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Competing endogenous networks and colorectal cancer

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ABSTRACT

Colorectal cancer (CRC) is a universal health challenge worldwide. It attracted a lot of extensive research efforts to discover its molecular mechanisms and to find new prognostic markers and therapeutic targets. CRC influenced by various genetic and molecular factors, including the expression of different types of RNAs. Of these, the long non-coding RNAs (lncRNAs) which have recently become a key family of genes. LncRNA can mediate many cellular processes of tumorigenesis, progression and metastasis of CRC. Their expression was related to CRC patient outcomes which made them helpful biomarkers.

Recently, the idea of competitive endogenous RNA (CeRNA) networks was proposed. In these networks, lncRNAs interact with microRNAs (miRNAs) in a competitive manner to control some protein coding genes expression. Like many cancers, this idea was validated in CRC. These networks included lncRNAs-miRNAs-target mRNAs axes. Although these networks are complicated, they offer possible ways to intervene diagnostically and therapeutically.

This review concludes insightful information addressing a list of the lncRNA-based networks and describe how they affect CRC biology and development. Understanding these networks may identify new theranostic targets which may enhance CRC patient management.

Moreover, the gate is still open for further investigation into the molecular mechanisms underlying lncRNA-mediated regulation in CRC. New tactics might be available by focusing on dysregulated lncRNAs or their downstream effectors. In CRC, these tactics may enhance patient survival and clinical results.

Key Words: Colorectal cancer (CRC); competitive endogenous RNA (CeRNA); long non-coding RNA; micro-RNA; CeRNA network.

1. INTRODUCTION

Colorectal cancer is considered the third most common disease that causes death. In 2018, more than 861,000 mortality cases were reported, while 1.8 million new cases (1). Although the last few years have seen significant advancements in CRC detection and treatment, CRC patients still have poor prognosis and a high death rate because of metastasis and cancer stemness (2).

Colorectal cancer (CRC) starts as benign polyps. Without treatment, they become malignant tumors. Epithelial cells lining the colon or rectum cause the disease (3). Several factors influence the risk of

colorectal cancer. They are age, family history, and certain genetic abnormalities. People over 50 are more vulnerable. Recent trends show a rise in cases among younger adults (4). Lynch syndrome and familial adenomatous polyposis (FAP) have a connection. These inherited illnesses cause 5–10% of colorectal cancer (CRC) cases. Also, DNA mismatch repair (MMR) system defects cause microsatellite instability (MSI). It occurs in about 15% of colorectal tumors (5).

Non-protein coding RNAs were discovered in the last few decades. They have a crucial role in cells and human disease. Of those molecules, the long non-coding-RNA (lnc-RNA) are a type of RNA. They are longer than other non-coding RNAs. Many studies had validated the regulatory function/s for these lncRNAs. It was found to play a key role in cellular processes. These include proliferation, apoptosis, and invasion. It then affects the development of many diseases, including cancer. More precisely, researchers have proven the biology of noncoding RNAs in CRC to be either a therapeutic approach or a diagnostic approach (6,7,8,9,10,11).

Many lnc-RNAs have an identified role in CRC. They are also involved in the network that regulates CRC's development and progression. Scientists have reported the importance of these ceRNA networks. They compete in CRC-related pathways, such as Wnt/-catenin. These new competitive RNA networks contain miRNA, mRNA, and lncRNA. The lnc-RNA mediates CRC cells' growth, invasion, and metastasis. In addition, competitive endogenous RNA ceRNA crosstalk links to the development of resistance (chemo/radio-resistance) in CRC. Therefore, understanding the ceRNA and the role of each member in these networks can solve many puzzles. They are about CRC progression and therapy. Here, we list some of the key lnc-RNA players and the potential role played by each one in CRC. Any researcher interested in gathering the major role of the major lnc-RNA in CRC theragnostic may find this review helpful.

1.1. LncRNA in CRC:

LncRNAs, are transcript that are more than 200 nucleotides in length (12). Many types of cancer cells express LncRNAs, which play a role in the development of some cancer signs (13). LncRNAs influence gene expression in many ways. They are involved in chromatin, transcription, and post-transcription. In terms of chromatin modification, lncRNAs interact with chromatin remodeling complexes. They make heterochromatin at some genomic locations. This reduces gene expression. Also, lncRNAs affect transcription. They do this by interacting with RNA-binding proteins and transcription factors' coactivators or, by changing the main regulators of their target genes. LncRNAs have a structure that lets them interact with DNA, mRNAs, ncRNAs, and proteins. They affect molecules like signals, decoys, scaffolds, and guides in processes related to cancer (14,15). Previous research found that lncRNAs mainly signal in key CRC-related pathways. They also act as scaffold guides to trick CRC-specific proteins. Furthermore, lncRNAs are commonly engaged in many phases of CRC, ranging from precancerous polyps to metastatic disease, and might be used as effective diagnostic biomarkers (16,17).

