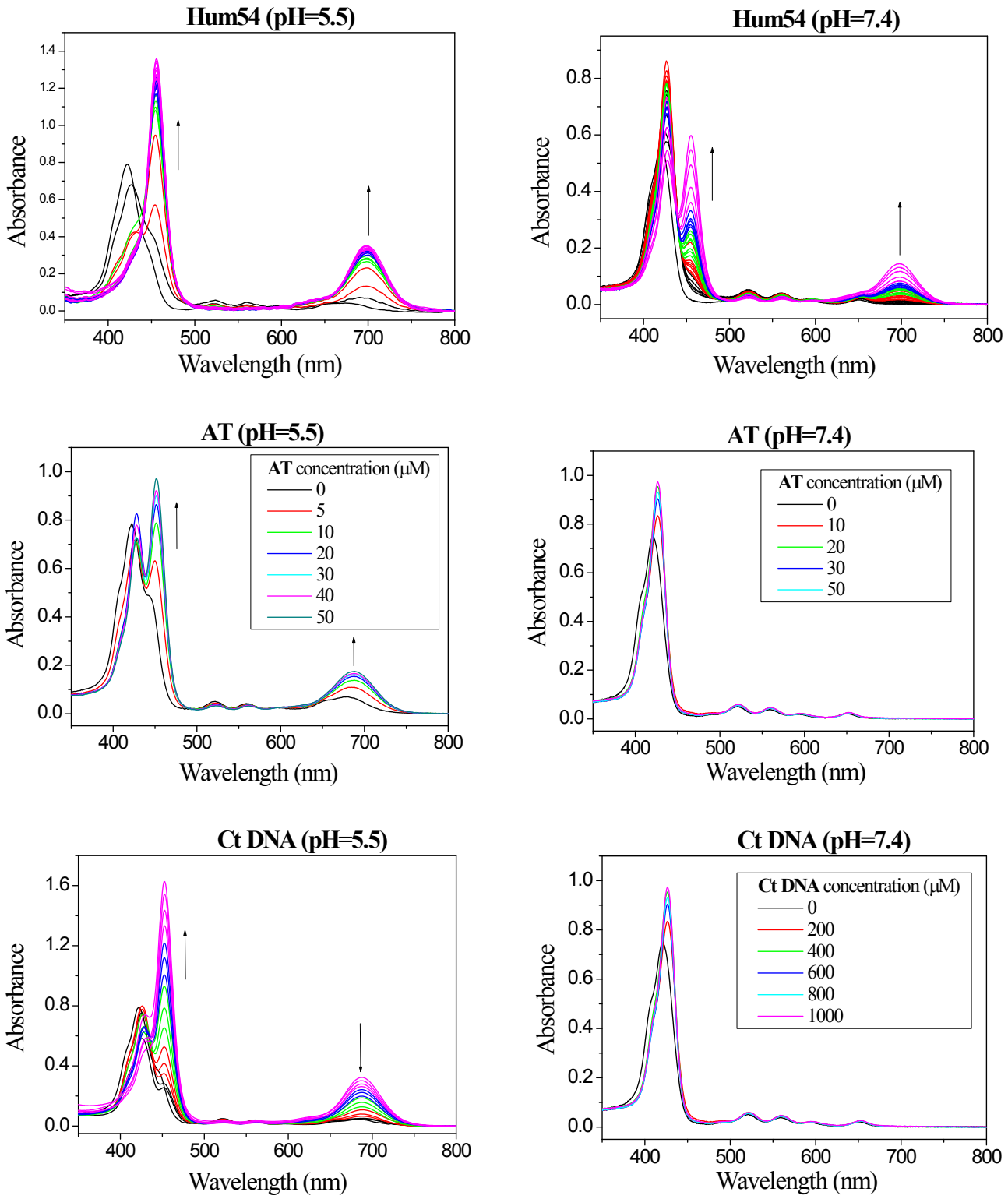


Figure S6. DNA concentration-dependent absorption spectrum changes of *i*-TMPipEOPP under acidic or neutral conditions. The concentrations of KRAS and M3Q are (arrow direction): 0, 0.3, 0.6, 1.0, 1.3, 1.6, 2.0, 2.3, 2.6, 3.0, 3.3, 3.6, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, 9.0, 10, 15, 20, 25, 30, 40 and 50 μM. For Hum48, another two concentrations of 0.15 and 0.45 μM were added. For Hum54, another two concentrations of 