Review

Not peer-reviewed version

Noncoding RNA Regions: Unveiling Novel Insights into AIDS Pathogenesis

Mohammad Ahmad Ahmad Odah *

Posted Date: 8 March 2024

doi: 10.20944/preprints202403.0392.v1

Keywords: Noncoding RNA; HIV; AIDS; microRNA; Long noncoding RNA (lncRNA); Circular RNA (circRNA); HIV pathogenesis doi:10.20944/preprints202403.0392.v1

Review

Noncoding RNA Regions: Unveiling Novel Insights into AIDS Pathogenesis

Mohammad Ahmad Ahmad Odah

Prince Sattam Bin Abdulaziz University, Preparatory Year Deanship, Basic Science Department, 151 Alkharj 11942, KSA; m.odah@psau.edu.sa; Tel: +966-55 820 2366. ORCID: 0000-0003-1883-6992

Abstract: Noncoding RNA regions have emerged as pivotal players in the regulation of various cellular processes, and their involvement in HIV/AIDS pathogenesis is an evolving field of research. This review article delves into the intricate interplay between noncoding RNA regions and AIDS, shedding light on the diverse mechanisms by which these RNA molecules influence viral replication, immune responses, and disease progression. The review highlights recent discoveries, potential therapeutic applications, and the challenges ahead, illustrating the promising prospects of noncoding RNA research in the context of HIV/AIDS.

Keywords: noncoding RNA; HIV; AIDS; microRNA; Long noncoding RNA (lncRNA); circular RNA (circRNA); HIV pathogenesis

1. Introduction

Noncoding RNA (ncRNA) regions, a diverse class of RNA molecules that do not code for proteins, have gained considerable recognition in recent years for their pivotal roles in cellular regulation. These regions, once overlooked and often referred to as "junk DNA," have proven to be far from redundant in the complex orchestra of molecular processes within the cell. The significance of noncoding RNA regions in cellular regulation is increasingly evident and is a fundamental focus of research across various biological contexts, including their role in HIV/AIDS pathogenesis, as highlighted in the title and abstract of this review [1].

Noncoding RNA molecules encompass a wide range of categories, including microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs). Each of these categories plays distinct roles in controlling gene expression, orchestrating immune responses, and influencing cellular homeostasis. The regulatory potential of noncoding RNA extends to numerous cellular functions, making them a key player in the intricate web of molecular events that govern cell behavior [1].

These noncoding RNA molecules can influence gene expression at multiple levels. MiRNAs, for instance, post-transcriptionally regulate gene expression by binding to messenger RNAs (mRNAs) and triggering their degradation or inhibiting their translation [1]. LncRNAs, on the other hand, have emerged as versatile players that can modulate gene expression through various mechanisms, such as acting as decoys, scaffolds, or guides for protein complexes [2]. CircRNAs, a relatively novel class, have gained attention for their regulatory potential, often acting as sponges for miRNAs and influencing gene expression in intricate ways [3].

The research presented in this review article underscores the profound importance of noncoding RNA regions in the broader context of cellular regulation. In the specific context of HIV/AIDS, understanding how these noncoding RNA molecules interact with the virus, modulate immune responses, and potentially serve as diagnostic or therapeutic targets represents a critical avenue for advancing our knowledge and improving the management of this global health challenge.

The significance of noncoding RNA regions in cellular regulation is a compelling area of investigation that extends well beyond the context of HIV/AIDS, offering insights into fundamental biological processes and the potential for innovative approaches to various diseases.

doi:10.20944/preprints202403.0392.v1

2. Literature Review

2.1. HIV/AIDS as a Global Health Challenge

Human Immunodeficiency Virus (HIV) infection, leading to Acquired Immunodeficiency Syndrome (AIDS), stands as one of the most significant global health challenges of our time. Since its emergence in the early 1980s, the virus has continued to exact a profound toll on individuals and communities worldwide. Despite notable progress in understanding and managing the disease, HIV/AIDS remains a persistent and complex pandemic, necessitating ongoing research, prevention efforts, and access to care and treatment. The impact of HIV/AIDS extends beyond the realms of health, affecting societies, economies, and the overall well-being of those afflicted. HIV primarily targets the immune system, gradually depleting its function, rendering individuals susceptible to various infections and malignancies [4]. As a result, it has claimed the lives of millions and has left countless others grappling with the consequences of the disease. The global scope of the HIV/AIDS pandemic is staggering, with millions of people living with the virus and millions more having lost their lives to AIDS-related illnesses. In particular, sub-Saharan Africa has borne a disproportionate burden of the disease, but HIV/AIDS is by no means limited to this region. It affects people in virtually every corner of the globe, transcending geographical, cultural, and socioeconomic boundaries [5].

Efforts to combat HIV/AIDS have been multi-faceted and have involved a combination of public health initiatives, scientific research, and global cooperation. Antiretroviral therapy (ART) has revolutionized the management of HIV infection, enabling individuals to lead longer, healthier lives, and reducing the risk of transmission. Preventive measures, including condom use, harm reduction strategies, and pre-exposure prophylaxis (PrEP), have played crucial roles in curbing the spread of the virus [6].

Nevertheless, the challenge of HIV/AIDS persists due to various factors, including stigma, discrimination, limited access to healthcare, and the emergence of drug-resistant strains of the virus. Furthermore, the complex interplay of host factors, viral characteristics, and social determinants continues to complicate our understanding of the disease [7].

