Differentially Expressed Genes Analysis in Schizophrenia

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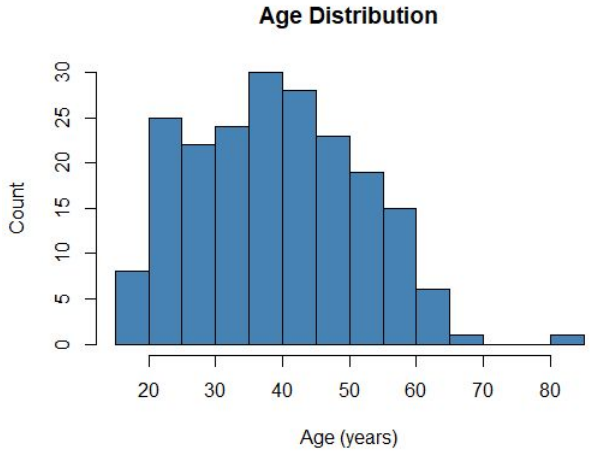
Dataset: GSE38484

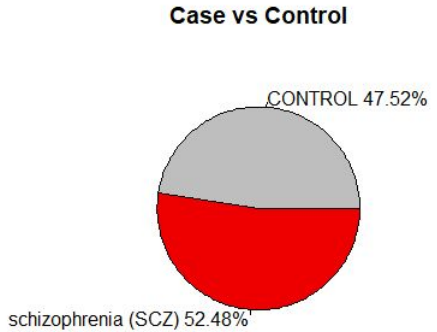
A gene co-expression network in whole blood of schizophrenia patients is independent of antipsychotic-use and enriched for brain-expressed genes

The **GSE38484** dataset, accessible through the **NCBI Gene Expression Omnibus** (GEO), comprises gene expression profiles from *whole blood samples* of individuals diagnosed with **schizophrenia** and healthy controls. Utilizing the *Illumina HumanHT-12 V3.0* expression bead chip platform, this dataset includes 202 samples—**106 from schizophrenia** patients and **96 from control** subjects. The study aimed to identify gene co-expression networks associated with schizophrenia, *independent of antipsychotic medication use*, and found enrichment for genes typically expressed in the brain.

The dataset data distribution

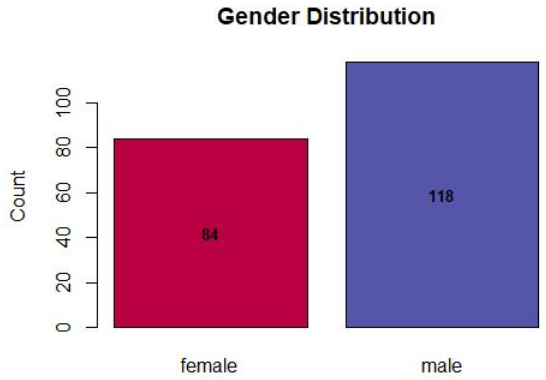


Age distribution over the entire dataset

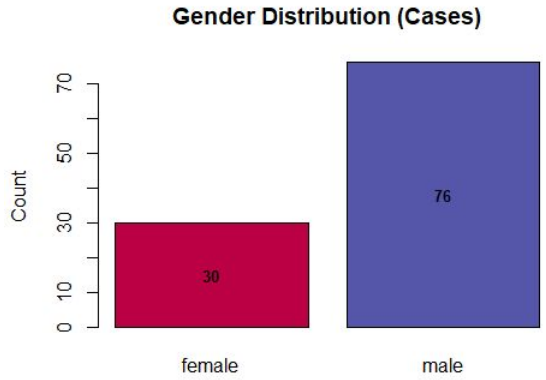


Control - Cases proportion in the dataset

The dataset data distribution



Gender distribution over the entire dataset



Gender distribution over the dataset schizophrenia cases

About the disease

Schizophrenia is a complex, **genetically influenced psychiatric disorder** that *affects how a person thinks, feels, and behaves*. It is primarily characterized by *positive symptoms* such as *hallucinations, delusions, and paranoia*, alongside *negative symptoms* like *social withdrawal* and *emotional blunting*, and *cognitive impairments* including *attention* and *memory deficits*. The disorder presents in various subtypes, one of which, **catatonic schizophrenia**, is marked by *abnormal motor activity*, ranging from complete immobility to excessive, purposeless movement. Globally, schizophrenia affects approximately **0.3–0.7% of the population,** with onset typically occurring in *early adulthood*. It is associated with **significantly reduced life expectancy**: males with schizophrenia live on average 14.5 years less, and females 13 years less, than the general population. Most patients in the ***GSE38484*** dataset are male and diagnosed with psychosis, reflecting both the demographic skew of the sample and the slightly higher prevalence and severity of the condition among men.

Dataset overview

Group	Accession	Title	Source name	Age	Gender	Status	Tissue
-	GSM943243	Human Whole blood RNA 38	CONTROL_whole blood	33	male	CONTROL	whole blood
-	GSM943244	Human Whole blood RNA 39	schizophrenia (SCZ)_whole blood	18	male	schizophrenia (SCZ)	whole blood
-	GSM943245	Human Whole blood RNA 40	schizophrenia (SCZ)_whole blood	24	female	schizophrenia (SCZ)	whole blood
-	GSM943246	Human Whole blood RNA 41	schizophrenia (SCZ)_whole blood	25	male	schizophrenia (SCZ)	whole blood
-	GSM943247	Human Whole blood RNA 42	schizophrenia (SCZ)_whole blood	49	male	schizophrenia (SCZ)	whole blood
-	GSM943248	Human Whole blood RNA 43	schizophrenia (SCZ)_whole blood	35	male	schizophrenia (SCZ)	whole blood
-	GSM943249	Human Whole blood RNA 44	CONTROL_whole blood	19	male	CONTROL	whole blood
-	GSM943250	Human Whole blood RNA 45	CONTROL_whole blood	53	male	CONTROL	whole blood
-	GSM943251	Human Whole blood RNA 46	CONTROL_whole blood	28	female	CONTROL	whole blood
-	GSM943252	Human Whole blood RNA 47	CONTROL_whole blood	31	female	CONTROL	whole blood
-	GSM943253	Human Whole blood RNA 48	CONTROL_whole blood	22	female	CONTROL	whole blood
-	GSM943254	Human Whole blood RNA 49	CONTROL_whole blood	38	female	CONTROL	whole blood
-	GSM943255	Human Whole blood RNA 50	CONTROL_whole blood	51	female	CONTROL	whole blood
-	GSM943256	Human Whole blood RNA 51	CONTROL_whole blood	34	female	CONTROL	whole blood
-	GSM943257	Human Whole blood RNA 52	schizophrenia (SCZ)_whole blood	29	female	schizophrenia (SCZ)	whole blood

Analysis overview

The analysis has been conducted through the avail of the **R** language and the **RStudio** development environment. The scripts can be found at this GitHub page.

Analysis steps:

1. Pre-processing
2. Filtering
3. Statistical significance
4. Principal Component Analysis
5. Functional Enrichment

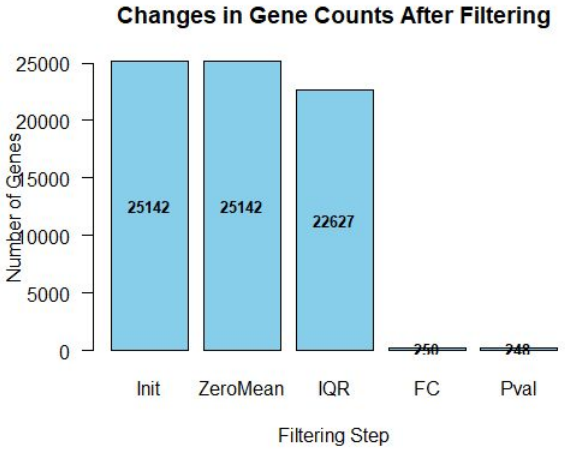
Pre-processing
Filtering
Statistical significance

To begin, the gene expression data was **pre-processed** by **removing** genes with **zero mean** expression and filtering out those with low variability using an **IQR threshold**. In the **filtering** phase, **log2 fold change** between *schizophrenia* and *control samples* has been calculated, keeping only genes with sufficient expression differences. Finally, **statistical significance** was assessed by performing **unpaired t-tests** and **adjusting p-values** using **FDR correction** to retain only the most confidently differentially expressed genes.

