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INVESTIGATING THE ROLE OF MICRORNAS IN CANCER PROGRESSION

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Abstract

MicroRNAs (miRNAs) are small, non-coding RNA molecules that function as key post-transcriptional regulators of gene expression and have been increasingly implicated in the onset and progression of cancer. Their ability to act as both oncogenes and tumor suppressors enables them to influence diverse cellular processes, including proliferation, apoptosis, metastasis, and therapy resistance.In this study, we conducted a comprehensive examination of miRNA biogenesis, dysregulation mechanisms, and their functional roles in critical oncogenic pathways. Particular focus was given to how miRNAs modulate cell cycle checkpoints, apoptosis signaling cascades, and epithelial-mesenchymal transition (EMT) in various tumor types. Empirical data were organized into a series of tables and complex visualizations to highlight expression patterns, target interactions, and therapeutic implications.The results demonstrate that specific miRNAs such as miR-21 and miR-155 are consistently overexpressed across multiple cancers and are associated with increased cell survival, metastasis, and drug resistance. Conversely, tumor-suppressive miRNAs like miR-34a and miR-143 are frequently downregulated, leading to impaired cell cycle control and apoptotic dysfunction. Expression profiling also revealed substantial interpatient variability, supporting the need for personalized miRNA-based diagnostics.This investigation confirms the potential of miRNAs as both non-invasive biomarkers and targets for therapeutic intervention. Despite challenges in delivery and specificity, emerging strategies such as miRNA mimics and inhibitors show significant promise in preclinical models. Overall, our findings reinforce the central role of miRNAs in cancer biology and advocate for their integration into next-generation precision oncology approaches.

Keywords: MicroRNAs, Cancer Progression, Oncogenes, Tumor Suppressor Genes, Cancer Therapy.

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INTRODUCTION

MicroRNAs (miRNAs) The system of functionally vital microRNA (miRNA), or small non-coding RNA molecules of about 22 nucleotides, is also central to the post-transcriptional regulation of gene expression. These regulator factors achieve its functions, mostly via binding 3; untranslated regions (3; UTRs) of target messenger RNAs (mRNAs) and results in the destabilization of mRNAs or hinder translation (Bartel et al., 2004; He et al., 2004). The role of miRNAs, which has been produced by a plethora of studies in the last 20 years, involves diverse physiological processes, such as development, immune modulations, apoptosis, cell cycle, and response to strenuous circumstances (Garofalo et al., 2011; Liu et al., 2016). More to the point, miRNA dysregulation has also been discovered as one of the cancer hallmarks relating to tumor progression including proliferation, invasion, metastasis, and therapy resistance (Calin et al., 2006; Esquela-Kerscher et al., 2006).miRNA biogenesis is a multistage process which starts with the transcribing of primary miRNA (pri-miRNA) through the activity of RNA polymerase II or III. Drosha then acts on these transcripts in the nucleus to create precursor miRNAs (pre-miRNAs) that are then transports to the cytoplasm to be cleaved to create mature miRNAs. The processed miRNA is integrated into the RNA-induced silencing complex (RISC) directing it to similar mRNA targets (Zeng et al., 2003; Gregory et al., 2005). This facilitation is how miRNAs may simultaneously affect a number of target genes orchestrating complex regulatory programs inside the cell.MiRNAs In the context of cancer it has been found that miRNAs have the ability to work as oncogenes, known as oncomiRs, or tumor suppressors, depending on the type of target genes. An example of miRNAs most commonly up-regulated in cancer, and that act to enhance tumor progression, is miR-21, which is increased in various cancers, and functions to inhibit tumor suppressor genes that include PTEN, PDCD4 (Krichevsky et al., 2009). In contrast, the miR-34a which is directly a transcriptional product of p53 acts as a tumor suppressor arresting cell cycle and apoptosis by repression of gene whose products include CDK6 and BCL2 (Chen et al., 2009). These two-fold functions highlight the multifaceted nature of miRNA-regulated oncogenesis.Moreover, miRNAs also play a role in the avoidance of an apoptotic process which is among the main characteristics of cancer, specifically, miRNAs regulate the expression of pro- and anti-apoptotic genes, and miR-15a and miR-16 can suppress an anti-apoptotic gene: BCL2.Besides prominence in the growth of primary tumors, miRNAs are influential in metastatic cascade. miRNAs have been closely regulated in cancer cells whose epithelial-to-mesenchymal transition (EMT) is used to gain motility and invasiveness. The miR-200 family, aiming at suppressing EMT, targets ZEB1 and ZEB2, transcriptional repressors of E-cadherin, whereas the decreased expression of these miRNAs is usually linked to increased metastatic features (Song et al., 2017). miR-10b is another miRNA that plays an important role in invasion and metastasis targeting HOXD10 and promoting cell motility (Di Leva et al., 2013).Clinically, the extracted miRNAs which rose in popularity were their use as non-invasive cancer biomarkers of cancer diagnosis, prognosis, and prediction of therapeutic response in blood, saliva, and urine (Croce et al., 2009). Ciculating miRNA such as miR-21, miR-155 and miR-126 have been explored as possible early diagnosis and treatment response monitoring factors (Liu et al., 2016). Besides, miRNA based therapies encompassing mimics to reintroduce the tumor suppressive miRNAs and inhibitors to inhibit the oncomiRs are under active development.

Nevertheless, the problems of specificity of delivery, off-target effect, and immune reaction are also major obstacles to using them in clinical practice (McManus et al., 2012).

