Dysregulated expression of miR-367 in disease development and its prospects as a therapeutic target and diagnostic biomarker (Review)

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Abstract. MicroRNA (miR)-367 has a wide range of functions in gene regulation and as such plays a critical role in cell proliferation, differentiation and development, making it an essential molecule in various physiological processes. miR-367 belongs to the miR-302/367 cluster and is located in the intronic region of human chromosome 4 on the 4q25 locus. Dysregulation of miR-367 is associated with various disease conditions, including cancer, inflammation and cardiac conditions. Moreover, miR-367 has shown promise both as a tumor suppressor and a potential diagnostic biomarker for breast, gastric and prostate cancer. The elucidation of the essential role of miR-367 in inflammation, development and cardiac diseases emphasizes its versatility in regulating various physiological processes beyond cancer biology. However, further research is necessary to fully understand the complex regulatory mechanisms involving miR-367 in different physiological and pathological contexts. In conclusion, the versatility and significance of miR-367 makes it a promising candidate for further study and in the development of new diagnostic and therapeutic strategies.

Contents

1. Introduction
2. miRNA biogenesis
3. Roles of miR-367 in disease pathogenesis
4. Conclusion and future perspectives

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1. Introduction

The discovery of the Lin-4 gene in the nematode, *Caenorhabditis elegans,* in 1993 by Lee *et al* (1) marked a major milestone in the field of RNA biology. Lin-4 encodes a small RNA molecule that was later found to belong to a larger family of RNA molecules known as microRNAs (miRNAs) (2). miRNAs are short (18-25 nucleotides), non-coding RNA molecules that play a crucial role in post-transcriptional regulation of gene expression by binding to the complementary mRNA at the 3'-untranslated region (UTR) and silencing the expression of the target gene (2). The binding of miRNAs to their target mRNA can lead to mRNA degradation or translational repression, depending on the degree of complementarity between the miRNA and the target mRNA. The 3'-UTR is the most common site for miRNA binding, but miRNAs can also interact with other regions of the target mRNA, such as the 5'-UTR, gene promoters and the coding region (2).

In terms of molecular mechanisms, gene expression is highly regulated through transcriptional, post-transcriptional and translational processes during development. miRNAs play a critical role in this complex regulatory network, requiring various feedback and feedforward mechanisms to ensure proper gene expression (3). miRNAs are versatile and important regulators of various cellular processes that influence the development and function of living organisms, and play crucial roles in fundamental biological events, such as cell differentiation (4), tissue regeneration (5), epithelial-mesenchymal transition (6), embryogenesis (7), proliferation, apoptosis and metabolism (8). A substantial body of clinical and preclinical evidence supports the role of miRNAs in various diseases, including cancer (9) and infectious (10), neurodegenerative (11), cardiovascular and immune-related diseases (12,13). Hence, miRNAs have emerged as promising biomarkers and therapeutic targets for a variety of diseases. Analyzing miRNA expression patterns is a promising method for detecting cancer, predicting disease prognosis and evaluating treatment efficacy (9,14). A key advantage of miRNAs is their high stability in bodily fluids and tissues. In the bloodstream, miRNAs are found in RNA-binding complexes

and/or exosomes, and their short length makes them resistant to degradation, improving their stability in various storage conditions (9,14). Studies have shown that miRNAs are markedly resilient in plasma and serum, maintaining their integrity despite exposure to RNase activity, extreme pH and multiple rounds of freezing-thawing (15,16).

The present review focuses on miR-367, a member of the miR-302/367 cluster found in the intronic region on the 4q25 locus of human chromosome 4 (17). This cluster, which includes miR-302a/b/c/d and miR-367, has been extensively studied and is involved in diverse neoplastic diseases through various modes of gene regulation. The miR-302/367 cluster is transcribed as a 1,974-nucleotide miRNA precursor for eight miRNAs, from a polycistronic miRNA gene containing the classical TATA box and polyadenylation signal (18). Regulated expression of the miR-302/367 cluster in the nucleus, cytoplasm and outside the cell, in addition to the exchange of its members between cells via exosomes, results in the differential expression and biological importance of the cluster (17,18). mir-367 has poor sequence homology with the other members of the miR-302/367 cluster and thus has mostly different mRNA targets and mechanisms of action compared with miR-302a/b/c/d (19). miR-302 family members were previously recognized as essential components of somatic cell reprogramming to generate pluripotent stem cells (20). In addition, the involvement of the miR-302/367 cluster in colorectal cancer is mostly mediated by the miR-302 family members (21). Despite the differences in sequences, targets and functions between miR-302a/b/c/d and miR-367, these miRNAs were commonly considered as a general miR-302/367 cluster in various contexts (17,18,20,21). Hence, it is crucial to examine the roles of miR-367 more specifically in cancer and other physiological processes due to its distinct targets and functions from miR-302.

