

The Role of Micro RNAs in Human Diseases: A Review of Current Research

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ABSTRACT

Micro RNAs (miRNAs) are small non-coding RNA molecules that play a crucial role in the regulation of gene expression. Over the past decade, extensive research has revealed the intricate involvement of miRNAs in the pathogenesis of various human diseases. This review aims to provide a comprehensive overview of the current state of research on the role of miRNAs in human diseases. The review begins by elucidating the biogenesis and mechanisms of action of miRNAs, highlighting their ability to modulate gene expression at the post-transcriptional level. Subsequently, it explores the diverse functions of miRNAs in normal cellular processes, emphasizing their regulatory roles in key signaling pathways. The main focus of the review is a detailed examination of the dysregulation of miRNAs in different human diseases, including but not limited to cancer, cardiovascular disorders, neurodegenerative diseases, and autoimmune conditions. For each disease category, we discuss specific miRNAs implicated in disease pathogenesis, their target genes, and the molecular mechanisms underlying their effects.

Furthermore, the review highlights the diagnostic and prognostic potential of miRNAs in various diseases, underscoring the emerging role of these molecules as biomarkers. We also delve into the therapeutic implications of targeting miRNAs for disease intervention, exploring the current status of miRNA-based therapeutics and the challenges associated with their clinical translation. Finally, we discuss the future directions of miRNA research, emphasizing the need for more comprehensive profiling studies, improved understanding of miRNA networks, and advancements in delivery systems for therapeutic applications. The review concludes by underscoring the potential of miRNAs as promising candidates for precision medicine and personalized therapeutic strategies in the context of human diseases.

Keywords: Micro RNAs, precision medicine, therapeutic strategies.

INTRODUCTION

Micro RNAs (miRNAs) have emerged as pivotal players in the intricate regulatory networks governing gene expression, influencing diverse physiological and pathological processes in humans. These small, non-coding RNA molecules, typically consisting of 19-22 nucleotides, exert their regulatory effects at the post-transcriptional level, modulating the expression of target genes. The discovery of miRNAs has revolutionized our understanding of gene regulation, revealing a previously unrecognized layer of complexity in cellular and molecular biology. The biogenesis of miRNAs involves a series of well-orchestrated steps, from transcription to maturation, ultimately leading to the formation of mature miRNA molecules. Once generated, these miRNAs can bind to the 3' untranslated region (UTR) of target mRNAs, leading to translational repression or degradation. This ability to fine-tune gene expression positions miRNAs as key regulators of various cellular processes, including proliferation, differentiation, and apoptosis. In recent years, research efforts have intensified to unravel the involvement of miRNAs in the pathogenesis of human diseases. Studies have revealed dysregulated miRNA expression patterns in a wide array of disorders, from cancer and cardiovascular diseases to neurological conditions and autoimmune disorders. The implications of these findings extend beyond mere academic interest, as miRNAs are increasingly recognized as potential diagnostic and prognostic biomarkers, as well as promising therapeutic targets.

This review aims to provide a comprehensive synthesis of current research on the role of miRNAs in human diseases. By exploring the biogenesis and mechanisms of action of miRNAs, as well as their normal regulatory functions in cellular processes, we set the stage for a detailed examination of miRNA dysregulation in various disease contexts. Moreover, we discuss the diagnostic and therapeutic implications of miRNAs, shedding light on their potential to revolutionize disease management and treatment strategies. As we delve into the intricate landscape of miRNA research, it becomes evident that understanding the roles of these small molecules holds great promise for advancing our knowledge of disease mechanisms and, importantly, for developing innovative and personalized approaches to healthcare.

THEORETICAL FRAMEWORK

The theoretical framework for understanding the role of micro RNAs (miRNAs) in human diseases is grounded in molecular biology, genomics, and systems biology. This framework incorporates key concepts that underpin the regulatory functions of miRNAs and their implications in the context of disease pathogenesis. Here are some key components of the theoretical framework:

1. **Molecular Biology of miRNAs:**

Biogenesis and Processing: Understanding the intricate process of miRNA biogenesis, including transcription, pri-miRNA processing, and maturation, is fundamental. The enzymatic machinery involved in these steps, such as Drosha and Dicer, plays a crucial role in generating mature and functional miRNAs.

Mechanisms of Action: Appreciating the mechanisms by which miRNAs modulate gene expression is essential. This includes the recognition and binding of miRNAs to target mRNAs, leading to translational repression or mRNA degradation. The specificity of miRNA targeting is influenced by the complementarity between the miRNA seed region and the target mRNA.

