Cross-Tissue Biomarkers for Hepatitis B Virus-Related Hepatocellular Carcinoma

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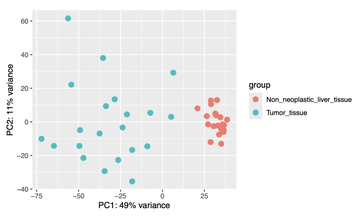
Introduction

Hepatitis B Virus (HBV) infection is a leading cause of hepatocellular carcinoma (HCC) worldwide. The development of cross-tissue biomarkers enables non-invasive diagnostics for early detection of HBV-related HCC. This study aims to identify gene expression patterns in blood and liver tissues to explore potential biomarkers detectable in blood, reducing the need for liver biopsies.

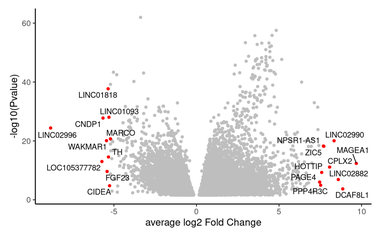
Methodology

- **Data Collection**: RNA-seq data from public sources, including healthy, HBV-infected, and HBV-HCC samples.
- **Transcript Quantification**: Kallisto was used for pseudo-alignment and transcript abundance estimation.
- **Differential Expression**: DESeq2 identified differentially expressed genes (DEGs) in blood and liver.
- **Visualization**: PCA and clustering heatmaps compared gene expression patterns across tissues.
- **Functional Enrichment**: ClusterProfiler analyzed DEGs for pathways linked to immune response and metabolism.
- **Cross-Tissue Comparison**: Identified biomarkers consistently expressed in both blood and liver for non-invasive HBV-HCC detection.

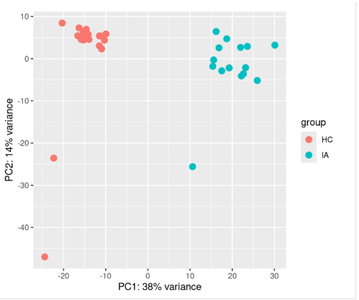
Visualization



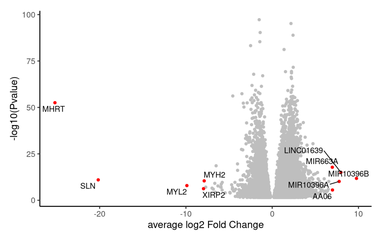
(a) PCA for Dataset 1



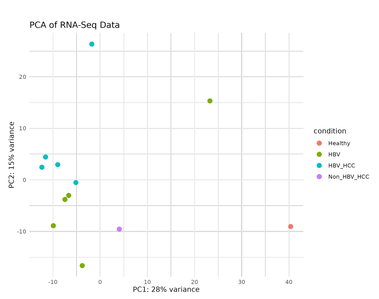
(b) Volcano Plot for Dataset 1



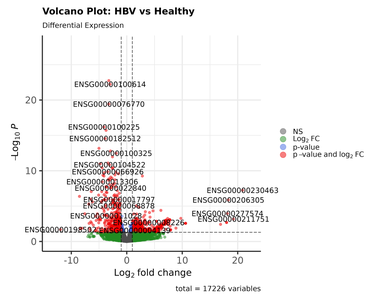
(c) PCA for Dataset 2



(d) Volcano Plot for Dataset 2



(e) PCA for Dataset 3

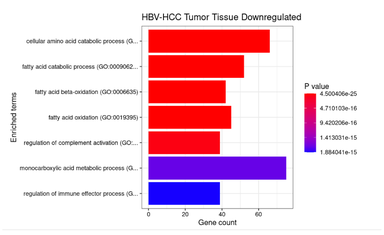


(f) Volcano Plot for Dataset 3

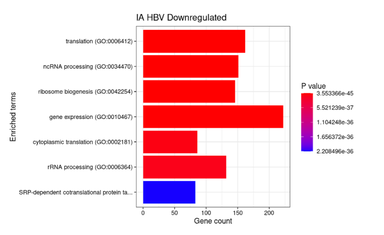
Figure: PCA plots and Volcano Plot for each of the three datasets, demonstrating gene expression patterns.

In these PCA and Volcano plots, we observe unique gene expression patterns across the datasets, indicating significant differential expression and clustering under varied conditions. This suggests potential key genes and molecular pathways that we plan to explore further.