Overall, the present review highlights the role of miR-367 in various physiological processes and cancer biology. A comprehensive understanding of miR-367 function may contribute to the development of new diagnostic and therapeutic strategies for a range of diseases. The potential of miR-367 as a therapeutic target warrants further investigation, and ongoing studies may reveal opportunities for its use in clinical settings.

2. miRNA biogenesis

The biogenesis of miRNAs begins with the processing of RNA transcripts either post- or co-transcriptionally (22). According to de Rie *et al* (23), most miRNAs are intragenic and originate from introns of protein-coding genes. By contrast, intergenic miRNAs are located between genes, therefore lacking a host gene, and are transcribed via their own polymerase II (Pol II) or polymerase III (Pol III) promoters (24).

In animals, miRNA biogenesis involves a series of steps, starting with the transcription of primary miRNA (pri-miRNA) from the DNA sequence and progressing to the generation of mature miRNA (22). Drosha, a class 2 ribonuclease III enzyme (25), plays a central role in this process by processing pri-miRNAs into precursor-miRNAs (pre-miRNAs) within the nucleus (26). After Drosha cleaves the pri-miRNA transcript, the resulting pre-miRNA is transported to the cytoplasm for further processing (27). This transport is facilitated by the Ras-related nuclear protein GTPase-dependent nuclear transport receptor, exportin-5 (28). In the cytoplasm, Dicer, a ribonuclease III enzyme, further processes the pre-miRNAs into functional 21 or 22-nucleotide miRNAs. These miRNAs are then incorporated into Argonaute proteins to form miRNA-induced silencing complexes (miRISCs), which regulate gene expression through post-transcriptional silencing of complementary target mRNAs (2). miRISC recruitment to target mRNAs can result in their degradation or translational repression, leading to gene silencing (29).

3. Roles of miR-367 in disease pathogenesis

miR-367 in cancer. Extensive cancer research has focused on miR-367, which has demonstrated tumor-suppressing activity through the targeting of oncogenes. In multiple types of cancer, including breast (30-32), gastric (33,34) and prostate cancer (35), higher levels of miR-367 have been associated with improved prognoses and survival rates. In addition, miR-367 has been recognized as a possible biomarker for diagnosing various types of cancer including breast (30,31) and gastric (33) cancer (Fig. 1).

Breast cancer. Breast cancer is a common cancer mainly found in women, accounting for 11.7% of all cancer diagnoses and 6.9% of cancer-related deaths globally in women (36). Studies have shown that miRNAs can be either upregulated (37) or downregulated (30,31) in patients with breast cancer and different levels can distinguish these patients from healthy individuals. Studies have shown that miR-367 is involved in the development and progression of breast cancer, and its dysregulation has been implicated in various aspects of breast cancer biology, including cell proliferation, apoptosis, invasion and metastasis (32,38).

In a recent study, Yang *et al* (30) discovered that miR-367-3p expression was significantly downregulated in the whole blood samples of patients with breast cancer with axillary lymph node metastasis (ALNM). This finding was particularly significant as it highlighted the potential diagnostic value of miR-367-3p in distinguishing between patients with breast cancer with or without ALNM. The presence of ALNM is a critical factor in determining the prognosis of patients with breast cancer and ALNs are the most common site for breast cancer metastasis (39). The results of the study demonstrated that low expression of miR-367-3p was associated with positive ALNM, larger tumor size and a more advanced tumor-node-metastasis stage (30). In addition, a study conducted by Liu *et al* (31) revealed a strong association between miR-367 expression and the clinicopathologic features and prognosis of breast cancer. It was found that the miR-367 expression level in the serum of patients with breast cancer was significantly lower than that of the control group. Moreover, the study demonstrated that the downregulation of miR-367 in patients with breast cancer was strongly correlated with advanced tumor stage, larger tumor size and lymph node metastasis. Furthermore, the study demonstrated that patients with breast cancer with low levels of miR-367 had significantly shorter disease-free and overall survival times compared with the control group. These findings suggest that miR-367 may play a critical role in the progression and prognosis of breast cancer and that circulating miR-367 has potential as a non-invasive biomarker for breast cancer.

