Supporting Information for

Conformation-Reconstructed Multivalent Antibody Mimic for Amplified Mitigation of Human Islet Amyloid Polypeptide Amyloidogenesis

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Figure S1. A) The size distribution of AuNPs, PEG@Au, SPEP@Au and SPEPS@Au evaluated by DLS. B) TEM image of the PEG@Au. C) TEM image of the SPEP@Au. D) TEM image of the SPEPS@Au. Scale bar: 200 nm.
Figure S2. Absorbance spectra of IAPP in the presence of AuNPs-based species with a molar ratio of IAPP:PEP 10:1. The spectra were recorded every 30 min for a total of 600 min. (A) IAPP with PEG@Au. (B) IAPP with SPEP@Au. (C) IAPP with SPEPS@Au.
Figure S3. The dynamic binding curves for IAPP interacting with PEG@Au, SPEP@Au and SPEPS@Au monitored at the resonant wavelength of 590 nm. IAPP concentration in all experiments: 42.0 μM.
Figure S4. MD simulation results (top view). (A) The refined binding pattern between SPEP@Au (green) and IAPP (red) with IAPP17-22 fragment shown in blue. (B) The refined binding pattern between SPEPS@Au (green) and IAPP (red) with IAPP17-22 fragment shown in blue.
Figure S5. The effects of SPEP/SPEPS on IAPP amyloidogenesis monitored by ThT assays and TEM imaging. (A) IAPP amyloidogenesis kinetics in the absence and presence of SPEP/SPEPS monitored by ThT assays with a molar ratio of IAPP:PEP 10:1. IAPP concentration in all experiments: 8 μM. (B-D) TEM images of samples collected at the end of kinetics studies. (B) IAPP alone. (C) IAPP with SPEP. (D) IAPP with SPEPS. Scale bar: 200 nm.
Figure S6. Characterization of SPEP@Au and SPEPS@Au with different ppN values (25 and 100). (A) The size distribution of SPEP@Au and SPEPS@Au with ppN values of 25 and 100 evaluated by DLS. (B) Absorbance spectra of SPEP@Au and SPEPS@Au with ppN values of 25 and 100. C) Zeta potentials of SPEP@Au and SPEPS@Au with ppN values of 25 and 100.
Figure S7. Inhibitory effects of AuNPs-based species with different ppN values on IAPP amyloidogenesis monitored by ThT fluorescence and TEM. (A) The kinetics of IAPP amyloidogenesis in the absence and presence of PEG@Au, SPEP@Au and SPEPS@Au monitored by ThT assays. The peptide density for SPEP@Au and SPEPS@Au was 25 ppN. (B) The kinetics of IAPP amyloidogenesis in the absence and presence of PEG@Au, SPEP@Au and SPEPS@Au monitored by ThT assays. The peptide density for SPEP@Au and SPEPS@Au was 100 ppN. The concentrations of IAPP and PEP were 8 μM and 0.8 μM respectively. (C-E) TEM images of samples collected at the end of ThT assays for IAPP in the presence of AuNPs-based species with ppN value of 25. (C) IAPP with PEG@Au. (D) IAPP with SPEP@Au. (E) IAPP with SPEPS@Au. (F-H) TEM images of samples collected at the end of ThT assays for IAPP in the presence of AuNPs-based species with ppN value of 100. (F) IAPP with PEG@Au. (G) IAPP with SPEP@Au. (H) IAPP with SPEPS@Au. Scale bar: 200 nm.
Figure S8. ROS generation induced by PEG@Au, SPEP@Au and SPEPS@Au, determined by measuring the DCF fluorescence intensity. $\lambda_{\text{ex}} = 485$ nm; $\lambda_{\text{em}} = 525$ nm.

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**Figure S9.** The stability of multivalent antibody mimic SPEPS@Au. (A) Absorbance spectra of SPEPS@Au that place for 7 d at 4 °C and when kept at 4 °C for 7 d or 90 °C for 10 min. (B) DLS evaluation of the size distribution of SPEPS@Au when kept at 4 °C for 7 d or 90 °C for 10 min.
Figure S10. (A) ThT-monitored kinetics of IAPP amyloidogenesis in the absence and presence of SPEPS@Au when kept at 4 °C for 7 d or 90 °C for 10 min. The molar ratio of IAPP:PEP was 10:1. IAPP concentration in all experiments: 8 μM. (B-D) TEM images of samples collected at the end of ThT assays. (B) IAPP alone. (C) IAPP with SPEPS@Au that kept at 4 °C for 7 d. (D) IAPP with SPEPS@Au that kept at 90 °C for 10 min. Scale bar: 200 nm.