

## COVID-19 Vaccines Confer a Prophylactic Effect on Common Cold

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### ABSTRACT

Common cold is an upper respiratory infection with relatively high mortality and infection rate. This is especially true among immunosuppressed individuals. The infection can be caused by human coronaviruses of which common cold coronaviruses-229E, -NL63, -OC43, and -HKU1 are the major etiological agents. These viruses also belong to the same family as the SARS-CoV-2 virus that cause the COVID-19 pandemic. The pandemic has led to the development of the various COVID-19 vaccines. The coronaviruses all express similar types of proteins, the membrane, spike, envelope protein, and the nucleocapsid. The spike protein is the main antigenic determinant and also induces an endoplasmic reticulum stress response. Cross-reactivity on the antigenic determinants between both groups of coronaviruses exists due to similar main antigenic orientation. Studies on the strength of the immune responses evoked by either SARS-CoV-2 or the human common cold coronaviruses towards each other is inconclusive; averagely demonstrating that antibodies (Abs) against SARS-CoV-2 can neutralize antigens (Ags) on common cold coronaviruses. Due to cross-reactivity, theoretically vaccines against SARS-CoV-2 can be used to fight common cold coronavirus infections due to the two expressing similar antigenic determinants that elicit an immune response for the homologous antigen.

Keywords: COVID-19, Common Cold Viruses, Vaccines, Immune Responses

## I. INTRODUCTION

Common cold is a relatively milder upper respiratory infection but possesses a very high mortality rate when it becomes severe. Human coronaviruses (HCoVs) account for an average of 7.5% of all the upper respiratory infections in adults and with a higher average of 30% in causing respiratory infection outbreaks related to a single HCoV species (Monto, 1991). The world health organization (WHO) documents that almost 650,000 people die yearly due to common cold-associated infection (WHO, 2017). One study conducted in Scotland illustrated that of the total viral etiology of common cold, coronaviruses account for 7% with the coronavirus OC43 variant being common among infants, children below five years, and the elderly (Heimdal et al., 2018). The coronavirus 229E is commonest in the adult age group from 17 years while coronavirus NL63 was more common in infants (Nickbakhsh et al., 2020). Another Norwegian study concluded that HCoV-OC43 and HCoV-NL63 result in an epidemic in the country among children every winter season and if the two viruses were absent, the causative agent would normally be HCoV-HKU-1 (Heimdal et al., 2018). HCoV-HKU-1 was first isolated from a single person in 2004 in Hong Kong. It later spread towards the end of the same year to Australia infecting about 10 people of whom mostly were children. The virus was then found to have spread to western hemisphere in 2005 and it was suspected to have gained worldwide distribution. Though it is prevalent in the world; it is less virulent compared to the other HCoVs, (Li et al., 2019). Other studies illustrate that the human coronaviruses (HCoVs) cause common cold epidemics unpredictably with each strain predominating in a given geographical location (Monto, 1991; Gaunt et al., 2010; Heimdal et al., 2018). Moreover, the HCoVs have been isolated from middle ear effusions demonstrating that common cold infection can be complicated with otitis media, another debilitating infection in children (Chonmaitree et al., 2008).

The HCoVs have been found to result in co-infection with certain severe lower respiratory infections such as pneumonia (Lieberman et al., 2010) and neurological diseases e.g., encephalitis (Ann et al., 2003). They result in influenza-like illness and cause acute exacerbations of chronic bronchitis. HCoV-OC43 has been shown to have the highest clinical impact of the HCoVs with an 8% fatality rate in long-term care facilities (Patrick et al., 2006). Although the illness is self-limiting, it lasts an average of 2 to 18 days while some patients even develop chronic disease. Thus, these patients are burdened with the responsibility of managing the clinical manifestations of the common cold and often than not, it makes a person unproductive and unable to go to work or perform at their best. This presents the need for common cold prophylaxis since currently there is no definitive treatment for the viral infection. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which has caused the deadly pandemic currently ravaging the world belongs to the same group of viruses as the human common cold viruses-229E, -NL63 (referred to as alpha coronaviruses), and -OC43, and -HKU1 (grouped as beta coronaviruses). They have similarities in terms of the proteins they express and as such display similar antigenic determinants. These determinants include the spike and membrane proteins. The spike protein is responsible for entry into host cells when the virus is inhaled. This spike protein is present in both the SARS-CoV-2 and common cold coronaviruses. The membrane protein is also present in both types of viruses and mediates the fusion of virions to host cell. SARS-CoV and HCoV-NL63 uses ACE2 as their receptor while the spike protein of other CoVs can in addition be activated by host proteases such as cathepsins.