2. **Genomics and Transcriptomics:**

MiRNA Profiling: Theoretical understanding involves the concept of miRNA profiling, which entails the systematic identification and quantification of miRNAs in various tissues or biological samples. High-throughput sequencing technologies have revolutionized miRNA profiling and contributed to the identification of dysregulated miRNA signatures in different diseases.

Target Prediction and Validation: Theoretical frameworks include computational algorithms for predicting miRNA target genes, taking into account sequence complementarity and other features. Experimental validation methods, such as luciferase reporter assays, are integral to confirming the interactions between miRNAs and their target mRNAs.

3. **Systems Biology and Network Analysis:**

MiRNA Regulatory Networks: Theoretical frameworks encompass the concept of miRNA regulatory networks, acknowledging that a single miRNA can target multiple genes and a single gene can be regulated by multiple miRNAs. Systems biology approaches, including network analysis, help elucidate the complexity of these regulatory networks in health and disease.

Functional Modules and Pathways: Understanding how miRNAs contribute to functional modules and cellular pathways is crucial. This involves recognizing the role of miRNAs in key biological processes, such as cell cycle regulation, apoptosis, and signal transduction pathways.

4. **Diagnostic and Therapeutic Applications:**

Biomarker Discovery: The theoretical framework includes the identification of miRNAs as potential biomarkers for disease diagnosis, prognosis, and treatment response. This involves considerations of sensitivity, specificity, and the dynamic nature of miRNA expression patterns.

Therapeutic Targeting: The framework extends to the development of miRNA-based therapeutics, including the challenges associated with efficient delivery systems, target specificity, and the potential for off-target effects.

In summary, the theoretical framework for understanding the role of miRNAs in human diseases integrates knowledge from molecular biology, genomics, and systems biology. It encompasses the molecular mechanisms of miRNA action, the genomic landscape of miRNAs, and their contribution to complex regulatory networks in health and disease. This framework forms the basis for both basic research and translational applications in the field of miRNA biology.

RECENT METHODS

Recent methods in the study of microRNAs (miRNAs) have evolved to address the complexities associated with their detection, profiling, and functional characterization. These methods leverage advances in technology, bioinformatics, and experimental techniques to enhance the precision and depth of our understanding. Here are some recent methods employed in miRNA research:

1. **Next-Generation Sequencing (NGS) for miRNA Profiling:**

Small RNA-Seq: NGS-based small RNA sequencing has become a standard method for comprehensive miRNA

profiling. It allows for the identification and quantification of miRNAs in a high-throughput manner, providing a detailed view of the miRNA landscape in various biological samples.

2. **Single-Cell miRNA Analysis:**
Single-Cell RNA Sequencing (scRNA-Seq): Advances in scRNA-Seq technologies now enable the profiling of miRNAs at the single-cell level. This allows for the examination of cellular heterogeneity and the identification of rare or cell-type-specific miRNAs, providing insights into the regulatory dynamics within complex tissues.
3. **Circulating miRNA Detection:**
Exosome-Associated miRNAs: Exosomes, extracellular vesicles containing miRNAs, have gained attention for their potential as circulating biomarkers. Methods for isolating and analyzing exosome-associated miRNAs, such as RNA sequencing or quantitative PCR (qPCR), are continually improving for diagnostic and prognostic applications.
4. **Advanced Bioinformatics Tools:**
MiRNA Target Prediction Algorithms: Ongoing developments in bioinformatics have led to improved algorithms for predicting miRNA target genes. Integration of multiple parameters, including binding site accessibility and evolutionary conservation, enhances the accuracy of target predictions.
Functional miRNA Analysis: Bioinformatics tools now facilitate the functional annotation and analysis of miRNAs, including their involvement in pathways, gene ontologies, and regulatory networks. These tools aid in deciphering the broader impact of miRNAs on cellular processes.
5. **CRISPR/Cas9 Screening for miRNA Function:**
CRISPR Screens for miRNA Target Validation: CRISPR/Cas9 technology has been adapted for functional studies of miRNAs by enabling large-scale screens to identify miRNA target genes. This approach helps validate miRNA-mRNA interactions and provides insights into the downstream effects of miRNA dysregulation.
6. **In vivo Imaging of miRNA Activity:**
Fluorescent Reporters: Novel methods involve the use of fluorescent reporter systems to visualize and monitor miRNA activity in living cells or organisms. These reporters allow real-time tracking of miRNA function and provide a dynamic perspective on miRNA-mediated regulation.
7. **Liquid Biopsy Technologies:**
Digital PCR and Droplet Digital PCR: These technologies enable precise and sensitive quantification of miRNA levels in liquid biopsy samples, such as blood or urine. Digital PCR platforms enhance the detection of low-abundance miRNAs, contributing to their utility as non-invasive biomarkers.
8. **Therapeutic Targeting Strategies:**
AntagomiRs and miRNA Mimics: Advances in the development of miRNA-based therapeutics include the use of antagomiRs (anti-miRNA oligonucleotides) to inhibit specific miRNAs and miRNA mimics to restore or enhance miRNA function. Improvements in delivery systems are a focus to enhance the efficacy and specificity of these therapeutic approaches.