Pre-processing

To ensure a clean and interpretable dataset, genes with no detectable expression were removed. Then, low-variability genes, those unlikely to contribute with meaningful biological differences, were filtered out based on interquartile range (IQR), preserving only those with sufficient variation across samples.

The dataset appeared to be **already log transformed and normalized**. The number of initial genes was 25.142.

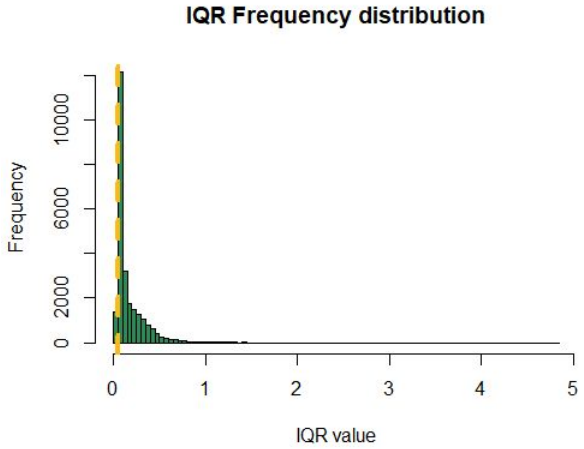


Number of genes after each filtering step

Pre-processing: IQR distribution

The **IQR frequency histogram** shows the distribution of **gene expression variability** across samples. The distribution is heavily **skewed** toward the origin, indicating that many genes had very low variation. These low-IQR genes were filtered out, helping retain only those with meaningful expression changes between schizophrenia cases and controls.

Genes with **IQR below the 10th percentile** of the IQR distribution were discarded, removing genes with low expression variability across all samples.

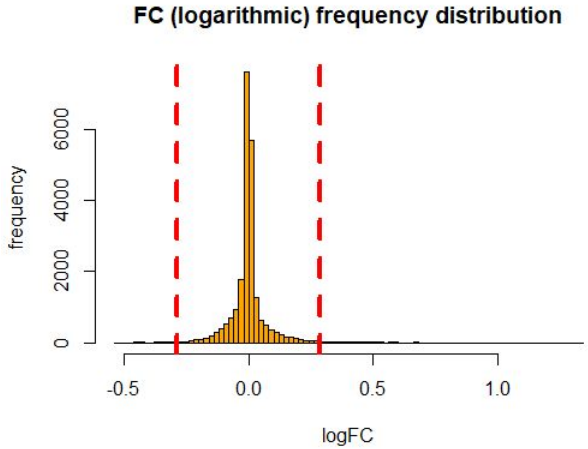


Compute : IQR = Q3 – Q1
Remove : variation ≤ quantile(IQR, 0.10)

Filtering: logFC distribution

This histogram displays the **distribution of log2 fold change (logFC)** values across all genes. The curve is centered around zero, indicating that *most genes have minimal differential expression* between schizophrenia and control samples.

The two red dashed vertical lines represent the filtering thresholds.
Genes falling between these thresholds are considered to have biologically insignificant changes and are excluded from further analysis. This ensures that retained genes show a meaningful degree of up- or down-regulation.



Compute: logFC = mean(case) − mean(control)
Filter out: | log2FC | < log2(1.22) ≈ 0.289

Statistical Significance: p-value

p-value Computation & Testing Method:

Each gene's expression difference was statistically tested using **Welch's t-test**, appropriate for the unpaired case-control dataset. This test assesses whether the average gene expression between schizophrenia and control groups differs significantly, providing p-values used for further filtering.

p-value Adjustment:

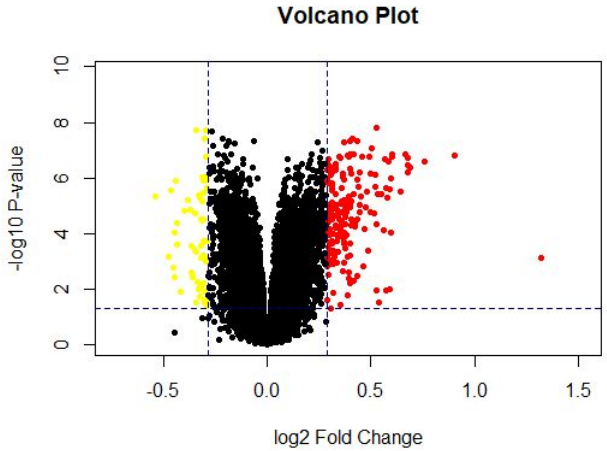
Raw p-values were adjusted using the **Benjamini-Hochberg False Discovery Rate** (FDR) method to correct for multiple testing. This step reduces the risk of false positives, ensuring that retained genes have statistically robust evidence of differential expression.

Filtering: volcano plot

Genes with an absolute fold change below a set threshold were filtered out, ensuring retention of genes with substantial differential expression.

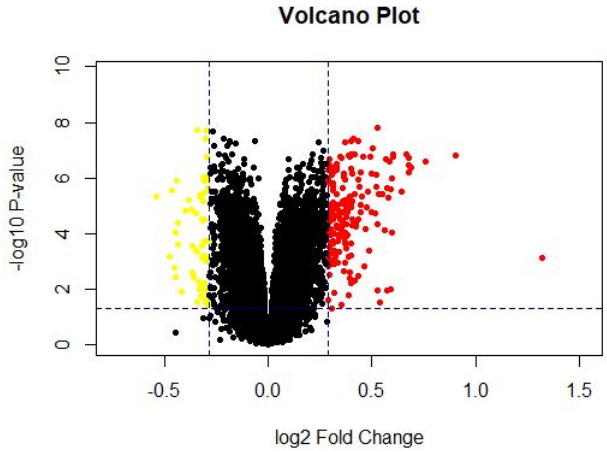
The log2 fold change (logFC) was computed for each gene as:

logFC = mean(case) – mean(control)

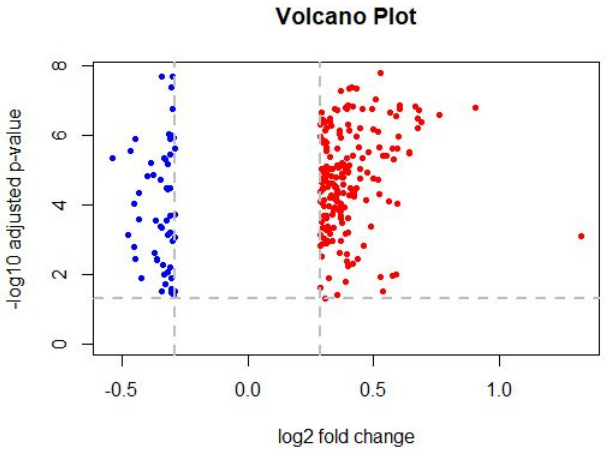


In black, points to be filtered out

Filtering: volcano plot



In black, points to be filtered out

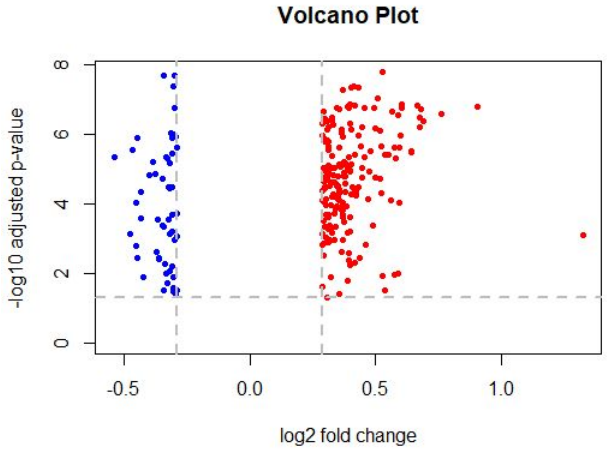


Plot after filtering

Filter criterion : $|\log2FC| < \log2(1.22) \approx 0.289$

Filtering: volcano plot

The volcano plot visualizes the trade-off between fold change and adjusted p-value. After filtering ~25,000 probes, about 250 highly significant genes remain. Upregulated genes are shown in red, downregulated in blue.



