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Supporting Information

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Inhibition of Amyloid Peptide Fibrillation by Inorganic Nanoparticles: Functional Similarities with Proteins**

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Additional TEM Images of Spherical Aggregates of $A\beta_{1\text{-}40}$ and CdTe NPs

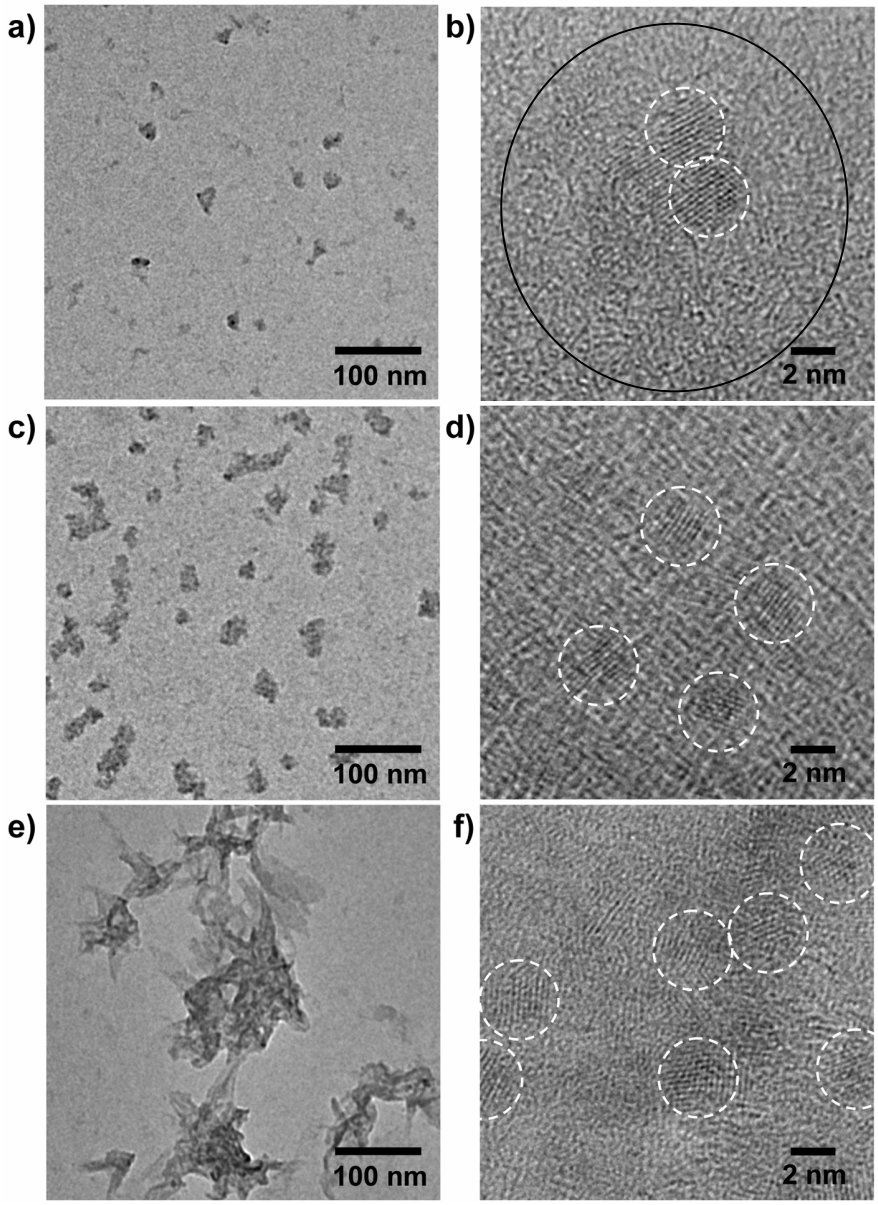

Figure S1. Normal (a, c, e) and HR (b, d, f) TEM images of aggregates consist of $A\beta_{1\text{-}40}$ and CdTe NPs. The molar ratios of [CdTe]/[$A\beta_{1\text{-}40}$] were (a, b) 0.01, and (c ~ f) 0.05. The lattice structures of CdTe NPs are marked by dashed circles in the HRTEM images.