1.1 and 1.2 μM were added. The concentrations of AT are labeled in the figures. The concentrations of Ct DNA (base concentration) at pH 5.5 are (arrow direction): 0, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, 200, 400, 600 and 1000 μM. The concentrations of Ct DNA (base concentration) at pH 7.4 are labeled in the figure.

5. Effects of *i*-TMPipEOPP on the stability of Hum48 and Hum54

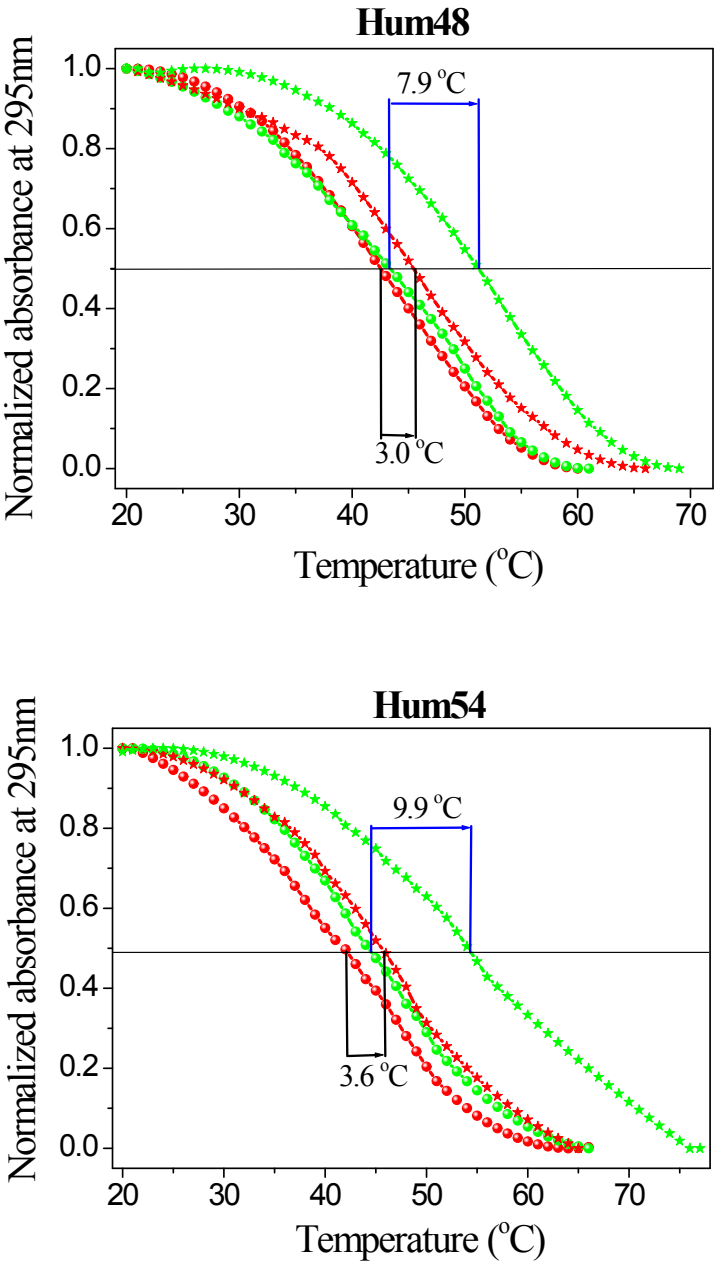
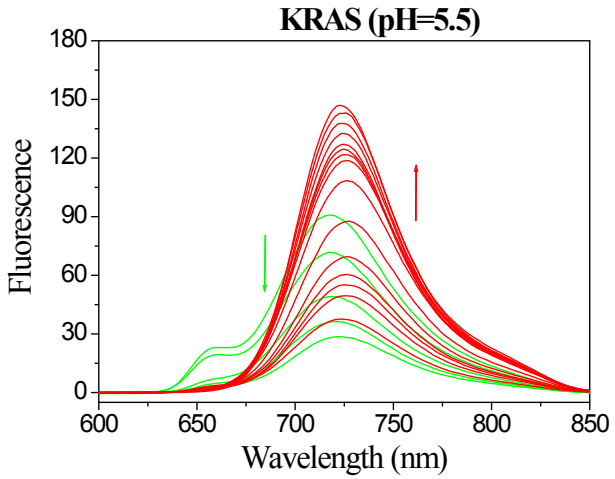


