**Supporting Information for**

# Enantioselective Targeting Left-handed Z-G-Quadruplex

## Experimental Section

### Materials and Methods

DNA sequences:

Tel22: 5'-AGGGTTAGGGTTAGGGTTAGGG-3'

Z-G4:5'-TGGTGGTGGTGGTTGTGGTGGTGGTGTT-3'

AS1411:5'-GGTGGTGGTGGTTGTGGTGGTGGTGG-3'

DNA oligomers were purchased from Sangon (Shanghai, China) and used without further purification. Concentrations of these oligomers were determined by measuring the absorbance at 260 nm after melting. Extinction coefficients were estimated by the nearest neighbor method by using mononucleotide and dinucleotide values. All the experiments were carried out in 10 mM Tris buffer (100 mM KCl, pH 7.2) unless stated otherwise.

The chiral metal complexes used in this paper were obtained by using a cellulose (~20 μm, Aldrich) column and eluting with sodium chloride aqueous solution. The purity is more than 95%, which was determined by ESI-MS and elemental analysis. UV-vis spectroscopy was used to determine the enantiomer concentration. The samples of purified M and P enantiomer were collected and freeze-dried for future use.

**UV melting experiment**: melting experiments were performed on a Cary 300 UV/Vis spectrophotometer equipped with a Peltier temperature control accessory. All UV/Vis

spectra were measured in 1.0-cm path-length cell. For metal complex-containing melting assays, the same concentration of corresponding metal complex aqueous solution was used as the reference solution. Absorbance changes at 295 nm versus temperature were collected at a heating rate of 0.5 °C·min$^{-1}$. Before measurement, the DNA samples were heated at 95 °C for 5 min, and gently cooled from 95 °C to room temperature. The concentration of the DNA used for UV melting experiments was 2 μM/strand.

**CD Spectroscopy**：CD spectra were recorded on a JASCO J-810 spectropolarimeter. CD spectra were recorded from 320 to 220 nm in 1 nm increments with an average time of 2 second and three scans were accumulated and automatically averaged. The various concentration of enantiomer was scanned as a control and subtracted from the spectra of metal complex/DNA mixture to eliminate its influence on DNA CD signal. The concentration of the DNA used for CD experiments was 2 μM/strand.

**Isothermal Titration Calorimetry (ITC)**: ITC assays were performed on a NANO ITC System (TA Instruments Inc., New Castle, DE, USA). Titrations were performed in 10 mM Tris buffer (pH = 7.2) containing 100mM KCl. Injections of 10 μL of 0.448 mM ligand was added from a computer-controlled microsyringe at an interval of 600 s into Z-G4 (20 μM) solution with stirring at 400 rpm at 25 ºC. The experimental data were analyzed with Nano Analyze software (TA Instruments Inc.) and were fitted to an independent model concurrently with a blank constant model to adjust for the heat of dilution. All measurements were from 25 injections of 0.448 mM M-0 into 1400 μL of DNA in 10 mM Tris-HCl, 100 mM KCl, pH = 7.2 buffer at 25 ºC. Each heat burst

curve was the result of a 10 μL injection of M-0 into the Z-G4 solution.

**Gel electrophoresis:** Native gel electrophoresis was carried out on acrylamide gel (15 %) and run at 4 ºC, 1×TB buffer containing 10 mM KCl and was silver stained. DNA was heated at 95 ºC for 5 min in 10 mM Tris buffer containing corresponding cation ($K^+$ or $Li^+$), and gently cooled from 95 ºC to room temperature, following by incubation at 4 ºC overnight. To prepare the final loading sample, the corresponding metal complexes were added to the annealed DNA samples and incubated at 4 ºC for 3 hours.

**NMR Spectroscopy:** samples for NMR were incubated in 10mM Tris-100 mM KCl buffer (pH 7.2) at 25 ºC with 10% $D_2O$ added. The final concentration of Z-G4 was 120 μM. The enantiomer was incubated with Tel22 at 25 ºC before measurement. NMR experiment was carried out on a Bruker 500 MHz AVANCE NMR spectrometer equipped with a triple-channel cryoprobe at 5 ºC.

