EXPLORING GENE NETWORK INTERACTIONS AND PATHWAYS IN THREE CANCERS: IDENTIFYING POTENTIAL THERAPEUTIC TARGETS AND DRUG CANDIDATES

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Abstract

In our work, we employed a bioinformatics approach to analyze publicly available gene expression data from the GEO database for these three cancer types. We aimed to identify shared differentially expressed genes **(DEGs)**, construct protein–protein interaction **(PPI)** networks, uncover hub genes, and explore transcription factor (TF)–gene and miRNA–gene regulatory networks using **Network Analyst** and **Cytoscape**. Furthermore, we performed **gene ontology** (GO) enrichment analysis and **pathway analysis** to understand the biological functions associated with these genes using **Enrichr**. The ultimate goal of this study is to reveal potential therapeutic targets and identify candidate drug compounds through the integration of drug–gene interaction data using the Enrichr platform.

Introduction

- Lung cancer, liver cancer, and cervical cancer are among the most prevalent and lethal cancers worldwide. Although they originate in different organs, they exhibit striking molecular and regulatory similarities including abnormal cell proliferation, genetic instability, and dysregulated gene expression - all of which play a pivotal role in their progression.
- Recent studies have shown that, although these cancers are distinct in their pathological features, they often involve overlapping patterns of differentially expressed genes (DEGs) and oncogenic pathways. These include pathways related to cell cycle dysregulation, DNA repair deficiencies, and immune evasion mechanisms, suggesting that there may be a shared genetic basis underlying their development. Understanding these common molecular drivers is essential for the development of therapeutic strategies and treatments that work across different types of cancer.

