Figure S7.1: AFM images of the supernatant of a BI amyloid fibril solution after ultracentrifugation at 100,000 X g for 1 hour. (A) A 10 µm area of a fibril including a height trace that shows that the short fibrils present in the image are approximately 3nm thick. (B) Shows a 20 µm AFM image of the ultracentrifugation supernatant. Few short fibrils and some disordered aggregates are present in the supernatant after ultracentrifugation. All the long BI fibrils present in Figure 51 have been effectively removed by ultracentrifugation leaving only short fibril fragments, small aggregates and soluble protein species in the supernatant. These images show that the ultracentrifugation protocol is effective at removing almost all of the fibrils present in solution.
Figure S8.1: Figure showing gel formation observed when 30mg/ml of HEWL was incubated at 65°C at 550rpm stirring speed. The figure shows the distribution of the gel and liquid phases due to the heterogeneous shearing in the magnetic stirring quartz cell.
Figure S8.2: Graphs showing the CD spectra at various temperatures for the denaturation (A) and renaturation (B) of HEWL. Major changes in the CD spectra are observed between 50 and 55°C.
Figure S8.3: Mean Residue Ellipticity of CD spectra at various wavelengths of the renaturation of HEWL at various temperatures. The figure shows that a major change in the alpha and beta secondary structure occurs between 40 and 65°C.

Figure S8.4: Mean Residue Ellipticity of CD spectra at various wavelengths of the denaturation of HEWL at various temperatures. The figure shows that a major change in the alpha and beta secondary structure occurs between 35 and 60°C.
Figure S8.5: Figure showing the CD values of HEWL in millidegrees at 265nm at different temperatures. The figure indicates a gradual loss of tertiary protein structure through the experiment. The loss of tertiary structure of the HEWL is more pronounced beyond 50°C.

Figure S8.6: Figure showing two examples of fitting the first order kinetic equation 7 using two fluorescence kinetic data sets obtained for 70°C (red squares, black line fitting equation) and 60°C (blue crosses, green dashed line fit). The graph shows that the equation has a very good fit with the kinetics data after the maximum rate of increase in fluorescence intensity (at about 1.5hrs) is reached.
Figure S8.7: Figure showing the differences between the ThT fluorescence of Aß incubated at 37°C with (solid black line) and without (dashed red line) inverting the cell at 5 minute intervals. Figures show the effects of extensive flocculation of the Aß fibrils on the resulting fluorescence signal if the flocs are not disrupted by the shaking protocol. The Aß sample grown without shaking was agitated at approximately 8 hours to break up the amyloid flocs that were compacting at the surface of the solution at the time point indicated on the figure to observe the effects of breaking up the flocs on the fluorescence signal. There appears no change after agitation and the flocs remain dispersed.

Figure S8.8: Figure showing the intrinsic fluorescence of 5 duplicate kinetic runs of HEWL that were used to plot the ThT trace in Figure 36, showing the variation in fluorescence intensity observed. It can be seen that there is significant variation in the intrinsic fluorescence values of HEWL between the runs, resulting in the very large standard deviation observed. However, the time intervals where the decrease in fluorescence intensity occurs remain similar between runs; hence the trends observed in Figure 36 are still valid despite the large standard deviation observed.
Figure S9.1: ThT fluorescence intensity over time for 2mg/ml GA incubated with 50uM ThT in 0.1% HCl. After 40 hours the ThT fluorescence signal only decreases by 0.2 A.U and this is believed to be due to the decrease in light scattering of the solution as seen in figure S2.2. Graph shows minimal change and minimal contribution to the ThT fluorescence intensity due to GA on ThT.

Figure S9.2: Light scattering intensity of GA incubated with ThT in 0.1% HCl (pH 1.5) over 40 hours. Light scattering measurement was taken at an excitation wavelength of 600nm with an emission wavelength of 605nm. Light scattering decreases over extended incubation showing that the particle size of the GA decreases due to extended incubation in acidic environments. This is most likely due to hydrolysis of the carbohydrate groups of the AG and AGP components of GA.
Figure S9.3: GPC light scattering traces of GA incubated in acidic conditions (2% HCl) before incubation, after 3 hours and after 24 hours. Traces show a decrease in the light scattering value as well as a right shift in the light scattering peak. This indicates a decrease in particle size that is most probably due to acid hydrolysis of the carbohydrate groups of the GA.