Single monomer binding to NPs

In the process of testing different hypothesis of NP inhibition of peptide assembly, we also looked at the possibility of direct covalent and hydrogen bond mediated binding of peptides to CdTe NPs. While it is chemically possible and results in scrambling of peptide conformation (Figure S2), the number of monomeric peptides that can be positioned around a single NPs and making direct covalent bonding to it is much smaller than what is observed in the experiment, i.e. 100-330.

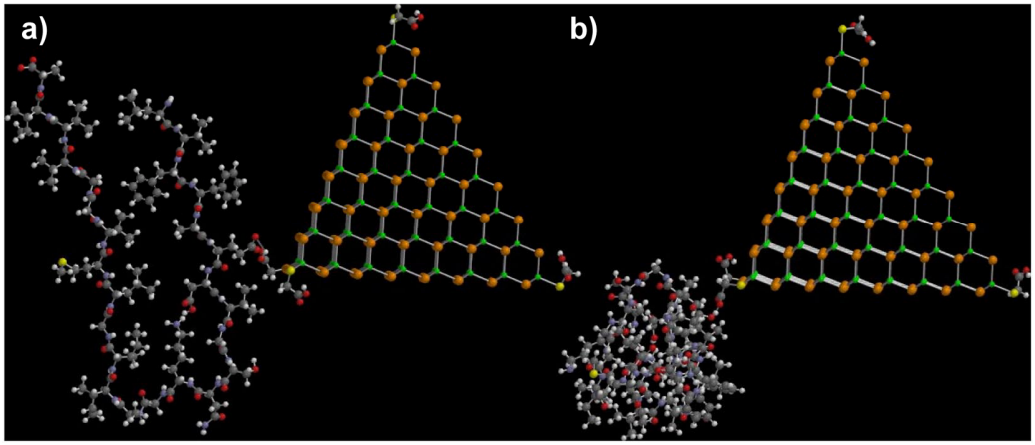

Figure S2. Molecular model for the conformation of $A\beta_{17-42}$ with CdTe NP before (a) and after (b) optimization by MMFF. CdTe NP is depicted as a tetrahedron consisting of Cd (green) and Te (brown) atoms. TGA molecule is present at each apex of tetrahedron with S (yellow), O (red), C (gray), and H (white) atoms. For the initial conformation, β-sheet structured $A\beta_{17-42}$ (Protein data bank code: 2BEG) was placed on the tetrahedral CdTe NP.

Number of Peptides in the Spherical Aggregates

The radius of an immobilized monomer was estimated using molecular mechanics with SPARTAN software package. Scrambled conformation of the peptide can be somewhat different depending on specific conformation. For the purpose of estimating an average volume of such conformations such model is probably one of the best possible because it is generated using realistic interatomic interactions in the globule. By assuming the scrambled peptide as a sphere, the radius of immobilized peptide was estimated as 1.3 nm.

To calculate the number of peptide molecules in a spherical aggregates (~ 18 nm in diameter), we applied simple space-filling condition. In Figure S3, the volume of total immobilized peptides is equal to the volume of a spherical aggregate subtracted by the volume of CdTe NP in a core.

$$\frac{4\pi}{3} r_{monomer}^3 N = \frac{4\pi}{3} (r_{aggregate}^3 - r_{CdTe}^3)$$

where, N is the number of immobilized peptides in the spherical aggregate, $r_{monomer}$, $r_{aggregate}$, and r_{CdTe} are the radius of the distorted monomer (Figure S2b), spherical aggregate, and CdTe NP, respectively. By using the values of $r_{monomer}$ = 1.3 nm, $r_{aggregate}$ = 9.0 nm, and r_{CdTe} = 1.75 nm, the number of peptide molecules in the spherical aggregate was evaluated as 329.

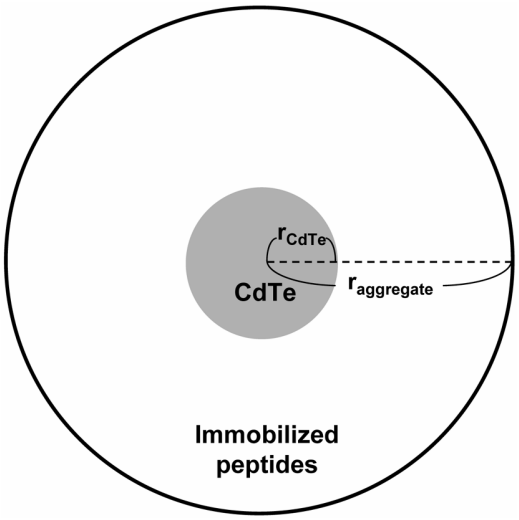

Figure S3. Geometry for the calculation of the number of peptides in the spherical aggregate.

