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 ^{o}C for 2 hours in a sealed vial for further dissolution and was then stored at -20 ^{o}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 ε_{262} =16 800 M^{-1} cm^{-1}.

Circular Dichroism measurements: Circular dichroism spectra were measured[2] 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 ^{o}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.

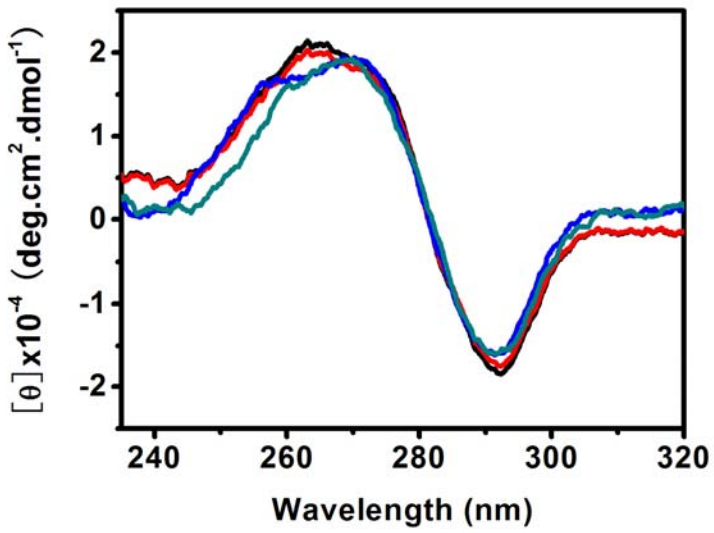


Fig. S1. Circular dichroism spectra of DNA-EuD complex in the absence of Aβ measured at different incubation time at 37 ^{o}C, in 10 mM Tris, pH 7.0 buffer. [DNA] = 100 μM; [EuD] = 50 μM. 0day(black); 1 day (red); 3 days (blue); 5 days (dark cyan).

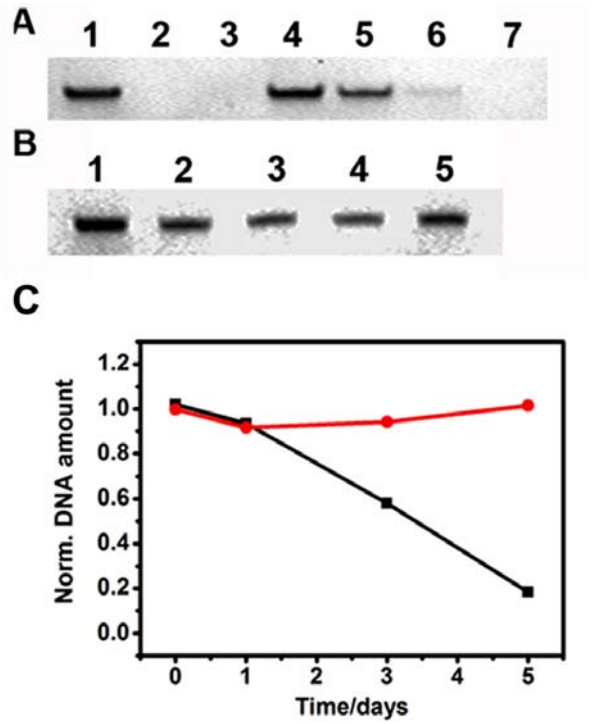


Fig. S2. The effect of Aβ1-40 on the sensitivity of DNA to DNase I. (A) Lane 1 was DNA without digestion. Lane 2 was digested DNA. Lane 3 was DNA digested in the presence of Aβ monomer. Lanes 4-7 were the digestion products of DNA-EuD complex after incubated with Aβ at 37 ^{o}C, in 10 mM Tris, pH 7.0 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 ^{o}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 ^{o}C for 0, 1, 3, and 5 days, respectively. The data were adopted from Fig. S2A and Fig. S2B.

