OMICS RESEARCH SYMPOSIUM

In silico analysis of Transcriptomics Profiling and Affected Biological pathways in Multiple sclerosis

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Introduction

Multiple sclerosis (MS) is a chronic autoimmune, inflammatory neurological disease that is widely associated with Grey and white matter degradation due to the demyelination of axons. Thus exposing the underlying causes of this condition can lead to a novel treatment approach for Multiple Sclerosis.

Given that characteristics the attempts to find the underlying causes of GML is poor. The main goal of our study was to identify the underlying reasons at the transcriptomics level for Grey Matter degeneration in Multiple sclerosis which is originally a White matter degenerative disease. Our main concern was to investigate the affected biological pathways due to the formation of lesions in Grey Matter after diagnosis of Multiple sclerosis.

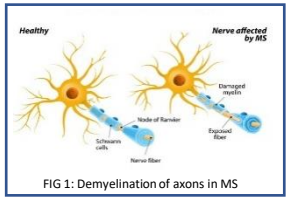
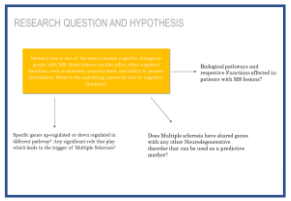


FIG 1: Demyelination of axons in MS



Methods

1. **Exploratory Analysis**

A. Principle Component Analysis (PCA) [FIG 3A to 3D]

2. **Comparative Analysis**

B. Differential Gene Expression (DGE)

The differential gene expression analysis was conducted using Welch's T-Test between Grey matter lesions and Control grey matter samples. As a result, 19677 genes (p.adj value <0.05, Fold change(>= ±1.5) were found to be significantly differentially expressed among these conditions based on differential gene expression analysis. It was observed that 438 of the genes were significantly upregulated and 1087 genes were downregulated in GML in comparison to CGM.

COMPARATIVE ANALYSIS

3. Heat Map and Hierarchical Clustering

H-clustering(Distance: Euclidean , Linkage: average) was performed to understand the clustering aspects of GML and Control samples based on their gene expression, especially after the selection of statistically significant genes, which is depicted in FIG 4

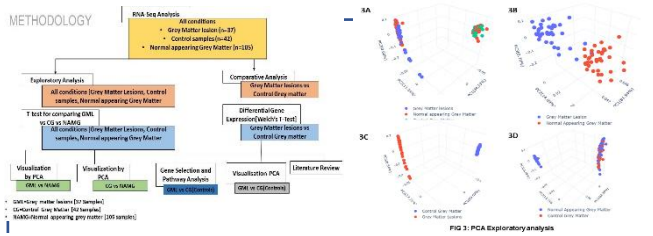


FIG 3: PCA Exploratory analysis

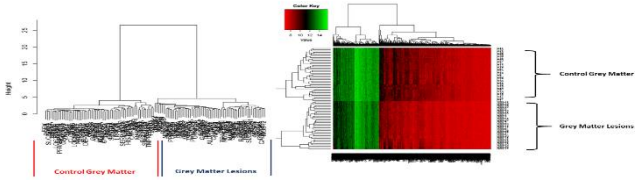


FIG: Hierarchical Clustering results as dendrograms. Red boxes clusters indicate the Control (Healthy) samples, and the blue one represents the clusters of the GML (lesions) samples.

FIG: Heat Map expressing the significantly differentially expressed genes

Results

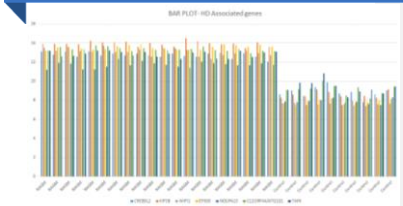


FIG: A Bar Plot representing the expression of 7 Huntington Disease associated genes in Multiple sclerosis Normal appearing Grey matter(without lesions) as well as Control (healthy) patients [Validation Data set]

It should be noted that in this study we have portrayed 7 genes (*CREB3L2, KIF5B, WIPI1, EP300, NDUFA1, ATG101, AND TAF4)* as the key features that may substantially contribute to loss of cognitive functions and progressive neurodegeneration involved in the MS pathogenesis.

People suffering from MS who might be potentially screened for HD can be looked upon for these genes in order to get signals for early onset of HD.

WIPI1, TAF4, and *CREB* protein-coding genes are the ones that are also associated with the early onset of Huntington's disease as well.

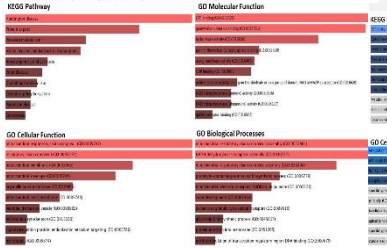


FIG: Gene ontology and KEGG Pathway analysis of Up regulated genes

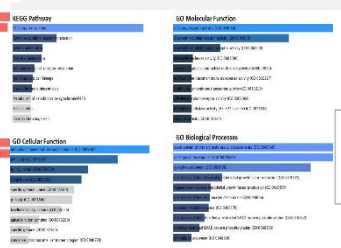


FIG: Gene ontology and KEGG Pathway analysis of Down regulated genes

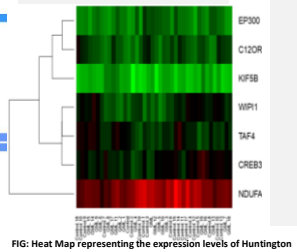


FIG: Heat Map representing the expression levels of Huntington Disease associated genes in Multiple sclerosis as well as Control (healthy) patients[Discovery Data Set]

Conclusions

This study shows that as per our KEGG Analysis pathways, the most affected pathway is the HD-associated pathway.

The associated genes with this pathway are *CREB3L2, KIF5B, WIPI1, EP300, NDUFA1, ATG101, AND TAF4*[as per Enrichr] as the key features that may substantially contribute to loss of cognitive functions in neurodegenerative disorders like Multiple sclerosis, Huntington's disease, and further on.

However, since our study was focused on samples of patients with multiple sclerosis, the involvement of certain genes that are also associated with HD is something of great importance.

In the future, intensive research is required to assess the precise effect of Multiple sclerosis on genes like *NDUAF1, EP300, and ATG101.* More comprehensive research is needed to support these findings stated above. As part of a future study, it would be interesting to understand the changes in MS pathogenesis and its effects on olfactory transduction, Development of Primary male sexual characteristics, GTP Binding protein, and Plasma Membrane component pathways.

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