Table S1. Thermodynamic Parameters for the Interaction of P-0/M-0 with Z-G4.

| | P-0 | M-0 |
|---|---|---|
| n | 1.5±0.3 | 1.1±0.2 |
| $\Delta G°_{25}$(kcal·mol$^{-1}$) | -5.9±0.6 | -8.9±0.4 |
| $\Delta H°$(kcal·mol$^{-1}$) | -11.0±0.8 | -20.1±0.6 |
| $T\Delta S°$(kcal·mol$^{-1}$K$^{-1}$) | -5.1±0.7 | -11.2±0.3 |

All data were derived from ITC experiments. $\Delta H°$ and n (stoichiometry) were directly obtained from ITC. $\Delta G°_{25}$ was obtained from the relation $\Delta G° = -RT\ln K_a$. TΔS° was obtained from the relation $T\Delta S° = \Delta H° - \Delta G°$. The values are the average of two independent measurements.

Table S2. Stabilization temperature ($\Delta T_m$) of Z-G4 by the enantiomers (1μM) of $[Ni_2L_3^0]^{4+}$, $[Ni_2L_3^3]^{4+}$ and $[Ni_2L_3^5]^{4+}$ in 10 mM Tris buffer (pH 7.2) containing 100 mM KCl. The concentration of the Z-G4 was 1μM/strand.

| Compound | $\Delta T_m$(℃) | |
|---|---|---|
| | P | M |
| $[Ni_2L_3^0]^{4+}$ | 0 | 6.1 |
| $[Ni_2L_3^3]^{4+}$ | 0.2 | 0.2 |
| $[Ni_2L_3^5]^{4+}$ | 0.2 | 0 |

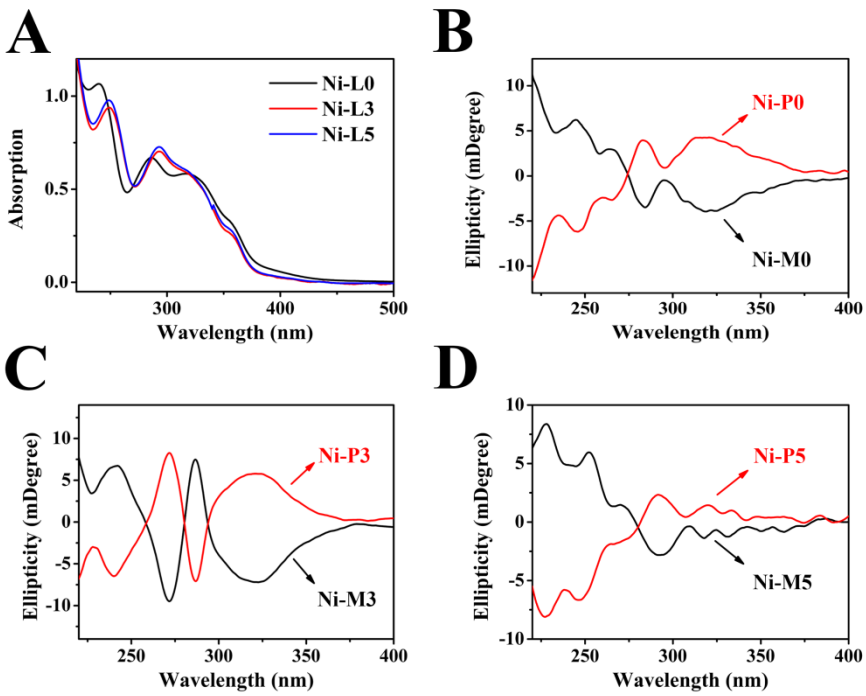


Figure S1. (A) UV/Visible absorbance spectra of racemic $[Ni_2L_3^{0}]^{4+}$ (black), $[Ni_2L_3^{3}]^{4+}$ (red), and $[Ni_2L_3^{5}]^{4+}$ (blue). CD spectra of M-0 and P-0 (B), M-3 and P-3 (C), M-5 and P-5 (D).

