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Editorial

Aβ Behavior on Neuronal Membranes: Aggregation and Toxicities

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A growing body of evidence suggests that the aggregation and toxic potentials of amyloidogenic proteins, including amyloid β-protein (Aβ), α-synuclein, and prion protein, emerge through the interaction of these proteins with neuronal and/or glial membranes. The aggregation and deposition of Aβ are the initial events of Alzheimer's disease (AD), and the toxicity of aggregated Aβ is the basis for the neuronal loss in AD brains. Thus, the Aβ behavior on neuronal membranes should be one of the critical issues to be clarified for our further understanding of the pathogenesis of AD and to develop therapeutic strategies. To accelerate studies in this field, we have invited original research articles as well as review articles that will provide novel information for our special issue.

The first three papers of this special issue describe the crucial involvement of lipid rafts, which are specific membrane microdomains on the cell surface that are rich in sphingolipids and cholesterol, in the production, aggregation, and toxicities of Aβ. The subsequent three papers focus on the gangliosides, which are the major constituent of lipid rafts, particularly in terms of their role in the induction of conformational changes of Aβ, leading to their aggregation and emerging toxicities.

The next two articles address how Aβ causes neuronal injury by showing the possibility of formation of amyloid channels in the neuronal membranes, resulting in the disruption of calcium homeostasis that is critical for the function and survival of neurons, and the possibility of generation of radicals. In regard to the Aβ toxicities, much attention has been paid to the argument that the accumulation of Aβ inside neurons may be the critical step. In this context, the next two papers propose a mechanism by which Aβ enters the neurons, which are followed by another two papers showing how the internalized Aβ acts pathologically inside neurons, emphasizing the possibility that the mitochondria may be a target of intraneuronal Aβ.

A further argument for the possible interaction between Aβ and neuronal membranes is presented in the next four papers. In these papers, it is presented how Aβ affects the properties of neuronal membranes or, conversely, how the alteration of membrane properties affects the processing of amyloid precursor protein (APP) leading to Aβ generation. Note that the metabolism of neuronal lipids, particularly sphingolipids and ceramide, can be regulated in association with APP processing.

The final paper of this special issue describes a foresighted aspect of science and technology of nanochemistry with respect to the pathological protein aggregation, which is likely based on the catalysts of membrane lipids, suggesting an opportunity for developing novel nanomedicines and nanodiagnostics for various amyloidoses.

We all look forward to seeing further expansion of studies in this field in the near future.

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