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**Review Article**

# COPD: Perspectives of Immune Peptide Therapy and Lung Cancer Prevention

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**Abstract:** Background: Chronic obstructive pulmonary disease (COPD) occurs due to chronic inflammation, which leads to thickening of the airway walls, increased mucus production and, ultimately, permanent changes in lung structure. Meta-analysis indicates an increased risk of lung cancer in patients with COPD, so timely and comprehensive cancer prevention is extremely important. Objective: Determine the mechanisms of interaction between immune peptides and immunocompetent cells, which lead to the elimination of pathogens and prevent the development of metaplasia on the background of chronic inflammation. Methods: Selection and analysis of open access scientific publications. Results: Restoring the ability of secretory cells to synthesize IgA and maintaining this synthesis at the appropriate level can provide the necessary protection of the respiratory system from infection. Strengthening immune surveillance over the mucous membrane promotes not only the elimination of pathogens, but also to the destruction and removal of disabled and infected cells and cells that have undergone metaplasia - this is how the immunity program is implemented to counteract infection and prevent cancer. Conclusion: The use of exogenous anti-infective peptides for the treatment and prevention of exacerbations of COPD in the context of antibiotic resistance, to stimulate airway immune function and to prevent cancer is currently considered a promising area in clinical pulmonology.

**Keywords:** COPD, Exacerbation, Antiinfective Peptides, Immune Correction, Lung Cancer Prevention

## 1. Introduction

One of the most common in the world is chronic obstructive pulmonary disease (COPD) - a progressive disease that causes shortness of breath, is prone to exacerbations and is life-threatening. Mortality from COPD continues to increase and ranks 4th among all causes of death in the general population. The prevalence of COPD in men over 40 in Europe ranges from 8% to 26%. [1-3]

Despite its prevalence, COPD is underdiagnosed, and many patients are not diagnosed until the disease progresses clinically. Recent basic scientific and clinical research has focused on early physiological and pathobiological changes in COPD, with the hope of improving diagnosis, providing treatment objectives, and identifying groups of patients who are most likely to benefit from early intervention. [4, 5]

Clinical experience in recent decades in many countries shows that chronic obstructive pulmonary disease is incurable. The main reason for the development of COPD is tobacco smoke as a result of smoking tobacco or inhaling secondary tobacco smoke. Not only current but also past smoking history should be assessed as the main risk factors for COPD. [6] Non-smokers who have experienced secondhand smoke in childhood and adulthood also have an increased risk of developing COPD. [7] Cigarette smoking has been identified as a cause of COPD in 50% –70% of patients in developed countries. [8] Other risk factors for COPD include occupational exposure (eg, dust, vapors, organic materials, evaporation, and chemicals), indoor and outdoor air pollutants (including biomass fuels), and aging. [6]

COPD occurs due to chronic inflammation, which leads to thickening of the airway walls, increased mucus production

and, ultimately, permanent changes in lung structure (Figure 1). [1] Lung changes may include destruction of the lung parenchyma, including the walls of the air sacs (alveolar), leading to fibrosis of the small airways (emphysema) and loss of elasticity; all of which can manifest as shortness of breath, coughing, and increased sputum production. [9-11]

It should also be noted that a meta-analysis indicates an increased risk of lung cancer in patients with COPD, so timely and comprehensive cancer prevention is extremely important. [12]