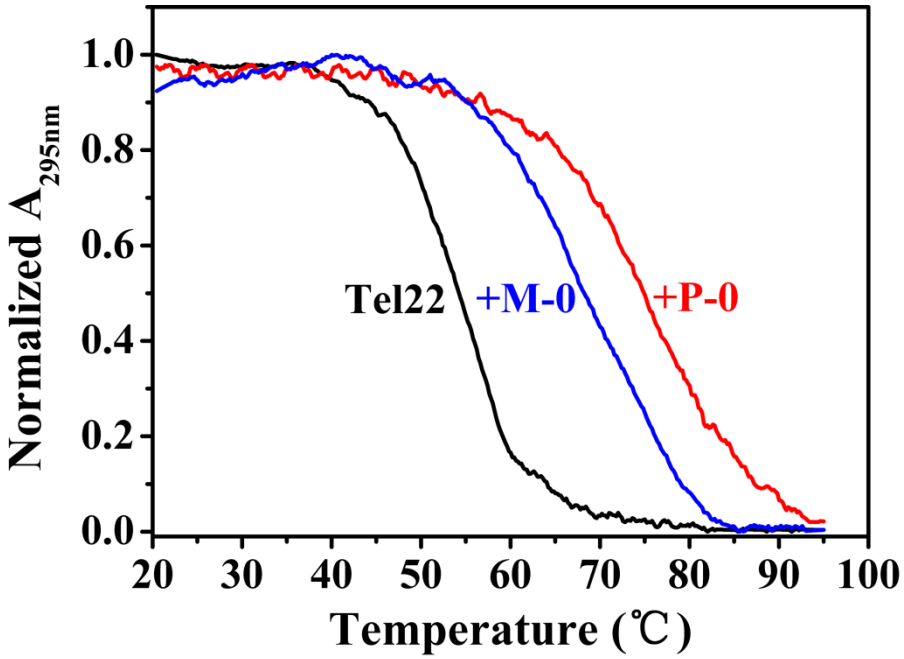


Figure S2. Melting spectra of Tel22 G-quadrupelx in the absence and presence of equivalent amount of P-0/M-0 in 10 mM Tris buffer containing 100 mM $K^+$, pH 7.2.