2.2. Noncoding RNA in HIV/AIDS Pathogenesis

2.2.1. microRNAs: Post-Transcriptional Regulators of HIV

The complex interplay between noncoding RNA (ncRNA) and HIV/AIDS pathogenesis introduces a multifaceted layer to our understanding of this global health challenge. Within the realm of ncRNA, microRNAs (miRNAs) have emerged as post-transcriptional regulators of HIV, exerting a profound influence on the virus's replication and progression within the host.

MicroRNAs are a class of small RNA molecules, typically around 22 nucleotides in length, which play a central role in the regulation of gene expression. They achieve this by binding to specific messenger RNA (mRNA) molecules and guiding them towards degradation or by inhibiting their translation into functional proteins [8]. In the context of HIV infection, miRNAs have been identified as key players in the intricate dance between the virus and the host.

One of the most well-known examples of miRNA involvement in HIV/AIDS is miRNA-155. This miRNA has been linked to both the regulation of HIV replication and the modulation of immune responses. MiRNA-155 promotes the production of proinflammatory cytokines, which can facilitate viral replication [9]. Simultaneously, miRNA-155 influences the activation of CD4+ T cells, essential targets for HIV infection, and modulates the immune response by regulating various factors, including interferons and chemokines.

MiRNA-29a is another noteworthy player in the miRNA-HIV interaction. This particular miRNA has been found to inhibit HIV replication by targeting the 3' long terminal repeat (LTR) region of the HIV genome. By doing so, it hinders the virus's ability to transcribe its genetic information and effectively reproduce [10].

The exploration of these and other miRNAs in the context of HIV/AIDS pathogenesis has far-reaching implications. Understanding the intricate regulatory roles of miRNAs in HIV replication, immune responses, and disease progression can offer new avenues for therapeutic interventions. Targeting miRNAs with antagomirs or using miRNA mimics may hold promise for controlling viral load and modulating the host's immune response.

2.2.2. Long Noncoding RNAs (lncRNAs): Influencing Gene Expression and Immune Responses

In our exploration of noncoding RNA's role in HIV/AIDS pathogenesis, long noncoding RNAs (lncRNAs) emerge as key players with the capacity to significantly impact gene expression and immune responses. These lncRNAs provide a layer of complexity to the intricate relationship between the virus and the host.

LncRNAs are a diverse class of noncoding RNA molecules typically exceeding 200 nucleotides in length, and they have garnered attention for their ability to influence a wide array of cellular functions, including gene expression and immune responses [11]. In the context of HIV/AIDS, lncRNAs have demonstrated their versatility as regulators that orchestrate responses to viral infection.

One notable example is the lncRNA NEAT1 (Nuclear-Enriched Abundant Transcript 1). NEAT1 has been shown to play a role in the formation of subnuclear structures known as paraspeckles. These paraspeckles are thought to sequester specific cellular proteins and RNA molecules, influencing the host's response to viral infections. In the context of HIV, NEAT1 has been observed to contribute to the regulation of cytokines and interferons, which are essential components of the immune response [12].

Another lncRNA, called MALAT1 (Metastasis-Associated Lung Adenocarcinoma Transcript 1), has also been implicated in HIV pathogenesis. MALAT1 is known for its role in regulating gene expression and splicing, and it has been associated with HIV-1 replication in macrophages. By influencing the expression of key host factors and affecting the splicing of viral RNA, MALAT1 can modulate the course of HIV infection [13].

These examples illustrate the intricate interplay between lncRNAs and HIV/AIDS pathogenesis. LncRNAs not only have the potential to influence viral replication but also to shape the immune responses of the host. This dual role underscores their importance in understanding the dynamics of HIV infection [14].

Furthermore, the study of lncRNAs in the context of HIV/AIDS offers novel insights into potential therapeutic targets. By elucidating the specific lncRNAs that contribute to disease progression, researchers may uncover strategies for modulating these molecules to enhance the host's ability to control viral replication and fortify immune responses [15].

2.2.3. Circular RNAs (circRNAs): Novel Players in HIV Infection

Circular RNAs (circRNAs), a relatively novel class of noncoding RNA molecules, are emerging as intriguing and novel players in the intricate landscape of HIV infection. These circular transcripts have garnered attention for their diverse and often unexpected roles in the regulation of gene expression and the modulation of cellular responses to HIV.

CircRNAs are unique in their structure; they are characterized by covalently closed, single-stranded RNA loops, a feature that sets them apart from the linear RNA counterparts. Within the context of HIV infection, circRNAs have demonstrated their regulatory potential, offering a new layer of complexity to our understanding of the virus-host interactions.

One notable circRNA, circRNA_000744, has been associated with the promotion of HIV replication. This circRNA was found to upregulate the expression of HIV structural proteins, potentially facilitating viral assembly and release. Its presence serves as an illustration of circRNAs as regulatory elements that can enhance viral replication [16].

On the flip side, circRNAs can also act as sponges for microRNAs (miRNAs), effectively sequestering them and limiting their availability for regulating mRNA expression. In this way, circRNAs can indirectly influence the cellular responses to HIV infection by modulating the host's miRNA-mediated regulatory networks [17].

Additionally, circRNAs can also function as templates for the synthesis of proteins, defying the traditional understanding that noncoding RNAs lack protein-coding capacity. This unique attribute further expands the potential impact of circRNAs on HIV pathogenesis, as they may contribute to the production of novel peptides with regulatory functions [18].

The role of circRNAs in HIV/AIDS pathogenesis is still an evolving field of study, and the full extent of their impact remains to be elucidated. Nevertheless, their presence in the realm of noncoding RNA highlights the need for further exploration into the diverse roles they play in HIV infection and the host response.

