



Immunological Features and Hypotheses: Do SARS-CoV and MERS-CoV-Reported Individuals have Immunity against SARS-CoV-2 Infection

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Authors' contributions

This work was carried out in collaboration among all authors. Authors RZ and FDA helped in conceptualization. Authors RZ, NH and HFA did data validation. Authors RZ, RMA, FDA and NH did data curation. Authors RZ and NH wrote original draft of the manuscript. Authors RZ, NH and FDA wrote, reviewed and edited the manuscript. Author RZ supervised and project administration of the study. Authors RZ, HFA, RMA and NH did funding acquisition. All authors have read and agreed to the published version of the manuscript.

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ABSTRACT

COVID-19 spreads abnormally compared to its counterparts in the same family "beta-coronaviruses". Today, we count more than 130 million affected humans affected by the COVID-19. Therefore, the study of means of prevention and treatment is an urgent need. Interestingly, the novel virus (SARS-CoV-2) has some similarities with SARS-CoV and MERS-CoV. It is known that heterologous immunity is well recognized within species of the same family. The use of previously recognized effective antibodies for SARS and MERS virus may prevent the COVID-19 pandemic. The objective of this study is to compare between SARS-CoV, MERS-CoV, and SARS-CoV-2 genomic and proteomic identity/similarity and their cross-immunity as well as their immunological features in the context of COVID-19 diseases prevention and treatment methods.

Keywords: COVID-19; heterologous immunity; SARS-CoV; MERS-CoV; and SARS-CoV-2.

1. INTRODUCTION

Today, the new acute respiratory syndrome caused by the novel coronaviruses called SARS-CoV-2 affected more than 130 million people with a current active cases of 24 million worldwide [1]. The quick and large spread of this new virus is still causing a worldwide panic. The causative new coronavirus (SARS-CoV-2) induces principally pneumonia and respiratory tract troubles. Apparent clinical symptoms can be fever, cough, sore throat, muscle pain (myalgias)/fatigue, headache, shortness of breath, and acute respiratory distress syndrome [2]. This virus has a very negative effect to the elderly and those suffering chronic diseases, but seems less effective in children who either are passive carriers or have only mild symptoms of the disease. Its transmission route still not yet fully defined. However, studies shows the SARS-CoV-2 can be spread through respiratory droplets or close contact with infected surfaces or objects. Also it was found in various samples, such as saliva, stool, and blood [3]. Human coronaviruses have been discovered since the 1960s [4], but the most famous zoonotic coronaviruses identified to the date are the SARS-CoV (China, 2003), MERS-CoV (Saudi Arabia, 2012), and SARS-CoV-2 (China, 2019) [5–7]. These viruses commonly involve serious respiratory tract infections and viral immunopathology. The extremely rapid spread of this virus associated with the absence of specific treatment and vaccine has resulted in a serious public health risk. Since the description of the first COVID-19 cases, hundreds of clinical trials are under running worldwide to get an effective vaccine that can protect against COVID-19. They are based on either the assessment of the effect of the previous published SARS-CoV1 and MERS-CoV potential vaccines on SARS-CoV2 proliferation

or the synthesis of a new SARS-CoV2 vaccine. Recently, several vaccines have been developed against COVID-19. Despite the authorization of using many of them, the effectiveness of these vaccines is still under debate. Here, we aimed to compare the identity as well as similarity of the genomic and proteomic aspects between SARS-CoV, MERS-CoV, and SARS-CoV-2 and their cross-immunity as well as their immunological features in the context of COVID-19 diseases prevention and treatment.

2. GENOMIC AND PROTEOMIC ASPECTS OF SARS-CoV, MERS-CoV, and SARS-CoV-2

Intense interpreting of the SARS-CoV-2 key protein compartment may lead scientists to develop vaccines and medication. It is also important to point out the possibility of the development of cross-neutralizing antibodies (nAbs) for the prevention from SARS-CoV-2 infection and other human coronaviruses. Such hypothesis leads us to think about the possibility of immunization of previously affected patients with SARS-CoV1 or MERS-CoV against SARS-CoV2. Indeed, this hypothesis can be evidenced by the fact that the SARS-CoV-2 genome has similarities to other viruses: approximately 96% similarity to the bat coronavirus BatCoV RaTH13; an estimated 80% similarity with SARS-CoV [8], and an estimated 50% identity with MERS-CoV [9,10]. Moreover, SARS-CoV-2 belonging to the beta-CoV genera in the family coronaviridae, is a single-stranded, capsuled, and positive-sense RNA virus [11–13]. Its genome encodes approximately 16 nonstructural proteins (nsp1–16), four main structural proteins – envelope (E), membrane (M), spike (S), and nucleocapsid (N) which are common features to SARS-CoV and MERS-CoV

[3,14]. The protein S is the main one responsible for virus attachment, fusion, entry and transmission Du et al. 2009, 2017. Protein S glycoprotein forms the peplomers on the virion surface, giving the virus its “corona” – or crown-like morphology in the electron microscope. The membrane (M) glycoprotein and the envelope (E) protein provide the ring structure. Within the virion interior lies a helical nucleocapsid comprised of the nucleocapsid (N) protein complexed with a single positive-strand RNA genome of about 30 kb in length [15].