Methodology

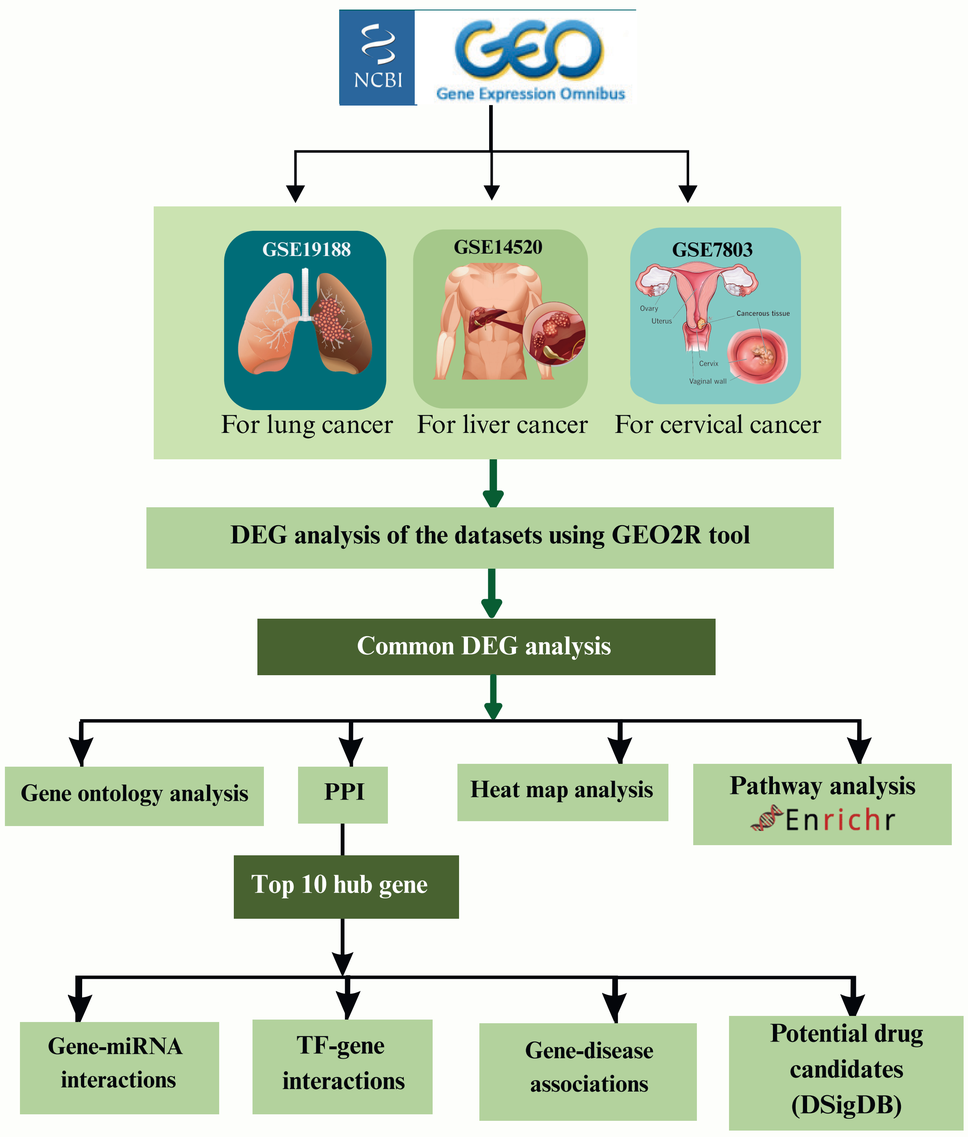


Figure 1: This methodology displays of the datasets are firstly collected for lung cancer, liver cancer, and cervical cacer from the Gene Expression Omnibus (GEO) at NCBI. Then, those datasets are preprocessed and filtered and found common DEGs. According to DEGs gene ontology and pathway analysis, help mainly understand the biological functions and therapeutic targets. Also, the PPI network provides topological information to determine hub genes. Finally, these hub genes are used to predict some significant miRNAs, TFs and potential drugs.

Results

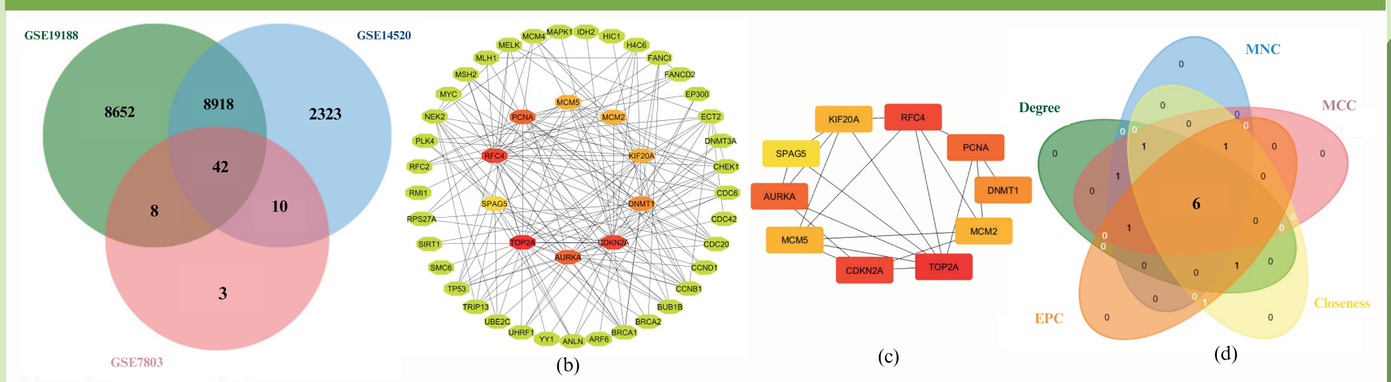


Figure 2. (a) The total number of DEGs as well as common DEGs using Venn Diagram (b) The STRING database (confidence cut off 600) was used to create this PPI network utilizing the common 42 DEGs (c) Top 10 hub-genes predicted by degree technique is represented using Cytoscape. (d) A Venn diagram was used to identify overlapping hub genes among top 10 hub-genes of various methods (Degree, MCC, MNC, EPC, Closeness).