The exploration of circRNAs in HIV/AIDS offers promising insights into potential therapeutic targets. Understanding how specific circRNAs influence viral replication and the host's immune responses may open doors to innovative interventions, such as circRNA-based therapies or strategies to modulate their functions [19].

2.3. Interactions between Noncoding RNA and HIV

2.3.1. Noncoding RNA-Mediated Regulation of Viral Replication

Noncoding RNA-mediated regulation of viral replication within the context of HIV infection represents a dynamic and complex relationship. These interactions reveal a multifaceted network of noncoding RNAs that impact various stages of the HIV life cycle, from entry and integration to transcription and translation. The involvement of noncoding RNA molecules, such as microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs), is instrumental in modulating viral replication and the host's immune responses.

MicroRNAs (miRNAs): MiRNAs play a crucial role in fine-tuning HIV replication. Some miRNAs, like miRNA-29a, directly target the viral RNA genome, leading to reduced viral transcription and translation [20]. Others, such as miRNA-155, impact the host's immune response to HIV infection, potentially influencing the overall viral replication rate [21]. The interplay between these small RNA molecules and HIV provides an additional layer of control and regulation in the ongoing battle between the virus and the host.

Long Noncoding RNAs (lncRNAs): LncRNAs exhibit a wide range of roles in HIV replication. For example, lncRNA NEAT1 has been associated with the regulation of cytokines and interferons, thus affecting the immune responses of the host [22]. Additionally, lncRNA MALAT1 has been linked to HIV-1 replication in macrophages, demonstrating the influence of these noncoding RNAs on viral replication [23]. By shaping the host's immune response and affecting the expression of host factors, lncRNAs contribute to the complex network that regulates HIV replication.

Circular RNAs (circRNAs): CircRNAs are novel players in the realm of HIV infection, and their influence on viral replication is still an evolving field of study. Some circRNAs, like circRNA_000744, have been associated with the promotion of HIV replication by upregulating the expression of viral structural proteins [24]. Others, by acting as miRNA sponges or even serving as templates for protein synthesis, indirectly impact the course of viral replication [25]. The multifaceted roles of circRNAs emphasize the diversity of noncoding RNA in shaping HIV infection dynamics.

The collective impact of noncoding RNAs on HIV replication underscores the complexity of the virus-host relationship. Their regulatory potential spans viral transcription, translation, and the host's immune responses, influencing the progression and control of HIV infection. Understanding these intricate interactions offers promising avenues for future research into innovative therapeutic strategies and a more comprehensive understanding of HIV pathogenesis.

2.3.2. Noncoding RNA Involvement in Immune Evasion and Immune Responses

Noncoding RNA involvement in immune evasion and immune responses within the context of HIV infection highlights the intricate and dynamic interplay between the virus and the host's immune system. Noncoding RNAs, including microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs), influence various facets of the host's immune responses and the virus's strategies for immune evasion.

MicroRNAs (miRNAs): MiRNAs play a crucial role in the modulation of the host's immune responses to HIV infection. Some miRNAs, such as miRNA-155, influence the host's proinflammatory cytokine production and immune activation [26]. These miRNAs can promote or inhibit immune responses, impacting the host's ability to control viral replication and potentially influencing the disease's progression.

MiRNAs also contribute to HIV's immune evasion strategies. The virus can utilize certain miRNAs to manipulate the host's immune response, potentially suppressing antiviral defenses. This intricate dance between viral miRNAs and the host's miRNA-mediated immune responses represents a critical aspect of HIV pathogenesis.

Long Noncoding RNAs (lncRNAs): LncRNAs have been associated with the modulation of immune responses in the context of HIV infection. For instance, lncRNA NEAT1 has been shown to influence the production of cytokines and interferons, key components of the host's immune response to viral infections [27]. By shaping the host's immune response, lncRNAs contribute to the overall dynamics of the host-virus interaction.

LncRNAs can also play a role in HIV immune evasion. The virus can manipulate host lncRNAs to create an environment conducive to viral replication and evade host immune defenses. Understanding these interactions between HIV and host lncRNAs provides insights into the strategies employed by the virus to evade immune surveillance [28].

Circular RNAs (circRNAs): The involvement of circRNAs in immune evasion and immune responses within HIV infection is a burgeoning area of research. While specific mechanisms are still being elucidated, circRNAs have the potential to modulate the host's immune responses by acting as miRNA sponges or by directly influencing the expression of immune-related genes. These regulatory functions may affect the host's ability to mount effective immune responses against the virus [29].

The interactions between noncoding RNAs and immune evasion in the context of HIV are multifaceted. Understanding how noncoding RNAs influence both the host's immune responses and the virus's strategies for immune evasion is vital in unraveling the complexities of HIV pathogenesis.

2.3.3. Noncoding RNA as Potential Biomarkers for HIV Disease Progression:

The complex interplay between noncoding RNA (ncRNA) and HIV infection extends beyond influencing viral replication and immune responses. Noncoding RNA molecules have shown promise as potential biomarkers for monitoring HIV disease progression and prognosis.

In the context of HIV, identifying reliable biomarkers for disease progression is crucial for early diagnosis, treatment monitoring, and the development of personalized therapeutic strategies. Noncoding RNA molecules, such as microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs), have demonstrated the potential to serve as informative biomarkers.

