Plasma cell-free RNA Profiling of Vietnamese Alzheimer's patients: A pilot study

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Introduction

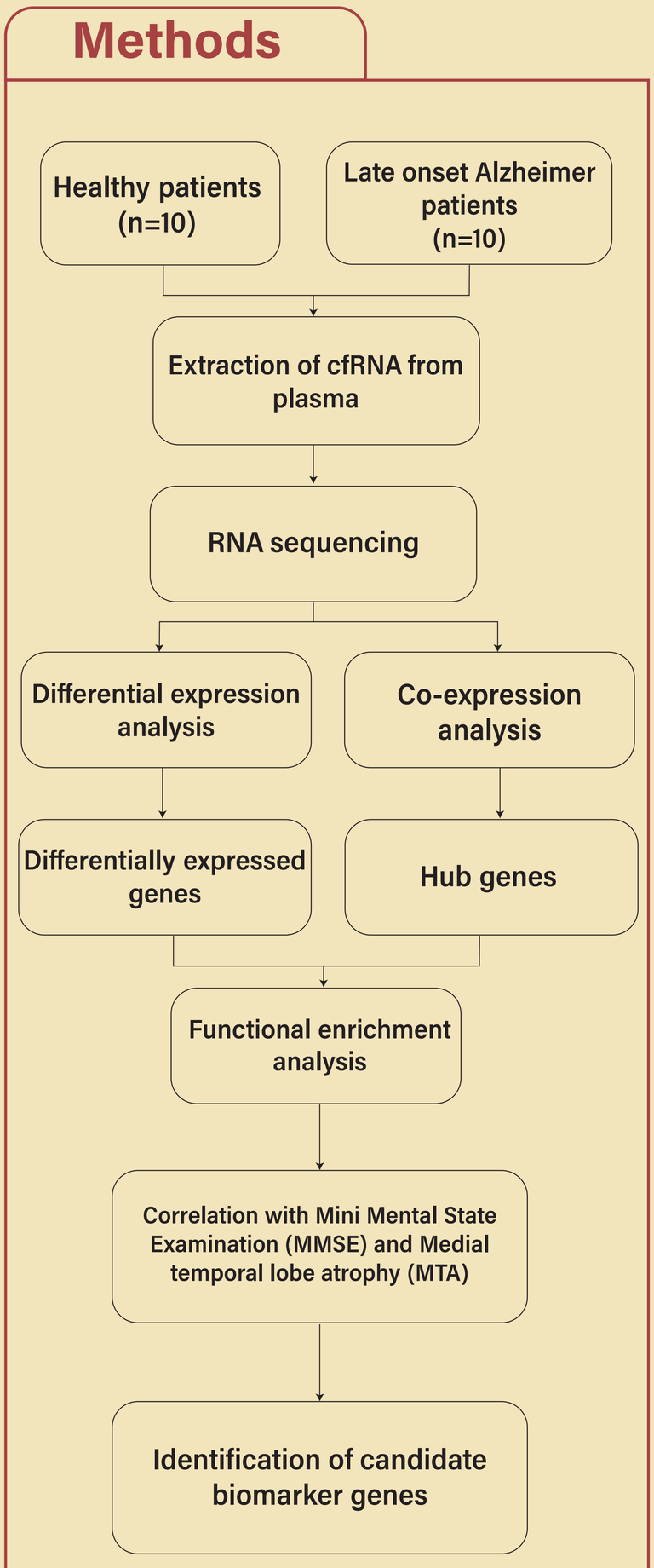
Circulating cell-free RNA (**cf-RNA**) is considered a potential hallmark for early diagnosis of **Alzheimer's Disease (AD)** as it can construe the **genetic expression level**, giving insights into the pathological progress at the outset. Profiles of cf-RNA in Caucasian AD patients have been investigated thoroughly, yet there was no report inspecting changes in Vietnamese population, or ASEAN groups. This study examined this gap, expecting the findings would support the development of point-of-care AD diagnosis.

By inspecting molecular changes in AD, these procedures can predict the pathology in advance, aiding the quality of life of Vietnamese in the rural area.

Goals

- **Identify which genes are key drivers of expression changes between the two groups, which are potentially relevant to the development and progression of Alzheimer's disease**
- **Examine whether the cfRNA transcripts significantly correlate with clinical measures of Alzheimer's disease severity to identify candidate cfRNA**

Methods



Results

Differential expression analysis shows contrast in transcriptomic profile of Alzheimer's patients

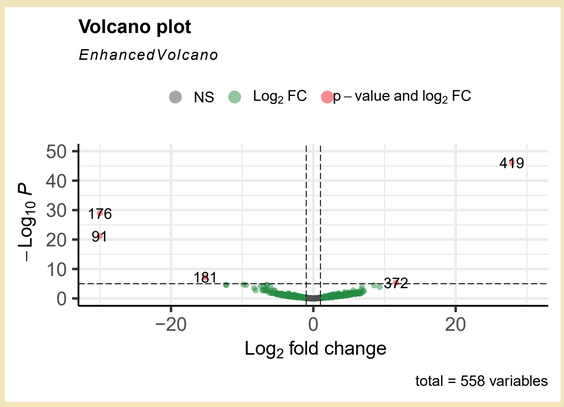


Figure 1: Volcano plot of the correlation between the log2foldchange and the adjusted p-value of 533 detected genes (grey - $p > 0.05$, green - $p < 0.05$; orange - $p < 0.0001$ and abs(log2foldchange) > 20)

