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Emerging Roles of Non-Coding RNAs in Immune Regulation and Disease Pathogenesis

Odile Patrick Thalia

Faculty of Biological Sciences Kampala International University Uganda

ABSTRACT

Non-coding RNAs (ncRNAs) have emerged as crucial regulators of immune responses and play significant roles in the pathogenesis of various diseases, including autoimmune disorders, cancers, and infectious diseases. This review explores the two main classes of ncRNAs: microRNAs (miRNAs) and long non-coding RNAs (lncRNAs). MiRNAs, typically 22 nucleotides in length, modulate gene expression post-transcriptionally by targeting messenger RNAs (mRNAs) for degradation or translational repression. They are essential in immune cell differentiation and activation, with dysregulated expression linked to autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. In contrast, lncRNAs, which exceed 200 nucleotides, influence immune responses through diverse mechanisms, including chromatin remodeling and interaction with proteins. They are implicated in both promoting and suppressing inflammation, contributing to autoimmune pathogenesis and cancer progression. Additionally, ncRNAs play a critical role in host-pathogen interactions, with pathogens exploiting ncRNA pathways to evade immune responses. Given their regulatory functions and potential therapeutic implications, ncRNAs represent promising targets for innovative treatments in immune-related diseases. Continued research into ncRNA biology will enhance our understanding of their roles in health and disease, paving the way for novel therapeutic strategies and biomarkers in precision medicine.

Keywords: Non-coding RNAs (ncRNAs), MicroRNAs (miRNAs), Long non-coding RNAs (lncRNAs), Autoimmune diseases, Therapeutic targets

INTRODUCTION

Non-coding RNAs (ncRNAs) represent a vast and diverse class of RNA molecules that do not encode proteins but play pivotal roles in regulating various biological processes, including gene expression, cell differentiation, and immune responses [1]. For many years, the focus of molecular biology has primarily been on protein-coding genes, relegating ncRNAs to the background. However, advancements in genomic and transcriptomic technologies have unveiled the significant impact of ncRNAs on health and disease [2]. Emerging evidence highlights the essential functions of ncRNAs as critical regulators of immune responses, contributing to the pathogenesis of a wide range of diseases, including autoimmune disorders, cancers, and infectious diseases.

NcRNAs are broadly classified into two major categories: small ncRNAs (such as microRNAs [miRNAs] and small interfering RNAs [siRNAs]) and long non-coding RNAs (lncRNAs) [3]. MiRNAs, typically around 22 nucleotides in length, regulate gene expression at the post-transcriptional level by binding to complementary sequences in messenger RNAs (mRNAs), leading to mRNA degradation or translational repression [4]. In contrast, lncRNAs are longer than 200 nucleotides and exhibit a wide range of regulatory mechanisms, including chromatin remodeling, transcriptional regulation, and interaction with various proteins and RNAs [5]. Recent research has illuminated the intricate roles of ncRNAs in immune regulation. MiRNAs are now recognized as crucial players in immune cell differentiation, activation, and function [6]. For example, specific miRNAs regulate the differentiation of T-helper cells and modulate the production of cytokines. Aberrant expression of miRNAs has been linked to several autoimmune diseases, where their dysregulation contributes to the uncontrolled activation of immune cells and the development of autoantibodies [7].

Long non-coding RNAs have also emerged as significant regulators of immune responses. They

can modulate the activity of immune cells, influencing inflammation and immune tolerance [8]. In autoimmune disorders, lncRNAs may play a role in the development of autoreactive T cells and the production of inflammatory cytokines [9]. Furthermore, in cancer, lncRNAs can act as oncogenes or tumor suppressors, affecting tumor progression and the immune response to tumors [10]. The relationship between ncRNAs and infectious diseases is equally compelling. Pathogens can manipulate the host's ncRNA pathways to evade immune responses, while the host's ncRNAs can target viral or bacterial RNA, enhancing the immune response [11,12]. This dynamic interaction between host and pathogen underscores the complexity of ncRNA involvement in infectious diseases. Given their critical roles in regulating immune responses and their implications in disease pathogenesis, ncRNAs present exciting opportunities for therapeutic interventions. Understanding the mechanisms by which ncRNAs influence immune regulation could lead to the development of innovative strategies for treating autoimmune diseases, cancers, and infections. As research continues to uncover the multifaceted roles of ncRNAs, their potential as biomarkers and therapeutic targets will become increasingly important in precision medicine and disease management.

