SUPPORTING INFORMATION

Mechanistic Investigation of the Inhibition of Aβ42 Assembly and Neurotoxicity by Aβ42 C-terminal fragments.

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Figure S1. PICUP–SDS-PAGE analysis. LMW Aβ42 (~20 μM) was mixed with increasing concentrations of CTF and photo-cross-linked immediately. The mixtures were fractionated by SDS-PAGE and silver-stained. Positions of molecular-weight markers are shown on the left. The concentrations of CTF are indicated at the bottom of each lane. A) Aβ42+Aβ(29–42). B) Aβ42+Aβ(32–42). C) Aβ(36–42) through Aβ(39–42).

Figure S2. Evaluation of Aβ(30–40) inhibition of Aβ42-induced toxicity. A) Cell death determined by the LDH-release assay in differentiated PC-12 cells in the presence of 10 μM Aβ42 and Aβ42:CTF concentration ratios ranging from 1:1 to 1:10. The data were normalized to full-kill and media controls and are reported as mean ± SEM (n = 18). B) Mouse primary hippocampal neurons were exposed to vehicle (n = 12), 3 μM Aβ42 (n = 8), or 1:10 Aβ42:Aβ(30–40) (n = 6), and the frequency and amplitude of mEPSCs were measured. Cells were perfused with vehicle for 5 min to establish baseline and then with peptide solutions for additional 20 min, and allowed to recover in vehicle solution for 15 min. The curves show the time dependence of mEPSC frequency after exposure to Aβ42 in the absence or presence of Aβ(30–40) over 40 min.

Figure S3. Correlation analysis. A) Linear regression analysis correlating inhibition of paranucleus formation for Aβ(29–42), Aβ(30–42), Aβ(31–42), and Aβ(33–42) with T_{50} of β-sheet formation by each CTF (*1*) ($r^2 = 0.96$, $p = 0.02$). B). Linear regression analysis correlating inhibition of paranucleus formation for Aβ(29–42), Aβ(30–42), Aβ(31–42), and Aβ(33–42) with rate of aggregation of each CTF (by itself) (*1*) ($r^2 = 0.94$, $p = 0.04$).

1. Li, H., Monien, B. H., Fradinger, E. A., Urbanc, B., and Bitan, G. (2010) Biophysical characterization of Aβ42 C-terminal fragments: inhibitors of Aβ42 neurotoxicity, Biochemistry 49, 1259–1267.

FIGURE S1

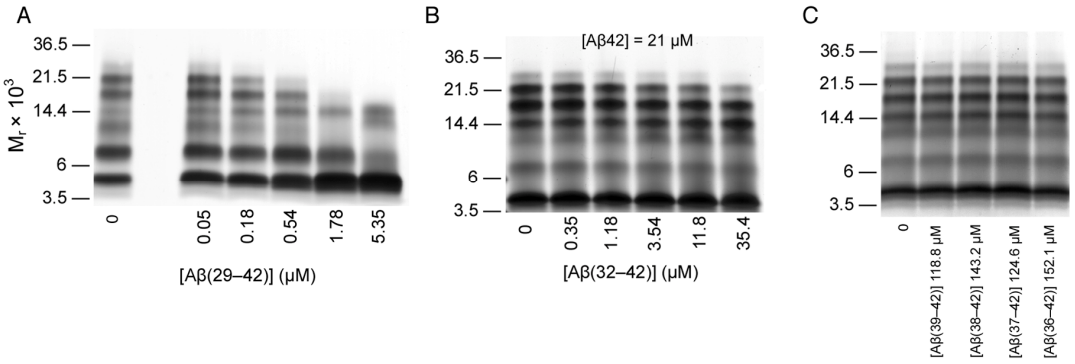

A
36.5
21.5
14.4
6
3.5
$M_r \times 10^3$
0
0.05
0.18
0.54
1.78
5.35
[Aβ(29–42)] (μM)
B
[Aβ42] = 21 μM
36.5
21.5
14.4
6
3.5
0
0.35
1.18
3.54
11.8
35.4
[Aβ(32–42)] (μM)
C
36.5
21.5
14.4
6
3.5
0
[Aβ(39–42)] 118.8 μM
[Aβ(38–42)] 143.2 μM
[Aβ(37–42)] 124.6 μM
[Aβ(36–42)] 152.1 μM

