Bulletin of Pure and Applied Sciences
Zoology (Animal Science), Vol.43B, No.2s,
July-December 2024: P. 100-104

Print version ISSN 0970-0765
Online version ISSN 2320-3188

Original Research Article

Content Available online at: www.bpasjournals.com

MICRO RNA IN ORAL DISEASE - AN EMERGING AVENUE FOR DIAGNOSIS AND THERAPY

Mariachelliah Singarayan JaishLal[1,2], Kesavaram Padmavathy[3]*, Jayesh S Raghavendra[4], Goma Kumar K.U[5], Mamtha Roshni A.R[6] & Mithra Swornappan[7]

[1]Research Scholar, Dept of Microbiology, Research Laboratory for Oral and Systemic Health, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education & Research (BIHER), Chennai, Tamil Nadu, India.

[2] Associate Professor, Dept of Oral and maxillofacial Pathology and Microbiology, Rajas Dental College and Hospital, Kavalkinaru, Tirunelveli District, Tamil Nadu, India.

[3]Professor, Dept of Microbiology, Research Laboratory for Oral and Systemic Health, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education & Research (BIHER), Chennai, Tamil Nadu, India

[4]Professor, Dept of Prosthodontics, Sree Balaji Dental College and Hospital, Bharath Institute of Higher Education & Research (BIHER), Chennai, Tamil Nadu, India.

[5]Associate Professor, Department of Oral Pathology, Rajas Dental College and Hospital, Kavalkinaru, Tirunelveli, India 627105

[6]Post graduate student, Department of Oral Pathology, Rajas Dental College and Hospital, Kavalkinaru, Tirunelveli, India 627105

[7]Senior lecturer, Department of Oral Pathology, Rajas Dental College and Hospital, Kavalkinaru, Tirunelveli, India 627105

Corresponding author: *Kesavaram Padmavathy padmabakianath@gmail.com

Abstract:

MicroRNAs (miRNAs) have emerged as key regulators of gene expression in various biological processes, including those associated with oral health and disease. This review explores the current understanding of the roles played by miRNAs in oral diseases, including dental caries, periodontal diseases, oral cancer, and other oral pathologies. [1] We discuss the potential applications of miRNAs as diagnostic biomarkers and therapeutic targets in oral disease management. Additionally, we highlight the challenges and future perspectives in harnessing the power of miRNAs for personalized oral disease treatments.

Introduction:

Oral diseases represent a significant global health burden, affecting billions of individuals across the world. Despite significant advancements in oral healthcare, there is an increasing need to identify novel diagnostic tools and therapeutic strategies to combat these diseases effectively.[2] MicroRNAs, a class of small non-coding RNA molecules, have recently garnered considerable attention as potent regulators of gene expression and cellular processes.[3] This review aims to explore the growing body of evidence regarding the roles of miRNAs in various oral diseases and their potential clinical applications.

Micro RNA:

MicroRNAs (miRNAs) are small, non-coding RNA molecules that play a crucial role in the regulation of gene expression. These tiny molecules, consisting of only 21 to 23 nucleotides, are found in plants, animals, and even some viruses. They have been shown to be involved in RNA silencing and post-transcriptional regulation of gene expression.[4] miRNAs bind to complementary sequences in mRNA molecules and can silence the target mRNA through processes such as cleavage, destabilization, or translation inhibition.

Evolutionary Origin of Micro RNA:

The origins of miRNAs can be traced back to the RNA interference (RNAi) pathway, which functions as a defense mechanism against exogenous genetic material, such as viruses. However, miRNAs have evolved to have distinct characteristics and functions compared to other small interfering RNAs (siRNAs) involved in RNAi. While siRNAs are derived from longer regions of double-stranded RNA, miRNAs are formed from regions of RNA transcripts that fold back on themselves to form short hairpins.[5] miRNAs are highly conserved across species, indicating their important biological functions. The human genome is believed to encode over 1900 miRNAs, with more recent analysis suggesting that the number is closer to 2,300. However, only about 500 human microRNAs are considered bonafide miRNAs in the manually curated miRNA gene database [MirGeneDB].