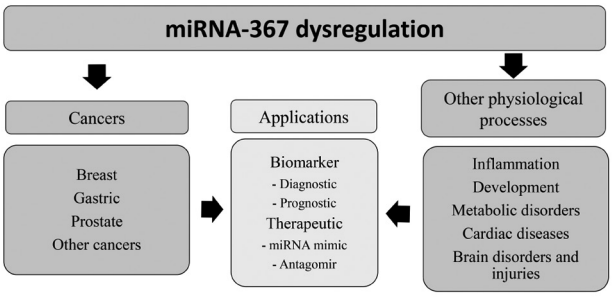

Figure 1. Dysregulation of miR-367 in various cancer types and physiological processes and its potential applications as a biomarker and therapeutic target. miR, microRNA.

A recent study investigating the involvement of miR-367-3p in breast cancer using the MCF-7 cell line also demonstrated its potential as a therapeutic target (32). The study found that miR-367-3p could induce apoptosis and suppress migration of MCF-7 cells by downregulating the expression of human choline kinase α, a key enzyme involved in breast cancer progression. Furthermore, bioinformatics analysis demonstrated that miR-367-3p was related to numerous potential targets, such as metal regulatory transcription factor 1 and phosphatase and tensin homolog, and multiple tumor-related pathways, including cell adhesion molecules, mammalian target of rapamycin and cellular senescence pathways, suggesting that it may play a crucial role in the development and progression of breast cancer (30). Overall, these findings highlight the potential clinical utility of miR-367-3p as a diagnostic marker and its potential role in breast cancer pathology.

Gastric cancer. According to GLOBOCAN 2020, an online database providing global cancer statistics and estimates of incidence and mortality rates in 185 countries for 36 types of cancer, gastric cancer is the fifth most common cancer and the fourth most common cause of cancer-related death worldwide (36). This disease remains difficult to cure, primarily due to most patients presenting with advanced disease, when prognosis is poor and treatment options have become limited (40). Thus, it is important to develop a method to identify and predict gastric cancer prognosis in clinical settings at the earlier stages of disease. miRNAs play a significant role in gastric cancer, influencing cell cycle, proliferation, apoptosis, migration and invasion (41). In addition, miR-367-3p acts as a tumor suppressor in gastric cancer (34). A study by Bin *et al* (33) found that miR-367 expression is downregulated in gastric cancer tissues and is linked to disease progression. The study also revealed that overexpression of miR-367 in gastric cancer cells inhibited migration and invasion by targeting Rab23, and that Rab23 overexpression reversed the inhibitory effect of miR-367. Thus, miR-367 is a crucial negative regulator of gastric cancer invasion and metastasis, indicating its potential as a therapeutic tool for treating this disease.

Tao *et al* (34) reported that miR-367-3p has the potential to bind to the 3'-UTR of high-mobility group AT-hook 2 (HMGA2) mRNA, an oncogene in gastric cancer. The study also demonstrated that miR-367-3p negatively regulated the expression of HMGA2 at both the mRNA and protein level in gastric cancer cells, as confirmed by luciferase reporter assays. Additionally, the levels of miR-367-3p and HMGA2 mRNA exhibited a negative correlation in gastric cancer tissues. By contrast, in a 2018 study by Liu *et al* (42), it was discovered that miR-367-5p functions as an oncogene in gastric cancer cells and targets $p27^{Kip1}$, which is a CDK inhibitor that regulates cell proliferation, cell motility and apoptosis. In addition, low expression of $p27^{Kip1}$ was associated with poor prognosis and high-grade tumors in gastric cancer. The study also found that the expression of circular RNA of Yes-associated protein 1 (circYAP1), which acted as a sponge for miR-367-5p, was significantly downregulated in gastric cancer tissues, and this low circYAP1 expression was associated with poor patient prognosis. circYAP1 upregulated the expression of $p27^{Kip1}$, but this effect was inhibited by miR-367-5p. Therefore, the study demonstrated that miR-367-5p targeted $p27^{Kip1}$ and that circYAP1 sponged miR-367-5p to upregulate $p27^{Kip1}$ expression in gastric cancer cells.

