## عنوان مقاله:

A Gene Expression Signature to Predict Chemotherapy Response of Colorectal Cancer Patients: Systems Biology Analysis on Transcriptomics Data and Experimental Validation


## محل انتشار:

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## خلاصه مقاله:

Introduction: Gene expression profiling has high potential in the identification of diagnostic, predictive, and therapeutic gene targets in human cancers such as colorectal cancer (CRC). Accordingly, in this study, an integrated systems biology analysis was done on several microarray datasets to identify key genes involved in CRC chemoresistance and also to differentiate peoples who benefit from chemotherapy. Subsequently, the findings were validated experimentally. Materials and Methods: Datasets were retrieved from Gene Expression Omnibus (GEO). Gene expression analysis was performed using the ExAtlas software. Gene enrichment analysis was done using g: profiler. Protein-Protein Interaction Network (PPIN) was constructed in STRING and visualized/analyzed by Cytoscape ۳.۸.۰. Significant modules were identified using the MCODE plugin in Cytoscape. The clinical importance of candidate genes was evaluated using ROC analysis and immunohistochemistry. Key candidate genes were validated using Real-Time PCR. Results: According to findings, ۲۶ datasets were selected. Gene expression analysis revealed ۶۴۶۳ Differentially Expressed Genes (DEGs), among which ۴۳۲۳ were unique and ۲۱۴۰ were related to overlapping DEGs between datasets. The overlapping DEGs with at least four shared datasets (n=۲۱۷ DEGs) were selected for further analysis. Overlapping DEGs were mainly enriched in the cellular process of response to chemicals stimulus. Most selected DEGs were enriched in KEGG pathways of cancer Benzo(a)pyrene metabolism and glucocorticoid receptor signaling. Fourteen hub genes and two significant modules were identified. Six hub genes (candidate genes) were contributed in significant modules. Among candidate genes, LCN۲, CXCL۸, and EGR۱ expression were significantly associated with chemotherapy response of CRC patients and chemosensitivity of CRC cell lines (P<۰.۰۵). Conclusion: This study revealed three genes signature for predicting chemotherapy responsiveness and treatment decision-making in CRC patients and also for therapeutic purposes.



## کلمات کلیدی:

colorectal neoplasm, Systems biology, Protein-Protein Interaction Network, ROC Analysis, Gene ontology, Antineoplastic Drug Resistance