S61-2 Pathological changes induced by amyloid-β in Alzheimer's disease

◯Kazuyuki TAKATA[1], Yoshihsia KITAMURA[1], Shun SHIMOHAMA[2], Takashi TANIGUCHI[1]
[1]Kyoto Pharm. Univ., [2]Sapporo Med. Univ. Sch. of Med.

Pathological hallmarks of Alzheimer's disease (AD) include senile plaques, neurofibrillary tangles (NFTs), and synaptic and neuronal loss. Senile plaques and NFTs are formed by accumulation of amyloid-β (Aβ) and hyperphosphorylated tau, respectively. Although the details of correlation between these AD pathologies are unclear, the Aβ accumulation is thought to be a primary event that influences other AD pathologies in the developmental cascade of AD. So far, we have studied microglial reactions as a pathological change induced by Aβ, and suggested that microglia phagocytose Aβ and play a critical role in the Aβ clearance system in brains. More recently, to clarify the effect of Aβ on neuronal pathologies, we investigated brains of Tg2576 mice, JNPL3 mice, and 3xTg-AD mice, which develops Aβ plaques, NFTs-like hyperphosphorylated tau accumulation, and both pathologies, respectively. As a result, we found a possibility that Aβ affects on the pathology of NFTs and induces an accumulation of actin assembly-related factor into the NFTs. It suggests that Aβ pathology promotes the NFTs maturation and induce the synaptic dysfunction via disturbance of actin assembly. Thus, Aβ pathology may be considered as a brain aging-promoting factor. Further studies on the Aβ-dependent pathological changes may contribute to a discovery of novel therapeutic targets for AD.