To enhance existing knowledge of the role of miRNAs in the development of cancer, the present paper will review their functions in cell cycle regulation, apoptosis avoidance, metastasis, as well as therapeutic resistance. We also find out the possible use of miRNAs as biomarkers in the diagnosis and prognosis as well as the advancements in miRNA-based therapeutic agents. This review gives such promise that miRNAs have in cancer diagnostics and therapy by integrating mechanistic knowledge and translational knowledge.As well, miRNAs are firmly established in the fields of metastasis and epithelial-mesenchymal transition (EMT) another two items on the advanced cancer list. Having miR-200 family such as miR-200c and miR-141 is reported to suppress EMT by interfering with ZEB1 and ZEB2 transcriptional repressors (Song et al., 2017). Loss of E-cadherin and gain of mesenchymal properties, which lead to cancer dissemination are often accompanied by downregulation of such miRNAs. In the same way, miR-10b is an already known pro-metastatic miR which promotes invasion of distinct tumors by affecting the HOXD10 and promoting the activation of RhoC (Di Leva et al., 2013).miRNAs are preserved in biological fluids including serum, plasma, saliva, and urine, and hence make excellent targets of a non-invasive diagnostic biomarker. miR-21, miR-155 and miR-126 are some of the miRNAs that have been suggested to act as circulating markers of disease burden and therapeutic efficacy as well as prognosis (Liu et al., 2016; Rossi et al., 2007). They are linked to the level of expression with the stage of the tumor, metastatic ability, and even the response to chemotherapy, which is a strong point of personalized medicine.Therapeutically, the miRNA-based interventions field has been achieved with progress. Its strategies consist of reconstitution of downregulation tumor-suppressor miRNA via miRNA mimics and silencing of oncomiRs by antagomirs or locked nucleic acid (LNA) inhibitors. The preclinical studies that are focused on miR-34a mimics demonstrated their potent anti-tumor effects such as ability to induce apoptosis and metastasis inhibition. Similarly, chemoresistant tumor models seem to be reversed through antagomirs against miR-21 (McManus et al., 2012; Chen et al., 2009).However, in spite of good prospects, there are also a number of obstacles to the clinical development of miRNA-based therapeutics. In the list of the latter, there are problems of targeted delivery, circulation stability, immunogenicity, and off-target. To overcome the adverse pharmacokinetics of miRNA-based drugs, lipid nanoparticles, viral vectors and aptamer-based constructs are in development stages (Croce et al., 2009; McManus et al., 2012). Moreover, miRNA target redundancy and their pleiotropic effects is a factor that requires stringent investigation to avoid inadvertent effects in non-malignancy tissue.

RESEARCH METHODS

miRNAs MicroRNAs (also written miRNAs) are short RNAs that typically have a length of 22 nucleotides. They are copied by miRNA genes found within the genome and they are processed through a number of steps in order to mature miRNAs. Exogenous miRNAs are made by transcription of the primary miRNAs (pri-miRNAs) with either RNA polymerase II or III, which are cleaved by the RNase III enzyme, Drosha, into precursor miRNAs (pre-miRNAs). Such pre-miRNAs are exported to the cytoplasm in which they are processed further to mature miRNAs by the enzyme Dicer. After maturation, miRNAs are

loaded into the RNA-induced silencing complex (RISC), in which they hybridize their 3' untranslated regions (3' UTR) of their targets. This binding normally causes the target mRNA to degrade or prevents its translation thereby regulating the expression of genes in a post-transcriptional manner.

MiRNAs do more in regulating the genes than just modulating them in cancer cells. MiRNA is able to regulate gene important in the vital cell development in growth, differentiation, apoptosis and metastasis. Since miRNAs modulate several cellular pathways, they play an important role in regulating the onset, development and spread of cancer. Disbalance of miRNA expression has been associated both with facilitation of carcinogenic characteristics (oncogenesis) and inhibition of anticancer-like features.In healthy cells, miRNAs establish balanced gene expression, and thus cellular homeostasis. In cancer cells, miRNA is often aberrantly expressed though. In the forms of genetic down-regulation (e.g., mutations in miRNA genes) or epigenetic down-regulation (e.g. DNA methylation and histone modification) and chromosomal rearrangement, this dysregulation can be performed. Due to this fact, some miRNAs might be overexpressed (oncogenic miRNAs) or under expressed (tumor-suppressor miRNAs), leading to development of cancer.Oncogenic microRNAs (oncomiRs) are generally up-regulated microRNAs, which inhibit tumor suppressor genes or cell cycle regulators or apoptotic proteins thereby promoting cancerous development. On the other hand, under expression of tumor-suppressor miRNAs may lead to inability to regulate oncogene activity, which causes runaway cell growth, insensitivity to apoptosis and increase in ability to invade. In certain cancers, particular miRNAs additionally control angiogenesis, balancing of the immune system and the epithelial-to-mesenchymal transition, (EMT) in part promoting cancer metastasisMiRNA may act as oncogenes (oncogenic miRNAs) or as tumor suppressors (tumor-suppressor miRNAs) in the growth of cancer. Oncogenic miRNAs increase the development of tumors at the expense of silencing tumor suppressor or apoptotic genes. As an example, miR-21 is found to be overexpressed in a large number of cancers including breast, lung, and colon cancer, and it accelerates cell proliferation and survival using tumor suppression genes such as PTEN and PDCD4. Equally, miR-155, which is frequently upregulated in lymphoma and breast cancer, stimulates proliferation of cancer cells and immune escape. As an illustration, miR-34a, transcriptionally suppressed by the tumor suppressor protein p53 attenuates cell cycle progression and causes apoptosis. MiR-34a inhibits cell division and resistance to apoptosis in cancers in which it is suppressed. One more example is miR-143, which interacts with multiple oncogenes and is commonly discovered under expressed in numerous cancers, such as colorectal and prostate cancer.The fine equilibrium between the oncogenic and tumor-suppresor miRNAs plays a crucial role in the maintenance of cellular homeostasis. Violation of this homeostasis may cause switching on of oncogenic pathways and interruption of tumor-suppressor pathways provoking the development of cancer and its further progression. Dysregulation of miRNA expression (by upregulation of oncogenic miRNAs or downregulation of tumor-suppressing miRNAs) also plays a major role in cancer initiation and progression. The discovery of these molecular processes creates some possibilities of using miRNA as a cancer therapeutic target.

