UNIVERSITI TEKNOLOGI MARA

THE EXPRESSION OF BIN1 GENE IN BLOOD OF ALZHEIMER'S DISEASE PATIENTS

RAJA NUR HAZIQAH BT RAJA ZULKARNAIN

Dissertation submitted in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy

BACHELOR OF PHARMACY (Hons.)

2015

ABSTRACT

Alzheimer's disease is a neurodegenerative disease which it shows slowly progressive loss of cognitive functions and would lead to dementia and death. The pathogenesis involves amyloid hypothesis and oxidative stress pathway. For amyloid hypothesis, there is an aggregation of β amyloid protein in the extracellular area of cortical region of brain. As for oxidative pathway, there is presence of neurofibrillary tangles formed inside the neurons. There are many genes showing expression in AD. In this study, BIN1 gene is used. The expression level of BIN1 gene in AD subjects is higher than the expression level of BIN1 gene in healthy subjects. The fold changes of the BIN1 gene in AD show that it express 8 times more than the BIN1 gene in healthy subjects. The finding of blood based biomarker to detect AD in early stages would reduce the burden of care taker and reduce mortality rate of AD thus would lead to increase the quality of life of AD patients.

ACKNOWLEDGEMENT

First of foremost, all praise to the almighty ALLAH who bless me with health, strength and peaceful mind to complete my project successfully.

I also would never have been able to finish my dissertation without the guidance of my supervisor, helps from friends and support from my family.

I would like to express my deepest gratitude to my advisor, Dr Richard Muhammad Johari James, for his excellent guidance, caring patience, and providing me with excellent atmosphere for doing research. I would like to thank my partner, Nurdiyana Yusof, for her support and was willing to help me. It would have been a lonely lab without her.

Many thanks to Nurul Syahidah, a postgraduate student and other lab assistants of Brain laboratory for their assistant throughout my lab work. My research would not have been possible without their help.

I would like to thank to all my friends and housemates for their support and willingness to help me regardless the time.

I would also like to thank my family member for always supporting me and encouraging me with their best wishes.

Finally, I would like to thank my best friend, Muhammad Ubaidah Syafiq bin Mustaffa, who are always there cheering up and stood by me through good times and bad.

Table of Contents

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

Alzheimer's disease (AD) is a neurodegenerative disorder characterised by loss of memory and other cognitive abilities (Sano et al., 1997). AD is the leading cause of dementia in developed countries which recent study shows that it afflicts 5.3 million individuals in the U.S. The prevalence of AD shows an age-related progression in the elderly. Approximately 25%-45% of individuals develop symptoms before 70 years (Olgiati, Politis, Papadimitriou, De Ronchi, & Serretti, 2011). The lifetime risk for AD for a 65 years individual is estimated to be 10.5%, with prevalence doubling every 5 years after age of 65, and by age of 80 years, it reaches nearly 50%. The costs of care related to AD in 2013 were more than $200 billion with the annual cost surpassing $1 trillion by 2050 (Fagan, 2014). Neuropathologically, AD include positive and negative features where positive features are amyloid plaques and cerebral amyloid angiopathy, neurofibrillary tangles, and glial responses ; and negative features are neuronal and synaptic loss (Serrano-Pozo, Frosch, Masliah, & Hyman, 2011). AD is progressive and ultimately fatal and there are early symptoms which are often mistaken as part of normal aging or manifestation of stress. The most common symptom is short-term memory loss and as the disease progresses, the symptoms like aggression, irritability, confusion and language problems as well as long-term memory loss are included (Barber, 2012).