SUPPORTING INFORMATION

The Ability of Rodent Islet Amyloid Polypeptide to Inhibit Amyloid Formation by Human Islet Amyloid Polypeptide Has Important Implications For the Mechanism of Amyloid Formation and the Design of Inhibitors.

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Figure S1: Sedimentation equilibrium studies of rat IAPP. The sample contained 30 μM rat IAPP in 20 mM Tris-HCl buffer solution at pH 7.4 and 25°C. The rotor speed was 48,000 rpm. The observed molecular mass was 4102.0, determined from a single-species fit; the expected mass is 3921.3. A plot of the residuals is shown below the data.

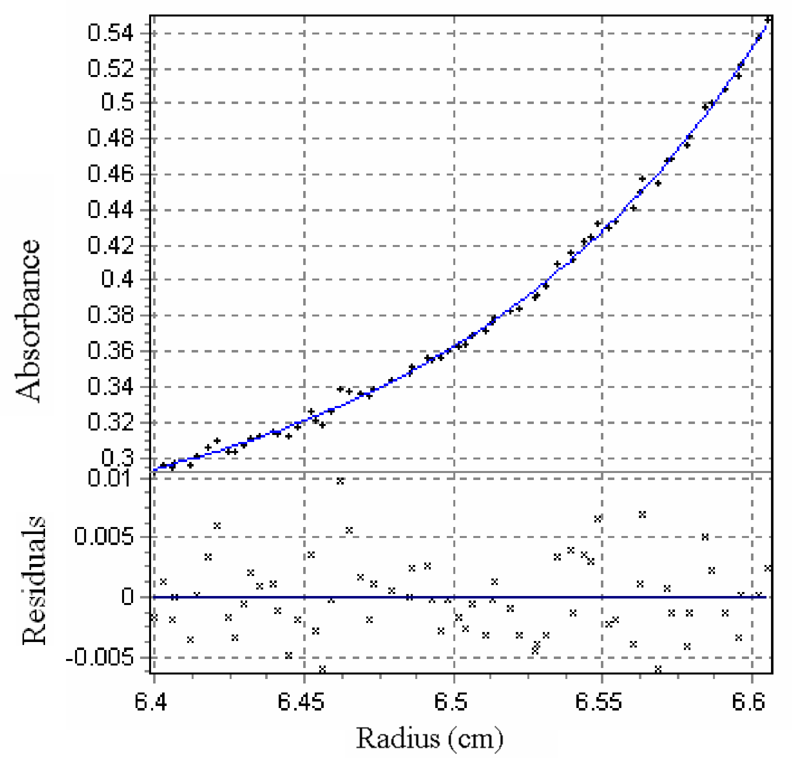


Figure S2: Plots of the derivative of the thioflavin-T fluorescence (F), vs time, dF(t)/dt, used to calculate T_{50} and the maximum rate. Panel B is an expansion of the first 5000s of panel A. The same color coding is used as employed in Figure 2.

