# MicroRNA: A New Promising Biomarker

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### Abstract

Understanding the molecular basis of life is at the center today, however, advances in the field of Molecular Biology and genomics improved the compassionate of the genetic basis of diseases in human. There is an increased interest in the function of non-coding RNA transcripts in early diagnosis and treatment to various diseases. MicroRNAs are classes of small non-coding RNAs that consist of 22-25 nucleotides, which are one of the most current forms of molecular characterization of tumours. The target MicroRNA regulates the mRNA translation that causes the subsequent decrease in the protein expression. This paper aims to review some of the accumulated literature that has proven that miRNAs are strong biomarkers in diagnosis and treatment of life threatening diseases such as cancer.

**Keyword**: MicroRNA; Cancer; Biomarker; Cardio progenitors

## Origin and Expression

Since the last decade immense research is being carried out on microRNA showing that the dysregulation, and its after effects in cellular and molecular mechanisms. However, the origin of the unique molecules is not yet clearly studied, studies suggest that a few circulating microRNAs originate from circulating tumor cells by various carrier molecules like HDL and AGO2. RNase and other factors degrade some of the carrier free miRNAs. Interestingly, microRNAs are found to be stable in RNase rich in plasma and serum [1].

Most of the studies proved that the aberrations in the MiRNA expression are the major cause of pathogenesis of human cancer. MiRNA is often found near the fragile sites or integration sites of Human Papiloma Virus. The integration alters the expression of MicroRNA by means of deletion, amplification, or genomic rearrangement. MicroRNA can be either tumor suppressor genes or oncogenes depending upon the target molecules. They can act as tumor suppressors when their overexpression targets the oncogenes whereas they can lead to the tumor formation when they are overexpressed against tumor suppressors. MiRNA alterations are involved in the initiation and progression of human cancer. The cause of the widespread differential expression of miRNA in malignant tumours may be due to their location when compared to normal cells. The expression profiling of miRNA studies proved that these genes might represent downstream targets of activated oncogenic pathways or target the protein coding genes that are involved in cancer [2].

## Role of miRNA in Cancer

Changes in MicroRNA expression have been linked to many cancers. Many studies reported that the molecules are admirable biomarkers and targets for cancer diagnosis and treatment. McBee et al. reported five miRNAs (miR-21,135b, 223) as possible biomarkers in the progression of cervical cancers [3]. Dip N et al. [4] reported the role of miR-100 in bladder carcinomas; the study proved the under expression of miR-100 through a molecular pathway, where miR-100 expression is the first event in the low-grade pTa UC (Urothelial Carcinomas) development [4]. Doss et al. conducted a computational study by applying computational tools, miRBase and UTRscan to validate miRNA and their targets by using colon cancer genes. The study emphasizes the approach in selecting the miRNAs and their targeting mRNAs [5].

Vitamin D is an effective anti-tumor agent (mostly prostate cancer) thus; the functional mechanism of tumor suppression activity facilitates clinical applications to Vit-D. miR-98 is a suppressor of prostate cancer cell growth. Tang et al. [6], reported transcrptionally induced mechanism of mir-98 by vitamin D (D3). This comprehensive study proved miR 98 as a therapeutic target for prostate cancer and biomarker for Vit D anti cancer mechanism.

MiRNA family members activate the mutations in 15-30% cancers. The mutations in the MiRNAs or polymorphisms in mRNA targeted by MiRNA also play a vital role in the progression of the cancer. These expression profiles are used for classification, diagnosis and progression of the human cancer [3]. Sun Y et al. [7] conducted a study to screen and to find out the role of miR-155 in breast cancer by using RT-qPCR and showed that increased level of miR-155 in breast cancer cells. The diagnostic power of miR-155 has been reported in this study via ROC analysis. Furthermore, the study has proved that administration of anticancer agents lead to continuous reduction of tumor burden and decreased levels of miR-155 [7].

Recent advances in miRNA research have revealed the presence of miRNA in human saliva which can act as a potential biomarker for detection of oral cancer. Yoshizawa and Wong [8] in their study performed miRNA profiling by using a highly sensitive and specific, Biosystem stem-looped RT based Taqman microRNA array and reported that salivary miRNA is a strong biomarker even at nanogram quantities [8]. Liver cancer is a highly distractive disease that lacks any therapy or validated diagnostic biomarker. The recent discoveries and emerging results in the field of miRNA research provides accurate diagnosis and specific prognosis for liver cancer therapy. Both upregulated and down-regulated miRNAs play a key role in liver cancer; miR-22 mir-121/122, and miR17-92 cluster are some of the known upregulated miRNAs, conversely, miR-122, miR199a, and *let-7*

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family are few down-regulated oncogenic miRs of liver cancer [9]. "*An In vitro study found that downregulation of miR-121 and miR-122 in liver cancers cells by antigo-miRNAs led to decreased cell growth*"[10].