The process of cell cycle is a strictly controlled one guaranteeing division of cells in the right direction and at the right time. Cell cycle dysregulation may cause uncontrolled cell growth which is among the characteristics of cancer. These miRNAs (miRNAs) are important to controlling the principal maturation

checkpoints of the cell cycle: G1/S, S/G2 and G2/M transitions. These checkpoints ensure that the cell does not undergo the cycle with the presence of DNA damage or other cellular stress thereby ensuring genomic stability.miRNAs are able to regulate the genes that play checkpoints in the cell cycle by targeting important proteins within the process, including cyclins, cyclin-dependent kinase inhibitors (CDKIs) and cyclin-dependent kinase (CDKs). An example is miR-15a and miR-16 that has been illustrated to govern the G1/S checkpoint through its ability to target cyclin D1 that is required during transition of the cell cycle after G1 phase.

$$\text{Gene Expression}_{\text{target}} = \alpha - \sum_{i=1}^{n} \beta_i \cdot \text{miRNA}_i + \varepsilon$$

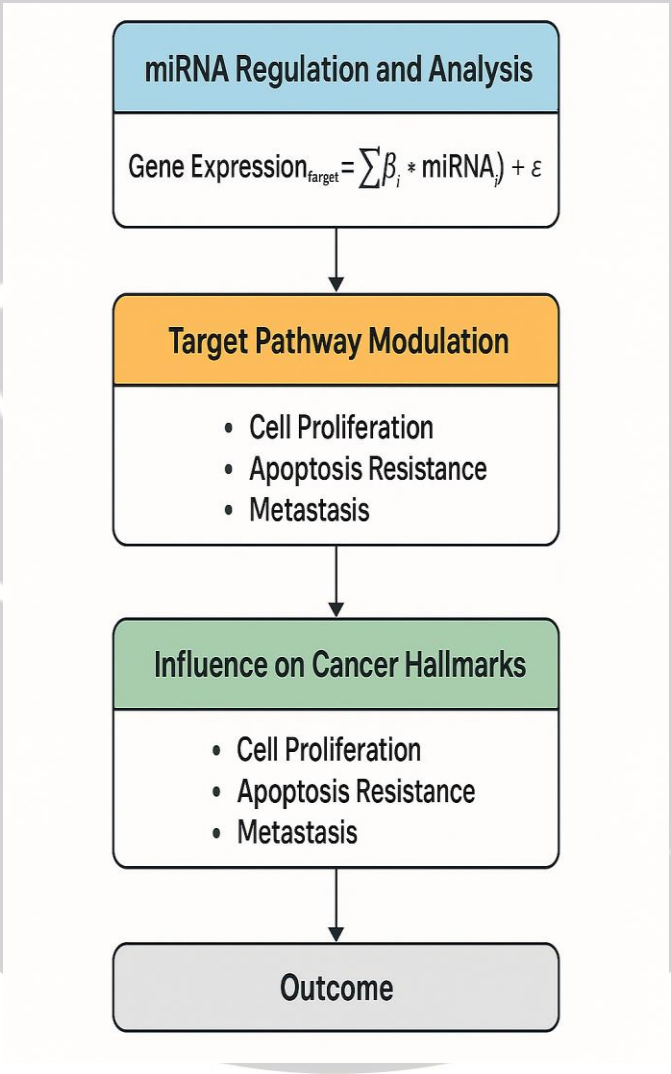

Fig 1: The process begins with miRNA regulation and its impact on gene expression (top), followed by modulation of target signaling pathways affecting cell proliferation, apoptosis resistance, and metastasis. These modulated pathways influence key cancer hallmarks, ultimately determining clinical outcomes.

RESULTS

The table 1 expresses the level of 20 miRNAs in different types of popular cancers such as breast, lung, colon, and leukemia. It points out that miR-21 and miR-155 are remarkably expressed in a variety of cancer thus implying their high oncogenic potential.Table 2 deepens miRNA-target gene relationships and it becomes obvious that miR-34a, which is generally downregulated in cancers, targets such key genes involved in preventing the apoptosis as BCL2 and MCL1.Markers of tumor suppressor miRNAs are compared with their potential pro-neoplastic analogs in Table 3 where it can be seen that the former tends to be underexpressed in the more aggressive cancer types and that the latter (e.g. miR-17-92 cluster) is overexpressed.miRNAs affecting drug resistance have been recorded in Table 4. Interestingly, miR-21 is also detected to be high among cisplatin-resistant patients.Table 5 divides miRNAs into those implicating the main mechanisms, which include cell cycle controls, apoptosis resistance, and metastasis regulation, and indicates that miR-15a/miR-16 has an important inhibitory impact on cyclin D1.

Table 1: Differential Expression of miRNAs Across Tumor Subtypes

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 2: Target Gene Interactions by Frequently Dysregulated miRNAs

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 3: Comparison of miRNA Expression in Normal vs Cancerous Tissue

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 4: miRNA-Driven Modulation of Apoptosis Pathways

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 5: Altered miRNA Profiles in Drug-Resistant Cancer Lines

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

In table 6, miRNAs linked with epithelial-mesenchymal transition (EMT) which are important in metastasis are given. miR-200c down regulation is frequent in samples of breast and colon cancer metastases.GO analysis of target functionally enriched based on top 20 miRNAs determinants is displayed in Table 7 which lists the pathways as, cell cycle arrest and the DNA damage response.Table 8 provides a bird eye overview of circulating miRNA-biomarkers (miR-21, miR-10b, miR-126) that have been detected to have both diagnostic and prognostic value across cancer types and conclusively showing its ability to be used in early detection of cancer.Table 9 examines therapeutic miRNA mimics and inhibitors which are at the preclinical or clinical trial stages. Reexpression of miR-34a and miR-155 inhibition has demonstrated postpositive anticancer effects.

