Supplementary Information

A snake venom peptide and its derivatives prevent Aβ$_{42}$ aggregation and eliminate toxic Aβ$_{42}$ aggregates *in vitro*

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Table S1. Secondary structure content of CDPs, based on CD-experiments

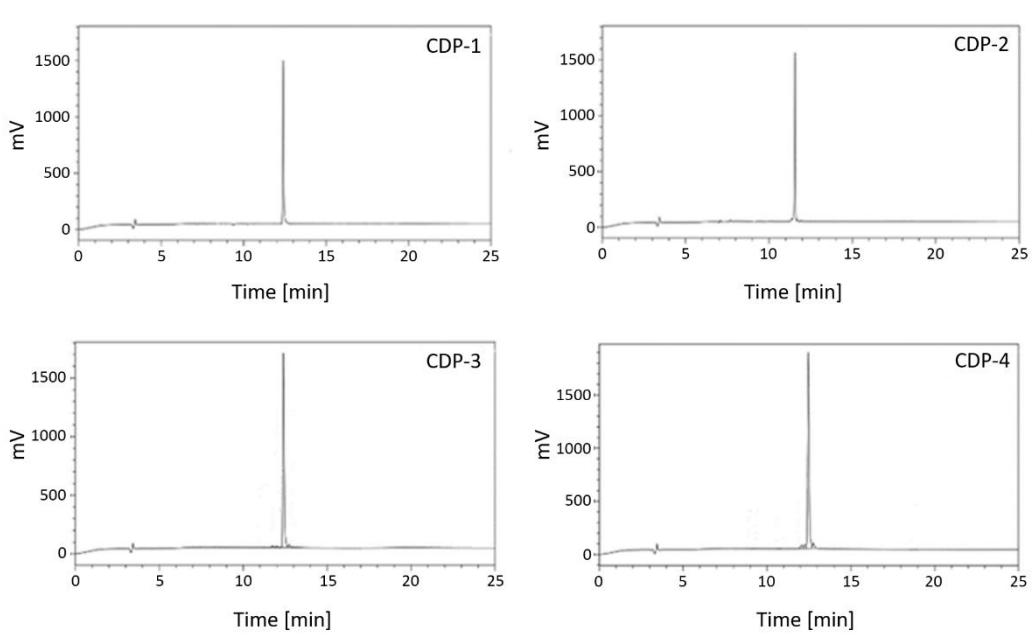

Figure S1. HPLC chromatograms of CDP-1 to CDP-4.

