

Weighted Gene Co-expression Network Analysis of Neutrophil Transcriptome Reveals Key Modules for Potential Early Blood-Based Diagnosis of Alzheimer's Disease

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- Three neutrophil gene co-expression modules (blue, brown and turquoise) were significantly associated with Alzheimer’s Disease.
- Functional enrichment revealed pathways involved in metabolism, neuronal regulation and homeostasis.
- Identified hub genes may serve as potential candidates for non-invasive neutrophilic blood-based early diagnostic biomarkers for Alzheimer’s Disease.

INTRODUCTION

Early detection of Alzheimer's disease (AD) remains a critical challenge, with limited non-invasive biomarkers available. Neutrophils, a major type of peripheral immune cell, may reflect central nervous system changes related to AD through alterations in gene expression. This study aims to identify highly co-expressed gene modules related to AD in neutrophils from Mildly Cognitively Impaired(MCI Stage) patients and Cognitively Normal(CN) persons using in silico Weighted Gene Co-expression Network Analysis (WGCNA) to uncover potential neutrophilic blood-based diagnostic markers.

- Several numbers of co-expression modules related to AD progression were identified from the WGCNA of this selected dataset.

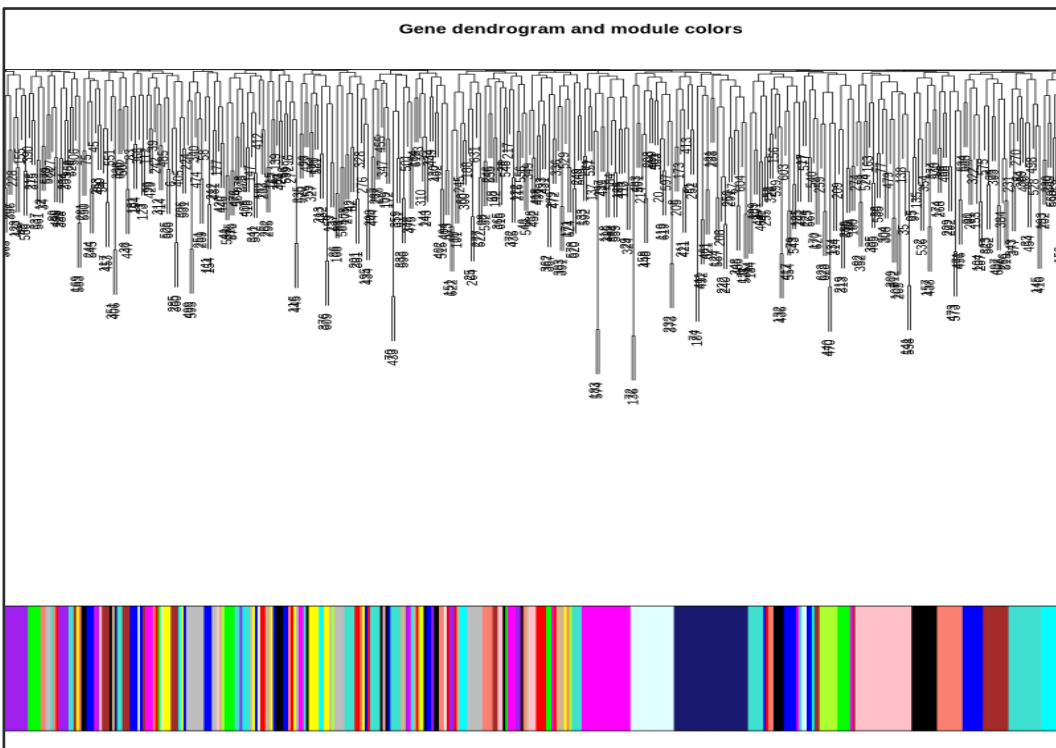


Figure 1: Gene dendrogram showing gene modules with their assigned colors

- Three co-expression networks were received as the most prominent key modules based on their significant association with the disease traits and biological relevance. They were blue, brown and turquoise networks.

