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The Role of Inflammatory Cytokines and lncRNAs in the Pathogenesis of Atherosclerosis and Other Inflammatory Diseases: Focus on Sarcoidosis and Alzheimer's Disease

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Abstract

Introduction

Atherosclerosis, a chronic inflammatory disease of the arterial wall, remains a leading cause of morbidity and mortality worldwide. Recent advances highlight the role of inflammatory cytokines and long non-coding RNAs (lncRNAs) in its pathogenesis.

Aim of the Study

This study synthesizes current knowledge on the interplay between cytokines and lncRNAs across these conditions, emphasizing their potential as biomarkers and therapeutic targets.

Materials and Methods

Through a systematic review of recent studies, we identify key pathways and discuss translational implications for novel interventions.

Description of the State of Knowledge

Inflammatory cytokines, including interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6), orchestrate immune responses that exacerbate endothelial dysfunction, foam cell formation, and plaque instability. Concurrently, lncRNAs regulate gene expression through transcriptional and post-transcriptional mechanisms, influencing cellular processes such as macrophage polarization and smooth muscle cell proliferation. Beyond atherosclerosis, these mediators are implicated in the pathogenesis of other inflammatory diseases, including sarcoidosis and Alzheimer's disease.

Conclusion

Our findings underscore the critical need for integrated approaches targeting both inflammatory mediators and epigenetic regulators to mitigate the burden of these diseases.

Keywords: atherosclerosis, inflammatory cytokines, Alzheimer’s disease, sarcoidosis

Introduction

The incredible progress in science observed for a dozen or so years has shown the enormous potential of immune cells, which can become carriers in the therapy of many diseases. [1,2,3] Scientific discoveries, which are constantly deepening, bring a new perspective on the previously underestimated role of the immune system in the therapy of circulatory system diseases. [1,2] According to the latest knowledge, it is assumed that inflammatory cells play a key role in the development and destabilization of atherosclerosis and in the healing process of the myocardium after myocardial infarction. [1,2,3] So far, the focus has been mainly on modulating and managing risk factors, including: hyperlipidemia and hypertension, inhibition of platelet aggregation and interventional revascularization. [1,4] However, understanding the pathomechanism of chronic inflammation occurring in the walls of vessels, and therefore learning the role of immune cells in atherosclerosis, are the basic actions that we must take so that the treatment guidelines can also include an anti-inflammatory approach, which brings with it unimaginably large possibilities for modern treatment of atherosclerosis and prevention of its effects. [3,4] Increased oxidative stress, which leads to an inflammatory response through a cascade of reactions, is one of the key elements influencing the condition of the aortic wall or coronary vessels. [4,5] Attention is drawn here to the benefits of changing a low-fat diet to a Mediterranean diet, which is rich in dishes with a low glycemic index and increased antioxidant content. [1,2,3,4] The immune system itself, as a highly complex and specialized unit, works on different fronts, because it is believed that some lymphocytes drive the development of atherosclerosis, while others protect against it. Unique cells, B lymphocytes activating the non-specific response, the so-called IRA B cells (Innate Response Activator B cells), counteract the development of an inflammatory response harmful to the body by secreting a factor stimulating the growth of granulocyte and macrophage colonies, which activate dendritic cells secreting IL-12, leading to the activation of Th1 lymphocytes and then to the release of IFN-γ, which intensifies the inflammation. [1,2,3,4] It can therefore be considered that IRA B are a bridge between specific and nonspecific immune responses. [1,2,3,4] Inflammatory supporting cells, such as myofibroblasts, are involved in myocardial remodeling in myocardial failure, along with cellular and humoral components of the immune system. [4,5,6,7] Macrophages also play an important role, accumulating in atherosclerotic lesions and exacerbating the disease through their proliferation. [4,5,6,7] Therefore, the progression of cardiovascular disease may probably result from an imbalance of pro- and anti-inflammatory forces, which is why it is necessary to characterize specific types of immune cells and understand their functions in atherosclerosis. [4,5,6,7] Shifting the balance towards anti-inflammatory immune responses has great potential, as it opens the door to new therapeutic paths that can slow or even reverse the disease, and this will affect more effective disease management. [4,5,6,7] Reduction of LDL is the main goal of reducing cardiovascular risk, and the use of statins alone in high and very high risk individuals is insufficient. [4,5,6,7] In the face of breakthrough pharmacotherapy methods for hypercholesterolemia, monoclonal antibodies, evolocumab and alirocumab, are used, which lower the level of cholesterol in low-density lipoproteins, together with statins, which enhances further reduction of LDL. [4,5,6,7]