Notations of 1-Letter Abbreviation of Each Residue in NMR Spectra.

F4	**R5**	**D7**	**S8**	**G9**	**Y10**	**E11**	**V12**
Phenylalanine	Arginine	Aspartic acid	Serine	Glycine	Tyrosine	Glutamic acid	Valine
Q15	**K16**	**L17**	**V18**	**F19**	**F20**	**E22**	**D23**
Glutamine	Lysine	Leucine	Valine	Phenylalanine	Phenylalanine	Glutamic acid	Aspartic acid
V24	**G25**	**S26**	**N27**	**G29**	**A30**	**I31**	**I32**
Valine	Glycine	Serine	Asparagine	Glycine	Alanine	Isoleucine	Isoleucine
G33	**L34**	**M35**	**V36**	**G37**	**G38**	**V39**	**V40**
Glycine	Leucine	Methionine	Valine	Glycine	Glycine	Valine	Valine

Oligomerization Condition: Sample Preparation, Western Blot, FT-IR and CD Spectroscopy.

To prepare oligomeric aggregates, $A\beta_{1-42}$ was selected because stable $A\beta_{1-42}$ oligomers can be more readily prepared compared to $A\beta_{1-40}$.[1,2] For the oligomerization, stock solution of $A\beta_{1-42}$ was prepared by dissolving the as-received lyophilized peptide (American Peptide Co. Inc.) into dimethyl sulfoxide (DMSO) to a final concentration of 1 mM. Then, the stock solution was added to sodium phosphate buffer without NaCl (10 mM, pH 7.5) to yield a 30 μM peptide solution in the presence and absence of CdTe NPs. The molar ratio of CdTe NPs to $A\beta_{1-42}$ was selected as 0, 0.01 and 0.05. Then the solutions were incubated at room temperature without stirring for 1 day.

For Western blot analysis, equal amounts of volume (typically 3 μL) from each sample was resolved by 4-12 % SDS-PAGE and transferred to Immobilon-P membranes (Millipore Corp.). The membranes were blocked with 10% nonfat milk in Tris-buffered saline containing 0.01 % Tween 20 (TBST) and then probed with primary antibody named 6E10 (Signet) overnight at 4 °C. The membranes were then washed and probed with a species-specific horseradish peroxidase-conjugated secondary

antibody (Santa Cruz Biotech.) for 90 minutes at room temperature, followed by ECL detection (Thermo Scientific).

The conformational change of $A\beta_{1-42}$ with and without CdTe NPs was monitored by circular dichroism (CD) spectrometer (Aviv, Model 62DS). Since DMSO has a strong absorbance in the far UV region, lyophilized peptide was first dissolved in aqueous solution of NaOH (100 mM) with a peptide concentration of 1 mM. Then, incubation solution was prepared as before. Prior to CD measurement, each sample was diluted with phosphate buffer to yield 15 μM $A\beta_{1-42}$ solution. CD spectra were recorded by 5 times and then averaged. FT-IR spectroscopy was performed on a Nicolet 6700 spectrometer.

Evaluation of van der Waals Interaction

The van der Waals energy (vdW) between two dissimilar spherical particles in a common medium is given by[3]

$$\mathrm{vdW} = \frac{A_{3-1-2}}{6}\left[\frac{2R_1R_2}{s^2+2R_1s+2R_2s} + \frac{2R_1R_2}{s^2+2R_1s+2R_2s+4R_1R_2} + \ln\left(\frac{s^2+2R_1s+2R_2s}{s^2+2R_1s+2R_2s+4R_1R_2}\right)\right] \text{ - (S1)}$$

where, A_{3-1-2} is Hamaker constant, R_1 and R_2 are radii of particles, and s is the center-to-center distance between two particles. The subscript 3-1-2 indicates that two particles of type 2 and 3 are separated by common medium of type 1.