Lung cancer is one of the leading death causing diseases. The survival rate is poor despite of the fact that many efforts have been constantly made for its prevention, diagnosis and treatment. Therefore, there is a great need to find a potential biomarker for early diagnosis and treatment. Hubaux et al. [11] presented the role of miRs in lung cancer through miRNA- regulated pathways. There are a lot of targets for lung cancer associated with miRs that have shown evident effects. *Let-7* and *miR17-92* members are involved in cell cycle regulation and apoptosis process of lung cancer [11]. Earlier studies have found that the up-regulation (miR-103, miR107) and down-regulation (miR155) of miRs are helpful to perceive pancreatic tumors [12], and miR21, miR29a, mir92, miR93, and miR126 are upregulated and miR-155, mir-99b and 27 are down-regulated in ovarian cancer [13].

Pancreatic cancer is the most death causing malignant cancer for which prognosis is very poor because of its rapidly spreading ability. As cancer studies progresses the correlation between miRNAs and human cancers have been reported. In addition, cancer research strongly believes on cancer stem cells role in cancer progression and regulation of miRNAs on CSCs as well. The connection between miRNAs and cancer stem cells have been revealed because the targets of certain miRNAs are associated with the expression of CSCs markers. In a recent study Ahmed et al. reviewed and reported the role of various miRNAs in pancreatic cancer, their specific targets and roles of CSCs and their expression profiles. The study concluded with deregulation in the expression of both miRNAs and mRNAs in the CSC and developing therapies for pancreatic cancer aggressiveness [14].

Advances in molecular biology and newly emerged techniques such as qPCR, miRNA microarray, and RNAome deep sequencing have indentified that miRNAs play a key role in human cancers including lung, colon, breast, oral, prostate, and liver. Vast research and studies have validated miRNAs as oncogenes or tumor suppressors. These molecules have a strong ability to target multiple genes and are involved in biological processes that make them as the predominant agent for cancer therapy. Recent research proved experimental basis for the utilization of miRNAs as new tools and targets for cancer therapy [15].

## miRNA in Cellular and Molecular Mechanisms

MicroRNAs play a pivotal role in cellular and molecular processes; cell proliferation and differentiation are basic and complex processes. Erythroposis mechanism is one among those, which is important and best studied where the significant role of miRNAs has been reported [16]. Thousands of miRNAs have been found in almost all organisms, which mediate the regulation of various cellular mechanisms such as apoptosis, carcinogenesis, and DNA damage response etc.

DNA damage response and repair is one of those critical processes that are protecting the genome from DNA damage. Cells induce a complex DDR that includes DNA repair, cell cycle check points etc. to secure the DNA from carcinogenic agents like UV light, and various chemical carcinogens. Proteins involved in DDR mechanism are regulated at both transcriptional and post-transcriptional levels. The expression levels of miRNAs can regulate the wide range of DDR and/ or DNA repair genes and modulate cellular sensitivity to DNA damage agents. miRNAs such as miR-24, 138, 96 and 182 have been implicated in DNA damage response or repair mechanism [17]. The roles of miRNAs in DDR to be studied and understanding the functions will provide strong evidence for designing novel therapies for cancer.

## MicroRNA as Cardiac Biomarker

Heart has a limited regeneration capacity and stem and cardiac progenitor cells (CPCs) have become a challenge for the cell therapy applications. Interestingly, recent research on cardiac progenitor cells showed that these progenitors are effectively influenced by miRs expression. Loperfido et al. [18] in their study proved that cardiac progenitors isolated from *sgcb* null mice, animal model limb-girdle muscular dystrophy type 2E has undergone an aberrant differentiation *in vivo* or *in vitro* due to the deregulation of miR669 [18]. Furthermore, the study proved that different heart pathologies are strictly associated with expression of miRNAs.

However, CPCs are multipotent of mycordium; it is difficult to achieve the maximum level of differentiation when these cells are implanted into a damaged myocardium. The improved knowledge of miRNAs enhances the use of CSCs in stem cell therapy. Regarding heart regeneration and the role of miRNAs, studies have reported that the molecules are capable to reprogramme the CSCs to attain three dimensional structure of cardiac muscle in its correct orientation. To put forth the applications of miRNAs in cardiac regeneration, recent studies have proved that nanoparticle bearing miRNAs are able to reprogramme isolated CPCs in a biodegradable tolerated 3D scaffold [19].

Since miRNA expression plays a significant role in genetic and cellular processes, various studies explored the effects of miRNAs in cardiovascular development and cardiac diseases. Many studies proved that microRNA is a promised biomarker for cardiac disease diagnosis. The studies conducted on miRNAs, reveal that 20 microRNAs are associated with acute myocardial infection with 90% sensitivity, 96% specificity and 93% accuracy. These miRNA signatures provide better results in diagnosis than any other single biomarker [20].

## Conclusion

Despite a lot of research to reveal the secret of the expression of the microRNAs and their chemistry, there is a need of more advanced techniques to understand the miRs at all cellular and molecular processes. Even though miRs could be potential biomarkers in various diagnostic methods, oncologists are waiting for a breakthrough in early diagnosis and treatment applications of microRNA. The vast diversity and wide spectrum of applications of miRNAs are closely associated with molecular pathways, diagnosis etc., are yet to be evaluated. Moreover, intensive study and continuous research is required in the development of molecular mimics of miRs, their targets, and effects in the patient. As many questions remains, there is a need of continuous research to bring out the molecular and cellular mechanisms involved in miRNA expression. This will lead to a better understanding of the functional roles of miRNAs and provide new insights into many human diseases.

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