Figure S9.4: GPC UV absorbance at 206nm of GA incubated in acidic conditions (2% HCl) before incubation, after 3 hours and after 24 hours. Traces show a slight right shift in the UV absorbance peak of the GA on incubation with acid. This indicates a small decrease in the size of the proteinaceous components of GA (i.e. AGP and GP) due to hydrolysis of part of the sugar side-chains; however the protein backbone remains largely intact in acid incubation under the conditions used.
Figure S9.5: GPC RI detector value traces of GA incubated in acidic conditions (2% HCl) before incubation, after 3 hours and after 24 hours. Traces show little change in the RI signal over the course of the incubation with the acid, indicating that the overall concentration of the macromolecules remains relatively constant. The large spike near the 45 minute mark is due to the solvent front.

Figure S9.6: A sample of seyal gum crystals used showing different coloured crystals in a heterogeneous mixture.
Figure S9.7: Absorbance spectra of pectin, GA and AGP. Graphs show that GA and AGP have very low absorbance at 280nm as compared to absorbance at 214nm. Pectin does show significant absorbance at 280nm which suggests presence of protein sample.
**Figure S10.1:** Synthesis of FA-diacid via ROMP (Ring opening metathesis polymerisation)\textsuperscript{242}, where X represents a CH group but can be replaced with other groups such as O to create other variants such as Oxy-FA. First step involves the polymerization of the monomer 5-Norbonene-2, 3-dicarboxylic anhydride using Grubbs 2\textsuperscript{nd} generation Catalyst in THF (Tetrahydrofuran). Second step involved hydrolysis of the anhydride and the final step involves acidification with HCl to give the acidic polymer. Synthesis was performed by the polymer science group of the University of Melbourne.

**Figure S10.2:** Absorbance spectra of 0.5mg/ml of FA-diacid (2 kDa). FA-diacid shows a strong absorbance at 280, 250 and 214nm that can interfere with calculations from absorbance readings obtained from ultracentrifugation.
**Figure S11.1:** Synthesis of PNGA from 5-Norbene-2-carbonitrile via ROMP. First step used LiAlH₄ (Lithium aluminum hydride) to reduce the nitrile group to an amine group. The second step reacts the amine with gluconolactone in boiling methanol to create an open sugar or poly-ol functional group. Finally, polymerization was conducted at room temperature in EVE (ethyl vinyl ether) at room temperature using Grubbs 1st generation catalyst in a mixture of methanol, water and DCM (Dichloromethane) to obtain PNGA. Synthesis was performed by the polymer science group of the University of Melbourne.

**Figure S11.2:** Synthesis of PNGE from Norbonene-2-carboxylic acid via ROMP. The first step involves reacting of the carboxylic acid with a protected glucose in DCC (Dicyclohexylcarbodiimide) to attach the glucose side chain via a decoupling reaction. The protected glucose was then deprotonated with TFA (Tetrahydrofuran). The last step in the reaction is polymerization of the product at room temperature in EVE using the using Grubbs 1st generation catalyst in a mixture of methanol, water and DCM (Dichloromethane) to obtain PNGA. Synthesis was performed by the polymer science group of the University of Melbourne.
Figure S11.3: Absorbance spectra of PNGA and PNGE showing relatively low absorbance at 280nm but a noticeable absorbance peak at ~250nm. Samples were dissolved in 0.1% HCL.
S12.1: Synthesis of glycosylated poly(valine-r-lysine) (ABL121)

Valine (145 mg, 1.24 mmol), TFA-lysine (299 mg, 1.24 mmol) and imidazole (170 mg, 2.50 mmol) were dissolved in MilliQ water (24.8 mL) in a 100 mL RB (round bottom) flask. Carbonyl diimidazole (806 mg, 4.97 mmol) was added, the flask was sealed and the mixture was stirred at room temperature for 12 h. The reaction mixture was transferred to a 500 mL RB flask, diluted with isopropanol (100 mL) and concentrated in vacuo. The residue was redissolved in methanol:isopropanol:TFA (2:4:2, 8 mL) and precipitated into diethyl ether (80 mL). The precipitate was collected via centrifugation, redissolved in methanol:isopropanol:TFA (4:2:1, 7 mL) and precipitated into diethyl ether (80 mL). The precipitate was collected via centrifugation and dried in vacuo (0.1 mbar, 50 °C) to afford poly(valine-r-(TFA-lysine)) as a white solid. The solid was suspended in methanol:water (19:1, 30 mL) and heated to 75 °C. K₂CO₃ (1 g) was added and the mixture was heated at 75 °C for 24 h to afford a clear solution. After cooling to room temperature, 15 mL of this solution was diluted with methanol (25 mL). Gluconolactone (800 mg, 4.50 mmol) was added and the mixture was heated at 75 °C for 24 h. The mixture was cooled to room temperature, concentrated in vacuo and the residue was dialysed (MWCO = 500-1000 Da) against water for 5 days. The dialysed solution was concentrated in vacuo to ca. 2 mL in volume and precipitated into acetone (40 mL). The precipitate was isolated via centrifugation and dried in vacuo (0.1 mbar, 45 °C, 12h) to afford glycosylated poly(valine-r-lysine) as a white solid (35 mg). Synthesis data and method obtained from Dr Anton Blencowe.
**Figure S12.2:** NMR spectrum of ABL 121. Peaks labeled in the figure are: $^1$H NMR (400 MHz, $D_2$O) $\delta_H$ 0.89-1.05 (m, CH(CH$_3$)$_2$), 1.40 (br s, CH$_2$), 1.57 (br s, CH$_2$), 1.78 (br s, CH$_3$), 2.08 (br s, CH(CH$_3$)$_2$), 3.26 (br s, CH$_2$N), 3.66-3.69 (m, CHOH), 3.76 (br s, 2CHOH), 3.82-3.85 (m, CHHOH), 4.10 (br s, CHN & CHHOH), 4.32 (br s, CHN & CHOH) ppm.

