

Editorial

The Structural Basis of Amyloid Formation

Alzheimer's disease is clearly one of the most important human disorders of the 21st century. With the increasing life expectancy, the rapidly growing prevalence of this disease will obviously bear profound social and economical implications, in addition to the medical ones. Therefore, understanding the etiology of Alzheimer's disease is a challenging yet very important task, which will likely open new venues toward therapy. At the molecular level, such understanding should initiate with exploring the process of amyloid formation as a key for delineating the mechanistic basis of plaque formation and for developing new drugs.

This special issue of *Current Alzheimer Research* is, indeed devoted to the *Structural Basis of Amyloid Formation*. We were privileged to receive for this issue, reports of recent work from several of the world leaders in the field of amyloid formation. The studies presented in this issue include both theoretical and experimental work and cover novel notions and directions that will be applicable not only to Alzheimer's disease but also to many other amyloid-associated disorders, including Parkinson's disease, Type II diabetes, Prion diseases and many more.

Structural studies of biological phenomena are traditionally based on physical, chemical and computational research methods. It is the convergence of power of such methods which makes this issue so special. The special issue starts with the study of the activity of the β -amyloid oligomers at the synaptic level (Cerpa *et al.* on page 233-243). The authors of this article describe the role of the Wnt signaling pathway in the synaptic activity of amyloid oligomers and suggest the use of molecular chaperons to target this activity. The actual nucleation of the fibril structures is studied computationally (Melquiond *et al.* on page 244-250). The use of simulations suggested that the rate limit step for oligomerization includes the central hydrophobic core.

The study of amyloid formation by yeast prion protein provides an intriguing model for the understanding of structural basis of oligomerization (Bousset *et al.* on page 251-259). This review describes the role of inherent asparagine and glutamine residues in the self-assembly of amyloid

structures. The special issue also includes the conceptual description of protein aggregation and its correlation with natively unfolded protein structures (Vladimir Uversky on page 260-287). In this review, the authors describe the fibrillogenesis process and the formation of partially folded structures by addressing the dynamic changes involved with the emergence of a definite structure.

For high-resolution study of amyloid formation and its inhibition, X-ray fiber analysis is being used (Kirschner *et al.* on 288-307). This article describes the use of fiber diffraction for the screening of amyloid inhibitors. Other biophysical techniques employed in this study provide key information regarding the molecular arrangement of amyloid assemblies. Ulrich Baxa describes on page 308-318, the development of structural models that are based on experimentally-derived biophysical parameters as well as correlation between models and the level of infectivity of amyloid assemblies.

The final review of this special issue describes the structural, functional and biological experiments used to study pre-fibrillar amyloid assemblies (Rahimi *et al.* on page 319-341). The authors describe the study of β -amyloid oligomers and compare it to other proteins that form amyloid assemblies in other diseases.

Taken together, these studies provide a fresh yet comprehensive view on amyloid formation with high resolution and precise kinetic parameters of major importance to all of the researchers in this field. We are certain that the readers will find this special issue of great interest and importance.

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