FIGURE S2

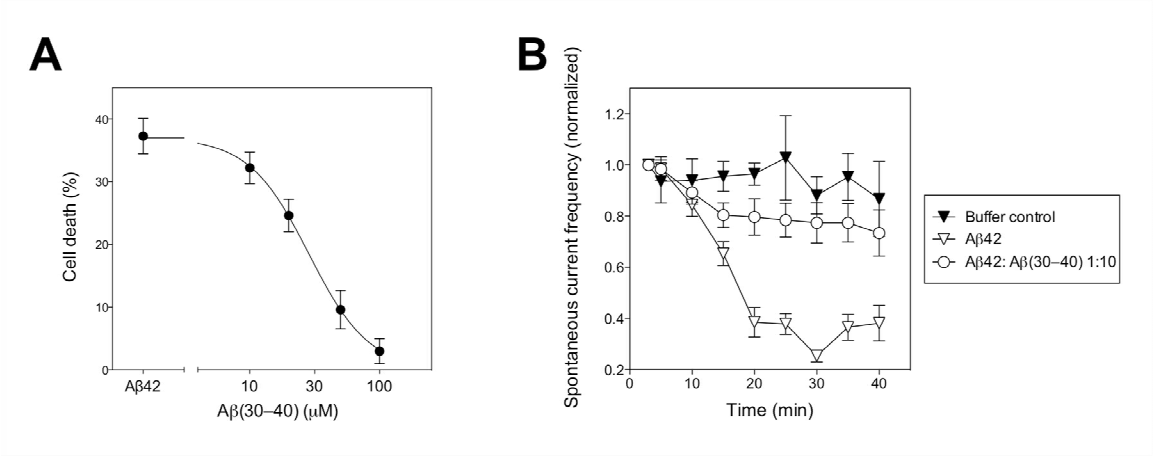
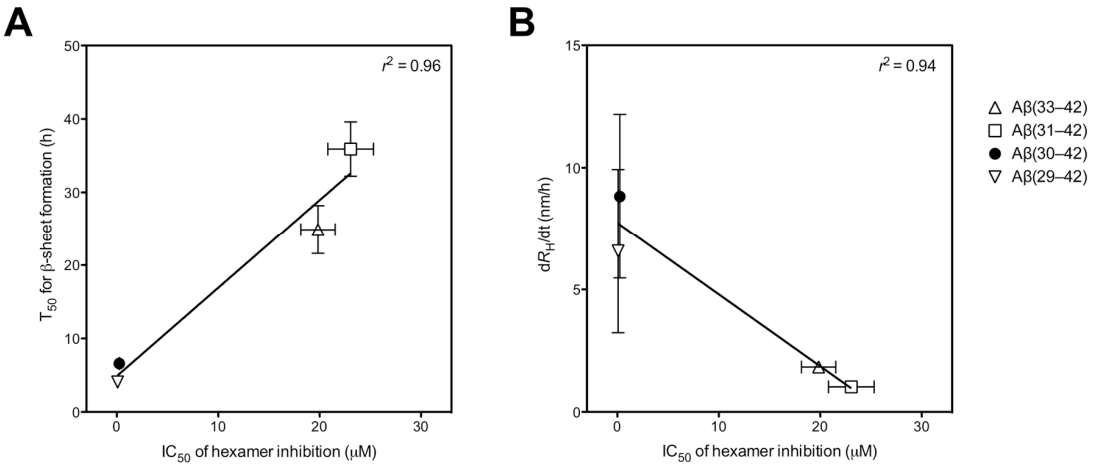

A
Cell death (%)
0
10
20
30
40
Aβ42
10
30
100
Aβ(30–40) (μM)
B
Spontaneous current frequency (normalized)
0.2
0.4
0.6
0.8
1.0
1.2
0
10
20
30
40
Time (min)
Buffer control
Aβ42
Aβ42: Aβ(30–40) 1:10

FIGURE S3


A
B
r^2 = 0.96
r^2 = 0.94
T_{50} for β-sheet formation (h)
dR_H/dt (nm/h)
IC_{50} of hexamer inhibition (μM)
IC_{50} of hexamer inhibition (μM)
Aβ(33–42)
Aβ(31–42)
Aβ(30–42)
Aβ(29–42)