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Original Article

The Role of Clusterin (CLU) in the Pathogenesis of Benign Prostatic Hyperplasia: Mechanisms and Potential as a Biomarker

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ABSTRACT
Background: Benign Prostatic Hyperplasia (BPH) is a common urological condition characterized by excessive proliferation of prostate epithelial and stromal cells, leading to lower urinary tract symptoms. Clusterin (CLU), a multifunctional glycoprotein, has been implicated in various cellular processes, including apoptosis regulation, inflammation, and autophagy. However, its exact role in BPH pathogenesis remains unclear.
Objective: This study aims to analyze the role of CLU in the molecular mechanisms underlying BPH and evaluate its potential as a biomarker for disease progression.
Method: A comprehensive analysis of recent literature was conducted to examine CLU expression in BPH tissues and its interactions with inflammatory pathways, hormonal regulation, and cellular homeostasis mechanisms such as apoptosis and autophagy. The study also reviewed CLU's involvement in epithelial-stromal interactions and its correlation with disease severity.
Results: Increased CLU expression in hyperplastic prostate tissues is associated with chronic inflammation, contributing to aberrant cell proliferation and apoptosis resistance. CLU interacts with inflammatory markers such as TNF-α and IL-6, promoting a microenvironment conducive to disease progression. Additionally, CLU is involved in autophagy dysregulation, which may further sustain cellular survival and resistance to apoptosis. Evidence suggests that hormonal factors, particularly androgens and estrogens, regulate CLU expression, linking it to prostate tissue remodeling. These findings highlight CLU as a potential biomarker for assessing BPH severity and progression.
Conclusion: CLU plays a critical role in BPH pathogenesis by modulating inflammatory responses, apoptosis, and cellular homeostasis. Its increased expression in hyperplastic prostate tissues suggests that it may serve as a novel biomarker for disease progression. However, further studies are needed to validate its clinical applicability and explore targeted therapies aimed at CLU modulation to improve BPH management.

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BACKGROUND

Benign Prostatic Hyperplasia (BPH) is a common condition in aging men, characterized by prostate enlargement that leads to lower urinary tract symptoms (LUTS). The prevalence of BPH increases with age and is one of the leading causes of reduced quality of life in men over 50 years old [1].

The pathophysiological mechanisms of BPH involve multiple factors, including hormonal changes, chronic inflammation, and dysregulation of growth factors. Recent studies have highlighted the critical role of the stromal microenvironment in BPH progression, with altered expression of various proteins that regulate apoptosis and prostate cell proliferation [2].

Clusterin (CLU) is a molecular chaperone protein involved in apoptosis, proteostasis, and cellular stress responses. Increased CLU expression has been observed in various pathological conditions, including prostate cancer and neurodegenerative diseases [3]. Recent studies indicate that CLU expression is also elevated in hyperplastic prostate tissue, particularly in patients with more severe LUTS [4].

Transcriptomic analyses of BPH tissues have revealed that cellular stress signaling pathways and apoptosis regulation are significantly influenced by CLU expression. This suggests that CLU may serve as a potential biomarker for assessing BPH progression [5]. Furthermore, experimental studies demonstrate that modulation of CLU expression affects stromal prostate cell proliferation, implicating its potential role in the development of molecular-targeted therapies for BPH [6].

Proteomic studies have also identified a strong association between CLU and growth factors involved in prostate tissue remodeling in BPH. This interaction presents a promising therapeutic target, particularly for patients who do not respond to conventional pharmacological treatments [7].

With the advancement of biomarker-based diagnostic technologies, further exploration of CLU's role in BPH is crucial. Additional research is needed to elucidate how CLU expression can be utilized as a predictor of disease progression and a potential therapeutic target in BPH management [8].

METHOD

This study employs a literature-based approach using secondary data to analyze the relationship between Clusterin (CLU) expression and the progression of Benign Prostatic Hyperplasia (BPH). The data utilized in this study are derived from scientific publications, biomolecular databases, and proteomic studies related to BPH.

The data sources for this study were obtained from international journals published between 2015 and 2025. The primary databases used include PubMed, ScienceDirect, Scopus, Web of Science, and Google Scholar. The keywords used in the literature search include "Clusterin AND Benign Prostatic Hyperplasia," "CLU expression AND BPH," "Molecular markers AND BPH progression," and "Proteomic analysis AND BPH."

This study includes only research that examines CLU expression in prostate tissue from patients with BPH and utilizes biomolecular analysis methods such as immunohistochemistry, PCR, or proteomics. Studies published in peer-reviewed journals in English or Indonesian within the specified timeframe are included in the analysis. Studies that focus solely on prostate cancer without addressing BPH, use animal or cell models without validation in human tissues, or are in the form of review articles, editorials, and case reports without quantitative analysis are excluded.

Data analysis is conducted using a descriptive-qualitative approach to identify CLU expression patterns in BPH prostate tissue and their correlation with disease progression and clinical symptoms. The findings are compared based on the analytical methods used to determine the extent to which CLU expression can serve as a potential biomarker for BPH assessment.