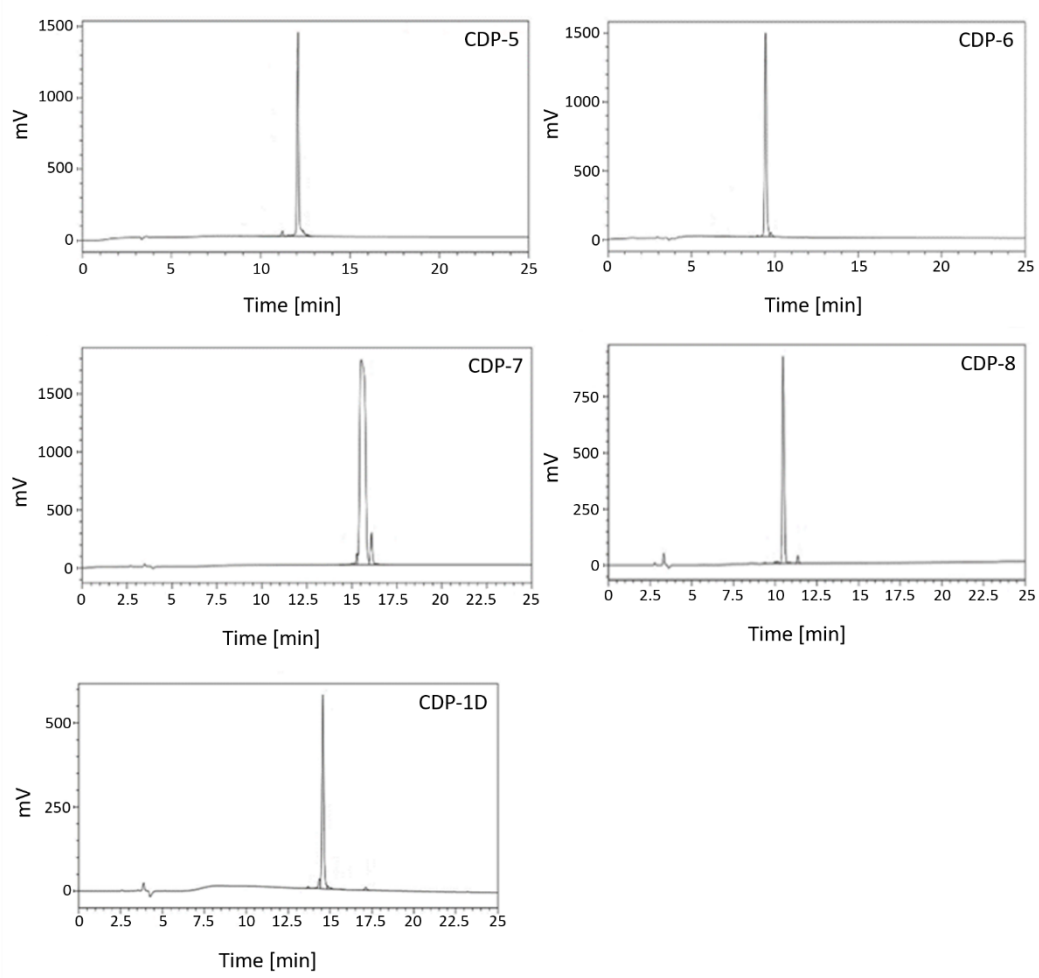

Figure S2. HPLC chromatograms of CDP-5 to CDP-8 and CDP-1D.

