

Dysregulated miRNAs Profile in Triple-Negative Breast Cancer: An in Silico Analysis

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Abstract

Background: Breast cancer remains the most prevalent malignancy among women globally, ranking as the second leading cause of cancer-related mortality. Approximately 70%-80% of patients with early-stage, non-metastatic disease are curable. Triple-negative breast cancer (TNBC) is characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2 expression. Contemporary therapeutic strategies in breast cancer are geared towards the individualization of treatment, including both de-escalation and escalation based on tumor biology and early therapeutic response. This study aims to identify significant miRNAs and genes that are dysregulated in TNBC, contributing to its pathogenesis.

Method: The dataset GSE38167 was retrieved from the Gene Expression Omnibus (GEO). Differential expression analysis of miRNAs between control and TNBC patient samples across various stages was conducted using R packages (GEOquery, limma, BiocGenerics, affy, and oligo). The multi-MiR package identified target genes of differentially expressed miRNAs (DEmiRNAs). A protein-protein interaction (PPI) network highlighted vital target genes, followed by gene ontology (GO) and KEGG pathway analyses to elucidate potential gene functions.

Results: Differential expression analysis revealed significant miRNAs with $|\log_2FC| > 2$ and adjusted $P < 0.05$. Upregulated miRNAs included hsa-miR-135b, hsa-miR-183, hsa-miR-18b, hsa-miR-96, and hsa-miR-7; downregulated miRNAs comprised hsa-miR-377, hsa-miR-376a, hsa-miR-145, hsa-miR-451, and hsa-miR-376c. Target genes for these DEmiRNAs were identified, with ten hub genes (MYC, HIF1A, JUN, FN1, CD44, ERBB2, MMP2, CCN2, THBS1, AXL) emerging from the PPI network. GO analysis indicated enrichment in positive regulation of DNA-templated transcription, nucleus, and RNA binding. KEGG pathway analysis identified focal adhesion as a significant enrichment pathway.

Conclusion: This study provides valuable insights into the regulatory mechanisms of miRNAs and their target genes in TNBC, offering a foundation for further research into the molecular underpinnings of this aggressive cancer subtype.

Keywords: Triple-negative breast cancer, Gene Expression Omnibus dataset, DEmiRNAs, Target genes

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