The Role of miRNAs in the Treatment and Regulation of Gastrointestinal Tumors

Weixiao Yuan
Hangzhou Xizi Experimental School, Hangzhou, China

Keywords: miRNA, Gastrointestinal Tumors, Biomarker.

Abstract: MicroRNA (miRNA) is a class of endogenous non-coding small RNA molecules that regulate gene expression at the post-transcriptional level by partially complementary binding to the 3'untranslated region (3'UTR) of target mRNA. This review summarizes miRNA's biogenesis and regulatory mechanisms, detailing the entire process from transcription and processing to maturation and functional exertion within the cell. Studies have shown that miRNA plays a crucial role in cell development, differentiation, proliferation, apoptosis, disease occurrence, and immune regulation. The development and progression of gastrointestinal tumors is a complex, multifactorial, and multistage process involving genetic factors, environmental factors, lifestyle, microbial infections, and precancerous lesions. Tumor cells promote their growth, invasion, and metastasis through genetic mutations, clonal evolution, and dynamic changes in the tumor microenvironment. This paper further explores the regulatory role of miRNA in gastrointestinal tumors and finds that specific miRNAs (such as miR-221, miR-125b, miR-320a-3p, etc.) significantly affect the progression of gastrointestinal tumors by regulating cell proliferation, apoptosis, metastasis, and invasion. In addition, miRNA, due to its stability and ubiquity in various biological fluids, shows potential as a tumor biomarker for early diagnosis and monitoring of tumor progression. Meanwhile, miRNA further influences tumor growth and development by regulating cells and metabolites in the tumor microenvironment. miRNA has excellent potential for application in controlling and treating gastrointestinal tumors. With the continuous progress of research and technology, miRNA is expected to become an essential tool for diagnosing and treating gastrointestinal tumors, providing new strategies and hope for cancer patients.

1 INTRODUCTION

As modern health issues gradually come to the forefront, gastrointestinal health problems among the Chinese population have become particularly prominent. The Chinese preference for greasy and salty foods has led to a significant burden on their gastrointestinal system, posing a considerable risk to their gastrointestinal health, with gastrointestinal tumors being especially typical. According to data from the National Cancer Center, in 2024, the annual incidence of gastric cancer in China exceeded 350,000 cases, ranking 5th among all malignant tumors; the number of deaths exceeded 260,000, ranking 3rd among malignant tumors. Chinese gastric cancer patients account for approximately 40%of the global total. This highlights the urgent need to pursue effective treatments and methods for gastrointestinal diseases, especially major diseases such as gastrointestinal tumors. The significant advancements in biology in recent years may have unveiled a glimpse into treating gastrointestinal tumors.

In 2024, the Nobel Prize in Physiology or Medicine was awarded to American scientist Victor Ambros and biologist Gary Ruvkun for discovering microRNA and its role in post-transcriptional gene regulation. MicroRNA is a type of RNA molecule transcribed from DNA, which regulates gene expression by affecting other RNA molecules transcribed from DNA. After the discovery of microRNA was made public, its immense potential in the medical field, especially in cancer treatment, was quickly recognized. The abnormal expression of oncogenes and tumor suppressor genes causes the emergence of cancer. If microRNA could regulate the expression of oncogenes and tumor suppressor genes in cancerous cells, treating cancer with microRNA would become a viable approach. Research has found that microRNA molecules such as microRNA-25, microRNA-451, and microRNA-625 play various

Yuan, W.
The Role of miRNAs in the Treatment and Regulation of Gastrointestinal Tumors.
DOI: 10.5220/0014464600004933

In *Proceedings of the 1st International Conference on Biomedical Engineering and Food Science (BEFS 2025)*, pages 207-211
ISBN: 978-989-758-789-4

roles in treating colorectal cancer. Therefore, microRNA has become a hot topic in colorectal cancer treatment. However, current research on microRNA is still relatively limited. As an emerging field, there are many unexplored areas, and the study of microRNA has a broad prospect for research and application. This study systematically analyzed the role and impact of microRNA in colorectal cancer by organizing and analyzing data, elucidating the mechanisms and pathways of microRNA in the development and metastasis of colorectal cancer, and providing a foundational plan for different stages of colorectal cancer diagnosis and treatment.