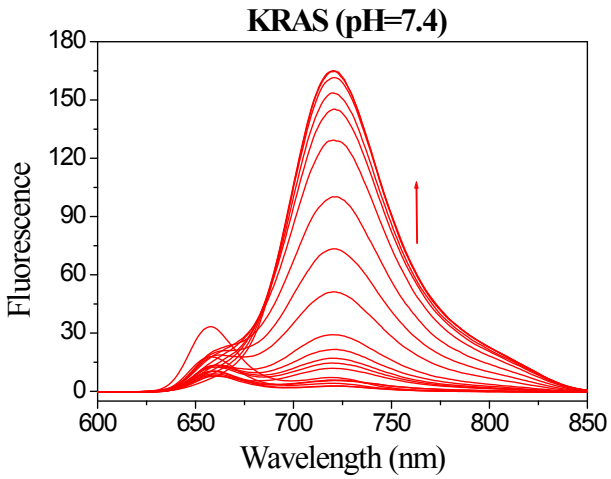
Figure S7. Melting temperature ($T_{1/2}$) detection of Hum48 and Hum54 in the absence (●) and presence (★) of 3 μM *i*-TMPipEOPP at pH of 7.4 (red) or 5.5 (green).

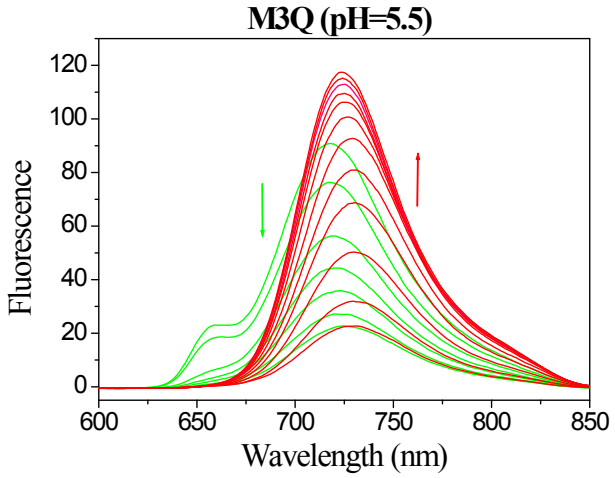
Table S1. G-quadruplex-stabilizing stability of *i*-TMPipEOPP

