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Surface Mediated Self-Assembly of Amyloid Peptides[1]

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Amyloid fibrils have been considered as causative agents in many neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, type II diabetes and amyloidosis. Amyloid fibrils form when proteins or peptides misfold into one dimensional crystals of stacked beta-sheets. In solution, amyloid fibrils form through a nucleation and growth mechanism. The rate limiting nucleation step requires a critical concentration much larger than those measured in physiological conditions. As such the exact origins of the seeds or oligomers that result in the formation of fully mature fibrils in the body remain topic intense studies. It has been suggested that surfaces and interfaces can enhance the fibrillization rate. However, studies of the mechanism and kinetics of the surface-mediated fibrillization are technologically challenging due to the small size of the oligomer and protofibril species. Using smart sample preparation technique to dry the samples after various incubation times we are able to study the kinetics of fibril formation both in solution and in the vicinity of various surfaces using high-resolution atomic force microscopy. These studies elucidate the role of surfaces in catalyzing amyloid peptide formation through a nucleation-free process. The nucleation free self-assembly is rapid and requires much smaller concentrations of peptides or proteins. We show that this process resembles diffusion limited aggregation and is governed by the peptide adhesion rate, two -dimensional diffusion of the peptides on the surface, and preferential interactions between the peptides. These studies suggest an alternative pathway for amyloid formation may exist, which could lead to new criteria for disease prevention and alternative therapies.

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