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p53: A Molecular Switch Determining Cell Fate Between Apoptosis and Differentiation

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Abstract

Apoptosis and differentiation are two critical cellular processes that share common molecular features, including, cytochrome c release and caspase activation. Despite these shared characteristics, the factors determining whether a cell undergoes apoptosis or differentiation remain poorly understood. In this study, we sought to identify the key genes and pathways that regulate cell fate decisions between these two processes. We first curated gene sets related to apoptosis and differentiation from the GSEA database, narrowing our focus to genes with high occurrence frequencies within each set. This led to the creation of refined gene sets that were analyzed using Enrichr. To validate these gene sets, we utilized 80 microarray samples from the GEO database and performed enrichment analysis with hallmark gene sets for apoptosis and differentiation. Remarkably, over 70% correlation was observed between our refined gene sets and hallmark gene sets, with substantial overlap in gene expression changes between apoptosis and differentiation samples. Further analysis revealed 16 common genes between the apoptosis and differentiation networks, with p53 exhibiting the highest betweenness centrality. Apoptosis and differentiation protein-protein interaction (PPI) networks were constructed using Cytoscape and then merged. Network analysis identified p53 as the most critical node in the final PPI network. To explore the functional role of p53, we analyzed its activity during differentiation using ISMARA and GEO datasets. We observed transient p53 activity during the differentiation of mesenchymal stem cells, consistent with reports that p53 dynamic regulates cell fate. Our findings highlight the pivotal role of p53 in balancing apoptosis and differentiation, providing insights into its function as a critical determinant of cell fate. Further research is needed to elucidate the precise

mechanism by which p53 and other key regulators control the balance between apoptosis and differentiation.

Keywords: Apoptosis; Differentiation; Cell fate; Cell signaling; p53

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