Biology of Mycoplasma Pneumonia and Its Vaccine Research Status

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Abstract: Mycoplasma pneumoniae is the main pathogen that causes pneumonia in hospitalized children. Existing treatment drugs have the disadvantage of insufficient resistance to varying degrees, and the discovery of drug-resistant strains has made it difficult to fully meet the needs of clinical intervention. The prevention of Mycoplasma pneumoniae infection remains unresolved, and the development and use of related vaccines have gradually become the focus of research. This article mainly provides an overview of the biology and vaccine research of Mycoplasma pneumoniae.

1. Introduction

Mycoplasma pneumoniae is a risk factor for community acquired pneumonia, with significant infectivity, mainly transmitted through respiratory droplets. Headache, myalgia, fever, dry cough, chest tightness, shortness of breath, and gastrointestinal symptoms are all common symptoms of Mycoplasma pneumoniae. Mycoplasma pneumoniae infection often manifests as self-limiting, and in recent years, due to increased drug resistance, the incidence rate of refractory pneumonia has increased. Mycoplasma pneumoniae can not only induce respiratory diseases such as atelectasis and obstructive bronchitis, but also carry the risk of damaging multiple organs such as the heart, brain, and kidneys. Vaccines are one of the important ways to prevent Mycoplasma pneumoniae infection [1]. Currently, live attenuated and inactivated vaccines against Mycoplasma pneumoniae have been gradually launched domestically and internationally for use in animal fields such as pigs, cows, and sheep. However, the highly targeted human Mycoplasma pneumoniae vaccine is still in the research and development stage. This study aims to explore the pathogenesis of Mycoplasma pneumoniae and review the application status of related vaccines.

2. Pathogenesis of Mycoplasma Pneumoniae Infection

The human body is susceptible to Mycoplasma pneumoniae, especially in children, whose respiratory and cardiovascular systems are not yet fully developed, which makes the clinical manifestations more complex and may lead to pulmonary and extrapulmonary complications. In the infection mechanism of Mycoplasma pneumoniae, adhesion is one of the important factors that induce pathological reactions, and mutant strains without adhesion ability have no pathogenicity. P1 protein is particularly important for the adhesion of Mycoplasma pneumoniae on its surface. P1 protein can bind to neuraminic acid receptors on the surface of respiratory epithelial cells, stably adhere to the cell surface, and extend microtubules into the cell to absorb nutrients. In addition, the duration of the disease may also be related to P1 adhesion. Related reports have shown that after initial infection with Mycoplasma pneumoniae, it can persist in the respiratory tract for several months, which may be related to the firm adhesion of Mycoplasma pneumoniae to the surface of epithelial cells and its invasion into the interior of epithelial cells, thereby escaping the immune killing effect of the body and effective drug intervention, leading to the transformation of patients into asymptomatic carriers or chronic infected individuals. There are relatively many literatures on the Pl protein of Mycoplasma pneumoniae. As a membrane surface protein, it has significant antigenic specificity and is usually used as a target for testing. However, Pl protein is not unique to Mycoplasma pneumoniae, and therefore its cross reactivity needs to be paid attention to [2].

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Regarding the immune damage induced by Mycoplasma pneumoniae, some reports suggest that after invading host cells, Mycoplasma pneumoniae can cause damage in some ways. Mycoplasma pneumoniae is transmitted through droplets from the respiratory tract, invading the patient's respiratory tract, and subsequently causing direct damage to the host cells. It should be noted that a toxin called community acquired respiratory distress syndrome toxin (CARDS TX) can cause organ damage, and lead to clinical symptoms such as fever in the patient.

