Transcriptomic Analysis of Differentially Expressed Genes in Triple-Negative Breast Cancer: Insights into Immune Cell Infiltration and the Tumor Microenvironment

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Background

Triple-negative breast cancer (TNBC) accounts for approximately 15% of breast cancers and is marked by aggressive behavior, high recurrence, and limited therapeutic options due to the absence of hormone receptors and HER2 expression.

Its molecular heterogeneity and immune-rich microenvironment influence prognosis and therapy response.

This study applied an in silico approach to identify gene expression signatures and immune-related markers distinguishing TNBC from HER2-positive and hormone receptor–positive subtypes.

Methods and Materials

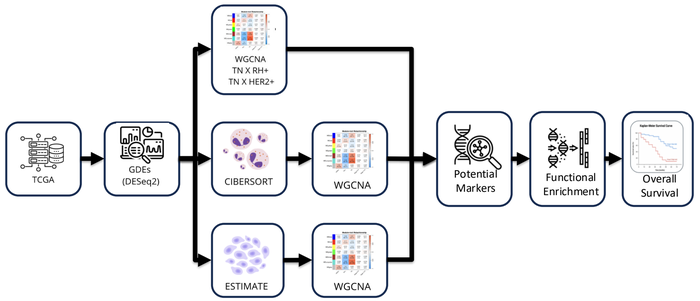


Figure 1. Schematic overview of the bioinformatic workflow. Transcriptomic (RNA-Seq) and clinical data from the *TCGA-BRCA cohort* were analyzed using an integrated approach. Differentially expressed genes were identified with *DESeq2*, immune and stromal scores estimated by *CIBERSORT* and *ESTIMATE*, and co-expression modules built with *WGCNA* correlated with these features. Functional enrichment and survival analyses were then applied to highlight potential prognostic markers in TNBC.

A total of 1,097 breast cancer samples from the TCGA-BRCA cohort were analyzed, comprising 162 triple-negative, 180 HER2-positive, and 755 hormone receptor-positive tumors. Clinical and transcriptomic data were integrated for subsequent analyses using DESeq2, CIBERSORT, ESTIMATE, and WGCNA.

Results

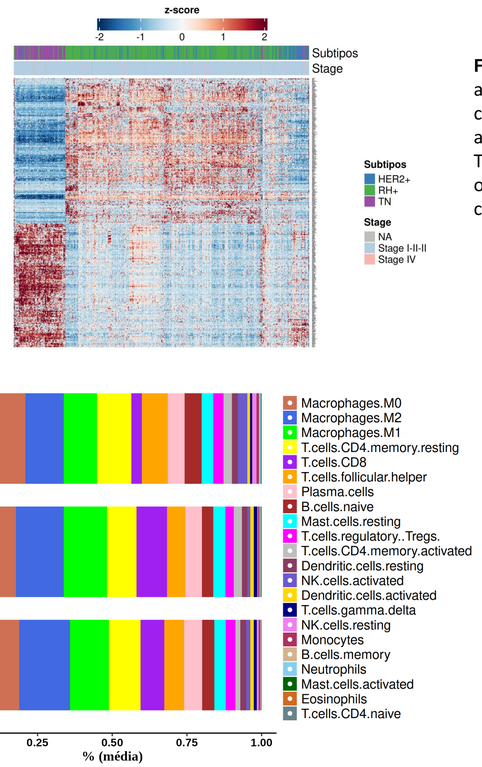


Figure 3. Relative immune cell fractions estimated by *CIBERSORT* across subtypes. TNBC shows higher levels of activated CD8⁺ T cells, M1 macrophages, and plasma cells, along with increased immune and stromal components, indicating an active tumor microenvironment.

Figure 2. Heatmap of differentially expressed genes (DEGs) among TNBC, HR+, and HER2+ subtypes in the TCGA-BRCA cohort. *DESeq2* identified 1,042 DEGs between TNBC and HR+ and 893 between TNBC and HER2+ (FDR < 0.05; $|\log_2 FC| > 1$). TNBC displays a distinct immune-enriched profile with activation of interferon signaling, cytokine interaction, and immune checkpoint pathways.

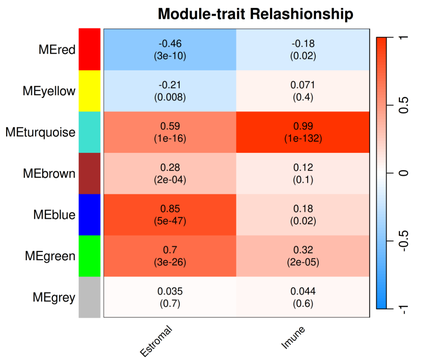


Figure 4. Correlation heatmap between *WGCNA* modules and *ESTIMATE* immune/stromal scores. The turquoise module (r = 0.99, p < 1e-130) was strongly immune-related, and the blue module (r = 0.85, p < 1e-40) associated with stromal features, reflecting adaptive immunity, cytotoxic activity, and extracellular matrix organization.

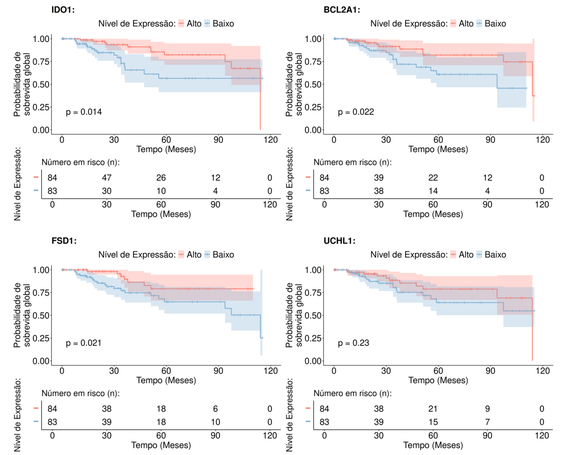


Figure 5. Kaplan–Meier curves for representative hub genes in TNBC. Higher expression of *IDO1, BCL2A1, UCHL1,*and *FSD1* was associated with better overall survival (p < 0.05), suggesting their potential as immune-related prognostic markers.

Conclusions

TNBC shows a distinct transcriptomic profile marked by **immune activation** and **stromal remodeling**.

Integration of gene-expression data with immune and stromal estimates revealed **modules strongly correlated** with the tumor microenvironment.

Hub genes — *IDO1, BCL2A1, UCHL1,* and *FSD1* — were linked to **better overall survival**, indicating their value as **prognostic markers**.

These results reinforce the importance of **bioinformatic analyses** in identifying molecular signatures that may guide **personalized therapy** in TNBC.

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