2 BIOGENESIS AND REGULATORY MECHANISMS OF MICRORNA

The miRNA coding sequence is first transcribed into an extended primary transcript (pri-miRNA) by RNA polymerase II (Pol II) (Emily et al. 2025), which is the unprocessed primary miRNA and typically features a polyadenylated 3'end and a 5'cap structure. The nascent pri-miRNA is cleaved by a microprocessor complex (composed of Drosha and DGCR8) near the junction between single-stranded RNA (ssRNA) and the dsRNA hairpin (referred to as the basal junction) into a precursor miRNA called pre-miRNA (Truong et al. 2024). This pre-miRNA is a hairpin-shaped precursor miRNA with a length of approximately 70 nucleotides. It is then explicitly recognized and bound by the nuclear export protein Exportin-5, mediating the atomic export of pre-miRNA precursors(pre-miRNAs) (Wang 2020). The pre-miRNA is recognized and bound by the ribonuclease Dicer in the cytoplasm. Dicer's C-terminal double-stranded RNA-binding domain (dsRBD) recognizes the GYM motif (Lee et al. 2023). After processing by Dicer, a small interfering RNA (siRNA) with a length of about 21–23 nucleotides is formed, completing the second processing of miRNA within the cell. Some pre-miRNAs are directly processed into mature miRNAs by Dicer. One strand of the siRNA, the guide strand, is loaded into the RNA-induced Silencing Complex (RISC), which plays a crucial role in both the small interfering RNA (siRNA) and microRNA(miRNA)pathways (Zhang et al. 2018). The other strand, the passenger strand (which is usually degraded), is ultimately wholly processed into the fully mature miRNA. Mature miRNAs play critical regulatory roles within the cell. If miRNAs are not entirely complementary to their target RNAs, they will inhibit the translation process, affecting peptide bond formation and ultimately reducing the expression of the corresponding proteins. When miRNAs are fully or almost entirely complementary to their target mRNAs, they can lead to the degradation of the target mRNA (this mechanism is more common in plants than animals). miRNAs play a crucial role in cell development and differentiation, cell proliferation and apoptosis, disease occurrence and immune regulation. This paper will focus on disease occurrence and cellular physiological mechanisms.

3 OCCURRENCE AND DEVELOPMENT OF GASTROINTESTINAL TUMORS

Genetic factors, microbial factors, environmental and lifestyle factors, and precancerous lesions are several of the main factors contributing to gastrointestinal tumors. Genetics is essential, as both gastric and colorectal cancers exhibit familial clustering. Mutations in genes such as *BRCA1/2* and *MLH1* are closely related to the occurrence of gastrointestinal cancer. Abnormal expression of MLH1 is associated with gene mutations and methylation, which may lead to a lack of mismatch repair (MMR) and subsequent malignant transformation of cells (Tian et al. 2025). Variants of *BRCA1* and *BRCA2* (Matykiewicz et al. 2025) also have many cancer risk factors. The intake of nitrites and polycyclic aromatic hydrocarbons, which are carcinogens found in high-salt pickled foods, increases the risk of gastrointestinal tumors. Fresh vegetables and fruits rich in vitamin C can block the synthesis of nitrosamines, thereby reducing the incidence of tumors. Harmful substances such as nicotine ingested through smoking can damage the gastrointestinal mucosa, reduce the body's immune capacity, and promote tumor development. In addition, dysbiosis of the gut microbiota and infections with Fusobacterium nucleatum and Helicobacter pylori can promote inflammatory responses, tumor development, and the conversion of nitrates to nitrites and nitrosamines. Helicobacter pylori has been classified as a Group 1 carcinogen by the International Agency for Research on Cancer and the World Health Organization, and its infection is considered a significant risk factor for gastric cancer (GC) (Liu et al. 2024). Some precancerous lesions,

such as chronic atrophic gastritis, gastric polyps, and gastric ulcers, may gradually evolve into gastric cancer.

In the development of gastrointestinal tumors, gene mutations and clonal evolution, the role of the tumor microenvironment, and metastasis and recurrence are essential influencing factors. Early tumor cells, such as cancer-associated fibroblasts and immune cells, accumulate sufficient growth advantages through gene mutations. As they grow, tumor cells accumulate more neutral mutations, leading to advanced tumors. Cells in the tumor microenvironment and metabolites such as lactate and glutamine provide essential carbon and nitrogen sources to sustain the growth of cancer cells, which can promote tumor growth, invasion, and metastasis during tumor development (Huang et al. 2024). Tumors can also metastasize through body fluids such as blood and lymph, leading to tumor recurrence. Gastrointestinal tumors trigger their occurrence and development through the above methods. Introducing miRNA regulation in this process can inhibit one or several links in the development of gastrointestinal tumors, thereby affecting the entire tumor occurrence and development process.