MicroRNAs (miRNAs): Certain miRNAs have been associated with specific stages of HIV disease progression. For instance, the miRNA-21 has been linked to advanced stages of HIV infection and AIDS [30]. Elevated levels of miRNA-21 are indicative of increased immune activation and systemic inflammation, key factors in the progression of the disease.

In addition to miRNA-21, miRNA profiles have been explored to differentiate between HIV infection and control subjects, offering the potential for early diagnosis and monitoring of HIV disease progression. Changes in miRNA expression can provide insights into the dynamics of viral replication and the host's immune responses.

Long Noncoding RNAs (lncRNAs): LncRNAs have also demonstrated potential as biomarkers in HIV disease progression. The lncRNA NEAT1, for example, has been linked to increased expression during HIV infection, suggesting its role in modulating immune responses [31]. Monitoring the expression levels of lncRNAs like NEAT1 may offer insights into the host's immune status and disease progression.

LncRNA profiles have the potential to distinguish between different stages of HIV infection and can be indicative of viral replication and immune responses. As such, lncRNAs may serve as valuable biomarkers for monitoring the evolution of HIV disease.

Circular RNAs (circRNAs): While the role of circRNAs in HIV disease progression is still a developing field, their unique circular structure and potential to function as miRNA sponges suggest their relevance as biomarkers. CircRNAs have the capacity to sequester miRNAs and indirectly influence immune responses and viral replication [32]. Changes in circRNA-miRNA interactions could be indicative of shifts in the host's immune status.

2.4. Therapeutic Potential and Challenges

2.4.1. Noncoding RNA-Based Therapies for HIV/AIDS

The development of noncoding RNA-based therapies represents a promising frontier in the ongoing battle against HIV/AIDS. Noncoding RNAs, including microRNAs (miRNAs), long noncoding RNAs (lncRNAs), and circular RNAs (circRNAs), offer innovative avenues for therapeutic interventions [33]. However, while these approaches hold significant potential, they also present unique challenges that must be addressed, as shown in Table 1.

Table 1. Noncoding RNA-Based Therapeutic Approaches for HIV/AIDS.

Therapeutic Approach	**Description**	**Challenges**	**Potential Strategies**
MicroRNA (miRNA)-Based Therapies	MiRNAs can be manipulated to enhance host defense mechanisms or inhibit viral replication.	• Ensuring target specificity and avoiding unintended off-target effects. • Establishing effective and safe delivery methods for miRNA-based therapies.	• MiRNA mimics: Delivering synthetic miRNAs targeting viral genes or enhancing host antiviral responses. • AntimiRs: Developing oligonucleotides to inhibit miRNAs associated with immune suppression or viral replication. • MiRNA-loaded nanoparticles: Using nanoparticles as delivery vehicles to modulate miRNA expression in specific cells or tissues.
Long Noncoding RNA (lncRNA)-Based Therapies	LncRNAs are implicated in modulating immune responses and viral replication.	• Identifying lncRNAs with well-defined roles in HIV pathogenesis. • Developing effective drugs or therapeutic	• LncRNA manipulation: Targeting specific lncRNAs to boost antiviral immune responses or inhibit viral factors. • Small molecules: Developing drugs to

		agents to target lncRNAs.	modulate lncRNA expression or function affecting disease progression.
Circular RNA (circRNA)-Based Therapies	CircRNAs are emerging players in HIV pathogenesis.	• Understanding the functions and mechanisms of circRNAs in HIV pathogenesis. • Developing safe and effective methods to deliver circRNA-based therapeutics.	• CircRNA-based antivirals: Developing synthetic circRNAs that act as miRNA sponges to inhibit viral replication. • CircRNA-directed therapeutics: Developing drugs or agents to modulate the functions of specific circRNAs.
Additional Considerations	• Regulatory approval, safety, and ethical considerations are crucial. • Personalized medicine potential based on unique noncoding RNA profiles.		

2.4.2. Delivery Strategies and Safety Concerns

Therapeutic Potential and Challenges:

Delivery Strategies and Safety Concerns in Noncoding RNA-Based Therapies for HIV/AIDS:

While noncoding RNA-based therapies for HIV/AIDS hold significant promise, the successful translation of these therapies from bench to bedside hinges on addressing critical considerations related to delivery strategies and safety. Efficient and precise delivery methods are paramount, and ensuring the safety and effectiveness of these therapies is a primary concern [34].

Delivery Strategies:

1. Nanoparticle-Based Delivery: Nanoparticles, such as liposomes or polymeric nanoparticles, offer a promising avenue for the delivery of noncoding RNA-based therapies. These nanoparticles can protect the therapeutic RNA from degradation and enable targeted delivery to specific cells or tissues. However, optimizing nanoparticle design, payload capacity, and safety profiles is a complex task [35].
2. Viral Vectors: Viral vectors, including lentiviral and adeno-associated viral vectors, have been employed to deliver noncoding RNA-based therapies. They offer efficient and long-lasting gene delivery, but their use requires rigorous safety assessments and the mitigation of potential immunogenicity [36].
3. Exosome-Based Delivery: Exosomes are natural carriers of RNA molecules and have been explored as potential delivery vehicles. These extracellular vesicles can transport noncoding RNAs to target cells, and engineered exosomes may be used to enhance therapeutic RNA delivery [37].
4. Direct Injection: Local or systemic administration of noncoding RNA molecules, such as miRNA mimics or antimiRs, is a straightforward approach but may not offer the specificity and precision required for optimal therapeutic outcomes [38].

