

miRNA: A PROMISING CANDIDATE FOR CLINICAL DIAGNOSIS AND TREATMENT

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Abstract: MicroRNA's (miRNA) are newly found small molecules which regulates most of the functions in our body. Serum level of these miRNA is very good indicator of the many pathological conditions. Since they directly involved in the gene regulation, they are important in the early diagnosis. They found to be effective in the prognosis also. They have gained the special preference in the cancer and viral disease diagnosis and treatment. In many other systemic pathologies, chronic conditions and autoimmune disorders also they have role. So an attempt has been made to have brief review on miRNA to get some basic findings on this topic.

Keywords: miRNA, cancer, cardiovascular disease.

Introduction

MicroRNA (miRNA) are non coding RNA molecules which consists of approximately 22 nucleotides which has role in regulation of gene expression, normally found in viruses, plants and animals [1]. The miRNA reveal was begun from 1993 with the discovery first miRNA lin-4 which 700 bp fragment by genetics in the nematode *Caenorhabditiselegans* (*C. elegans*) and is involved in developmental timing [2]. It involved in differentiation, apoptosis, proliferation and metastasis of cells [3]. There after many discoveries has begun, secondly let-7 in 2000 and also it has been reported that it is conserved to the human also by detecting in tissues like brain, heart, kidney, liver, lung, trachea, colon ,small intestine, spleen stomach and thymus. This discovery in the year of 2000 revolutionized and now thousands of miRNA are discovered. Some data bases are also been established, such as miR Base, miR2 disease, HMDD, etc. These miRNA regulate about ~50% genome. Till now more than 18000 miRNA are explored. These have key regulatory role in numerous diseases such as cancer, cardiovascular disease, metabolic disorders, neurological pathologies, renal diseases,

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hepatological conditions, auto immune disorders, obesity, reproductive disorders, gastro enterological conditions, musculoskeletal disorders and viral diseases. Hence miRNA become valid biomarkers for diagnostic and prognostic purposes. The miRNA level is altering in the tissue and fluids especially in the blood. So serum miRNA level is one of the best biomarker in many cancerous conditions. The role of miRNAs in vertebrate development and disease was also identified [3].

Discoveries in miRNA biology

Since 1993, miRNA was discovered in *C.elegans*, a lot of new discoveries has been done and still that going on. First break through came in year 2000, when miRNA was found in human and later on in 2005 this miRNA was used in synthesis of transgenic mouse. In 2006, researchers found a correlation between the miRNA and cardiovascular system and in 2009, it was consider as a marker for cardiovascular disease [4].