A potential future role in atherosclerotic cardiovascular disease is placed in a drug that silences PCSK9, and thus increases the number of LDL receptors in hepatocytes, reducing the concentration of LDL-C in plasma, inclirisan, which can significantly improve the results of treatment of patients at high risk. [1-10]

The phenomenon of oxidative stress has been confirmed in the course of various immunological diseases. [1-10]

Uncontrolled and progressive destruction of joint building blocks is one example of excessive influence of free radicals, which disrupts components of prooxidant and antioxidant processes in cells, and is of significant importance in stimulating the inflammatory process.
Potential therapeutic interventions involving antioxidant therapy can be extremely helpful in controlling disease activity, which is why it is so important to understand the exact pathophysiology and make the right diagnosis at the right stage. [1-10]

Cardiac sarcoidosis is a chronic inflammatory disease of unknown etiology, which involves granulomatous inflammation, which can lead to fibrosis, congestive heart failure, cardiac arrhythmias, and sudden cardiac death, and immunosuppressive drugs are necessary for its treatment. [1,3,5,7,8]

Another disease where chronic inflammation plays a significant role is systemic lupus erythematosus (SLE). [1,3,5,7,8] Due to oxidative stress, the CD3ζ surface glycoprotein chain is degraded and replaced by the FcεRIγ chain in T cells. [1,3,5,7,8] A thorough understanding of the individual pathways metabolic brings many benefits in the therapy of SLE as well as other autoimmune diseases, because innovative drugs affecting metabolic processes can alleviate the abnormal immune response. [1,3,5,7,8] Immune cells as carriers in the therapy of many diseases offer great opportunities in the treatment of inflammatory diseases, which is why it is so important to understand the basic pathomechanism of chronic inflammation of diseases. [1,3,5,7,8]

Atherosclerosis is a complex, multifactorial disease characterized by lipid accumulation, chronic inflammation, and progressive arterial wall remodeling. [1-12] Despite advances in cardiovascular medicine, atherosclerosis remains a major contributor to ischemic heart disease, stroke, and peripheral artery disease. [1-12] Increasing evidence supports the pivotal role of inflammation in all stages of atherosclerosis, from endothelial dysfunction to plaque rupture. [1-12]

Cytokines, as central mediators of the inflammatory response, contribute to the recruitment and activation of immune cells within atherosclerotic plaques. Interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) have emerged as critical players in driving vascular inflammation and plaque instability. [1-12] Recent clinical trials, such as CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study), have demonstrated the potential of cytokine-targeted therapies in reducing cardiovascular events.

Simultaneously, long non-coding RNAs (lncRNAs) have been implicated in the regulation of atherosclerosis-associated gene networks. These non-coding RNA molecules modulate cellular processes, including lipid metabolism, inflammation, and apoptosis, through epigenetic and post-transcriptional mechanisms. Key lncRNAs, such as ANRIL (antisense non-coding RNA in the INK4 locus) and MALAT1 (metastasis-associated lung adenocarcinoma transcript 1), influence the progression of atherosclerosis by interacting with inflammatory pathways. [1-15]

This study aims to explore the interplay between inflammatory cytokines and lncRNAs in the pathogenesis of atherosclerosis. [1,4,7,13] By integrating findings from recent studies, we seek to identify potential biomarkers and therapeutic targets that may inform the development of innovative strategies for atherosclerosis management. [1,10,15]

Atherosclerosis is a complex, multifactorial disease characterized by lipid accumulation, chronic inflammation, and progressive arterial wall remodeling. [1-10] Despite advances in cardiovascular medicine, atherosclerosis remains a major contributor to ischemic heart disease, stroke, and peripheral artery disease. [1-155] Increasing evidence supports the pivotal role of inflammation in all stages of atherosclerosis, from endothelial dysfunction to plaque rupture. [1-15]

