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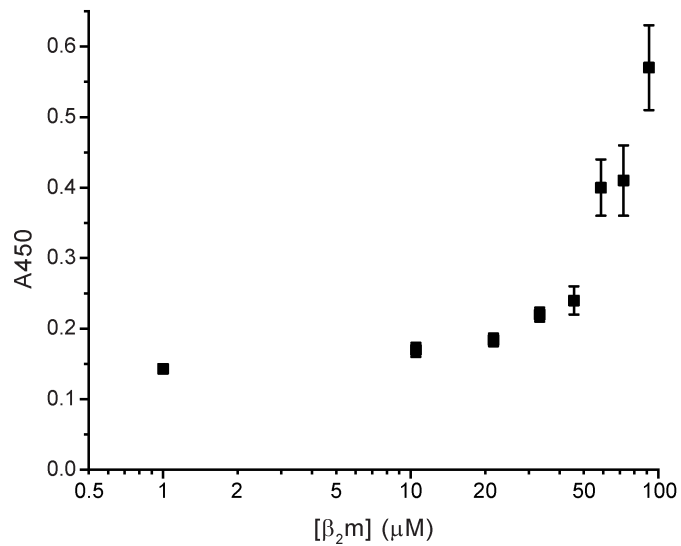
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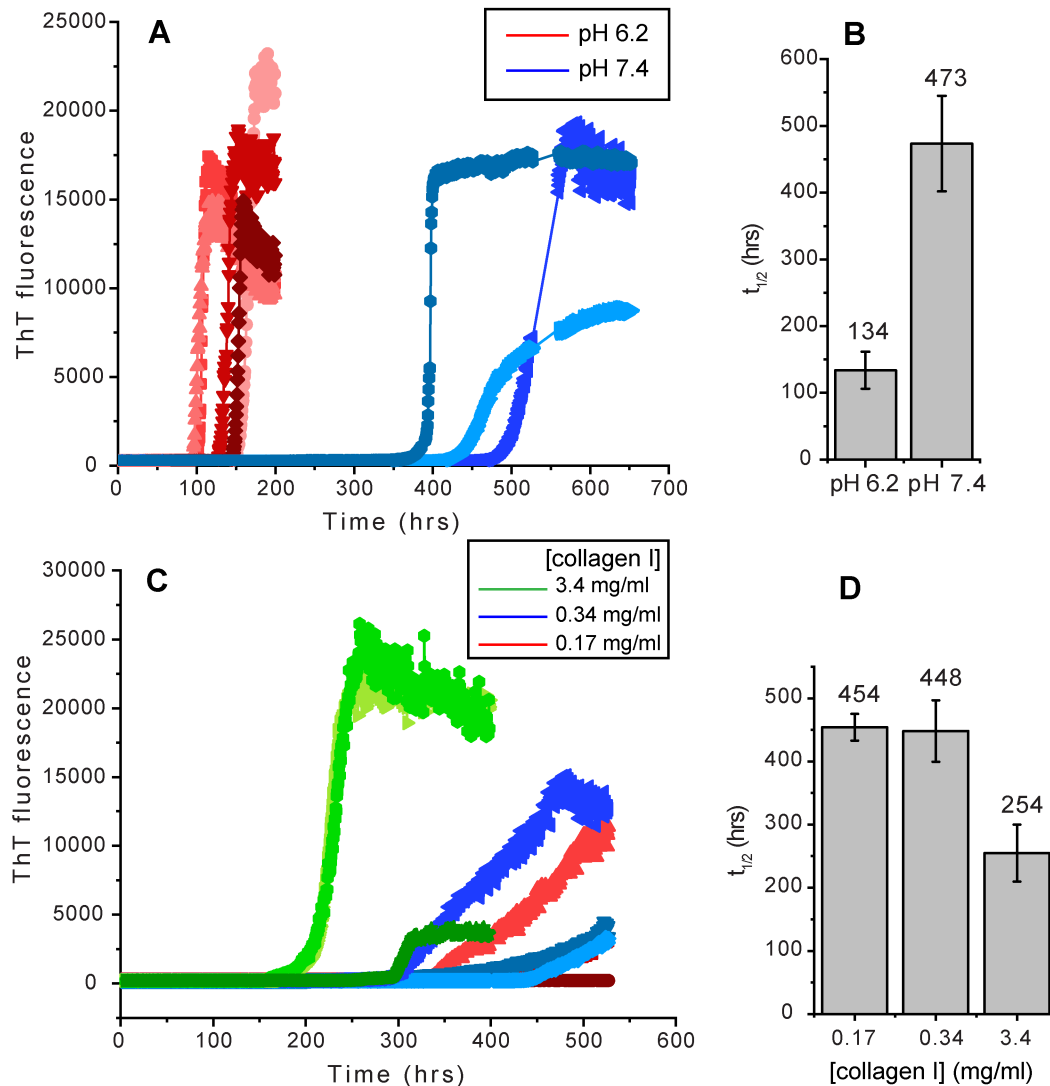
# Collagen I weakly interacts with the $\beta$ -sheets of $\beta_2$ -microglobulin and enhances conformational exchange to induce amyloid formation