Recently, the ravaging SARS-CoV-2 prompted the development of vaccines to scale down infection severity and mortality rate across the world. These vaccines include: mRNA vaccines such as Moderna and Pfizer - NTech vaccines; vector vaccines such as Johnson & Johnson, AstraZeneca, and the University of Oxford vaccine and; the protein subunit vaccine such as the Novovac vaccine (Forni & Mantovani, 2021). They induce a state of adaptive immunity but do not prevent the acquisition of the virus. The antigenic similarity between SARS-CoV-2 and HCoVs lies in the fact that they express the same surface proteins which act as the antigenic determinants and thus induce a more or less similar immune response. Immunopathogenesis of the HCoVs and SARS-CoV-2 take a similar path. The viruses infect the respiratory airways where they are phagocytosed by the antigen presenting cells (APCs). The APCs release the pathogen- and damage-associated molecular patterns which leads to recruitment of lymphocytes, monocytes and neutrophils.

The overall effect is hyper secretion of pro-inflammatory cytokines inducing a positive feedback and production of antibodies by the b lymphocytes. In an immunocompetent person, this process eliminated the infection and infection manifestations are usually mild to moderate. However, in immunocompromised individual, immune response is dysregulated and exaggerated causing widespread inflammation in the lungs. The antibodies are however short-lived and less frequently undergo somatic hyper mutation (Fung & Liu, 2021). Vaccines against SARS-CoV-2 when given to a patient could potentially induce an immune response against HCoV-2 due to cross-reactivity. It is therefore reasonable to assert theoretically that if antibodies against the SARS-CoV-2 virus lead to enhanced immune response towards common cold HCoVs, then vaccines developed for COVID-19 could be used as prophylactic medicines for common cold due to coronaviruses.

#### IV. DISCUSSION

Most humans have been exposed to the human common cold coronaviruses that have led to production of Abs to neutralize the viruses. However, the infection is usually self-limiting and recurrent. This means that every time the common cold epidemic occurs, individuals have to suffer the cost of not going to work and bearing the feeling of unwellness. This reduces productivity during such times and causes discomfort among the patients. The viral etiologies for the common cold belong to the same family as the virus that has caused the current Coronavirus Diseases-2019 (COVID-19)- the SARS-CoV-2 virus. These two groups of viruses share the same set of proteins they synthesize and express (Liu et al., 2021). Thus, a rational question is do this humoral immune response confer immunity against SARS-CoV-2 infections? Or even reduce the extent of severity of the infection?

Research and clinical studies paint a mixed picture. Some scholars suggest and illustrate that exposure to Human coronaviruses induces the formation of antibodies either monoclonal or mixed that cross-react with antigens present on the SARS-CoV-2 virus, especially the N and the S2 proteins to neutralize the virus lessening disease development and mortality rate (Li et al., 2020, Khan et al., 2020, Mveang Nzoghe et al., 2020, Ma et al., 2020, To et al., 2020). Other studies suggest otherwise that previous exposure to human coronaviruses may lead to the development of Abs but without immunity to the SARS-CoV-2 virus (Guo et al., 2020, Shrock et al., 2020, Anderson et al., 2020, Nguyen-Contant et al., 2020). Overall, SARS-CoV-2-unexposed individuals demonstrate the presence of Abs that cross-react with to SARS-CoV-2 Ags to trigger a weak to moderate immune response in the population.

