UNIVERSITI TEKNOLOGI MARA

MAP2K1 GENE AS POTENTIAL BLOOD-BASED BIOMARKER FOR EARLY DETECTION OF ALZHEIMER'S DISEASE

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Dissertation submitted in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.)

Faculty of Pharmacy

2014

ACKNOWLEDGEMENTS

Firstly, Alhamdulillah because of Him Who has blessed me with health, patience and permission to complete this thesis in the given time. I want to express my deepest and sincere gratitude to those who have contributed to the completion of this thesis.

I also want to express special thanks to my supervisor, Professor Dato' Dr. Abu Bakar Abdul Majeed and co-supervisor, Dr. Ainon Zahariah Samsudin for all of the support, guidance, advice and knowledge given to me.

Special thanks to the Dean of the Faculty of Pharmacy, UiTM, for providing the opportunity to carry out this work, and staff of Brain Research Laboratory for their valuable time in helping to complete the research.

Last but not least, my thanks go to my family and colleagues for their understanding and support.

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ABSTRACT

Background: Alzheimer' disease (AD) is the most common subtype of dementia which accounts for 60-80% of dementia characterized as a brain disorder usually affecting the elderly. It is associated with slow, progressive loss of function of the brain. By 2050, prevalence in Malaysia is expected to rise to 453,900 with annual new cases of 138,800. Though a variety of testing approaches are available, however, it is often difficult to make an accurate diagnosis of early stage of AD. There are currently no biochemical markers available for preclinical detection of definitive AD. MAP2K1 is gene of interest for potential blood-based biomarker as it involves in signalling pathways which regulate various cellular activities such as proliferation, differentiation, survival and death. Impairment in control of MAPK signalling pathways has been shown to be implicated in AD. In this study, comparison of expression of MAP2K1 gene and correlation with previous microarray study have been established.
Method: Phase 2 samples consist of a total of 30 samples of healthy, AD, MCI and VAD. Blood samples were collected and RNA extraction was conducted to generate cDNA. All blood samples were subjected to qPCR analysis. Relative quantification of the data obtained was analysed using Pfaffl's mathematical model. The data obtained were correlated with previous microarray study.
Results: Relative mRNA expression level in AD was upregulated 5.64-fold as compared to healthy subjects whereas for MCI and VA, it was downregulated 38-fold and 0.23-fold, respectively. As $p<0.0001$, there is significant difference in MAP2K1 expression between AD and other subtypes of dementia which are MCI and VAD. The direction of expression of MAP2K1 gene is following data obtained from previous microarray study.
Conclusion: MAP2K1 gene was found to be a potential blood-based biomarker for early detection of Alzheimer's disease as it showed a significantly higher level of mRNA expression as compared to healthy, MCI and VAD.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Alzheimer' disease (AD) is the most common subtype of dementia which accounts for 60-80% of dementia (Gauthier, 2007) characterized by a brain disorder usually in older people and associated with slow, progressive loss of function of the brain (Akter et al., 2012). Global estimation of AD is expected to increase from the current estimated 25 million to 63 million in 2030, and by 2050, the number of people affected is estimated to be over 100 million (Wimo et al., 2003). This figure is expected to double every 20 years (Ferri et al., 2005). The incidence of dementia in Asia Pacific region is expected to increase from 4.3 million in 2005 to 19.7 million in 2050. Individual country data for the estimated old and new cases of dementia are summarized in the **Table 1.1**.

Table 1.1 Estimated prevalence and incidence of dementia in selected countries and year in Asia Pacific Region

'000 people	2005		2050	
	Prevalence	Incidence	Prevalence	Incidence
Australia	195.4	60.2	664.1	199.7
China	5,541.2	1,721.0	27,004.4	8,269.0
India	3,248.5	1,026.8	16,290.1	4,974.6
Indonesia	606.1	191.4	3,042.0	932.0
Japan	1,871.2	570.2	4,873.1	1,4517.7
Malaysia	63.0	20.1	453.9	138.8
Pakistan	330.1	107.3	1,916.2	584.3
Philippines	169.8	54.8	1,158.9	353.9
Singapore	22.0	6.8	186.9	56.7
Thailand	229.1	71.4	1,233.2	377.0

[Adapted from Alzheimer's Disease International, 2006]