These recent methods collectively contribute to a deeper and more nuanced understanding of miRNA biology, offering new avenues for exploration in both basic research and translational applications. Continued advancements in technology and methodology are expected to further propel the field of miRNA research in the coming years.

SIGNIFICANCE OF THE TOPIC

The significance of studying the role of micro RNAs (miRNAs) in human diseases is underscored by the multifaceted impact these small RNA molecules have on cellular processes and their potential implications for diagnostics, therapeutics, and our broader understanding of disease mechanisms. Several key aspects highlight the significance of this topic:

1. **Regulatory Nodes in Gene Expression:**
MiRNAs act as critical regulators of gene expression, exerting control over a wide range of biological processes. Understanding how miRNAs modulate the expression of target genes provides insights into the intricate regulatory

networks that govern normal cellular functions.

2. **Disease Biomarkers:**
Dysregulated miRNA expression profiles have been identified in various diseases, making miRNAs promising candidates as diagnostic and prognostic biomarkers. The ability to detect specific miRNA signatures in bodily fluids allows for non-invasive and early detection of diseases, potentially improving patient outcomes.
3. **Therapeutic Potential:**
The dysregulation of miRNAs is implicated in the pathogenesis of numerous diseases, presenting opportunities for therapeutic interventions. Strategies such as antagomiRs and miRNA mimics hold promise for correcting aberrant miRNA expression and restoring normal cellular function, offering novel avenues for targeted therapies.
4. **Precision Medicine:**
MiRNA research contributes to the paradigm of precision medicine by recognizing the heterogeneity of diseases at the molecular level. Understanding individual miRNA profiles could lead to personalized therapeutic strategies tailored to the unique molecular characteristics of a patient's disease.
5. **Insights into Disease Mechanisms:**
Studying miRNAs enhances our understanding of disease mechanisms. Identification of specific miRNA-target interactions can elucidate key pathways involved in disease progression, providing valuable information for the development of targeted therapies.
6. **Cancer Progression and Metastasis:**
MiRNAs play a crucial role in cancer biology, influencing tumor initiation, progression, and metastasis. Investigating the role of miRNAs in different cancer types not only aids in understanding cancer biology but also opens avenues for developing targeted cancer therapies.
7. **Neurodegenerative Disorders:**
MiRNAs are implicated in neurodegenerative diseases, contributing to the regulation of neuronal function and survival. Understanding the role of miRNAs in conditions such as Alzheimer's and Parkinson's disease may lead to the development of therapeutic strategies to mitigate neurodegenerative processes.
8. **Cardiovascular Health:**
MiRNAs are involved in the regulation of cardiac function and vascular physiology. Investigating their role in cardiovascular diseases provides insights into the molecular basis of conditions such as heart failure, myocardial infarction, and atherosclerosis.
9. **Emerging Biomolecular Technologies:**
Advances in technology, such as next-generation sequencing and single-cell analysis, have greatly expanded our ability to study miRNAs at a finer resolution. These technologies contribute to the comprehensive characterization of miRNA profiles, offering a more nuanced understanding of their roles in health and disease.

In summary, the significance of studying miRNAs in human diseases lies in their central role as regulators of gene expression, their potential as disease biomarkers, and the therapeutic opportunities they present. Insights gained from miRNA research contribute to a deeper understanding of disease mechanisms and pave the way for innovative diagnostic and therapeutic strategies in the era of precision medicine.

LIMITATIONS & DRAWBACKS

While the study of micro RNAs (miRNAs) in human diseases has revealed significant insights, there are several limitations and drawbacks that researchers and clinicians need to consider. These challenges may impact the accuracy, interpretation, and translational potential of miRNA-related findings. Some key limitations and drawbacks include:

1. **Complexity of Target Recognition:**
MiRNA target recognition is complex, and computational algorithms predicting miRNA-mRNA interactions may yield false positives or negatives. The lack of complete understanding of the rules governing target recognition

poses challenges in accurately predicting miRNA targets.