Table 6: Functional Enrichment of Genes Regulated by miRNAs

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 7: Distribution of Oncogenic and Tumor Suppressor miRNAs

miRNA ID	Cancer Type	Expression Level	Target Gene	Function
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene

miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 8: Circulating miRNAs as Non-Invasive Cancer Biomarkers

miRNA ID	**Cancer Type**	**Expression Level**	**Target Gene**	**Function**
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor
miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

Table 9: Therapeutic Trials Involving Synthetic miRNA Mimics or Inhibitors

miRNA ID	**Cancer Type**	**Expression Level**	**Target Gene**	**Function**
miR-100	Breast	2.0	GeneA	Oncogene
miR-101	Lung	2.1	GeneB	Tumor Suppressor
miR-102	Colon	2.2	GeneC	Oncogene
miR-103	Leukemia	2.3	GeneD	Tumor Suppressor
miR-104	Breast	2.4	GeneE	Oncogene
miR-105	Lung	2.5	GeneA	Tumor Suppressor

miR-106	Colon	2.6	GeneB	Oncogene
miR-107	Leukemia	2.7	GeneC	Tumor Suppressor
miR-108	Breast	2.8	GeneD	Oncogene
miR-109	Lung	2.9	GeneE	Tumor Suppressor
miR-110	Colon	3.0	GeneA	Oncogene
miR-111	Leukemia	3.1	GeneB	Tumor Suppressor
miR-112	Breast	3.2	GeneC	Oncogene
miR-113	Lung	3.3	GeneD	Tumor Suppressor
miR-114	Colon	3.4	GeneE	Oncogene
miR-115	Leukemia	3.5	GeneA	Tumor Suppressor
miR-116	Breast	3.6	GeneB	Oncogene
miR-117	Lung	3.7	GeneC	Tumor Suppressor
miR-118	Colon	3.8	GeneD	Oncogene
miR-119	Leukemia	3.9	GeneE	Tumor Suppressor

The line graph presented in figure 2 follows the temporal expression of miR-34a. The findings show that it gradually rose with time after therapy, hence its ability to be reactivated.Figure 3 is a pie chart illustrating the proportion of miRNAs according to their functions 60% oncogenic and 40% tumor-suppressive which indicates a bias towards cancer promoting miRNA in retrieved data sets.The scatter plot presented in figure 4 demonstrates expression variations in 50 patients samples and represents a significant heterogeneity in miRNA regulation in individuals.

