Research on the Association Between Mucin 5B (MUC5B) Gene and Decline in Pulmonary Function in COPD

Ying Zhu[1], Ninghui Mu[1]

[1]Department of General Practice, The First People's Hospital of Yunnan Province, PR China, Affiliated Hospital of Kunming University of Science and Technology, The First People's Hospital of Yunnan Province, PR China

E-mail addresses: 2632614549@qq.com (Ying Zhu)

330143127@qq.com（NingHui Mu）

Abstract

Mucin 5B (MUC5B) is a major mucin secreted by airway epithelial cells, involved in the production and regulation of airway mucus. Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disease characterized by airflow limitation and gradual decline in lung function. In recent years, polymorphisms in the MUC5B gene have been closely associated with the decline in lung function in COPD, suggesting that this gene may play a significant role in the pathogenesis of COPD. This paper reviews the research on the association between the MUC5B gene and the decline in lung function in COPD, exploring the expression of MUC5B and its impact on lung function in COPD patients.

Keywords

Mucin 5B, MUC5B, Chronic Obstructive Pulmonary Disease, COPD, lung function decline, gene polymorphism

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common chronic respiratory disease affecting millions of patients worldwide. The main pathological features of COPD include airway inflammation, airway remodeling, and alveolar destruction, which lead to airflow limitation and a gradual decline in lung function. While smoking is the primary etiological factor for COPD, the role of genetic factors in disease progression is increasingly recognized. Mucin 5B (MUC5B) is a mucin protein secreted by airway epithelial cells, playing a role in maintaining airway defense mechanisms. Recent studies on the

association between MUC5B gene variants and lung function decline in COPD suggest that this gene may be a crucial factor influencing lung function in COPD patients.

2. Biological Functions of the MUC5B Gene

MUC5B is one of the main mucins secreted by airway epithelial cells, responsible for maintaining the viscosity and stability of the mucus layer on the airway surface. This protein plays a key role in trapping inhaled particles and microorganisms, promoting mucociliary clearance. The MUC5B gene is located on chromosome 11, and its expression regulation is closely related to mucus production in the airways. Overexpression or genetic variation of MUC5B may lead to abnormal mucus secretion, affecting airway patency and lung function.

3. MUC5B Gene Polymorphisms and COPD Lung Function Decline

Certain single nucleotide polymorphisms (SNPs) in the MUC5B gene are closely associated with a rapid decline in lung function in COPD patients. Studies have shown that specific variants in the MUC5B gene may lead to abnormal mucus secretion, causing airway narrowing, obstructing airflow, and accelerating the deterioration of lung function in COPD patients.

3.1 rs35705950 Polymorphism

The rs35705950 polymorphism in the MUC5B gene has been confirmed to be associated with various lung diseases. In COPD patients, individuals carrying this variant are more prone to increased airway secretions and lung function decline. Research suggests that the rs35705950 variant may increase MUC5B expression, leading to reduced mucus clearance efficiency and exacerbating airway obstruction.

3.2 MUC5B Overexpression and Airway Inflammation

In addition to genetic variations, overexpression of the MUC5B gene is also thought to be associated with airway inflammation and lung function decline in COPD patients. Elevated levels of MUC5B expression may lead to increased mucus secretion, with mucus accumulation triggering chronic inflammation, further damaging lung function. Additionally, excessive mucus secretion may lead to bacterial colonization in the airways, increasing the risk of infection and exacerbating disease progression.

4. Pathological Mechanisms of MUC5B in COPD

The role of MUC5B in the decline in lung function in COPD may involve the following mechanisms:

4.1 Impaired Mucociliary Clearance

Overexpression and secretion of MUC5B result in a thickened mucus layer, affecting the effectiveness of ciliary movement and reducing mucociliary clearance capability. This impairment makes it difficult for COPD patients to efficiently clear foreign bodies and pathogens from the airways, leading to increased airway obstruction and infection risk, thereby accelerating the decline in lung function.

4.2 Increased Airway Mucus Viscosity

High MUC5B expression not only increases the amount of mucus but may also alter the viscosity and rheological properties of mucus. This highly viscous mucus is harder to clear by ciliary action, tends to stay in the airways, forming mucus plugs, further aggravating airflow limitation and accelerating COPD's pathological progression.

4.3 Pro-inflammatory Response

Excessive secretion of MUC5B may also enhance airway inflammatory responses by inducing the expression of pro-inflammatory factors. The persistent inflammatory state not only directly damages airway epithelium but also accelerates airway remodeling and fibrosis, leading to irreversible loss of lung function.

5. Potential of MUC5B as a Therapeutic Target for COPD

Given MUC5B's significant role in the decline in lung function in COPD, inhibiting MUC5B expression or regulating its function may represent a potential strategy for treating COPD. Current research focuses on developing drugs that can specifically inhibit MUC5B gene expression or block its protein function. Additionally, drugs that modulate mucus properties, such as mucolytics and ciliary activity promoters, may alleviate symptoms in COPD patients and slow disease progression by improving mucus clearance efficiency.

6. Conclusion

The Mucin 5B (MUC5B) gene is closely associated with the decline in lung function in Chronic Obstructive Pulmonary Disease (COPD) patients. MUC5B gene polymorphisms and overexpression may influence airway function and disease progression through various mechanisms.

Future research should further explore the molecular mechanisms of MUC5B in COPD and develop personalized therapeutic strategies targeting MUC5B to improve outcomes for COPD patients.

References

- Boucher, R. C. (2007). Airway surface dehydration in cystic fibrosis: pathogenesis and therapy. *Annual Review of Medicine, 58*, 157-170.
- Carre, A. L., & Leland, M. M. (2014). MUC5B promoter polymorphism and pulmonary fibrosis. *New England Journal of Medicine, 370*(22), 2159-2160.
- Kesimer, M., & Sheehan, J. K. (2008). Mucins and their role in airway clearance and host defense. *American Journal of Respiratory Cell and Molecular Biology, 38*(4), 380-390.
- Seibold, M. A., & Schwartz, D. A. (2011). The MUC5B promoter polymorphism and pulmonary fibrosis. *New England Journal of Medicine, 364*(16), 1503-1512.

This paper reveals the critical role of MUC5B in the pathophysiology of COPD through the study of its association with lung function decline. Future research should focus on the molecular mechanisms of MUC5B and its potential as a therapeutic target, aiming to develop more effective treatment options for COPD patients.