Contrastingly, other evidence has shown that individuals exposed to SARS-CoV-2 illustrated enhanced responses towards common cold human coronaviruses infections (HCoVs) (Nguyen-Contant et al., 2020, Anderson et al., 2020, Shrock et al., 2020, Yonker et al., 2020, Song et al., 2021). This upregulation of the response is attributed to the cross-reactivity of the SARS-CoV-2 antibodies with the HCoVs and again the antigenic determinants in play here are the S2 and N. Altogether, exposure to the HCoVs or SARS-CoV-2 results in the formation of Abs that cross-react with antigens present on either virus and in particular the S2 and the N protein. Thus, if infection with the SARS-CoV-2 virus causes the development of Abs that cross-react with antigens on HCoVs leading to an upregulated response against the HCoVs, could vaccines against the SARS-CoV-2 virus be used as a prophylactic intervention to scale down infection with common cold HCoVs? Theoretically, this is possible. The main antigenic determinant for the coronaviruses is the spike protein (S) which also functions to facilitate viral attachment and fusion to host cells. It is a type I membrane protein that is cleaved by the host proteases to S1 and S2 subunits.

The Ectodomain of the spike protein is modified by disulfide bonds while its endo domain is palmitoylated. The receptors for this spike protein differ depending on the HCoV in question. HCoV-229E uses the cell surface peptidase-aminopeptidase N as its receptor while SARS-CoV-2 and HCoV-NL63 utilize the angiotensin-converting enzyme as their receptor. HCoV-OC63 and HCoV-HKU1 glycanated receptors having the 9-O-acetylated sialic acid (Liu et al., 2021). This is beneficial since the antigenic determinant; the S protein is similar for all the HCoVs. Although they have disparate receptors in the host for fusion and entry, the immune response that develops usually focuses on the ligand which is the same for all the HCoVs.

The current COVID-19 vaccines are either *mRNA* or viral vector vaccines which when administered induce the body to produce antibodies against the spike protein or the virions' structure which is similar to the structure and spike protein expressed in HCoV. Thus, administration of the COVID-19 vaccines leads to the generation of an immune response aimed at eliminating the main antigenic determinant-the S protein since it evokes endoplasmic reticular stress and provokes immune response induction. As such, when these vaccines are administered in patients co-infected with the common cold HCoVs, cross-reactivity occurs which leads to the generated immune response also fighting and clearing the common cold HCoVs. This furthermore leads to immunological memory which may clear future HCoVs without the development of clinical symptoms which decreases disease burden for chronic common cold patients. Further, to put into consideration, these vaccines against SARS-CoV-2 aim at stimulating the immune system to develop immunologic memory to fight the current and future SARS-CoV-2 infection lessening the disease severity, thus providing a wider scope for an immune response since some of the viruses e.g. Moderna vaccine causes host cells to express the spike protein from the *mRNA* administered.

## I. CONCLUSION

In conclusion, SARS-CoV-2 and common cold HCoVs belong to the same family of coronaviruses and these two groups of viruses express similar types of viral proteins including viral morphology. The main antigenic protein in both groups is the spike protein which though binds to different receptors, largely evokes similar immune responses and cross-reactivity occurs because the two groups of viruses share the same antigenic determinants. Thus, the immune response generated against SARS-CoV-2 can also eliminate and fight HCoVs. Since vaccines against the SARS-CoV-2 induce humoral response against the spike protein, then hypothetically can be used to induce an immune response which due to cross-reactivity, fights and eliminates the HCoVs and thus can be used prophylactically against common cold infections caused by HCoVs.

## II. RECOMMENDATIONS

Based on theoretical review of available literature & perspectives, we recommend as follows:

- COVID 19 vaccines confer partial immunity for common cold (HCoV Ags) and;
- Further research be conducted to accurately identify and quantify the antigenic homology between SARS-CoV-2 and HCoVs

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