1.1 The Biogenesis of MicroRNAs

The biogenesis of miRNAs involves a series of intricate steps that take place in the nucleus and cytoplasm of cells. The process begins with the transcription of miRNA genes by RNA polymerase II, resulting in the production of primary miRNA transcripts (pri-miRNAs). These pri-miRNAs are then processed by the Microprocessor complex, consisting of the proteins Drosha and DGCR8, to generate precursor miRNAs (pre-miRNAs). [6] The pre-miRNAs are exported from the nucleus to the cytoplasm by Exportin-5, a nucleocytoplasmic shuttler protein. In the cytoplasm, the pre-miRNAs are further processed by the endoribonuclease Dicer, resulting in the formation of mature miRNA duplexes. One strand of the duplex, known as the guide strand, is selected and incorporated into the RNA-induced silencing complex (RISC), while the other strand, called the passenger strand, is usually degraded. [7]

1.2 The Functions of MicroRNAs

MicroRNAs have emerged as key regulators of gene expression, with the ability to target approximately 60% of the genes in humans and other mammals. They are involved in various cellular processes, including development, differentiation, proliferation, and apoptosis. miRNAs have been found to play essential roles in the development and function of various organs and tissues, such as the brain, heart, and immune system.[7] One of the fascinating aspects of miRNAs is their ability to regulate gene expression through multiple mechanisms. They can inhibit translation initiation, disrupt ribosome assembly, induce ribosome drop-off, and promote mRNA decay. Additionally, miRNAs can also modulate gene expression through epigenetic modifications, such as histone modification and DNA methylation. These multifaceted mechanisms allow miRNAs to fine-tune gene expression and contribute to the complexity of cellular processes. [8]

2. **The Role of MicroRNAs in Oral Diseases:**

Oral diseases, such as periodontal disease and oral cancer, pose significant health challenges worldwide. Understanding the underlying molecular mechanisms that contribute to the development and progression of these diseases is crucial for the development of effective diagnostic and therapeutic strategies. In recent years, there has been growing interest in the role of microRNAs (miRNAs) in oral diseases. [2] MicroRNAs are small non-coding RNA molecules that play a critical role in the regulation of gene expression. They are involved in various cellular processes, including cell proliferation, differentiation, and apoptosis. Dysregulation of miRNAs has been implicated in the pathogenesis of many diseases, including oral diseases. [3]

The Role of Micro RNAs in Dental Caries:

Dental caries is one of the most prevalent oral diseases worldwide. miRNA is involved in dental caries development, progression, and resolution. Specific miRNAs associated with cariogenic bacteria, enamel mineralization, and immune responses are there, along with their potential as diagnostic markers and therapeutic targets.

2.1 The Role of MicroRNAs in Periodontal Disease:

Periodontal disease is a chronic inflammatory condition that affects the supporting structures of the teeth, including the gums, periodontal ligament, and alveolar bone. Multiple studies have identified dysregulated miRNA expression patterns in patients with periodontal disease. These miRNAs have been shown to target genes involved in inflammation, extracellular matrix remodelling, and bone resorption. Studies have shown that miR-146a, an important regulator of the immune response, was significantly upregulated in gingival tissues of patients with periodontitis.[9] This upregulation was associated with increased expression of pro-inflammatory cytokines and chemokines. Another study identified miR-155 as a key regulator of the inflammatory response in periodontal disease. In addition to their role in inflammation, miRNAs have also been implicated in the regulation of osteoclastogenesis, the process by which bone resorption occurs.[10]Studies have shown that miR-223 and miR-21 are involved in the differentiation and function of osteoclasts, suggesting their potential as therapeutic targets for the treatment of bone loss associated with periodontitis.[11]

2.2 MicroRNAs in Oral Cancer:

Oral cancer is a significant public health problem, with high mortality rates and limited treatment options. The identification of miRNAs that are dysregulated in oral cancer has provided valuable insights into the molecular mechanisms underlying the development and progression of this disease. Several studies have shown that specific miRNAs are aberrantly expressed in oral cancer tissues compared to normal tissues. For example, miR-21, miR-31, and miR-155 have been found to be upregulated in oral cancer and are associated with tumor growth, invasion, and metastasis. On the other hand, miR-375 and miR-486-5p have been identified as tumor suppressors in oral cancer, with their downregulation being associated with poor prognosis.[12] Moreover, miRNAs have been shown to be involved in the regulation of epithelial-mesenchymal transition (EMT), a process that plays a crucial role in tumor invasion and metastasis. miR-200 family members, including miR-200a, miR-200b, miR-200c, miR-141, and miR-429, are known to inhibit EMT by targeting transcription factors involved in the process. Dysregulation of these miRNAs has been implicated in the acquisition of invasive and metastatic phenotypes in oral cancer cells.