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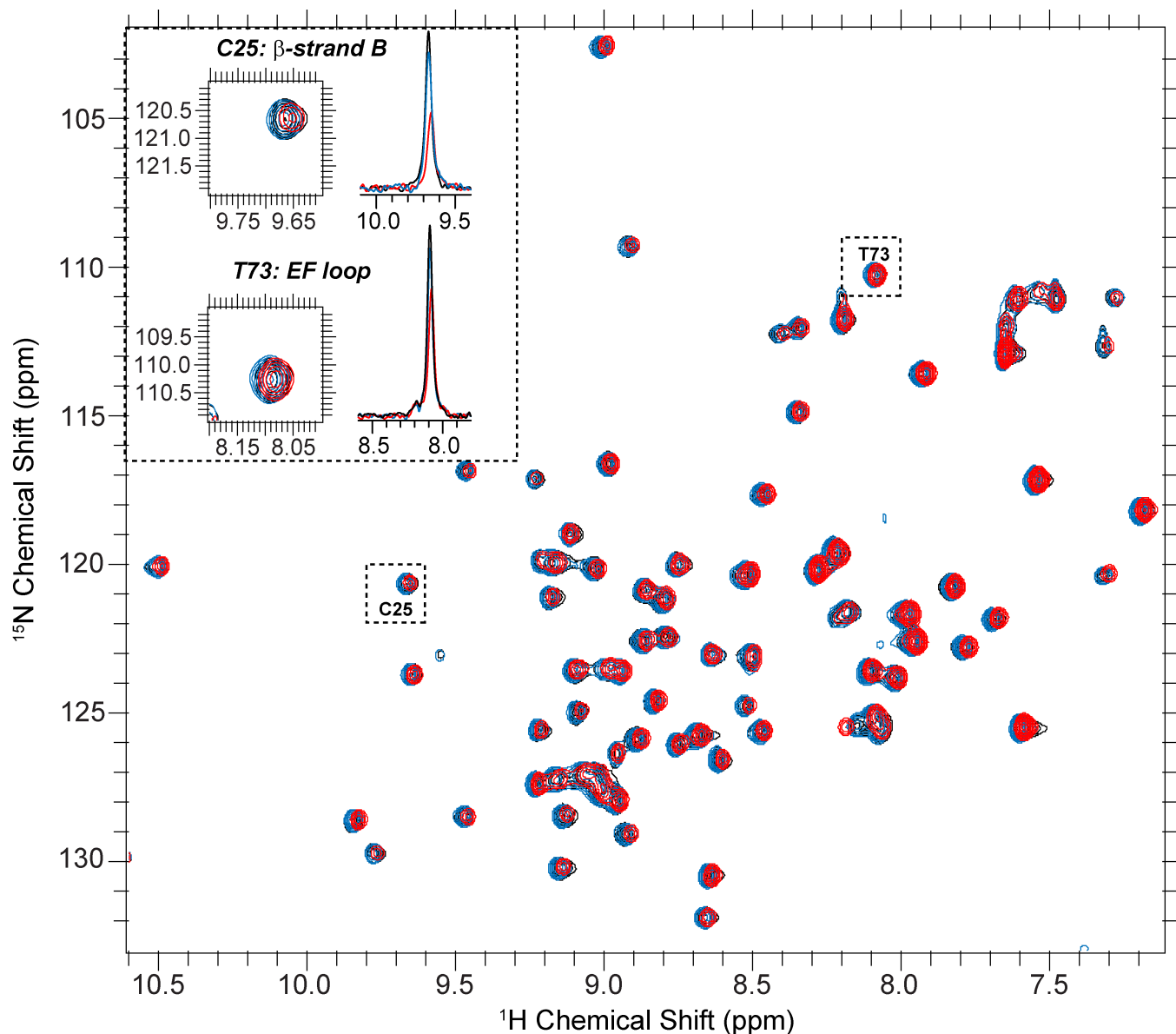
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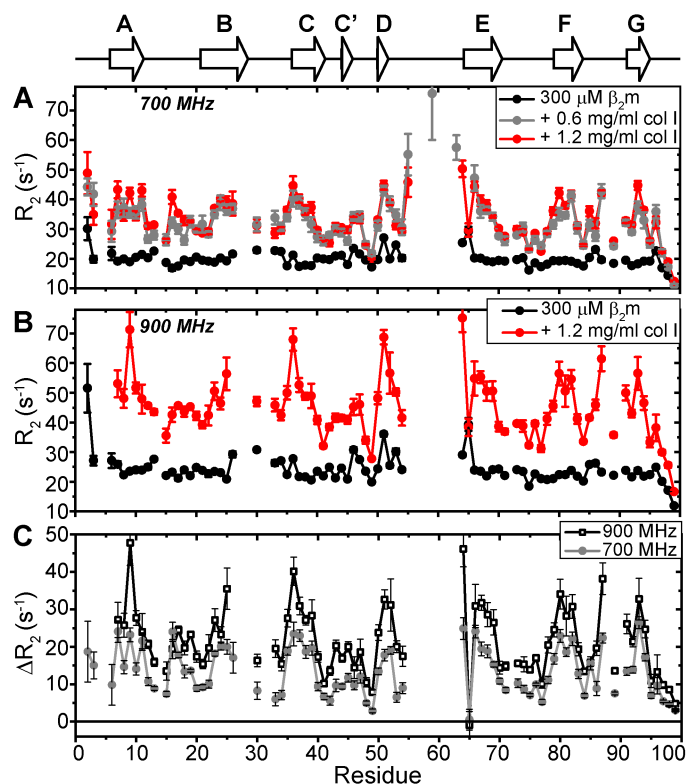
**Figure S1. Weak  $\beta_2m$ -collagen I binding as assessed by ELISA.** Dose-dependent binding of varying concentrations of  $\beta_2m$  (1–100  $\mu M$ ) to immobilized collagen I at pH 7.4. The x-axis is plotted on a logarithmic scale. Each point is the average absorbance at 450 nm of triplicates within the same plate. The error bars represent the standard deviation of the triplicates.