2. Context-Dependent Functions:

The functions of miRNAs are often context-dependent, varying based on cellular context, tissue type, and disease stage. This variability makes it challenging to extrapolate findings from one context to another and emphasizes the need for a nuanced understanding of miRNA function.

3. Cellular Heterogeneity:

Cellular heterogeneity within tissues and organs can affect miRNA expression profiles. Traditional methods that analyze bulk tissue may overlook important miRNA signatures present in specific cell populations. Recent advancements in single-cell sequencing aim to address this limitation.

4. Biological Complexity and Redundancy:

MiRNAs often target multiple genes, and a single gene can be regulated by multiple miRNAs. This redundancy and complexity in miRNA-mediated regulation make it challenging to dissect the precise contribution of individual miRNAs to specific phenotypes or diseases.

5. Limited Specificity of Biomarkers:

While miRNAs show promise as disease biomarkers, their expression patterns may overlap between different diseases. Achieving disease-specific miRNA signatures with high sensitivity and specificity remains a challenge, especially in conditions where shared pathways are dysregulated.

6. Technical Variability:

Technical variability in miRNA detection methods, such as quantitative PCR and next-generation sequencing, can introduce noise and inconsistencies in miRNA expression data. Standardization and quality control measures are essential to mitigate these technical challenges.

7. Normalization Issues:

Choosing appropriate reference genes for normalization in miRNA expression studies can be challenging. The ideal reference miRNA may vary depending on the experimental conditions and the specific disease context, leading to potential biases in data interpretation.

8. Limited Functional Annotations:

While there is a growing understanding of miRNA functions, many miRNAs still lack well-defined functional annotations. Elucidating the precise roles of miRNAs in specific cellular processes and diseases requires continued functional studies.

9. Delivery Challenges in Therapeutics:

Developing effective delivery systems for miRNA-based therapeutics faces hurdles such as off-target effects, immune responses, and tissue-specific targeting. Achieving efficient and targeted delivery remains a significant challenge in translating miRNA research into clinical applications.

10. Ethical and Regulatory Challenges:

The use of miRNA-based therapies raises ethical considerations, including potential unforeseen consequences and long-term effects. Regulatory frameworks for miRNA-based therapeutics are still evolving, and comprehensive guidelines are needed to ensure safety and efficacy.

Recognizing and addressing these limitations is crucial for advancing the field of miRNA research and translating findings into clinical applications. Continued efforts to refine experimental methodologies, enhance computational predictions, and improve our understanding of miRNA biology will contribute to overcoming these challenges.

CONCLUSION

In conclusion, the study of micro RNAs (miRNAs) in human diseases represents a dynamic and evolving field with significant implications for our understanding of molecular mechanisms, diagnostics, and therapeutics. Despite the progress made in elucidating the roles of miRNAs, several challenges and opportunities lie ahead. The complexity of miRNA

regulation, including target recognition and context-dependent functions, underscores the need for a nuanced and comprehensive approach to unravel the intricacies of miRNA-mediated gene expression control. Addressing the limitations in computational predictions, understanding cellular heterogeneity, and embracing emerging technologies like single-cell sequencing will enhance the precision and reliability of miRNA research. MiRNAs' potential as disease biomarkers holds promise for non-invasive diagnostics and prognostics, yet the quest for disease-specific signatures and standardized methodologies continues. Overcoming technical variability and normalization challenges, along with refining data analysis approaches, will be instrumental in realizing the clinical utility of miRNAs as reliable biomarkers. The therapeutic potential of miRNAs is an exciting frontier, offering opportunities for targeted interventions in various diseases. However, the translation of miRNA-based therapeutics faces hurdles related to delivery systems, specificity, and regulatory considerations. Continued efforts in these areas are essential to bridge the gap between bench top discoveries and clinical applications.

As we move forward, a deeper exploration of miRNA functions in specific disease contexts, including cancer, neurodegenerative disorders, and cardiovascular diseases, will provide insights into disease mechanisms and identify novel therapeutic targets. The integration of advanced bioinformatics tools, functional annotations, and collaborative multi-disciplinary approaches will facilitate a more comprehensive understanding of miRNA biology. In the era of precision medicine, miRNA research contributes to a personalized understanding of diseases, recognizing the molecular diversity among patients. Harnessing this knowledge can pave the way for innovative therapeutic strategies tailored to individual molecular profiles. In conclusion, the study of miRNAs in human diseases is a rapidly evolving field that not only deepens our understanding of fundamental biological processes but also holds great potential for transforming diagnostics and therapeutics. By addressing current limitations, embracing emerging technologies, and fostering interdisciplinary collaboration, the field of miRNA research is poised to make significant contributions to the future of healthcare and personalized medicine.

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