Molecular Mechanism of Cisplatin Resistance

RNA-Seq Analysis of Human Lung Cancer Cells

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1. Executive Summary

In this project, we analyzed the transcriptomic landscape of **Cisplatin-Resistant** vs. **Sensitive** lung cancer cells (A549 cell line). The goal was to identify key molecular mechanisms driving drug resistance.

Key Findings: 1. **Oxidative Stress Response** is significantly upregulated in resistant cells. 2. **Metabolic Reprogramming** (Glucose transport) is activated to support cell survival. 3. **Cell Adhesion** pathways are altered, suggesting potential metastatic features.

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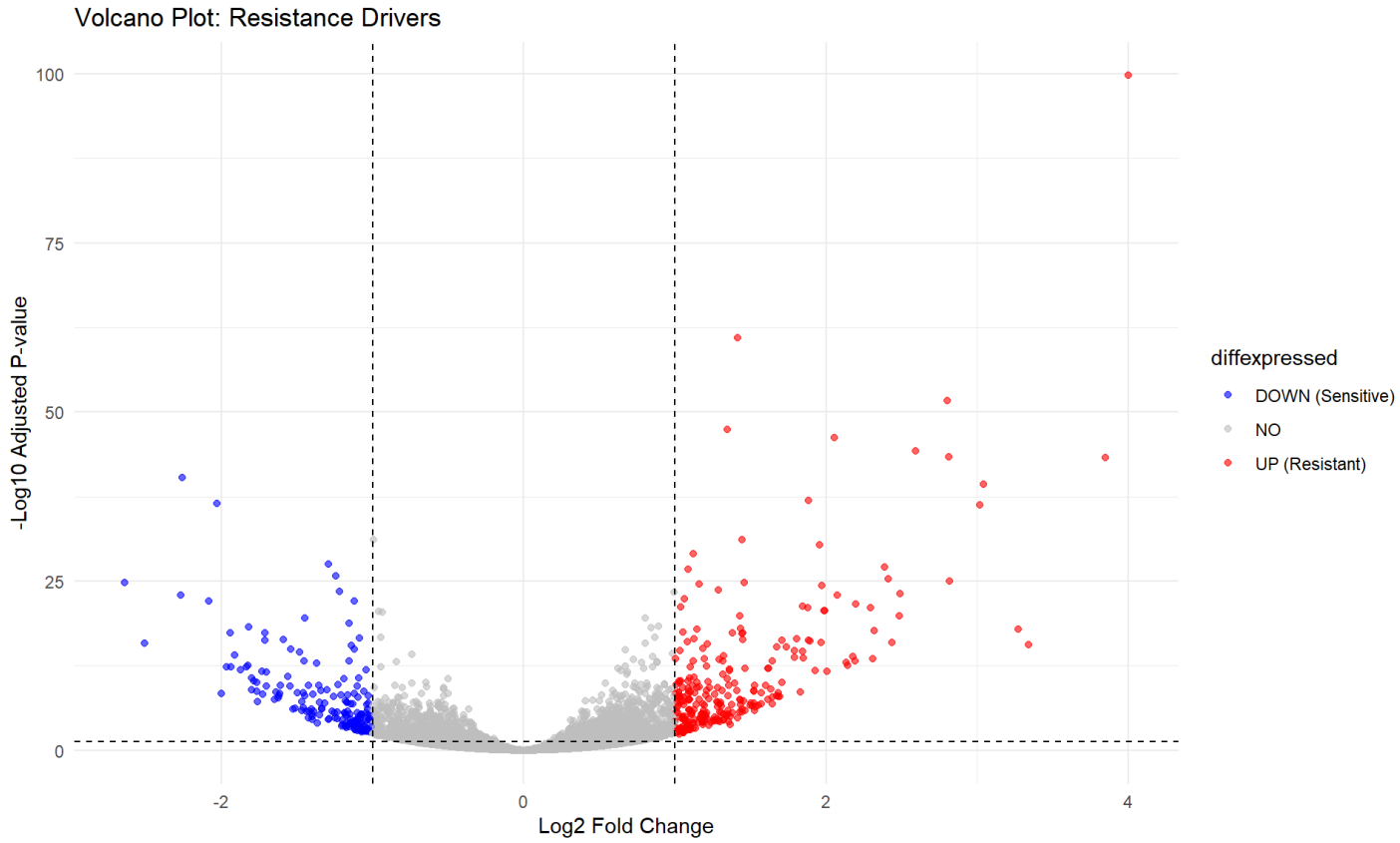
2. Differential Expression Analysis

We compared gene expression profiles to identify Up-regulated (Resistance drivers) and Down-regulated genes.

Volcano Plot Visualization

The plot below illustrates the global distribution of differentially expressed genes. Red points indicate genes with significant upregulation in resistant cells (Log2FC > 1, P-adj < 0.05).