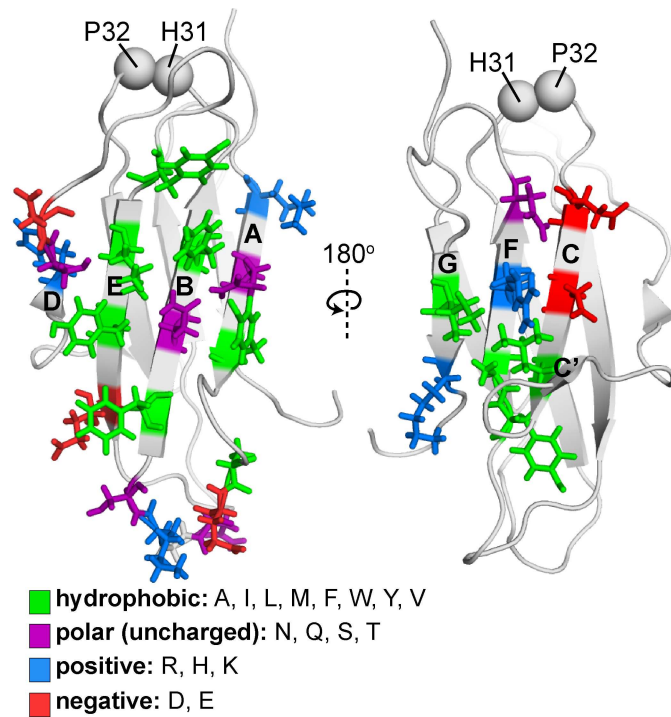
**Figure S2. Collagen I-induced amyloid formation of  $\beta_2m$  observed by ThT fluorescence.** A) ThT fluorescence curves of 85  $\mu M$   $\beta_2m$  with 3.4 mg/ml collagen I in 10 mM sodium phosphate buffer pH 6.2 (red shades) or pH 7.4 (blue shades). The pH 7.4 data are the same data presented in Figure 1 in the main text. Data were acquired at 37  $^{\circ}C$  with shaking (600 rpm). B) Average half-times ( $t_{50}$  values) of  $\beta_2m$  amyloid formation in the presence of 3.4 mg/ml collagen I at pH 6.2 or pH 7.4 calculated from the ThT fluorescence curves in panel A. Error bars represent the standard deviation of  $t_{50}$  values calculated from the multiple curves in the same condition. The mean  $t_{50}$  value (hrs) is given above each bar. C) ThT fluorescence curves of 85  $\mu M$   $\beta_2m$  in the presence of collagen I at different concentrations (green shades- 3.4 mg/ml, blue shades- 0.34 mg/ml, red shades- 0.17 mg/ml) in 10 mM sodium phosphate buffer, pH 6.2. D) Average  $t_{50}$  value of  $\beta_2m$  amyloid formation in the presence of different concentrations of collagen I at pH 6.2 calculated from the ThT fluorescence curves in panel C. Error bars represent the standard deviation of  $t_{50}$  value calculated from the multiple curves in the same condition. The mean  $t_{50}$  value (hrs) is given above each bar.