Moreover, overexpression of miR-367-3p was found to promote growth, migration and epithelial-mesenchymal transition of gastric cancer cells, while inhibition of this miRNA led to the opposite effect (43). Based on the contrasting effects of miR-367 (possibly due to whether it is miR-367-3p or 5p) on the pathogenesis of gastric cancer, the use of this miRNA as a therapeutic target or biomarker is dependent on the pathway involved.

Prostate cancer. Prostate cancer is a common type of cancer in males. Siegel *et al* (44) reported that >248,530 cases of prostate cancer will be diagnosed in 2021, resulting in 34,130 deaths. While prostate-specific antigen is commonly used as a marker to diagnose and predict the progress of prostate cancer, its effectiveness is limited due to false-positive outcomes, which can result in the unnecessary treatment of non-aggressive cancer and incorrect decisions for treating cases of relapse (45). Consequently, there is a significant need for new approaches to identify and predict prostate cancer prognosis in clinical settings at earlier stages of disease.

Studies have shown that miR-367 is dysregulated in prostate cancer and plays a role in prostate cancer pathogenesis (46,47). A recent study by Du *et al* (35) demonstrated that miR-367-3p inhibited the expression of Rab23 and the Hedgehog signaling pathway in prostate cancer cells. Rab23 is a GTPase family member and is known to play a critical role in tumor progression (48). The Hedgehog signaling pathway is a downstream pathway of Rab23, and its overactivation has been implicated in oncogenic occurrence and development. Notably, miR-367-3p is downregulated in prostate cancer, and overexpression of miR-367-3p has been found to impede cell proliferation, invasion, and migration as demonstrated by *in vitro* and *in vivo* experiments (35). Furthermore, Du *et al* (35) found that miR-367-3p downregulates the Hedgehog pathway, leading to the regulation of key transcription factors, Gli1 and Gli2, which are responsible for cell proliferation, differentiation and angiogenesis. These findings suggest that miR-367-3p exerts tumor-suppressive effects by targeting critical genes and cell signaling pathways, making it a promising target for further investigation of prostate cancer treatment.

Other cancer types. Kaid *et al* (49) discovered that miR-367 may be a therapeutic target and a marker in aggressive embryonal central nervous system tumors, and it may facilitate prognosis and early diagnosis of this disease. Circulating miR-367 is also upregulated in acute lymphoblastic

leukemia (ALL), making it a potential therapeutic target and a distinguishing factor between patients with ALL and healthy individuals (50).

In endometrial cancer, miR-367-3p expression levels are correlated with the International Federation of Gynecology and Obstetrics stage and lymph node metastasis (51). High expression of miR-367-3p results in high survival rates, suppression of cancer cell metastasis and inhibition of malignant tumor behaviors. This is achieved through the downregulation of HMGA2 by miR-367-3p, as shown by Ma *et al* (51). The study also suggested that the miR-302a-5p/367-3p-HMGA2 axis could be used as a diagnostic biomarker for endometrial carcinoma metastasis and prognosis, and as a therapeutic target.

miR-367 may play a crucial role in the progression of cutaneous melanoma and may be a promising target for the treatment of this disease. A study by Long *et al* (52) demonstrated that miR-367 enhanced the proliferation and invasion of cutaneous malignant melanoma. The upregulation of miR-367 was observed in both melanoma tissues and cell lines, and its level in tumor tissues was found to be positively correlated with tumor thickness, stage, lymph node involvement, distant metastasis and patient survival rate. Moreover, a higher expression of miR-367 promoted the growth, migration and invasion of melanoma cells, while lower levels of miR-367 had an inhibitory effect on cell proliferation and invasion.

miR-367 has also been implicated in non-small cell lung cancer (NSCLC). Yu *et al* (53) found that overexpression of miR-367-3p lead to the downregulation of serum and glucocorticoid regulated kinase 3, resulting in the inhibition of NSCLC cell proliferation and migration.