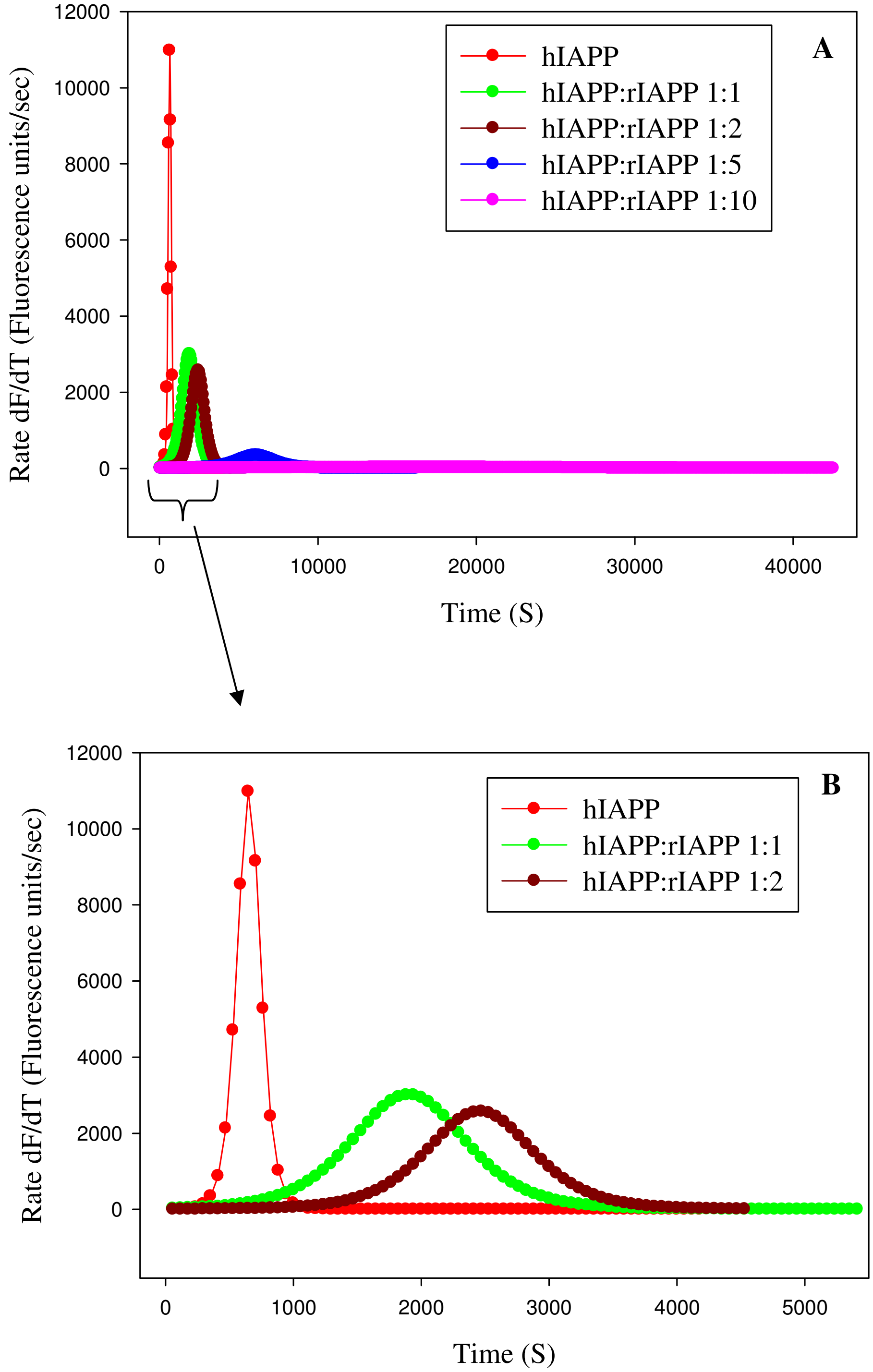


Figure S3: CD experiments provide direct evidence for an interaction between human and rat IAPP. (A) Experimental CD spectra of human IAPP (black) and rat IAPP (red) collected at the end of the kinetic experiments shown in Figure 2. (B) The experimental CD spectrum of a 1:1 mixture of rat and human IAPP collected at the end of the kinetic experiments (black) is compared to the spectrum expected if the peptides did not interact (red). The calculated spectrum was generated by the numerical sum of the two spectra shown in panel A. (C) The experimental CD spectrum of a 2:1 mixture of rat and human IAPP collected at the end of the kinetic experiments (black) is compared to the spectrum expected if the peptides did not interact (red). (D) The experimental CD spectrum of a 5:1 mixture of rat and human IAPP collected at the end of the kinetic experiments (black) is compared to the spectrum expected if the peptides did not interact (red). The calculated spectra in panels C and D were generated by the weighted numerical sum of the spectra shown in panel A.