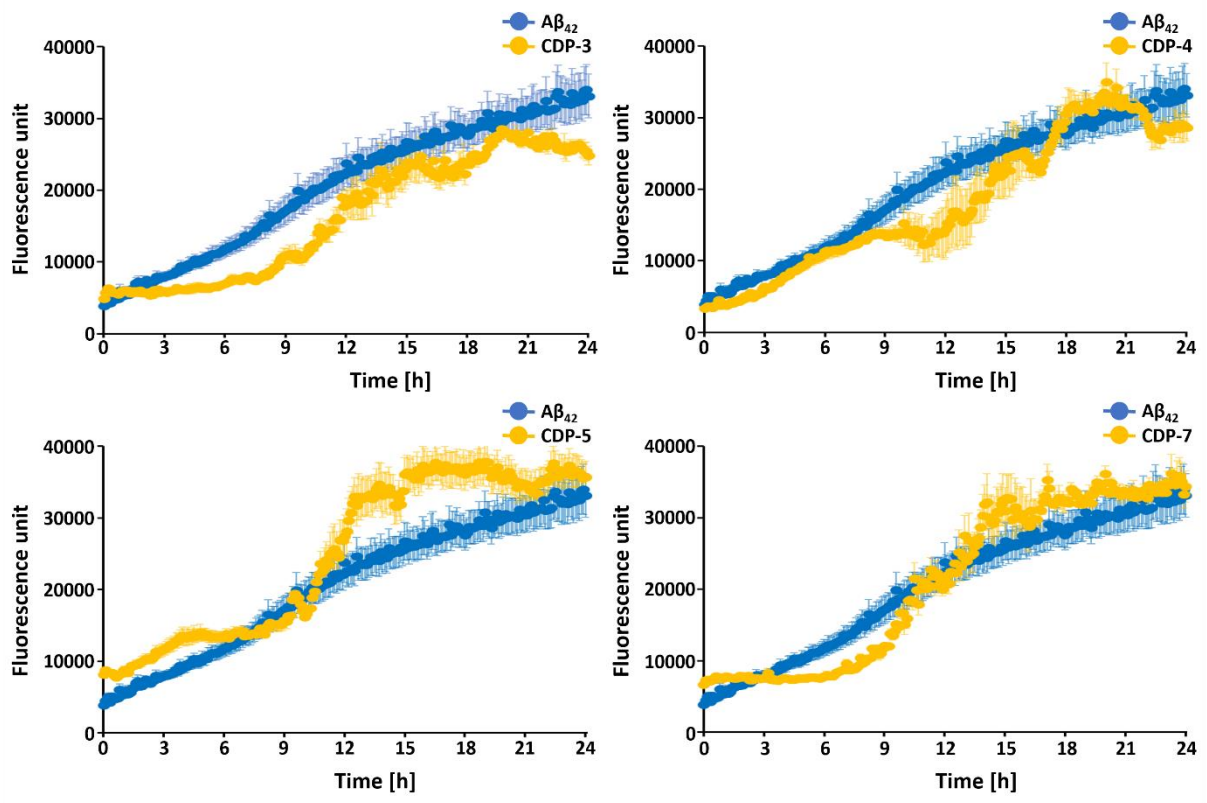

Figure S3. Effect of CDP-3, -4, -5 and -7 on Aβ42 aggregation using ThioflavinT assays. The ThT fluorescence signal with only Aβ42 is shown in blue. In orange, the action of CDP-3, -4, -5 and -7 in the signal of ThioflavinT. **A:** Effect of CDP-3 against Aβ42 aggregation. **B:** Effect of CDP-4 against Aβ42 aggregation. **C:** Effect of CDP-5 against Aβ42 aggregation and **D:** Effect of CDP-7 against Aβ42 aggregation. Data shown are the mean ± SEM from three independent measurements (n = 3).

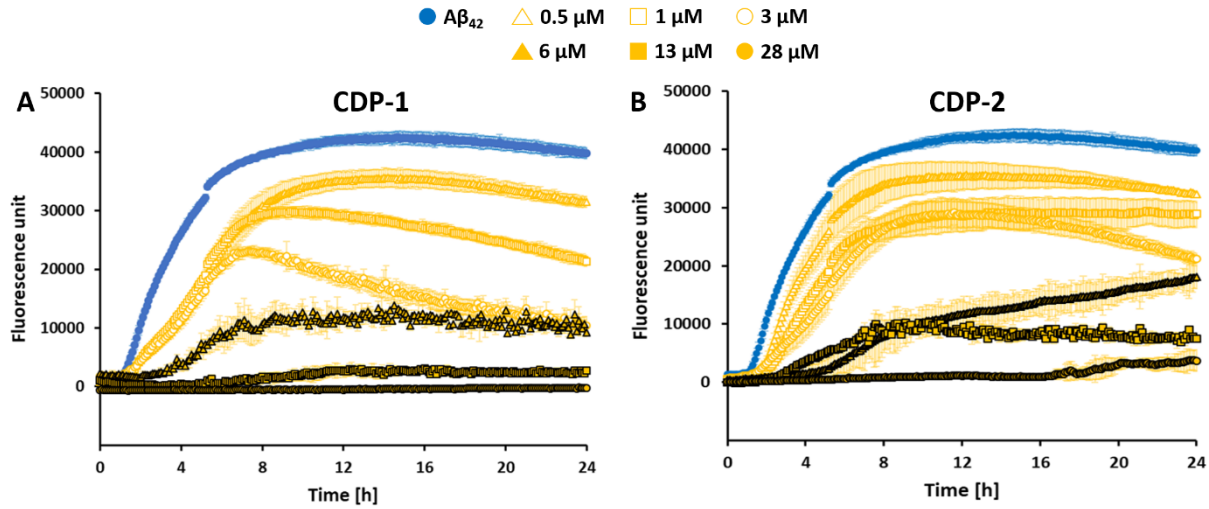

Figure S4. Dose dependency of CDP-1 and CDP-2 against the Aβ42 aggregation. The ThT fluorescence signal with only Aβ42 is shown in blue. In orange, the action of CDP-1 and -2 at different concentrations in the signal of ThioflavinT. Effect CDP-1 (**A**) and CDP-2 (**B**) doses (0.5, 1, 3, 6, 13 and 28 μM) on Aβ42 aggregation. Data shown are the mean ± SEM from three independent measurements (n = 3).

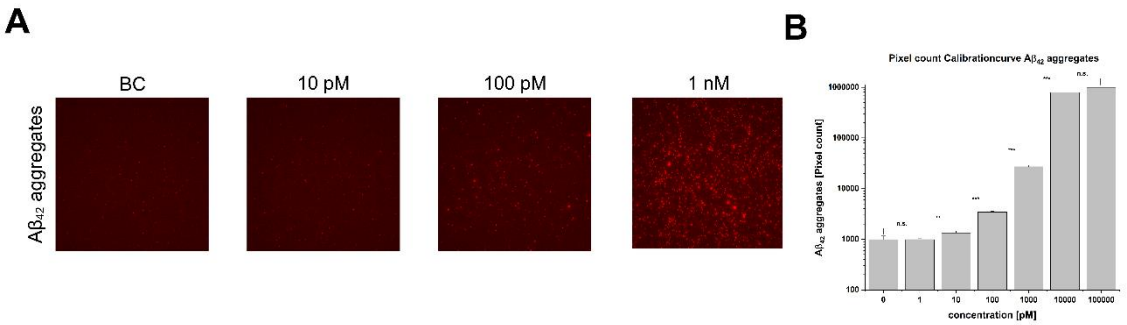

Figure S5. sFIDA with Aβ aggregates in different concentrations. A: TIRM images and **B:** Pixel count of the Aβ aggregate standard curve. Data shown are the mean ± SEM from three independent measurements (n = 3). Asterisks mean that the data differ from the control significantly at *: $p<0.05$, **: $p<0.01$ and ***: $p<0.001$ levels according to analyses by a two sample t-test.

