Differential Gene Expression Analysis of GSE39870

1. Introduction

Breast cancer progression is strongly influenced by Estrogen Receptor (ER) activity, which regulates genes involved in cell proliferation and survival. The tumor suppressor p53 mediates apoptosis in response to DNA damage. Doxorubicin, a DNA-damaging chemotherapeutic agent, activates apoptosis-related signaling pathways primarily through p53-dependent mechanisms. To examine the transcriptional response to doxorubicin treatment, a GSE microarray dataset derived from treated MCF7 breast cancer cells was analyzed.

2. Methods

Module: Differential Gene Expression Analysis of Doxorubicin Response in Breast Cancer Cells
Dataset: GSE39870 (Doxorubicin vs Vehicle)
Platform: Affymetrix Human Genome U133 Plus 2.0 Array
Number of samples: 6
Analysis method: limma
Cutoff: FDR < 0.01 and |log2FC| > 1
Enrichment analysis: GO and KEGG

3. Results

Differentially Expressed Genes

A total of 126 genes were differentially expressed, indicating substantial transcriptional changes induced by doxorubicin treatment.

- Number of upregulated genes: 68
- Number of downregulated genes: 58

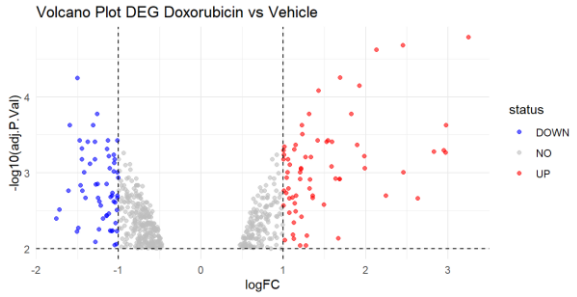
The most significantly upregulated genes included:

- TNFRSF10C — TNF receptor superfamily member 10c
- GPR87 — G protein-coupled receptor 87
- FAS — Fas cell surface death receptor

The most significantly downregulated genes included:

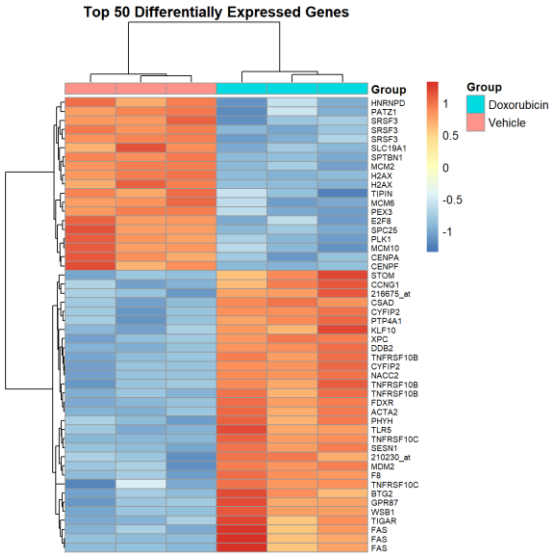
- LHX2 — LIM homeobox 2
- KIF20A — kinesin family member 20A
- NDC80 — NDC80 kinetochore complex component
- PLK1 — polo-like kinase 1
- KIF14 — kinesin family member 14

The volcano plot demonstrates clear separation between significantly upregulated and downregulated genes, indicating strong transcriptional response following doxorubicin exposure.



Top 50 Differentially Expressed Genes

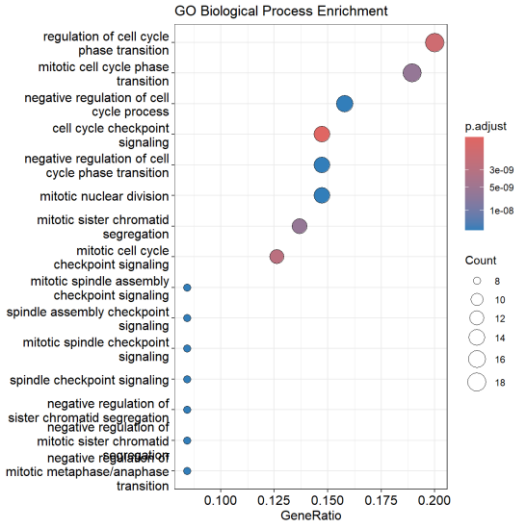
The top 50 most significant differentially expressed genes were selected for hierarchical clustering analysis and displayed using heatmap visualization.



GO Enrichment

GO enrichment analysis revealed significant enrichment in biological processes including:

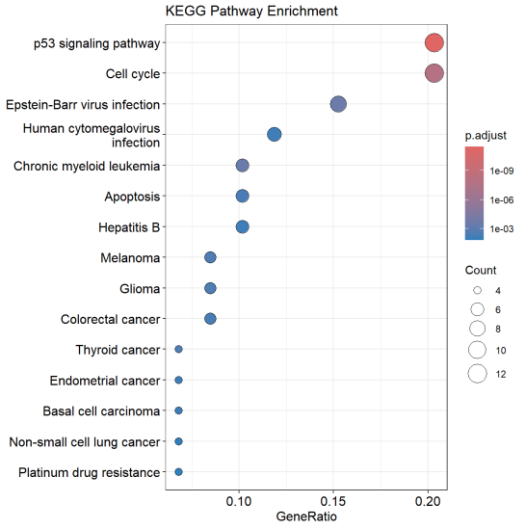
- Regulation of cell cycle phase transition
- Cell cycle checkpoint signaling
- Mitotic cell cycle checkpoint signaling
- Mitotic cell cycle phase transition
- Mitotic sister chromatid segregation



KEGG Pathway

KEGG pathway enrichment analysis identified significant pathways such as:

- p53 signaling pathway
- Cell cycle
- Epstein-Barr virus infection
- Chronic myeloid leukemia
- Thyroid cancer



Biological Interpretation

Up-regulated genes (TNFRSF10C, GPR87, FAS) play a role in the activation of the apoptosis pathway. This shows that doxorubicin triggers cell death mechanisms in response to DNA damage. Conversely, down-regulated genes (LHX2, KIF20A, NDC80, PLK1, and KIF14) play a role in the cell cycle, so their decrease indicates inhibition of cell division and cell cycle arrest.

GO enrichment indicates involvement in cell cycle regulation and mitotic checkpoints, reflecting impaired division control due to DNA stress. The most significant KEGG pathway is the p53 signaling pathway, which plays a role in the response to DNA damage and the induction of apoptosis. This suggests that doxorubicin triggers the p53 mechanism to control cell proliferation and promote cell death under conditions of severe DNA damage.

4. Conclusion

DEG analysis on the GSE39870 dataset showed that doxorubicin treatment resulted in 126 significantly altered genes, consisting of 68 upregulated genes and 58 downregulated genes. Upregulated genes were associated with apoptosis, while downregulated genes were linked to cell cycle and mitosis. GO and KEGG enrichment highlighted mitotic checkpoint processes and the p53 signaling pathway, indicating that doxorubicin induces DNA damage–mediated stress, activates p53, suppresses proliferation, and promotes apoptosis in ER-positive breast cancer cells.