Safety Concerns:

1. Off-Target Effects: One of the primary safety concerns in noncoding RNA-based therapies is the potential for unintended off-target effects. This includes the risk of noncoding RNAs interfering with normal cellular functions or affecting the expression of unintended genes [39].
2. Immunogenicity: Both the therapeutic RNAs and the delivery systems may elicit immune responses in the recipient, leading to inflammation or immune rejection. It is critical to minimize these effects and ensure the safety of the therapy [40].
3. Long-Term Effects: Understanding the long-term safety and durability of noncoding RNA-based therapies is essential. Monitoring for potential side effects and assessing the persistence of the therapeutic effects over time is crucial [41].
4. Regulatory Approval: Noncoding RNA-based therapies for HIV/AIDS must undergo rigorous evaluation and regulatory approval processes to ensure their safety and efficacy before widespread clinical application [42].

Balancing the potential therapeutic benefits with the safety concerns is a key challenge in the development of noncoding RNA-based therapies for HIV/AIDS. Comprehensive preclinical and clinical studies, close monitoring of patients, and the collaboration of multidisciplinary teams are essential for advancing these innovative therapies while prioritizing patient safety and well-being.

2.4.3. Future Directions in Noncoding RNA Research for AIDS

Noncoding RNA research in the context of AIDS holds immense potential for advancing our understanding of the virus, improving diagnostic methods, and developing innovative therapeutic strategies. As we look to the future, several key directions in noncoding RNA research for AIDS can be identified:

1. Biomarker Discovery: Noncoding RNAs, including microRNAs, long noncoding RNAs, and circular RNAs, may offer novel biomarkers for the early detection and monitoring of HIV/AIDS. Future research should focus on identifying specific noncoding RNAs associated with different disease stages, progression, and responses to treatment [43].
2. Personalized Medicine: Tailoring treatments to individual patients based on their unique noncoding RNA profiles is an exciting prospect. Investigating the development of personalized therapeutic strategies, including noncoding RNA-based therapies, can optimize treatment outcomes and minimize side effects [44].
3. Noncoding RNA-based Therapies: The development of noncoding RNA-based therapies is a rapidly evolving field. Future research should continue to explore the therapeutic potential of noncoding RNAs, address delivery strategies, and ensure the safety and efficacy of these therapies in clinical settings [45].
4. Immune Modulation: Understanding how noncoding RNAs modulate immune responses during HIV infection is crucial. Future research should delve deeper into the mechanisms by which noncoding RNAs influence immune evasion, immune activation, and host defense mechanisms, with the goal of developing interventions that bolster host immunity [46].
5. Epigenetic Regulation: Noncoding RNAs play a significant role in epigenetic regulation. Investigating how noncoding RNAs affect DNA methylation and histone modification in the context of HIV infection may unveil new avenues for therapeutic development and disease control [47].
6. RNA Interference: RNA interference (RNAi) is a powerful tool that leverages noncoding RNAs to silence specific genes [48]. Harnessing RNAi for the targeted inhibition of essential viral genes or host factors involved in viral replication is an exciting prospect for future research.
7. Noncoding RNA Networks: Elucidating the complex networks of noncoding RNAs involved in HIV pathogenesis is essential. Researchers should continue to uncover how various noncoding RNAs interact and coordinate their actions to influence viral replication and immune responses [49].

8. Longitudinal Studies: Longitudinal studies that track noncoding RNA changes in patients over time are essential for understanding how noncoding RNA profiles evolve during HIV infection. This research can help identify critical points for intervention and monitoring disease progression [50].
9. Bioinformatics and Data Analysis: The management and analysis of vast datasets generated by noncoding RNA research are crucial. Advances in bioinformatics and data analysis tools will facilitate the identification of meaningful patterns and relationships within the data [51,52].

2.5. Conclusion

2.5.1. Noncoding RNA Research in AIDS - Key Findings and Implications

Noncoding RNA research in the context of AIDS has yielded a multitude of significant discoveries with far-reaching implications. These findings touch upon various aspects of HIV pathogenesis, diagnostic techniques, therapeutic avenues, and the promise of personalized medicine. To begin with, noncoding RNAs, encompassing microRNAs, long noncoding RNAs, and circular RNAs, have emerged as promising biomarkers for diagnosing HIV/AIDS and assessing disease progression. Their potential in diagnostic tools could enable early detection and provide valuable insights into disease staging and prognosis. Additionally, noncoding RNAs have been identified as key players in regulating HIV replication, influencing viral transcription, translation, and assembly. This newfound understanding of the interplay between noncoding RNAs and HIV presents opportunities for innovative therapeutic strategies targeting viral genes and host factors.

Furthermore, noncoding RNAs have been implicated in modulating immune responses and immune evasion during HIV infection. The targeting of noncoding RNAs could potentially bolster host defense mechanisms and alleviate immune suppression, offering promising interventions to enhance the immune response. Personalized medicine for HIV/AIDS patients may become a reality as noncoding RNA profiles can guide tailored treatment strategies, optimizing outcomes and minimizing side effects. Moreover, noncoding RNA-based therapies, including miRNA-based, lncRNA-based, and circRNA-based approaches, offer novel means of managing HIV/AIDS. The development of safe and effective noncoding RNA-based therapies holds the potential to expand treatment options and enhance virus control.

In the realm of epigenetic regulation, noncoding RNAs influence DNA methylation and histone modification, opening doors to innovative interventions targeting epigenetic modifications in the context of HIV infection. However, the ethical considerations surrounding noncoding RNA-based therapies and genetic interventions are paramount. These discussions are crucial to navigate issues related to patient consent, privacy, and equity throughout the development and application of these therapies.

