UNIVERSITI TEKNOLOGI MARA

MICROARRAY-BASED BLOOD GENE EXPRESSION MARKER FOR DETECTION OF ALZHEIMER'S DISEASE

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Thesis submitted in fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Neuroscience)

Faculty of Pharmacy

November 2018

ABSTRACT

Convenient biomarkers are important not only to assist detection of Alzheimer's Disease (AD) but also to uncover potential drug targets that can be manipulated to slow down the disease progression. This study therefore was conducted to identify and validate candidate blood biomarkers for detection of AD. Blood samples for total RNA extraction were collected and gene expression analysis performed on the Agilent Technologies Microarrays. When comparing the gene expression of 90 AD patients and 90 Non-Demented Controls (NDCs), Partial Least Square Discrimination Analysis (PLSDA) was used to develop a disease classifier algorithm. This algorithm correctly predicted the class of 157/180 (accuracy 87.2%), including 81/90 AD samples (sensitivity 90.0%) and 76/90 NDCs (specificity 84.4%) in training cohort. There was also a good separation between AD and NDC with the area under the receiver operating characteristic curve (ROC AUC) of 0.88. In the present study, the genes regulation (*ABCA9, CNOT8, SESN1, UCP3, MAP2K1, DDIT4*) in the real-time quantitative PCR (RT-qPCR) results for training cohort corroborated 100% with the microarray data for all six tested genes (Pearson correlation coefficient 0.95). The performance of selected significant genes was then tested using RT-qPCR in yet another independent cohort comprising 25 AD patients, 25 NDCs, 12 individuals with mild cognitive impairment (MCI) and 12 subjects with vascular dementia (VaD). The combination of six genes gave an overall correct classification of 82.0%, including 21/25 AD samples (sensitivity 84.0%) and 20/25 NDCs (specificity 80.0%). Furthermore, the algorithm also discriminated AD from MCI and VaD in 10/12 patients (specificity 83.3%) and 9/12 patients (specificity 75.0%) respectively. The most important results in the present study is, however, the high performance of the combined blood biomarker panel and the robustness such a panel offers in a future test compared to single markers.

Keywords: Gene Expression; Alzheimer's disease, Biomarkers, Blood, Microarray Analysis

ACKNOWLEDGEMENT

Firstly, I wish to thank God for giving me the opportunity to embark on my PhD and for completing this long and challenging journey successfully. My gratitude and thanks go to my supervisor Professor Dato' Dr. Abu Bakar Abdul Majeed as well as co-supervisors, Associate Professor Dr. Kalavathy Ramasamy, Professor Dr. Chin Ai-Vyrn, Professor Dr. Philip Poi Jun Hua, Professor Dr. Tan Maw Pin and Associate Professor Dr. Shahrul Bahyah Kamaruzzaman for their continuous support and guidance throughout the duration of my study.

I would also like to thank all members of Brain Research Laboratory and Memory Clinic of University Malaya Medical Centre (UMMC) who had helped me throughout the course of this project. Thank you to all participants who volunteered for this clinical study and their family members for their understanding about the importance of this research. Without their immense help, this project could not have been completed.

Finally, special thanks to my beloved husband and children for their patience, understanding and encouragements that give me the impetus to further my study. This thesis is also dedicated to my loving mother and the memory of very dear late father for the vision and determination to educate me. This piece of victory is dedicated to both of you. Alhamdulillah.

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