

ncRNAs: Master Regulators in Disease and Therapy

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Introduction

Non-coding RNAs (ncRNAs) represent a diverse and rapidly expanding class of RNA molecules that do not encode proteins but instead perform crucial regulatory functions within cells. These molecules are now understood to be central orchestrators of gene expression and cellular processes, playing pivotal roles in both maintaining health and driving disease pathogenesis. The intricate world of ncRNAs includes various types, such as microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), each possessing distinct structures and mechanisms of action. Understanding their complex regulatory networks provides promising avenues for novel diagnostic biomarkers and therapeutic strategies in modern medicine.

The involvement of ncRNAs in human health is extensive, with significant implications across numerous disease areas. For example, non-coding RNAs play pivotal roles in the development and progression of various cancers. Different types of ncRNAs, including microRNAs, long non-coding RNAs, and circular RNAs, can act as oncogenes or tumor suppressors, influencing cell proliferation, apoptosis, metastasis, and drug resistance. Understanding their complex regulatory networks provides promising avenues for novel diagnostic biomarkers and therapeutic strategies in oncology [1].

The intricate interplay between non-coding RNAs and epigenetic mechanisms is crucial in the pathogenesis of various neurological disorders, including Alzheimer's disease and Parkinson's disease. These ncRNAs modulate gene expression without coding for proteins, impacting neuronal function, neuroinflammation, and disease progression. Targeting these regulatory pathways could open doors to new therapeutic approaches for neurodegenerative conditions [2].

Further illustrating their diverse roles, Long non-coding RNAs (lncRNAs) are emerging as critical players in the complex orchestration of immune responses and the development of autoimmune diseases. These molecules regulate immune cell differentiation, activation, and cytokine production, highlighting their potential as therapeutic targets and diagnostic markers in immunological disorders [3].

Meanwhile, Circular RNAs (circRNAs) represent a fascinating class with distinct circular structures, conferring high stability and unique regulatory functions. Their crucial involvement in cardiovascular diseases, modulating processes like cardiac remodeling, angiogenesis, and atherosclerosis, positions them as promising diagnostic and prognostic biomarkers, as well as potential therapeutic targets, in heart conditions [4].

MicroRNAs (miRNAs) are another fundamental class, small and conserved ncRNAs that critically regulate gene expression post-transcriptionally. They impact a wide array of biological processes, including metabolism. The dysregulation

of miRNAs in various metabolic diseases such as diabetes, obesity, and Non-Alcoholic Fatty Liver Disease (NAFLD) illustrates their potential as both diagnostic tools and therapeutic interventions for these prevalent conditions [5].

Beyond initiating diseases, non-coding RNAs also contribute significantly to treatment challenges. Drug resistance presents a significant hurdle in cancer therapy, and ncRNAs are increasingly recognized for their involvement in this complex phenomenon, especially in gastric cancer. They contribute to chemoresistance and targeted therapy resistance by modulating various cellular pathways, including apoptosis, autophagy, and Epithelial-Mesenchymal Transition (EMT), underscoring their potential as targets to overcome drug resistance in cancer treatment [6].

The unique characteristics of non-coding RNAs, such as their stability in bodily fluids and tissue-specific expression, make them excellent candidates for biomarkers. Evidence consistently points to the utility of various ncRNAs, including miRNAs, lncRNAs, and circRNAs, as diagnostic and prognostic indicators across a spectrum of human diseases, offering insights into their clinical translation for early detection and disease monitoring [7].

Fundamentally, ncRNAs operate as master regulators of gene expression through a myriad of mechanisms, influencing everything from chromatin remodeling to post-transcription. Different ncRNA classes, like miRNAs and lncRNAs, interact with DNA, RNA, and proteins to fine-tune gene activity, underscoring their fundamental importance in maintaining cellular homeostasis and driving developmental processes [8].

Moreover, the interplay between hosts and viruses involves a complex dance, with non-coding RNAs playing significant roles in modulating both viral replication and host immune responses. Host-encoded ncRNAs can suppress or promote viral infections, and conversely, viral ncRNAs can manipulate host cellular machinery. Understanding these interactions offers novel perspectives for developing antiviral therapies and diagnostic strategies against infectious diseases [9].

The profound regulatory capabilities of non-coding RNAs have further positioned them as attractive candidates for therapeutic interventions across a spectrum of human diseases. Discussions around cutting-edge strategies for delivering ncRNA-based therapies, including gene editing tools and oligonucleotide-based approaches, highlight their potential in treating cancers, cardiovascular disorders, and neurodegenerative diseases, moving ncRNA research closer to clinical reality [10].

Description

Non-coding RNAs (ncRNAs) are dynamic molecular entities that regulate gene expression and cellular function without translating into proteins. This diverse group includes microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), each contributing uniquely to biological processes. Their complex regulatory networks are crucial for maintaining cellular homeostasis, and their dysregulation is frequently associated with the onset and progression of various human diseases. These RNAs influence cellular activities ranging from proliferation and apoptosis to differentiation and immune responses, making them central to a comprehensive understanding of human health and disease [1, 8]. The sheer breadth of their influence underscores their importance in fundamental biology.

