



PCI-25

## **Elucidation of the role of chronic inflammation underlying pathogenesis of Alzheimer's disease**

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### **Abstract**

Alzheimer's disease (AD), the most common form of progressive dementia, is characterized by two pathological features in the brain, extracellular senile plaques and intracellular neurofibrillary tangles. Senile plaques consist of amyloid- $\beta$  peptide ( $A\beta$ ) generated from amyloid precursor protein (APP) through proteolytic processing. Then, neurofibrillary tangles are formed by aggregation of tau protein which acts as a stabilizer of microtubules under the physiological conditions. In AD research, amyloid cascade hypothesis is the most acceptable hypothesis that amyloid deposition triggers tau aggregation during aging. On the other hand, chronic inflammation in the brain also affects higher brain dysfunction with aging. In AD brain, massive microgliosis and astrogliosis as inflammatory responses were observed at around  $A\beta$  plaques. But the detailed mechanisms connecting  $A\beta$  depositions with neuroinflammation to tau aggregation remained unclear.

Recently, we have generated a novel type of AD model mouse manipulated by the knock-in paradigm, because previous AD model mouse, such as APP transgenic mouse, has artificial aspects which confused to understand the mechanism of AD pathogenesis. Using the novel mouse model, I will elucidate the mechanisms and the role of chronic inflammation in the brain underlying pathogenesis of Alzheimer's disease. This study will contribute to resolve the pathological mechanism of AD and to find the drug discovery for prevention, treatment and delay of onset of the disease.