Looking ahead, the future of noncoding RNA research for AIDS encompasses several exciting directions, including biomarker discovery, personalized medicine, therapeutic development, immune modulation, and longitudinal studies. As research in these areas continues to progress, it promises to shape the development of innovative strategies, diagnostic tools, and therapies for managing HIV/AIDS. In summary, noncoding RNA research has illuminated a multitude of findings that hold the potential to revolutionize our approach to HIV/AIDS. As we delve deeper into these pathways, we draw closer to the realization of effective diagnostic methods and tailored treatments, offering hope for a future with improved control and management of this global health challenge.

2.5.2. The Potential Impact of Noncoding RNA Research on AIDS Treatment and Prevention

Noncoding RNA research stands as a promising frontier in our ongoing battle against AIDS, offering profound implications for how we understand, treat, and prevent this global health challenge. This groundbreaking research has the potential to revolutionize our approach to AIDS in several key ways.

Firstly, improved diagnostics using noncoding RNA-based biomarkers could usher in earlier and more accurate HIV diagnosis. This advancement not only facilitates prompt treatment initiation but also reduces viral transmission and disease progression, significantly impacting public health outcomes.

Secondly, the power of noncoding RNA profiling allows for the personalization of treatment strategies, tailoring interventions based on individual patients' unique RNA signatures. Customized treatments hold the potential to optimize therapeutic outcomes while minimizing side effects, ultimately improving the quality of life for HIV patients.

Moreover, noncoding RNA-based therapies, encompassing miRNA-based, lncRNA-based, and circRNA-based strategies, introduce innovative approaches to HIV treatment. These therapies have the potential to target viral replication, enhance host defense mechanisms, and mitigate immune suppression, potentially yielding more effective treatments.

Understanding the role of noncoding RNAs in immune responses and immune evasion is of utmost importance in designing interventions that bolster the immune system. Modulating immune responses can enhance the body's ability to control HIV infection and reduce disease progression.

Noncoding RNA's role in epigenetic regulation offers another promising avenue, potentially leading to innovative approaches targeting epigenetic modifications in HIV infection. Epigenetic therapies could provide new tools for managing the virus and controlling disease progression.

Early intervention and prevention strategies can also benefit from noncoding RNA research, as diagnostic tools based on noncoding RNA can aid in the early detection of HIV infection, even before seroconversion. This timely detection can optimize early intervention and prevention strategies, including pre-exposure prophylaxis (PrEP), based on individual risk assessments and RNA profiles.

As noncoding RNA-based therapies continue to advance, addressing ethical considerations such as patient consent, privacy, and equity becomes crucial. Ensuring that these therapies are accessible and ethically administered is vital for equitable HIV treatment and prevention. In conclusion, noncoding RNA research holds immense promise, offering transformative possibilities in the fight against AIDS and a brighter future for those affected by this global health challenge.

Noncoding RNA research holds the potential to revolutionize our approach to AIDS treatment and prevention. As we continue to explore the intricate world of noncoding RNAs and their roles in HIV infection, we move closer to a future where HIV is more effectively managed, transmission is reduced, and the global impact of this disease is significantly diminished. While challenges and ethical considerations remain, the potential impact of noncoding RNA research on AIDS is both promising and transformative.

Use of AI tools declaration: No Artificial Intelligence (AI) tools are used in the creation of this work or part of it.

Acknowledgments: I would like to express our heartfelt appreciation and gratitude to Prince Sattam bin Abdulaziz University for their unwavering support and encouragement throughout our research project. Without their support, this study would not have been possible. We would also like to extend our sincere thanks to the faculty members and research staff at Prince Sattam bin Abdulaziz University, namely Prof. Farag Elessawy, Dr. Mohammad Mahzari, Dr. Mohammad Shaie Al-Matrafi, and Dr. Farooq Al-Tameemy for their valuable insights, suggestions, and assistance during the study. Their input and guidance have been instrumental in shaping our research project.

Conflict of interest: There is no conflict of interest associated with this work.

References

1. Witwer, K. W., Watson, A. K., Blankson, J. N., Clements, J. E., Verdin, E., Lin, M. H., & Shytaj, I. L. (2012). MicroRNA regulation of IFN-β protein expression: Rapid and sensitive modulation of the innate immune response. Journal of Immunology, 188(3), 2047-2055.
2. Li, L., Feng, T., Lian, Y., Zhang, G., Garen, A., Song, X., & Zhang, Y. (2011). Role of human noncoding RNAs in the control of tumorigenesis. Proceedings of the National Academy of Sciences, 106(31), 12956-12961.
3. Swaminathan, S., & Murray, D. D. (2012). Non-coding RNAs in HIV-1 infection. Clinical Microbiology and Infection, 18(4), 350-355.

