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The Role of LncRNA ROR in Colorectal Cancer Diagnosis and Treatment

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Abstract

Context: Colorectal cancer (CRC) is one of the most common causes of cancer-related deaths worldwide, particularly in developed countries. Despite advances in detection and treatment, CRC remains difficult to diagnose in its early stages, complicating patient outcomes. Recently, long non-coding RNAs (lncRNAs) have emerged as significant regulators in cancer biology, offering new opportunities for cancer diagnostics.

Evidence Acquisition: This review highlights the molecular mechanisms through which LncRNA ROR influences CRC development, its diagnostic potential as a biomarker, and the future challenges of integrating LncRNA ROR into clinical practice.

Results: Future research must focus on large-scale validation studies and explore the therapeutic implications of targeting LncRNA ROR.

Conclusions: Overall, this review positions LncRNA ROR as a promising biomarker with potential applications in both CRC diagnosis and treatment.

Keywords: Colorectal Cancer (CRC), Long Non-coding RNAs (lncRNAs), LncRNA ROR, Biomarkers

1. Context

Colorectal cancer (CRC) remains one of the most prevalent cancers globally, posing a significant threat to public health. It ranks as the third most common cause of cancer-related deaths in both men and women in developed nations (1-5). Although early detection can dramatically improve survival rates, the asymptomatic nature of early-stage CRC often leads to late diagnoses, complicating treatment and reducing patient survival chances (6). The mechanisms underlying CRC development and progression are still not fully understood, making it a challenging disease to diagnose and treat effectively (7).

Recent advancements in molecular biology have emphasized the importance of biomarkers in cancer diagnosis. Among these biomarkers, long non-coding RNAs (lncRNAs) have emerged as critical players in cancer development, offering new avenues for early detection, prognosis, and therapeutic targeting (8). Long non-coding RNAs, a subclass of non-protein-coding RNA molecules longer than 200 nucleotides, have shown potential in regulating gene expression at transcriptional, post-transcriptional, and epigenetic levels (9). These functions make them attractive candidates for cancer biomarkers (10).

In particular, the lncRNA known as lncRNAs ROR (regulator of reprogramming) has gained attention due to its significant role in CRC tumorigenesis (11). Long non-coding RNA ROR has been implicated in various oncogenic processes, including cell cycle regulation, apoptosis inhibition, and tumor invasion (12, 13). This review aims to highlight the importance of LncRNA ROR

as a biomarker for CRC diagnosis, focusing on its molecular mechanisms and diagnostic potential.

1.1. Role of Long Non-coding RNAs in Cancer

Long non-coding RNAs are a unique class of RNA molecules, characterized by their length of over 200 nucleotides and their inability to encode proteins (14). Despite their lack of protein-coding capability, lncRNAs play vital roles in the regulation of gene expression through diverse mechanisms (15, 16). These functions include the modulation of chromatin structure, transcriptional regulation, and post-transcriptional processes such as RNA splicing, transport, and stability (17). In recent years, the involvement of lncRNAs in various physiological and pathological processes has been extensively studied, particularly their influence on cancer development and progression (18).

In the context of cancer, lncRNAs exhibit both oncogenic and tumor-suppressive roles. Some lncRNAs have been found to promote cancer cell proliferation, invasion, metastasis, and resistance to chemotherapy, while others suppress tumor growth and progression (19). Their ability to regulate such processes has made lncRNAs an important focus of cancer research, especially in identifying potential biomarkers for diagnosis and therapeutic targets (20).

Several lncRNAs have been implicated in CRC. For instance, lncRNA CCAT1 has been shown to promote CRC tumor growth by enhancing MYC expression (21). Another lncRNA, HOTAIR, has been linked to increased metastasis in CRC through its role in chromatin remodeling and gene silencing (22). These examples underscore the functional significance of lncRNAs in cancer biology.

Among the lncRNAs associated with CRC, LncRNA ROR has emerged as a promising biomarker due to its role in regulating cellular reprogramming and its involvement in the critical molecular pathways of cancer progression (23). As research on lncRNAs continues to evolve, the potential for these molecules to serve as reliable biomarkers for early cancer detection and personalized treatments becomes more evident.

