SELF-ASSEMBLY, DYNAMICS, AND POLYMORPHISM OF hIAPP(20-29) AGGREGATES AT SOLID-LIQUID INTERFACES

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The misfolding and subsequent assembly of proteins and peptides into insoluble amyloid structures play important roles in the development of numerous diseases [1]. The dynamics of self-assembly and the morphology of the resulting aggregates critically depend on various environmental factors and especially on the presence of interfaces [2,3]. Here, we show in detail how the presence of surfaces with different physicochemical properties influences the assembly dynamics and especially the aggregate morphology of hIAPP(20-29) [4], an amyloidogenic fragment of the peptide hormone human islet amyloid polypeptide (hIAPP), which is involved in the development of type 2 diabetes. Time-lapse atomic force microscopy is employed to study the assembly dynamics of hIAPP(20-29) and the morphology of the resulting aggregates in bulk solution as well as at hydrophilic and hydrophobic model surfaces. We find that the presence of hydrophilic mica surfaces promotes fibrillation when compared with the assembly in bulk solution and results in a more pronounced polymorphism. Three fibrillar species are found to coexist on the mica surface, that is, straight, coiled, and ribbon-like fibrils, whereas only the straight and coiled fibrils are observed in bulk solution after comparable incubation times. In addition, the straight and coiled fibrils assembled at the mica surface have significantly different dimensions compared with those assembled in bulk solution. The three fibrillar species found on the mica surface most likely form independently by lateral association of arbitrary numbers of protofibrils with about 2 nm height. On hydrophobic hydrocarbon surfaces, fibrillation is retarded but not completely suppressed, in contrast to previous observations for full-length hIAPP(1-37). Our results show that peptide-surface interactions may induce diverse, peptide-specific alterations of amyloid assembly dynamics and fibrillar polymorphism. They may therefore contribute to a deeper understanding of the molecular processes that govern amyloid aggregation at different surfaces.

Keywords: Amyloid, Atomic Force Microscopy, Biointerfaces

References:


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