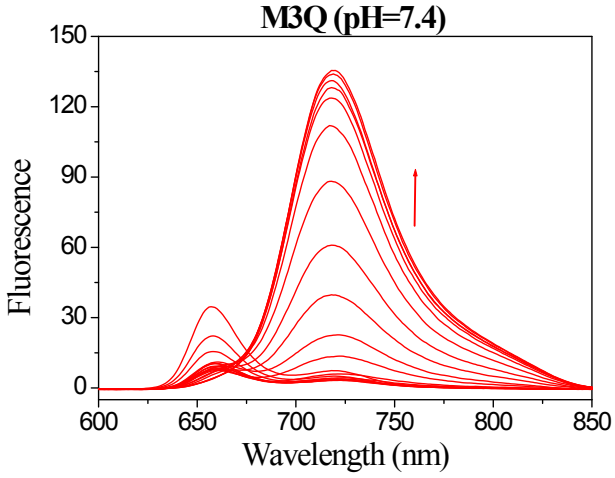
	pH=5.5		pH=7.4	
	DNA	DNA + *i*-TMPipEOPP	DNA	DNA + *i*-TMPipEOPP
Hum24	55.1	68.6	54.3	59.5
Hum48	43.3	51.2	42.5	45.5
Hum54	44.5	54.4	42.2	45.8

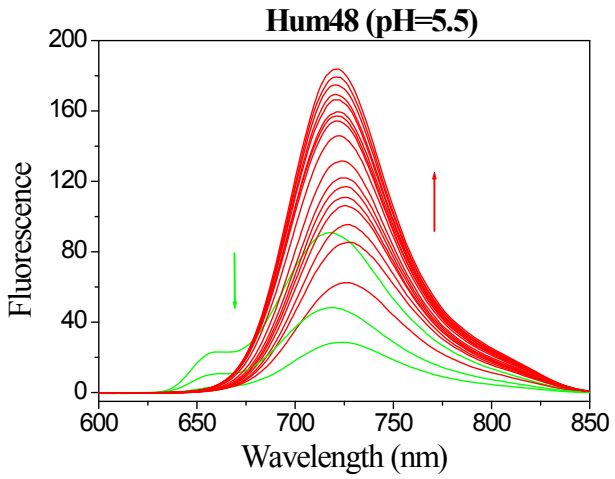
6. Fluorescence titration spectra of *i*-TMPipEOPP by different DNAs