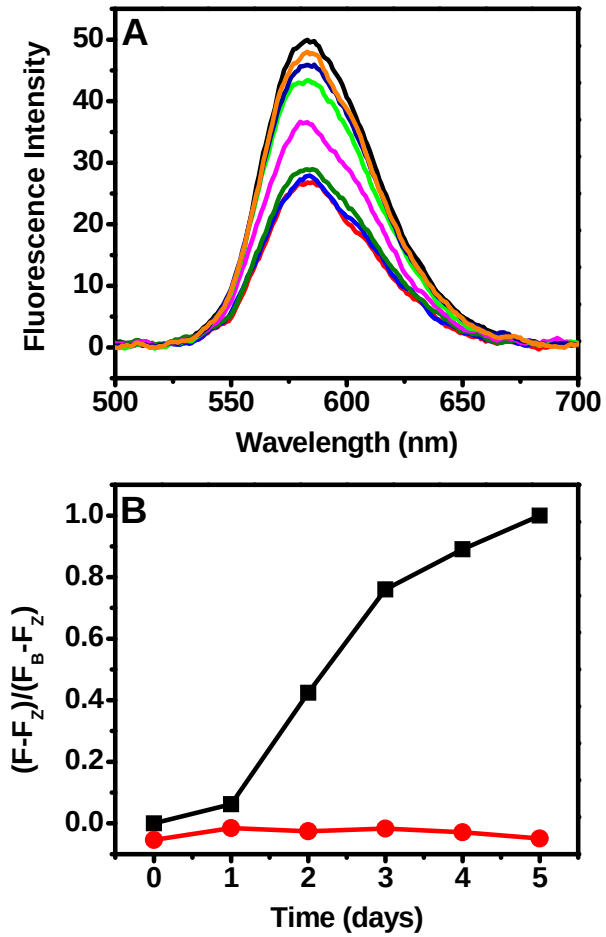


Fig. S3. (A) Fluorescence spectra of EB when bound to DNA-EuD in the presence of Aβ1-40. The proportion of DNA-EuD and Aβ1-40 is the same as that used in the CD experiments. EB fluorescence was increased with increasing the incubation time: 0 day(blue); 1 day(olive); 2 days(magenta); 3 days(green); 4 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.

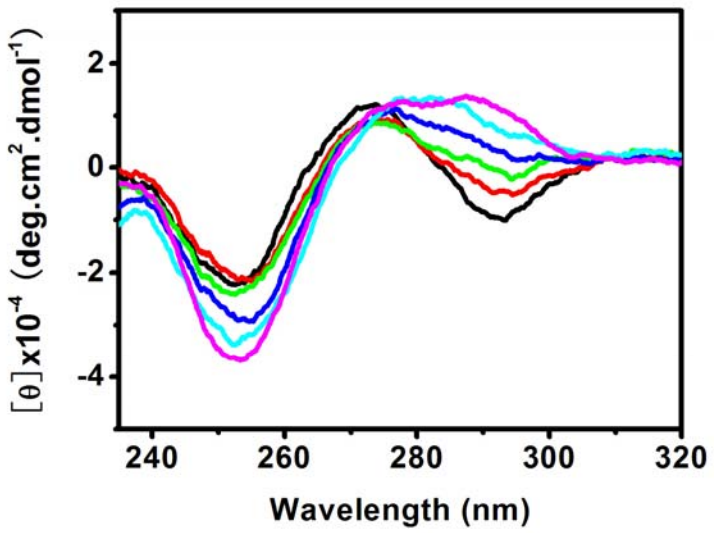


Fig. S4. Circular dichroism spectral changes of DNA induced by Aβ1–40 in 40% EG at RT. Spectra were collected after addition of Aβ1–40 for 30 minutes. 10 μM DNA in the absence (black) or presence of Aβ 1–40: 1 μM (red); 2 μM (green); 3 μM (blue);4 μM (cyan). 10 μM DNA in 10 mM Tris, pH 7.0 buffer (magenta).

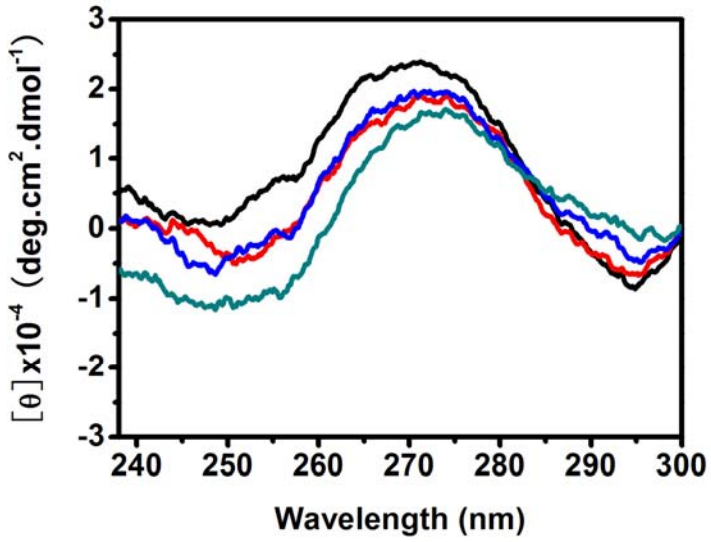
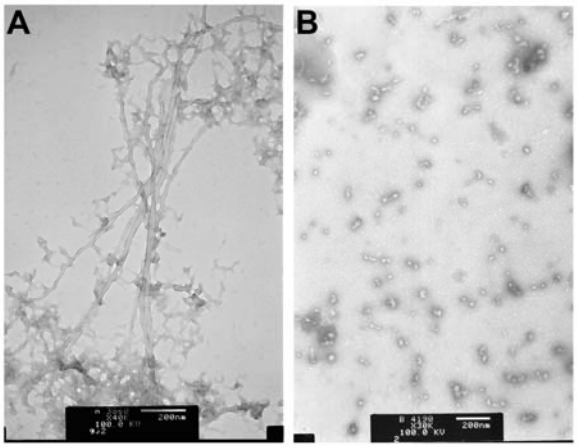


