CHAPTER I

INTRODUCTION

Rationale for the study

Alzheimer's disease (AD) is a multifactorial disease and most common form of dementia, affecting 10% of individuals older than 65 and nearly 50% of those older than 85 of age (Imbimbo, et al., 2005) with a prevalence of more than 35 million worldwide (Querfurth and LaFerla, 2010). The disease has many signs or symptoms that can be observed such as memory loss that disrupts daily life, challenges in planning or solving problems, confusion of time or place, trouble understanding visual images and spatial relationships, problems of learning new words especially speaking or writing, misplacing things and losing the ability to retrace steps, decrease or poor judgment, withdrawal from work or social activities and changes in mood and personality. These signs or symptoms in this disease have risk caused from both non-genetic and genetic risk factors. Non-genetics risk factors are head injury, high density lipoprotein cholesterol alcohol drinking, etc. Genetic risk factors cause from many genes that have single nucleotide polymorphisms or mutation on Amyloid precursor protein gene (*APP*), Presenilin1 gene (*PSEN1*), Presenilin2 gene (*PSEN2*) gene and Apolipoprotein E gene (*APOE*). In 2001, there were about 135,000 potential AD patients in Thailand (Sukying, 2007). Thai government has allocated budget to the treatment of AD patients and to prevent its citizens from the disease. Currently, several studies have been executed in Thailand including utilizing Thai herbs treatment to prevent memory loss, or finding single nucleotide polymorphisms (SNPs) of genes involved in AD in Thai population for a possible pre-diagnosis. This research will attempt to identify SNP genotypes in *PSEN1* using association study, which involves in AD pathogenesis to be used in pre-diagnosis of AD patient in Thai population.

Purpose of the study

1. To study SNPs of *PSEN1* in Thai AD patients.

2. To identify tag single nucleotide polymorphisms (tag SNPs) in *PSEN1* from HapMap website.

3. To genotype the identified tag SNPs in *PSEN1* in control and Thai AD subjects.

4. To analyze statistical association between the genotyped tag SNPs of *PSEN1* in control and Thai AD subjects using association studies.

Hypothesis

Identifying and genotyping SNPs in *PSEN1* in Thai AD patients using association study might find some SNPs significantly associated with Thai AD patients.

Scope of the study

1. This study identified tag SNPs in *PSEN1* from HapMap website as reported in Han Chinese from Beijing, China.

2. This study genotyped the identified tag SNPs of *PSEN1* in Thai AD subjects and controls from Chiangmai Neurological Hospital, Chiangmai, Thailand.

3. Genotyping of *PSEN1* SNPs was performed by DNA sequencing technique.

4. Interpretation of SNP frequencies in *PSEN1* was performed by the association study.

Keyword (s)

Single nucleotide polymorphisms (SNPs), Association studies, Presenilin1 gene (*PSEN1*), Thai Alzheimer's disease patients

Benefits

1. Association studies of genotypic frequencies of identified tag SNPs in *PSEN1* among Thai AD onset might be revealed.

2. Ministry of Public Health can gain the knowledge from the research to use for pre-diagnostic and risk assessments, which can influence the healthcare plans in the future.