SINGLE NUCLEOTIDE POLYMORPHISMS ASSOCIATION STUDIES OF PRESENILIN 1 GENE IN THAI ALZHEIMER'S DISEASE PATIENTS

KONGLA SOPACHAI

A Thesis Submitted to the Graduate School of Naresuan University
in Partial Fulfillment of the Requirements
for the Master of Science Degree
in Medical Sciences (International Program)
April 2012

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This thesis entitled "Single nucleotide polymorphisms association studies of presenilin1 gene in Thai Alzheimer's disease patients" submitted by Kongla Sopachai in partial fulfillment of the requirements for the Master of Science Degree in Medical Sciences (International Program) is hereby approved.

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ABSTRACT

Single nucleotide polymorphisms (SNPs) in amyloid precursor protein (*APP*) and presenilin (*PSEN*) gene are known to cause early onset Alzheimer's disease (EOAD) but different in ethnic groups. The purposes of this research were to study SNPs association studies of presenilin 1 gene (*PSEN1*) in Thai Alzheimer's disease patients. The studies were following with as case-control study using HapMap database to identify the SNPs. The identified tagSNPs in the *PSEN1* of Han, Chinese from Bejing, Chaina as a model for Thailand are rs3025780 (Intron 3), rs214273 (Intron 3), rs362340 (Intron 4), rs165932 (Intron 8), rs165933 (Intron 8) and rs10146743 (Intron 9). The 15 Alzheimer's disease patients and 15 controls were recruited using activities of daily living, behaviors and cognitive function evaluation from Memorial Clinic, Chiangmai Neurological Hospital, Chiangmai, Thailand. This study reported that 13.33% showed as GA heterozygous alleles in rs165933 for both Alzheimer's disease patients and controls. In Alzheimer's disease patients, the GA heterozygous was about 20%, when only 6.66% showed in the controls. Association studies using odd ratio (95% CI) in the rs165933 in *PSEN1* showed GG, GA and AA alleles at 0.33 (95% CI = 0.0275-4.0359), 4.20 (95% CI = 0.3320-53.1253), and 0.24 (95% CI=0.0188-3.0117), respectively. Therefore, the rs165933 (Intron 8) genotypes (GG and GA alleles) could be a candidate SNPs marker of *PSEN1* in Thai population.

However, large sample size both Alzheimer's disease patients and controls must be verified.

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ABBREVIATIONS

A	=	Adenine
AD	=	Alzheimer's disease
APP	=	Amyloid precursor protein gene
APP	=	Amyloid precursor protein
APOE	=	Apolipoprotein E gene
Aβ	=	Amyloid beta
BDI	=	Thai Beck Depression Inventory criteria
B_G	=	Genetic effect
bp	=	base pair
C	=	Cytosine
°C	=	degree Celsius
dNTP	=	Deoxyribonucleotide triphosphate
DNA	=	Deoxyribonucleic acid
E	=	Binary exposure factor (1=exposed, 0=unexposed)
EDTA	=	Ethylenediaminetetraacetic acid
EOFAD	=	early onset familial Alzheimer's disease
G	=	Glycine
G	=	Genotype (AA,Aa, or aa) at a candidate locus
g	=	Earth's gravitational acceleration
HapMap	=	Haplotype mapping
HCl	=	Hydrogen chloride
HWE	=	Hardy-weinberg equilibrium
htSNPs	=	haplotype tagging Single Nucleotide Polymorphisms
kbp	=	kilo base pairs
kDa	=	kilo dalton
LD	=	linkage disequilibrium
M	=	Molar
mM	=	mili molar
MAF	=	minor allele frequencies

ABBREVIATIONS (CONT.)

MD	=	mental disorder
NPs	=	Neuritic plaques
N	=	nitrogen
NFTs	=	Neurofibrillary tangles
NINCDS–ADRDA	=	National Institute of Neurologic and Communicative Disorders and Stroke–Alzheimer's disease and Related Disorders Association
OR	=	Odd ratio
PSEN1	=	Presenilin1 protein
PSEN1	=	Presenilin1 gene
PSEN2	=	Presenilin2 protein
PSEN2	=	Presenilin2 gene
P_o	=	Baseline disease risk
R_E	=	Environmental relative risk (or odds ration)
R_G	=	Genetic relative risk (or odds ratio)
R_{GE}	=	Interaction effect (Relative-risk ratio, or odds ratio ratio)
rsSNPs	=	reference single nucleotide polymorphisms
SPSS	=	Statistical Package for Social Sciences
SBE	=	Single base extension
SNPs	=	single nucleotide polymorphisms
sAPP	=	soluble amyloid precursor protein
T	=	Thymine
TAE	=	Tris-Acetate-Ethylenediaminetetraacetic acid
TE	=	Tris-Ethylenediaminetetraacetic acid
TMSE	=	Thai Mini Mental State Examination
Tm	=	melting temperature
tag SNPs	=	Tag single nucleotide polymorphisms