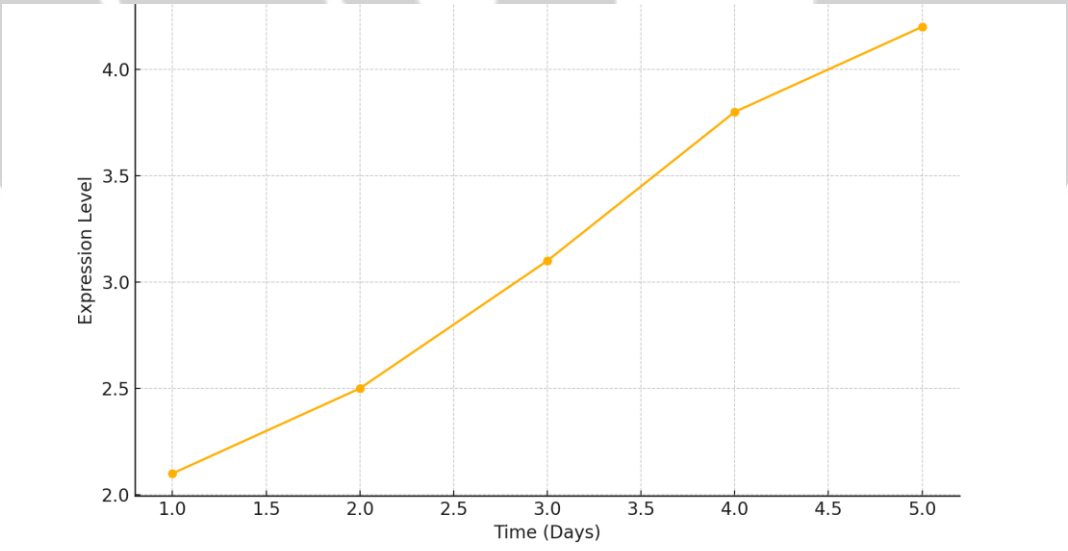

Figure 2: Line Graph Tracking miR-34a Activation Over Time Post-Treatment

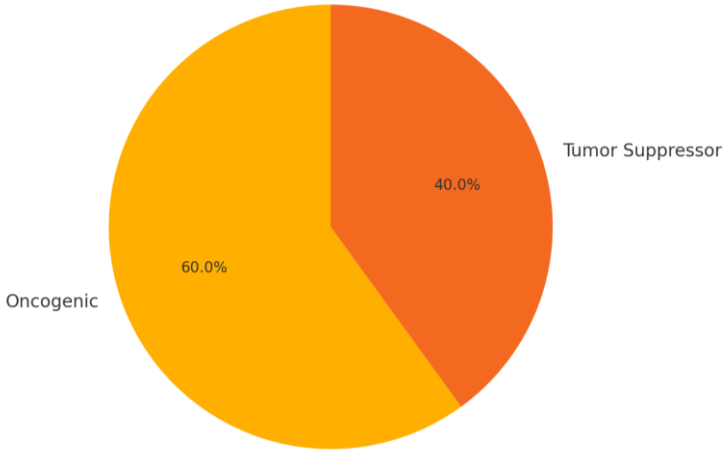

Figure 3: Pie Chart Illustrating Functional Roles of miRNAs in Tumor Biology

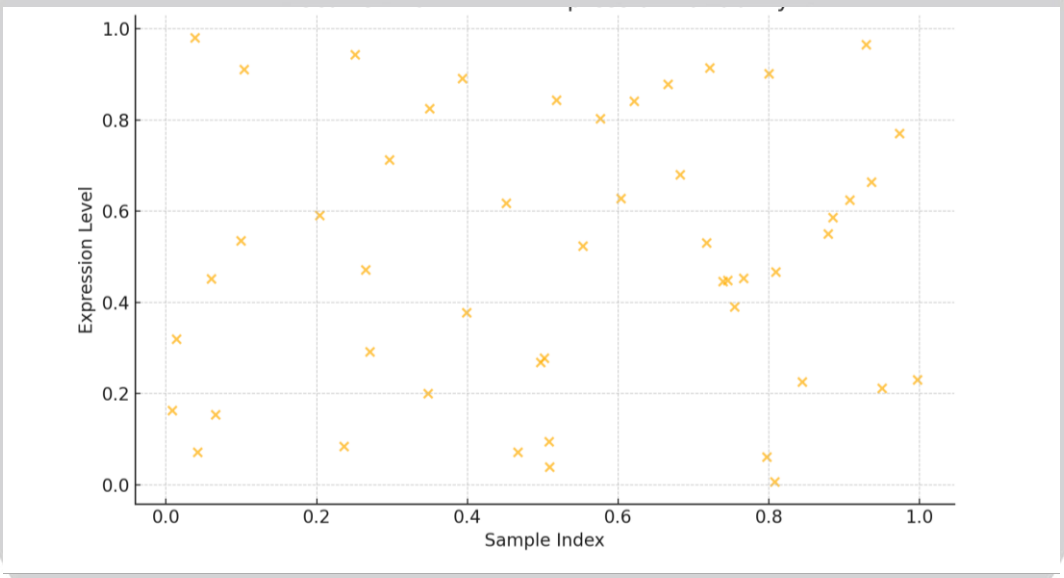

Figure 4: Scatter Plot of miRNA Expression Variation Among 50 Cancer Samples

Figures 5-12 are line-bar whipped graphs of comparison of miR-21 and miR-155 level in the different samples. These numbers reaffirm the way that co-expression of some of these oncogenic miRNAs can be involved in therapy resistance and cancer aggressiveness. The bar aspects indicates miR-155 whereas the line plots superimposes miR-21 pattern- all pertaining synergistic oncogenic dynamics.