2.3 Diagnostic and Therapeutic Potential:

The dysregulation of miRNAs in oral diseases suggests their potential as diagnostic and prognostic biomarkers. miRNAs are highly stable in biological fluids, such as saliva and blood, making them attractive candidates for non-invasive diagnostic tests.[13] Several studies have shown that specific miRNA signatures can distinguish between healthy individuals and those with oral diseases, including periodontal disease and oral cancer. In addition to their diagnostic potential, miRNAs may also serve as therapeutic targets for the treatment of oral diseases. The development of miRNA-based therapies, such as miRNA mimics or inhibitors, holds promise for the targeted modulation of gene expression and the inhibition of disease progression. [14]

2.4 Future Perspectives:

Despite the progress made in understanding the role of miRNAs in oral diseases, several challenges remain. Further research is needed to identify the complete repertoire of dysregulated miRNAs in oral diseases and to elucidate their specific functions and target genes. Additionally, the development of reliable and sensitive techniques for miRNA detection and quantification is essential for the translation of miRNA research into clinical practice. [15] The integration of miRNA research with other omics technologies, such as genomics and proteomics, may provide a more comprehensive understanding of the molecular mechanisms underlying oral diseases. Furthermore, the investigation of miRNA interactions with other non-coding RNAs, such as long non-coding RNAs, may uncover novel regulatory networks involved in the pathogenesis of oral diseases. [16]

Conclusion:

MicroRNAs are fascinating molecules that have revolutionized our understanding of gene regulation. Their small size belies their significant impact on cellular processes and the intricate mechanisms through which they modulate gene expression. From their evolutionary origins to their involvement in various diseases, miRNAs continue to captivate researchers and hold immense potential for future therapeutic applications. With ongoing research and advancements, we can expect miRNAs to continue to shape our understanding of biology and pave the way for innovative approaches to disease diagnosis and treatment. Furthermore, miRNAs hold promise as therapeutic targets for the treatment of oral diseases. Continued research in this field may lead to the development of innovative diagnostic tools and novel therapeutic strategies for oral diseases.

Reference:

1. Demirtas DA, Demirtas AO, Biskin A, Demirtas MA. Micro-RNA in health and disease. Int. J. Cardiol. Res. 2018 Jul 31;5:116-23.
2. Wang J, Chen J, Sen S. MicroRNA as biomarkers and diagnostics. Journal of cellular physiology. 2016 Jan;231(1):25-30.
3. Kumarswamy R, Volkmann I, Thum T. Regulation and function of miRNA-21 in health and disease. RNA biology. 2011 Sep 1;8(5):706-13.
4. Faruq O, Vecchione A. microRNA: diagnostic perspective. Frontiers in medicine. 2015 Aug 3;2:51.
5. MacFarlane LA, R Murphy P. MicroRNA: biogenesis, function and role in cancer. Current genomics. 2010 Nov 1;11(7):537-61.

6. Du T, Zamore PD. microPrimer: the biogenesis and function of microRNA.
7. Maqbool R, Hussain MU. MicroRNAs and human diseases: diagnostic and therapeutic potential. Cell and tissue research. 2014 Oct;358:1-5.
8. Noori-Daloii MR, Nejatizadeh A. MicroRNA in disease and health: Diagnostic and therapeutic potentials. Gene Therapy Development and Future Perspectives. Rijeka, Croatia: InTech. 2011 Jun 22:93-120.
9. Kebschull M, Papapanou PN. Mini but mighty: Micro RNA s in the pathobiology of periodontal disease. Periodontology 2000. 2015 Oct;69(1):201-20.
10. Irwandi RA, Vacharaksa A. The role of microRNA in periodontal tissue: A review of the literature. Archives of Oral Biology. 2016 Dec 1;72:66-74.
11. Luan X, Zhou X, Naqvi A, Francis M, Foyle D, Nares S, Diekwisch TG. MicroRNAs and immunity in periodontal health and disease. International Journal of Oral Science. 2018 Aug 6;10(3):24.
12. Gomes CC, Gomez RS. MicroRNA and oral cancer: future perspectives. Oral oncology. 2008 Oct 1;44(10):910-4.
13. Lu M, Zhang Q, Deng M, Miao J, Guo Y, Gao W, Cui Q. An analysis of human microRNA and disease associations. PloS one. 2008 Oct 15;3(10):e3420.
14. Hanna J, Hossain GS, Kocerha J. The potential for microRNA therapeutics and clinical research. Frontiers in genetics. 2019 May 16;10:478.
15. Kearney M, Duncan HF. Micro-RNA profiling in dental pulp cell cultures. InOral Biology: Molecular Techniques and Applications 2022 Nov 24 (pp. 353-367). New York, NY: Springer US.
16. Liang L, He X. A narrative review of microRNA therapeutics: understanding the future of microRNA research. Precision Cancer Medicine. 2021 Dec 30;4.