

Structural Studies of Amyloid-Forming Peptides from the Yeast Prion Sup35 Suggests Features of the Amyloid State

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Despite the importance of protein aggregates in prion and other amyloid diseases, little is known at the atomic level of the structure of amyloid. Sup35, a prion-like protein in yeast, forms fibrillar amyloid assemblies intrinsic to its prion function. We have identified several peptides from the N-terminal prion-determining domain of Sup35 that exhibit the amyloid properties of full-length Sup35, including cooperative kinetics of aggregation, fibril formation, binding of the dye Congo red, and the characteristic cross-beta X-ray pattern.

Microcrystals of these peptides also share the principal properties of the fibrillar amyloid, including a highly stable, beta-sheet rich structure and the binding of Congo red. Unfortunately, these materials will not grow single crystals of size sufficient for diffraction analysis.

The X-ray powder pattern of the microcrystals extend to resolutions as great as 0.9 Å resolution, and yield the unit cell dimensions of the well ordered structure. High resolution x-ray powder diffraction data can be indexed to a monoclinic unit cell of dimensions 23.41Å x 4.89Å x 21.18Å, $\beta = 103.86^\circ$ (See Figure.) These dimensions restrict possible atomic models of the crystalline peptides, and demonstrate that they form packed beta-sheets.

The intensities are being interpreted in terms of atomic models, which may illuminate the nature of the amyloid state and the action of prions.

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