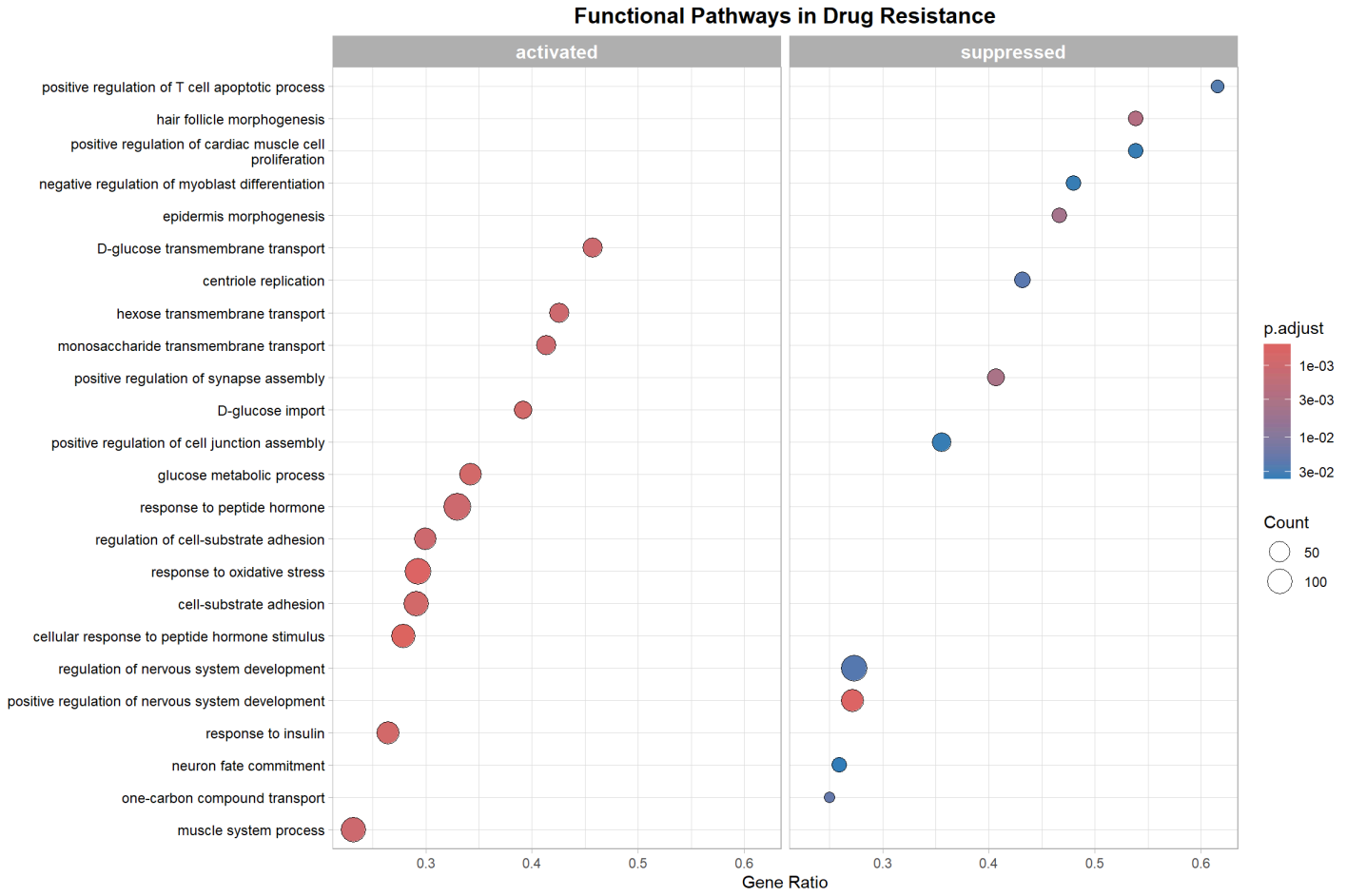


3. Pathway Enrichment Analysis (GSEA)

To understand the biological function of these genes, we performed Gene Set Enrichment Analysis (GSEA).

Mechanism of Resistance

The Dotplot below reveals the top activated and suppressed biological pathways.



Interpretation: The analysis confirms that **Response to Oxidative Stress** and **Glucose Import** are the primary mechanisms utilized by cancer cells to survive Cisplatin treatment. —

5. Protein-Protein Interaction (PPI) Network

To identify “Hub Genes” and potential drug targets, we analyzed the protein interaction network using the **STRING database**. This analysis reveals functional clusters and master regulators of the resistance mechanism.

Network Visualization

The graph below shows the interaction between the top 50 upregulated genes. *(Nodes with more connections are considered Hub Genes)*.

