Review Article

CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

Minireview: Designing next generation human metapneumovirus (HMPV) vaccine

Clin Exp Vaccine Res. 2025 Apr;14(2):116-118
https://doi.org/10.7774/cevr.2025.14.e12
pISSN 2287-3651·eISSN 2287-366X

Mohammed Ibrahim Saeed

Medical Laboratory Department, Gulf Medical University, Ajman, United Arab Emirates

OPEN ACCESS

Received: Feb 19, 2025
Revised: Feb 26, 2025
Accepted: Feb 26, 2025
Published online: Mar 18, 2025

Corresponding author:
Mohammed Ibrahim Saeed, PhD
Medical Laboratory Department, Gulf Medical University, Al Jerf 1, P.O. Box 4184 Ajman, United Arab Emirates.
Tel: +971-6-7431333 (Ext:1227)
Email: moibsaeed@yahoo.com

The recently circulating human metapneumovirus (HMPV) is a serious respiratory infection that affects immunocompromised persons, the elderly, and children. HMPV infections can cause significant morbidity, including pneumonia, bronchiolitis, and worsen chronic respiratory diseases. Despite the clinical burden, there is still no licensed HMPV vaccine. This short review examines the mechanisms underpinning next generation HMPV vaccines, the gene involved, the significant epitopes, the immunological responses they elicit, and the potential impact on herd immunity.

Keywords: Human metapneumovirus; Vaccine; Epitopes; Mucosal immunity

INTRODUCTION

Human metapneumovirus (HMPV) structure of the virion

HMPV is a single strand RNA virus with negative reprinting. It has a nucleocapsid made up of proteins and RNA genomes, and is coated with a lipid envelope with glycoproteins on its surface. The genome encodes several important structural proteins. Nucleocapsid: forms a nucleocapsid by attaching to RNA. Phosphoproteins: improve replication and stabilize the RNA genome. Matrix: promotes virus buds and assembly. Fusion (F): facilitating virus fusion at the membrane of the host cell. Glycoproteins support virus adhesion to host cells. Polymerase: responsible for transcription and RNA replication.

HMPV epitopes and genes

Since the viral F and hemagglutinin-neuraminidase (HN) proteins are required for viral entry into host cells, these are the primary targets for HMPV vaccine development [1]. The HMPV genome, which codes for structural proteins that allow host interaction and immune recognition, serves as the genetic underpinning for these proteins [2]. The F helps the viral envelope and host cell membrane fuse together. Antibodies that neutralise the F protein can prevent this F and the virus from infecting cells. The HN protein plays a role in viral release by binding to sialic acid receptors on the host cell's surface. Antibodies against HN can prevent viruses from adhering and infecting individuals [3]. Vaccine design is based on the identification of surface epitopes, or exposed regions of proteins that the immune system recognize. The basic goals of vaccine developers are surface epitopes that elicit T-cell cellular

immune responses and B cell epitopes that produce neutralising antibodies.

Mechanisms of HMPV vaccines

The primary goal of the HMPV vaccine trial is to protect against the virus by eliciting humoral and cellular immune responses. B cells, which produce antibodies against viral antigens, play the key role in humoral immunity. Antibodies against the virus F protein, which promotes viral F with host cells, are thought to be necessary for avoiding HMPV infection. The virus's capacity to infect cells can be blocked by neutralising antibodies that target both the F and HN proteins [4]. T cells, particularly cytotoxic CD8+ T cells, play a critical role in the elimination of virus-infected cells as part of cellular immunity. To support humoral and cellular immune responses, helper T cells (CD4+) activate B cells and cytotoxic T cells. Memory immunity: vaccines are designed to develop memory B and T cells, which will be able to recognise the virus and activate an immune response when it is encountered again [4].

Types of HMPV vaccines

A number of challenges have hampered the development of HMPV vaccines, including the virus's ability to evade immune responses and the difficulty in developing post vaccination immunity that provide long-term protection. Inactivated vaccine, which use inactivated viral particles to generate an immune response without the risk of disease transmission, are among the many vaccine development strategies under investigation [5].

Inactivated vaccines may not give long-term protection, therefore they typically require adjuvants to improve their efficiency. Live attenuated vaccine uses weakened virus strains that can still replicate but do not cause sickness. Although live attenuated are known for their capacity frequently generate strong immunological responses, but, they may not be recommended for those with weakened immune systems [5]. Subunit vaccines can induce protective immune response, they target specific viral proteins, such as F and HN. Although these vaccines require an adjuvants or carriers to be more effective, and compared to live vaccines, they are generally safer and better controlled [6]. After its success with coronavirus disease 2019 (COVID-19), mRNA vaccines for HMPV have gained more concern and they may provide promising success in future protection towards HMPV [7]. To provoke an immune response, these vaccines encode viral protective epitopes, which are then expressed by the vaccinee's host cells. Viral vector-based HMPV vaccines: these vaccines designed to carry HMPV genes for viral epitopes that offer protection towards the virus after being expressed into host cells via viral vectors such as adenoviruses, eliciting parenteral immune response [8].

HMPV VACCINES INDUCED IMMUNE RESPONSES

Parenteral immunity

The primary goal of the humoral response is to induce the production of neutralising antibodies, namely against the F and HN proteins. These antibodies block the virus from penetrating host target cells, effectively stopping the viral replication and preventing from infection. Cellular response: T cell-mediated immunity, particularly CD8+ cytotoxic T cells, is responsible for the majority of virus-infected cell elimination. CD4+ T helper cells activate both cytotoxic T cells and antibody-producing B cells. A significant cellular immune response is required to eliminate the virus from the body and prevent further infection.