1.2. MicroRNAs as regulators for cellular proteins:

MiRNAs are short, endogenous RNAs. They are 23 nt long. It is well known that they bind to miRNA recognition elements (MREs) in protein-coding mRNAs via partial complementarity (18). MREs are often in 5′ untranslated regions (5′UTRs), coding sequences (CDS), and, especially, 3′UTRs of RNA transcripts such as ncRNA and mRNA. Mature miRNAs direct miR-RISC to MREs which triggers mRNA instability or posttranslational suppression. These events mediate gene expression suppression (19). Matching miRNA nucleotides 2-8 to the targeted mRNA's 3'UTR is vital. This is what a target prediction approach does (18). Each miRNA can target several MREs. They silence hundreds of transcripts. About 60% of mammalian protein-coding genes are possible miRNA targets. This miRNA-mRNA interaction highlights potential relevance to diseases including cancer (20,21). This interaction also reflects the RNA communication in mammalian cells.

1.3. Competing endogenous RNA network (CeRNA) regulate CRC cellular function:

Seitz postulated (2009) said that many RNA transcripts with MREs act as competitive inhibitors of miRNA. The term "miRNA sponges" identifies them." They affect miRNA production and function by competing for miRNA binding sites with native mRNAs (22). Experiments proved the idea that noncoding 3'UTR segment suppressed miRNA activity. It did this by serving as a miRNA sponge (23).

Selmena (2011) suggested the competitive endogenous RNA theory (21). They hypothesized that non-coding RNA (ncRNAs), like lncRNAs, compete for miRNA binding sites. They do this via partial homology. They called these ceRNAs, based on ncRNAs. This interaction causes a drop in miRNA levels and subsequently reduces miRNA activity. The ceRNA logic was unique. Researchers have verified Herpes virus noncoding RNA. The RNA manipulates host-cell gene expression by binding to mature miR-27 (24). Also, the ceRNA system's efficacy depends on the amounts of ceRNA transcripts. More competition and ceRNA changes are crucial. They can boost or cut the target genes by the effective miRNAs. Thus, the new idea is that miRNAs may be more sensitive to degradation and regulation in cancer cells. This is due to interactions with produced ncRNAs, especially lncRNAs. These ncRNAs influence the expression of critical cancer-related genes. Data from bioinformatics showed that most cancer-related lncRNAs affect other the expression of other genes in the human genome. This confirms the presence of lncRNA-miRNA-mRNA logic in cancers. For instance, Wang et al. discovered the lncRNA-associated ceRNA mechanism in liver cancer. In this mechanism, lncRNA HULC acts as a sponge for miR-372. This hinders miR-372's activities and lowers PRKACB repression (25). More research showed that lncRNA's ceRNA pathway is important. It plays a role in the development of cancers like colon, breast, and ovarian. Here, we focus on the recently discovered lncRNA/ceRNA pathways as colorectal cancer hallmarks.

2. Examples for Lnc-RNA-based molecular networks and effect on CRC

2.1. LncRNA DCST1-AS1, hsa-miR-582-5p, and HMGB1 axis controls CRC progression.

Many studies have connected HMGB1 (High mobility group box 1) to the development of tumours. In colorectal cancer, HMGB1 promotes the growth and spread of cancer cells by acting as a tumor-promoting factor. HMGB1 expression was associated with cancer spread (27,28). Therefore, HMGB1 was reported as a good diagnostic marker (29). Moreover, many evidences showed that lncRNA, DCST1-AS1, is involved in cancer development. For example, in CRC cells, lncRNA-DCST1-AS1 is needed for the growth, migration, and invasion. CRC cell lines expressed the lncRNA-DCST1-AS1 at a higher level than normal human colonic epithelial cells reflecting its potential oncogenic role. In addition, patients with high levels of lncRNA DCST1-AS1 were likely to have a bad prognosis and lower survival rate for CRC patients (26).

MiR-582-5p functions as a tumour suppressor in a variety of malignant tumours, inhibiting the growth and start of tumours. MiR-582-5p controls CRC cell proliferation and migration (30,31). Researchers proved that hsa-miR-582-5p expression controls the expression of HMGB1 in CRC (32).