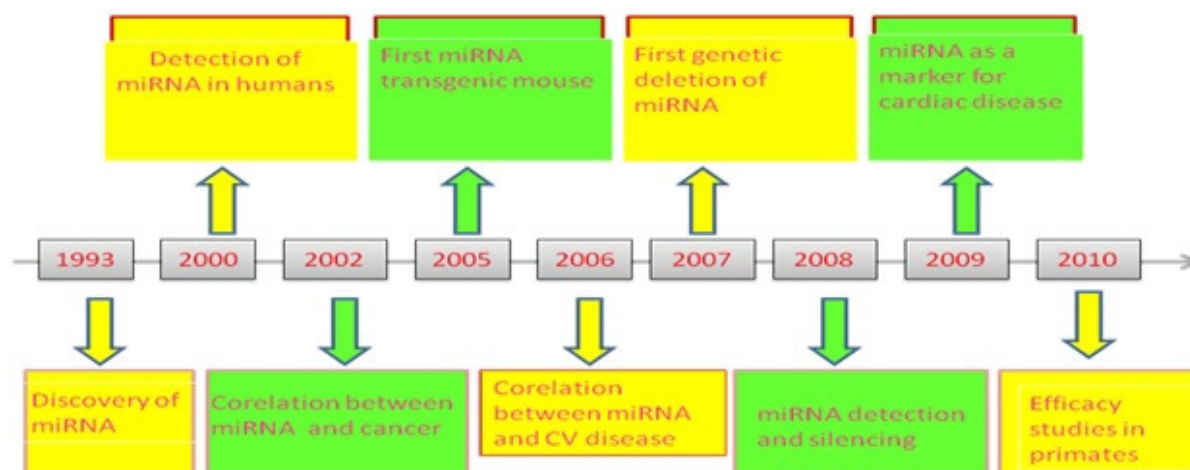


Fig. 1 Biological discoveries of miRNA

miRNA in clinical diagnosis and prognosis

In 2002, the role of miRNA in chronic lymphocytic leukemia condition in humans reported [5]. From this many more discoveries are carried out in the field of cancer. Many techniques such as microarrays, deep sequencing, bead flow cytometry, quantitative RT-PCR and Klenow enzyme. Altered miRNA expression had been reported in almost all type of cancer [6]. In cardiovascular diseases also some reports are evident to say that there is an altered miRNA expression. In some chronic inflammatory diseases & auto immune disorders such as rheumatoid arthritis are also associated with miRNA. MicroRNA is potential diagnostic marker in lupus erythematosus and lupus nephritis. These have been linked to neurodegenerative diseases such as Alzheimer's disease, Parkinson's and Huntington disease [7].

The miRNA is also reported to have prognosis in lung cancer patients. They concluded that low let-7 expression levels have a significantly shorter survival. miRNA also play role as bio marker in the diagnosis of tumor samples removed from biopsies and surgery. Circulating miRNA has evolved as most important diagnostic tool in disease diagnosis especially in cancer conditions.

miRNA in cancer

Mature miRNA promotes the association of large protein complex called RNA induced silencing complex (RISC) with specific region in the 3' untranslated region (3' UTR) of target gene [8]. Single miRNA can target 10-100 of mRNAs. This association inhibits the target gene by mRNA degradation or translation inhibition [9].

miRNA profiling of pancreas can distinguish different types of pancreatic cancers [10]. Expression pattern of miRNA also serve as reliable tool to predict therapeutic outcome of leukemia and colon cancer. miR-21 and miR-155 are found to be elevated in many tumor conditions [11].

These also act as tumor suppressors. Expression of let-7 dramatically inhibits tumor growth in lung cancer module in vivo. Some miRNA acts as both oncogene as well as tumor suppresser depending on cellular environment. Disruption of miRNA biogenesis pathway can alter the homeostasis of normal cellular physiology. RNase III enzyme drosha involves in the processing of miRNA. Altered drosha processing has been described for tumor suppressers miR-7 in glioblastoma [12]. Chromosomal abnormalities associated with cancer may also give rise to miRNA processing.

Export of pre- miRNA from nucleus is carried out by exportin-5 [13]. In some tumor condition this export is altered and pre-miRNA is shuttled in nucleolus. Since miRNA represent critical regulation of cell proliferation differentiation and survival. Alteration in expression of miRNA is clearly linked with cancer conditions. Hence the miRNA are used in the diagnostic tool for cancer identification, classification and also as therapeutic agents. But many researches have to be undertaken for clear understanding of mechanisms of regulations. Ultrasensitive electrochemical bio sensors for detection of circulating miRNA based on DNA amplification [14].