**Figure S3. Minimal chemical shift perturbation with residue-specific intensity losses observed by titration of collagen I into  $\beta_2m$ .**  $^1H$ - $^{15}N$ -HSQC spectra of 300  $\mu M$   $\beta_2m$  in TBS, pH 7.4 containing 0.5 mg/ml casein in the absence (black) or presence of different concentrations of collagen I (blue- 0.12 mg/ml collagen I and red- 1.2 mg/ml collagen I). The inset shows a zoom-in on the 2D contours and the extracted  $^1H$  1D projections of a residue that has a higher degree of peak intensity loss (Cys 25,  $I/I_0 = 0.48$ ) and one that has a low level of intensity loss (Thr 73,  $I/I_0 = 0.76$ ) upon addition of collagen I. Experiments were conducted in 10%  $D_2O$  at 700 MHz  $^1H$  Larmor frequency and 10°C.



**Figure S4. Perturbation of  $\beta_2m$   $^{15}N$ - $R_2$  values at different magnetic field strengths.** A) Residue-specific  $^{15}N$ - $R_2$  measurements at 700 MHz  $^1H$  Larmor frequency of 300  $\mu M$   $\beta_2m$  in the absence (black) or presence of 0.6 mg/ml (gray) or 1.2 mg/ml (red) collagen I in TBS, pH 7.4 containing 0.5 mg/ml casein.  $^{15}N$ - $R_2$  data in the absence (black) or presence of 1.2 mg/ml collagen I (red) are replotted from Figure 2B in the main text. B)  $^{15}N$ - $R_2$  measurements at 900 MHz  $^1H$  Larmor frequency of 300  $\mu M$   $\beta_2m$  in the absence (black) or presence (red) of 1.2 mg/ml collagen I in TBS, pH 7.4 containing 0.5 mg/ml casein. C) Residue-specific  $^{15}N$ - $\Delta R_2$ s at 700 MHz (gray) or 900 MHz (black), taken as the difference in  $^{15}N$ - $R_2$  of  $\beta_2m$  in the absence or presence of 1.2 mg/ml collagen I. All experiments were conducted in 10% D<sub>2</sub>O and 10°C. All error bars are propagated from the fitting errors.



**Figure S5. Amino acid composition of the  $\beta_2m$  interface for collagen I interactions.** Amino acids determined to be at the  $\beta_2m$ -collagen I interface by  $^{15}N$ -DEST and that have side-chains oriented toward the interaction surface are shown in stick representation and colored by amino acid type (hydrophobic= green; polar, uncharged= purple; positive charge= blue; negative charge= red). His 31 and Pro 32 are shown as spheres. Both  $\beta_2m$   $\beta$ -sheets are composed of a mixture of hydrophobic and hydrophilic amino acids, with the ABED  $\beta$ -sheet displaying several aromatic rings. Structural models are based on PDB: 2XKS<sup>1</sup>.

## REFERENCES

1. Eichner, T.; Kalverda, A. P.; Thompson, G. S.; Homans, S. W.; Radford, S. E., Conformational conversion during amyloid formation at atomic resolution. *Mol Cell* **2011**, *41*, 161-72.