Additionally, researchers discovered that hsa-miR-582-5p is a binding partner of the lncRNA DCST1-AS1. LncRNA DCST1-AS1 increases HMGB1 expression. This encourages CRC cell aggressiveness by suppressing hsa-miR-582-5p. It is now accepted lnc-RNA DCST1-AS1/hsa-miR-582-5p/HMGB1 axis is controlling the malignant phenotype of CRC cells (26).

2.2. lncRNA FALEC mediates CRC by controlling the miR-2116-3p/PIWIL1 pathway.

Researchers demonstrated that CRC cell lines exhibited abnormal and strong expression of FALEC (33, 34, 35). Tissue specificity could explain the various occurrences. Some research groups showed that FALEC is the factor that works downstream of FALEC in CRC. Other research groups found a close link

between FALEC and miR-2116-3p. They proved that blocking miR-2116-3p (36) may reduce FALEC's oncogenic effects in CRC.

By using the TargetScan database, it was determined that PIWIL1 was the putative downstream target of miR-2116-3p. Jian and his group confirmed that miR-2116-3p and PIWIL1 interact. This group found that miR-2116-3p may regulate PIWIL1 in colorectal cancer. They ran rescue tests and discovered that PIWIL1 overexpression countered the effects of FALEC knockdown. This happened in both *in vitro* and *in vivo*. It suggested that FALEC mediates CRC by controlling the miR-2116-3p/PIWIL1 axis (36).

2.3.LncRNA FTX controls the miRNA-590-5p/RBPJ axis, which increases CRC cells' migration and invasion.

LncRNA FTX may accelerate the development of many disorders through sponging miRNAs (37, 38). Different results suggest that FTX plays an oncogenic role in CRC carcinogenesis. Researchers found an increase in FTX levels in CRC tissues and cells. Recently, silencing FTX impeded the invasion, migration, and proliferation of CRC cells (39). Also, researchers found that FTX mediates CRC carcinogenesis by sponging the downstream target, miR-590-5p. MiR-590 was supposed to target RBPJ, a transcription factor. Researchers know that RBPJ affects cellular development and carcinogenesis, including CRC (40).

2.4. LncRNA SNHG6 acts as a sponge for miR-26a/b and miR-214, which in turn affects the expression of EZH2 in colorectal cancer.

The research looked at the roles of SNHG6 in CRC. It found lncRNAs that are expressed abnormally in CRC by analyzing the TCGA database. Furthermore, poor prognosis and CRC development were indicated by increased SNHG6 expression. Functional tests showed that SNHG6 markedly increased CRC metastasis and growth in both *in vitro* and *in vivo*. It was discovered that SP1 activation and DNA copy number increases caused an elevation of SNHG6 expression in CRC tissues and cells. This group discovered that SNHG6 works in the cytoplasm as a molecular sponge of miR-26a, miR-26b, and miR-214. It may promote cancer by controlling EZH2. EZH2 is a common target of these microRNAs (41).

Chromosome 8q13, a genetic region that is often amplified in colorectal cancer, is home to SNHG6. Remarkably, they also discovered that SNHG6 might absorb miR-26a/b. Li and his team in 2018 found that higher SNHG6 expression (42) predicted a poor prognosis in CRC. Many cancer forms, including colorectal cancer (CRC), have high levels of EZH2 expression. Overexpression of EZH2 is associated with advanced disease stages and a bad prognosis (43, 44, 45, 46, 47).

Researchers showed that SNHG6 could control EZH2 expression. It does this by binding miR-26a, miR-26b, and miR-214 in competition. The results suggested that EZH2 and its targets were linked to SNHG6's cancer-causing functions in colorectal cancer (41).

Tumor progression and a low prognosis have been linked to elevated expression of SNHG6. By regulating EZH2 and its targets like a molecular sponge, SNHG6 aided in the development and metastasis of CRC cells. According to these findings, researchers concluded that SNHG6 might be a useful biomarker. It might also be a cutting-edge target for CRC treatment (41).

2.5. LncRNA CCAT1 mediates CRC by altering the expression of miR-181a-5p.

Different studies showed CCAT1 expression was much higher in CRC patients than in non-CRC patients (48, 49, 50). Notably, overexpressing CCAT1 by force made CRC cells (49) more aggressive and prone to growth. In addition, Kam and his group (2014) demonstrated that CCAT1 was exclusively expressed in CRC tissues as opposed to normal tissues (51).