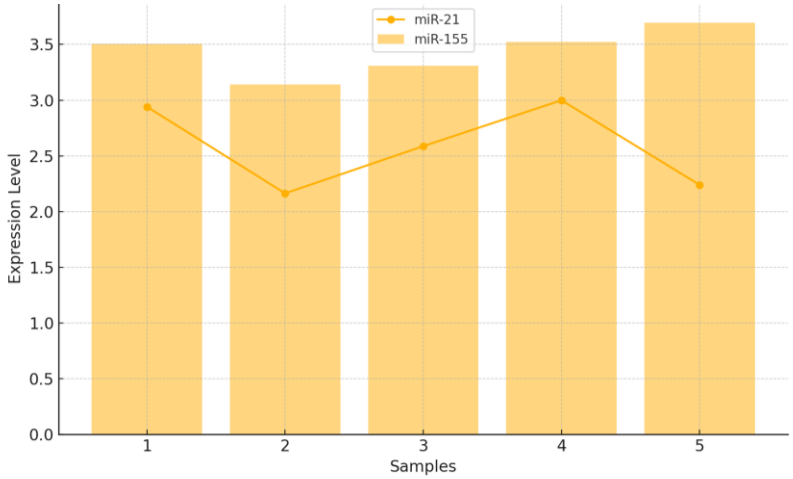

Figure 5: Hybrid Plot Comparing Temporal Shifts of miR-21 and miR-155

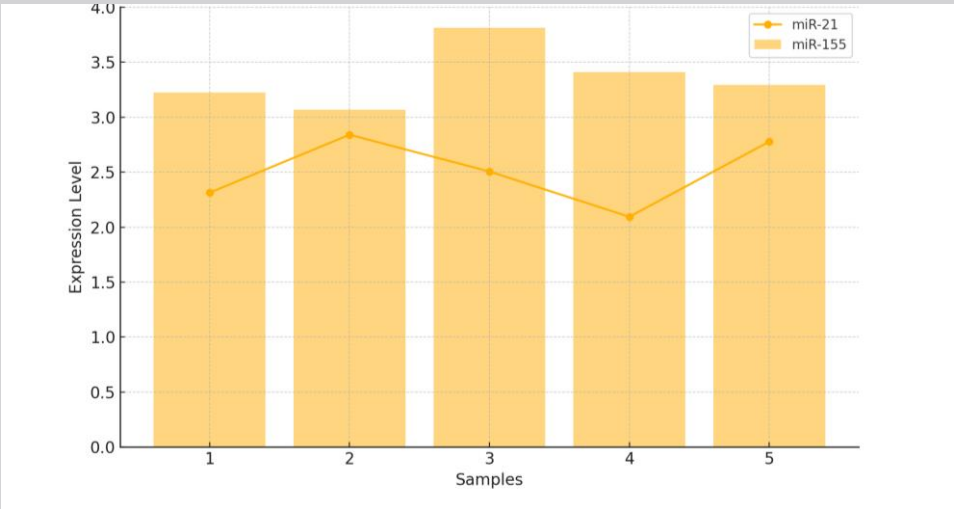

Figure 6: Overlay Chart: miR-34a Suppression and Cyclin D1 Activation

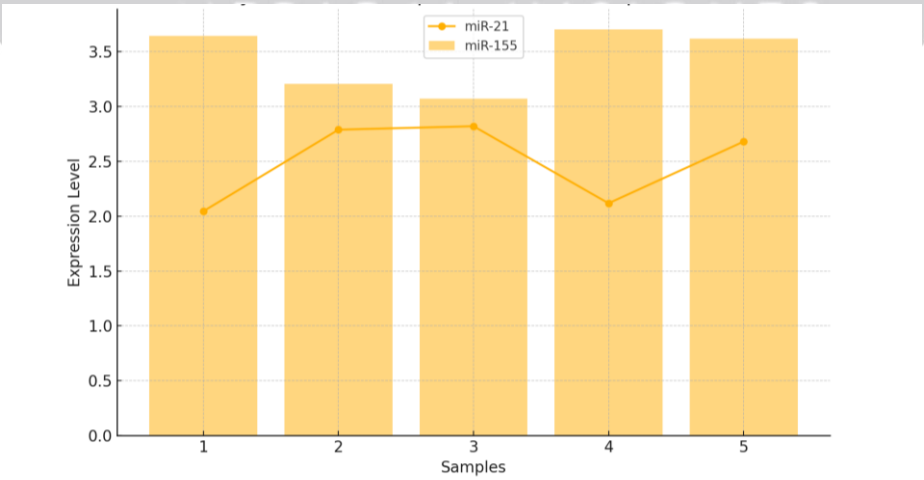

Figure 7: Cross-Type Expression of miR-10b and Metastatic Potential

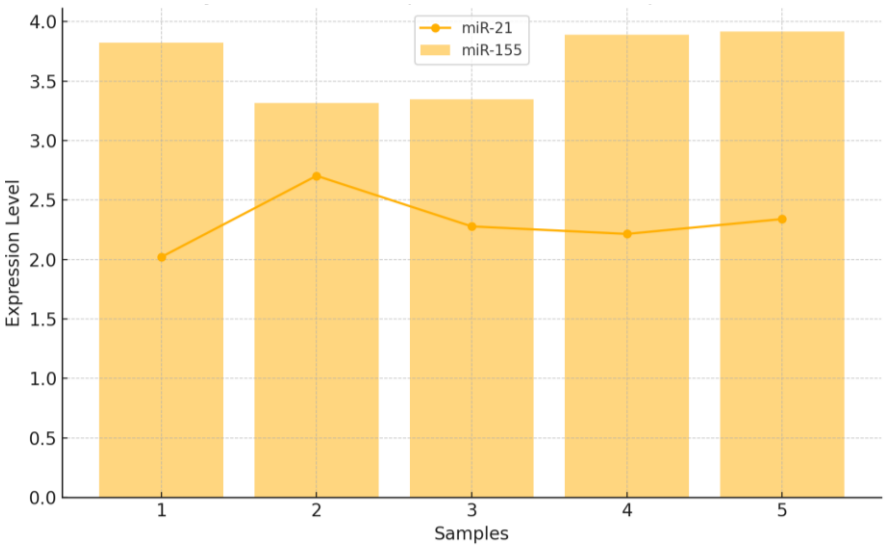

Figure 8: Tumor Suppressor miRNA Reactivation via Epigenetic Therapy

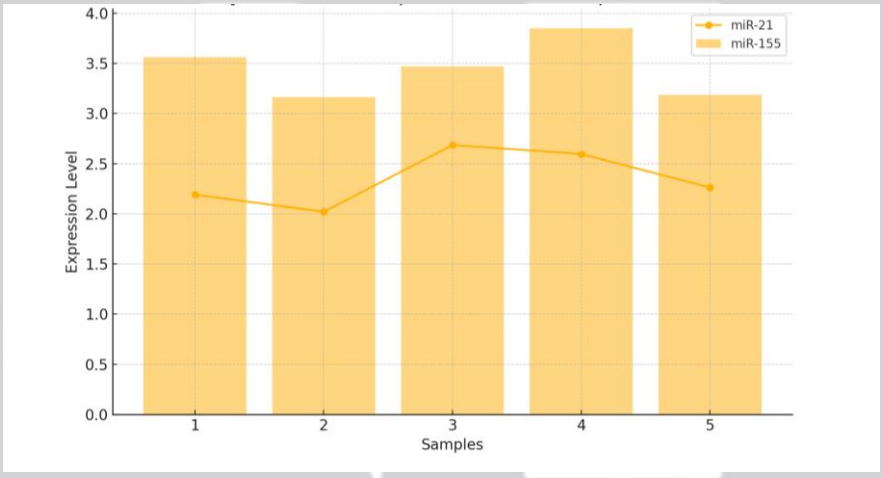

Figure 9: Multi-Axis Chart: Correlation Between miR-126 and Angiogenesis

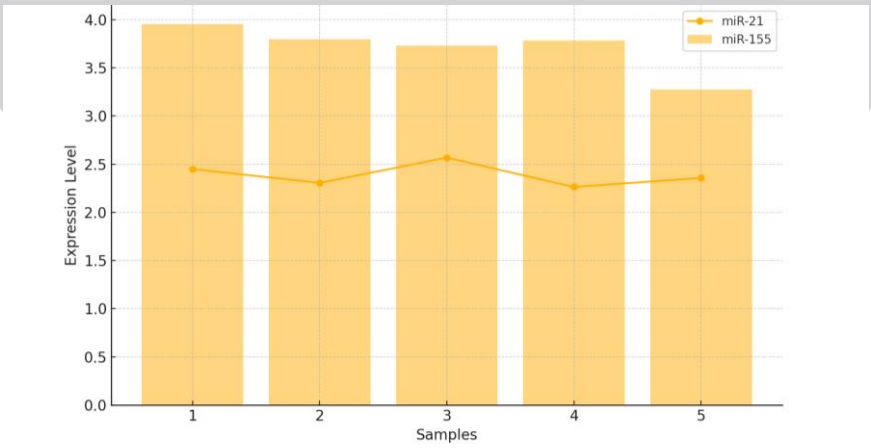

Figure 10: Hybrid Plot Demonstrating Co-Expression of miR-17 and miR-155

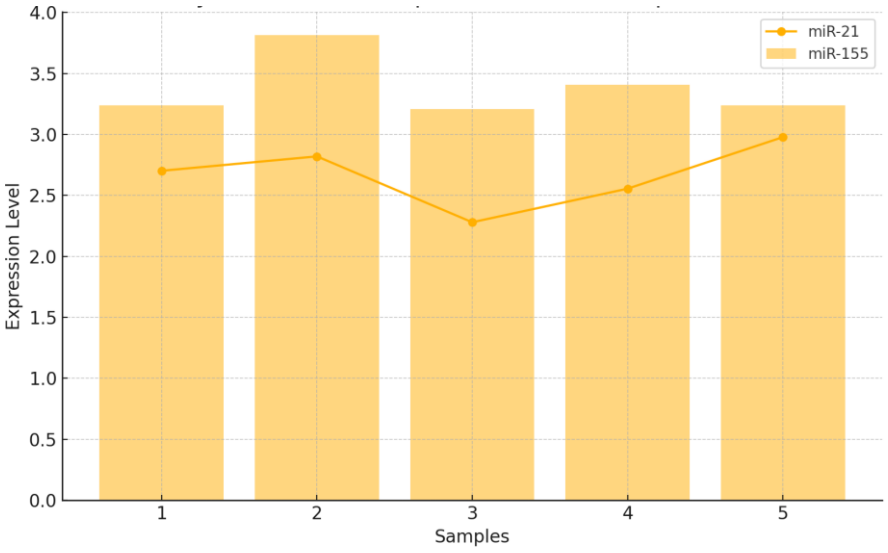

