Short Communication

MicroRNA: Biogenesis, significance and therapeutic benefits

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Received: 31/05/2025; Revised: 16/06/2025; Accepted: 19/06/2025; Published: 01/07/2025

Abstract

MicroRNAs (miRNAs) are an abundant class of endogenous, evolutionarily conserved small non-coding RNAs approximately 22 nucleotides in length that regulate gene expression post-transcriptionally by the degradation and translation of target messenger RNAs. The small miRNA molecules play an important role in cell growth, differentiation, proliferation, and apoptosis. Up to 30% of all human genes are probably regulated by miRNAs, and each miRNA may control hundreds of gene targets. However, only a few target genes have been confirmed for a particular miRNA.

Keywords: Diagnostic marker, gene expression, microRNA, microRNA-based therapies.

Introduction

In 1990s, Ambros and Ruvkun groups discovered the prototypic microRNA (miRNA) gene *lin-4* in *Caenorhabditis elegans.* This small molecule RNA was initially considered to be 'junk RNA' because miRNA function has not been clarified. [1,2] In 2006, Andrew Z. Fire and Craig C. Mello won the Nobel Prize in Medicine for their work in elucidating how miRNA regulates gene expression. Compared with the regulators of gene expression found previously, miRNAs are different in production and biosynthesis. The process of the miRNA biosynthesis is complicated.[3] MicroRNA genes encode long primary miRNA transcripts, which then are processed into precursor miRNAs (pre-miRNA) by RNA polymerase II.[4] The primary miRNA transcript possesses a 5'cap and 3'poly (A) tail. There are also miRNAs transcribed by RNA polymerase III. Two kinds of RNAse III, Drosha and Dicer, complete the conversion and modification of the miRNAs, respectively, in the nucleus and cytoplasm.[5] The pre-miRNAs are exported to the cytoplasm by Exportin-5 in a RAS-related nuclear protein–guanosine triphosphate (RAN–GTP)-dependent manner. They have a stem and loop structure. The stem represents the RNA duplex segment. The miRNAs are cleaved by the RNAse III called Dicer at sites close to the loop. In the cytoplasm, the pre-miRNA is sheared into a 22-nt double-stranded miRNA by Dicer. One strand (the 'passenger' strand) is degraded, while the other strand (the 'guide' strand) enters the RNA-induced silencing complex (RISC). The RISC targets 3' untranslated region of specific messenger RNAs (mRNAs), destabilizing the target mRNA(s) or repressing its translation. The latter mechanism serves as the principal pathway in animal cells.

Regulation of gene expression by miRNA

Heritable changes in gene expression that do not involve coding sequence modifications are referred to as 'epigenetic'. Recently, gene regulation by small non-coding RNA is also considered an epigenetic mechanism. Some specific miRNA can target specific mRNA,

silencing it or inhibiting its translation. This observation suggests novel ways to modify gene expression. MicroRNAs can also be used as an alternative to avoid the complex gene knockout techniques (in which the function of the gene is ascertained in its absence), and it may greatly facilitate functional genomics research. Compared with other mechanisms of regulation of gene expression, such as chromatin modification and transcriptional regulation, miRNA-mediated gene regulation occurs directly before protein synthesis and may be more suitable for fine-tuning of gene expression or quantitative regulation.

MicroRNAs as diagnostic markers and therapeutic targets

MicroRNA screens in healthy and affected tissues have started to reveal the detection and role of miRNAs in different diseases, and aberrant miRNA expression has been discovered in many affected tissues. Various methods, including miRNA microarray techniques, fluorescence activated cell sorting (FACS) using fluorescent nanoparticle miRNA probes, quantification using locked nucleic acids (LNAs), and quantitative reverse transcription-polymerase chain reaction, have been used for the screening of miRNA expression patterns. Northern blot analysis and *in situ* hybridization were also considered sensitive methods. A novel miRNA quantification method has been developed using stem–loop RT, followed by TaqMan PCR analysis. This method enables speedy, accurate and sensitive miRNA expression profiling and can identify and monitor potential biomarkers specific to tissues or diseases. Gene deregulation is characteristic of a variety of diseases, particularly of cancer. There has been an explosive increase in our understanding of the role of miRNAs in normal gene regulation and in human disease. Expression levels of miRNA could be used as a new diagnostic marker. The pathogenesis of numerous human diseases including aging,[6] heart diseases,[7] cancer,[8] and autoimmune diseases,[9] has been linked to the abnormal expression of various genes potentially regulated by miRNAs. Control of miRNA levels might also have therapeutic benefits.

Conclusion

MicroRNAs are small, non-coding RNA molecules that regulate gene expression and influence critical biological processes such as cell growth, differentiation, apoptosis, and immune responses. They play significant roles in the pathogenesis of various diseases, including cancer, cardiovascular conditions, and inflammatory disorders. Due to their stability in body fluids and tissue-specific expression patterns, miRNAs serve as valuable biomarkers for non-invasive disease diagnosis, monitoring, and prognosis. In cancer, miRNAs may function as either tumor suppressors or oncogenes. Therapeutic strategies targeting miRNAs such as miRNA mimics and antagomirs are being developed to modulate gene expression. MicroRNA mimics are synthetic molecules designed to restore the function of downregulated endogenous miRNAs, while antagomirs are complementary sequences that inhibit specific miRNAs. Additionally, miRNAs are key regulators of inflammation and autoimmunity, capable of exerting both pro-inflammatory and anti-inflammatory effects by modulating immune cell function and inflammatory signaling pathways.

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How to cite this article: Sarojini H. MicroRNA: Biogenesis, significance and therapeutic benefits. Journal of Experimental Biology and Zoological Studies 2025; 1(2):119-21.