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Exosomal Micrornas Derived from HIV-infected Macrophages

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Abstract

Exosomes are extracellular vesicles that play crucial roles in intercellular communication by transporting various biomolecules, including microRNAs (miRNAs). In the context of HIV infection, exosomes derived from infected cells, particularly macrophages, have gained attention for their potential role in viral pathogenesis and immune modulation. This review focuses on exosomal microRNAs derived from HIV-infected macrophages, exploring their biogenesis, composition, functional roles in viral persistence and immune evasion and potential as biomarkers or therapeutic targets. Understanding the interplay between exosomal miRNAs and HIV pathogenesis can provide insights into novel strategies for disease management and therapeutic intervention.

Keywords: Exosomes • MicroRNAs • HIV

Introduction

Human Immunodeficiency Virus (HIV) infection remains a global health challenge despite significant advances in Antiretroviral Therapy (ART). Macrophages are important cellular reservoirs for HIV, contributing to viral persistence and immune evasion. Exosomes, small extracellular vesicles released by cells, play critical roles in intercellular communication by transferring bioactive molecules, including microRNAs (miRNAs), between cells. Exosomal miRNAs derived from HIV-infected macrophages have emerged as potential mediators of viral pathogenesis and immune dysregulation. This review aims to comprehensively explore the current understanding of exosomal miRNAs in the context of HIV infection, with a specific focus on macrophage-derived exosomes. It will discuss the biogenesis and composition of exosomes, mechanisms of miRNA packaging into exosomes and the functional roles of exosomal miRNAs in modulating viral replication, immune responses and disease progression. Furthermore, it will highlight the diagnostic and therapeutic implications of exosomal miRNAs as biomarkers or targets for novel therapeutic strategies against HIV [1].

Literature Review

Exosomes are small (30-150 nm) extracellular vesicles of endocytic origin released by various cell types, including macrophages, upon fusion of Multi Vesicular Bodies (MVBs) with the plasma membrane. They carry a cargo of proteins, lipids, RNAs (including miRNAs) and other biomolecules that reflect the physiological state of the donor cell. The composition of exosomes can be influenced by cellular activation, stress, or pathological conditions such as HIV infection. Macrophage-derived exosomes exhibit specific markers such as CD9, CD63, CD81 and TSG101, which are involved in their biogenesis and secretion [2]. These exosomes encapsulate a diverse repertoire of miRNAs, which can regulate gene expression in recipient cells upon internalization. Exosomal miRNAs derived from HIV-infected macrophages play pivotal roles in viral pathogenesis by influencing various aspects of viral replication and immune modulation. Studies have identified specific miRNAs, such as miR-29a, miR-155 and miR-223, enriched in exosomes from HIV-infected macrophages, which can target host factors involved in viral replication or immune responses. Exosomal miRNAs can directly target HIV transcripts or host factors essential for viral replication, thereby inhibiting viral production and spread. For instance, miR-29a has been shown to target HIV Long Terminal Repeat (LTR) sequences, leading to suppression of viral transcription in recipient cells. Exosomal miRNAs can modulate immune responses by targeting immune-related genes in recipient cells, affecting immune cell activation, differentiation and cytokine production. MiR-155, for example, regulates inflammatory responses and T cell activation pathways, influencing the host immune environment during HIV infection [3].

Exosomal miRNAs may contribute to viral persistence by promoting latency establishment or reactivation in infected cells. They can regulate cellular pathways involved in HIV latency maintenance, such as chromatin remodeling and transcriptional regulation. Exosomal miRNAs show promise as diagnostic biomarkers for HIV infection and disease progression. Their presence and specific profiles in circulation or bodily fluids, such as blood plasma or cerebrospinal fluid, may reflect the viral load, immune status and treatment response of HIV-infected individuals [4]. Moreover, exosomal miRNAs could serve as targets for novel therapeutic strategies aimed at disrupting viral replication, modulating immune responses, or reversing HIV latency. Profiling exosomal miRNAs from HIV-infected macrophages and recipient cells could identify signature patterns associated with disease progression, antiretroviral drug resistance, or comorbidities such as neurocognitive impairment (HIV-Associated Neurocognitive Disorders, HAND). Manipulating exosomal miRNA profiles or inhibiting specific miRNAs could offer new avenues for therapeutic intervention. Strategies include using antagomiRs to block miRNA function or exosome engineering to deliver therapeutic miRNAs or antiviral agents to target cells [5].

Discussion

The role of exosomal miRNAs derived from HIV-infected macrophages in viral pathogenesis and immune modulation represents a dynamic area of research with significant implications for HIV biology and clinical management. Understanding the mechanisms by which these miRNAs are packaged into exosomes, their functional effects on recipient cells and their potential as diagnostic markers or therapeutic targets is critical for developing effective strategies to combat HIV infection. The interplay between exosomal miRNAs and viral persistence, immune dysregulation and treatment outcomes underscores their multifaceted roles in HIV pathogenesis. Future research directions should focus on elucidating specific miRNA-mediated pathways involved in viral latency, reservoir establishment and immune

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evasion strategies employed by HIV-infected macrophages. Integration of high-throughput sequencing technologies, bioinformatics analyses and experimental validation will advance our understanding of exosomal miRNA dynamics during HIV infection and inform the development of personalized therapeutic approaches [6].

Conclusion

Exosomal microRNAs derived from HIV-infected macrophages represent key mediators of viral pathogenesis, immune dysregulation and disease progression in HIV infection. Their packaging into exosomes, transport to recipient cells and modulation of gene expression highlight their significance in intercellular communication and viral persistence. Moreover, exosomal miRNAs hold promise as biomarkers for disease diagnosis and progression monitoring, as well as potential targets for therapeutic intervention strategies aimed at disrupting viral replication or modulating immune responses. Continued research efforts are essential to elucidate the complex interactions between exosomal miRNAs and HIV pathogenesis, leveraging this knowledge to develop innovative diagnostic tools and therapeutic strategies. By targeting exosomal miRNAs derived from HIV-infected macrophages, we can advance towards more effective management and eradication of HIV/AIDS, ultimately improving outcomes for affected individuals worldwide.

Acknowledgement

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Conflict of Interest

None.

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