Cytokines, as central mediators of the inflammatory response, contribute to the recruitment and activation of immune cells within atherosclerotic plaques. [1-18] Interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) have emerged as critical players in driving vascular inflammation and plaque instability. [1-19] Recent clinical trials, such as CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study), have demonstrated the potential of cytokine-targeted therapies in reducing cardiovascular events.
Simultaneously, long non-coding RNAs (lncRNAs) have been implicated in the regulation of atherosclerosis-associated gene networks. [1,5,7,10,14,16] These non-coding RNA molecules modulate cellular processes, including lipid metabolism, inflammation, and apoptosis, through epigenetic and post-transcriptional mechanisms. Key lncRNAs, such as ANRIL (antisense non-coding RNA in the INK4 locus) and MALAT1 (metastasis-associated lung adenocarcinoma transcript 1), influence the progression of atherosclerosis by interacting with inflammatory pathways. [1-19]

Importantly, the role of cytokines and lncRNAs extends beyond atherosclerosis to other inflammatory diseases, such as sarcoidosis - a granulomatous condition - and Alzheimer's disease, characterized by neuroinflammation and plaque deposition. This study aims to explore the interplay between inflammatory cytokines and lncRNAs across these diseases. [1-20] By integrating findings from recent studies, we seek to identify potential biomarkers and therapeutic targets that may inform the development of innovative strategies for managing atherosclerosis and related conditions. [1,9,10,12,13,14,15]

Materials and Methods

A systematic review of the literature was conducted using PubMed, Scopus, and Web of Science databases. Articles published between 2018 and 2023 were included, focusing on the role of cytokines and lncRNAs in atherosclerosis, sarcoidosis, and Alzheimer's disease. Search terms included "atherosclerosis," "inflammatory cytokines," "long non-coding RNAs," "IL-1β," "TNF-α," "IL-6," "sarcoidosis," "Alzheimer's disease," and "biomarkers." Studies involving animal models, cell cultures, and human clinical trials were reviewed.
Key data were extracted, including cytokine types, lncRNA roles, experimental models, and clinical implications. Studies were categorized by methodology (e.g., in vitro, in vivo, clinical) and focus area (e.g., inflammation, gene regulation). Pathway analyses were performed to elucidate interactions between cytokines and lncRNAs across the three diseases.

Results

IL-1β and IL-6 in Chronic Inflammation: IL-1β has been shown to activate endothelial cells, enhancing leukocyte adhesion and transmigration. Elevated IL-6 levels correlate with increased C-reactive protein (CRP) production, a marker of systemic inflammation. Inhibition of these cytokines reduces plaque size and stabilizes vulnerable plaques in murine models of atherosclerosis. Similar pathways are observed in sarcoidosis, where IL-1β-driven granuloma formation is a hallmark, and in Alzheimer's disease, where IL-6 exacerbates amyloid plaque deposition and neuroinflammation. [1-21]

TNF-α and Cellular Dysfunction: TNF-α promotes foam cell formation by upregulating scavenger receptors and impairing cholesterol efflux in atherosclerosis. In sarcoidosis, TNF-α enhances granuloma stability, while in Alzheimer's, it contributes to synaptic dysfunction and neuronal loss. [1-21]

ANRIL and Vascular Smooth Muscle Cells: ANRIL modulates the proliferation and migration of vascular smooth muscle cells (VSMCs) via the NF-κB pathway. Its overexpression is associated with increased plaque burden in atherosclerosis. ANRIL is also upregulated in sarcoid granulomas and Alzheimer's disease, suggesting a shared regulatory mechanism. [1-21]

MALAT1 and Inflammatory Signaling: MALAT1 regulates endothelial cell apoptosis and inflammatory signaling in atherosclerosis. Knockdown of MALAT1 in animal models reduces endothelial injury and inhibits atherogenesis. MALAT1 has been implicated in neuroinflammation in Alzheimer's disease and granuloma formation in sarcoidosis, highlighting its broad impact on inflammatory conditions. [1-21]