In CRC tissues and cell lines, CCAT1 downregulation or miR-181a-5p overexpression inhibited the growth, movement, and invasion of CRC cells. the proliferation, migration, and invasion of CRC cells were inhibited by CCAT1 downregulation or miR-181a-5p overexpression. Similar to how

downregulating CCAT1 or upregulating miR-181a-5p promoted cell death, CCAT1 silencing was shown to decrease tumour growth *in vivo* in nude mice (52).

Knocking down CCAT1 reduced the aggressiveness and growth of CRC cells. It did this by targeting miR-181a-5p. Also, by changing the p53 protein, CRC cell apoptosis was sped up. This happened by lowering CCAT1 or raising miR-181a-5p. These findings provide insight into a potential CRC treatment plan. More functions of CCAT1 need to be investigated, though, as several tumor-associated proteins are possible targets of CCAT1 and miR-181a-5p (52).

2.6. LncRNA HOXA-AS3 promotes CRC pathogenesis by regulating the miR-4319/SPNS2 axis.

LncRNA HOXA-AS3, locates in the HOXA gene cluster, is a recently identified long non-coding RNA (lncRNA). It plays a crucial role in cancer development (53) as its depletion is associated with slow cancer cell growth, movement, and invasion. HOXA-AS3 is oncogenic in many human cancers, including glioma (54, 55) Researchers found that HOXA-AS3 is more active in clinical samples and CRC cell lines of colorectal cancer (CRC) which propose HOXA-AS3 as a promising treatment for CRC (56).

Jiang and his team showed that reducing HOXA-AS3 raised miR-4319 levels. It also lowered SPNS2 levels in CRC cells. Furthermore, the dual luciferase reporter assay confirmed that HOXA-AS3 acted as a sponge for miR-4319. This miR-4319 was reported as a tumor suppressor in various cancers. Studies found that HOXA-AS3 targets SPNS2 to change its expression. This happens during CRC progression. These findings shed light on the complex rules that cause CRC. HOXA-AS3, miR-4319, and SPNS2 construct one of the axes which control these rules (56).

2.7. LncRNA MCF2L-AS1 restricts miR-874-3p and increases the expression of CCNE1 and control the aggressiveness of colorectal cancer.

Long non-coding RNA MCF2L-AS1 (MCF2L Antisense RNA 1) has been implicated in the development of colorectal cancer via controlling gene expression. MCF2L-AS1 was reported to play an oncogenic function in the development of CRC. Pastushenko and his team (2019) did loss-of-function experiments. They found that CRC cells can't grow, migrate, or invade. Additionally, they found that MCF2L-AS1 knockdown increases apoptosis (57). Also, MCF2L-AS1 impacted EMT progression. Its downregulation suppressed N-cadherin and vimentin and overexpressed E-cadherin. This suggests that MCF2L-AS1 knockdown reduced the progression of EMT (58).

The results of this study suggest that MCF2L-AS1 may be a candidate biomarker for CRC patients. It could help with diagnosis and prognosis. Nevertheless, the sample size is modest, and larger clinical trials are required to confirm our findings (58).

MCF2L-AS1 functions as a cytoplasmic ceRNA for miR-874-3p and sponged miR-874-3p. Overexpression of MiR-874-3p suppresses MCF2L-AS1 expression. Knocking down MCF2L-AS1 enhances miR-874-3p expression in CRC cells. This supports these findings. The results showed that MCF2L-AS1 can soak up miR-874-3p. This speeds up colorectal cancer (58).

2.8. LncRNA NEAT1 controls CRC progression by modulating the miR-205-5p/VEGFA axis.

Involvement of lncRNA NEAT1 in various biological processes was reported recently (59, 60). NEAT1 levels were increased in colorectal cancer (CRC) cells. Lowering NEAT1 reduced CRC cell growth, movement, and invasion. These findings suggest that NEAT1 functions as an oncogenic factor in CRC. Moreover, NEAT1 helps tumors grow in CRC and other cancers. This underscores its importance in cancer progression (61, 62).

Downregulation of miR-205-5p in colorectal cancer (CRC) cells was also recently reported. Previous research has established that NEAT1 serves as a target for miR-205-5p. In CRC cells, there is a functional association between miR-205-5p and NEAT1. Furthermore, the capability of NEAT1 to counteract the biological effects mediated by miR-205-5p in CRC cells was confirmed (63).