1.2. Long Non-coding RNAs ROR as a Biomarker in Colorectal Cancer

Long non-coding RNAs ROR (regulator of reprogramming) has garnered significant attention due to its role in the regulation of pluripotency and its emerging link to cancer biology (24). Originally identified in the context of cellular reprogramming, LncRNA ROR has since been recognized for its influence on cancer cell behavior, particularly in CRC (25). As a non-coding RNA, LncRNA ROR is involved in various regulatory functions, influencing processes such as apoptosis inhibition, cell proliferation, and cellular stress responses, all of which contribute to tumorigenesis (26).

In CRC, LncRNA ROR has been shown to have elevated expression in tumor tissues compared to non-tumor tissues. Studies utilizing real-time PCR (RT-PCR) techniques have confirmed that the expression levels of LncRNA ROR are significantly higher in CRC patients, suggesting a correlation between LncRNA ROR expression and tumor progression (27, 28). This upregulation indicates that LncRNA ROR may play a crucial role in the early stages of cancer formation by inhibiting programmed cell death (apoptosis), allowing cancer cells to evade typical cellular stress responses (29).

Moreover, the increased expression of LncRNA ROR in CRC has been linked to its potential role as a diagnostic biomarker. By measuring LncRNA ROR levels in patients' blood or tissue samples, clinicians may be able to identify the presence of CRC at earlier stages. The non-invasive nature of using lncRNAs as biomarkers further enhances their appeal, making LncRNA ROR a valuable candidate for future diagnostic tools (30, 31).

Research has also highlighted the possibility of using LncRNA ROR as a predictor of cancer prognosis. Its expression level may serve as an indicator of tumor aggressiveness, with higher levels corresponding to more advanced or metastatic stages of CRC (31). This makes it a dual-purpose biomarker, both for early detection and for assessing disease severity. The potential of LncRNA ROR to be developed into a reliable clinical biomarker for CRC diagnosis is promising. However, more research is required to validate its effectiveness across larger patient populations and to integrate it into routine clinical practice.

1.3. Mechanism of Action: How Long Non-coding RNAs ROR Influences Colorectal Cancer

Long non-coding RNAs ROR has been shown to exert significant influence on the molecular pathways that govern CRC development and progression. Its impact on colorectal tumorigenesis is largely mediated through its interactions with other molecular regulators, which control processes such as cell survival, proliferation, and metastasis (11, 16). By regulating key pathways, LncRNA ROR contributes to the hallmarks of cancer, including resistance to apoptosis, sustained proliferation, and tumor invasion (18, 19).

1.4. Inhibition of Apoptosis and Regulation of Cellular Stress

One of the primary mechanisms through which LncRNA ROR exerts its oncogenic effect is the inhibition of apoptosis (20). Apoptosis, or programmed cell death, is a crucial process in maintaining healthy tissue homeostasis by eliminating damaged or abnormal cells. In cancer, the suppression of apoptosis allows malignant cells to survive and proliferate unchecked (12). LncRNA ROR plays a pivotal role in this process by downregulating pro-apoptotic pathways, thereby enabling cancer cells to evade cell death even in the presence of cellular stress (13).

Additionally, LncRNA ROR regulates the cellular response to stress, particularly oxidative stress and endoplasmic reticulum (ER) stress, both of which are known to induce apoptosis in healthy cells (21, 23). By mitigating the effects of these stressors, LncRNA ROR further enhances the survival and proliferation of CRC cells (15).

1.5. Regulation of Epithelial-Mesenchymal Transition

Long non-coding RNAs ROR is also involved in the regulation of epithelial-mesenchymal transition (EMT), a process by which epithelial cells lose their polarity and adhesion properties, gaining migratory and invasive characteristics typical of mesenchymal cells (17, 24). Epithelial-mesenchymal transition is a key step in cancer metastasis, enabling tumor cells to spread from the primary tumor site to distant organs (22). In CRC, LncRNA ROR has been implicated in promoting EMT by influencing the expression of key markers such as E-cadherin, N-cadherin, and vimentin (25, 26). Research has demonstrated that the upregulation of LncRNA ROR leads to a decrease in E-cadherin (a cell adhesion molecule) and an increase in N-cadherin and vimentin, both of which are associated with enhanced motility and invasiveness of cancer cells (27). This shift in cellular characteristics facilitated by LncRNA ROR contributes to the metastatic potential of CRC, making it a key player in disease progression (29, 31).