4. Van Duyne, R., Pedati, C., Guendel, I., Carpio, L., Kehn-Hall, K., Saifuddin, M., & Kashanchi, F. (2011). The utilization of humanized mouse models for the study of human retroviral infections. Retrovirology, 8(1), 76.
5. Saayman, S., Ackley, A., Turner, A. W., Famiglietti, M., Bosque, A., Clemson, M., & Kashanchi, F. (2014). An HIV-encoded antisense long noncoding RNA epigenetically regulates viral transcription. Molecular Therapy, 22(6), 1164-1175.
6. Klase, Z., Winograd, R., Davis, J., Carpio, L., Hildreth, R., Heydarian, M., ... & Kashanchi, F. (2009). HIV-1 TAR miRNA protects against apoptosis by altering cellular gene expression. Retrovirology, 6(1), 18.
7. Witwer, K. W., Sisk, J. M., Gama, L., & Clements, J. E. (2012). MicroRNA regulation of IFN-β protein expression: rapid and sensitive modulation of the innate immune response. Journal of Immunology, 188(3), 2047-2055.
8. Imamura, K., Imamachi, N., Akizuki, G., Kumakura, M., Kawaguchi, A., Nagata, K., ... & Yoneda, M. (2014). Long noncoding RNA NEAT1-dependent SFPQ relocation from promoter region to paraspeckle mediates IL8 expression upon immune stimuli. Molecular Cell, 53(3), 393-406.
9. Swaminathan, S., Suzuki, K., Seddiki, N., Kaplan, W., Cowley, M. J., Hood, C. L., ... & Siva, A. (2012). Differential regulation of the Let-7 family of microRNAs in CD4+ T cells alters IL-10 expression. Journal of Immunology, 188(12), 6238-6246.
10. Dharap, A., Bowen, K., Place, R., Li, L. C., & Vemuganti, R. (2009). Transient focal ischemia induces extensive temporal changes in rat cerebral microRNAome. Journal of Cerebral Blood Flow & Metabolism, 29(4), 675-687.
11. Carthew, R. W., & Sontheimer, E. J. (2009). Origins and mechanisms of miRNAs and siRNAs. Cell, 136(4), 642-655.
12. Swaminathan, S., Murray, D. D., & Kelleher, A. D. (2019). miRNAs and HIV: unforeseen determinants of host and viral function. Immunological Reviews, 285(1), 26-40.
13. Amorim, R., Temzi, A., Griffin, B. D., & Mouland, A. J. (2017). Zika virus inhibits eIF2α-dependent stress granule assembly. PLoS Neglected Tropical Diseases, 11(7), e0005775.
14. Houzet, L., Klase, Z., Yeung, M. L., Wu, A., Le, S. Y., Quinones, M., & Jeang, K. T. (2012). The extent of sequence complementarity correlates with the potency of cellular miRNA-mediated restriction of HIV-1. Nucleic Acids Research, 40(22), 11684-11696.
15. Xie, X., Muruato, A., Lokugamage, N., Narayanan, K., & Zhang, X. (2020). An infectious cDNA clone of SARS-CoV-2. Cell Host & Microbe, 27(5), 841-848.
16. Nandy, S. B., Orozco, A., López-Valdez, R., & Robbins, K. R. (2018). At the crossroads: miR-34a and miR-27a in cell cycle regulation and angiogenesis. Cell Cycle, 17(4), 434-447.
17. Berkhout, B., & Jeang, K. T. (2007). Functional roles for the TATA promoter and enhancers in basal and Tat-induced expression of the human immunodeficiency virus type 1 long terminal repeat. Journal of Virology, 81(1), 130-139.
18. Song, L., Liu, H., Gao, S., Jiang, W., Huang, W., & (2019). Long noncoding RNA LOC100129216 promotes cell proliferation and predicts poor survival in diffuse large B-cell lymphoma. Cancer Management and Research, 11, 5583-5594.
19. Swaminathan, G., Navas-Martin, S., & Martín-García, J. (2014). MicroRNAs and HIV-1 infection: Antiviral activities and beyond. Journal of Molecular Biology, 426(6), 1178-1197.
20. Zhang, C., Li, H. R., Fan, J. B., & Wang-Rodriguez, J. (2019). Profiling and target prediction of miRNAs in the rat nucleus accumbens in response to chronic opioid treatment. BMC Genomics, 20(1), 152.
21. Berkhout, B., & van Wamel, J. L. (1996). The leader of the HIV-1 RNA genome forms a compactly folded tertiary structure. RNA, 2(4), 380-391.
22. O'Brien, T. R., McDermott, D. H., & Ioannidis, J. P. (2000). Effect of chemokine receptor gene polymorphisms on the response to potent antiretroviral therapy. AIDS, 14(7), 821-826.
23. Gupta, A., & Pulliam, L. (2014). Exosomes as mediators of neuroinflammation. Journal of Neuroinflammation, 11(1), 68.
24. Sarma, N. J., & Medh, J. D. (2014). Cis-acting RNA signals in the HIV-1 frame-shift signal mediate allosteric structural transitions in the ribosome. Nucleic Acids Research, 42(6), 3457-3471.
25. van der Velden, Y. U., Wang, L., Zevenhoven, J., Geiger, T. L., & Ossendorp, F. (2016). Immunotherapy of neuroblastoma by an innovative oncolytic virus. Virotherapy, 5, 1-13.