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## Warning:  we couldn't map to STRING 11% of your identifiers
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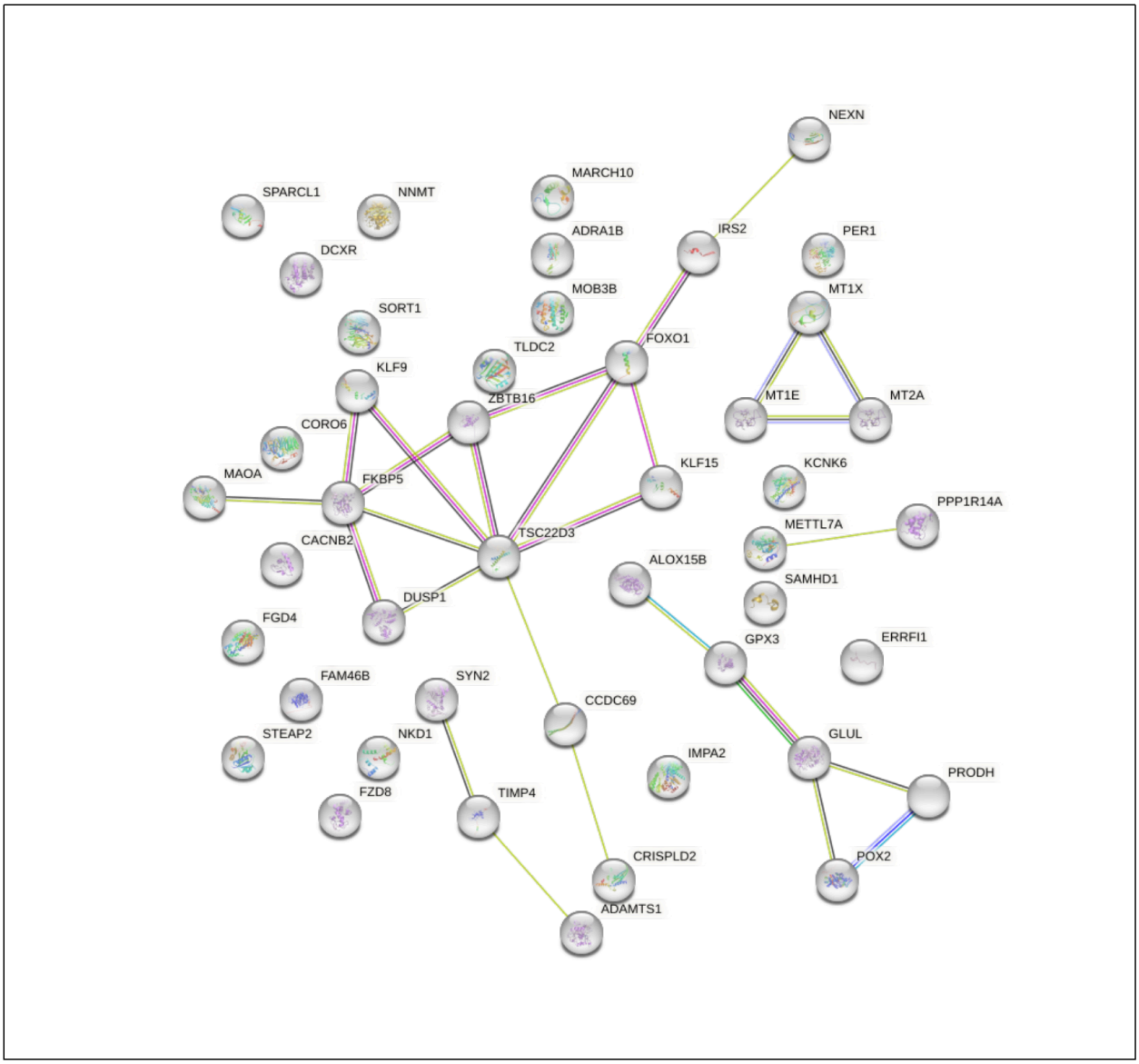
proteins: 45
interactions: 27
expected interactions: 5 (p-value: 3.35e-12)



Key Findings: The network analysis highlights highly connected proteins (Hub Genes) such as **Metallothioneins** and **FOXO1**, suggesting them as central drivers of cisplatin resistance.

4. Data Availability (Interactive Table)

The table below shows the top significant genes. You can search and filter this table.

Show 5 **entries** **Search:**

Table 1: Top 100 Differentially Expressed Genes

	log2FoldChange	pvalue	padj

ENSG00000152583	3.999069167885835	9.88999146049434e-105	1.838054912932873e-100
ENSG00000148175	1.417331406132504	1.221958656837328e-65	1.135505081866087e-61
ENSG00000179094	2.801774473258751	3.132380998427908e-56	1.940510028526089e-52
ENSG00000134686	1.349265459513949	8.043913437150226e-52	3.737403280735924e-48
ENSG00000125148	2.053923652833972	1.609198136649421e-50	5.981389473925896e-47

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