Roles of miR-367 in various physiological processes miR-367 and other diseases. miR-367 has traditionally been studied for its potential as a tumor suppressor and diagnostic biomarker in cancer research. However, previous studies have highlighted its significance in regulating essential genes involved in inflammation (54), development (55,56), metabolic disorders (57), cardiac diseases (12,58), brain disorders (59,60) and pregnancy disorders (61). These findings demonstrate the multifaceted role of miR-367 in controlling diverse physio-logical processes beyond cancer (Fig. 1).

Inflammation. miR-367 has been found to play a crucial role in regulating inflammation in various diseases. Yuan *et al* (54) demonstrated that miR-367 negatively regulated the inflammatory response of microglia by targeting interleukin 1 receptor-associated kinase 4 (IRAK4) in intracerebral brain hemorrhage (ICH). The study found that ICH downregulated the expression of miR-367 and upregulated the expression of IRAK4 in primary microglia. It was also demonstrated that miR-367 suppressed IRAK4 expression by directly binding to its 3'-UTR region. Furthermore, miR-367 inhibited NF-κB activation and the production of downstream proinflammatory mediators including interleukin 6 (IL-6), IL-1b and tumor necrosis factor α (TNF-α). Knocking down IRAK4 expression in microglia inhibited both NF-κB activation and the production of proinflammatory mediators. Additionally, the study found that miR-367 could reduce brain oedema, improve neurological functions and inhibit the expression of proinflammatory cytokines in ICH mice. In addition, miR-367 has also been found to regulate the inflammatory response of microglia by targeting the transcription factor, CCAAT enhancer binding protein α, which promotes microglia M2 polarization (62). The same study also demonstrated that miR-367 attenuated ICH-induced inflammatory injury and could potentially be applied for the management of ICH. The administration of miR-367 has also been shown to ameliorate neurological function by reducing neurological injury and brain oedema (54). The microglia-mediated inflammatory response plays a critical role in the pathogenesis of ICH, which is the most severe cerebrovascular disease and is characterized by high mortality and disability rates (62). Thus, controlling the production of pro-inflammatory mediators represents a promising strategy to prevent brain injury following ICH.

Stroke is a severe disease that can be categorized into ischemic or hemorrhagic stroke. Ischemic stroke is particularly burdensome, accounts for 85% of strokes and currently lacks effective treatment strategies, especially for reducing neuroinflammation that leads to cell death (63). miRNAs may provide new therapeutic options for neuroinflammation associated with ischemic stroke (64). In a study by Tabet *et al* (65), miR-367 was found to be associated with ischemic stroke. The study found that miR-367-3p was reduced in brain homogenates following sustained ischemia and G protein-coupled receptor class C group 5 member A (GPRC5A) expression, a target gene of miR-367-3p, was increased. Furthermore, miR-367-3p and GPRC5A were co-expressed in human cortical neurons (HCN-2 cell line) and inhibition of miR-367-3p led to increased expression of GPRC5A in mouse primary neurons, indicating that the loss of miR-367-3p suppression of GPRC5A (due to the reduced levels of this miRNA during ischemia) may contribute to neuroinflammation in ischemic stroke. As for hemorrhagic stroke, miR-367 has been found to attenuate neurobehavioral and neuropathological changes in hemorrhagic stroke by improving blood-brain barrier integrity, suppressing neuroinflammation and reducing neuronal apoptosis, as demonstrated by Xu *et al* (66).

Myocardial infarction (MI) is a common and serious ischemic cardiomyopathy with high morbidity and mortality rates globally (67). A recent study by Wang *et al* (68) demonstrated that miR-367-5p was directly involved in the pathogenesis of MI through targeting and inhibiting the expression of cyclooxygenase 2 (COX2). This study confirmed that miR-367-5p downregulation or COX2 overexpression leads to cellular dysfunction of cardiomyocytes. Moreover, knockdown of miR-367-5p has been found to promote the secretion of inflammatory cytokines, such as IL-1β, IL-6 and TNF-α, which exacerbate the inflammatory response in patients with MI (68). These findings suggest that miR-367-5p could be relevant for the treatment of MI.