Overview of MicroRNAs

MicroRNAs (miRNAs) are small, endogenous ncRNAs that play a crucial role in post-transcriptional regulation of gene expression. They are processed from longer primary transcripts and function by binding to the 3' untranslated region (3' UTR) of target mRNAs, leading to their degradation or translational inhibition [13]. MiRNAs are involved in various biological processes, including cell differentiation, proliferation, and apoptosis [14].

Role in Immune Cell Differentiation and Function

MiRNAs are essential regulators of immune cell differentiation and function. For instance, specific miRNAs are crucial for the differentiation of T helper cells. MiR-155 is upregulated during T cell activation and is required for the differentiation of Th1 and Th2 cells [15]. Conversely, miR-146a has been shown to inhibit the production of pro-inflammatory cytokines in macrophages, thus functioning as a negative regulator of inflammation [16]. In B cells, miR-17-92 cluster is involved in promoting differentiation into plasma cells and regulating antibody production [17].

MicroRNAs in Disease Pathogenesis

The dysregulation of miRNAs has been implicated in the pathogenesis of several diseases. In autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), altered expression of miRNAs contributes to the aberrant activation of immune cells and the production of autoantibodies [18]. For example, decreased levels of miR-146a in SLE patients lead to enhanced activation of dendritic cells and increased production of type I interferons, which are crucial for the disease's progression [19]. In cancer, miRNAs can act as oncogenes or tumor suppressors, depending on their target genes. For instance, the upregulation of miR-21 is associated with tumor progression and poor prognosis in various cancers. MiR-34, a known tumor suppressor, can induce apoptosis and inhibit proliferation in cancer cells [20]. Moreover, miRNAs are involved in the tumor microenvironment, influencing the immune response against tumors and affecting tumor immunoediting.

Long Non-Coding RNAs in Immune Regulation

Long non-coding RNAs (lncRNAs) are defined as ncRNAs longer than 200 nucleotides that do not encode proteins. They play diverse roles in gene regulation and are involved in various cellular processes, including chromatin remodeling, transcriptional regulation, and splicing [5]. LncRNAs can interact with proteins, DNA, and RNA to influence gene expression at multiple levels [21].

Role in Immune Responses

LncRNAs are emerging as crucial regulators of immune responses. They can modulate the differentiation and function of various immune cells. For example, lnc-IL7R is essential for Th cell differentiation and cytokine production. LncRNA NEAT1 is implicated in regulating the production of pro-inflammatory cytokines in macrophages and plays a role in the formation of paraspeckles, which are nuclear structures involved in the regulation of gene expression [22].

Long Non-Coding RNAs in Disease Pathogenesis

The dysregulation of lncRNAs has been associated with various diseases. In autoimmune disorders, lncRNAs can influence the development of autoreactive T cells and the production of autoantibodies. For instance, lncRNA LincRNA-p21 is involved in the regulation of inflammation and has been implicated in the pathogenesis of RA and SLE [23]. In cancer, lncRNAs can function as oncogenes or tumor suppressors. The lncRNA HOTAIR is overexpressed in various cancers and is associated with poor prognosis. It can promote cancer cell metastasis by reprogramming chromatin structure and inhibiting tumor suppressor genes [24]. Additionally, lncRNAs can modulate the immune response to tumors, influencing tumor progression and response to immunotherapy [25].

Non-Coding RNAs in Infectious Diseases

NcRNAs also play critical roles in the immune response to infectious diseases. Pathogens can exploit the host's ncRNA machinery to enhance their virulence or evade the immune response. For instance, some viruses, such as the human immunodeficiency virus (HIV) and hepatitis C virus (HCV), can manipulate the expression of host miRNAs to facilitate their replication and persistence [26]. Conversely, the host's ncRNAs can be crucial for controlling viral infections. For example, specific miRNAs can target viral RNA, inhibiting its replication and promoting antiviral responses [27]. In response to infections, the expression of various miRNAs and lncRNAs can be modulated to regulate the immune response and maintain homeostasis.

Therapeutic Potential of Non-Coding RNAs

The emerging understanding of ncRNAs in immune regulation and disease pathogenesis has opened new avenues for therapeutic interventions. Modulating the expression of specific miRNAs and lncRNAs presents a novel strategy for treating autoimmune diseases, cancers, and infections.

