



The Role of Non-Coding RNAs in Immune Regulation and Disease Pathogenesis

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Abstract

Non-coding RNAs (ncRNAs) have emerged as key players in the regulation of immune responses and the pathogenesis of various diseases. This review highlights the diverse roles of ncRNAs, including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), in modulating immune cell functions, inflammatory processes, and disease development. We discuss the mechanisms by which ncRNAs regulate gene expression, signaling pathways, and immune cell differentiation, highlighting their potential as therapeutic targets for immune-related disorders. Furthermore, we explore the diagnostic and prognostic implications of ncRNA dysregulation in autoimmune diseases, cancer, infectious diseases, and other immune-mediated disorders. Understanding the intricate network of ncRNA-mediated immune regulation provides novel insights into disease pathogenesis and unveils promising avenues for the development of innovative therapeutic strategies.

Keywords: Non-coding RNAs; Immune regulation; MicroRNAs; Long non-coding RNAs; Circular RNAs; Disease pathogenesis

Introduction

The immune system plays a critical role in defending the host against pathogens and maintaining tissue homeostasis. Dysregulation of immune responses contributes to the pathogenesis of various diseases, including autoimmune disorders, cancer, infectious diseases, and inflammatory conditions [1]. Recent advances in molecular biology have uncovered the complexity of gene regulation beyond protein-coding sequences, revealing the importance of non-coding RNAs (ncRNAs) in modulating immune functions and disease processes. In this review, we provide an overview of the roles of ncRNAs in immune regulation and their implications in disease pathogenesis.

MicroRNAs (miRNAs) in Immune Regulation

MicroRNAs (miRNAs) are small non-coding RNAs approximately 19–22 nucleotides in length that post-transcriptionally regulate gene expression by binding to target mRNAs, leading to mRNA degradation or translational repression (Table 1) [2]. In the context of the immune system, miRNAs play critical roles in the regulation of immune cell development, differentiation, and function. For instance, miR-155 is involved in the activation of T cells and the polarization of macrophages towards an inflammatory phenotype. Conversely, miR-146a acts as a negative regulator of innate immune responses by targeting key signaling molecules such as IRAK1 and TRAF6.

Long Non-Coding RNAs (lncRNAs) in Immune Modulation

Long non-coding RNAs (lncRNAs) are a heterogeneous group of transcripts longer than 200 nucleotides that lack protein-coding capacity (Table 2) [3]. Emerging evidence suggests that lncRNAs play diverse roles in immune regulation by modulating chromatin remodeling, transcriptional regulation, and post-transcriptional processes. For example, lncRNA HOTAIR regulates the expression of inflammatory genes in macrophages by interacting with chromatin-modifying complexes. Additionally, lncRNA NEAT1 promotes the activation of the innate immune response by facilitating the formation of paraspeckles and the nuclear retention of immune-related transcripts.

Circular RNAs (circRNAs) in Immune Responses

Circular RNAs (circRNAs) are a class of covalently closed RNA molecules generated through back-splicing events. Although initially considered as byproducts of pre-mRNA splicing, circRNAs have emerged as important regulators of gene expression at the transcriptional and post-transcriptional levels [4,5]. In the immune system, circRNAs have been implicated in the modulation of immune cell functions, cytokine production, and inflammatory responses. For instance, circRNA circHIPK3 regulates macrophage activation and polarization by sponging miR-124 and derepressing the expression of its target genes.

Dysregulation of ncRNAs in Disease Pathogenesis

Aberrant expression of ncRNAs has been associated with the pathogenesis of various immune-related disorders, offering potential diagnostic and prognostic biomarkers. In autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus, dysregulated miRNAs and lncRNAs contribute to the dysregulation of immune responses and the perpetuation of chronic inflammation [6,7]. Similarly, altered expression of ncRNAs has been observed in cancer, infectious diseases, and inflammatory conditions, highlighting their multifaceted roles in disease pathogenesis.

Therapeutic Targeting of ncRNAs

Given their critical roles in immune regulation and disease pathogenesis, ncRNAs represent attractive therapeutic targets for the development of novel treatment strategies. Approaches such as antagomirs, antisense oligonucleotides, and small molecule inhibitors have been explored to modulate the expression and activity of specific

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Table 1: Examples of microRNAs (miRNAs) in Immune Regulation.

miRNA	Target Genes/Pathways	Function
miR-155	SOCS1, SHIP1, PU.1, TAB2, etc.	Promotion of T cell activation and inflammation
miR-146a	IRAK1, TRAF6, STAT1, etc.	Negative regulation of innate immune responses
miR-124	CDK6, STAT3, NF-κB, etc.	Modulation of macrophage polarization and inflammation

Table 2: Long Non-Coding RNAs (lncRNAs) in Immune Modulation.

lncRNA	Target Genes/Pathways	Function
HOTAIR	HOXD gene cluster, EZH2, etc.	Regulation of inflammatory gene expression in macrophages
NEAT1	Paraspeckle formation	Promotion of innate immune response through nuclear retention of immune-related transcripts
MALAT1	NF-κB pathway, SRSF1, etc.	Modulation of inflammatory gene expression and T cell activation

ncRNAs for therapeutic purposes [8]. Furthermore, the development of delivery systems that enable targeted delivery of ncRNA-based therapeutics holds promise for precision medicine approaches in immune-mediated disorders.

Conclusion

Non-coding RNAs exert profound effects on immune regulation and disease pathogenesis through diverse mechanisms of action. Elucidating the functions of ncRNAs in immune cell biology and inflammatory processes provides insights into the development of diagnostic biomarkers and therapeutic interventions for immune-related disorders. Continued research into the roles of ncRNAs in immune regulation promises to uncover novel therapeutic targets and strategies for the treatment of autoimmune diseases, cancer, infectious diseases, and other immune-mediated conditions.

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