Development. During neurulation, the neural plate, which is predominantly composed of neural progenitor cells (NPCs), undergoes a series of complex and highly dynamic morpho-logical changes, including bending, bilateral lifting, folding and fusion, to form the closed neural tube (69). Precise control of NPC behaviors, such as proliferation, differentiation and survival, is essential for coordinating this process and preventing open neural tube defects (NTDs). miRNAs are ideal regulators for orchestrating these cellular behaviors for normal neural tube (NT) formation by binding to multiple

targets that regulate the planar cell polarity pathway (70). A mouse development study demonstrated that miR-302/367 expression started in the embryonic region after implantation and became restricted to the anterior neural tube by embryonic day 8.5 (55). Furthermore, Yang *et al* (56) conducted a study that demonstrated the significance of miR-302/367 in mammalian NT formation and the survival of developing embryos. The results showed that miR-302/367 regulated NPC proliferation, differentiation and perseverance by inhibiting cyclin D1/D2 and fibroblast growth factor 15 gene expression at the post-transcriptional level. Depletion of miR-302/367 leads to early differentiation, increased cell proliferation and cell death, which could cause NTD.

Research has revealed that mammalian primed pluripotent stem cells are particularly vulnerable to cell death stimuli as they possess a low apoptotic threshold. A key mechanism that regulates apoptosis in the post-implantation epiblast is the miRNA-mediated pathway (55). Research conducted on cultured cells indicates that the miR-302/367 cluster has crucial functions in regulating pluripotency, differentiation, cell cycle progression and apoptosis in embryonic stem cells or primed pluripotent stem cells (55). This study also indicated that three miRNA families, namely miR-20, miR-92 and miR-302/367, played a crucial role in controlling the mitochondrial apoptotic machinery by precisely regulating the levels of the proapoptotic protein, Bcl-2-like 11. These miRNA families act as a necessary buffer for sustaining the survival of stem cells that are primed for both differentiation and cell death.

Cardiac diseases. Atrial fibrillation (AF) is a heart rhythm disorder characterized by irregular and fast heartbeats that can affect blood flow and oxygen delivery (71). According to the 2019 Global Burden of Disease study, there was an estimated 59.7 million (95% uncertainty interval, 45.7 million to 75.3 million) cases of atrial flutter (AF) in 2019, an ~2-fold increase compared with the number of cases in 1990 (72,73). Since AF can lead to serious complications, such as stroke, heart failure and dementia, there is a growing interest in preventing this condition. Certain studies have suggested that miRNAs may play a role in the development of AF (74,75), and have shown that miRNAs found in the bloodstream could be used as biomarkers to identify AF (76,77). The potential of miR-367 as a diagnostic biomarker for AF was highlighted in a recent study by Cao and Cui (58). The identification of differentially expressed miRNAs in AF revealed that miR-367 exhibited greater diagnostic utility than other miRNAs. The aberrant expression of miR-367 in the atrial tissues of patients with AF suggests its use as a non-invasive diagnostic tool for distinguishing between healthy individuals and those with AF (58).

In addition, Hu *et al* (12) validated the role of miR-367-3p in regulating the development of cardiac fibrosis, a condition characterized by the accumulation of extracellular matrix proteins in the cardiac interstitium, which can lead to cardiac dysfunction (78). The study (12) found that the expression of miR-367-3p was lower in patients with cardiac fibrosis compared with the non-fibrosis controls, and further analysis revealed that CD69, a protein involved in the immune response, was a target of miR-367-3p. Downregulation of CD69 by miR-367-3p mimics and CD69 small interfering RNA indicated that CD69 expression was associated with a decrease in cytokine levels and the upregulation of T helper 17 cells. These findings indicate that miR-367-3p plays a critical role in regulating cardiac fibrosis by targeting CD69 and modulating the immune response.