This study has limitations, as it does not involve direct experimental validation, making the reliability of the results dependent on the quality and methodology of the analyzed studies. Additionally, variations in CLU analysis methods across different studies may introduce heterogeneity in data interpretation.

RESULT

The expression of Clusterin (CLU) has been linked to the progression of Benign Prostatic Hyperplasia (BPH), particularly in regulating cellular proliferation and apoptosis. Studies indicate that CLU plays a role in cellular protective mechanisms, allowing prostate cells to withstand oxidative stress and apoptosis [3]. Elevated

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CLU expression has been observed in prostate tissues of patients with more severe BPH, suggesting a correlation between CLU levels and disease progression [4].

Further proteomic analysis has identified CLU's involvement in interactions between epithelial and stromal prostate cells, contributing to increased cellular proliferation under hyperplastic conditions [5]. Studies have shown that heightened CLU expression in hyperplastic prostate tissue is also associated with resistance to apoptosis induced by hormonal changes and other environmental factors [6].

A transcriptomic-based study found that CLU is involved in signaling pathways regulating cell proliferation and differentiation within prostate tissue, potentially contributing to the excessive growth observed in BPH patients [7]. Additional research suggests that CLU expression may serve as a potential biomarker for assessing BPH severity and predicting disease progression [8].

Recent studies have also revealed that CLU interacts with various inflammatory factors involved in BPH pathogenesis. Researchers have found that CLU expression increases alongside elevated levels of proinflammatory cytokines such as TNF-α and IL-6 in hyperplastic prostate tissue [9]. Furthermore, CLU's role in prostate cell homeostasis has become clearer with the discovery of its association with autophagy pathways in hyperplastic prostate tissue [10].

Although multiple studies have confirmed CLU's role in BPH pathogenesis, several challenges remain in its clinical application. Variability in CLU expression measurement techniques and differences in patient characteristics may impact research consistency. Therefore, further studies with more standardized methodologies are required to validate CLU as a biomarker or therapeutic target in BPH [11,12].

DISCUSSION

The study results indicate that Clusterin (CLU) expression plays a crucial role in regulating cellular proliferation and apoptosis in hyperplastic prostate tissue. Increased CLU expression is associated with the progression of Benign Prostatic Hyperplasia (BPH), primarily through interactions with inflammatory factors and cellular signaling pathways [3,4]. Several studies have revealed that CLU can act as a cytoprotective protein, helping prostate cells survive oxidative stress conditions, which frequently occur during hyperplasia [5,6].

In the context of BPH, chronic inflammatory processes play a significant role in inducing structural and functional changes in prostate tissue. High CLU expression has been observed in prostate tissue with significant inflammatory infiltration, suggesting that this protein may be involved in regulating the local immune response [7,9]. Additionally, studies have highlighted the relationship between CLU and proinflammatory cytokines such as TNF-α and IL-6, which are known to trigger prostate cell proliferation and contribute to more severe urinary obstruction in BPH patients [10,11].

Beyond its role in inflammation regulation, CLU has also been found to interact with autophagy pathways in hyperplastic prostate tissue. Autophagy is a crucial cellular process for maintaining homeostatic balance, and dysfunction in this mechanism may lead to uncontrolled cell growth. Recent studies have shown that increased CLU expression in hyperplastic prostate tissue is associated with alterations in autophagy activity, potentially contributing to resistance against natural apoptotic mechanisms [12,14].

Furthermore, CLU expression in prostate tissue is linked to epithelial and stromal cell differentiation and proliferation. Proteomic and transcriptomic studies have identified CLU's role in mediating communication between these cells, ultimately contributing to increased prostate tissue volume in BPH [6,8,13]. Molecular analyses suggest that CLU expression may be influenced by hormonal changes, particularly androgens and estrogens, which are key players in BPH development [5,9].

Although various studies have confirmed CLU's involvement in BPH pathogenesis, challenges remain in translating these findings into clinical practice. Variability in CLU expression measurement methods and differences in patient characteristics may affect study outcomes. Therefore, further research with more standardized approaches is necessary to validate CLU's potential as a biomarker or therapeutic target in BPH [13,15].

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CONCLUSION

Clusterin (CLU) plays a crucial role in the development of Benign Prostatic Hyperplasia (BPH) through mechanisms involving inflammation regulation, cellular proliferation, and resistance to apoptosis. Increased CLU expression in hyperplastic prostate tissue suggests that this protein may serve as a potential biomarker for assessing disease progression. Additionally, CLU's involvement in autophagy pathways highlights its role in cellular homeostasis, presenting a novel therapeutic target to slow BPH progression.

Although scientific evidence strongly supports the association between CLU and BPH pathogenesis, further research is needed to clarify the molecular mechanisms underlying CLU's interaction with inflammatory and hormonal factors. Standardizing methods for measuring CLU expression in prostate tissue is also essential to enhance its validity as a clinical biomarker. A deeper understanding of CLU's role could pave the way for more targeted and effective therapies for BPH, ultimately improving clinical outcomes for patients.

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