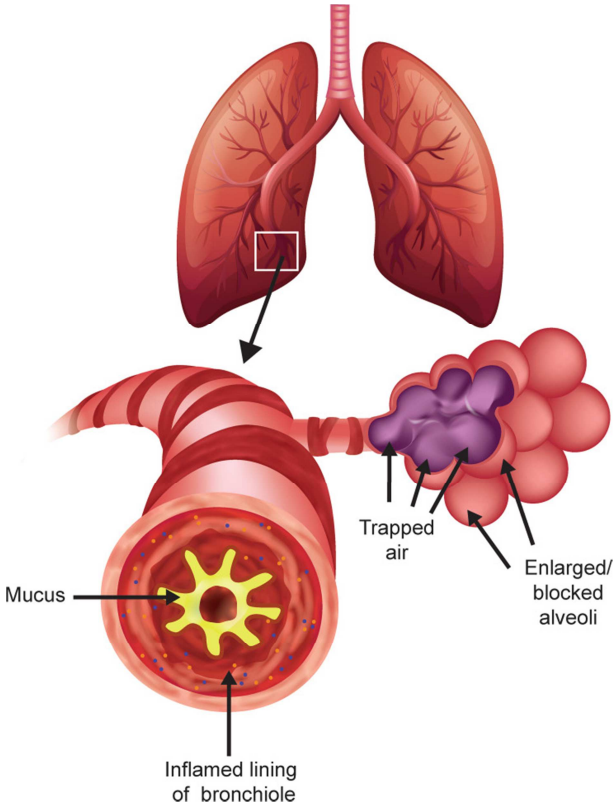


***Figure 1.*** *Pathophysiology of chronic obstructive pulmonary disease. During COPD, airway inflammation can lead to thickening of the airway walls, increased mucus production, and damage to the alveoli and alveolar ducts, leading to an increase in air space / emphysema, and potentially air entrapment. [1]*

## 2. Methods

To write this review article, we used the method of selection and analysis of open access scientific publications. All factual material, illustrations and research results presented in this article refer to the original source, which corresponds to the number of the original publication in the bibliography.

## 3. Results

The goal of pulmonologists to treat exacerbations of COPD is to minimize the damaging effects of the current exacerbation and prevent further exacerbations. Approximately 80% of patients with exacerbations can be treated on an outpatient basis, the decision to hospitalize is made by a specialist: family doctor, therapist, pulmonologist.

Because the most common cause of exacerbations of COPD is considered to be a respiratory infection, so in the presence of indications, antibiotics are prescribed. Exacerbations of COPD can be caused by seasonal viral infections, so it is extremely important to maintain the immune protection of the mucous membranes of the respiratory tract at the proper level. During the Sars-Cov2 pandemic, immune prevention of COPD exacerbations becomes even more clinically and socially relevant. [13-15]

It is also important that in exacerbations of COPD, the timely appointment of supportive immunocorrection can reduce the time to recovery and reduce the risk of early recurrence. Immunocorrection using immune anti-infective peptides is recognized as one of the most promising techniques at the present stage, in the era of multiple resistance to drugs (MDR - multi-drug resistance) [17, 21].

COPD is characterized by chronic inflammation of the airways and periodic episodes of deterioration in respiration and lung function, which are called acute exacerbations of COPD. Such episodes are associated with increased inflammation of the airways and are often provoked by infection. Patients with COPD have frequent exacerbations, despite the relatively high effectiveness of existing standard therapy. Therefore, it is obvious that a targeted and more effective prevention strategy is needed.

Immunoglobulins are glycoprotein molecules that are secreted by B lymphocytes and plasma cells and play a crucial role in the adaptive immune response against many pathogens. Altered serum immunoglobulin levels were observed in patients with immunodeficiency and inflammatory diseases. Serum immunoglobulin has also been identified as a potential biomarker of COPD exacerbations, but it should be noted that class A secretory immunoglobulin (IgA) plays a crucial role in protecting the airway mucosa. [22-24]

IgA is a specialized weapon of the body against the penetration of viruses and bacteria into the cells of mucous membranes. Therefore, restoring the ability of secretory cells to synthesize IgA and maintaining this synthesis at the appropriate level can provide the necessary protection of the respiratory system from infection, in particular by the Sars-Cov-2 virus [23]

In recent years, to restore immune homeostasis in various diseases are increasingly using drugs that contain anti-infective peptides. Finally, it is well known that immune proteins play a key role in the immune responses of living organisms. The International Institute of Biotherapy has developed and implemented in clinical practice an innovative method of anti-relapse immunocorrection, which is based on the use of immune anti-infective proteins. Innovative immune drug is called «Arecur» - from the English anti-reccurence («against recurrence»). Immune proteins in the drug are RJP-1 and defensins, have antibacterial and antiviral properties. [16, 20, 21, 26]. It is also noteworthy that due to their properties, formed by evolution over millions of years, immune peptides in the conditions of hyperproduction of proinflammatory cytokines due to the effect of competitive substitution are able to reduce inflammation. Conversely, when enhanced

immunity is required, peptides activate the required number of immunocompetent cells.