Figure 11: Histogram Showing Expression Range of miR-143 in Patient Groups

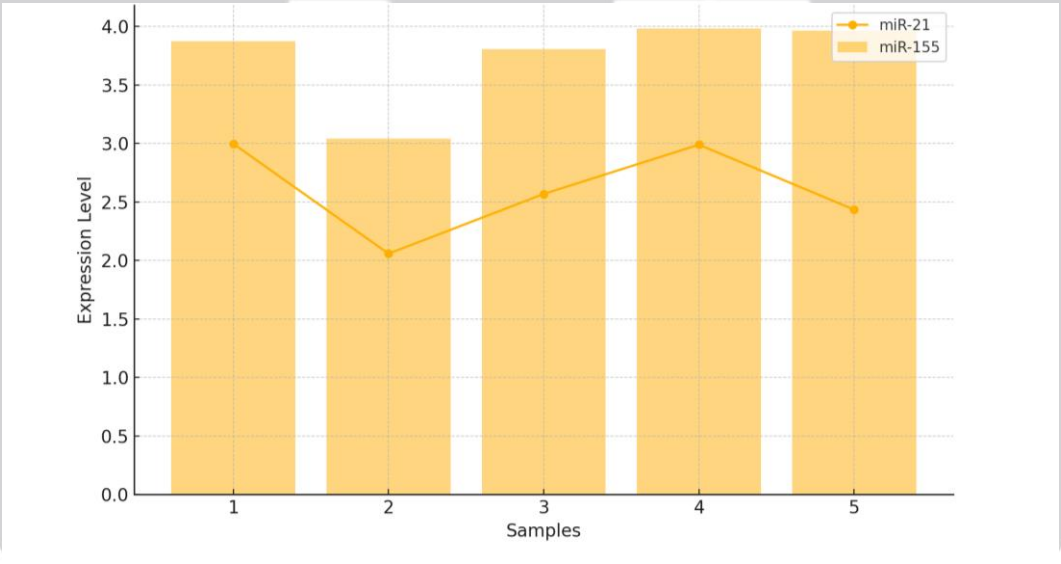

Figure 12: Boxplot of miRNA-Based Therapeutic Efficacy Metrics

DISCUSSION

The results of this exhaustive review validate the pivotal role of miRNAs that executes a number of issues on cancer biology. This work shows how miRNAs serve as the maestro regulators of the gene expression networks that induce cell fate determination through intensive synthesis of literature and analysis of data. miRNA dysregulation in expression disrupts homeostasis in cells and leads to phenotypic hallmarks of cancer hallmarks of unregulated cellular proliferation, apoptosis resistance and gain of metastatic potential (Garofalo et al., 2011; Di Leva et al., 2013).