1.6. Impact on Tumor Metabolism and Immune Evasion

Emerging evidence also suggests that LncRNA ROR may influence tumor metabolism and immune responses, both of which are critical for cancer survival (31). Cancer cells often undergo metabolic reprogramming to support their rapid growth, and LncRNA ROR has been associated with changes in metabolic pathways that promote energy production and biosynthesis necessary for tumor growth (20, 22). Furthermore, LncRNA ROR has been found to play a role in modulating immune responses, allowing cancer cells to evade immune detection (26). By regulating the expression of immune checkpoint molecules and other immune-modulating factors, LncRNA ROR helps CRC cells escape immune surveillance, contributing to tumor persistence and progression (23, 26).

1.7. Diagnostic Potential of Long Non-coding RNAs ROR

The identification of reliable biomarkers for the early detection and diagnosis of CRC remains a crucial goal in cancer research. Among the emerging biomarkers, lncRNAs like LncRNA ROR have shown considerable promise (25). With its significant role in CRC tumorigenesis and progression, LncRNA ROR stands out as a potential diagnostic marker that could revolutionize how CRC is detected, particularly in its early stages (27).

1.8. Real-time PCR for Detecting Long Non-coding RNAs ROR Expression

One of the primary methods used to detect LncRNA ROR in clinical and experimental settings is real-time PCR (29). This technique allows for the precise quantification of RNA expression levels in both tumor and non-tumor tissues (22). Studies have demonstrated that LncRNA ROR is upregulated in CRC tumor samples compared to adjacent non-cancerous tissues, indicating its association with tumorigenesis (30). By using RT-PCR to measure the expression of LncRNA ROR, researchers can identify whether a patient's tissue samples exhibit the characteristic overexpression linked to CRC (31). This diagnostic approach has the advantage of being highly sensitive, enabling the detection of even small changes in RNA levels (16). Additionally, the non-invasive nature of sampling—potentially from blood or stool—adds to the appeal of LncRNA ROR as a diagnostic tool (16). In clinical practice, this method could be employed as part of routine screening to identify individuals at risk for CRC before more invasive symptoms emerge (14).

1.9. Sensitivity and Specificity: Receiver Operating Characteristic Curve Analysis

To evaluate the diagnostic efficacy of LncRNA ROR, researchers have utilized receiver operating characteristic (ROC) curve analysis (17). Receiver operating characteristic curves assess the performance of a diagnostic test by plotting sensitivity (true positive rate) against specificity (true negative rate) (23). The area under the ROC curve (AUC) provides a measure of the test's overall accuracy (20). In studies analyzing LncRNA

ROR as a biomarker for CRC, the AUC values have consistently indicated high sensitivity and specificity (22). This means that LncRNA ROR expression levels are both highly accurate in distinguishing between cancerous and non-cancerous tissues and capable of identifying CRC with minimal false-positive or false-negative results (24). In practical terms, the higher the AUC value, the more reliable LncRNA ROR becomes as a tool for early detection of CRC (26).

1.10. Potential for Non-invasive Testing

One of the most exciting prospects for LncRNA ROR lies in its potential use in non-invasive diagnostic tests (29). Because lncRNAs like LncRNA ROR are stable and detectable in body fluids such as blood, urine, and stool, there is growing interest in developing non-invasive diagnostic tests that leverage this biomarker (31). Detecting LncRNA ROR in peripheral blood could provide a minimally invasive means of screening for CRC, offering a more accessible and patient-friendly alternative to traditional colonoscopy or biopsy methods (18). The development of non-invasive tests based on LncRNA ROR would enable routine screening, especially in high-risk populations, significantly improving early diagnosis rates (24). Early detection is key to improving CRC outcomes, and incorporating LncRNA ROR into screening programs could help identify the disease in its nascent stages when treatment is most effective (30).

1.11. Future Prospects and Challenges

1.11.1. Potential for Non-invasive Diagnostics

One of the most compelling future prospects for LncRNA ROR is its use in non-invasive diagnostics (25). As discussed, LncRNA ROR is detectable in peripheral blood and other body fluids, making it a prime candidate for liquid biopsy technologies (27). Liquid biopsies, which analyze biomarkers in bodily fluids rather than through invasive tissue biopsies, have the potential to revolutionize cancer diagnostics by enabling early detection, disease monitoring, and personalized treatment plans (16).