Cao Nannan et al. [3] have shown through research that CARDS TX not only appears in damaged lung areas, but also can enter the bloodstream and further activate Nod-like receptor protein 3/interleukin-1 β, the interleukin-18 pathway, mediate the occurrence and development of severe Mycoplasma pneumoniae pneumonia, while also participating in the local lung injury mechanism in patients with this disease. Sun Hui et al. stated that [4], the serum lactate dehydrogenase index and the expression of CARDS TX in bronchoalveolar lavage fluid increased, the erythrocyte sedimentation rate increased, and the probability of children with Mycoplasma pneumoniae pneumonia with ≥ 2/3 lung lesions developing into refractory Mycoplasma pneumoniae pneumonia increased. Ma Xiang et al. proposed [5] that after acute infection with Mycoplasma pneumoniae, the CARDS toxin index will gradually decrease and can still be detected six months after the onset of the disease. Its expression level may be related to the cough and asthma symptoms and clinical severity of the child. The 3D structure of these toxins has also been gradually elucidated.

3. Diagnosis and Treatment

The diagnostic methods for Mycoplasma pneumoniae infection include serological antibody diagnosis, Mycoplasma pneumoniae isolation and culture method, nucleic acid diagnosis method, and antigen diagnosis method. The lack of typicality in the characteristics of various tissues, organs, and lung lesions caused by Mycoplasma pneumoniae infection makes it difficult to judge the disease based on clinical manifestations. Serological testing is a commonly used diagnostic technique for Mycoplasma pneumoniae infection in China at present. Culture method is the gold standard and the best way to detect Mycoplasma pneumoniae, but it has high cultivation conditions and requires a long time. Many clinical departments have not been able to establish a sound detection system, which is mostly used for retrospective judgment and analysis, and its clinical value is limited. Enzyme-linked immunosorbent assay (ELISA) is a type of serological detection that is simple in operation and can detect specific IgM and IgG antibodies against Mycoplasma pneumoniae. The tracer is usually selected from enzyme labeled anti-human immunoglobulin antibodies to evaluate IgG and IgM in serum. It can also detect non-complement dependent antibodies, especially IgA class antibodies, so it can play a corresponding reference value in identifying Mycoplasma pneumoniae infection in the respiratory tract. Compared with conventional Mycoplasma culture methods, enzyme-linked immunosorbent assay (ELISA) takes less time, only a few hours, and no cross reactions were found with other common respiratory pathogens. However, this testing method also has shortcomings, such as the need to prepare two serum samples from different periods during the testing process. The nucleic acid testing method has good sensitivity and specificity, and can detect Mycoplasma pneumoniae infection in early clinical practice. However, many medical institutions currently lack complete equipment and clear quality control standards, which increases the difficulty of clinical diagnosis of Mycoplasma pneumoniae.

At present, the treatment for Mycoplasma pneumoniae pneumonia in clinical practice mainly includes fiberoptic bronchoscopy, antibiotic therapy, immunosuppressive agents, and other methods. Azithromycin is widely used in the clinical treatment of Mycoplasma pneumoniae pneumonia, with advantages such as fast absorption, wide antibacterial spectrum, and outstanding stability under gastric acid conditions after medication. In addition, Azithromycin has a half-life of up to 70 hours, and can maintain strong blood drug concentrations in the tissue for a long time after medication. Some studies suggest that Azithromycin has a definite effect in the treatment of Mycoplasma pneumoniae infection, with significant antibacterial effects and long-lasting efficacy. However, during the intervention process, attention should be paid to the accumulation of drugs in the body and the post-antibiotic effects to prevent liver and kidney damage [6]. Macrolide antibiotics are one

of the main methods, and for acute patients, the inflammatory response can be controlled through immunosuppressive agents. Fiberoptic bronchoscopy treatment can effectively diagnose the local pathological state of the lungs. If the treatment with macrocyclic acetic acid antibiotics is ineffective, it is necessary to comprehensively consider various pathogenic factors, evaluate the resistance of Mycoplasma pneumoniae, and then take sensitive drugs for corresponding intervention. Currently, there is a significant resistance rate of Mycoplasma pneumoniae resistant bacteria to macrolide antibiotics in China. Based on this, the development of Mycoplasma pneumoniae vaccines is an effective means of preventing Mycoplasma pneumoniae infection.