4 REGULATORY AND THERAPEUTIC ROLES OF MICRORNA IN THE OCCURRENCE AND DEVELOPMENT OF GASTROINTESTINAL TUMORS

During the occurrence and development of gastrointestinal tumors, miRNA plays a vital role in regulating cell proliferation and apoptosis. In promoting cell proliferation, miR-221 promotes cell cycle progression by targeting proteins, thereby facilitating cell proliferation. The expression level of miR-221 may be closely related to the occurrence and development of gastric cancer, and a series of miRNA genes such as miR-221 may become an essential target for the diagnosis and treatment of gastric cancer and other digestive tract and organ tumors in the future (Tao et al. 2010). In regulating apoptosis, miR-125b targets Bcl-2 family proteins to inhibit cell proliferation and induce apoptosis. In regulating tumor metastasis and invasion, some miRNAs promote the metastasis and invasion of gastrointestinal tumor cells by regulating genes related to epithelial-mesenchymal transition. For example, miR-320a-3p is downregulated in many tumors, and its downregulation is associated with enhanced invasion and migration capabilities of tumor cells. MicroRNA 320a-3p may become a potential target for GC immunotherapy by inhibiting PD-L1 gene expression (Asghariazar et al. 2025). Therefore, enhancing the expression of miRNAs that inhibit tumor cell proliferation and metastasis and promote tumor cell apoptosis through genetic engineering may help control the progression of gastrointestinal tumors.

MicroRNAs are abnormally expressed in many gastrointestinal tumors, so they can be used as a detection marker to reflect the development status of tumors and thus serve as a tumor marker for auxiliary diagnosis. MicroRNAs are considered promising candidates for clinical biomarkers because of their stable characteristics and ubiquity in easily accessible biofluids obtained through non-invasive and minimally invasive means (Metcalf et al. 2024). Studies have shown that tumor-specific DNA and RNA are often found in the plasma of cancer patients (Metcalf et al. 2024) and can be used as potential tumor markers for early diagnosis. In addition, miRNAs can also be used as therapeutic agents to complement the treatment of gastrointestinal tumors. For example, miRNA-34a exhibits significant tumor-suppressive effects in gastric cancer and can serve as a targeted therapy. Moreover, miRNAs can regulate the tumor microenvironment to affect tumor progression. For example, cancer-associated fibroblasts (CAFs) play an essential role in the tumor microenvironment, and miRNAs can influence tumor growth and development by controlling the interaction between CAFs and tumor cells (Nedaeinia et al. 2024). On the other hand, miRNAs can also be combined with other therapeutic methods for combined tumor therapy. Studies have found that miRNAs are promising immunotherapy adjuvants that can enhance the effectiveness of tumor treatment (Yadav et al. 2024).

5 OUTLOOK ON THE APPLICATION OF MICRORNA IN THE TREATMENT OF GASTROINTESTINAL TUMORS

Many miRNA molecules have been found to regulate tumor cells, so using miRNA for tumor treatment has

a broad prospect and promotes cancer treatment research. However, although researchers have achieved phased results in the regulatory mechanisms, functional analysis, and tumor association of miRNA, many fundamental scientific issues in this field have not been clarified. First, the expression regulation network of miRNA itself has not been fully explained, and the molecular mechanisms of its transcriptional activation or inhibition still need to be further explored. Secondly, there is still a lack of systematic research evidence on whether the regulatory role of miRNA in tumor occurrence and development is tissue-specific or universally associated with everyday cell physiological activities and other disease processes. The unresolved nature of these core issues indicates that miRNA-related research still needs a long period of theoretical exploration and technological breakthroughs. In addition, how to transform the regulatory mechanisms of miRNA on gastrointestinal tumors into clinically operable diagnostic and therapeutic strategies remains a key direction for translational medical research. Therefore, promoting the transformation of basic research results into clinical treatment has become an important development direction in this field.

6 CONCLUSION

MicroRNA (miRNA), as a class of crucial molecules regulating gene expression, has demonstrated significant potential in the occurrence, development, and treatment of gastrointestinal tumors. By controlling biological processes such as cell proliferation, apoptosis, metastasis, and invasion, miRNA plays a vital role in tumor progression. Studies have found that specific miRNAs (such as miR-221, miR-125b, miR-320a-3p, etc.) are abnormally expressed in gastrointestinal tumors and are closely related to the biological behavior of tumors. In addition, due to their stability and widespread presence in various biological fluids, miRNAs are considered to have the potential as tumor biomarkers for early diagnosis and monitoring of tumor progression. MiRNAs can also serve as therapeutic targets; by regulating their expression or function, tumor cell proliferation, metastasis, and invasion can be inhibited, and cell apoptosis can be induced. For example, miRNA-34a exhibits significant tumor-suppressive effects in gastric cancer, revealing its potential as a targeted therapeutic approach. Moreover, miRNAs can influence tumor growth and development by regulating cells (such as cancer-associated fibroblasts) and metabolites (such as glutamine) in the tumor microenvironment, providing new ideas for comprehensive treatment.