MicroRNA-based Therapies

MiRNA mimics and inhibitors (antagomiRs) are being explored as therapeutic agents. For example, delivering miR-146a mimics could potentially restore its function and inhibit inflammation in autoimmune diseases. Conversely, the use of miR-21 inhibitors may enhance the efficacy of cancer immunotherapy by targeting immune suppression within the tumor microenvironment [28].

Long Non-Coding RNA-based Therapies

Targeting lncRNAs offers another promising therapeutic approach. The development of small molecules that can modulate lncRNA function or inhibit their interactions with proteins could provide novel treatment options for various diseases [29]. For example, inhibiting the oncogenic lncRNA HOTAIR may enhance the efficacy of existing cancer therapies by restoring the expression of tumor suppressor genes.

CONCLUSION

Non-coding RNAs, including microRNAs and long non-coding RNAs, are emerging as critical regulators of immune responses and play significant roles in the pathogenesis of various diseases. Their involvement in immune cell differentiation, inflammatory processes, and disease progression underscores their potential as therapeutic targets and biomarkers. As our understanding of ncRNAs continues to evolve, harnessing their regulatory potential may offer innovative strategies for treating autoimmune disorders, cancers, and infectious diseases, ultimately advancing the field of precision medicine. Continued research into the functions and mechanisms of ncRNAs will be essential for developing effective therapeutic interventions and improving patient outcomes.

REFERENCES

1. Fu XD. Non-coding RNA: a new frontier in regulatory biology. National science review. 2014 Jun 1;1(2):190-204.
2. Das S, Shah R, Dimmeler S, Freedman JE, Holley C, Lee JM, Moore K, Musunuru K, Wang DZ, Xiao J, Yin KJ. Noncoding RNAs in cardiovascular disease: current knowledge, tools and technologies for investigation, and future directions: a scientific statement from the american heart association. Circulation: Genomic and Precision Medicine. 2020 Aug;13(4):e000062.
3. Sharma S, Yang IV, Schwartz DA. Epigenetic regulation of immune function in asthma. Journal of Allergy and Clinical Immunology. 2022 Aug 1;150(2):259-65.
4. Pandey S, Shreya S, Jain BP. Post-transcriptional gene regulation: an overview. Post-Transcriptional Gene Regulation in Human Disease. 2022 Jan 1:33-53.
5. Zhang X, Wang W, Zhu W, Dong J, Cheng Y, Yin Z, Shen F. Mechanisms and functions of long non-coding RNAs at multiple regulatory levels. International journal of molecular sciences. 2019 Nov 8;20(22):5573.
6. Xu SJ, Hu HT, Li HL, Chang S. The role of miRNAs in immune cell development, immune cell activation, and tumor immunity: with a focus on macrophages and natural killer cells. Cells. 2019 Sep 24;8(10):1140.
7. Dasgupta I. MicroRNA regulation in autoimmune diseases. InPost-Transcriptional Gene Regulation in Human Disease 2022 Jan 1 (pp. 205-237). Academic Press.
8. Pi YN, Qi WC, Xia BR, Lou G, Jin WL. Long non-coding RNAs in the tumor immune microenvironment: biological properties and therapeutic potential. Frontiers in immunology. 2021 Jul 6;12:697083.
9. Mehmandar-Oskuie A, Jahankhani K, Rostamlou A, Mardafkan N, Karamali N, Razavi ZS, Mardi A. Molecular mechanism of lncRNAs in pathogenesis and diagnosis of auto-immune diseases, with a special focus on lncRNA-based therapeutic approaches. Life Sciences. 2023 Dec 1:122322.
10. Zhang L, Xu X, Su X. Noncoding RNAs in cancer immunity: functions, regulatory mechanisms, and clinical application. Molecular cancer. 2020 Dec;19:1-2.