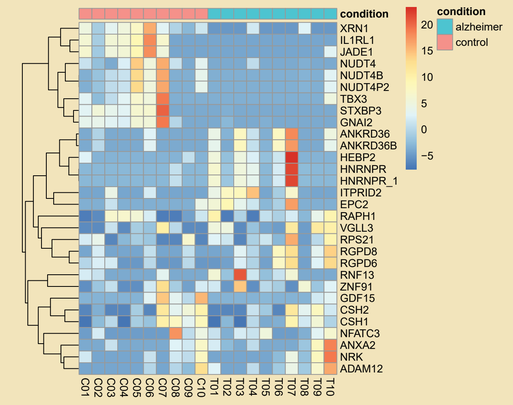


Figure 2: Clustered heatmap of expression of the top 30 genes with the highest variance

Gene co-expression analysis highlights key genes within modules

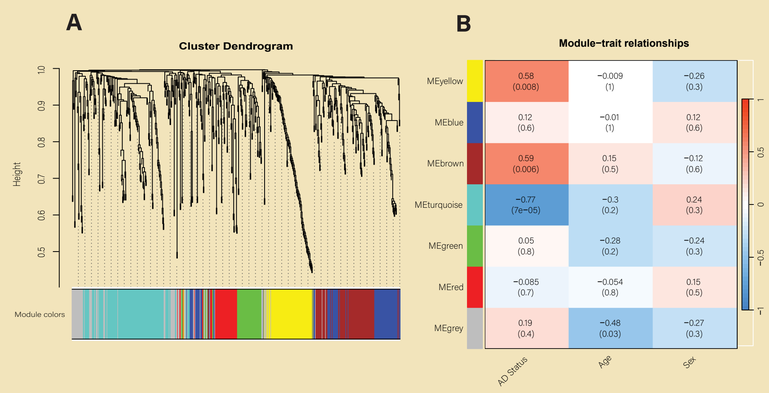


Figure 3: (A) Gene cluster dendrogram of the modules detected by hierarchical clustering (B) Correlations between modules and traits: Alzheimer's disease status, Age, and Sex

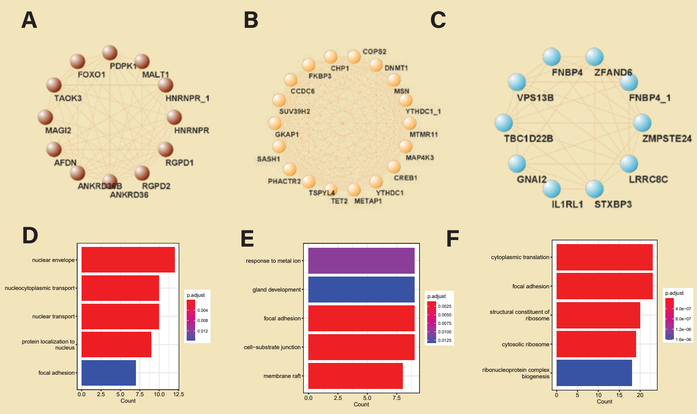
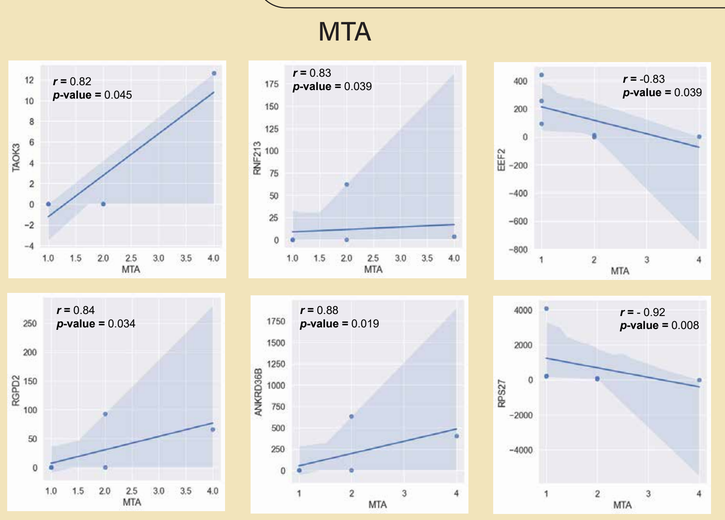


Figure 4: (A, B, C) Network visualization of the significant gene modules,from left to right: *brown, yellow, and turquoise.* Hub genes in each module are labeled. (D, E,F) Gene Ontology functional enrichment of the modules

Candidate genes show correlation with AD clinical measures



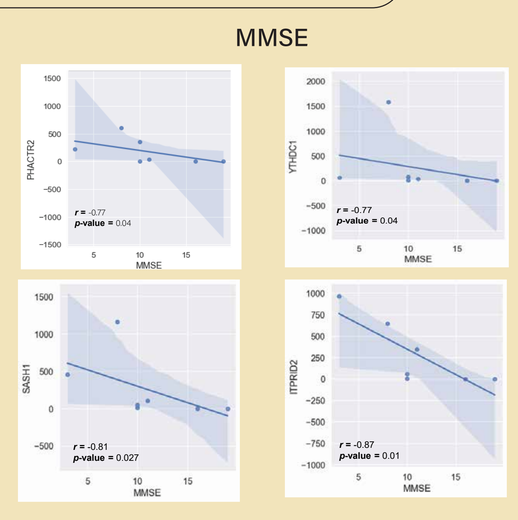


Figure 5: Correlation between MTA-score and the normalised transcript counts (median of ratios)

Figure 6: Correlation between MMSE-score and the normalized transcript counts (median of ratios)

Conclusions

(1) We have identified some gene clusters that are potentially related to structural changes inside the brains of AD-patients.

(2) We have identified some candidate genes (YTHDC1, SASH1, ITPRID2. ANKRD36B, TAOK3, EEF2, RNF213) that are highly correlated with Alzheimer's disease severity.

Future directions

Validate the identified candidate genes with a larger cohort of samples to ascertain their value in early diagnosis of Alzheimer's disease

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