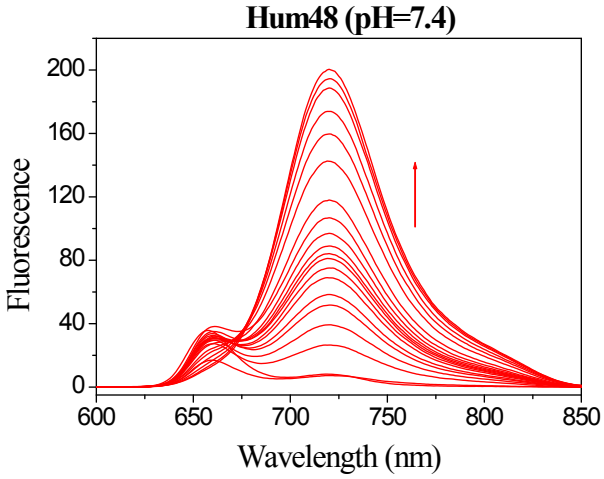












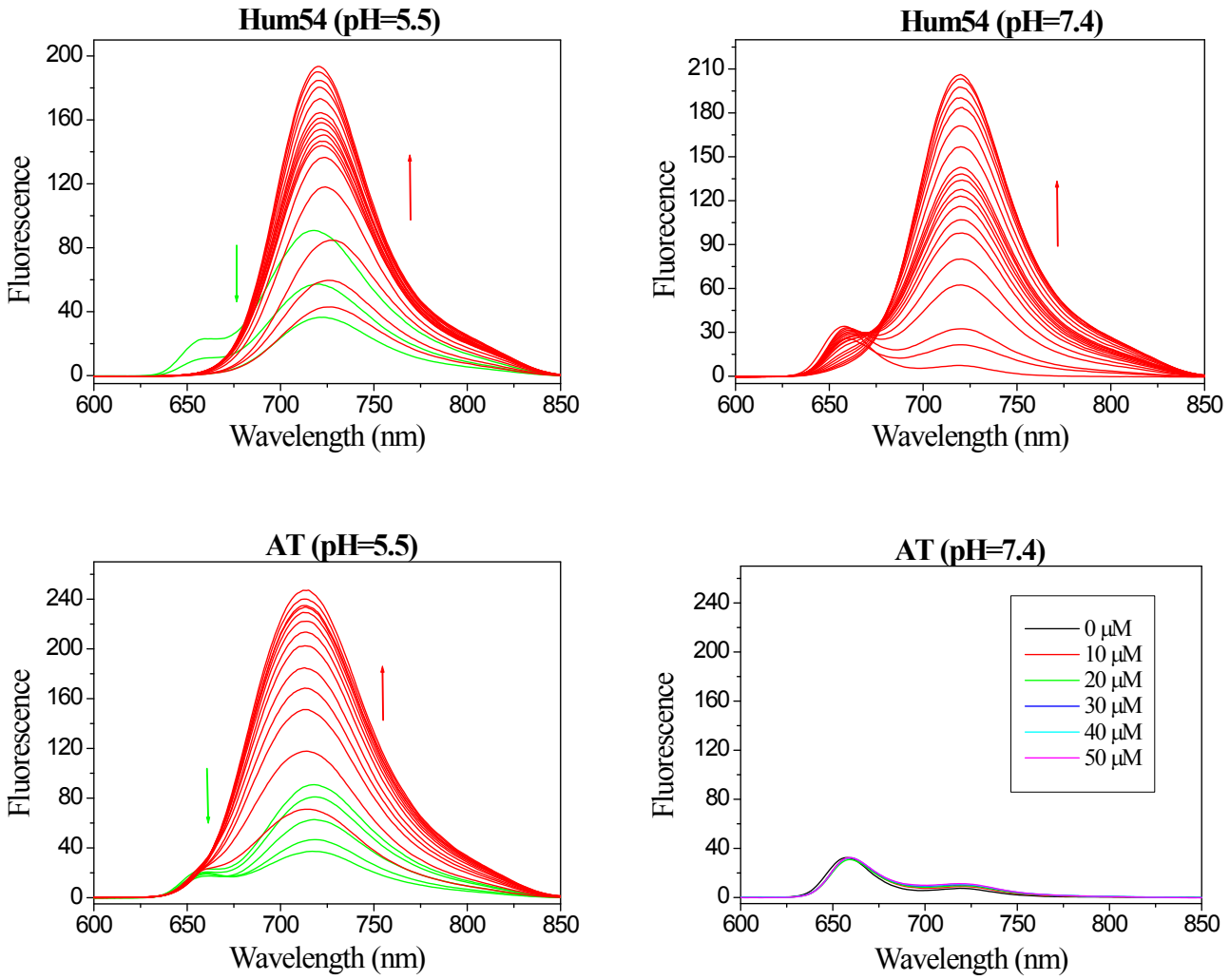


Figure S8. DNA concentration-dependent fluorescence spectrum changes of *i*-TMPipEOPP under acidic or neutral conditions. The concentrations of KRAS and M3Q are (arrow direction): 0, 0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4, 1.6, 1.8, 2, 3, 4, 6, 10, 14, 20, 30, 40 and 50 μM. The concentrations of Hum48 and Hum54 are (arrow direction): 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.5, 2, 3, 5, 7, 10, 15, 20 and 25 μM. The concentrations of AT at pH 5.5 are (arrow direction): 0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 7, 8, 10, 20, 30 and 50 μM. The concentrations of AT at pH 7.4 are labeled in the figure.

