CHAPTER 9

Non-amyloid structure of the Aβ(1−42) polypeptide in presence of a permanent chaperone

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Conceptual diagram which illustrates structural stabilization of a polypeptide in the presence of an external molecule. The biologically active form requires interaction with a scaffold − a cellular membrane, another protein or a suitable compound.

The structure of the Aβ(1−42) amyloid has been compared with its non-amyloid form, with particular focus on fragments identified as amyloid seeds. The presented results enable us to identify conformational changes involved in the amyloid transformation process.

Ever since the discovery of prions, the structure of amyloid aggregations and the mechanisms by which they emerge have puzzled molecular biologists [1,2].

Radical conformational rearrangements in the absence of mutations appear to contradict the prevalent view that the protein's 3D structure is fully encoded in the composition of its chain [3].

Particular attention has been accorded to proteins in which conformational rearrangements produce structures capable of unrestricted growth, resulting in fibrillar complexes [4]. This phenomenon is of great importance in biological research since amyloid fibrils cause a variety of pathological

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conditions in living organisms [5]. In particular, they may accumulate in brain tissue, leading to neurodegeneration [6].

The insolubility of amyloids greatly hampers analysis of their structural properties. In order to overcome these obstacles prior to invention of solid-state NMR [7] amyloidogenic peptides were complexed with other molecules, including other proteins, in order to ensure solubility [8–11].