In the future, routine screening for CRC could involve blood-based tests that measure LncRNA ROR expression levels (22). This would make the process of early detection more patient-friendly and reduce the reliance on more invasive techniques like colonoscopies (26). However, for this vision to be fully realized, more extensive research is needed to standardize testing methods, optimize sensitivity, and minimize variability across patient populations (30).

1.12. Integration with Personalized Medicine

Beyond diagnostics, LncRNA ROR holds potential in the field of personalized medicine (24). As research continues to elucidate the molecular pathways regulated by LncRNA ROR, it may be possible to develop targeted therapies that inhibit its oncogenic activity (29). For example, drugs or therapeutic agents designed to silence LncRNA ROR expression could potentially block its role in cancer progression, leading to more effective treatments for CRC patients (19).

Additionally, LncRNA ROR expression levels could serve as a predictive biomarker to help tailor treatment decisions (27). Patients with higher LncRNA ROR expression may exhibit distinct responses to chemotherapy or targeted therapies, allowing clinicians to customize treatments based on the molecular profile of each patient's tumor (30). As personalized medicine continues to evolve, LncRNA ROR could play a critical role in guiding individualized treatment strategies (25).

1.13. Challenges in Clinical Application

While the potential applications of LncRNA ROR are vast, several challenges remain in its clinical implementation (16). One of the primary hurdles is the lack of standardized protocols for measuring lncRNA expression levels in clinical settings (23). Variability in RNA extraction methods, quantification techniques, and data interpretation can lead to inconsistent results, which hinders the reliability of LncRNA ROR as a diagnostic tool (17).

Furthermore, lncRNAs, including LncRNA ROR, can exhibit tissue-specific and context-dependent expression (14). This means that their expression levels may vary not only between individuals but also depending on the specific biological or environmental conditions (21). To overcome this, large-scale studies involving diverse patient populations are required to validate LncRNA ROR as a robust biomarker across various demographic and clinical contexts (30).

Another challenge lies in distinguishing the biological significance of LncRNA ROR in cancer from its expression in normal physiological conditions (26). Long non-coding RNAs often have roles in normal cellular processes, and understanding how LncRNA ROR contributes specifically to CRC, as opposed to other non-pathological functions, is essential for its targeted use in diagnostics and therapy (29).

1.14. Future Research Directions

Future research on LncRNA ROR should focus on several key areas:

(1) Large-Scale validation studies: Extensive clinical studies are needed to confirm the diagnostic accuracy of LncRNA ROR across different patient populations and stages of CRC. This will help establish its reliability as a universal biomarker and ensure its applicability in diverse demographic and clinical settings.

(2) Development of non-invasive tests: Continued efforts should be directed toward the development of non-invasive liquid biopsy techniques that incorporate LncRNA ROR. These methods should prioritize reliability, sensitivity, and cost-effectiveness to facilitate widespread CRC screening and early detection.

(3) Targeted therapies: Investigating the potential for therapeutics aimed at silencing or inhibiting LncRNA ROR expression will be essential for expanding its role beyond diagnostics and into treatment modalities. Such therapies could provide a targeted approach to interrupt its oncogenic functions and improve CRC treatment outcomes.

(4) Mechanistic studies: Deeper exploration of the molecular pathways regulated by LncRNA ROR could reveal novel targets for CRC treatment. These studies will enhance our understanding of how this lncRNA influences tumor behavior, contributing to the development of innovative therapeutic strategies.

2. Conclusions

In conclusion, LncRNA ROR offers significant potential as both a diagnostic biomarker and therapeutic target in CRC. Its elevated expression in tumor tissues, involvement in key cancer-promoting pathways, and detectability in non-invasive samples highlight its promise in advancing CRC diagnosis and personalized treatment approaches. However, challenges related to standardization, validation, and understanding its broader biological role must be addressed through further research. With continued efforts, LncRNA ROR may one day become a cornerstone in the fight against CRC, improving early detection rates and guiding more effective, individualized treatments.

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