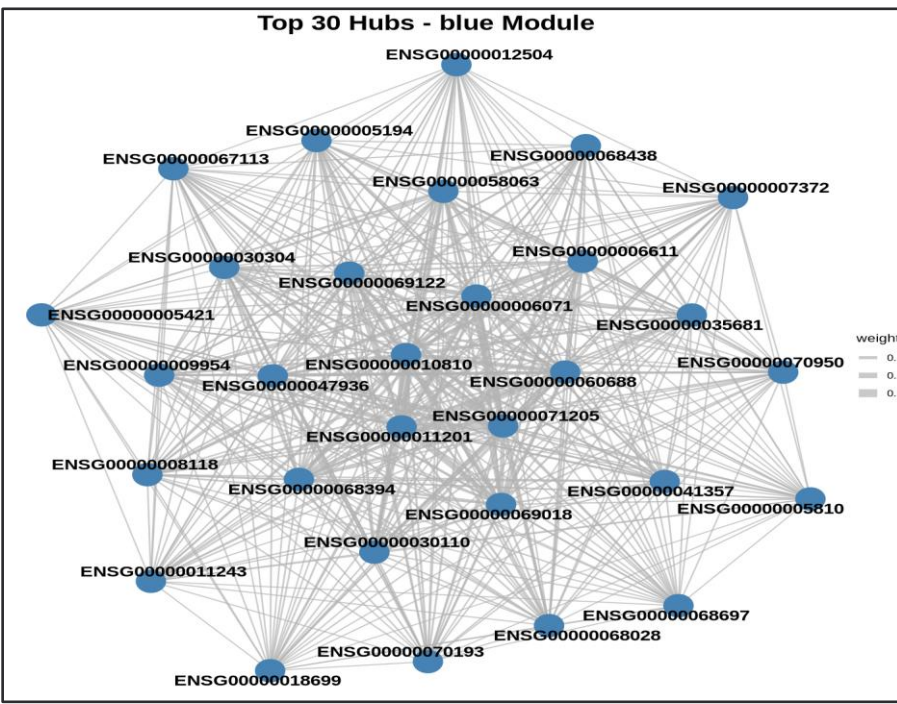


Figure 2: Co-expression network of the top 30 hub genes identified in the Blue Module

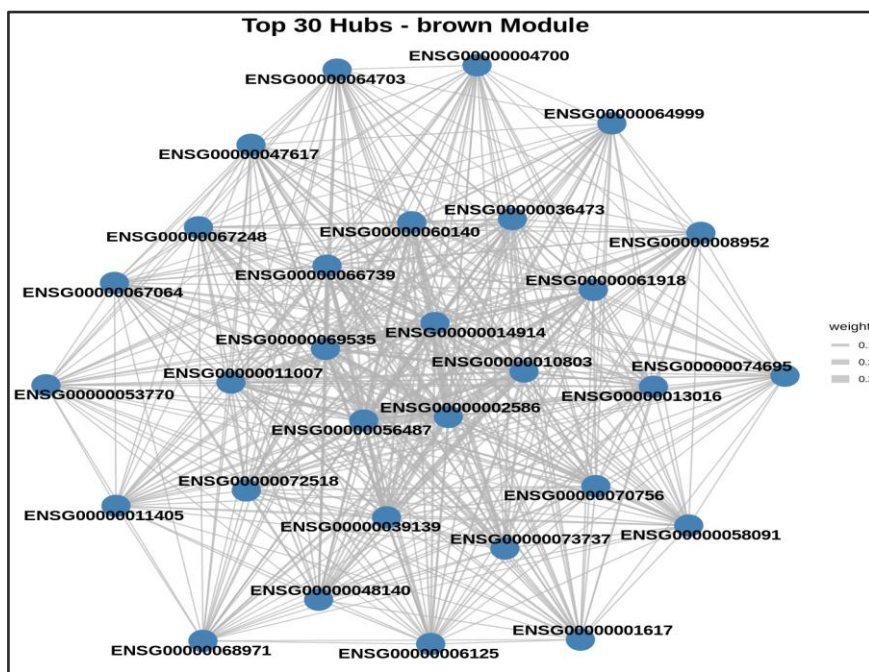


Figure 3: Co-expression network of the top 30 hub genes identified in the Brown Module