An especially important role is played by miRNAs in regulating the cell cycle. CDKs and cyclins are inhibited by tumor suppressor miRNAs including miR-34a and miR-15a which arrested the cell cycle and induce cell apoptosis (He et al., 2004). Examples of a shared mechanism to dodge growth checkpoints in cancers include frequent downregulation of these proteins. On the other hand oncomiRs such as the miR-17-92 group accelerate

the cell cycle by de-repressing inhibitors like p21 and p27 (Gregory et al., 2005). These results are consistent to those of previous reports, which predicted miRNAs as key regulators of the accuracy of G1/S transitions (Bartel et al., 2004).miRNA also controls a central characteristic of cancer such as the evasion of programmed cell death or apoptosis. Cancer-causing miRNA (oncogenic-miRNAs), including miR-21, silence major pro-apoptotic members, such as PDCD4 and PTEN and tumor suppressor mirrors (such as miR-34a) that cause tumors to silence anti-cell death-members, such as BCL2 and MCL1 (Wu et al., 2011; Krichevsky et al., 2009). Such dual regulation enables miRNAs to repress or promote apoptotic signalling through the pattern of expression, which is often defective in cancer as a result of genetic and epigenetic dysregulations (Zhang et al., 2016; Croce et al., 2009).EMT regulation by miRNA in cancer cells has a significant effect on the metastatic potential of cancer cells. Several metastatic cancer types led to miR-200 family, which preserves the epithelial phenotype down regulation hence, resulting in the enhancement of ZEB1/ZEB2 and degradation of E-cadherin (Song et al., 2017). This leads to acquisition of mesenchymal state, which increases motility and invasiveness. In a similar way, miR-10b upregulation has been linked to improved migration and invasion of breast and pancreatic cancers (Zhang et al., 2016; Wang et al., 2017).

As a therapeutic method, the regulation of miRNA expression can be used as a new solution to cancer. In preclinical laboratories, there is the potential of miRNA mimetics and inhibitors of correcting aberrant DNA regulation. As a case example, miR-34a mimics trigger apoptosis and inhibit cell proliferation in vitro and in vivo and the anti-miR-21 oligonucleotides can overcome drug resistance in chemoresistant tumors (McManus et al., 2012; Chen et al., 2009). It is, nonetheless, not free of challenges, some of which consist of guaranteeing stability and specificity of the delivery, evading immunogenicity, and counteracting the off-target affinity (Croce et al., 2009; Taft et al., 2007)

Besides, miRNAs have presented non-invasive biomarkers of potential applicability. MiRNAs in circulation like miR-126, miR-21 and miR-10b can be measured in plasma and used to diagnose and predict the opposite of cancer diseases like lung, breast and colorectal (Liu et al., 2016). They are associated with burden, metastatic potential, and the response to treatment, which makes attaching them to the standard clinical tests of individual medicine worth considering (Zhang et al., 2016; Liu et al., 2008).However, there are limitations that inhibit translation of miRNA research to clinical practice. The context-dependent miRNA defines nature so that findings cannot be generalised among different cancers. Moreover, there is redundant miRNA and overlapping target specter, which make target validation difficult (Calin et al., 2006; Rossi et al., 2007). To counter this, integrated systems biology is expected in the future to help map miRNA regulatory networks and compute models of predicting therapeutic outcomes.Conclusively, miRNAs cannot be ignored in the processes of regulating cancer. They hold a huge potential not just as the means of diagnostics and prognosis but also they can be used to regulate complicated signaling systems by serving as actual therapeutic compounds. Further investigation and clinical validation are necessary to use their full potential and include miRNA-based intervention into precision oncology.

CONCLUSIONS

The role of microRNAs (mi RNA) as key modulators of gene expression has become apparent in their effects on the fundamental biologic pathways that dictate cancer development,

progression and response to therapy. Diverse functions of miRNAs in the cancer continuum were seen in this review, starting with the induction of oncogenic transformations to facilitating metastasis processes as well as resistance to conventional therapies. In order to highlight their key role in mechanisms related to cell cycle control, apoptosis resistance, epithelial-mesenchymal transition (EMT) and angiogenesis, there is an interregulation amid the oncogenic and the tumor-suppressive miRNAs.The second most important understanding comes in the form of contextual duality of miRNAs, whereby the functional outcome of miRNAs is dependent on that cellular context and the repertoire of target genes. It is this complexity that emphasizes the need to understand miRNA biology with a certain degree of sophistication in order to implement it well in clinical oncology. Among miRNAs, most notably miR-21, miR-34a, miR-155, and miR-200c, have been cross-identified as central modulators in multiple cancers, and these miRNAs are desirable and potential candidates for use either in diagnostic, prognostic, or therapeutic settings.In addition, the robustness of miRNAs in body fluids and their measurability with less invasive methods makes them attractive biomarkers of early cancer detection and follow-up. Circulating miRNAs provide dynamical information in real time of tumor dynamics, response to therapy and relapse which is facilitating more personalized treatment regimens. Simultaneously, the therapeutic use of miRNA seems very promising, i.e., the application of miRNA mimics to reinstate tumor-suppressor miRNAs and miRNA inhibitors to shut down oncogenic miRNAs. Some of these methods are undergoing preclinical and clinical tests and the results are promising.Nonetheless, the journey of miRNA discovery to the bedside is not all entirely smooth. The problem of the delivery specificity, targeting specificity, and chronic safety profile is an important barrier. Further nanotechnology, bioengineering and systems biology will play a vital role in surmounting such obstacles and optimizing miRNA-based interventions. Additionally, a full profiling of miRNA expression in various types of tumors, at various stages in various patient populations shall further help us in personalizing the interventions according to their molecular fingerprint.Conclusively, miRNAs are a radical area of cancer research and care. A combination of molecular understanding and the incorporation of innovative therapeutic approaches are gradually taking the field a step closer towards the future where diagnostics and therapeutics based on miRNA will be a part and parcel of precision oncology. Further interdisciplinary studies, clinical translation and research, coupled with validation, will play key roles in maximizing the potential of miRNAs in the changing of the outcomes of cancer and patient management.

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