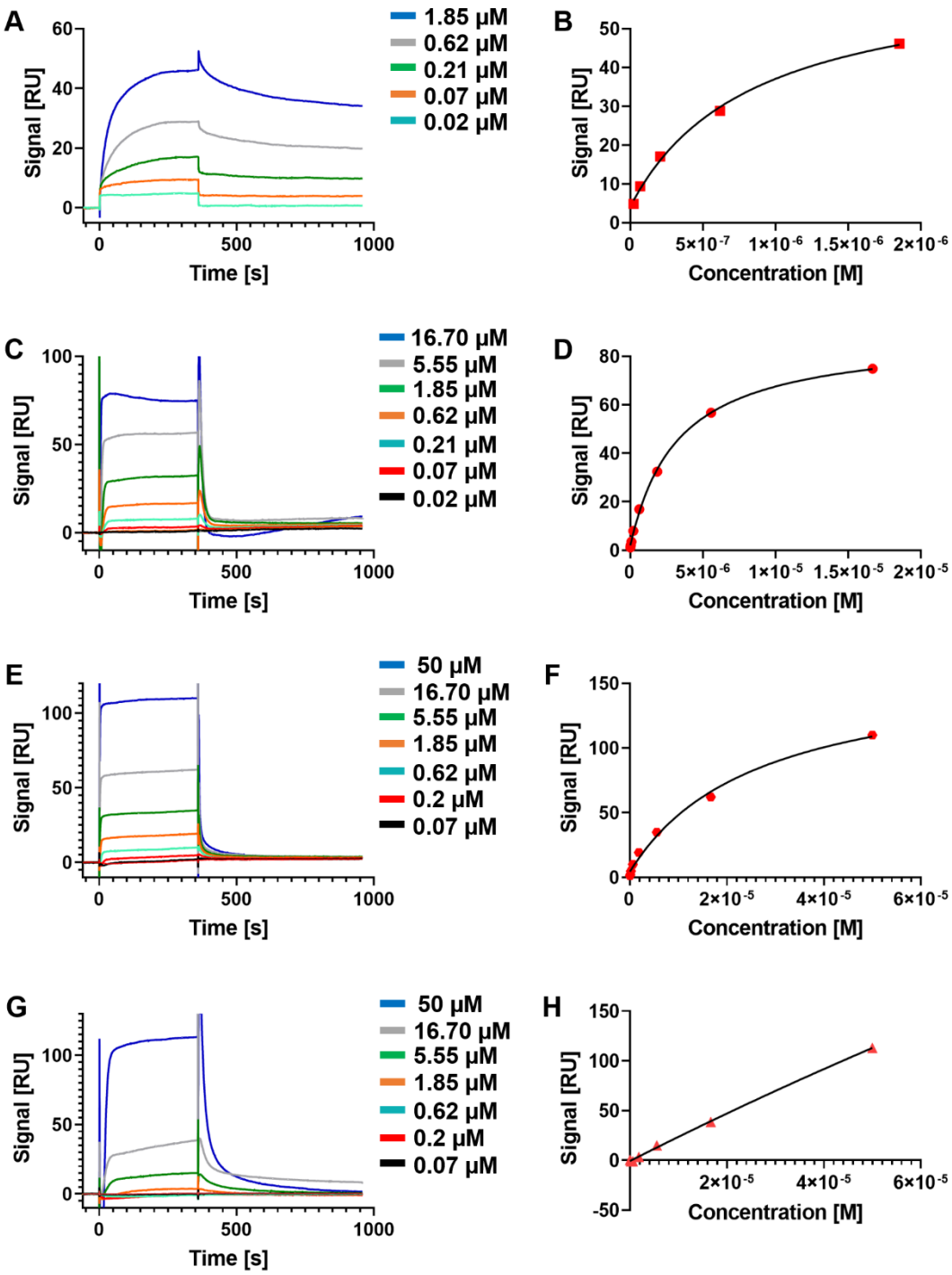

Figure S6. Biacore SPR kinetic analyses of peptides to Aβ42. The sensorgram and saturation curve of the titration are shown. Sensorgrams were obtained by using a different concentration of peptides (Coloured sensorgrams represent different concentrations in µM). Binding curves were fitted to a steady-state affinity model to get K_D values. CDP-1 (**A**, **B**), CDP-2 (**C**, **D**), CDP-6 (**E**, **F**) and CDP-8 (**G**, **H**).

