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A network-based approach to uncover the potential genes, microRNAs and pathways in colorectal cancer pathogenicity

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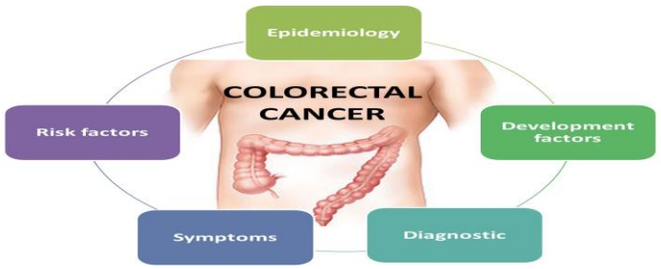
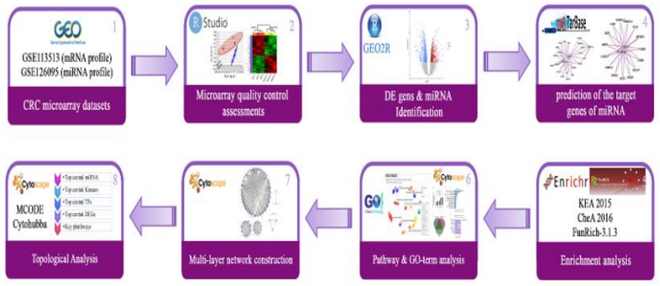
Background

Colorectal cancer (CRC) is one of the most prevalent malignancies worldwide. Despite various conducted surveys and experiments around the CRC, the pathogenicity of this disease is not clear enough. The present study aimed to apply a systematic approach to make valuable insight into the involved genes and their regulatory layers that can shed light on CRC pathogenicity



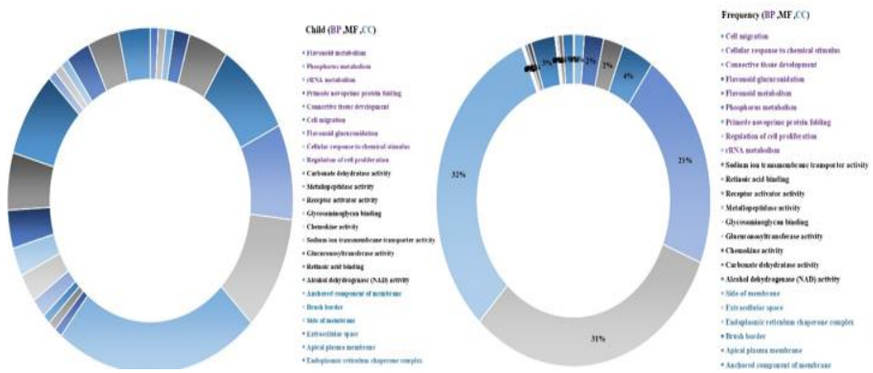
Materials and Methods

In the current survey, GSE126095 microRNA profiles, and gene microarray dataset GSE113513 re-analyzed through <0.05 |log fold change (FC)|≥1 parameter to recognize differentially expressed genes (DEGs) and MicroRNAs (DEMs). Principal component analysis (PCA) was used for analyzing the quality of datasets. Furthermore, the DEGs related kinases (KEA) and transcription factors (ChEA) were retrieved by using the EnrichR database. In addition, a multi-layer network composed of DEGs, KEA, ChEA was constructed and analyzed by using Cytoscape application. Finally, the functional and pathway enrichment analyses were applied, using Cytoscape ClueGO plugin.



Results

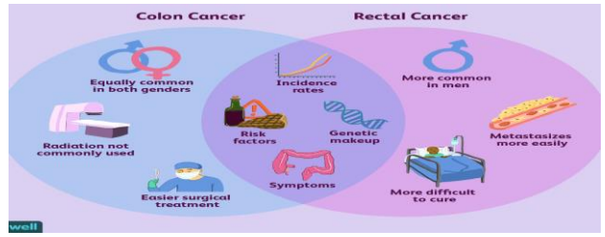
Top 10 hub genes, miRNAs, TFs and kinases extracted from multilayer network, Module 1 of the merged network was chosen for further investigation, most of the edges and nodes were connected with RHO GTPase effectors, Cdc20-mediated mitotic protein degradation, rRNA processing and the senescence associated secretory phenotype, based on GO and pathway enrichment analysis . Most DEGs are related to import and biological pathways such as Wnt/β-catenin, flavonoids metabolism pathway and UDP glucuronosyltransferases pathway. Moreover, top-most central TP53, AR, CTNNB, POU3F2, FOXA1, NR3C1, PIAS1, PPAR were identified as genes in the network that play a significant role in CRC.



Top Central Kinase	Top Central Transcription Factor (TF)	Top Central DE genes	Top Central miRNA
CSNK2A1	NR3C1	TP53	miR-1244
CDK6	FOXA1	AR	miR-4708-3p
CSNK1G1	PAX3	CTNNB1	miR-133b
MAPK8	MYCN	POU3F2	miR-34a-3p
CSNK1G2	FOXA1	NR3C1	miR-4328
CSNK1G3	TP53	FOXA1	miR-548ap-5p/miR-548j
MAPK1	AR	PPAR	miR-188-5p
MAPK9	CTNNB1	PIAS1	miR-224-5p
CDK7	POU3F2	GNAI1	miR-766-5p
CHEK2	CLOCK	CDK1	miR-133a

Conclusion

Our research followed a systematic approach to identifies reliable molecular biomarkers and biological pathways for CRC screening and diagnosis, as well as prognosis and potential treatment targets.



References

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