Multivalent Macromolecules Redirect Amyloid Beta Aggregation and Reduce Its Cytotoxicity
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**Purpose**
Amyloid beta (A-beta) peptide aggregation is the process of forming insoluble proteinaceous aggregates, which is associated with Alzheimer’s disease. Although it is not yet clear by which mechanism toxic A-beta oligomers and fibrils form, strategies that intervene with the A-beta aggregation and prevent fibril formation have shown their potential applications in therapeutics for Alzheimer’s disease. Here, we introduce multivalent polymer-peptide conjugates (mPPCs) that redirect fibrillar assembly of A-beta and reduce the cytotoxicity of A-beta aggregates. The mPPCs were rationally designed to target A-beta intermediates formed prior to critical nucleation.

**Methods**
polymer-peptide synthesis, Thioflavin T fluorescence assay, AFM, TEM, cell viability assay

**Results**
Thioflavin T kinetics fluorescence assays demonstrate that mPPCs suppress A-beta fibrillogenesis. Atomic force microscopy and transmission electron microscopy studies show that A-beta self assembles into uniform zero dimensional nanospheres in the presence of mPPCs, while A-beta alone self assembles into one-dimensional fibrils in micrometer. Cell viability assays indicate that mPPCs reduce the cytotoxicity of A-beta aggregates in a dose-dependent manner.

**Conclusion**
We envision that mPPCs may offer an opportunity for potential development of diagnostics and therapeutics in Alzheimer’s disease. This work is one example of designing a polymer that disrupts protein aggregation via beta-sheet formation.