The Hamaker constant can be further described as[3]

$$A_{3-1-2} = A_{1-1} + A_{2-3} - A_{1-2} - A_{1-3} \cong A_{3-1-3}^{1/2}\, A_{2-1-2}^{1/2} \text{ --------- (S2)}$$

where, A_{3-1-3} and A_{2-1-2} are the Hamaker constant for independent particles of type 3 and 2 in a medium of type 1, respectively.

Here, we are interested in the comparison of the vdW between CdTe NPs and Aβ ($vdW_{CdTe\text{-}A\beta}$) with that between organic NPs and Aβ ($vdW_{organic\text{-}A\beta}$). Since the peptide molecule in our interests is the one that is not bound to CdTe NPs, we assumed Aβ adopts a spherical shape. The shape of CdTe NPs was also assumed as a sphere. After that, Equation (S1) was employed for the estimation of $vdW_{CdTe\text{-}A\beta}$ / $vdW_{organic\text{-}A\beta}$. By choosing organic NPs having the same size with CdTe NPs and water as a medium, $vdW_{CdTe\text{-}A\beta}$ / $vdW_{organic\text{-}A\beta}$ can be further simplified as

$$\frac{W_{CdTe-A\beta}}{W_{organic-A\beta}} = \frac{A_{CdTe-water-A\beta}}{A_{organic-water-A\beta}} \cong \frac{A^{1/2}_{CdTe-water-CdTe}}{A^{1/2}_{organic-water-organic}} \frac{A^{1/2}_{A\beta-water-A\beta}}{A^{1/2}_{A\beta-water-A\beta}} = \frac{A^{1/2}_{CdTe-water-CdTe}}{A^{1/2}_{organic-water-organic}} \quad \text{--------- (S3)}$$

The value of $A_{CdTe\text{-}water\text{-}CdTe}$ was assumed as 4.9×10^{-20} J that is for a closely related semiconductor CdS interacting in water.[4] For $A_{organic\text{-}water\text{-}organic}$, we selected the value for polystyrene particles as a representative case and was 3.9×10^{-21} J.[5] From these values, $W_{CdTe\text{-}A\beta}$ / $W_{organic\text{-}A\beta}$ was estimated as 3.5.

To evaluate the value of vdW energy, Hamaker constant of $A_{A\beta\text{-}water\text{-}A\beta}$ was assumed as 3.1 k_BT (~ 1.3×10^{-20} J), which is a theoretical value of protein-water-protein interaction.[6] From the selected Hamaker constants, vdW energy was evaluated from Equation (S1). For the calculation, the radii of both CdTe NPs and organic NPs were selected as 1.75 nm. If we take 5 nm for NP-to-peptide distance and 3 nm for the size of Aβ aggregate, the value of $vdW_{CdTe\text{-}A\beta}$ and $vdW_{organic\text{-}A\beta}$ were evaluated as 2.8×10^{-3} k_BT (~ 1.7×10^{-3} kcal/mol) and 8.0×10^{-4} k_BT (~ 4.7×10^{-4} kcal/mol), respectively. While the vdW interaction is weak but it is effective short-range interaction and can effectively compete against Coulombic repulsion, particularly for nanostructured materials.[7]

UV-Vis and Fluorescence of CdTe NPs

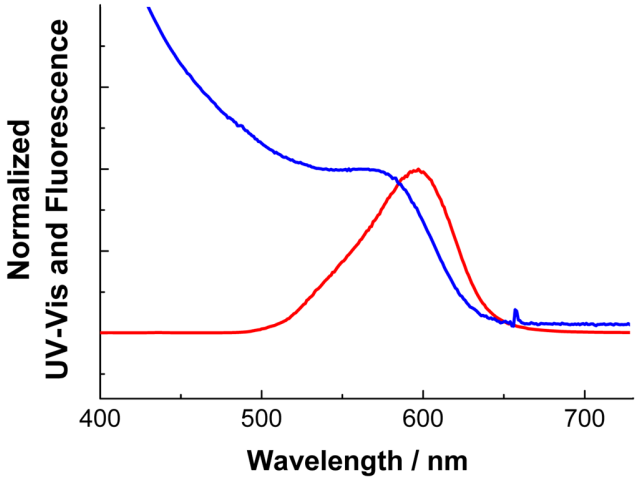

Figure S4. Normalized UV-Vis absorbance (blue line) and fluorescence (red line) of CdTe NPs.

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