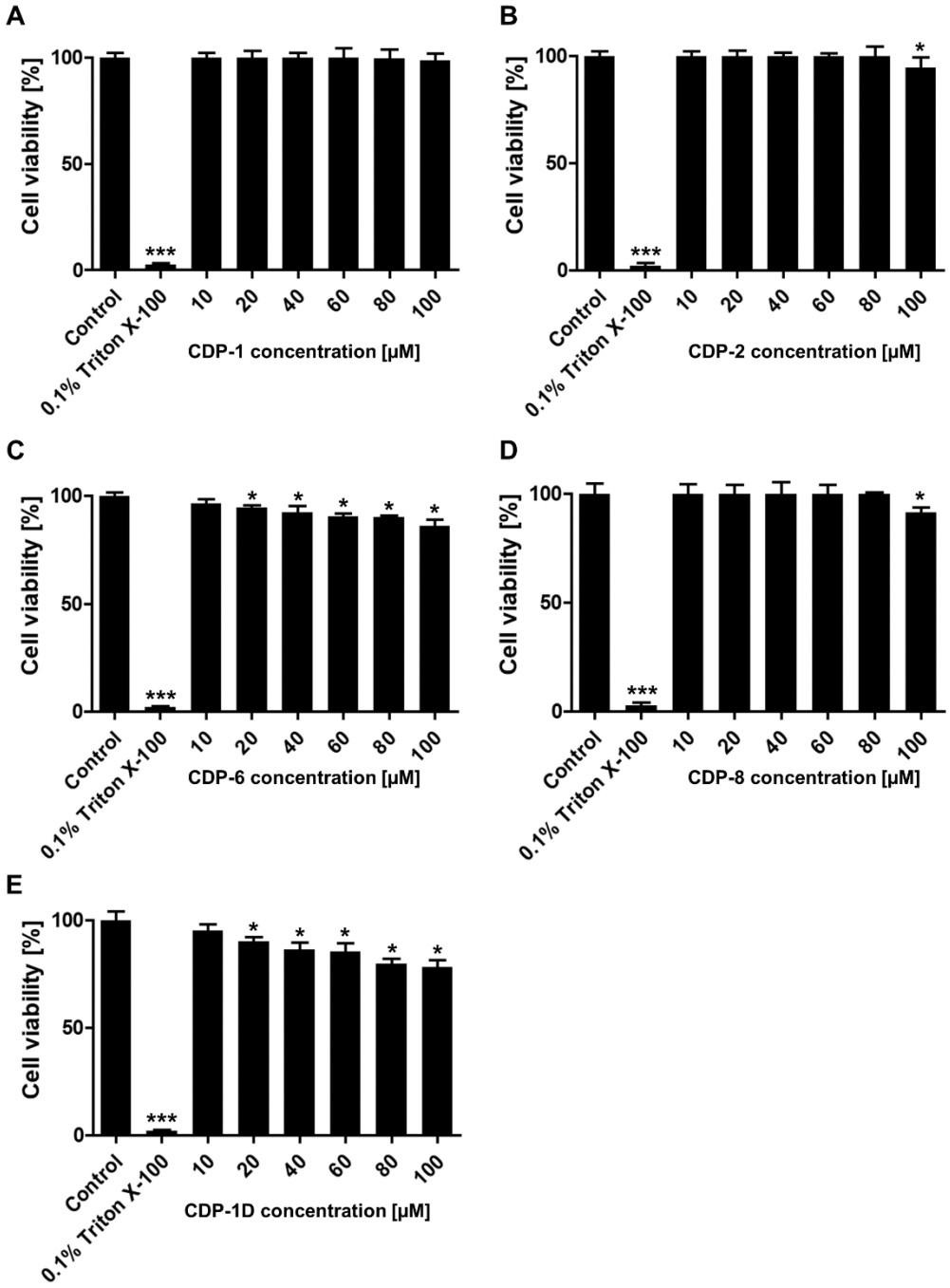

Figure S7. MTT assay of CDPs on SH-SY5Y cells. MTT assay evaluated the cytotoxicity of four L-peptides and one D-peptide, each at a concentration range between 0 to 100 μM. The control shows the cell viability without peptide, and 0.1% Triton x-100 was used as a negative control. **A:** CDP-1, **B:** CDP-2, **C:** CDP-6, **D:** CDP-8 and **E:** CDP-1D. Data shown are the means ± SD from three independent measurements (n = 3). Asterisks mean that the data differ from the control significantly at *: $p<0.05$ and ***: $p<0.001$ levels according to analyses by two-way ANOVA.