Plot after filtering

RPS4Y1 and NRGN

The gene **RPS4Y1** is the most significantly upregulated gene in schizophrenia samples. Its expression is clearly higher in patients compared to controls, with a noticeable shift in distribution and a very low adjusted p-value (0.00077), indicating strong differential expression.

On the other hand, **NRGN** is the most downregulated gene. Its average expression in schizophrenia patients is lower than in controls, and this difference is also highly statistically significant (adjusted p-value = 4.6e−06).

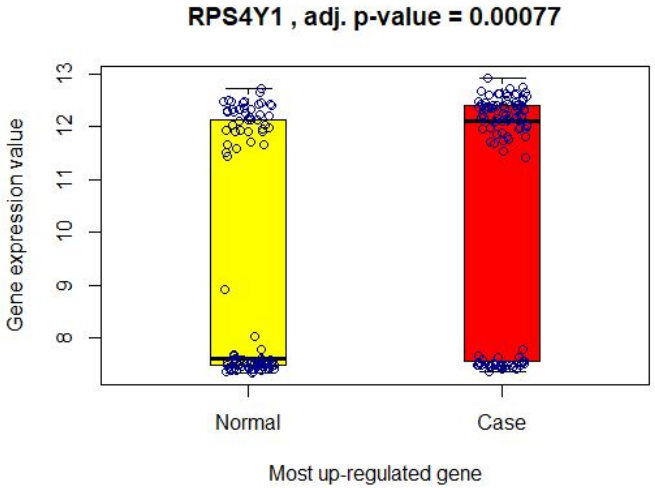
This contrast highlights how some genes are activated while others are suppressed in the disease state, pointing to complex molecular dysregulation.

This genes will be of interest for further analysis.

Boxplot of RPS4Y1 (Most Upregulated Gene)

Expression in the control group is centered near the first quartile, indicating lower and tightly clustered values. In contrast, the case group has expression values near the fourth quartile, showing consistent and elevated upregulation.

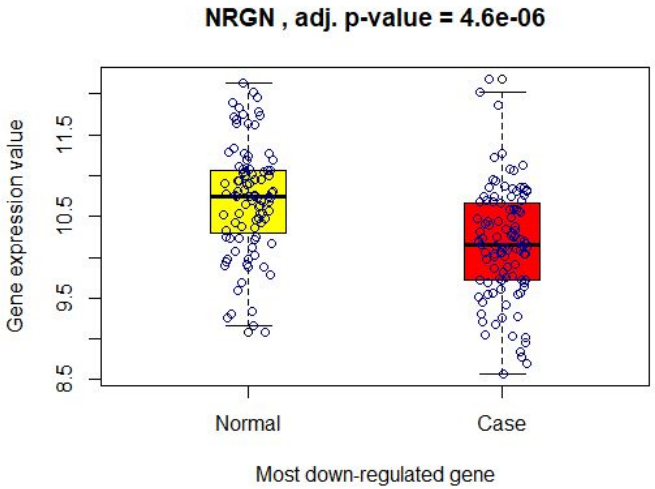
The small adjusted p-value confirms statistical significance after **FDR** correction, supporting **RPS4Y1** as a robust biomarker candidate.



The boxplot displays the expression levels of RPS4Y1, the most upregulated gene, across control (yellow) and schizophrenia (red) samples

Boxplot – NRGN (Most Downregulated Gene)

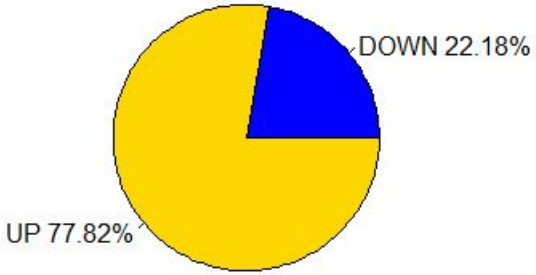
The overall shift in distribution is statistically robust, with an adjusted p-value of *4.6e–06*, confirming that the downregulation of NRGN is both substantial and significant. This suggests that **NRGN** might play a relevant role in the biological differences seen in the disorder due to downregulation.



The boxplot displays the expression levels of NRGN, the most downregulated gene, across control (yellow) and schizophrenia (red) samples

Regulation Proportions

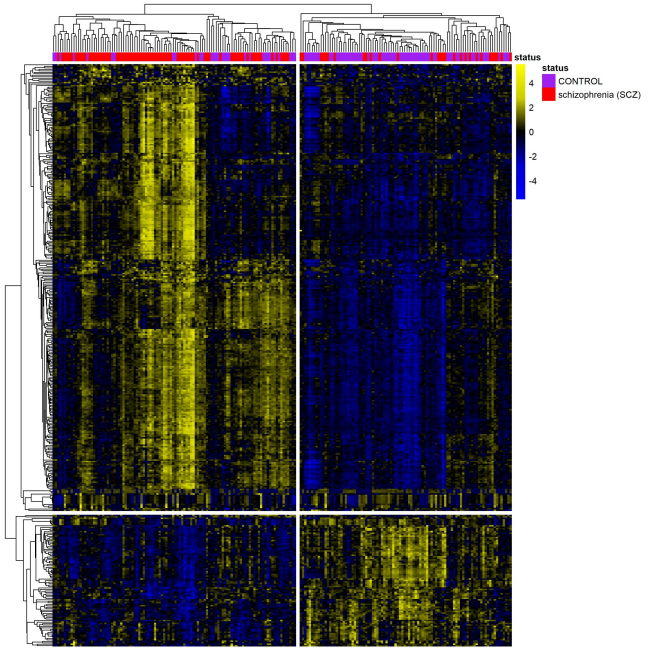
After all filtering steps, **77.82%** of the remaining differentially expressed genes are upregulated. This asymmetry could reflect systemic activation of certain pathways or compensatory mechanisms in schizophrenia.



Clustering: Heatmap of Differentially Expressed Genes

Rows represent genes, columns represent samples, with color-coded expression (blue: downregulated, yellow: upregulated).

This pattern supports the effectiveness of DEG filtering and highlights distinct expression profiles between the two conditions, providing strong evidence of biological differences.

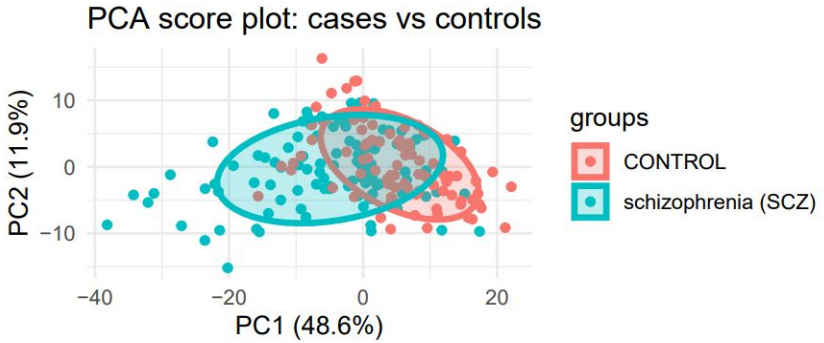


Principal Component Analysis

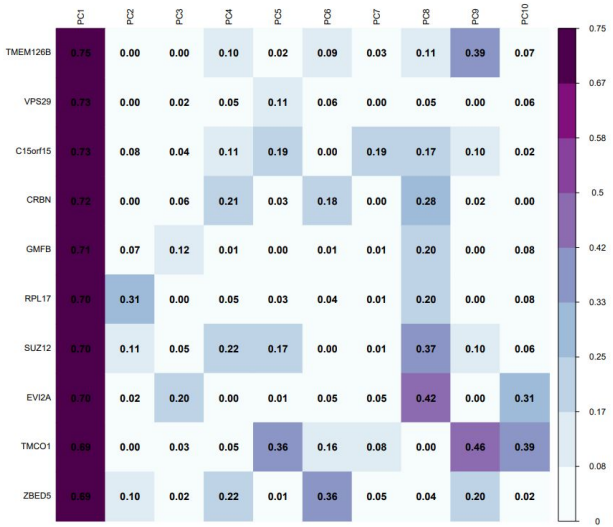
PCA was used to reduce the dimensionality of the expression matrix of differentially expressed genes, simplifying thousands of gene features into a few principal components. This should allow for visual separation of schizophrenia and control samples based on expression patterns.