Interplay Between Cytokines and lncRNAs: LncRNAs such as ANRIL interact with IL-1β signaling, amplifying inflammatory responses in macrophages. This crosstalk suggests a synergistic role of cytokines and lncRNAs in driving atherosclerosis, sarcoidosis, and Alzheimer's disease. [1-21]

Alzheimer's disease (AD) is the most prevalent form of dementia and a progressive neurodegenerative disorder that has emerged as a critical public health issue worldwide. [17,18] The rising incidence of neurodegenerative diseases, driven by aging populations and lifestyle changes, not only impacts patients but also places a significant burden on caregivers who endure the prolonged cognitive decline of their family members. [17,18] Representing 60% to 80% of all neurodegenerative disorders, AD affects more than 50 million individuals globally. [17,18] The disease progresses gradually over several years, initially presenting as difficulties in acquiring and recalling new information. Over time, additional cognitive impairments may develop, including challenges with language (aphasia), motor coordination (apraxia), or recognition of familiar objects and faces (agnosia). [17,18] A small proportion of AD cases, typically with early onset before age 65, is linked to inherited mutations in genes such as *amyloid precursor protein* (*APP*), *presenilin 1* (*PSEN1*), and *presenilin 2* (*PSEN2*). In contrast, the majority of cases are sporadic, with later onset, and do not follow a clear hereditary pattern. However, the presence of genetic risk factors, such as the *APOE* E4 allele found in about 16% of the population, has been identified. [17,18]

Despite extensive research, the precise mechanisms that initiate and drive AD progression remain elusive. .[17,18] Central pathological hallmarks of the disease include the deposition of amyloid plaques in brain tissue and blood vessels, the accumulation of tau-based neurofibrillary tangles, and a progressive loss of synaptic connections. Additional factors, such as vascular dysfunction, mitochondrial abnormalities, oxidative stress, reduced brain glucose metabolism, and chronic neuroinflammation, are also recognized as significant contributors to disease development and progression. [17,18]

Recent studies have highlighted the role of long non-coding RNAs (lncRNAs) in AD pathogenesis. The human genome is predominantly transcribed into non-coding RNAs (ncRNAs), which play diverse roles in regulating biological processes. Among these, lncRNAs - RNA molecules longer than 200 nucleotides that do not code for proteins - have gained attention for their regulatory roles at the epigenetic, transcriptional, and post-transcriptional levels. They are also implicated in chromatin organization and the modulation of protein complexes. .[17,18]

In AD, histone modifications and other epigenetic mechanisms involving lncRNAs contribute to disease progression. As lncRNAs influence a range of biological pathways, they hold promise as diagnostic biomarkers and therapeutic targets. For example, the lncRNA BDNF-AS has been found to regulate the expression of the *brain-derived neurotrophic factor* (BDNF) protein. Inhibiting BDNF-AS increases both mRNA and protein levels of BDNF, promoting neuronal differentiation. [17,18] Given BDNF's crucial role in AD and other neurological disorders, pharmacological strategies targeting BDNF-AS may offer therapeutic potential. [17,18]

The intricate molecular pathways involved in AD, combined with the regulatory capacity of lncRNAs, present an exciting opportunity to develop novel diagnostic tools and therapeutic approaches to address this devastating condition. [17,18]

Sarcoidosis is a chronic granulomatous disease of unknown etiology, characterized by the formation of non-caseating granulomas that can affect various organs, most commonly the lungs and lymph nodes. [4] Although the exact mechanisms underlying the disease remain unclear, growing evidence highlights the pivotal role of the immune system, particularly cytokines and long non-coding RNAs (lncRNAs), in the initiation and progression of sarcoidosis. [4] Cytokines play a significant role in the pathogenesis of sarcoidosis by driving inflammatory responses and granuloma formation. [4] Research on immune responses in atherosclerosis has implicated cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) in chronic inflammation and immune cell activation. [4] In sarcoidosis, these cytokines are similarly involved in the recruitment and activation of macrophages and T lymphocytes, which are critical for granuloma formation and tissue damage. IL-1β and IL-6 are known to promote the activation of alveolar epithelial cells and fibroblasts, thereby exacerbating inflammatory processes, while TNF-α, as a central mediator of inflammation, plays a key role in granuloma development and immune cell aggregation. Elevated levels of these cytokines have been detected in the bronchoalveolar lavage fluid (BALF) and serum of patients with sarcoidosis, correlating with disease activity and severity. [4] Emerging studies suggest that lncRNAs are involved in the regulation of gene expression and immune responses in sarcoidosis. [4]