Fig. S5. Circular dichroism spectral changes of DNA-EuD induced by incubation with Aβ1–40 aggregates. DNA-EuD complex was titrated by Aβ aggregates measured at 37 ^{o}C, in 10 mM Tris, pH 7.0 buffer. Spectra were collected after addition of Aβ1–40 for 30 min. 0 μM Aβ (black); 5 μM Aβ (red); 10 μM Aβ (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 ^{o}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℃, in 10 mM Tris, pH 7.0 buffer for 5 days (Scale bars, 200 nm). Detailed information was described in Experimental section.

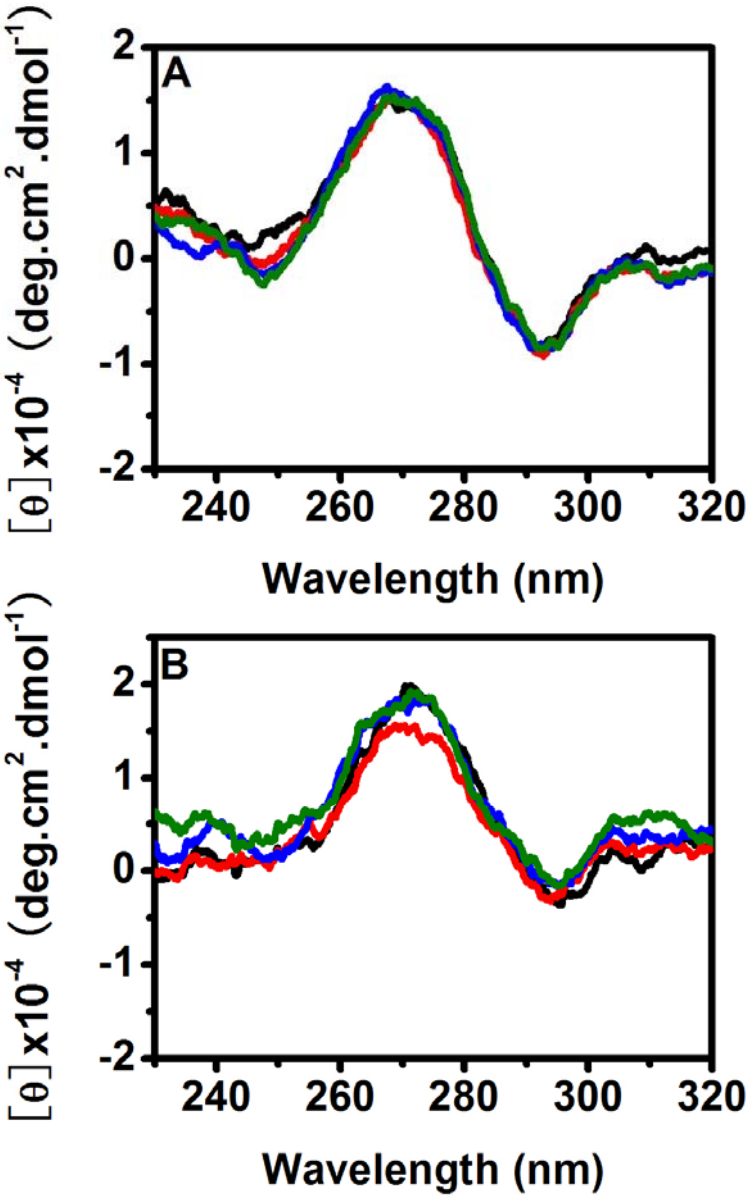


Fig. S7. CD spectra of DNA-EuD (100 μM) complex after incubated with Aβ1-12 (A) or Aβ25-35 (B) (100μM) for different time at 37 ^{o}C, in 10 mM Tris, pH 7.0 buffer. 0 day (black); 1 day (red); 3 days (blue); 5 days (dark cyan).

References:

1. a)H. Yu, J. Ren, X. Qu, *Biophys. J.*, 2007, **92,** 185; b) J. Geng, H. J. Yu, J. S. Ren and X. G. Qu, *Electrochem. Commun.*, 2008, **10,** 1797; c) H. Yu, J. Ren and X. Qu, *Chembiochem*, 2008, **9,** 879.

2. a)X. Li, Y. Peng and X. Qu, *Nucleic. Acids Res.*, 2006, **34,** 3670; b)H. Zhang, H. Yu, J. Ren and X. Qu, *Biophys. J.*, 2006, **90,** 3203.