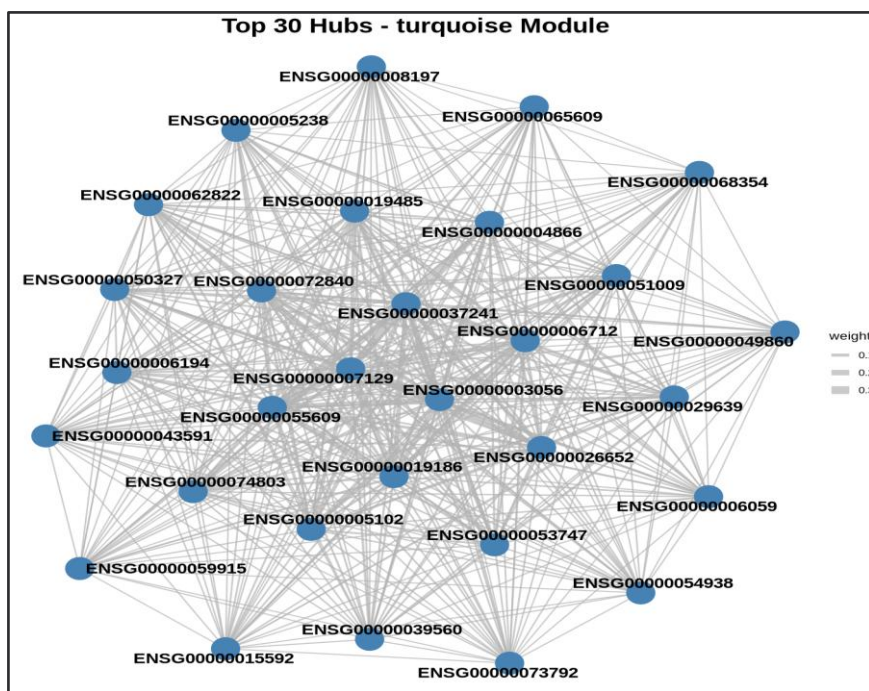


Figure 4: Co-expression network of the top 30 hub genes identified in the Turquoise Module

- The blue module comprised genes which are enriched in metabolic and homeostatic pathways, including phospholipid metabolic process, glucose homeostasis and carbohydrate homeostasis.
- The brown module demonstrated enrichment in neuronal and transport-related functions, including regulation of neuron projection development, calcium ion transmembrane transport and cell projection organization.
- The turquoise module was associated with regulatory and metabolic processes, including methylation, rhythmic behavior and energy homeostasis.