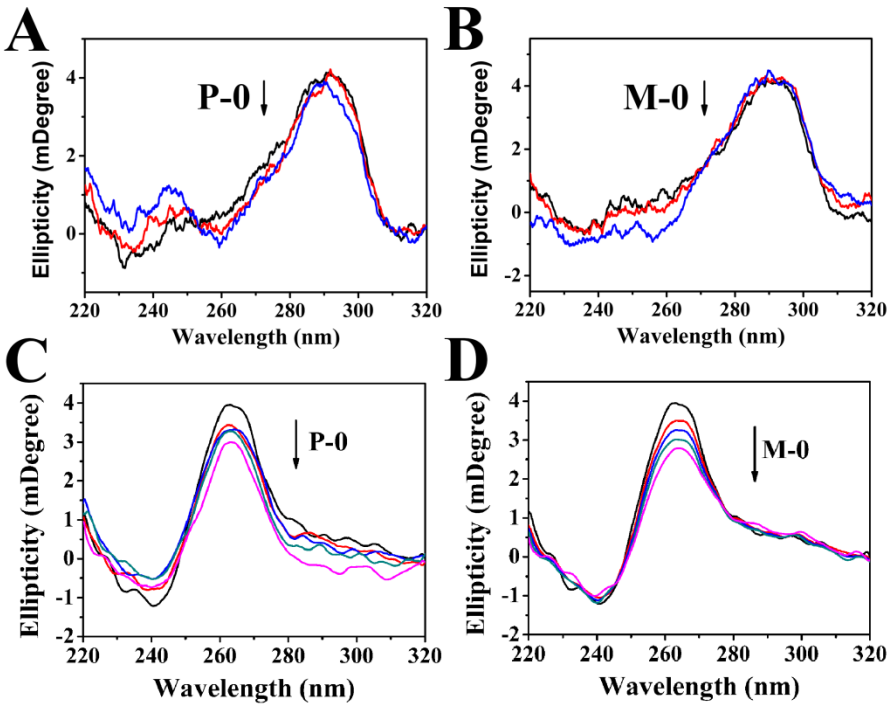


Figure S3. CD titration of Tel22 G-quadruplex with P-0 (A) and M-0 (B) in 10 mM KCl, 10 mM Tris buffer (pH 7.2). The concentration of the enantiomer was varied from 0 μM to 2 μM. CD titration of AS1411 G-quadruplex with P-0 (C) and M-0 (D) in 100 mM KCl, 10 mM Tris buffer (pH 7.2). The concentration of the enantiomer was varied from 0 μM to 2 μM.

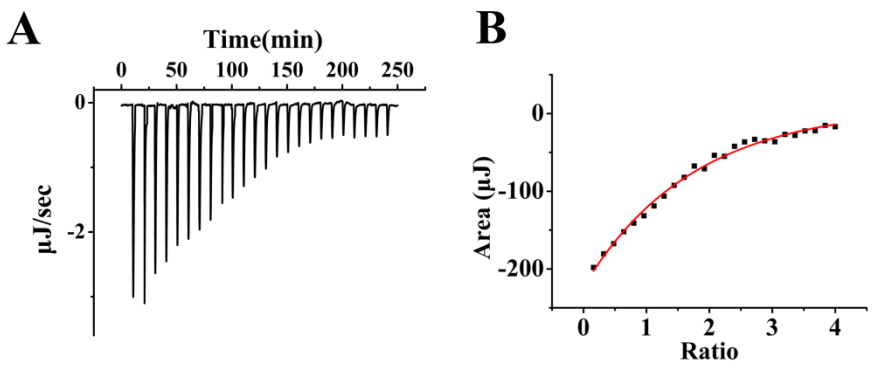


Figure S4. (A) ITC spectrum for the titration of P-0 into the solution of Z-G4. (B) Corresponding normalized heat signals versus molar ratio obtained from A.

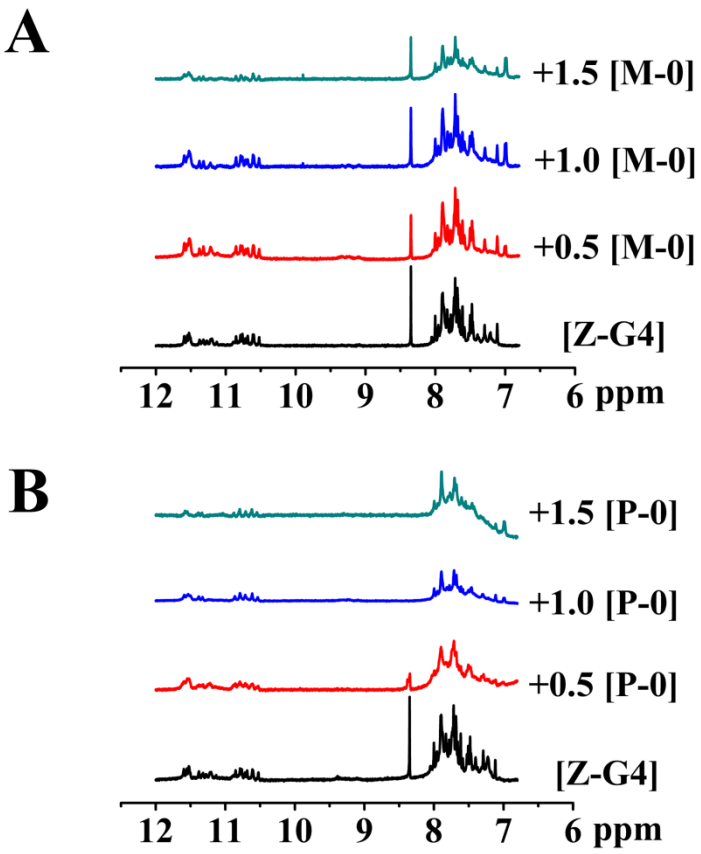


Figure S5. NMR titration of Z-G4 with Z-G4 with M-0 and P-0 at various [Ligand]/[Z-G4] ratios.

