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Targeting Gastric Cancer: RNA Sequencing-Based Gene Analysis and Drug Repurposing

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ABSTRACT

Introduction: Gastric cancer (GC) is one of the significant health issues, ranked as the third leading cause of cancer-related deaths worldwide. The standard treatments show limited efficacy, highlighting the necessity of innovative therapeutic approaches. Drug repurposing is a promising approach that decreases drug development time and costs by utilizing the existing FDA-approved drugs initially developed to treat other diseases for treating incurable conditions. RNA sequencing, a next-generation sequencing technology, allows detailed analysis of gene expression profiles. Our study aimed to identify potential drugs for GC treatment via drug repurposing, focusing on RNA sequencing data. Enrichment analysis of differentially expressed genes (DEGs) was performed to investigate gene functions across biological processes, cellular components, and molecular functions and uncover key pathways and protein-protein interactions (PPIs) involved in GC.

Methods and Materials: We downloaded the GSE122796 expression profiles from the GEO database containing three gastric cancer samples and three normal adjacent tissues. We used the GEO2R web tool to compare them and identify DEGs. Potential candidate drugs that could reverse the expression of DEGs were identified using the iLINCS database. These drugs were screened through DrugBank and literature reviews. To gain insights into molecular function, cellular components, and biological processes, we utilized the GO (Gene Ontology) database. Key pathways involved in GC were identified using the KEGG database available in the Enrichr tool. PPIs were analyzed using the STRING database.

Results: We identified 20,113 DEGs, including 1,620 upregulated and 1,405 downregulated genes, and then selected genes with |log2 fold change| 1. Potential candidate drugs obtained from iLINCS included Amcinonide and Clofazimine, which were considered as final drugs. GO analysis revealed that DEGs were predominantly involved in extracellular matrix organization in biological processes, monocarboxylic acid binding in molecular functions, and collagen-containing extracellular matrix in cellular components. KEGG pathway analysis highlighted significant enrichment in protein digestion and absorption. PPI network analysis identified ITGA3, ITGA2, ITGB5, and COL1A2 as hub genes.

Conclusion and Discussion: We identified two drugs, Clofazimine and Amcinonide, which haven't previously been reported for treating GC. Clofazimine, an antimicrobial dye used in leprosy treatment, has demonstrated growth suppression effects on various cancer types through different mechanisms, including interference with intrinsic apoptosis. Amcinonide, a topical corticosteroid, has also shown anti-cancer impact by reversing the expression of the oncogene DAPK1 in liver carcinoma. Enrichment analysis provided insights into their cellular and molecular characteristics and identified hub genes that play crucial roles in the pathogenesis of GC. This study will enhance our understanding of GC; however, due to the limitations of in silico studies, further studies are recommended to improve the management of this condition.

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