PCA: Score plot

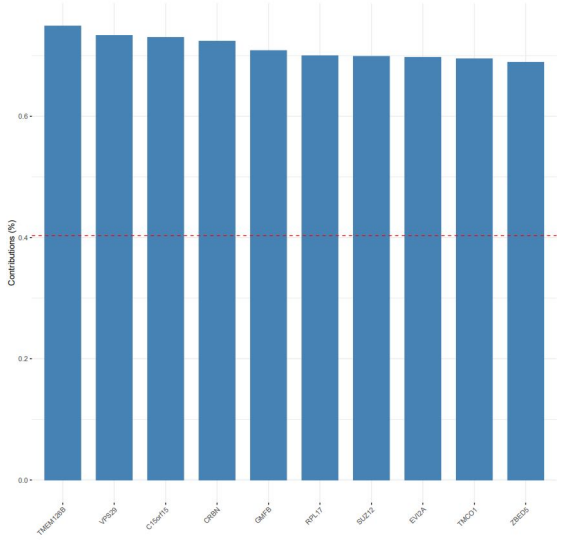
The plot shows the data projected onto the first and second principal components, which capture the largest variance in the dataset. However, the considerable overlap between schizophrenia cases and controls indicates that these components do not clearly separate the groups, limiting the interpretability of the data through PCA in this context.



PCA: Contributions



Contribution matrix



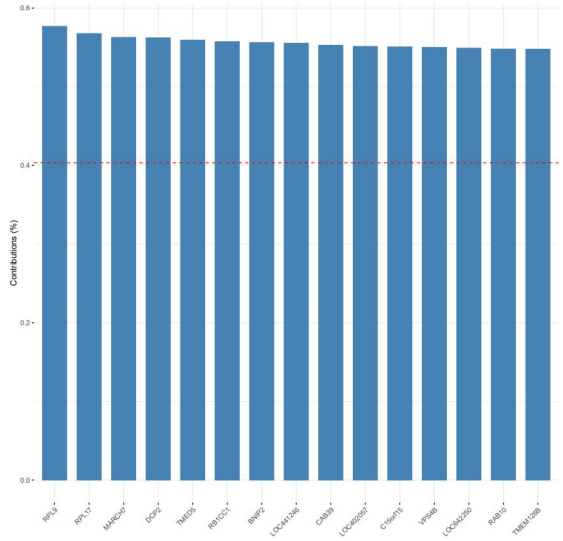
Top 10 contributors to PC1:
TMEM126B, VPS29, C15orf15, CRBN, GMFB, RPL17, SUZ12, EVI2A, TMCO1, ZBED5

PCA: Top contributions PC1 - PC3

Interesting genes:

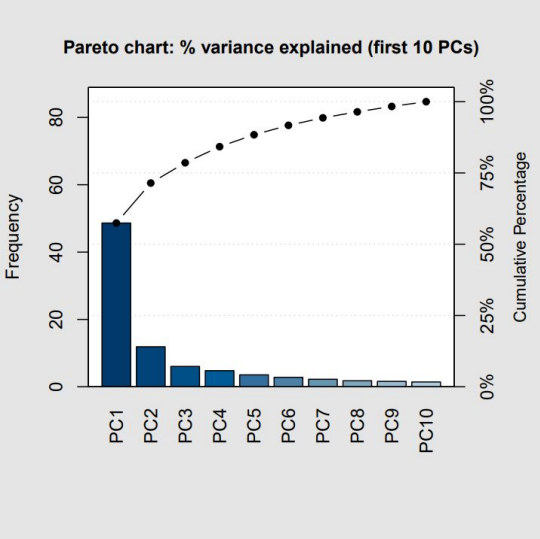
RPL17 & **RPL9**: ribosomal proteins, translation

RB1CC1: autophagy, neurogenesis

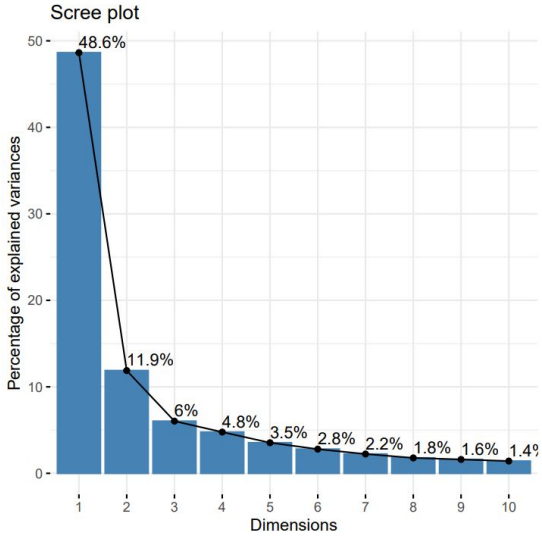


Top 10 contributors to PC1-PC3:
RPL9, RPL17, MARCH7, DCP2, TMED5, RB1CC1, BNIP2, LOC441246, CAB39, LOC402057, C15orf15, VPS4B, LOC642250, RAB10, TMEM126B,

PCA: Pareto chart & Scree plot



Pareto chart



Scree Plot

Functional Enrichment Analysis

In this study, functional enrichment analysis was performed to interpret the biological significance of differentially expressed genes (DEGs) identified in schizophrenia. Using the EnrichR R package, upregulated and downregulated gene sets were analyzed against curated databases to uncover overrepresented biological processes, molecular functions, pathways, and disease associations.

Functional Enrichment Analysis

Enrichment plots for both upregulated and downregulated gene sets have been generated to illustrate significant associations.

Parameters:

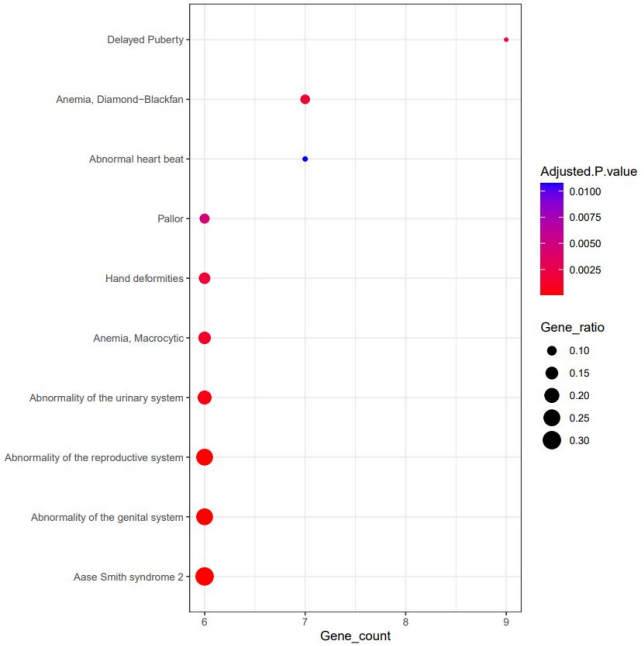
- Top Terms Displayed: 10
- P-value Threshold: 0.15

Databases Queried:

- DisGeNET
- GO Molecular Function
- GO Biological Process
- KEGG 2021 Human

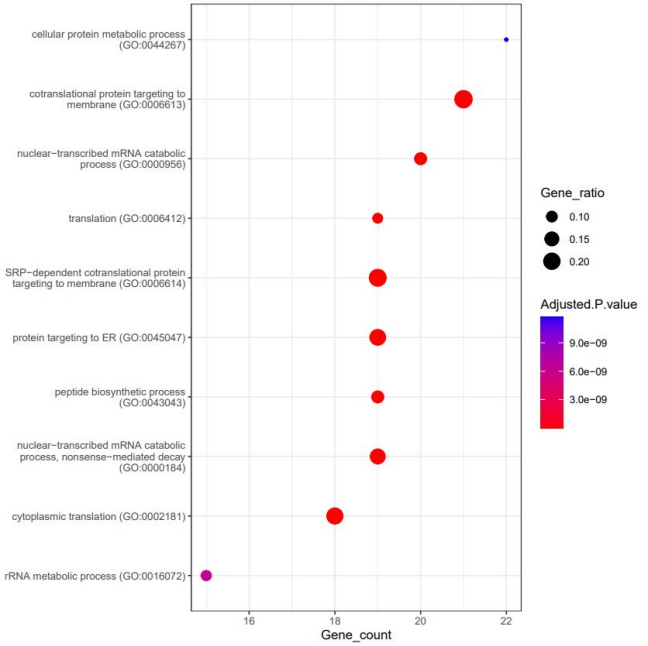
Upregulated DisGeNET Enrichment

The dotplot highlights that the most significant disease associations for upregulated genes include anemia and developmental disorders, suggesting that the same genes altered in schizophrenia may also play roles in blood and developmental conditions.



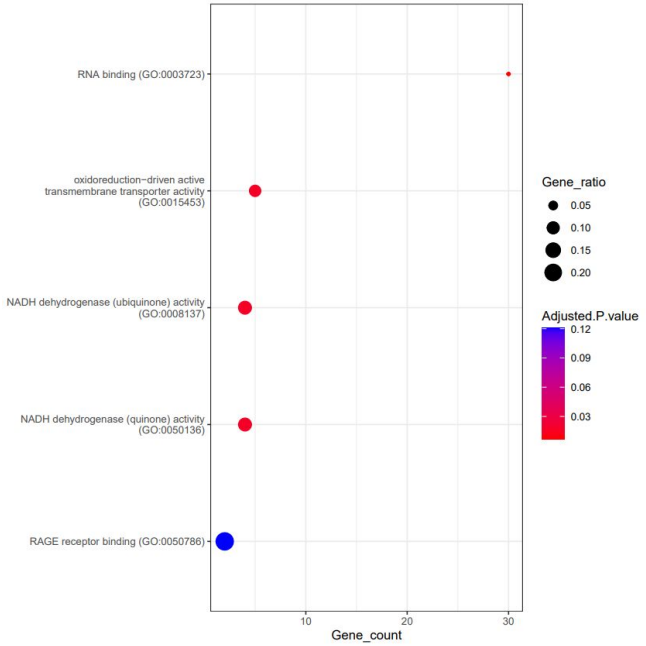
Upregulated GO Biological Process

Enrichment analysis reveals top processes related to protein synthesis and targeting, such as cotranslational transport to membranes and general translation, indicating a broad upregulation of the cell's protein-production in schizophrenia samples.



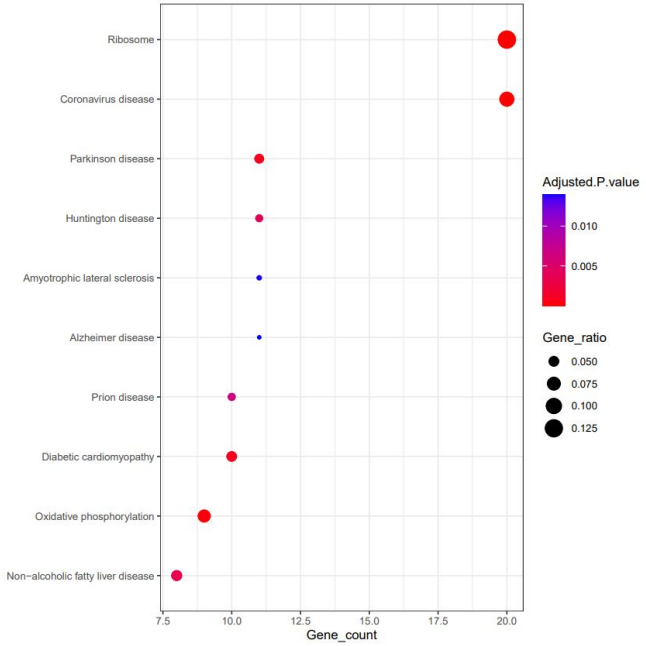
Upregulated GO Molecular Function

The GO-MF dotplot reveals **RNA-binding** as the most significant molecular function among upregulated genes, with many genes (including **RPS4Y1** and **RPL17**) contributing to RNA processing and stability. This suggests that post-transcriptional regulation and RNA metabolism may be key mechanisms affected in schizophrenia.



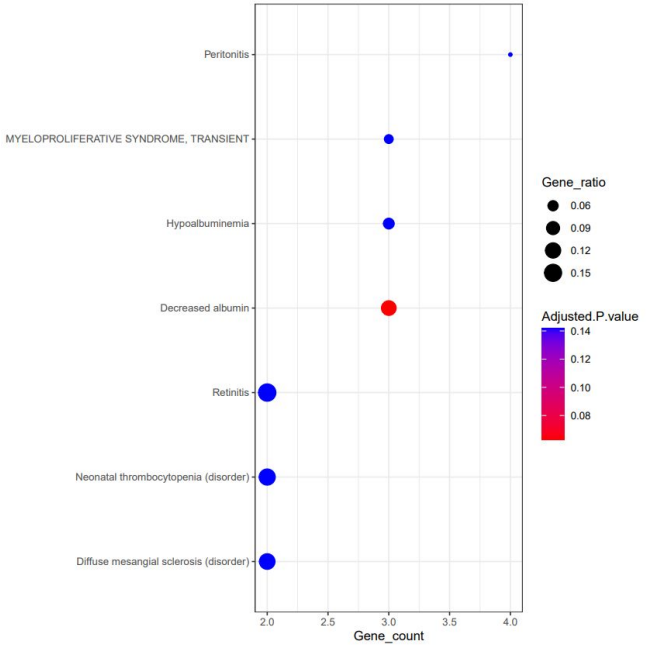
Upregulated KEGG Pathways

KEGG enrichment identifies the **ribosome pathway** as the most overrepresented, followed (by gene ratio) by coronavirus disease and oxidative phosphorylation. Again, the prominence of ribosomal genes confirms translation dysregulation.



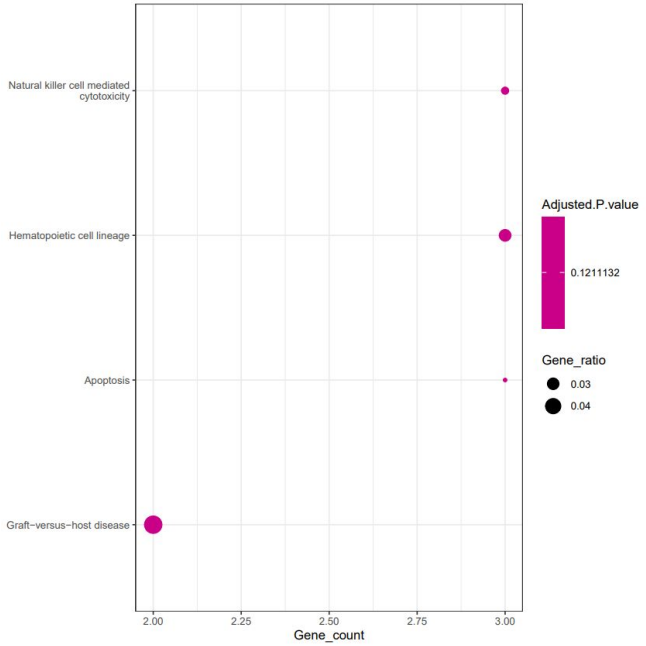
Downregulated DisGeNET Enrichment

Although fewer in number and with higher p-values, downregulated genes show associations with hypoalbuminemia and immune-related conditions such as peritonitis.



