

Non-fibrillar amyloidogenic protein assemblies— Common cytotoxins underlying degenerative diseases

Farid Rahimi, editor

Deskripsi Lengkap: <https://lib.ui.ac.id/detail?id=20417827&lokasi=lokal>

Abstrak

Amyloid-forming proteins are implicated in over 30 human diseases. The proteins involved in each disease have unrelated sequences and dissimilar native structures, but they all undergo conformational alterations to form fibrillar polymers. The fibrillar assemblies accumulate progressively into disease-specific lesions in vivo. Substantial evidence suggests these lesions are the end state of aberrant protein folding whereas the actual disease-causing culprits likely are soluble, non-fibrillar assemblies preceding the aggregates. The non-fibrillar protein assemblies range from small, low-order oligomers to spherical, annular, and protofibrillar species. Oligomeric species are believed to mediate various pathogenic mechanisms that lead to cellular dysfunction, cytotoxicity, and cell loss, eventuating in disease-specific degeneration and systemic morbidity. The particular pathologies thus are determined by the afflicted cell types, organs, systems, and the proteins involved. Evidence suggests that the oligomeric species may share structural features and possibly common mechanisms of action. In many cases, the structure–function interrelationships amongst the various protein assemblies described in vitro are still elusive. Deciphering these intricate structure–function correlations will help understanding a complex array of pathogenic mechanisms, some of which may be common across different diseases albeit affecting different cell types and systems.