Alzheimer's & Parkinson's Disease: Open Access

Editorial

Therapeutic Perspectives of Alzheimer's Disease - a

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ABSTRACT

Alzheimer's disease (AD) is the most common dementia that leads to a progressive deterioration of cognitive function with memory loss. With increasing ageing population in our society, AD influences more and more people in their late life. Although significant advances have been made in the pathological process of AD after its discovery for over a century, the effects targeting the assumed clarified pathogenesis for the treatment of AD are still elusive.

The two pathologic hallmarks of AD have been considered as extracellular plaques of amyloid-β peptide aggregates and intracellular neurofibrillary tangles composed of hyperphosphorylated microtubular protein tau [1]. The β-amyloid deposition constitutes the plaques that are composed of a 39–42 amino acid peptide (Aβ), which is the proteolytic product of the amyloid precursor protein (APP) [2]. The hyperphosphorylated tau protein aggregates to form insoluble particles in cells and cause intracellular neurofibrillary tangles. Since the discovery of the pathological features of AD, tremendous efforts have been make to fight against the progress of AD. The immunotherapy can represent an innovative strategy developed in recent years.

The amyloid cascade hypothesis has been formulated over last 20 years [3]. The key of this theory is that accumulation and aggregation of Aβ initiate the neurodegenerative cascade that leads to neuronal loss and cognitive decline. In this respect, the immunotherapy aiming to prevent Aβ deposition and clean the existing Aβ has been developed. The primary results are encouraging with passive immunotherapy, which demonstrated that application of monoclonal antibody against some epitopes of Aβ reduced the Aβ burden and prevented Aβ aggregation [4,5]. However, the clinical efficacy was not satisfactory, no cognitive benefit has been achieved in AD patients with passive immunotherapy against Aβ [6]. In a recent study in animal model of AD, Aβ-targeting antibody fails to repair neuronal dysfunction by using *in vivo* two-photon images in mice, besides, it can increase the neuronal hypersensitivity in the cerebral cortex [7], which may be a feature of early neuronal dysfunction in AD [8].

Although active immunity against Aβ is more effective to remove or clarify the amyloid plagues, immunization with Aβ did not prevent the progression of AD and did not even improve the survival of patients [9], not to mention of increased risk of meningoencephalitis due to requirement of adjuvant for the vaccine [10]. In this respect, DNA vaccine may hold some promise, since no adjuvant is required for DNA vaccine.

The above results give another reason to argue against the amyloid cascade hypothesis [11]. In fact, the Aβ plague and tau pathology have been proposed to function independently [12]. The amyloid load has been considered to have a poor correlation with cognitive deficit, in contrast, tau pathology and neurofibrillary tangle are more closely correlated with the severity of the disease [13,14]. The immunotherapy targeting tau protein has therefore become a new promising opportunity. In animal models, anti-tau antibodies have been demonstrated to reduce the tau aggregates and improve the motor neuronal function in mice [15,16]. The clinical efficacy for tau immunotherapy is expected in the near future.

With the development of second generation of DNA sequencing techniques, lower and more reliable genetic screening service for dementia is becoming more and more accessible for cases with genetic mutation. With that in hand, early application of immunotherapy becomes possible and may achieve considerable cognitive benefits.

The complicated nature of pathogenesis of AD indicates that comprehensive measurement is required to prevent or block the development of this disorder. Other therapeutic strategies aiming to prevent the pathological cascade are also emerging, such as anti-oxidative stress, anti-inflammation, and cell therapy, every minimal efficacy of which would be counted to contribute to the future therapeutic renovation for AD. For example, long-term treatment with an antagonist of corticotropin-releasing factor, a stress-coping hormone that has been associated with pathology of tau protein and amyloid, reduces the brain's stress circuitry activity and slows the progressive cognitive decline in mice [17]. Neural stem cell therapy has also been demonstrated to reduce the amyloid plagues, prevent neuronal loss, and improve the synaptic plasticity and cognitive function in mouse model of AD [18,19].

With a new journal, SRL Alzheimer's & Parkinson's disease, has been launched, the researchers fighting against AD and Parkinson's disease will own a new platform to communicate and this may provide more robust motivation to push the development of novel therapies for these degenerative diseases forward. Since more and more people are jumping into the research field of AD and Parkinson's disease, it is also the opportunity for this journal to establish its own reputation through recruiting high quality papers and attracting prestigious scientists to input their cutting-edge approaches and discoveries in this journal.

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