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Review

The role of lipid–protein interactions in amyloid-type protein fibril formation

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Abstract

Structural transition of polypeptide chains into the β-sheet state followed by amyloid fibril formation is the key characteristic of a number of the so-called conformational diseases. The multistep process of protein fibrillization can be modulated by a variety of factors, in particular by lipid–protein interactions. A wealth of experimental evidence provides support to the notion that amyloid fibril assembly and the toxicity of pre-fibrillar aggregates are closely related and are both intimately membrane associated phenomena. The present review summarizes the principal factors responsible for the enhancement of fibril formation in a membrane environment, viz. (i) structural transformation of polypeptide chain into a partially folded conformation, (ii) increase of the local concentration of a protein upon its membrane binding, (iii) aggregation-favoring orientation of the bound protein, and (iv) variation in the depth of bilayer penetration affecting the nucleation propensity of the membrane associated protein. The molecular mechanisms of membrane-mediated protein fibrillization are discussed. Importantly, the toxicity of lipid-induced pre-fibrillar aggregates is likely to have presented a very strong negative selection pressure in the evolution of amino acid sequences.

Keywords: Protein–lipid interactions; Membrane-induced protein aggregation; Amyloid fibrils