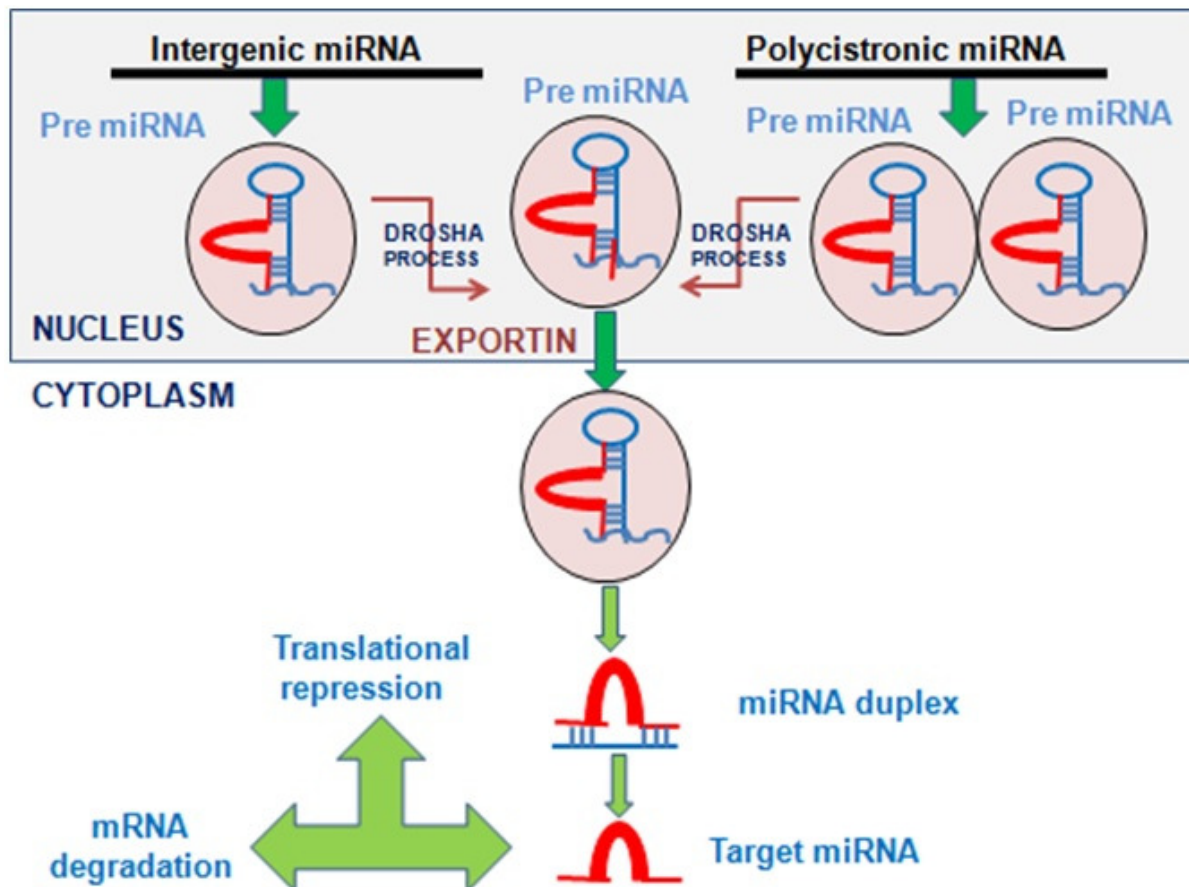


Fig.2 Biogenesis of miRNA and its action.

miRNA in viral diseases

Interferons are cytokines produced in response to viral infection by the infected cells which stimulates uninfected cells to create an antiviral state [15]. These interferons induce expression of some genes along with miRNA expression, these miRNA acts to made cell to non permissive for viral replication. By exploring these facts in recent years studies are conducted to take the help in diagnosis and treatment of the viral diseases. Like cancer drug discovery the miRNA are expected to be the remedy for the viral disease. Researches have been conducted concerned with the disease like marek’s and infectious bursal disease and successes still lot many are there in feature [16].

Conclusion

miRNA is the new topic and have the bright feature in the field of clinical diagnosis and therapy. In the field veterinary science study about the detail structure and functions of miRNAs are less but these are boon in diagnosis and treatment in many conditions with special preference to cancer conditions and viral diseases. Constraints in front of miRNA

studies are that methodologies for miRNA detection and analysis are still evolving since topic is recently introduced. miRNA are smaller in size, varied GC content, complex bio synthesis pathway etc. are also challenging in quantification. But also since 1993 the miRNA publications growing exponentially indicates bright future of miRNA as diagnostic tool.

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