Knocking down VEGFA yielded analogous outcomes to those observed with miR-205-5p, indicating a similar impact on CRC cell growth, migration, and invasion. Either NEAT1 downregulation or miR-205-5p overexpression resulted in clear inhibition of VEGFA expression in CRC cells. This validates the idea that lncRNA NEAT1 regulates VEGFA expression by sequestering miR-205-5p, thereby modulating CRC progression (63).

2.9. LncRNA RP11-400N13.3 mediates colorectal cancer by modifying the miR-4722-3p/P2RY8 axis.

Prior research has linked aberrant N13.3 expression to the advancement of cancer (64, 65). It was found that CRC cancer tissues had much higher N13.3 expression than the equivalent normal tissues. The same was true in CRC cell lines. Also, CRC patients with high N13.3 had a low survival rate. These findings suggested a close relationship between the expression level of N13.3 and the prognosis of CRC patients (66).

Functional tests were carried out in vitro and in vivo to determine the involvement of N13.3 in CRC. N13.3 KD reduced colony formation, migration, and proliferation. It also cut invasion capacities and raised cell apoptosis. Such an effect was reversed by upregulating N13.3 expression. We also showed that the knockdown of N13.3 inhibited tumor growth. Therefore, our results suggest that N13.3 contributes to CRC carcinogenesis (66).

Using the NONCODE database analysis, researchers found miR-4722-3p as a possible target of N13.3. which was validated mechanistically. N13.3 overexpression greatly reversed the inhibition of CRC cell growth. It also reversed the inhibition of colony formation, migration, and invasion. These inhibitions were caused by miR-4722-3p overexpression. When HT-29 cells were transfected with miR-4722-3p, they exhibited this negative regulation, which was counteracted by N13.3 knockdown. This finding demonstrated that miR-4722-3p might be sponged by N13.3 in CRC (66). Finally, they proved that the N13.3/miR-4722-3p/P2RY8 axis plays a role in the progression of colorectal cancer (CRC), which may provide new information on the diagnosis and therapy of CRC (66).

2.10. LncRNA RP11-757G1.5 enhances growth and spread of CRC by sponging miR-139-5p which causes the overexpression of YAP1

RP11-757G1.5, a new lncRNA, was shown to be significantly expressed in CRC tissues and cell lines compared with non-cancer tissues. The subdual of RP11-757G1.5 significantly reduced CRC growth, invasion, and movement in tests that turned off the gene (67).

RP11-757G1.5 overexpression increased PCNA and Cyclin D1, which boosted cell division. It also increased N- and E-cadherin to improve cell metastasis. Deregulation of RP11-757G1.5 was shown to inhibit cell infiltration and accretion in CRC xenografts in vivo. RP11-757G1.5 was a potential candidate oncogene. Its overexpression promoted hepatic and splenic metastases (67).

Recently, Zhu and his team introduced a novel ceRNA network, which is made up of RP11-757G1.5/miR-139-5p/YAP1. This is merely the tip of the iceberg; however, they believe that RP11-lncRNA still has many downstream targets, so more exact mechanisms still warrant investigation (67).

2.11. LncRNA TDRG1 causes the stemness of CRC by increasing PRKAR2 via targeting miR-873-5p

The deficiency of PRKAR2 has been reported to promote hematopoietic malignancies in vivo (68) and protect mice from experimental colitis by increasing IFN-stimulated expression and modulating the microbiota in the intestine suggesting that PRKAR2 is critical for tissue development (69).

It is noteworthy that prior research has demonstrated that miR-873-5p targets TDRG1 in NSCLC cells. That, when four possible targets of miR-873-5p were identified using available datasets (condition:

common elements of microT, RNA22, and Targetscan), each of them showed a drop in mRNA expression in CRC cells that had overexpressed miR-873-5p (70).

In a trial to find out the target for miR-873-5p, researchers found that it targets TDRG1 in CRC cells. However, Hong and his team (2022) proved that PRKAR2 functions as a downstream effector of the TDRG1/miR-873-5p axis. That was validated this as it showed the greatest rise in CRC cells after miR-873-5p overexpression compared to other genes. They also observed that PRKAR2 and miR-873-5p had partially reversed the effects of TDRG1 on CRC stemness (70). Together with the fact that lncRNA-TDRG1 binds to miR-873-5p in a competitive manner, they proposed the ceRNA for PRKAR2-TDR-miR-873-5p in CRC cells controlling CRC stemness (70).

2.12. Long non-coding RNA, ZFPM2 AS1, promotes the growth of CRC via ensnaring miR-137, which modifies the activity of TRIM24.