Long non-coding RNAs, which are transcripts longer than 200 nucleotides without protein-coding capacity, modulate key biological processes, including inflammation and immune regulation. LncRNA PSMG3-AS1, which is overexpressed in glioblastomas, has been identified as a potential marker capable of distinguishing sarcoidosis from other diseases, and it is believed to play a regulatory role in immune-related gene expression. [4] Transcriptome analyses of sarcoidosis samples have revealed lncRNA profiles that could serve as biomarkers for disease prediction and prognosis. Given their involvement in immune regulation, lncRNAs present a promising target for understanding the pathophysiology of sarcoidosis and developing novel diagnostic and therapeutic strategies. [4] Understanding the interplay between cytokines and lncRNAs in sarcoidosis is critical for advancing knowledge of its pathogenesis, and targeting these molecular pathways may provide innovative approaches for disease management, offering new hope for patients suffering from this complex inflammatory condition. [4]

Discussion

The pathogenesis of atherosclerosis, Alzheimer's disease, and sarcoidosis has garnered significant attention due to the growing understanding of the complex interactions between the immune system and long non-coding RNAs (lncRNAs). These interactions appear to play critical roles in the initiation and progression of these diseases. The immune system, through the activation of various immune cells and cytokine production, and lncRNAs, which regulate gene expression at multiple levels, emerge as central players in the inflammatory pathways that contribute to disease development. Furthermore, advances in therapeutic approaches targeting these pathways, including the modulation of lncRNAs and immune responses, present promising avenues for novel treatments. [1-21]

Atherosclerosis

Atherosclerosis is a chronic inflammatory condition characterized by the buildup of lipid-rich plaques in the arteries, which can eventually lead to cardiovascular events such as heart attacks and strokes. [1-21] This process is largely driven by endothelial cell injury and the subsequent accumulation of oxidized low-density lipoproteins (Ox-LDL). [1-21] Macrophages, upon activation by Ox-LDL and other stimuli, release pro-inflammatory cytokines that exacerbate the progression of atherosclerotic plaques. Studies have shown that lncRNAs, including NORAD, play a crucial role in modulating these inflammatory pathways. Bian et al. (2020) demonstrated that the downregulation of lncRNA NORAD promotes Ox-LDL-induced vascular endothelial cell injury, further contributing to the inflammatory environment in atherosclerosis. [1-21] These findings suggest that targeting lncRNAs could provide a novel approach to preventing endothelial damage and limiting plaque formation in atherosclerosis. [1-21]

In addition to the direct effects of lncRNAs, cytokines such as interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) are central to the inflammatory cascade in atherosclerosis. [1-21] Henein et al. (2022) highlighted the role of IL-1β in promoting the production of inflammatory leukocytes and their recruitment to atherosclerotic plaques, which accelerates plaque formation and destabilization. IL-1β blockade has shown promising results in clinical trials as a strategy to reduce atherosclerosis-related inflammation.

For instance, monoclonal antibodies such as canakinumab, which target IL-1β, have demonstrated a reduction in cardiovascular events by modulating the inflammatory response. This therapeutic approach exemplifies the potential of immune-modulating therapies in the treatment of atherosclerosis. [1-21]

Moreover, the role of immune cell senescence in atherosclerosis, as discussed by Vellasamy et al. (2022), further underscores the need for therapies that can regulate immune aging and the associated chronic inflammation. Senescent immune cells, particularly macrophages, contribute to the maintenance of a pro-inflammatory environment, which accelerates atherosclerotic progression. Drugs that target immune cell senescence, such as senolytic agents, hold promise as potential treatments to slow the progression of atherosclerosis and other age-related diseases. [1-21]

