

EXAMINATION OF UPREGULATED 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 upregulated 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.

Upregulated miRNAs identified in CRC pathogenesis.

hsa-mir-17-92	hsa-miR-135a	hsa-miR-92a-3p	hsa-miR-210
hsa-mir-20	hsa-miR-203a-3p	hsa-miR-942	hsa-miR-221
hsa-mir-21	hsa-miR-301a-3p	hsa-miR-191	hsa-miR-107
hsa-mir-135	hsa-miR-31-5p	hsa-miR-32-5p	hsa-miR-223
hsa-mir-144	hsa-miR-410	hsa-miR-338-5p	hsa-miR-4260
hsa-mir-92a	hsa-miR-452	hsa-miR-590-5p	
hsa-mir-106a	hsa-miR-494	hsa-miR-6716-5p	
hsa-mir-106b	hsa-miR-501-3p	hsa-miR-1229	
hsa-miR-135b	hsa-miR-590-3p	hsa-miR-25-3p	
hsa-mir-10b	hsa-miR-6803-5p	hsa-miR-125b	

List of the biological pathways identified from predicted target genes of upregulated miRNAs.

Pathway	p-value	#genes	#miRNAs
TGF-beta signaling pathway	9.34E-12	54	25
Fatty acid metabolism	8.36E-06	24	19
FoxO signaling pathway	3.31E-05	76	22
Hippo signaling pathway	0.000263	83	26
N-Glycan biosynthesis	0.0011974	24	18
Axon guidance	0.0014637	68	24

Results

- We identified 35 upregulated miRNAs from studies of patients with CRC. We then identified a list of the biological pathways identified from downregulated miRNAs target genes.
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- We further investigated the highlighted pathways and found unique miRNAs associated with these pathways. Namely, hsa-mir-296-3p and hsa-mir-198-3p 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-296b-3p and hsa-mir-198-3p. Further work is necessary to identify specific roles of these miRNA candidates as biological markers or therapeutic targets for patients with CRC.