The Presence and Potential Role of Tilted Peptides in Amyloidogenic Proteins

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Amyloidogenic proteins are of interest in the study of transconformational processes because they undergo a major conformational change. This change leads to amyloid fibril formation through the self-assembly of their misfolded form.

Amyloid fibrils are involved in several diseases such as Alzheimer's, Parkinson's or Creutzfeldt-Jakob disease. From a structural point of view, it is established that these fibrils have varying lengths at up to a few micrometers, they are unbranched, and the individual β strands are oriented perpendicular to the long axis of the fibril. The conformational changes induce an increase in the β content. However, little is known about the mechanisms of transconformation, the subsequent aggregation and the toxicity of these proteins. The study of these misfolded proteins, especially the study of their conformation, is difficult due to their tendency to aggregate in solution.

We found it interesting to study the potential role of tilted peptides in transconformational mechanisms because they possess several properties that may be involved in this process. They can adopt an α or β conformation, depending on the environment and when helical, they can destabilize the hydrophilic/hydrophobic interface of an organised system. They were notably found in the domain undergoing transconformation in the Aβ protein (Alzheimer's disease) and in PrP (prion diseases). They may have an important role in the first step of the transconformational process ; their destabilizing properties could also be involved in the toxicity of these proteins.