

Head-to-tail cyclization of a heptapeptide eliminates its cytotoxicity and significantly increases its inhibition effect on amyloid β -protein fibrillation and cytotoxicity

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Electronic Supplementary Material

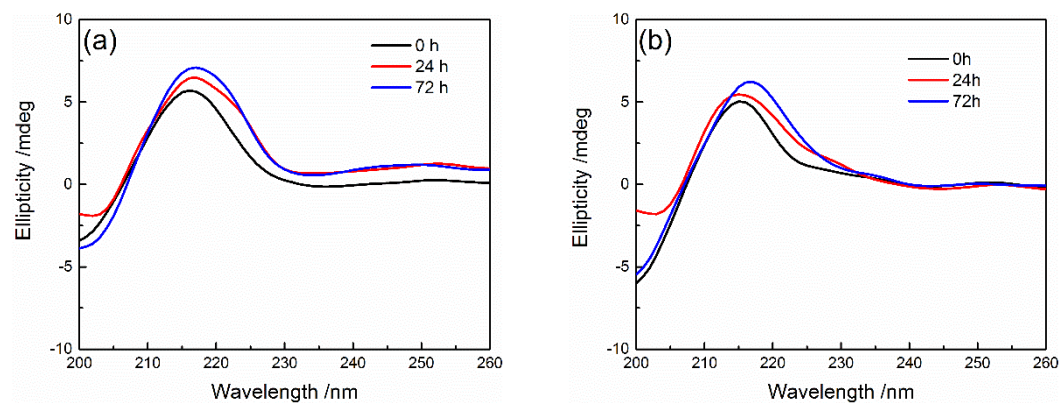


Fig. S1 Far-UV CD spectra of (a) LK7 (100 μ M), (b) cLK7 (100 μ M).

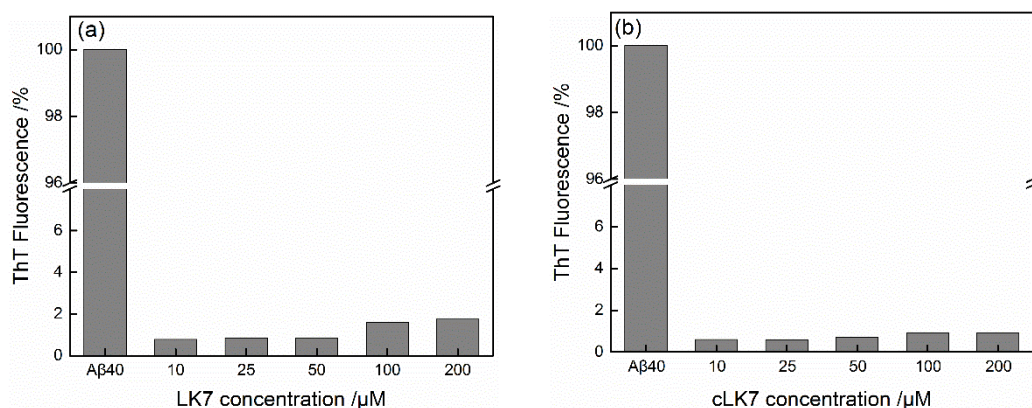


Fig. S2 ThT fluorescence intensity caused by the heptapeptides in comparison with that of A β ₄₀. (a) LK7, (b) cLK7. The datas were obtained by average of three measurements and standard deviations were <0.2%. The fluorescence intensity of A β ₄₀ after incubation for 72 h was set to 100%. All samples were incubated at 37 °C for 72 h.

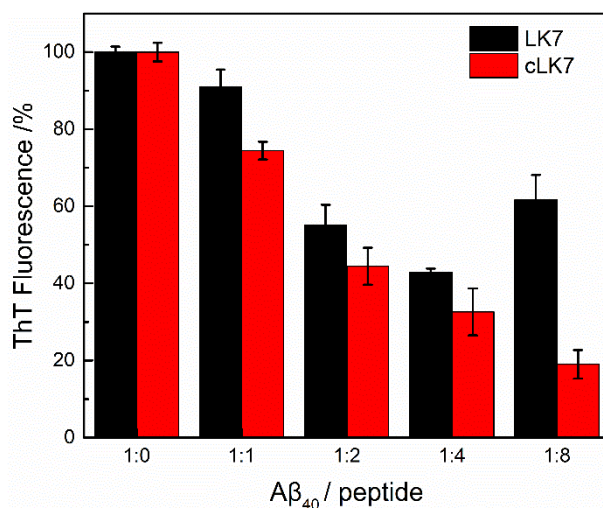


Fig. S3 Effect of the two peptides on A β ₄₀ fibrillation measured by ThT fluorescent assays. A β ₄₀ concentration was 25 μM . The fluorescent intensity of A β ₄₀ only after incubation for 72 h was set to 100%. Each experiment was repeated three times and error bars represent the standard deviation of the fluorescent intensity.

