SUPPORTING INFORMATION

Alzheimer’s Disease Amyloid Beta Converting Left-handed Z-DNA Back to Right-handed B-Form

Experimental Section

Sample preparation: Aβ 1-40 (lot no. U10012) and Aβ 1-12 (lot no. 122K1377) Aβ 25-35 (lot no. 70K49532) were purchased from American Peptide and Sigma individually and prepared as previously described. 1 Briefly, the powdered Aβ peptide was first dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) at the concentration of 1 mg/ml. The solution was shaking at 4 °C for 2 hours in a sealed vial for further dissolution and was then stored at -20 °C as a stock solution. Before use, the solvent HFIP was removed by evaporation under a gentle stream of nitrogen and peptide was dissolved in 10 mM Tris buffer, pH 7.0. The 34 mer DNA oligonucleotide (dGdC)17 (lot no. W52857) was synthesized by Sangon and used after annealing. The concentration of DNA[13,33] was determined by ultraviolet absorbance measurements using the extinction coefficient $\epsilon_{262} = 16,800 \text{ M}^{-1} \text{ cm}^{-1}$.

Circular Dichroism measurements: Circular dichroism spectra were measured2 from 230 nm to 320 nm on a JASCO J-810 spectropolarimeter with a computer-controlled water bath. The optical chamber of CD spectrometer was deoxygenated with dry purified nitrogen (99.99%) for 45 min before use and kept the
nitrogen atmosphere during experiments. Three scans were accumulated and automatically averaged.

**Fluorescence measurements:** Fluorescence data were collected on a Jasco-FP6500 spectrofluorimeter.\(^2\) EB was used as a fluorescent probe to characterize DNA conformation because EB had less affinity for left-handed Z-DNA and its fluorescence was much weaker than that of its B-DNA complex. Fluorescence spectra were monitored at different incubation time. The EB emission signals were recorded at 585 nm with an excitation wavelength 480 nm.

**DNase I nuclease digestion and PAGE experiments:** Samples were incubated for a defined period of time at 37 °C in Tris buffer before initiating hydrolysis at the same temperature by adding 0.4 units DNase I and 1 mM Mg\(^{2+}\). After 10 min digestions were stopped by adding stop solution (EGTA). Electrophoresis was carried out by using 20% acrylamide at 60 V for 3 h at room temperature. The gels were silver-stained.

**Electron Microscopy:** Samples (10 µl) were spotted onto carbon-coated copper grids for 30 min. The grids were blotted with filter paper to remove excess buffer and the sample was stained with 1.5\% (w/v) phosphotungstic acid (pH 7.0). Grids were blotted again and air-dried before analysis on a transmission electron microscope (JEOL JEM-1011), operating with a voltage of 100 kV.
Fig. S1. Circular dichroism spectra of DNA-EuD complex in the absence of Aβ measured at different incubation time at 37 °C, in 10 mM Tris, pH 7.0 buffer. [DNA] = 100 μM; [EuD] = 50 μM. 0 day (black); 1 day (red); 3 days (blue); 5 days (dark cyan).
Fig. S2. The effect of Aβ1-40 on the sensitivity of DNA to DNase I. (A) Lane 1 was DNA without digestion. Lane 2 was digested DNA. Lane 3 was DNA digested in the presence of Aβ monomer. Lanes 4-7 were the digestion products of DNA-EuD complex after incubated with Aβ at 37 °C, in 10 mM Tris, pH 7.0 buffer for 0, 1, 3, 5 days, respectively. The proportion of DNA-EuD and Aβ1-40 is the same as that used in the CD experiments; (B) As controls, Lanes 1-4 were the digestion products of DNA-EuD complex after incubated in the absence of Aβ1-40 at 37 °C for 0, 1, 3, and 5 days, respectively. Lane 5 was DNA-EuD without digestion. (C) Plots of the amount of undigested DNA after incubated in the presence (black square) or absence (red circle) of Aβ1-40 at 37 °C for 0, 1, 3, and 5 days, respectively. The data were adopted from Fig. S2A and Fig. S2B.
Fig. S3. (A) Fluorescence spectra of EB when bound to DNA-EuD in the presence of Aβ1-40. The proportion of DNA-EuD and Aβ1-40 is the same as that used in the CD experiments. EB fluorescence was increased with increasing the incubation time: 0 day (blue); 1 day (olive); 2 days (magenta); 3 days (green); 4 days (royal); 5 days (orange); DNA alone (black); DNA-EuD (red); (B) Normalized EB fluorescence at 585 nm as a function of incubation time in the presence (black squares) or absence (red circles) of Aβ.
Fig. S4. Circular dichroism spectral changes of DNA induced by Aβ1−40 in 40% EG at RT. Spectra were collected after addition of Aβ1−40 for 30 minutes. 10 μM DNA in the absence (black) or presence of Aβ1−40: 1 μM (red); 2 μM (green); 3 μM (blue); 4 μM (cyan). 10 μM DNA in 10 mM Tris, pH 7.0 buffer (magenta).
Fig. S5. Circular dichroism spectral changes of DNA-EuD induced by incubation with Aβ1−40 aggregates. DNA-EuD complex was titrated by Aβ aggregates measured at 37 °C, in 10 mM Tris, pH 7.0 buffer. Spectra were collected after addition of Aβ1−40 for 30 min. 0 μM Aβ (black); 5 μM Aβ (red); 10 μM Aβ (blue); 20 μM Aβ (dark cyan). [DNA] = 100 μM; [EuD] = 50 μM. Aβ 1-40 aggregates were prepared by incubation in 10mM Tris (pH 7.0) containing 40%EG at 37°C for 1 hour.
Fig. S6. TEM images of Aβ1-40 in the absence (A) or presence (B) of DNA-EuD complex after incubation at 37°C, in 10 mM Tris, pH 7.0 buffer for 5 days (Scale bars, 200 nm). Detailed information was described in Experimental section.
Fig. S7. CD spectra of DNA-EuD (100 μM) complex after incubated with Aβ1-12 (A) or Aβ25-35 (B) (100μM) for different time at 37 °C, in 10 mM Tris, pH 7.0 buffer. 0 day (black); 1 day (red); 3 days (blue); 5 days (dark cyan).
References:
