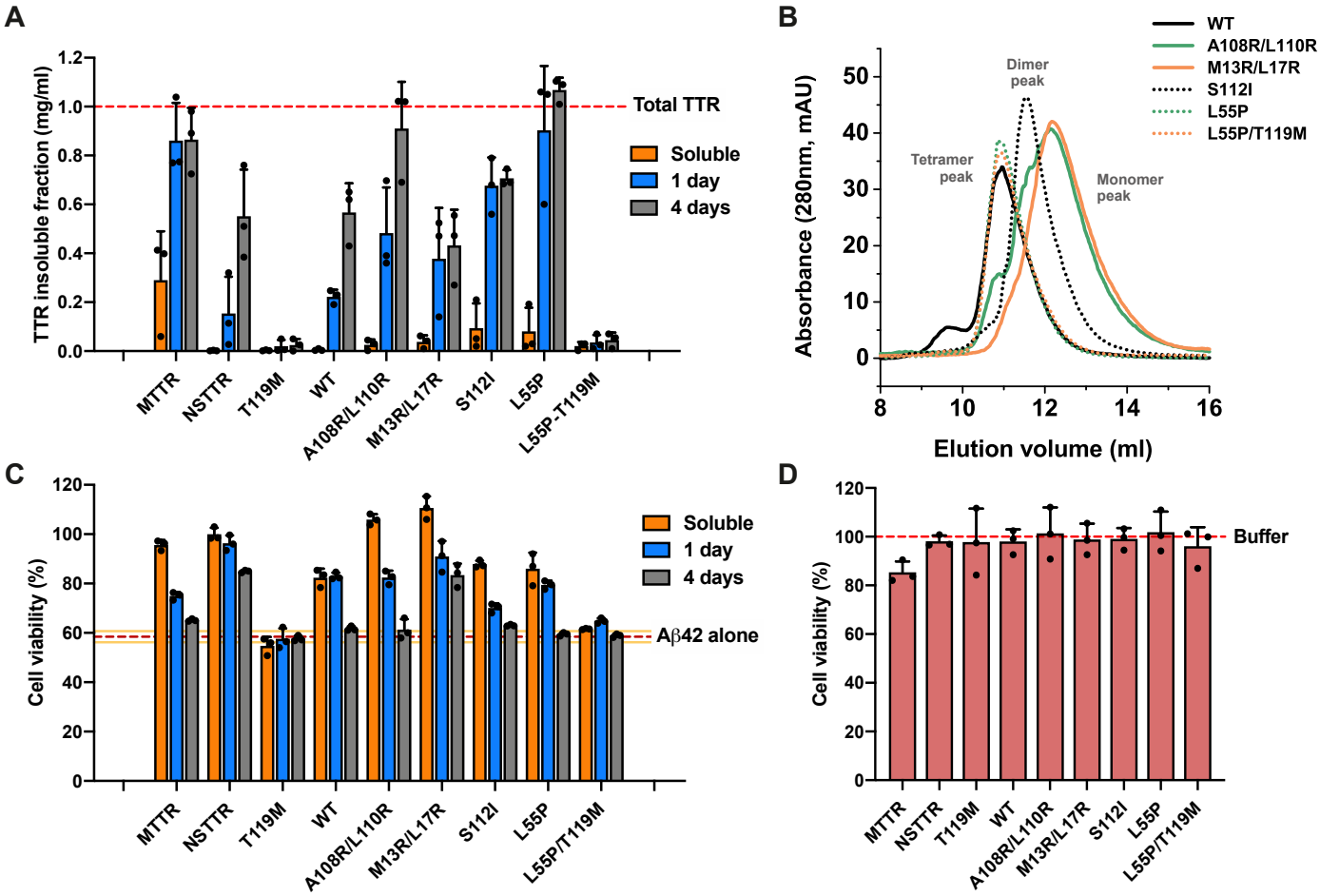
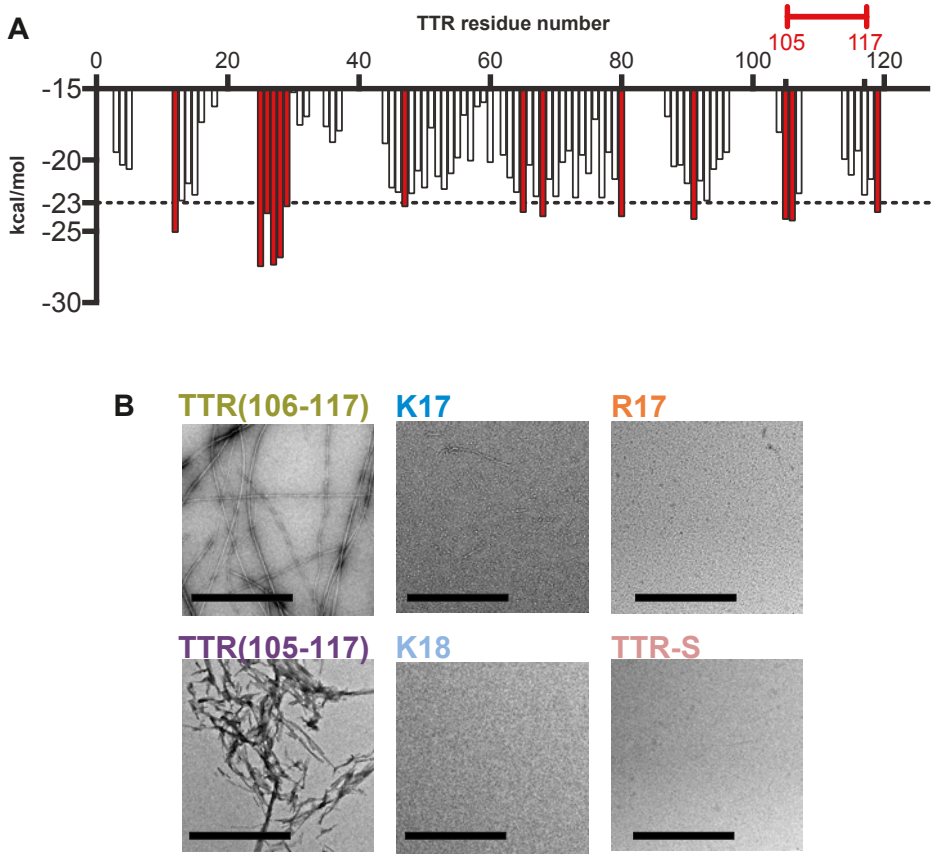
Supplementary Figure 1



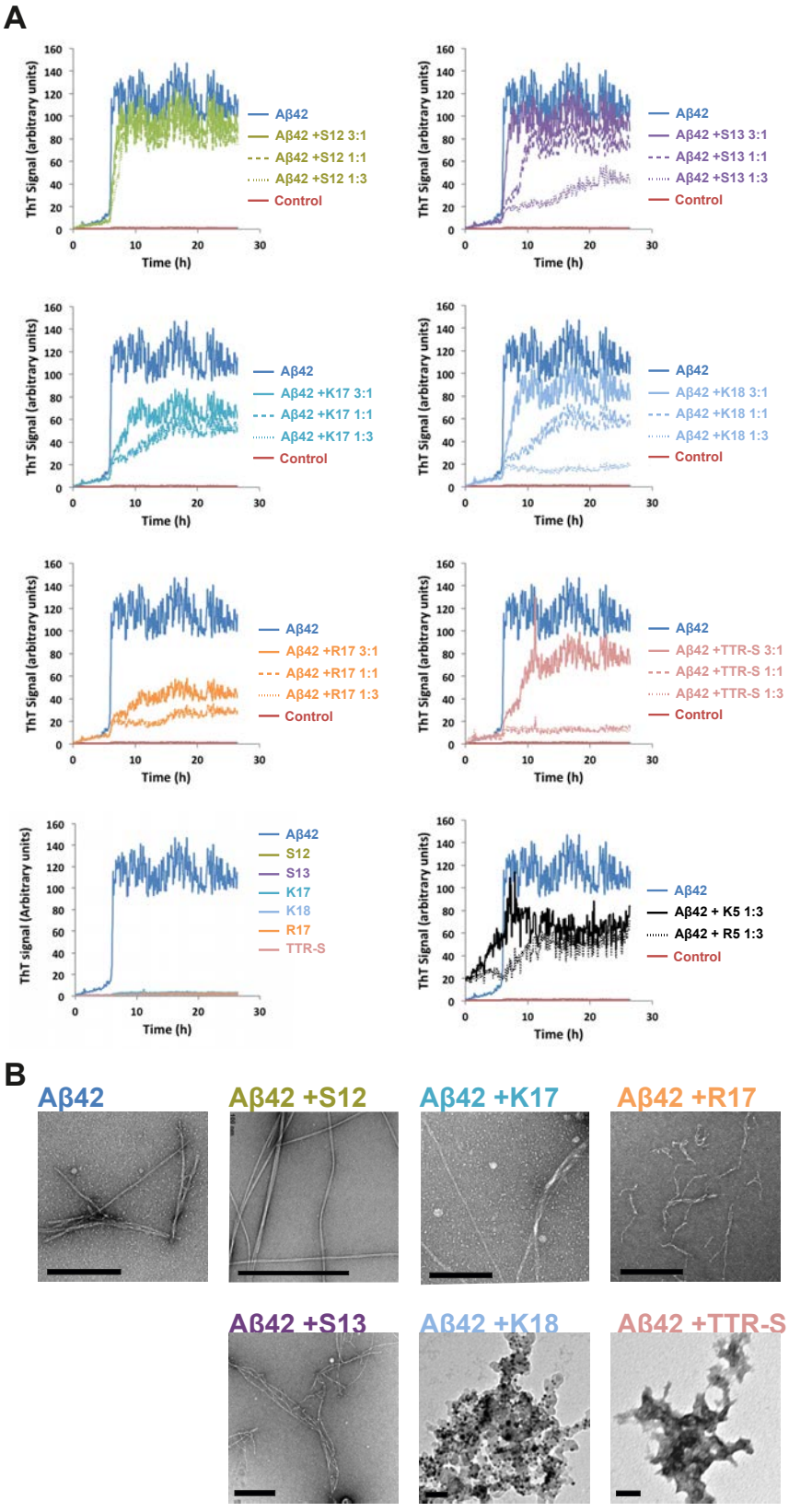
Supplementary Figure 1. Inhibition of Aβ42 cytotoxicity by TTR variants. (A) Aggregation assay of TTR variants followed by protein concentration of insoluble fractions collected prior incubation, or after 1, and 4 days of incubation at 37º C, as labeled. **(B)** Size exclusion chromatography of soluble TTR variants at pH 7.4. **(C)** Cytotoxicity assay of Aβ42 in the presence of TTR variants at different stages of aggregation, followed by MTT reduction. A five-fold molar excess of soluble TTR (50 μM, considering monomeric concentration), and aggregated samples collected after 1 and 4 days of incubation was added to soluble 10 μM Aβ42 and incubated overnight. Samples were added to HeLa cells, and MTT reduction was measured after 24 hours. Buffer-treated cells were considered 100% viability and used for normalization. **(D)** Cytotoxicity of TTR variants in the absence of Aβ42 measured by MTT reduction. TTR final concentration was kept the same as for **(C)**, 50 μM.

Supplementary Figure 2



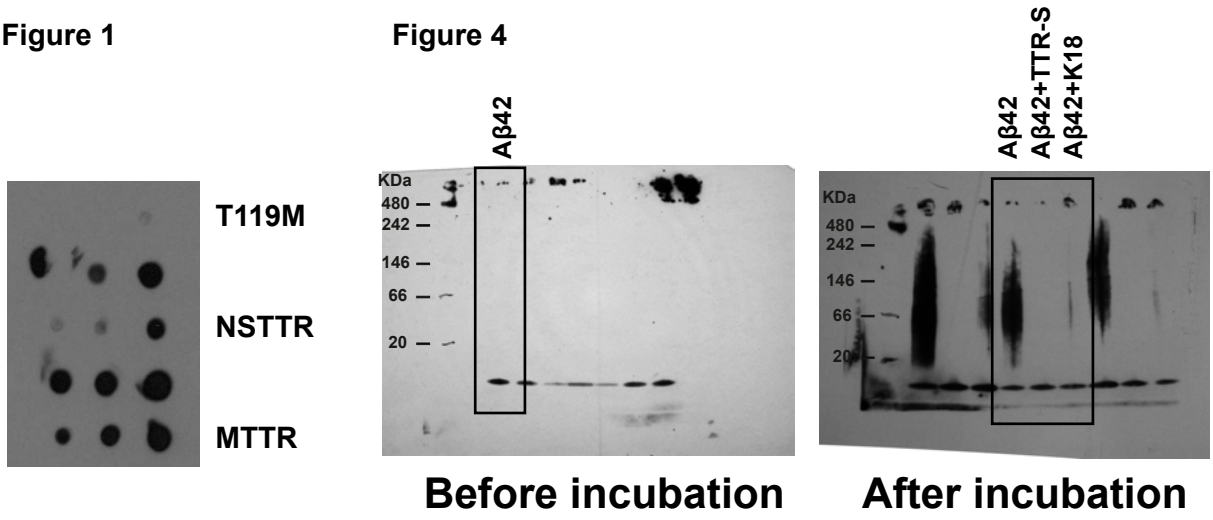
Supplementary Figure 2. Evaluation of TTR-derived peptides in the absence of Aβ42. (A) Propensities of steric zipper formation of each 6-residue segment within the TTR sequence. Computationally predicted segments with steric zipper propensities are represented with *red bars*. The segment identified from docking modeling is marked with a red bracket. **(B)** Electron micrographs of TTR-derived peptides after 26 hours of incubation at 37°C. Scale bar, 200 nm.

Supplementary Figure 3



Supplementary Figure 3. Evaluation of the inhibitory effect of TTR-derived peptides. (A) Thioflavin T (ThT) fluorescence was measured from samples containing 10 μM Aβ42 in the presence and absence of TTR-derived peptides at several molar ratios, as labeled. TTR-derived peptides were added at the starting point. Peptide sequences are listed in Table 2. Buffer was used as negative control. All samples were incubated at the same time, but data were separated into independent graphs to facilitate visualization. Thus, the curves of the control Aβ42 in the absence of inhibitors are the same for all graphs. **(B)** Electron micrographs of samples collected from ***A***, incubated for 26 hours in the presence and absence of 3-fold molar excess of peptides, as labeled.

Supplementary Figure 4



Supplementary Figure 4. Uncut Gels. These images were used for Figure 1 and Figure 4, as labeled.