Downregulated KEGG Pathways

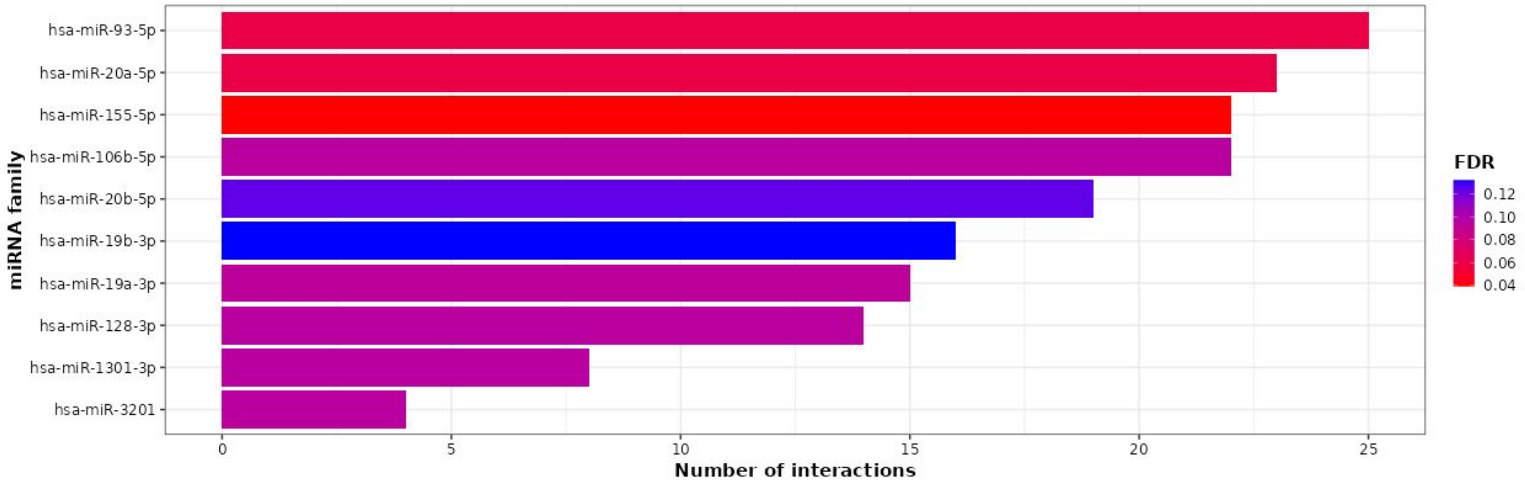
The dotplot for downregulated genes shows only pathways with **high adjusted p-values**, such as hematopoietic cell lineage and immune cell functions, indicating that there are **no robust, statistically significant pathway** enrichments among the downregulated gene set.



Further analysis: miRNA

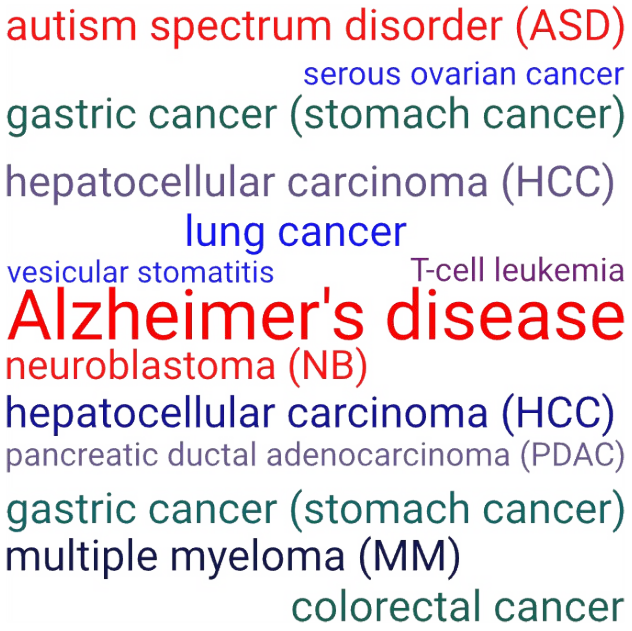
Upregulated and downregulated gene sets were analyzed using **mienturnet**, querying the **miRTarBase** database for experimentally validated **miRNA–target interactions**. This analysis identified the most significantly enriched **microRNAs** associated with each gene set. The results offer insights into the post-transcriptional regulatory landscape potentially involved in schizophrenia.

miRNA Analysis: upregulated genes

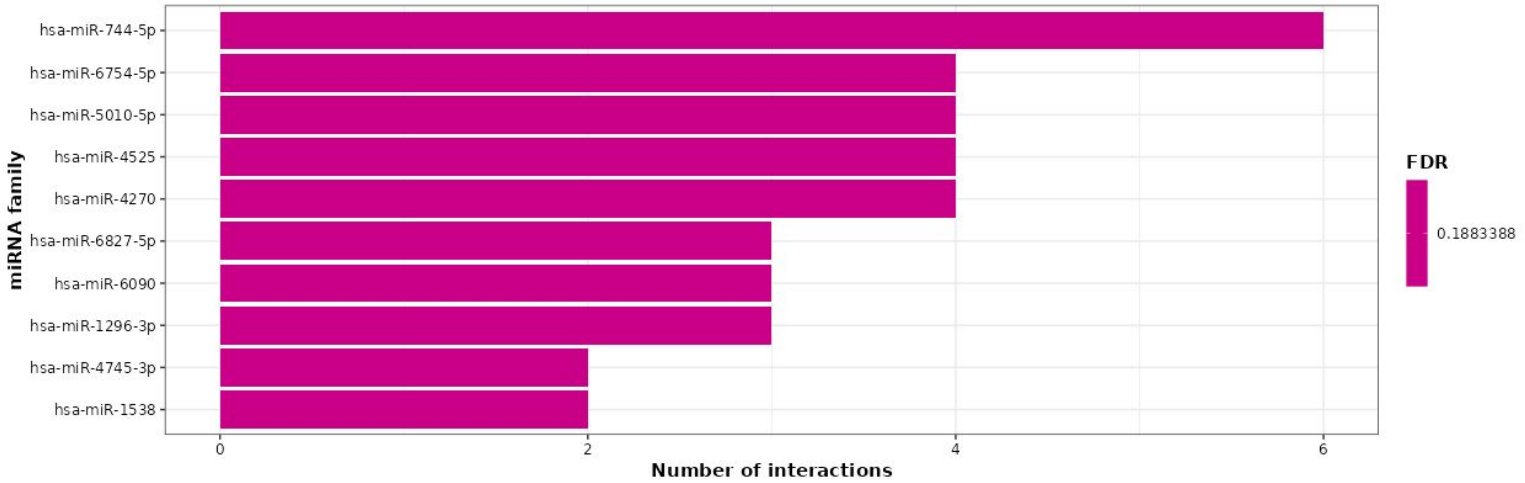


miRNA Analysis

On the right, a word cloud displays diseases associated with the microRNA hsa-miR-93-5p. Notably, this microRNA has been implicated in neuropsychiatric conditions such as autism spectrum disorder and Alzheimer's disease. These associations may suggest a potential link with schizophrenia or related neurological disorders.



miRNA Analysis: downregulated genes



Literature-based research

The main objective is to connect the top hints (e.g. NRGN, RPS4Y1) and key miRNAs (miR-93-5p, miR-155-5p, miR-128-3p) to published schizophrenia evidence.

Overview:

1. NRGN - Neurogranin
2. RPS4Y1
3. TMEM126B
4. RB1CC1
5. RPL17 and RPL9
6. hsa-miR-128-3p
7. hsa-miR-155-5p
8. Transcription factors

NRGN Down-Regulation and Synaptic Signaling

What it does:

Neurogranin (NRGN) is a postsynaptic calmodulin-binding protein essential for calcium-mediated signaling, **synaptic plasticity**, and **working-memory formation**.