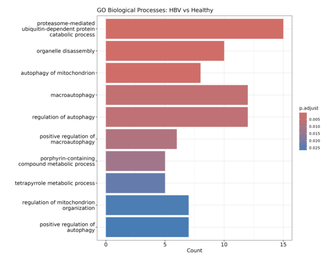
Functional Enrichment



(a) Enrichment for Dataset 1



(b) Enrichment for Dataset 2

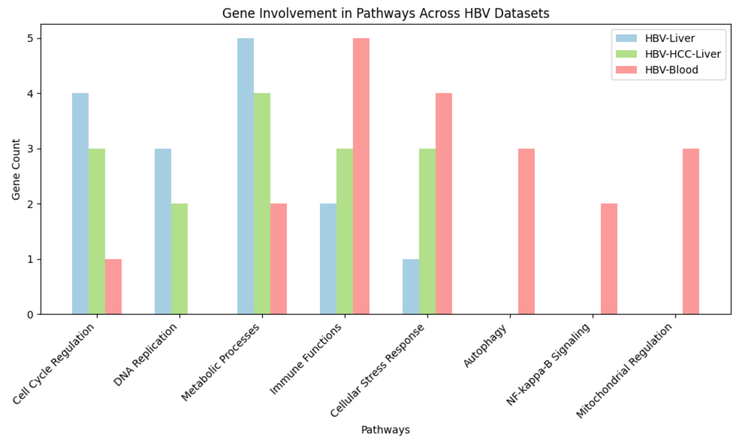


(c) Enrichment for Dataset 3

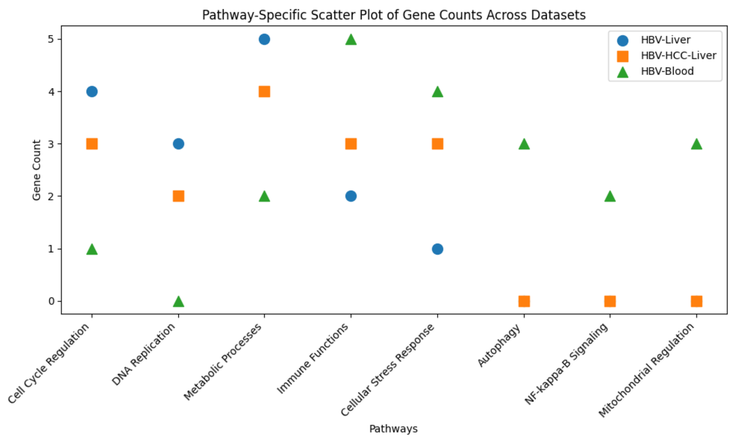
Figure: Functional enrichment plots showing key pathways for each dataset.

Pathway Visualization

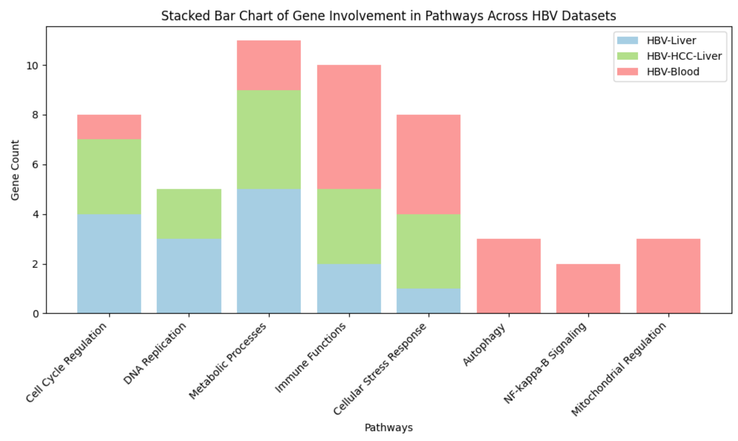
This section presents visualizations of common pathways across blood and liver datasets, focusing on immune response, metabolism, and cell proliferation. These visualizations highlight the potential for cross-tissue biomarkers in non-invasive HBV-HCC detection.



(a) Pathway Visualization - Plot 1



(b) Pathway Visualization - Plot 2



(c) Pathway Visualization - Plot 2

Figure: Visualizations highlighting common pathways across blood and liver datasets.

Conclusion

Findings suggest that immune and stress response pathways in blood samples mirror liver tissue, indicating that blood-based biomarkers for HBV-HCC are feasible. This cross-tissue consistency provides a basis for non-invasive diagnostics for early liver cancer detection.

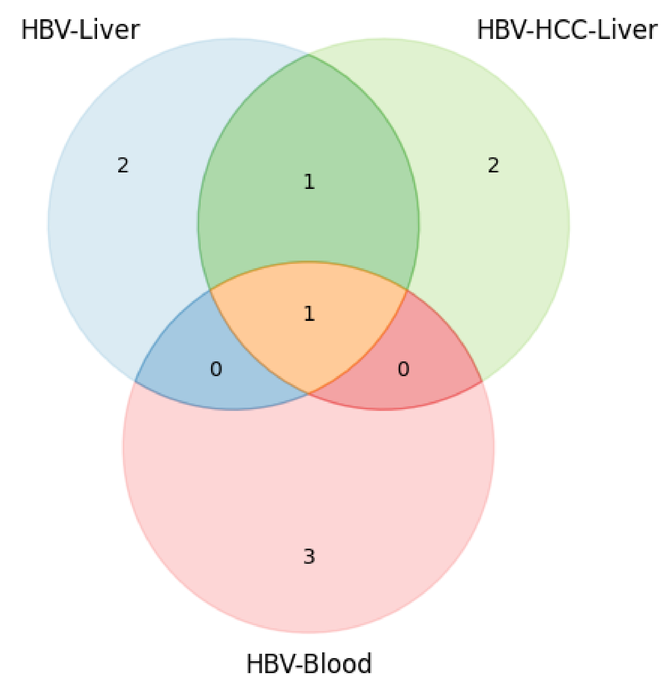


Figure: Illustrative representation of blood-based biomarkers for HBV-HCC detection.

Limitations

- Potential batch effects due to multi-source data integration.
- Kallisto may not capture novel transcripts absent from the reference transcriptome.
- Further validation is required across larger, diverse patient cohorts.

Applications

- **Non-Invasive Diagnostic Tool**: Potential for blood-based tests as alternatives to liver biopsies for early HBV-HCC detection.
- **Public Health Screening**: Screening programs could leverage these biomarkers in HBV-prevalent regions.
- **Personalized Medicine**: Biomarkers can guide individualized treatment based on gene expression profiles.
- **Research in HBV-HCC Pathogenesis**: Insights into disease progression and potential therapeutic targets.

Data Availability

The RNA-seq data used in this study is publicly available from NCBI Gene Expression Omnibus (GEO)].

- Dataset 1 : `https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE94660`
- Dataset 2 : `https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE230397`
- Dataset 3 : `https://www.ncbi.nlm.nih geo/query/acc.cgi?acc=GSE236281`