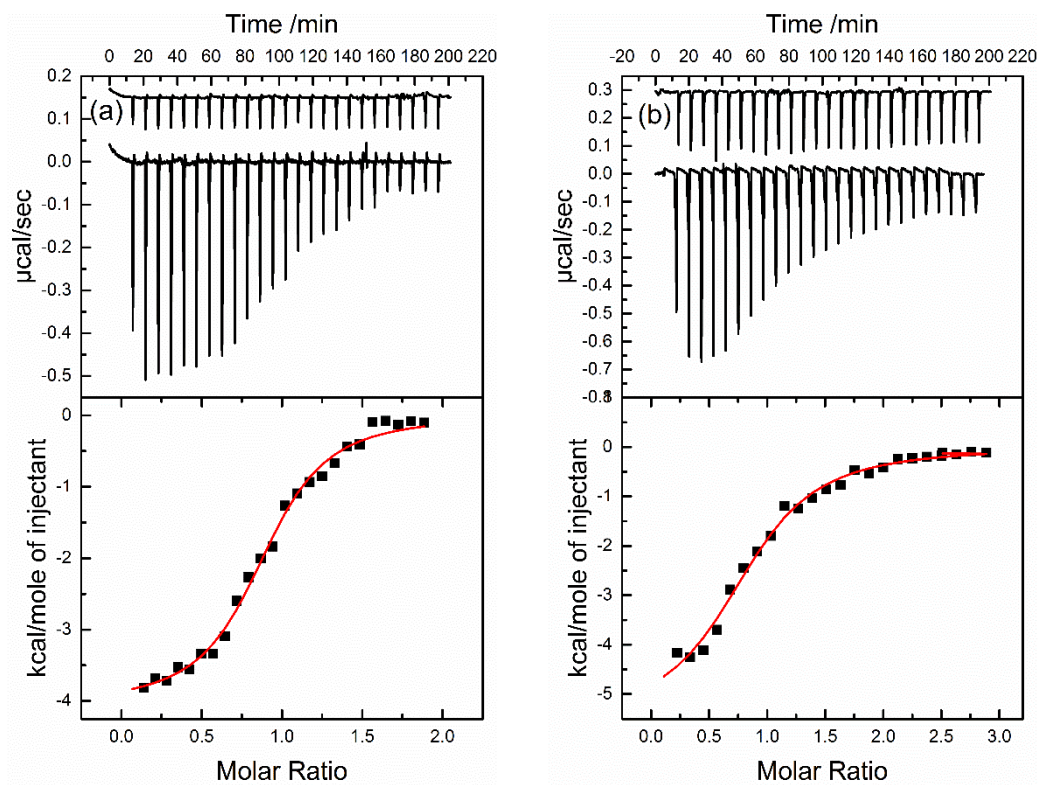


Fig. S4 ITC measurements of the interactions between $A\beta_{40}$ and (a) LK7 or (b) cLK7.

In each figure, the top panel shows the base-line subtracted heat signals obtained by a series of injections; the blank injection of peptides into the ITC cell containing only buffer is also shown and has been vertically offset for clarity. The bottom panel shows the integrated heats in each injection versus molar ratio of peptides to $A\beta_{40}$ together with a fit using a one-site binding model.

Table S1. Estimated secondary structural content obtained from BeStSeL web server (<http://bestsel.elte.hu/>) for the LK7 and cLK7 in 100 μ M. ^{a)}

		Antiparallel β -sheet (%)	Turn (%)	Others (%)	NRMSD ^{b)}
LK7	0 h	22.4	31.7	45.9	0.085
	24 h	33.4	32.0	34.6	0.072
	72 h	33.0	34.1	32.9	0.058
cLK7	0 h	31.9	25.3	42.8	0.087
	24 h	28.0	27.8	44.2	0.076
	72 h	31.8	27.0	41.2	0.093

a) Helix and parallel β -sheet structures did not appear in the secondary structures of either LK7 or cLK7.

b) NRMSD refers to the normalized root mean square deviation.

Table S2. Estimated secondary structural content obtained from BeStSeL web server (<http://bestsel.elte.hu/>) for the various A β samples.

	Helix (%)	Antiparallel β -sheet (%)	Parallel β -sheet (%)	Turn (%)	Others (%)	NRMSD ^{a)}
A β ₄₀ only 0 h	18.6	25.5	4.6	5.2	46.2	0.042
A β ₄₀ only 72 h	5.2	22.2	39.4	8.4	24.8	0.016
A β ₄₀ : LK7=1:1 72 h	5.9	23.1	35.6	7.4	28.0	0.022
A β ₄₀ : LK7=1:2 72 h	4.7	19.2	30.8	10.4	34.9	0.053
A β ₄₀ : LK7=1:4 72 h	8.8	14.7	32.6	4.4	39.5	0.091
A β ₄₀ : LK7=1:8 72 h	10.3	20.8	34.9	8.2	25.8	0.077
A β ₄₀ :cLK7=1:1 72 h	8.2	25.7	32.8	7.2	26.1	0.045
A β ₄₀ :cLK7=1:2 72 h	5.6	27.1	21.9	12.7	32.7	0.058
A β ₄₀ :cLK7=1:4 72 h	8.8	35.1	6.1	10.5	39.5	0.071
A β ₄₀ :cLK7=1:8 72 h	20.4	30.9	1.5	8.7	38.5	0.025

a) NRMSD refers to the normalized root mean square deviation