Although significant progress has been made in the study of miRNA in gastrointestinal tumors, it is still in its infancy, and many key issues remain unresolved. For example, the regulatory mechanisms of miRNA expression, its specific role in tumorigenesis, and how to translate research findings into clinical applications are still pressing issues. Future research directions should include: in-depth exploration of the regulatory mechanisms of miRNA and its specific role in tumorigenesis; development of efficient miRNA delivery systems for precise treatment; investigation of the combined application of miRNA with other therapeutic approaches (such as chemotherapy and immunotherapy) to enhance therapeutic effects; and validation of miRNA as a tumor biomarker and therapeutic target through large-scale clinical trials. In summary, miRNA has excellent potential for application in regulating and treating gastrointestinal tumors. With the continuous progress of research and technology, miRNA is expected to become an essential tool for diagnosing and treating gastrointestinal tumors, bringing new hope to cancer patients.

REFERENCES

Asghariazar, V., Makaremi, S., Amani, N. et al. 2025. MicroRNA 320a-3p up-regulation reduces PD-L1 expression in gastric cancer cells: an experimental and bioinformatic study. Sci Rep. 15, 8239.

Emily M. King, Amanda R. Panfil. 2025. Dynamic Roles of RNA and RNA Epigenetics in HTLV-1 Biology, Viruses, 10.3390/v17010124, 17, 1, (124).

Huang, Y., Meng, F., Zeng, T. et al. 2024. IFRD1 promotes tumor cells' “low-cost” survival under glutamine starvation via inhibiting histone H1.0 nucleophagy. Cell Discov. 10, 57.

Lee YY, Kim H, Kim VN. 2023. Sequence determinant of small RNA production by DICER. Nature. Mar;615(7951):323-330.

Liu, Y., Miao, R., Xia, J. et al. 2024. Infection of Helicobacter pylori contributes to the progression of gastric cancer through ferroptosis. Cell Death Discov. 10, 485.

Matykiewicz, J., Adamus-Białek, W., Wawszczak-Kasza, M. et al. 2025.The known genetic variants of BRCA1, BRCA2 and NOD2 in pancreatitis and pancreatic cancer risk assessment. Sci Rep. 15, 1791.

Metcalf, G.A.D. 2024. MicroRNAs: circulating biomarkers for the early detection of imperceptible cancers via biosensor and machine-learning advances. Oncogene. 43, 2135–2142.

Nedaeinia, R., Najafgholian, S., Salehi, R. et al. 2024. The role of cancer-associated fibroblasts and exosomal miRNAs-mediated intercellular communication in the tumor microenvironment and the biology of carcinogenesis: a systematic review. Cell Death Discov. 10, 380.

Tao CH, Su JL, Huang ZG, et al. 2010. Effects of abnormal expression of miR-221 on proliferation and apoptosis of gastric cancer cell lines[J]. Journal of Tongji University (Medical Science). 31(2):44-46,54.

Tian, Z., Yang, L., Yang, R. et al. 2025.The prognostic and immunomodulatory role of the MMR system in patients with stomach adenocarcinoma. Sci Rep. 15, 180.

Truong VA, Chang YH, Dang TQ, Tu Y, Tu J, Chang CW, Chang YH, Liu GS, Hu YC. 2024. Programmable editing of primary MicroRNA switches stem cell differentiation and improves tissue regeneration. Nat Commun. Sep 27;15(1):8358.

Wang, J., Lee, J.E., Riemondy, K. et al. 2020. XPO5 promotes primary miRNA processing independently of RanGTP. Nat Commun. 11, 1845.

Yadav, R., Khatkar, R., Yap, K.CH. et al. 2024.The miRNA and PD-1/PD-L1 signaling axis: an arsenal of immunotherapeutic targets against lung cancer. Cell Death Discov. 10, 414.

Zhang, R., Jing, Y., Zhang, H. et al. 2018. Comprehensive Evolutionary Analysis of the Major RNA-Induced Silencing Complex Members. Sci Rep. 8, 14189.