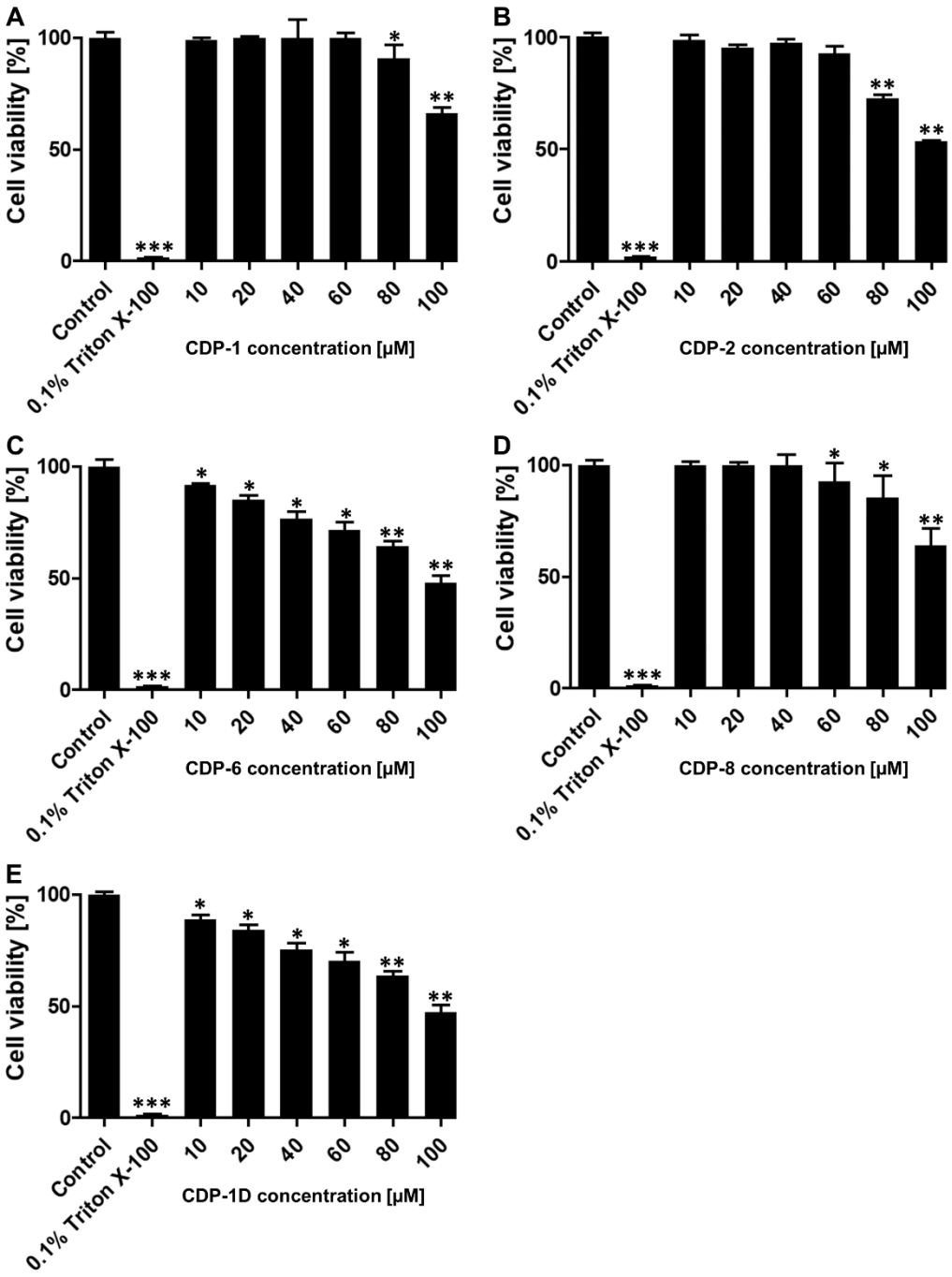

Figure S8. MTT assay of CDPs on HEK293 cells. MTT assay evaluated the cytotoxicity of four L-peptides and one D-peptide, each at a concentration range between 0 to 100 μM. The control shows the cell viability without peptide, and 0.1% Triton x-100 was used as a negative control. **A:** CDP-1, **B:** CDP-2, **C:** CDP-6, **D:** CDP-8 and **E:** CDP-1D. Data shown are the means ± SD from three independent measurements (n = 3). Asterisks mean that the data differ from the control significantly at *: $p<0.05$, **: $p<0.01$ and ***: $p<0.001$ levels according to analyses by two-way ANOVA.