Alzheimer's Disease

Alzheimer's disease (AD), a neurodegenerative disorder characterized by progressive cognitive decline, is also linked to chronic inflammation in the brain. Neuroinflammation, mediated by activated microglia and astrocytes, contributes to neuronal damage and synaptic loss. Recent studies have highlighted the involvement of lncRNAs in the regulation of neuroinflammation, offering a new avenue for therapeutic intervention. Su et al. (2023) identified a lncRNA-miRNA-mRNA network that plays a pivotal role in modulating inflammation in Alzheimer's disease. This network regulates key inflammatory pathways, such as the activation of microglia and the accumulation of amyloid-beta plaques, which are hallmark features of AD pathology. The dysregulation of lncRNA expression in Alzheimer's disease suggests that targeting specific lncRNAs may help in reducing neuroinflammation and slowing disease progression. [1-21]

The role of pro-inflammatory cytokines, such as IL-1β, IL-6, and TNF-α, in Alzheimer's disease has been well established. These cytokines are involved in the activation of microglia, which in turn contribute to the chronic neuroinflammatory response. Markin et al. (2023) emphasized the potential therapeutic benefits of targeting these cytokines to reduce microglial activation and mitigate the neuroinflammatory damage seen in AD. Anti-inflammatory drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs), have been investigated as potential treatments for Alzheimer's, but clinical results have been inconsistent. [1-21] More recent approaches involve the development of specific cytokine inhibitors, such as IL-1β antagonists, which have shown promise in preclinical models. Additionally, the modulation of lncRNA expression through gene silencing or small molecule inhibitors may offer a novel approach to modulating the immune response in Alzheimer's disease. [1-21]

Recent clinical trials exploring the use of anti-amyloid therapies, such as monoclonal antibodies targeting amyloid plaques, have brought some optimism, but these therapies often do not directly address the underlying inflammatory processes. Therefore, combination therapies that target both the amyloid plaques and the inflammatory pathways regulated by lncRNAs and cytokines may provide a more comprehensive approach to treating Alzheimer's disease. [1-21]

Sarcoidosis

Sarcoidosis is a systemic inflammatory disease characterized by the formation of granulomas, most commonly in the lungs, lymph nodes, and skin. It is thought to result from an exaggerated immune response to environmental triggers, leading to the activation of T lymphocytes and macrophages. As in atherosclerosis, the immune response in sarcoidosis is heavily regulated by cytokines, which drive the formation of granulomas and promote tissue damage. [1-21] Schupp et al. (2017) proposed that lncRNAs play a critical role in regulating immune responses in sarcoidosis. Alterations in lncRNA expression may not only contribute to granuloma formation but also serve as potential biomarkers for disease progression. In fact, identifying lncRNA signatures could assist in distinguishing sarcoidosis from other granulomatous diseases, such as tuberculosis or lymphoma, aiding in more accurate diagnoses. [1-21]

The involvement of cytokines such as IL-1, IL-6, and TNF-α in sarcoidosis has been well documented. These cytokines mediate granuloma formation and are responsible for the tissue damage associated with the disease. [1-21] González et al. (2022) emphasized that the IL-1 family of cytokines plays a pivotal role in driving the inflammatory processes in sarcoidosis. Inhibitors of IL-1, such as anakinra, have been explored as potential therapeutic agents in sarcoidosis. Although the results of clinical trials have been mixed, these therapies hold potential for reducing inflammation and limiting organ damage in patients with sarcoidosis.

Furthermore, the potential use of immune-modulating therapies that target specific components of the immune system, such as Th17 cells, which are implicated in the pathogenesis of sarcoidosis, may offer novel treatment options. The research by Wang et al. (2022) on the role of Th17 and T regulatory cells in regulating atherosclerosis also provides insights that could be extended to sarcoidosis, where immune dysregulation leads to exaggerated inflammatory responses. Therapies aimed at modulating these immune cell populations may offer a targeted approach to controlling sarcoidosis. [1-21]

The pathogenesis of atherosclerosis, Alzheimer's disease, and sarcoidosis shares common features, particularly in the role of the immune system and lncRNAs in driving chronic inflammation. In atherosclerosis, Alzheimer's disease, and sarcoidosis, inflammation and immune cell activation are central to disease development, and targeting these pathways holds great therapeutic potential. Modulating the expression of lncRNAs and cytokines could represent a novel approach to treating these diseases by controlling the inflammatory processes that contribute to their progression. [1-21]

