TEMPERATURE DEPENDENT CHANGES IN STRUCTURE AND SEEDING POTENTIAL OF AMYLOID FIBRILS

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Amyloids are self-assembled and highly ordered peptide or protein aggregates, which are usually rich in beta-sheet structures. Their formation is linked to several neurodegenerative diseases, such as Alzheimer's, Parkinson's or prion diseases. Recently is has been shown that prolonged incubation may induce structural changes in amyloid fibrils [1][2].

Prion proteins (PrP) were incubated at 37 °C in a 2 M GuHCl, pH 6 buffer with a final concentration of 0.5 mg/ml for 3 days with constant sample rotation at 10 rpm. The generated fibril samples were additionally incubated at 60 °C for different amounts of time. Each sample was sonicated and their seeding potential, as well as Thioflavin T binding ability and fibril stability were tested at different denaturant concentrations.

PrP fibril incubation lead to an increased stability under higher denaturant concentrations, suggesting a change in their structure upon incubation at a higher temperature. There was also a noticeable difference in their ThT binding capacity, as incubation resulted in a sizable shift of ThT fluorescence emissions. Finally, the seeding potential was affected negatively at lower and positively at higher denaturant concentrations.

The results of PrP fibril incubation at an elevated temperature all point towards a restructurization into higher stability amyloid assemblies (Fig. 1), suggesting that temperature and time are an important factor not only during the initial aggregation of amyloid proteins, but also after the fibrils are already generated.

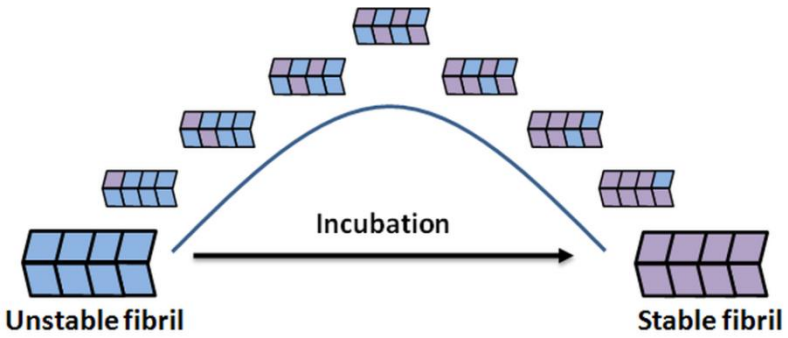

Fig. 1. Prion amyloid fibril restructurization into a higher stability assembly.

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[2] M N. J. Cobb, M. I. Apostol, S. Chen, V. Smirnovas, and W. K. Surewicz, "Conformational Stability of Mammalian Prion Protein Amyloid Fibrils Is Dictated by a Packing Polymorphism within the Core Region," *J. Biol. Chem.*, vol. 289, no. 5, pp. 2643–2650, Jan. 2014.