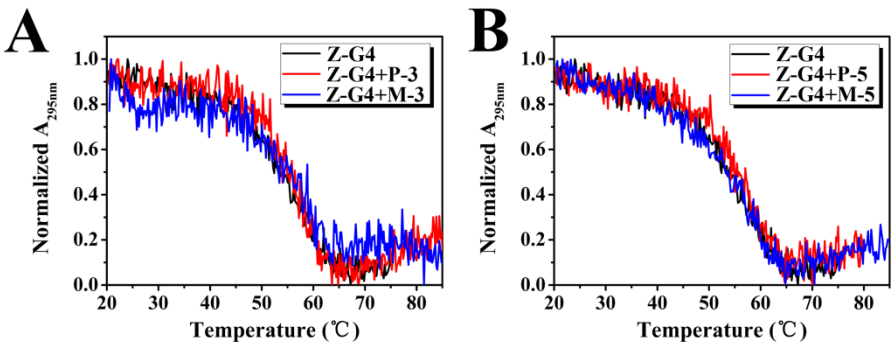


Figure S6. UV melting profiles of the Z-G4 G-quadruplex in the absence and presence of P-3/M-3/P-5/M-5 in 10 mM Tris buffer (pH 7.2) containing 100 mM $K^+$.

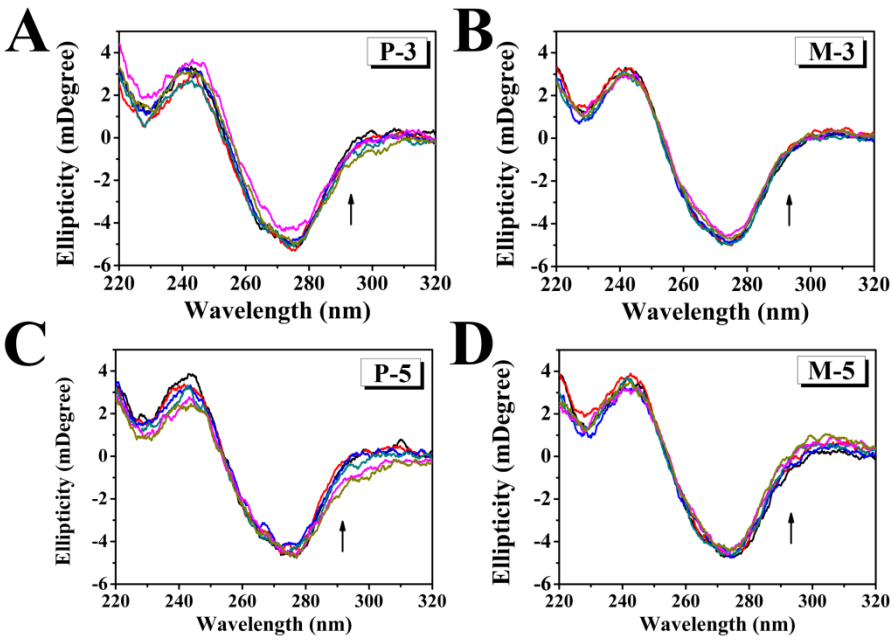


Figure S7. CD titration of Z-G4 G-quadruplex with P-3 (A)/M-3 (B)/P-5 (C)/M-5 (D) in 100 mM KCl, 10 mM Tris buffer (pH 7.2). The concentration of the enantiomer was varied from 0 μM to 6 μM.