EXAMINATION OF DOWNREGULATED MIRNAS AND ASSOCIATED PATHWAYS IN COLORECTAL CANCER: A SYSTEMATIC REVIEW

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Introduction

- Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths worldwide.
- Many biological molecules play a significant role in the pathogenesis of CRC including miRNAs, small RNA molecules that regulate the translation and stability of specific target mRNAs.
- Given the involvement of miRNAs on all fronts of CRC including pathogenesis, diagnosis, prognosis and potential therapy, it is imperative to fully understand their role within this deadly disease.
- With this study, we examined unique miRNAs which were upregulated in patients with CRC.

Methods

- We searched PubMed and the Cochrane Database of Systematic Reviews (CDSR) through Wiley from 2016 to 2022 for keywords “miRNA”,” micro-RNA”, “colon cancer”, “colorectal cancer”, “CRC”.
- From this data, we performed computational analysis using MicroInspector, miRanda, PicTar, RNA22, DIANA, softwares and identified unique upregulated miRNAs.
- We further examined the list of the biological pathways identified from predicted target genes of downregulated miRNAs and selected the top 4 pathways of clinical significance.
- We then filtered common miRNAs between these selected pathways and identified unique miRNAs between the top 4 pathways.

Downregulated miRNAs identified in CRC pathogenesis

hsa-miR-296	hsa-miR-20a	hsa-miR-1	hsa-miR-186-5p	hsa-miR-4319
hsa-miR-22	hsa-miR-885-3p	hsa-miR-708	hsa-miR-181a-5p	hsa-miR-362
hsa-miR-217	hsa-miR-6868-5p	hsa-miR-520e	hsa-miR-16-5p	hsa-miR-200b-3p
hsa-miR-198	hsa-miR-622	hsa-miR-519b-3p	hsa-miR-148a	hsa-miR-185
hsa-miR-184	hsa-miR-375	hsa-miR-330	hsa-miR-139-5p	hsa-miR-143-3p
hsa-miR-502	hsa-miR-27b	hsa-miR-324-5p	hsa-miR-873-5p	hsa-miR-141-3p
hsa-miR-30d	hsa-miR-218	hsa-miR-302a	hsa-miR-760	hsa-miR-1271
hsa-miR-30a	hsa-miR-206	hsa-miR-28-5p	hsa-miR-548c-5p	hsa-miR-1258
hsa-miR-216a	hsa-miR-126	hsa-miR-204	hsa-miR-500a-5p	hsa-miR-125
hsa-miR-214	hsa-miR-1249	hsa-miR-200	hsa-miR-488	

List of the biological pathways identified from predicted target genes of downregulated miRNAs

Pathway	p-value	#genes	#miRNAs
MAPK signaling pathway	2.79E-08	158	26
ErbB signaling pathway	6.69E-08	60	25
PI3K-Akt signaling pathway	2.87E-06	197	28
Rap1 signaling pathway	3.71E-06	127	26

Results

- We identified 59 downregulated miRNAs from studies of patients with CRC. We then identified a list of the biological pathways identified from downregulated miRNAs target genes.
- We then identified a list of the biological pathways identified from upregulated miRNAs target genes.
- Namely, hsa-mir-135b-3p and hsa-mir-191-3p were identified, suggesting that these miRNAs may play an important role in those pathways.

Conclusion

MicroRNAs play an important role in CRC initiation, progression, and development through manipulation of cell stemness, angiogenesis, apoptosis, and the epithelial–mesenchymal transition (EMT) of tumor cells. With this study we identified unique clinically relevant metabolic pathways of CRC affected by downregulated miRNAs. We also identified the unique miRNAs hsa-mir-135b-3p and hsa-mir-191-3p. Further work is necessary to identify specific roles of these miRNA candidates as biological markers or therapeutic targets for patients with CRC.