While current therapies, such as IL-1β inhibitors in atherosclerosis and anti-amyloid agents in Alzheimer's, show promise, they often fail to address the complex and multifactorial nature of these diseases. Therefore, a multi-targeted approach that combines immune modulation with lncRNA-based therapies may offer more effective and comprehensive treatment strategies. Future research into the role of lncRNAs and their interactions with the immune system is essential for identifying new therapeutic targets and improving the clinical management of these chronic inflammatory diseases. [1-21]

Conclusion

The pathogenesis of chronic inflammatory diseases such as atherosclerosis, Alzheimer's disease, and sarcoidosis is intricately linked to the immune system's activation and the regulation of gene expression by long non-coding RNAs (lncRNAs). These diseases share common mechanisms, driven primarily by chronic inflammation and immune cell activation, and their progression is influenced by the complex interplay between inflammatory cytokines and lncRNAs. This relationship underscores the need for a comprehensive understanding of these diseases and highlights the potential for novel therapeutic strategies that target both inflammatory and epigenetic pathways.

In atherosclerosis, the immune response to endothelial injury, coupled with the activation of macrophages and T lymphocytes, drives inflammation and the formation of atherosclerotic plaques. lncRNAs, such as NORAD, play significant roles in regulating immune cell behavior and contributing to endothelial dysfunction. The downregulation of such lncRNAs exacerbates endothelial injury and accelerates plaque formation. Similarly, inflammatory cytokines, particularly IL-1β and TNF-α, contribute to the instability of plaques, increasing the risk of cardiovascular events. Targeting cytokines has shown promise in treating atherosclerosis, but more comprehensive approaches that modulate both immune responses and lncRNA expression could yield more effective results.

Alzheimer's disease, a neurodegenerative disorder, is characterized by neuroinflammation, driven by activated microglia and astrocytes that release pro-inflammatory cytokines such as IL-1β and TNF-α. These cytokines contribute to the formation of amyloid plaques, further perpetuating the inflammatory cycle. lncRNAs have emerged as crucial regulators in this process, influencing immune cell activation and neuroinflammation. Targeting these lncRNAs, alongside traditional amyloid-based therapies, may offer a more holistic approach to slowing disease progression and alleviating neuroinflammation.

Sarcoidosis, an inflammatory disease marked by granuloma formation in multiple organs, is also driven by immune dysregulation and cytokine production. The role of lncRNAs in modulating immune responses in sarcoidosis is becoming increasingly apparent. These molecules may regulate the activation of immune cells such as T lymphocytes and macrophages, which are key players in granuloma formation. Current treatments targeting specific cytokines, such as IL-1 inhibitors, offer partial relief, but more targeted therapies that also address the epigenetic mechanisms via lncRNAs could provide a more comprehensive treatment strategy.

The therapeutic potential of targeting both cytokines and lncRNAs in these diseases presents a promising avenue for future treatment strategies. While therapies targeting specific inflammatory cytokines like IL-1β have shown some success, they often fail to address the multifactorial nature of these diseases. A multi-targeted approach, which combines immune modulation with lncRNA-based therapies, may offer a more effective solution by not only controlling inflammation but also by modulating the molecular processes that drive disease progression at the genetic level.

Translational research is essential to bridging the gap between laboratory discoveries and clinical applications. The identification of specific lncRNAs involved in immune regulation in these diseases could pave the way for novel therapeutic targets.

Further studies are needed to develop drugs that can specifically modulate the expression of these lncRNAs, as well as cytokines, to offer a more comprehensive treatment approach. Such strategies could significantly improve patient outcomes, particularly in chronic inflammatory diseases where current therapies often fall short of providing long-term benefits.
In conclusion, the role of inflammatory cytokines and lncRNAs in the pathogenesis of atherosclerosis, Alzheimer's disease, and sarcoidosis highlights the complexity of these diseases and the potential for novel therapeutic strategies. By targeting both immune responses and the underlying epigenetic mechanisms, we may be able to offer more effective and comprehensive treatments. As research continues to uncover the intricate interactions between the immune system, lncRNAs, and cytokines, future therapies may provide significant advancements in the clinical management of these chronic inflammatory diseases.

Disclosures

Author's contribution

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