Finding: Post-mortem studies of schizophrenia prefrontal cortex (Brodmann areas 9 and 32) demonstrate a **dramatic reduction in NRGN immunoreactivity** (–72% in layer III of area 9; –50% in layer V), without loss of neuron number, indicating loss of synaptic protein rather than cell death.

Ruano D et al., Association of the gene encoding neurogranin with schizophrenia in males. PMID: 17140601
Broadbelt K, Ramprasaud A, Jones LB, Evidence of altered neurogranin immunoreactivity in areas 9 and 32 of schizophrenic prefrontal cortex. PMID: 16797925

RPS4Y1 Up-regulation and Translational Dysregulation

What it does:

RPS4Y1 encodes a Y-chromosome–specific 40S ribosomal protein that participates in the initiation of mRNA translation; The increased expression of RPS4Y1 in males may reflect sex-specific changes in protein synthesis pathways in schizophrenia, potentially contributing to differences in disease manifestation between males and females.

"**RPS4Y1** and **DDX3Y** showed the strongest signal for shared familial risk among male twins"

Finding: Studies have identified **RPS4Y1** (along with DDX3Y) as significantly **upregulated** in **male individuals** with schizophrenia, suggesting a potential link between Y chromosome gene expression and the disorder.

Tiihonen J, Koskuvi M, Storvik M, Hyötyläinen I, Gao Y, Puttonen KA, et al.
"Sex-specific transcriptional and proteomic signatures in schizophrenia". Nature Communications. 2019, 10:3933.

TMEM126B and Mitochondrial Complex I

What it does:

TMEM126B is a mitochondrial protein essential for assembling Complex I, a key component in **cellular energy production**.

Finding: While TMEM126B mutations are known to cause **mitochondrial disorders**, there is currently no direct evidence linking TMEM126B expression to schizophrenia. *No findings correlating TMEM126B to schizophrenia have been found.*

RB1CC1 and Autophagy Dysregulation in Schizophrenia

What it does:

RB1CC1, is a crucial component of the ULK1 complex that initiates **autophagy**, a cellular process essential for maintaining neuronal health and function.

Alias: FIP200

Finding: A study identified a patient with schizophrenia who had an **extra copy of the RB1CC1 gene**, leading to its overexpression. This genetic change may disrupt normal autophagy processes.

Wen, J., Zellner, A., Braun, N.C. et al. "Loss of function of FIP200 in human pluripotent stem cell-derived neurons leads to axonal pathology and hyperactivity". *Transl Psychiatry 13, 143 (2023)*, 13:143.

RB1CC1: Autophagy

What is autophagy?

Autophagy, a term derived from the Greek words “auto,” meaning self, and “phagy,” meaning eating, is a biological process that allows cells to degrade and recycle their own components. It is a critical cellular mechanism for maintaining homeostasis and adapting to various stresses.

Possible correlation:

Disruption in autophagy due to **RB1CC1 overexpression** could contribute to the development of schizophrenia by affecting how brain cells maintain their health.

RPL17 and RPL9 Expression in Schizophrenia

What they do:

RPL17 and **RPL9** are genes that encode components of the 60S large ribosomal subunit, playing essential roles in **protein synthesis** within cells.

Finding: Research has identified **upregulation of RPL17** in individuals with schizophrenia, suggesting a potential link between ribosomal protein expression and the disorder. Additionally, studies indicate that dopamine-induced alterations in gene co-expression networks in schizophrenia are enriched for ribosomal proteins, including **RPL9**,highlighting the involvement of translation in the disease's pathogenesis.

Hori H, Nakamura S, Yoshida F, et al. Integrated profiling of phenotype and blood transcriptome for stress vulnerability and depression. J Psychiatr Res. 2018;104:202–210. PMID: 30103068
Song X, Liu Y, Pu J, et al. Transcriptomics Analysis Reveals Shared Pathways in Peripheral Blood Mononuclear Cells and Brain Tissues of Patients With Schizophrenia. Front Psychiatry. 2021;12:716722. PMID: 34630179

hsa-miR-128-3p in Synaptic Excitability

What it does (from the cited study):

A brain-enriched microRNA that shapes neuronal structure and firing properties by regulating the intellectual-disability gene PHF6. Blocking miR-128 causes excessive dendritic branching and reduces neuronal excitability.

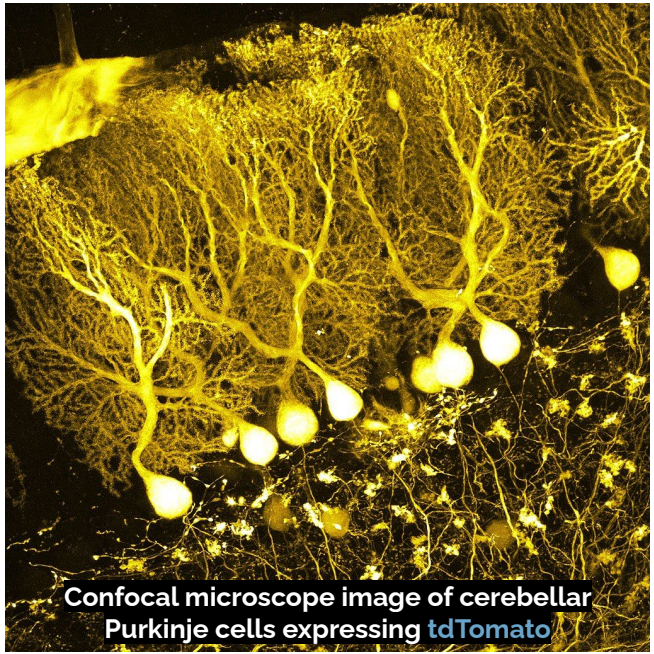
Finding: Prematurely increasing miR-128 levels in developing upper-layer cortical neurons leads to simpler dendritic arbors and a marked rise in intrinsic excitability (more action potentials evoked per current injection). Co-expression of PHF6 restores normal dendritic complexity and firing behavior, confirming PHF6 as the key downstream effector.

Franzoni E, Booker SA, Parthasarathy S, Rehfeld F, Grosser S, Srivatsa S, Fuchs HR, Tarabykin V, Vida I, Wulczyn FG. miR-128 regulates neuronal migration, outgrowth and intrinsic excitability via the intellectual disability gene Phf6. Elife. 2015 Jan 3;4:e04263. doi: 10.7554/eLife.04263. PMID: 25556700; PMCID: PMC4337614.

hsa-miR-128-3p in Synaptic Excitability

"Within the upper layers, premature miR-128 expression reduces the complexity of dendritic arborization, associated with altered electrophysiological properties."

Franzoni E, Booker SA, Parthasarathy S, Rehfeld F, Grosser S, Srivatsa S, Fuchs HR, Tarabykin V, Vida I, Wulczyn FG. miR-128 regulates neuronal migration, outgrowth and intrinsic excitability via the intellectual disability gene Phf6. Elife. 2015 Jan 3;4:e04263. doi: 10.7554/eLife.04263. PMID: 25556700; PMCID: PMC4337614.



hsa-miR-155-5p

What it is: A pro-inflammatory microRNA highly expressed in immune cells (macrophages, microglia), known to regulate cytokine signaling via targets like SOCS1 and SHIP1.

Finding: In a case–control study of 225 paranoid schizophrenia patients vs. 225 matched healthy controls, peripheral blood miR-155 levels were significantly higher in patients (mean fold-change = 1.8; $p < 0.01$)

"miR-155 expression was significantly elevated in peripheral blood of paranoid schizophrenia patients compared to healthy controls."