Impact of vaccines and herd immunity

When herd immunity covers a large portion of the population acquires immunity to a virus, it help to contain the virus and prevents the infection from spreading throughout the community. Broad vaccination coverage is critical to the concept of herd immunity in order to contain HMPV, especially among vulnerable groups such as small children, the elderly, and those with compromised immune systems. Lower transmission rates may arise from an effective HMPV vaccine that provides long-term immunity by reducing the incidence of symptomatic infections. Adequate vaccination coverage may significantly diminish the virus's ability to spread across the community, resulting in long lasting herd immunity. Although the threshold for herd immunity varies, it is widely agreed that for herd immunity to be effective, 75%–90% of the population must be immune [9].

CURRENT HPMV VACCINE DEVELOPMENT

The HMPV vaccine development process is not as advanced as the manufacture of COVID vaccines. However, none have moved beyond the preclinical stage. The virus's ability to evade immune responses, as well as our lack of understanding of long-term immunity, remain 2 important barriers to developing an HPMV vaccine. The preliminary results of the HPMV vaccine study have shown promising potential to prevent respiratory infections in the future [10]. Vaccine developers are refining vaccine formulations with an

emphasis on viral protective epitopes immunogenicity, delivery carrier, and boosting long-lasting highly neutralizing postvaccination immunity.

Current gap: challenges and future directions

Despite tremendous progress in the development of the HMPV vaccine trials, a number of difficulties need to be overcome the followings issues. Antigenic variation: mutations in HMPV gene that induces the protective epitopes can affect its antigenic properties, making it partly or completely fail to provide recognizable protective immunity to the circulating virus strains. Vaccine efficacy and safety: while live attenuated vaccines are effective, they can be risky, particularly for persons with compromised immune systems. Similarly, inactivated vaccines may not elicit a strong enough immune response. Immunity durability: herd immunity requires long-term immunity. For the vaccine-induced immunity to be successful in preventing virus spread, it need the development of novel delivery strategy to prolong the immunogenicity of HMPV vaccines. Therefore continued search into new vaccine platforms such as mRNA vaccines and nanoparticle-based delivery systems may result in a safer and more effective HMPV vaccine. For the development of effective HPMV vaccines, researchers and vaccine manufacturers should collaborate to develop univalent or multivalent HPMV vaccines that combine HPMV with other respiratory viruses.

WHAT WILL BE THE IDEAL HMPV VACCINE

Induction of balanced multiple types of immune response seem crucial for developing the best protective and effective optimum HMPV vaccine. The ideal vaccine will need to evoke both parenteral (humoral and cellular responses), in addition to increased mucosal immunity in term of specific sIgA antibodies at the viral earlier entry to target cells. Induction of combined immune responses will collectively enabling all-encompassing defenses mechanisms against HMPV by blocking early viral replication, while also preventing initial infection (via antibodies) and destroying viral infected cells by T cells.

CONCLUSION

Finally, developing an HMPV vaccine is a realistic method to reducing the burden of respiratory infections caused by this virus. Long-term protection necessitates an understanding of immunity mechanisms, the discovery of key genetic components, and the creation of vaccines that elicit mucosal, humoral and cellular immune responses. Herd immunity, achieved through mass vaccination, is a feasible goal that might significantly reduce HMPV transmission. However, continued research and development next generation vaccine with novel design, delivery means, epitope stabilizers are needed to address challenges such as antigenic diversity, vaccine safety, and immunization durability.

ORCID iDs
Mohammed Ibrahim Saeed
https://orcid.org/0000-0002-3530-1351

Funding
None.

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Cox RG, Williams JV. Breaking in: human metapneumovirus fusion and entry. Viruses 2013;5:192-210. PUBMED | CROSSREF
2. Wei T, Wang C, Ma F, et al. Whole genome sequencing and evolution analyses of human metapneumovirus. Virus Genes 2023;59:524-31. PUBMED | CROSSREF
3. Melero JA, Mas V. The pneumovirinae fusion (F) protein: a common target for vaccines and antivirals. Virus Res 2015;209:128-35. PUBMED | CROSSREF
4. Márquez-Escobar VA. Current developments and prospects on human metapneumovirus vaccines. Expert Rev Vaccines 2017;16:419-31. PUBMED | CROSSREF
5. Ren J, Phan T, Bao X. Recent vaccine development for human metapneumovirus. J Gen Virol 2015;96:1515-20. PUBMED | CROSSREF
6. Aerts L, Rhéaume C, Carbonneau J, et al. Adjuvant effect of the human metapneumovirus (HMPV) matrix protein in HMPV subunit vaccines. J Gen Virol 2015;96:767-74. PUBMED | CROSSREF
7. Ma S, Zhu F, Xu Y, et al. Development of a novel multi-epitope mRNA vaccine candidate to combat HMPV virus. Hum Vaccin Immunother 2024;20:2293300. PUBMED | CROSSREF
8. Ogonczyk Makowska D, Hamelin MÈ, Boivin G. Engineering of live chimeric vaccines against human metapneumovirus. Pathogens 2020;9:135. PUBMED | CROSSREF
9. Anderson RM, Vegvari C, Truscott J, Collyer BS. Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination. Lancet 2020;396:1614-6. PUBMED | CROSSREF
10. Lee YZ, Han J, Zhang YN, et al. Rational design of uncleaved prefusion-closed trimer vaccines for human respiratory syncytial virus and metapneumovirus. Nat Commun 2024;15:9939. PUBMED | CROSSREF