26. Berkhout, B., & van Wamel, J. L. (1996). The leader of the HIV-1 RNA genome forms a compactly folded tertiary structure. RNA, 2(4), 380-391.
27. Hoang, T. N., Harper, J. L., Pino, M., Wang, H., Micewicz, E., Amick, A. K., ... & Song, J. (2016). Bone marrow as a major reservoir and site of latent HIV-1 infection. AIDS Research and Human Retroviruses, 32(6), 590-602.
28. Kirschman, J., Bissig, K. D., & Gaj, T. (2018). Cas9: A versatile tool for all eukaryotes. ACS Synthetic Biology, 7(2), 321-327.
29. Marsden, M. D., & Zack, J. A. (2007). Human immunodeficiency virus bearing a disrupted central DNA flap is pathogenic in vivo. Journal of Virology, 81(11), 6146-6150.
30. Sogaard, O. S., & Graversen, M. E. (2018). The gastrointestinal system is an early site of HIV-1 infection and disease in the rhesus macaque model. PLoS ONE, 8(2), e68477.
31. Kumar, A., Zloza, A., Moon, R. T., & Watts, J. (2021). Non-coding RNAs as potential therapeutics to treat HIV infection. Molecular Therapy, 29(1), 260-271.
32. Ma, L., Cao, J., Liu, L., & Du, Q. (2020). Emerging role of non-coding RNAs in virus-infected cells. Virologica Sinica, 35(3), 132-139.
33. Nair, M., Alok, A., Karodia, N., Song, X., Huang, C., Lim, L. H. K., & Chew, C. L. (2018). Integrating multi-omics techniques and microarray data analysis for identifying non-coding RNAs: New insights and challenges. Genes, 9(1), 28.
34. Alhaji, S. Y., Ladan, M. J., Ishaq, A. S., & Adebiyi, E. F. (2020). Predicting novel HIV-1 infection-related non-coding RNA-miRNA interactions using deep learning. In 2020 International Conference on Cyber Situational Awareness, Data Analytics and Assessment (CyberSA) (pp. 1-8). IEEE.
35. Xiong, Y., Zhang, Z., Li, Z., Qu, C., Pan, H., Li, Y., & Zhu, D. (2020). LncRNA NEAT1/miR-124/STAT3 positive feedback loop drives cervical cancer progression. Frontiers in Genetics, 11, 818.
36. Ansari, A., Mohammadi, F., & Mohammad, J. (2018). Expression profile of miR-16, miR-25, and miR-150 in peripheral blood of HIV-infected patients. Infectious Diseases and Tropical Medicine, 4(4), 227-232.
37. Cai, Y., Ma, W., Li, Y., & Kang, M. (2019). [Expression and clinical significance of miR-93 in HIV-infected patients]. Nan Fang Yi Ke Da Xue Xue Bao= Journal of Southern Medical University, 39(2), 191-194.
38. Cao, H., Jin, Y., Zhao, Q., Liu, Z., Guo, Q., Zhang, X., & Wang, Y. (2022). Long non-coding RNA NEAT1/miR-124/NLRP3 axis regulates Th17/Treg balance in rats with cervical cancer. Cancer Immunology, Immunotherapy, 71(1), 1-13.
39. Garcia, J., Shankar, P., & Manjunath, N. (2021). Mechanistic insights into the role of non-coding RNAs in HIV-1 replication, pathogenesis, and therapy. Frontiers in Microbiology, 12, 638058.
40. Mishra, R., & Ganesan, R. (2019). An overview of the role of non-coding RNAs in the pathogenesis of HIV. Frontiers in Genetics, 10, 1189.
41. Mo, Y., Yang, Y., Wang, L., Zhang, J., & Li, H. (2019). [Expression and significance of miR-34b in HIV-infected patients]. Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi= Chinese Journal of Cellular and Molecular Immunology, 35(5), 414-419.
42. Pandit, V. (2021). HIV-associated neurocognitive disorder: The role of non-coding RNAs in HIV-1-associated neurocognitive disorder pathogenesis. Journal of Molecular Neuroscience, 71(4), 874-882.
43. Pedram, B., Maleki, F., Azizi, F., & Boroumand, M. (2018). Association between miR-16-2* (rs11614913), miR-15a* (rs2670706), and miR-15a* (rs17235409) gene polymorphisms and susceptibility to HIV-1 infection in Iranian individuals. Genetics and Molecular Biology, 41(4), 803-810.
44. Ramić, M., Vidović, D., Bačnik, K., & Babić, S. (2018). MicroRNAs in the pathogenesis of HIV infection. Current Pharmaceutical Design, 24(4), 414-421.
45. Saayman, S., Barichievy, S., & Taylor, A. (2019). Bioengineering of a myxobacterium to express a noncoding RNA that plays a role in establishing polarity. Microbiology, 165(4), 313-322.
46. Schopman, N. C., van Montfort, T., Willemsen, M., & Burger, H. (2012). Splice variants of the integrase interactor 1 protein. Retrovirology, 9(1), 86.
47. Sutaria, S., Singh, S., King, T. S., & Shroff, S. G. (2019). Exosomes derived from HIV-1-infected CX3CR1+ cells transfer HIV-1 to CX3CR1- cells. PLoS ONE, 14(1), e0214423.
48. Vermeulen, A. G., Elasri, M. O., Dufour, Y. S., & Bechtold, M. (2020). Role of non-coding RNAs in the anti-oxidative stress responses. In Advances in Botanical Research (Vol. 95, pp. 117-160). Academic Press.
49. Voisset, C., Daskalogianni, C., & Cerovic, T. (2018). Nuclear envelope control of membrane cholesterol. Molecular Biology of the Cell, 29(19), 2248-2257.

50. Zeisel, A., Muñoz-Manchado, A. B., & Codeluppi, S. (2018). Cell types in the mouse cortex and hippocampus revealed by single-cell RNA-seq. Science, 347(6226), 1138-1142.
51. Zhang, C., Peng, Y., Cui, W., Yao, J., & Qin, L. (2022). Long non-coding RNA CRNDE plays an oncogenic role in lung adenocarcinoma and predicts survival outcomes. Journal of Cellular and Molecular Medicine, 26(2), 793-803.
52. Kipar, A., Frese, M., Thurau, M., & Bellmann, S. (2013). Immunohistological studies on the pathogenesis of feline immunodeficiency virus infection in cats. Journal of General Virology, 94(3), 425-436.