Ghazaryan H, Zakharyan R, Petrek M et al. "Expression of micro-RNAs miR-31, miR-146a, miR-181c and miR-155 and their target gene IL-2 are altered in schizophrenia: a case-control study". F1000Research 2019, 8:2077

Transcription factors

Transcription factors (**COMMD6**, **CYP1B1**, **FOXN2**, **PSMA6**, **S100A12**, **S100A8**, **TAX1BP1**, **ZNF281**, **ZNF683**) were retrieved from our DEG list via **BioMart**. A targeted PubMed search shows that **S100A8**and **S100A9** are consistently reported as *up-regulated neuroinflammatory markers in schizophrenia* post-mortem brain and peripheral fluids. **S100A12** supports the hypothesis that the disorder has an immunological and neuroinflammatory component in its etiology**. No PubMed-indexed associations with schizophrenia were found for CYP1B1, FOXN2, TAX1BP1, ZNF281, PSMA6, COMMD6 or ZNF683**, indicating limited evidence for their involvement in the disorder.

Sharma G, Malik A, Tripathi S, Deshmukh V, Patil A. Gene expression analysis of Schizophrenia. Bioinformation. 2024 Nov 5;20(11):1441-1446. doi: 10.6026/9732063002001441. PMID: 40162448; PMCID: PMC11953522.
Gardiner EJ, Cairns MJ, Liu B, Beveridge NJ, Carr V, Kelly B, Scott RJ, Tooney PA. Gene expression analysis reveals schizophrenia-associated dysregulation of immune pathways in peripheral blood mononuclear cells. J Psychiatr Res. 2013 Apr;47(4):425-37. doi: 10.1016/j.jpsychires.2012.11.007. Epub 2012 Dec 4. PMID: 23218666; PMCID: PMC7094548.

Conclusions

The observed up-regulation of ribosomal genes (RPS4Y1, RPL17/RPL9) alongside the down-regulation of NRGN in peripheral blood mirrors published findings of enhanced translational activity and synaptic protein loss in schizophrenia. Likewise, increased miR-155-5p and decreased miR-128-3p levels reflect the neuroinflammatory and excitation–inhibition imbalances reported in CNS studies, confirming that our DEG and miRNA signatures are consistent with existing schizophrenia literature.

Overall Differential Expression Profile

The analysis of **GSE38484** whole-blood samples revealed a clear pattern of gene regulation in schizophrenia. The most pronounced **up-regulation** of **RPS4Y1** and ribosomal proteins **RPL17/RPL9** suggests a systemic boost in translation, particularly in male patients, given RPS4Y1's Y-linked specificity. In contrast, **NRGN** emerged as the top **down-regulated** transcript, echoing post-mortem findings of synaptic protein loss in prefrontal cortex layers III and V. These opposing extremes, ribosomal activation versus neurogranin suppression, underscore a complex peripheral mirror of central synaptic dysregulation.

Pathway Enrichment & miRNA Regulatory Clues

Functional enrichment pointed the **ribosome** as the most **over-represented KEGG pathway** among up-regulated genes, with **GO terms** dominated by **RNA binding and translation initiation**, an indication that translational dysregulation might be a robust blood signature for schizophrenia. *Down-regulated genes failed to generate statistically significant pathway hits*. On the post-transcriptional front, **miR-155-5p** and **miR-128-3p** surfaced as **key miRNAs targeting inflammation and synaptic-plasticity** transcripts. While miR-155's peripheral elevation aligns with an activated immune phenotype, the down-regulation of miR-128 hints at disrupted excitation–inhibition balance, both recapitulating central nervous system observations .

Interpretation, Limitations & Next Steps

The concordance between **NRGN down-regulation** and **known synaptic deficits** validates our blood-based approach as a proxy for brain pathology. Although explored in the **RPS4Y1** analysis, the pronounced ribosomal signature raises questions about **sex-specific translation effects,** indicating the need for deeper exploration. However, **PCA** revealed substantial overlap between cases and controls, indicating that peripheral expression patterns alone may lack sufficient discriminative power for diagnostics. Ultimately, combining top gene hits (NRGN, RPS4Y1) with miRNA regulators (miR-155, miR-128) into a multi-omic panel could enhance both mechanistic insights and clinical utility.

References

- **Papers:**
  - Ruano D, Aulchenko YS, Macedo A, Soares MJ, Valente J, Azevedo MH, Hutz MH, Gama CS, Lobato MI, Belmonte-de-Abreu P, Goodman AB, Pato C, Heutink P, Palha JA. Association of the gene encoding neurogranin with schizophrenia in males. J Psychiatr Res. 2008 Jan;42(2):125-33. doi: 10.1016/j.jpsychires.2006.10.008. Epub 2006 Nov 30. PMID: 17140601
  - Broadbelt K, Ramprasaud A, Jones LB. Evidence of altered neurogranin immunoreactivity in areas 9 and 32 of schizophrenic prefrontal cortex. Schizophr Res. 2006 Oct;87(1-3):6-14. doi: 10.1016/j.schres.2006.04.028. Epub 2006 Jun 22. PMID: 16797925
  - Tiihonen, J., Koskuvi, M., Storvik, M. et al. Sex-specific transcriptional and proteomic signatures in schizophrenia. Nat Commun 10, 3933 (2019). https://doi.org/10.1038/s41467-019-11797-3
  - Wen, J., Zellner, A., Braun, N.C. et al. Loss of function of FIP200 in human pluripotent stem cell-derived neurons leads to axonal pathology and hyperactivity. Transl Psychiatry 13, 143 (2023). https://doi.org/10.1038/s41398-023-02432-3
  - Hori H, Nakamura S, Yoshida F, Teraishi T, Sasayama D, Ota M, Hattori K, Kim Y, Higuchi T, Kunugi H. Integrated profiling of phenotype and blood transcriptome for stress vulnerability and depression. J Psychiatr Res. 2018 Sep;104:202-210. doi: 10.1016/j.jpsychires.2018.08.010. Epub 2018 Aug 6. PMID: 30103068.

References

- **Papers:**
  - Song X, Liu Y, Pu J, Gui S, Zhong X, Chen X, Chen W, Chen X, Chen Y, Wang H, Cheng K, Zhao L, Xie P. Transcriptomics Analysis Reveals Shared Pathways in Peripheral Blood Mononuclear Cells and Brain Tissues of Patients With Schizophrenia. Front Psychiatry. 2021 Sep 22;12:716722. doi: 10.3389/fpsyt.2021.716722. PMID: 34630179; PMCID: PMC8492981.
  - Ghazaryan H, Zakharyan R, Petrek M et al. Expression of micro-RNAs miR-31, miR-146a, miR-181c and miR-155 and their target gene IL-2 are altered in schizophrenia: a case-control study [version 1; peer review: 1 approved, 1 approved with reservations]. F1000Research 2019, 8:2077 (https://doi.org/10.12688/f1000research.19900.1
  - Franzoni E, Booker SA, Parthasarathy S, Rehfeld F, Grosser S, Srivatsa S, Fuchs HR, Tarabykin V, Vida I, Wulczyn FG. miR-128 regulates neuronal migration, outgrowth and intrinsic excitability via the intellectual disability gene Phf6. Elife. 2015 Jan 3;4:e04263. doi: 10.7554/eLife.04263. PMID: 25556700; PMCID: PMC4337614.
  - Sharma G, Malik A, Tripathi S, Deshmukh V, Patil A. Gene expression analysis of Schizophrenia. Bioinformation. 2024 Nov 5;20(11):1441-1446. doi: 10.6026/9732063002001441. PMID: 40162448; PMCID: PMC11953522.
  - Gardiner EJ, Cairns MJ, Liu B, Beveridge NJ, Carr V, Kelly B, Scott RJ, Tooney PA. Gene expression analysis reveals schizophrenia-associated dysregulation of immune pathways in peripheral blood mononuclear cells. J Psychiatr Res. 2013 Apr;47(4):425-37. doi: 10.1016/j.jpsychires.2012.11.007. Epub 2012 Dec 4. PMID: 23218666; PMCID: PMC7094548.

References

- **Sources:**
  - https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE38484
  - https://www.ncbi.nlm.nih.gov/
  - https://www.mirbase.org/
  - http://userver.bio.uniroma1.it/apps/mienturnet/
- **Images:**
  - https://commons.wikimedia.org/wiki/File:All_that_glitters_in_the_brain.jpg
- **Slides:**
  - https://github.com/pietro-nardelli/sapienza-ppt-template

Thank you for the attention!