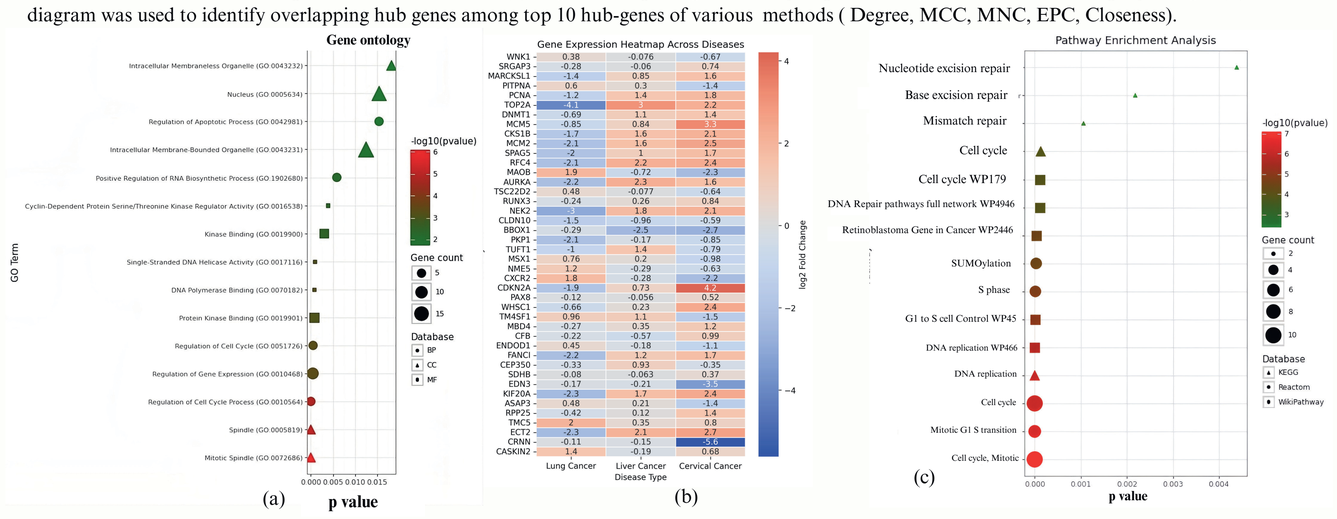


Figure 3. (a) Diagram illustrating GO terms of biological process, cellular component and molecular function (b) Heatmap analysis (c) Diagram illustrating pathways from KEGG, Reactome and Wikipathway

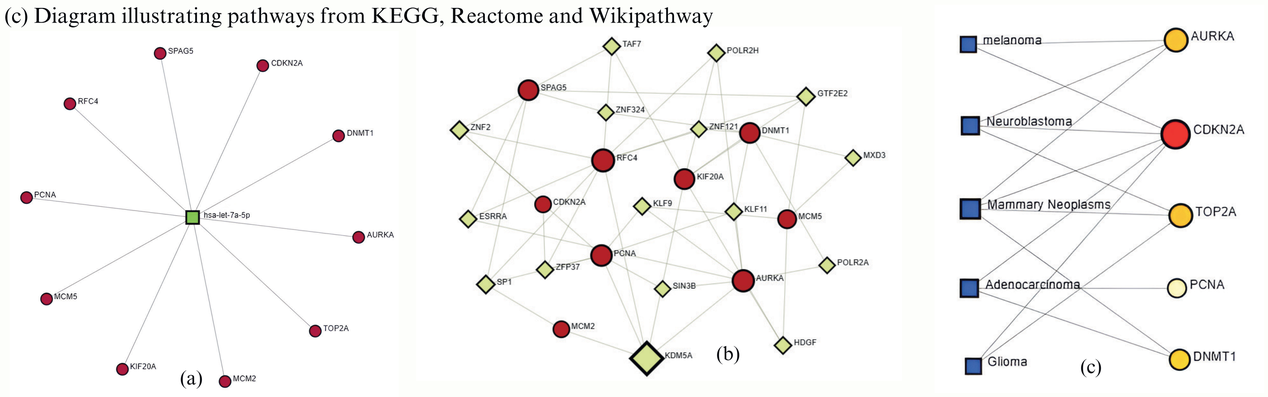


Figure 4. (a) The 11 most important nodes of the gene-miRNA interactions network (b) The 25 most important nodes of the gene-TF interaction network (c) The interaction between hub genes (red to yellow based on connections) and cancer types (diseases) through gene-disease associations

Table 1: Top 5 potential drugs that may have regulatory effects on selected three cancers

Drug Name	P - value	Target Gene
Resveratrol CTD 00002483	1.053e-11	TOP2A, DNMT1, RFC4, PCNA, SPAG5, CDKN2A, MCM5, KIF20A, AURKA, MCM2
Enterolactone CTD 00001393	1.383e-1	TOP2A, DNMT1, RFC4, PCNA, SPAG5, MCM5, KIF20A, AURKA, MCM2
Genistein CTD 00007324	3.350e-7	TOP2A, DNMT1, PCNA, SPAG5, KIF20A, AURKA, MCM2
Methaneseleninic acid CTD 00000412	1.246e-8	TOP2A, PCNA, CDKN2A, MCM5, AURKA, MCM2
Trifluridine MCF7 DOWN	4.872e-7	TOP2A, KIF20A, AURKA

Discussion & Conclusion

Our findings:

- Gene-miRNA interaction network suggests **hsa-let-7a-5p**'s high degree of interaction suggests it plays a pivotal role in gene regulation.
- TF-gene interaction suggests **KDM5A** stands out for its epigenetic control over hub genes.
- Gene-disease interaction network emphasizes the importance of **CDKN2A** as a key gene in multiple cancers
- Lastly **Resveratrol,** targeting the most hub genes, presents a promising potential drug candidate with the ability to modulate cell cycle and DNA repair pathways.

These findings emphasize the importance of gene-miRNA, gene-TF, and drug-gene interactions in understanding cancer progression and guiding targeted therapy development.

Future works

Future research in this area aims to perform molecular docking based on the hub proteins using phytochemical plants and also perform molecular dynamic simulations and create a single generic drug to treat several related illnesses, offering a fresh perspective.

References

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