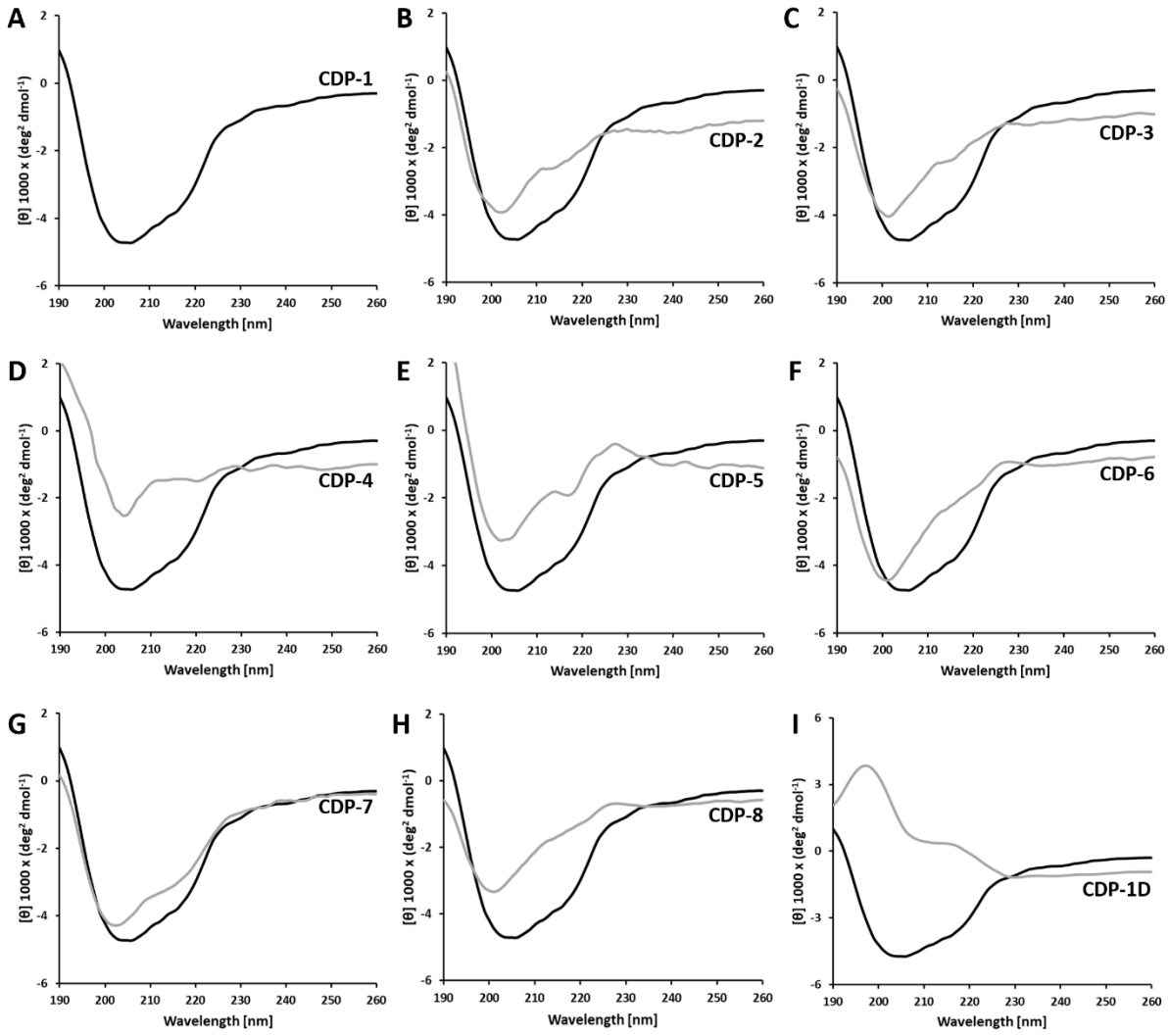

Figure S9. CD-spectra of CDPs. The CD spectra of the peptides are shown in reference to the spectrum of CDP-1. All peptides were solved in ddH_2O, and the peptide concentration was 30 µM. **A:** CDP-1, **B:** CDP-2, **C:** CDP-3, **D:** CDP-4, E: CDP-5, **F:** CDP-6, **G:** CDP-7, **H:** CDP-8 and **I:** CDP-1D.

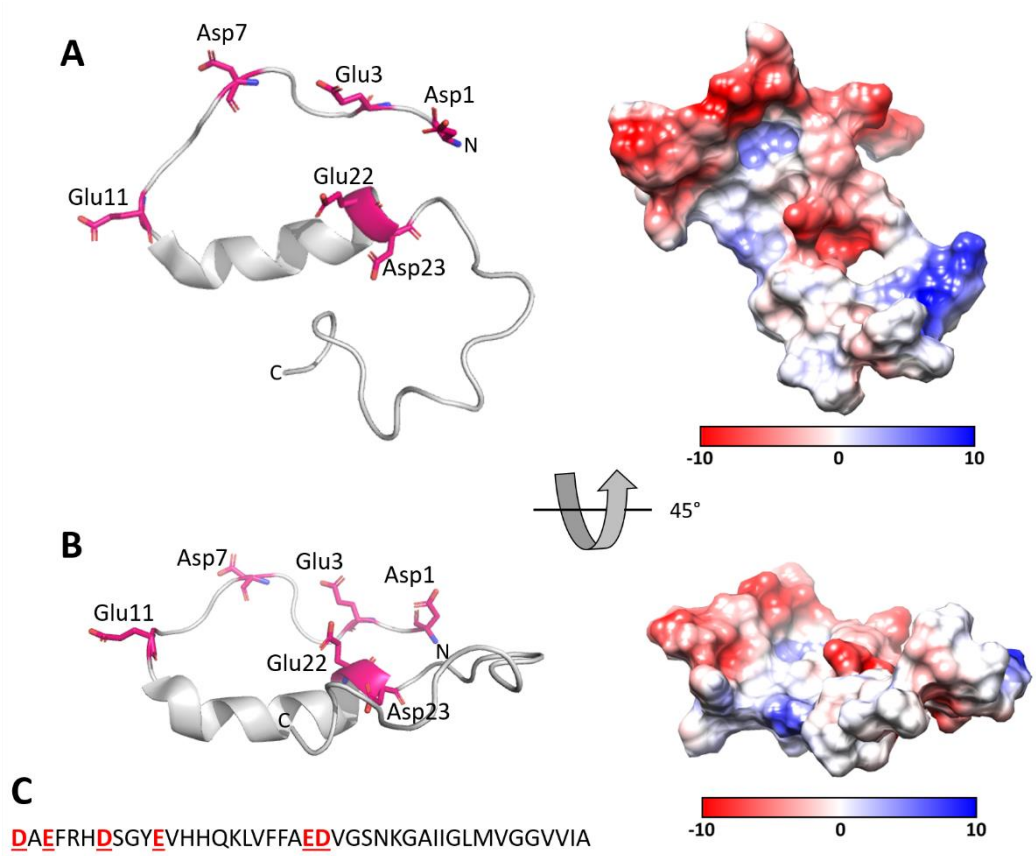

Figure S10. Negatively charged residues in the Aβ structure and surface. Ribbon view and coloumbic surface representation of the Aβ monomer structure (PDB: 2LFM). Residues with negative charges are highlighted as sticks. **A:** Ribbon and surface view of the Aβ monomer and **B:** bent forward 45°. **C:** Sequence of Aβ42, the negatively charged residues are highlighted.

Table S1. Secondary structure content of CDPs, based on CD-experiments[1].

	Secondary structure		
Peptides	α-helix [%]	β-strand [%]	Others [%]
CDP-1	25	-	75
CDP-2	3	-	97
CDP-3	4	-	96
CDP-4	7	-	93
CDP-5	4	-	96
CDP-6	6	-	94
CDP-7	8	-	92
CDP-8	6	-	94

[1]Secondary structure determination was performed using the online tool BeStSel (https://bestsel.elte.hu/index.php).