Coronary artery disease refers to constriction of the arteries that supply blood and oxygen to the heart (79). Off-pump coronary artery bypass (OPCAB) surgery is a technique that involves grafting veins or arteries to bypass the narrowed or blocked areas, thus improving blood flow and reducing the risk of death from coronary artery disease (80). However, individuals who undergo this procedure may experience complications related to coagulation and hemostasis (81). Thus, there is a need to investigate the molecular mechanisms underlying the impact of OPCAB. Sun *et al* (13) conducted a comprehensive investigation into the molecular mechanisms underlying the efficacy of OPCAB surgery. Through the analysis of differentially expressed genes (DEGs) and miRNAs, miR-367 was identified as a crucial regulatory factor in the immune response following OPCAB surgery. Specifically, miR-367 was shown to modulate the expression of early growth response (EGR) 2, a key regulator of the Toll-like receptor signaling pathway and immune inflammation feedback. Thus, the miR-367 expression level in patients post-OPCAB may serve as an informative marker for monitoring immune responses. These findings provided valuable insights into the molecular mechanisms underlying the effectiveness of OPCAB surgery and have important implications for improving patient outcomes in the treatment of coronary heart disease.

Brain disorders or injuries. Schizophrenia is a multifaceted neurodevelopmental disorder for which the underlying mechanisms remain unclear. As such, there is a pressing need to understand the molecular mechanisms of schizophrenia, identify potential biomarkers and devise new treatment strategies. A recent study identified miR-367 as a promising biomarker for schizophrenia, with evidence indicating its involvement in the regulation of DEGs, such as SMAD7 and EGR1 (59). The study suggested that the miR-367-SMAD7-EGR1 and miR-367-SMAD7-aryl hydrocarbon receptor nuclear translocator axis could serve as potential biomarkers for schizophrenia. Thus, understanding the function of miR-367 in the molecular mechanisms of schizophrenia could aid in the development of diagnostic biomarkers and effective therapeutic strategies for this complex neurodevelopmental disorder.

In addition, Svenningsen *et al* (60) highlighted the significance of miR-367 in depression. In this study, rats exposed to the learned helplessness rat model of depression displayed alterations in miRNA expression levels in the medial and lateral habenula, with miR-367 being one of the four miRNAs significantly regulated in the lateral habenula. This finding suggests that miR-367 may play a role in depression, as changes in its expression were observed in a relevant brain region associated with the disorder. Additionally, it was found that the target genes of miR-367 are involved in neurotransmission, specifically neutrophin and ErbB signaling, further supporting its role in depression (60). Understanding the precise role of miR-367 in depression could provide valuable insights into the pathogenesis of the disease and lead to the development of novel treatment approaches.

4. Conclusion and future perspectives

miR-367 is a versatile miRNA involved in various physiological processes, including cell proliferation, differentiation, self-renewal and reprogramming. miR-367 dysregulation has been implicated in numerous diseases, including cancer, and recent studies have indicated that miR-367 could be a therapeutic target and biomarker of disease. The investigation of miR-367 regulation and its potential use in the prognosis and treatment of various diseases offers encouraging opportunities for future clinical applications. As aforementioned, miR-367 may either act as an oncogene or tumor suppressor depending on the type of cancer. In future, anti-miR-367 oligonucleotides (antagomirs) or miR-367 mimics could be used as therapeutics to either block or restore the activity of miR-367 for tumor suppression. The level of miR-367 in circulating serum has been used as a prognostic marker for breast (31) and testicular germ cell (82,83) cancer. However, more studies to investigate the correlations between miR-367 serum levels and various stages of diseases would enhance the potential of this miRNA as a biomarker. The combined tumor suppression effects of miR-367 and other miRNAs or drugs, such as aspirin (84), should also be explored in the future. However, further research is necessary to fully understand the complex regulatory mechanisms involving miR-367 in different contexts and to identify potential off-target effects of miR-367-targeted therapies. Studies to verify the targets of miR-367 are also required to elucidate the pathways involved in disease development.

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Authors' contributions

SM drafted the manuscript. LLF and WCST verified the contents and revised the manuscript. SAH, GBYT and BYK critically revised and edited the manuscript. Data authentication is not applicable. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

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Patient consent for publication

Not applicable.

Use of artificial intelligence tools

During the preparation of this work, ChatGPT was used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the AI tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

Competing interests

The authors declare that they have no competing interests.

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