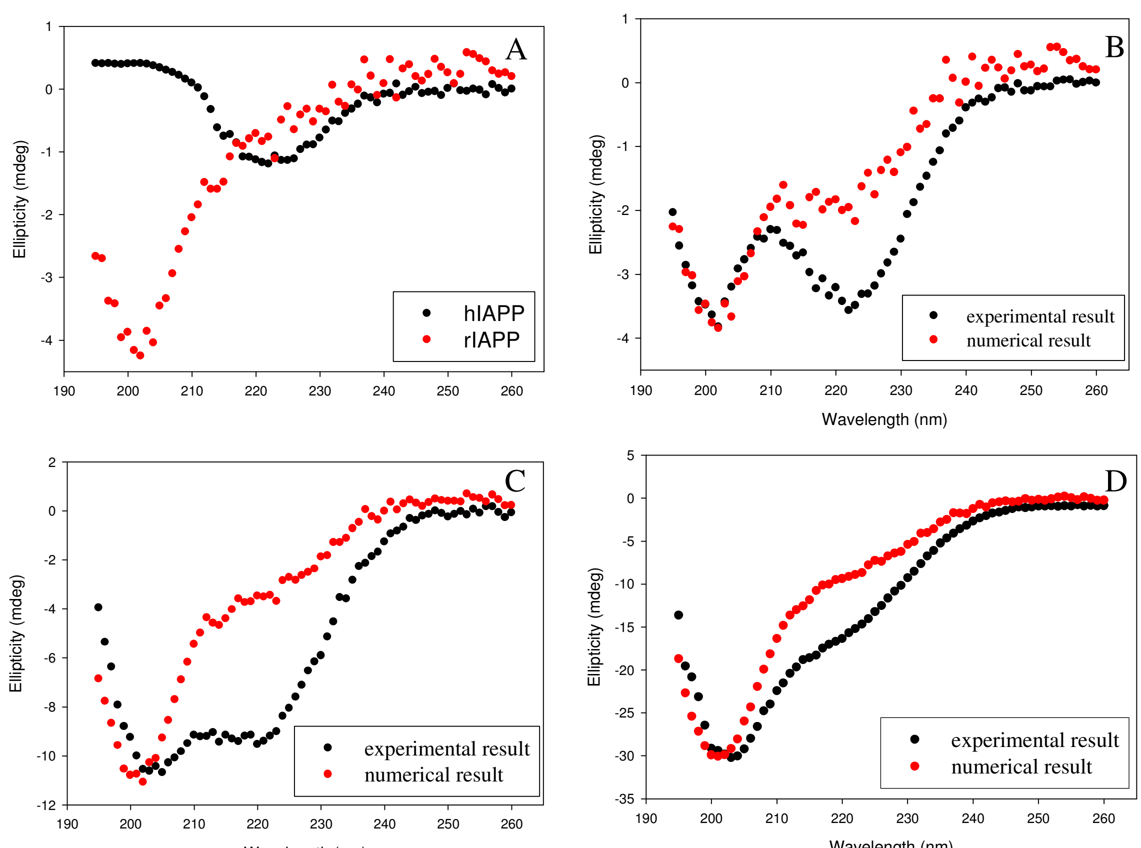


Figure S4: Gel filtration confirms that the A13P rat IAPP and F15D rat IAPP mutants are monomeric. Samples were injected at 160 μM peptide into a superdex 75 10/300 GL column in 20 mM Tris-HCl pH 7.4 buffer. Wild type rat IAPP, which is known to be monomeric, was used as a standard. Each mutant elutes with the same retention time as wild type rat IAPP. (A) Red, A13P-rat IAPP; black, rat IAPP. (B) Blue, F15D-rat IAPP; black, rat IAPP.

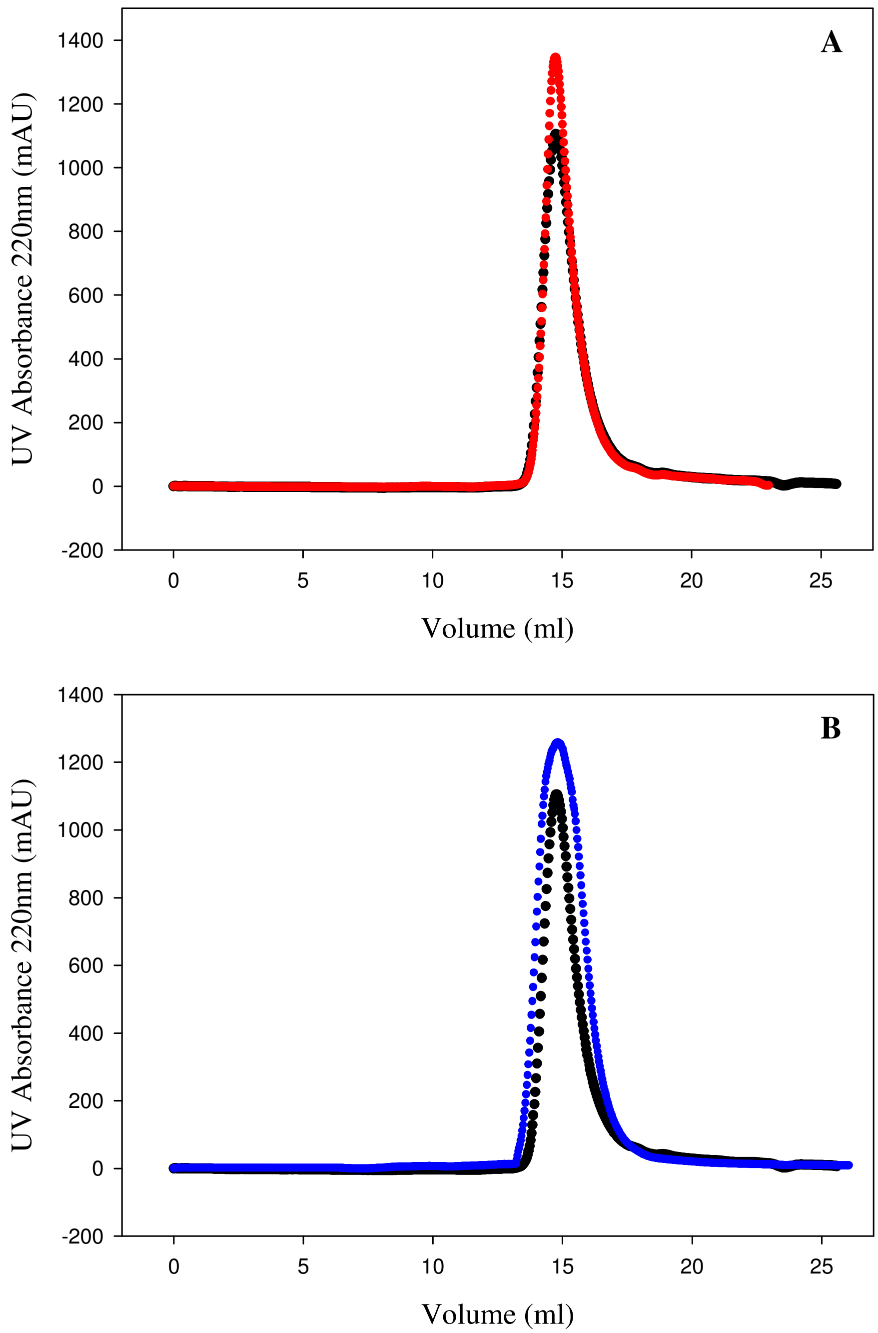
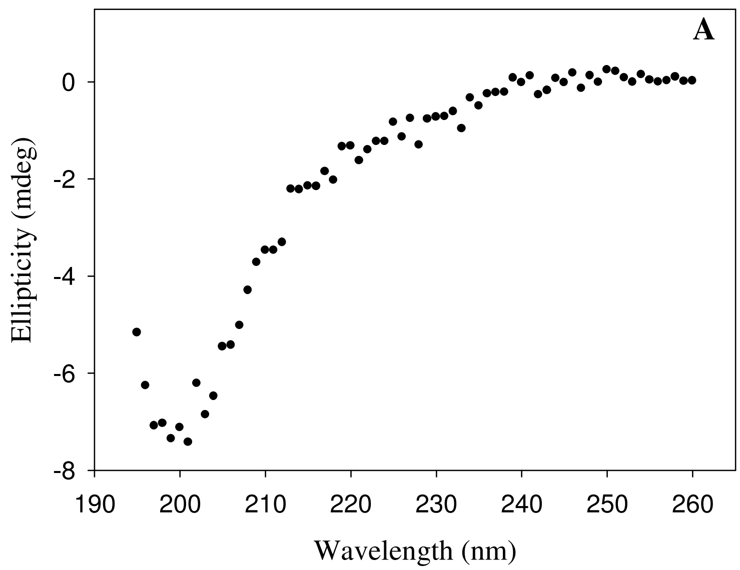