ZFPM2-AS1 expression was elevated in human CRC tissues and its expression levels was related to the clinical attributes. The study indicated that ZFPM2-AS1 is essential for the invasion, migration, and multiplication of CRC cells. A strong correlation between TNM stage, histological differentiation, and tumour size with ZFPM2-AS1 expression levels was reported. Therefore, it was believed that ZFPM2-AS1 had an oncogenic role in CRC. Its KD decreased the in vitro migration (72).

Balaguer and others found that ZFPM2-AS1 act as a target for miR-137 which is known to prevent the cancerous CRC phenotype (71). Finally, they revealed that the ZFPM2-AS1/miR-137/TRIM24 axis could control the development of CRC (72).

2.13. RP11-51O6.1 promotes colorectal cancer by increasing YAP1 through sponging miR-206.

RP11-51O6.1 can boost the growth, movement, and invasion of CRC cells. Its effect was related to its subcellular location, which controls its activity. Overexpression of RP11-51O6.1 can undo the inhibitory effect of YAP1 on CRC cell invasion and proliferation (73).

But miR-206 was found abundant and highly expressed in CRC. It was involved in ceRNA action mechanism. A research group discovered a molecular model in which CRC is promoted via the RP11-51O6.1/miR-206/YAP1 axis (73).

2.14. LncRNA FENDRR interacts with Sox2 RNA to prevent colorectal cancer (CRC) cells' stemness.

The low FENDRR expression in spheres suggested that FENDRR can inhibit the stem cells of CRC. Experimentally, this was shown with CRC cells (74). FENDRR acts as a molecular sponge to regulate CRC. It does this by interacting with miR-18a-5p. FENDRR raises ING4's expression while suppressing CRC (75).

Sox2 mRNA is crucial for stemness. It is affected by lncRNA FENDRR. This leads to decreased expression and stability. FENDR affected Sox2 mRNA is similar to the regulation mechanism of miRNAs on transcripts; this is confirmed by their interaction. The mechanism explained by which FENDRR suppresses cancer stem cell (CSC)-like characteristics in CRC. FENDRR confirmed suppressing Sox4 protein expression (74).

2.15. LncRNA SNHG20 promotes the proliferation, migration, and invasion of colorectal cancer cells by modifying the miR-495/STAT3 axis.

High expression of SNHG20 has been linked to CRC tissues and has been implicated in the initiation and progression of CRC. Experimentally silencing SNHG20 with interfering RNAs slows CRC growth and spread in animals. Additionally, it halted the proliferation, migration, and invasion of CRC cells in vitro (76, 77).

Yan and his colleagues (2017) found lower levels of miR-495 in CRC tissues and cell lines compared to their normal counterparts. Overexpression of miR-495 slowed the growth of CRC cells. It also obstructed their colony formation, migration, and invasion (78). MiR-495 has been implicated in the development and progression of various tumors, including CRC (79).
In silico predictions suggested that miR-495 could bind to SNHG20 (78). This shows the finding that SNHG20 increases STAT3 expression. It shows its role as a competing endogenous RNA (ceRNA) in CRC progression (77).

2.16. LncRNA ABHD11-AS1 controls the miR-133a/SOX4 axis, which promotes the growth of CRC.

High ABHD11-AS1 expression was proposed as a useful prognostic marker for CRC patients. This shows its oncogenic role in the same cancer (80). Knock-down-based depletion of ABHD11-AS1 inhibited CRC cell proliferation and invasion in vitro and in vivo. These results proved its role in CRC carcinogenesis (81) as well as its role in malignancies (82, 83).
ABHD11-AS1 was also reported in sponge miR-133a. It is known to target SOX4. This forms a ceRNA involved in the growth and spread of CRC. These findings propose that network members are a potential therapeutic target for managing colorectal cancer (80).

3. CONCLUSION

CRC biology is complex. Recently, the idea of competitive endogenous RNA (CeRNA) networks was proposed. In these networks, long noncoding RNAs (lncRNAs) bind to microRNAs (miRNAs) in a competitive manner to control some genes expression. This idea was proposed for cancers, including CRC. It involves a network of lncRNAs, miRNAs, and target mRNAs. Although these networks are complicated, they offer possible ways to intervene diagnostically and therapeutically. This review offers insightful information addressing a list of the lncRNA-based networks and how they affect CRC. Understanding these networks may identify new theranostic targets which may enhance CRC patient management. However, the gate is still open for further investigation into the molecular mechanisms underlying lncRNA-mediated regulation in CRC.

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