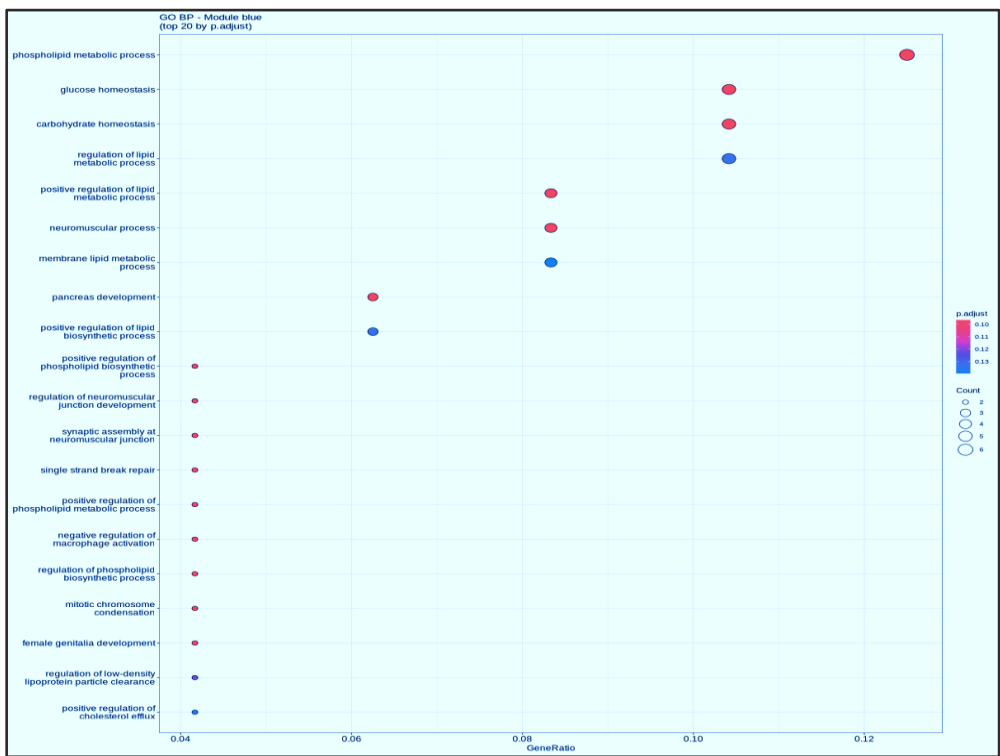


Figure 5: The GO-BP Dot plot of the Blue Module

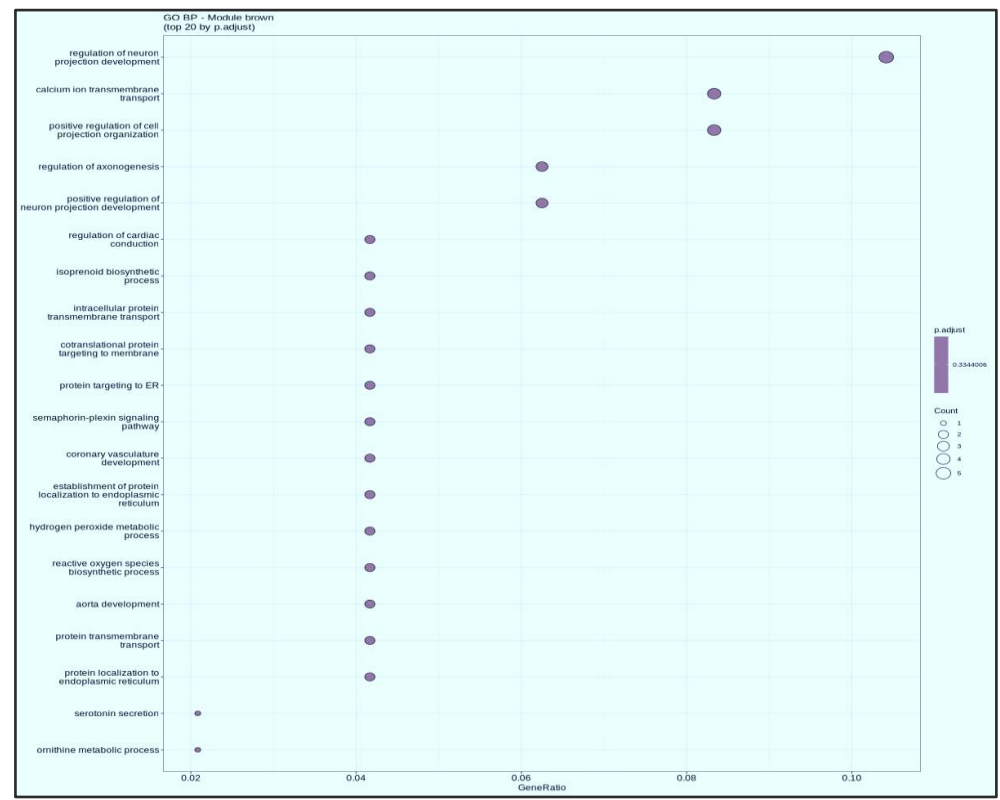


Figure 6: The GO-BP Dot plot of the Brown Module

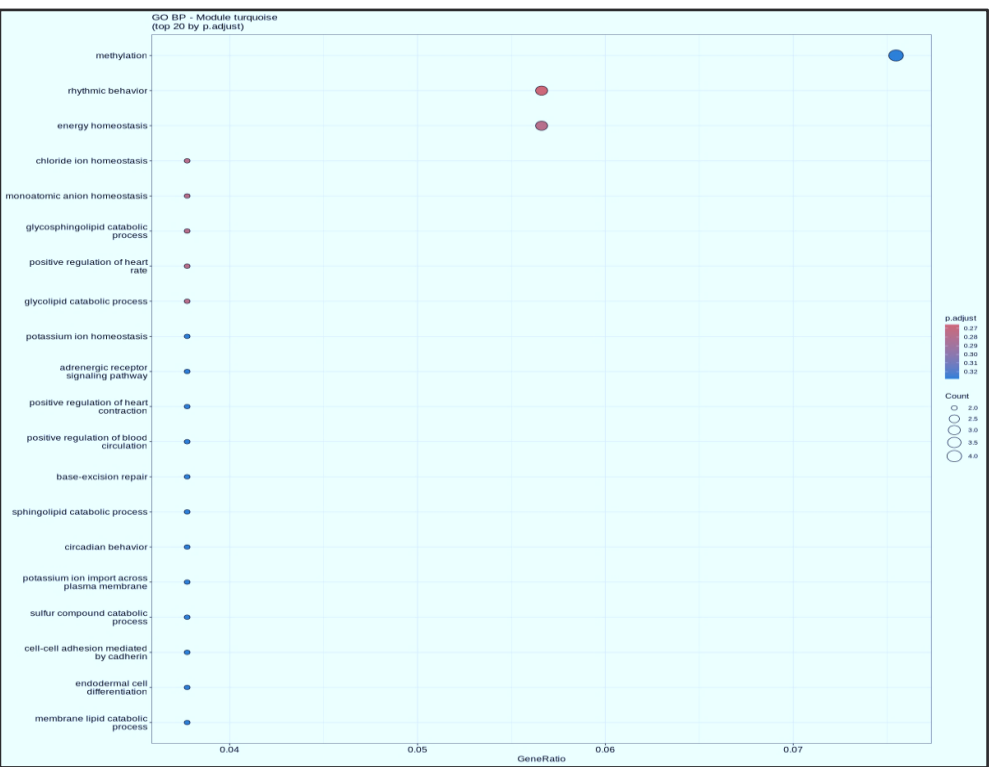


Figure 7: The GO-BP Dot plot of the Turquoise Module

CONCLUSION

- This ongoing *in silico* analysis demonstrates distinct co-expressed gene modules in the neutrophil transcriptome linked to AD, emphasizing pathways in metabolism, neuronal and homeostasis.
- These findings, derived from processed public RNA-seq data, suggest novel candidates for neutrophilic peripheral blood based early diagnostic biomarkers, with planned experimental validation to confirm their clinical utility.

REFERENCES

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2.Tang, R., & Liu, H. (2019). Identification of Temporal Characteristic Networks of Peripheral Blood Changes in Alzheimer's Disease Based on Weighted Gene Co-expression Network Analysis. *Frontiers in Aging Neuroscience*, 11(MAY).<https://doi.org/10.3389/fnagi.2019.00083>

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METHODS

