

## Editorial

# A $\beta$ Behavior on Neuronal Membranes: Aggregation and Toxicities

**Katsuhiko Yanagisawa,<sup>1</sup> Jacques Fantini,<sup>2</sup> Avijit Chakrabartty,<sup>3</sup> and Anne Eckert<sup>4</sup>**

<sup>1</sup> Research Institute, National Center for Geriatrics and Gerontology, Obu, Aichi 474-8522, Japan

<sup>2</sup> Centre de Recherche en Neurobiologie et Neurophysiologie de Marseille (CRN2M), Université de la Méditerranée Aix-Marseille II et Université Paul Cézanne Aix-Marseille III, CNRS UMR 6231, INRA USC 2027, 13284 Marseille Cedex 07, France

<sup>3</sup> Department of Medical Biophysics, Ontario Cancer Institute, University of Toronto, TMDT 4-305, 101 College Street, Toronto, ON, Canada M5G 1L7

<sup>4</sup> Neurobiology Laboratory for Brain Aging and Mental Health, Psychiatric University Clinics, University of Basel, 4025 Basel, Switzerland

Correspondence should be addressed to Katsuhiko Yanagisawa, [katuhiko@ncgg.go.jp](mailto:katuhiko@ncgg.go.jp)

Received 1 March 2011; Accepted 1 March 2011

Copyright © 2011 Katsuhiko Yanagisawa et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

A growing body of evidence suggests that the aggregation and toxic potentials of amyloidogenic proteins, including amyloid  $\beta$ -protein (A $\beta$ ),  $\alpha$ -synuclein, and prion protein, emerge through the interaction of these proteins with neuronal and/or glial membranes. The aggregation and deposition of A $\beta$  are the initial events of Alzheimer's disease (AD), and the toxicity of aggregated A $\beta$  is the basis for the neuronal loss in AD brains. Thus, the A $\beta$  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 A $\beta$ . 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 A $\beta$ , leading to their aggregation and emerging toxicities.

The next two articles address how A $\beta$  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 A $\beta$  toxicities, much attention has been paid to the argument that the accumulation of A $\beta$  inside neurons may be the critical step. In this context, the next two papers propose a mechanism by which A $\beta$  enters the neurons, which are followed by another two papers showing how the internalized A $\beta$  acts pathologically inside neurons, emphasizing the possibility that the mitochondria may be a target of intraneuronal A $\beta$ .

A further argument for the possible interaction between A $\beta$  and neuronal membranes is presented in the next four papers. In these papers, it is presented how A $\beta$  affects the properties of neuronal membranes or, conversely, how the alteration of membrane properties affects the processing of amyloid precursor protein (APP) leading to A $\beta$  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.

*Katsuhiko Yanagisawa*  
*Jacques Fantini*  
*Avijit Chakrabartty*  
*Anne Eckert*