7. Effects of *i*-TMPipEOPP on the CD spectra of Hum48 and Hum54

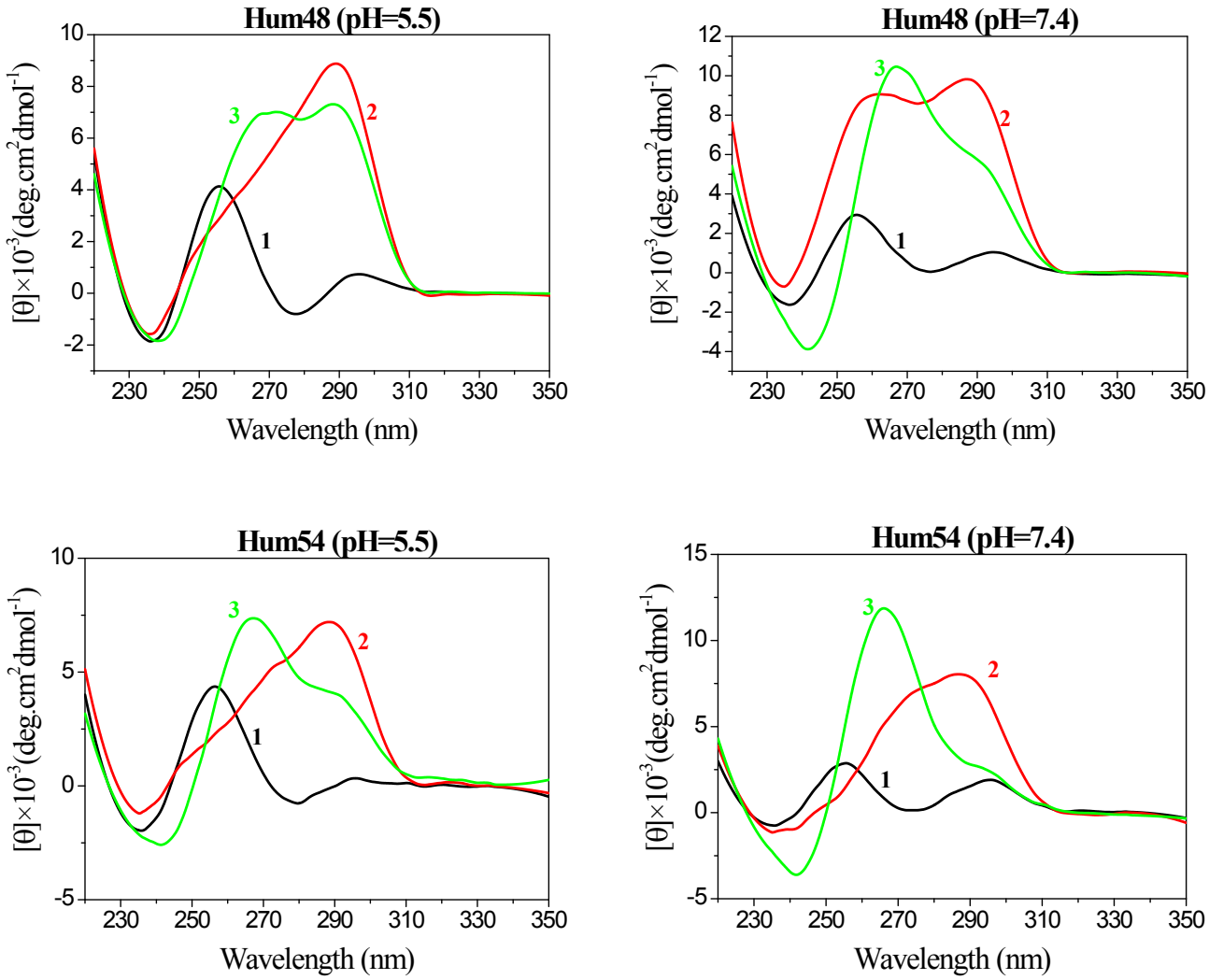


Figure S9. Effects of *i*-TMPipEOPP on the CD spectra of Hum48 or Hum54 under acidic and neutral conditions. (1) DNA; (2) DNA + 50 mM K^+; (3) DNA + 50 mM K^+ + 5 μM *i*-TMPipEOPP.