4. Related Vaccine Research

4.1 Peptide Vaccine

P30, P1, and other adhesion proteins are important adhesion factors of Mycoplasma pneumoniae, possessing immunoreactivity and immunogenicity. They can induce specific neutralizing antibodies. In addition, immunogenicity also includes polysaccharides, P116, CARDS TX, lipoproteins, and lipids, which can provide new directions for vaccine development. Analysis suggests that antibodies specific to P116 exist in the serum of patients infected with Mycoplasma pneumoniae. CARDS TX is a novel virulence protein expressed by Mycoplasma pneumoniae and plays a major role in the pathogenesis of Mycoplasma pneumoniae. A foreign analysis has shown that the C-terminus of CARDS TX can produce antibody reactions to Mycoplasma pneumoniae infection. Anti-CARDS TX antibodies have been found in the serum of Mycoplasma pneumoniae infected individuals in both the acute infection and recovery stages, and antibody levels are higher in the recovery stage. These research reports provide a reference basis for the development of peptide vaccines to prevent Mycoplasma pneumoniae infection. Peptide vaccines have the characteristics of simple composition and easy control, but due to the lack of strong immunogenicity and low relative molecular weight, adjuvants need to be added to induce a strong immune response.

Antibodies formed by the stimulation of the glycolipid structure of Mycoplasma pneumoniae do not have a high host protective effect, and vaccines using glycolipids as antigens are difficult to induce long-term protective immunity, and there is a risk of cross reactivity immunity. In addition, analysis showed that compared to the placebo group, mice vaccinated with the lipid fraction of Mycoplasma pneumoniae lipoprotein did not reduce the pathogen load, and may also experience more severe lung inflammation, indicating that the lipid fraction of Mycoplasma pneumoniae lipoprotein may be a pathogenic factor for vaccine-enhanced diseases.

4.2 Recombinant Protein Subunit Vaccine

The subunit vaccine is a vaccine developed using important immunogenic components of pathogenic bacteria. Due to the relatively small molecular weight of the double-stranded circular genome of Mycoplasma pneumoniae, the proteins that can be encoded are relatively limited. Among the limited coding proteins, the surface proteins P1 and P30 related to Mycoplasma pneumoniae adhesion are particularly important during its pathogenic period. The recombinant protein subunit vaccine, as a candidate vaccine for preventing Mycoplasma pneumoniae infection, eliminates irrelevant or harmful components in pathogen antigens through gene recombination technology and retains the original antigenic effector components [7]. In addition, the recombinant protein subunit vaccine can induce a certain immune response in the body, but its cost is not low. Its effectiveness as a dominant vaccine against Mycoplasma pneumoniae still needs further research and analysis.

4.3 DNA Vaccine

The mechanism of action of DNA vaccines is to recombine antigen genes into relevant vectors, inject them into the body after processing, and express corresponding antigens in the body, stimulating the body to form antibodies. Foreign reports have found that a DNA vaccine is produced by fusing the P1 protein gene with the Escherichia coli heat-labile toxin B subunit gene, which can

form immune protection against Mycoplasma pneumoniae infection in a mouse model with less pathological inflammation. Compared to traditional vaccines, DNA vaccines are easier to store, construct, and transport, do not pose a risk of infection, and can form a longer immune response. However, there are still many obstacles that need to be addressed when applying DNA vaccines to the human body, such as immune tolerance and injection routes.

5. Conclusion

In summary, in recent years, the risk of diseases induced by Mycoplasma pneumoniae has been continuously increasing, and it has gradually progressed into a public health problem that is increasingly threatening physical and mental health. Developing more efficient vaccines based on the biological characteristics of Mycoplasma pneumoniae may become an important direction for preventing Mycoplasma pneumoniae pneumonia in the future. Although some new vaccine strategies have been gradually developed, there is still no clinical vaccine available at this stage. With the in-depth exploration of the pathogenesis of Mycoplasma pneumoniae and the emergence of new vaccination methods, as well as successful experience in animal experiments, more new ideas have been provided for the development of therapeutic Mycoplasma pneumoniae vaccines in the future. Further exploration is needed to improve the effectiveness and safety of vaccines.

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