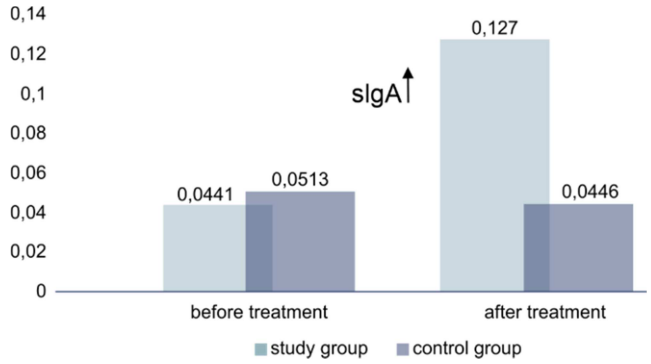


***Figure 2.*** *Increased levels of sIgA (pkg / ml) of the mucosa after administration of exogenous immune peptides. [25]*

The mechanism of activation by immune proteins of immune cells is quite simple: when accumulated, immune peptides attach to cell membranes in the target organ and, thus, provoke their productive interactions with T-lymphocytes, NK-cells and macrophages.

Thus, the probability of detection and destruction of atypical cells in the foci of metaplasia increases and preventive immune prophylaxis of bronchial carcinoma is realized. [12, 16, 18, 19]. Most importantly, contact of exogenous peptides with the mucosa stimulates the membranes of immunocompetent cells and increases the expression of secretory immunoglobulin A - the body's main weapon against pathogenic bacteria and viruses (Figure 2) [25].

To date, clinical data are accumulating to suggest that the use of the anti-relapse immunocorrector Arecur in the form of inhalations protects the airways of patients from infection and thus prevents possible frequent recurrences of COPD. The use of Arecur inhalations is most effective according to the preventive scheme, before the SARS season - 1 inhalation per day, a course of 10 inhalations, preventive courses are recommended for patients with COPD at least 2 times a year. If exacerbation still occurs, inhalation is used during the recovery period after lowering the temperature. Not only during the rehabilitation period after exacerbation of COPD, but also in general for the prevention of seasonal viral infections and for the assistance of cellular immunity in effectively counteracting pathogens, it is recommended to take Arecur capsules: 1 capsule 2 times a day for 1 month during the cold season. Arecur is fully compatible with antibacterial drugs and anti-inflammatory therapy. A wide range of therapeutic peptides opens up great clinical prospects for the use of antirelapse immunocorrection in viral respiratory infections, bronchitis and pneumonia, so research in this area should be continued.

# 4. Discussion

Studies have shown that contact of immune peptides with mucosal cells significantly increases the expression of secretory immunoglobulin A. [25] The ability of immune proteins to stimulate macrophage migration and induce apoptosis of atypical cells opens new possibilities for the use of antirelapse immunocorrection [26] Encouraging clinical results of the use of immune proteins for the prevention of cancer recurrence were obtained [27, 28].

Studies in recent years have shown that antimicrobial peptides, both endogenous and exogenous, play a crucial role in protecting the body and especially the mucous membranes of the respiratory tract from the penetration of pathogenic microflora. [29-31]

In addition, the evolutionary properties of anti-infective peptides to destroy pathogens are complemented by their unique ability to activate productive cell-cell and cell-viral interactions between T-lymphocytes, dendritic cells, macrophages and pathogens. [32-34] This leads not only to protection against infection and disease development, but also to the effective destruction of pathogens and more productive and rapid recovery, particularly during exacerbations of COPD. Increasing the level of immune peptides in the bronchial mucus also stimulates more productive utilization of toxic residues of pathogens and infected cells by the macrophage system, and ultimately their evacuation with sputum.

Therefore, the addition of exogenous anti-infective peptides to endogenous ones to kill the infection in the context of antibiotic resistance, to stimulate airway immune function and to prevent cancer is currently considered a promising area in clinical pulmonology. [35-36]

Given the above, we believe that the study of the effectiveness of anti-infective immune peptides in the treatment of respiratory diseases must continue, especially given that in recent years there has been a gradual development of resistance to generally accepted methods of therapy.

# 5. Conclusions

The use of exogenous anti-infective peptides for the treatment and prevention of exacerbations of COPD is an innovative and promising area of modern pulmonology.

The ability of peptides to stimulate and restore the normal level of synthesis of immunoglobulin A provides protection of the mucous membranes of the respiratory tract from infection, which is extremely important for patients with COPD.

An important characteristic of peptides is not only their ability to destroy pathogens, but also genetically programmed properties to stimulate the immune response by assisting T-lymphocytes and macrophages in determining the danger and in removing infected and potentially atypical cells.

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