

MONITORING IMMUNOGLOBULIN LIGHT CHAIN AMYLOID FIBRIL FORMATION ON SURFACES USING ATOMIC FORCE MICROSCOPY

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Light chain (or AL) amyloidosis is characterized by the pathological deposition of insoluble fibrils of immunoglobulin light chain (LC) fragments in various tissues, blood vessels, and on basement membranes. In the present investigation, the in vitro assembly of a recombinant amyloidogenic LC variable domain, SMA, on various surfaces was monitored using atomic force microscopy (AFM). SMA forms fibrils on native mica at pH 5.0, conditions under which amorphous aggregates are predominantly formed in solution. Two types of fibril growth were observed: bi-directional assembly of sub-unit aggregates and elongation growth from preformed amorphous cores. No fibrils were observed on hydrophobic or positively charged modified mica surfaces, or at pH >7.0. Our studies show that SMA fibril formation is surface dependent. SMA presumably binds to negatively charged surfaces and this accelerates fibril formation. This suggests that fibrillation may be driven by interactions at the interface. Since AFM permits the direct observation of the growth of individual aggregates, it provides a significant advantage over conventional techniques based on an ensemble measurement.