11. Moure UA, Tan T, Sha L, Lu X, Shao Z, Yang G, Wang Y, Cui H. Advances in the immune regulatory role of non-coding RNAs (miRNAs and lncRNAs) in insect-pathogen interactions. Frontiers in Immunology. 2022 Apr 6;13:856457.
12. Cheng Y, Liang Y, Tan X, Liu L. Host long noncoding RNAs in bacterial infections. Frontiers in Immunology. 2024 Sep 2;15:1419782.
13. O'Brien J, Hayder H, Zayed Y, Peng C. Overview of microRNA biogenesis, mechanisms of actions, and circulation. Frontiers in endocrinology. 2018 Aug 3;9:402.
14. Doghish AS, Ismail A, El-Mahdy HA, Elkady MA, Elrebehy MA, Sallam AA. A review of the biological role of miRNAs in prostate cancer suppression and progression. International journal of biological macromolecules. 2022 Feb 1;197:141-56.
15. Xu SJ, Chen JH, Chang S, Li HL. The role of miRNAs in T helper cell development, activation, fate decisions and tumor immunity. Frontiers in Immunology. 2024 Jan 9;14:1320305.
16. Gilyazova I, Asadullina D, Kagirova E, Sikka R, Mustafin A, Ivanova E, Bakhtiyarova K, Gilyazova G, Gupta S, Khusnutdinova E, Gupta H. MiRNA-146a—A Key Player in Immunity and Diseases. International Journal of Molecular Sciences. 2023 Aug 14;24(16):12767.
17. Xie J, Du Y, Liu D, Wu J, Yang K, He X, Zhao J, Hong P, Liao K, Zhang H, Hong Y. The miR-17∼ 92 miRNAs promote plasma cell differentiation by suppressing SOCS3-mediated NIK degradation. Cell Reports. 2023 Aug 29;42(8).
18. Lopez-Pedrera C, Barbarroja N, Patiño-Trives AM, Luque-Tévar M, Torres-Granados C, Aguirre-Zamorano MA, Collantes-Estevez E, Pérez-Sánchez C. Role of microRNAs in the development of cardiovascular disease in systemic autoimmune disorders. International Journal of Molecular Sciences. 2020 Mar 16;21(6):2012.
19. Mortazavi-Jahromi SS, Aslani M, Mirshafiey A. A comprehensive review on miR-146a molecular mechanisms in a wide spectrum of immune and non-immune inflammatory diseases. Immunology Letters. 2020 Nov 1;227:8-27.
20. Syed RU, Banu H, Alshammari AD, Alshammari MD, Kadimpati KK, Khalifa AA, Aboshouk NA, mofareh Almarir A, Hussain A, Alahmed FK. MicroRNA-21 (miR-21) in breast cancer: From apoptosis dysregulation to therapeutic opportunities. Pathology-Research and Practice. 2024 Aug 30:155572.
21. Herman AB, Tsitsipatis D, Gorospe M. Integrated lncRNA function upon genomic and epigenomic regulation. Molecular Cell. 2022 Jun 16;82(12):2252-66.
22. Shin HS, Shin JJ, Park J, Arab I, Suk K, Lee WH. Role of macrophage lncRNAs in mediating inflammatory processes in atherosclerosis and sepsis. Biomedicines. 2023 Jul 5;11(7):1905.
23. Gao Y, Li S, Zhang Z, Yu X, Zheng J. The role of long non-coding RNAs in the pathogenesis of RA, SLE, and SS. Frontiers in medicine. 2018 Jul 3;5:193.
24. Zhu C, Wang X, Wang Y, Wang K. Functions and underlying mechanisms of lncRNA HOTAIR in cancer chemotherapy resistance. Cell death discovery. 2022 Sep 13;8(1):383.
25. Entezari M, Taheriazam A, Orouei S, Fallah S, Sanaei A, Hejazi ES, Kakavand A, Rezaei S, Heidari H, Behroozaghdam M, Daneshi S. LncRNA-miRNA axis in tumor progression and therapy response: An emphasis on molecular interactions and therapeutic interventions. Biomedicine & Pharmacotherapy. 2022 Oct 1;154:113609.
26. Gupta A, Swaminathan G, Martin-Garcia J, Navas-Martin S. MicroRNAs, hepatitis C virus, and HCV/HIV-1 co-infection: new insights in pathogenesis and therapy. Viruses. 2012 Oct 26;4(11):2485-513.
27. Trobaugh DW, Klimstra WB. MicroRNA regulation of RNA virus replication and pathogenesis. Trends in molecular medicine. 2017 Jan 1;23(1):80-93.
28. Seyhan AA. Trials and tribulations of MicroRNA therapeutics. International Journal of Molecular Sciences. 2024 Jan 25;25(3):1469.
29. Arun G, Diermeier SD, Spector DL. Therapeutic targeting of long non-coding RNAs in cancer. Trends in molecular medicine. 2018 Mar 1;24(3):257-77.

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