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Amyloid Aggregation

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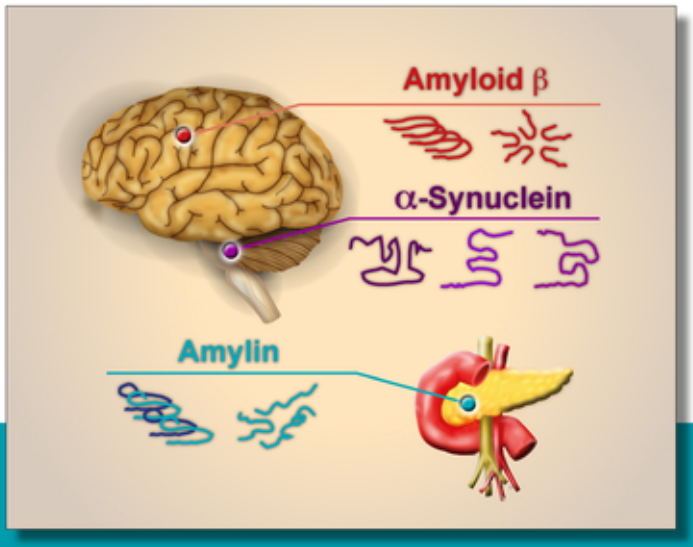

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Special Issue: Amyloid Aggregation

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Amyloid diseases are a large and diverse group of illnesses in which symptoms have been identified with the self-assembly of specific proteins into ordered amyloid aggregates. Examples of such amyloidogenic proteins and the associated diseases are amyloid β (Aβ) and Alzheimer′s disease, α-synuclein and Parkinson′s disease, and amylin or islet amyloid protein (IAPP) and Type 2 diabetes. Interest in the self-assembly of amyloidogenic proteins has increased in recent years with growing numbers of experimental, theoretical, and computational studies. There are now tens of identified disease related amyloid proteins as well as functional amyloids, all sharing key universal features of protein self-assembly to form ordered amyloid aggregates.

Amyloidogenic proteins are typically soluble, monomeric, and intrinsically disordered proteins that undergo remarkable conformational changes associated with a process of aggregation and self-assembly involving the formation of oligomers, protofibrils, and mature fibrils. For certain proteins, studies have identified oligomers as the toxic species in this self-assembly process. As such, it is of great interest and importance to investigate the nature of amyloid oligomers. The study of oligomers, however, is exceptionally demanding as they are often found to be only partially ordered intermediate species with short lifetimes. Therefore, an important challenge to the field is the development of new computational and experimental techniques that can provide insight into the structure and properties of the elusive amyloid oligomers.

A further complex issue believed to be critical to the study of amyloid diseases is the effect of metal ions, such as Cu(II) and Zn(II), on amyloidogenic protein aggregation. It has been suggested that these metal ions bind to amyloidogenic proteins and promote aggregation as well as the formation of reactive oxygen species. Currently, both computational and experimental studies are focused on testing a variety of intriguing hypotheses related to the nature of metal-amyloid interactions.

In recent decades, there have been extensive efforts to develop novel inhibitors and modulators as potential therapeutics for amyloidogenic protein aggregation and the development of amyloid disease. To date, drug therapies have been used to effectively treat the symptoms of some amyloid diseases, but failed to prevent or arrest disease progression. Recent studies are focused on new strategies for the development of amyloid disease therapeutics. One promising approach focuses on inhibiting the formation of toxic oligomers. However, there is a sense that therapeutic innovation is needed in order to effectively address the development and progression of the great diversity of amyloid diseases.

The current special issue presents eighteen research articles and reviews that represent leading efforts to probe the properties of amyloidogenic proteins and establish at the molecular level their relation to amyloid disease. New computational or experimental techniques needed to effectively characterize the nature of toxic amyloid oligomers are described. Other studies focus on the investigation of the enzymes critical to the genesis of Aβ providing insight that may be valuable to the development of enzyme modulators as disease therapeutics. Exciting reports are made describing new techniques to study the molecular mechanisms of amyloidogenic protein aggregation and activity. Finally, new insight is provided on the effect of metal ions on amyloid aggregation and the development of new therapeutic strategies for the prevention of amyloid diseases.

A unique feature of this special issue is the representation of a wide range of techniques currently applied to investigate amyloidogenic protein aggregation, including theoretical concepts, computational tools, in vitro methods, and in vivo studies. Moreover, the studies that are presented in this issue illustrate multidisciplinary topics, combining principles and methodologies from biology, chemistry, physics, engineering,

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and biotechnology. This multidisciplinary scientific approach described in reports from leading scientific groups provides an exceptional progress report on efforts to fundamentally understand and effectively address amyloid diseases. It is our hope that this special issue will assist the current and next generations of researchers in solving key challenges standing between our present knowledge and the effective future prevention of amyloid disease.

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