Figure S5: CD spectra of the A13P and F15D mutants of rat IAPP. Spectra were recorded from aliquots removed at the end of the kinetic runs shown in Figure 6 and Figure 7 and contained 16 μM peptide, 2% HFIP, 25 μM thioflavin-T, 20 mM Tris-HCl at pH 7.4. The samples were incubated for 6000 seconds with constant stirring, a time which larger than that required for pure human IAPP or mixtures of human IAPP with the mutants to form amyloid. (A) A13P rat IAPP. (B) F15D rat IAPP.



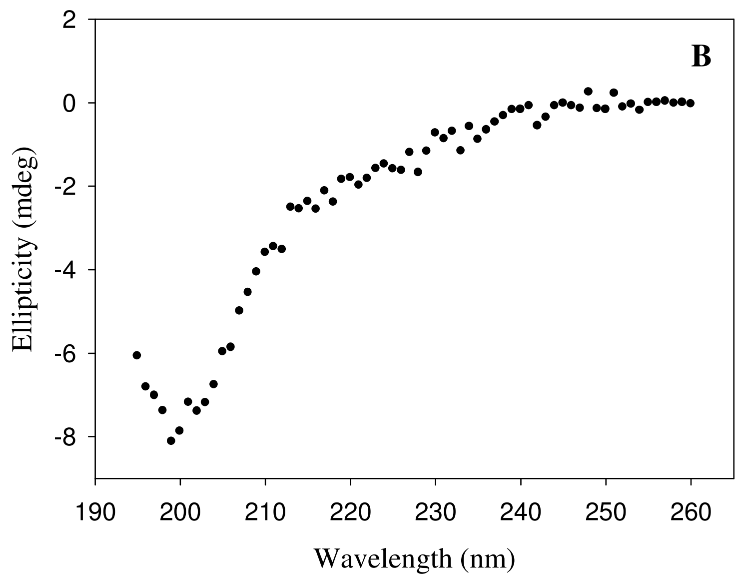


Figure S6: Predicted % helicity vs residue as calculated using the AGADIR algorithm of Serrano and coworkers (http://agadir.crg.es/protected/correctlogin.jsp).Calculations assumed a linear sequence (no disulfide), pH 7.4, 20 mM ionic strength. Black, rat IAPP; Blue, F15D rat IAPP; Red, A13P rat IAPP.