CHAPTER 1

Introduction

1.1. Background

Dementia is a clinical syndrome characterized by the manifestation of language disturbance, difficulties in memory, changes in psychological aspects, and impairment in doing daily activity. It is one of the leading causes of disability in later life, in terms of the global burden of disease, as it contributes to approximately 11.2% of years lived with disability. Also, it has the highest percentage when compared to other diseases, such as stroke, heart disease and cancer (Burns & Iliffe, 2009a).

Alzheimer disease (AD) is the most common cause of Dementia. It is a progressive neurodegenerative disorder that is characterized by three main groups of symptoms; cognitive dysfunction, psychiatric symptoms, and difficulties in doing daily life tasks (Burns & Iliffe, 2009b). Cognitive dysfunctions are related to memory loss, language disturbance, and executive dysfunction, whereas the psychiatric symptoms are composed of depression, hallucinations and other non-cognitive symptoms. The last group of symptoms consists of difficulties in doing daily life tasks, such as eating and dressing. The symptoms will progress from mild cognitive impairment such as memory loss to severe AD, where typically in this stage, the patient is bedbound (Burns & Iliffe, 2009b). AD can be differentiated from other dementia diseases through its pathological hallmarks which are the presence of amyloid plaque and neurofibrillary tangles (NFTs) in the brain.

Age is one of the principal risk factors in AD. The risk of getting AD will increase alongside with age. Thus, in super age societies like Japan, where more than 20% of the total population is above 65 years old, are racing to find potential effective treatments for this disease. In 2018, it affected around 46.8 million individuals worldwide, and it is predicted that the number of populations with

AD will double every 20 years due to the aging population (Nguyen., 2018). Besides, due to its increasing number of cases, the social and economic burden associated with Alzheimer's disease has increased 2.2 times from 2002 to 2011, from ¥755.9 to ¥1,653.4 billion (Montgomery, Ueda, Jorgensen, Stathis, Cheng & Nakamura., 2017).

In the previous two decades, more than 400 potential treatment candidates have failed to pass trials (Sasaguri et al., 2017). Thus, finding an effective treatment for AD is crucial, especially in aging countries. The Alzheimer's Disease International Organization is currently calling governments to set aside funds with a minimum of one million of the societal cost of dementia to be dedicated to the research of AD (Patterson, 2018). Currently, approved treatments for AD consist of cholinesterase inhibitor and low-affinity N-Methyl-D- aspartate receptor antagonist (Lane, Hardy & Schott., 2018). The treatments only improve the symptoms of the patients, such as memory and alertness; in addition, the progression of AD remains unchanged and keeps worsening (Weller & Budson., 2018).

Despite the high failure rate in finding AD treatments, many potential treatments are also emerging, one of them is IL-33. A study done by Fu et al. (2016), shows mice that have been injected with IL-33 for two days with the dosage of 200 μg had lower Amyloid β (Aβ) area and improved cognitive function compared to the vehicle-treated control. The current project will provide insight into the effect of Interleukin-33 (IL-33) long-term injection towards the cognitive function of APP/PS1dE9 mice.

1.2. Research Objective

The purpose of this study is to follow-up the effect of IL-33 treatment, in terms of cognitive function and Amyloid β (Aβ) presence in the brain, in APP/PS1 mice that have been treated with IL-33 for six and a half months.

This experiment hypothesizes that IL-33 treated APP/PS1 mice will have a better cognitive function and lower quantity of Amyloid β (Aβ) in the brain compared to vehicle-treated APP/PS1 mice, and the results will be comparable to wildtype mice.