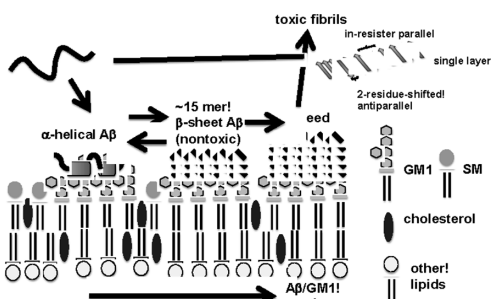
IS02-4

Toxic A β amyloids formed on neuronal membranes: their mechanism of formation and structure

○ Katsumi MATSUZAKI[1]
[1]Kyoto Univ. Grad. Sch. of Pharm. Sci.

The abnormal aggregation of A β is considered to cause Alzheimer's disease (AD). Yanagisawa et al. discovered a specific form of A β bound to GM1 ganglioside (GA β) in neuronal membranes from the brain of early AD patients, and proposed that GA β acts as a template for the formation of A β aggregates [1]. This hypothesis was proved in vivo using the anti GA β antibody [2]. We have elucidated the following mechanisms for the GM1-mediated abnormal aggregation of A β by various physicochemical techniques [3–4]. 1) A β specifically recognizes and binds to cholesterol-induced clusters of GM1. 2) At lower A β densities on the membrane, the peptide assumes an α -helix-rich structure whereas at higher densities, it is converted to a β -sheet-rich oligomer composed of ~15 A β molecules. 3) A further increase in A β density leads to the formation of toxic amyloid fibrils, the structure of which is a unique tape-like one composed of a single layer of mixed in-resister parallel/2-residue-shifted antiparallel β -sheets.



[1] K. Yanagisawa et al., ***Nat. Med.*** 1, 1062 (1995). [2] H. Hayashi et al., ***J. Neurosci.*** 21, 4894 (2004). [3] K. Matsuzaki, ***Acc. Chem. Res.*** 47, 2397 (2014). [4] Y. Okada et al., ***ACS Chem. Neurosci.***, in press (2018).