A significant area of ncRNA research focuses on their intricate involvement in complex diseases like cancer, neurological disorders, and metabolic conditions. In oncology, ncRNAs are recognized for their pivotal and often dual roles as either oncogenes or tumor suppressors. They actively impact cell proliferation, metastasis, apoptosis, and critically, contribute to drug resistance mechanisms, particularly highlighted in gastric cancer where overcoming chemoresistance is a major therapeutic challenge [1, 6]. For neurological disorders such as Alzheimer's and Parkinson's diseases, ncRNAs interact profoundly with epigenetic mechanisms to modulate neuronal function and neuroinflammation, thereby shaping disease progression and presenting novel avenues for therapeutic development [2]. Similarly, miRNAs are critically implicated in a range of metabolic diseases, including diabetes, obesity, and Non-Alcoholic Fatty Liver Disease (NAFLD), where their consistent dysregulation suggests significant potential as both diagnostic markers and therapeutic interventions [5]. Complementing this, the unique circular structure of circRNAs grants them high stability and distinct regulatory functions, underpinning their significant roles in cardiovascular diseases by modulating processes like cardiac remodeling, angiogenesis, and atherosclerosis [4].

Beyond these specific disease contexts, ncRNAs are essential regulators of the immune system and are intimately involved in host-pathogen interactions. Long non-coding RNAs, for instance, are pivotal in orchestrating innate and adaptive immune responses and are deeply implicated in the development of autoimmune diseases through their precise influence on immune cell differentiation, activation, and cytokine production [3]. Concurrently, non-coding RNAs play a multifaceted role in viral infections, with both host-encoded ncRNAs suppressing or promoting viral infections, and conversely, viral ncRNAs manipulating host cellular machinery. Understanding these complex interactions offers novel perspectives for developing targeted antiviral therapies and refined diagnostic strategies against infectious diseases [9]. At a more fundamental level, ncRNAs operate as master regulators of gene expression through a myriad of mechanisms, influencing everything from chromatin remodeling to post-transcriptional modification. Different ncRNA classes, like miRNAs and lncRNAs, interact dynamically with DNA, RNA, and proteins to fine-tune gene activity, underscoring their fundamental importance in maintaining cellular homeostasis and driving developmental processes [8].

The remarkable stability of ncRNAs in bodily fluids and their tissue-specific expression patterns make them exceptionally valuable as biomarkers. This characteristic positions various ncRNAs, including miRNAs, lncRNAs, and circRNAs, as promising diagnostic and prognostic indicators across a wide spectrum of human diseases. Their potential for clinical translation in early detection, disease monitoring, and even predicting therapeutic responses is substantial, providing crucial insights into disease progression and treatment efficacy [7]. Furthermore, the profound and versatile regulatory capabilities of non-coding RNAs have naturally led to their intense exploration as therapeutic targets. Cutting-edge strategies for delivering ncRNA-based therapies, such as gene editing tools and oligonucleotide-based approaches, are currently being developed and refined with promising applications in treating intractable conditions like cancers, cardiovascular disorders, and neurodegenerative diseases. This movement of ncRNA research closer to clinical reality signifies a major paradigm shift in therapeutic development [10]. This com-

prehensive understanding of ncRNA biology opens up broad possibilities for future medical advancements and personalized medicine.

Conclusion

Non-coding RNAs (ncRNAs), including microRNAs, long non-coding RNAs, and circular RNAs, are crucial players in cell biology and disease. They exert profound regulatory influence without encoding proteins, impacting various cellular functions and maintaining homeostasis. Research reveals their pivotal roles in the development and progression of cancers, where they can act as oncogenes or tumor suppressors, affecting cell proliferation, apoptosis, metastasis, and contributing to drug resistance. Beyond oncology, ncRNAs are implicated in the intricate interplay with epigenetic mechanisms underlying neurological disorders such as Alzheimer's and Parkinson's diseases, modulating neuronal function and neuroinflammation.

Here's the thing, lncRNAs are specifically recognized for orchestrating immune responses and developing autoimmune diseases, regulating immune cell differentiation and cytokine production. Similarly, circRNAs have critical involvement in cardiovascular diseases, influencing cardiac remodeling and atherosclerosis. miRNAs, on the other hand, show significant dysregulation in metabolic conditions like diabetes and obesity. The unique characteristics of ncRNAs, such as their stability in bodily fluids and tissue-specific expression, make them excellent candidates for diagnostic and prognostic biomarkers across a wide spectrum of human diseases. What this really means is, ncRNAs are involved in host-virus interactions, modulating both viral replication and host immune responses. Their profound regulatory capabilities also position them as attractive candidates for therapeutic interventions, with emerging strategies for ncRNA-based therapies showing promise in treating various conditions.

Acknowledgement

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Conflict of Interest

None.

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