

UNIVERSITI TEKNOLOGI MARA

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

AINON ZAHARIAH BT SAMSUDIN

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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*, *SESNI*, *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

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