**Figure S12.3:** Absorbance spectra of GHP and P-GHP showing minimal absorbance at 280nm but significant absorbance at 214nm. GHP was dissolved in 0.1% HCl while P-GHP was dissolved in 0.1% HCl with 25μM of ThT and was later used for CD measurements. The absorbance contribution of 25μM ThT was subtracted from the raw values of the P-GHP before plotting using a previously obtained absorbance spectra of ThT.
Figure S12.4: Figure showing the relationship between bound ThT concentration in μM and estimated % conversion to amyloid calculated from ultracentrifugation. NA refers to points from amyloid kinetic experiments with no additive. PNGA and PNGE for BI points were plotted using the estimated % conversion using method 2. Points are labelled with the additive that was incubated with the protein. Numbers before the additive name indicate the concentrations in mg/ml. Point labels without numbers had the inhibitors at 2 mg/ml except for the following points: 1) FA-diacid was at 1.25 μM, 2) GHP, PNGA and PNGE with HEWL were at 0.2 mg/ml, 3) GHP and P-GHP with BI were at 0.2mg/ml and 4) P-GHP with Aβ was at 0.5mg/ml. Also included is a rough line of best fit, however due to the large spread of values, it is unclear if all 3 proteins shared the same line of best fit. Notably the PNGE experiments tend to have a higher amount of bound ThT as compared to points with similar estimated fibril content, while FA-diacid tends to have a lower bound ThT for the % amyloid conversion.
Figure S12.5: Figure showing the relationship between plateau fluorescence and bound ThT concentration in μM calculated from ultracentrifugation. NA refers to points from amyloid kinetic experiments with no additive. Points are labelled with the additive that was incubated with the protein. Numbers before the additive name indicate the concentration in mg/ml. Point labels without numbers had the inhibitors at 2 mg/ml except for the following points: 1) FA-diacid was at 1.25 μM, 2) GHP, PNGA and PNGE with HEWL were at 0.2 mg/ml, 3) GHP and P-GHP with BI were at 0.2 mg/ml and 4) P-GHP with Aβ was at 0.5 mg/ml. Also included is a rough line of best fit, however due to the large spread of values it is unclear if all 3 proteins shared the same line of best fit. Notably the PNGE experiments tend to have a higher amount of bound ThT as compared to points with similar fluorescence value. Also it can be seen that the large fibrils in 2mg/ml GA and 2mg/ml AGP showed the unusually high fluorescence value as compared to the bound ThT value, and they are shown in this diagram as the two outliers.
Figure S12.6: Figure showing the relationship between fluorescence and estimated % conversion to amyloid calculated from ultracentrifugation. NA refers to points from amyloid kinetic experiments with no additive. PNGA and PNGE for BI points were plotted using the estimated % conversion using the simple method. Points are labelled with the additive that was incubated with the protein. Numbers before the additive name indicate the concentration in mg/ml. Point labels without numbers had the inhibitors at 2 mg/ml except for the following points: 1) FA-diacid was at 1.25 μM, 2) GHP, PNGA and PNGE with HEWL were at 0.2 mg/ml, 3) GHP and P-GHP with BI were at 0.2mg/ml and 4) P-GHP with Aβ was at 0.5 mg/ml. Also included is a rough line of best fit, however due to the large spread of values it cannot be determined if all 3 proteins share the same line of best fit. Notably the PNGE experiments tend to have a higher amount of bound ThT for the estimated fibril content, while FA-diacid has a lower bound ThT for % conversion. Also it can be seen that the large fibrils in 2mg/ml GA and 2mg/ml AGP showed unusually high fluorescence value as compared to the bound ThT value, and they appear in this diagram as the two outliers.

Appendix references

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Appendix

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