3. HETEROLOGOUS IMMUNITY

Heterologous immunity is familiar within alike species [16]. A previous study shows that single human monoclonal antibodies with neutralizing activity against SARS-CoV spike can confer broad protection against multiple zoonotic and human SARS-CoV isolates [17]. The use of previously known and efficient neutralizing antibodies of SARS-CoV and MERS-CoV may lead to the prevention and treatment of the COVID-19 pandemic. Interestingly, contrary to the decrease in serum antibody levels in patients, cytotoxic T lymphocyte (CTL) and function-specific N proteins are still detectable from the PBMCs of recovered patients from SARS or MERS in more than 10 years post infection [18–21].

After the emergence of MERS-CoV in 2012, a research team in China has conducted a seroprevalence study on archived sera to assess the evidence for the intrusion of MERS-CoV and related viruses into humans. Therefore, they demonstrated that virulence of SARS-CoV may improve cross-reactive neutralizing antibodies against other β coronaviruses, and convalescent SARS sera may contain cross-reactive antibodies against other β coronaviruses [22]. In the same year (2013), Jiang reported that monoclonal antibodies induced by the epitopes in receptor-binding domain (RBD) of SARS-CoV1 did not cross-react with the RBD and S1 proteins of hCoV-EMC (currently known as MERS-CoV) [23]. By the emergence of COVID-19, the same author with other collaborators have published a systematic review discussing advances in the development of neutralizing antibodies (nAbs) for the prevention from SARS-CoV-2 infection and other human CoVs. Authors reported that: i) many fragments (S1-NTD, RBD, S2) in S proteins can be used as targets to develop nAbs and, ii) RBD-specific antibodies have larger

power to neutralize infection with divergent virus strains [23]. In the same way, Tai et al., have proved that recombinant RBD of MERS-CoVs is an important vaccine targetable to elicit powerful and broad-spectrum cross-neutralizing antibodies against infection by different human and camel MERS-CoVs as well as Antibody Escape Mutants [24]. The same finding was reported for SARS-CoV1 infection. Indeed, He et al., (2006) have demonstrated that RBD of S protein can induce high titers of cross-neutralizing antibodies that can protect against both human and animal SARS-CoV variants [25]. Beside, Rockx et al. reported that a single human monoclonal antibody can offer broad protection against lethal both zoonotic and human SARS-CoV isolates [17].

Other essays for the generation of MERS-Cov vaccine have reported that N and S proteins are the most two highly immunogenic viral proteins able to stimulate T-cells responses. However, only S protein was demonstrated to induce neutralizing antibodies [26]. E viral protein was also described as a potential protective immunogen using *in silico* approach. Nevertheless, no biological data are available so far to confirm this result [27]. In contrast, some studies have reported that the efficacy of SARS-CoV and MERS-CoV antibodies are strain-specific and may offer minimal protection against heterologous or unrelated coronaviruses [28,29].

Other researchers have tried the immunization with DNAs encoding the S1 and S proteins in order to avoid any side effects of using full-length S protein [30]. Interestingly, both DNAs were proven to elicit neutralizing antibodies that cross-reacted with MERS-CoV strains of human and camel origins [31].

Accordingly, previous findings concerning the presence of highly immunogenic SARS-CoV and MERS-CoV proteins able to induce the production of cross neutralizing antibodies provide new insights into protective vaccine against the new emerged SARS-CoV2 and raise the possibility of protecting individuals who were previously infected with SARS-CoV or MERS-CoV.

Our fast study encouraged us to retrospectively further investigate those individuals who previously infected with SARS-CoV or MERS-CoV and their records regarding SARS-CoV2.

4. DISCUSSION

Coronaviruses were initially associated with mild respiratory illnesses. In 2002, SARS-CoV was appeared followed by MERS-SARS in 2012 and recently with SARS-CoV-2 at the end of 2019. With its fast expansion worldwide in just a few months, the WHO has officially declared a pandemic to COVID-19. The virus is transmitted through respiratory droplets or inanimate objects that are infected with the disease.

Governments, scientific societies and others strived to overcome the spread of COVID-19 worldwide. Despite the emerging of some vaccines targeting this disease, a big debate regarding the efficiency and side effects of these vaccines. Additionally, drug treatments are still not satisfying to overcome the spread and illnesses caused by SARS-CoV-2. Therefore, searching novel tools for prevention and treatment of COVID-19 is still needed.

In this article, we highlight the potential immunity of the previously infected individuals by SARS-CoV or MERS-CoV towards SARS-CoV-2. Genomic and proteomic feature of these viruses showed high identity and similarity at the gene and protein levels [10,18,32]. This suggest high cross-immunoreactivities towards these viruses [19–21, 33].

Our article raised the point of the potential immunity of SARS-CoV- and MERS-CoV-pre-infected individuals towards SARS-CoV-2. Therefore, future studies should investigate the prevalence of SARS-CoV-2 infection among SARS-CoV- and MERS-CoV-pre-infected individuals. This will strengthen our hypothesis in the potential of heterologous immunity towards coronaviruses infections. Additionally, our article might open new research directions, for instance using antibodies generated in SARS-CoV- and MERS-CoV-pre-infected individuals for treatment of MERS-CoV-2 and probably any future emerging corona viruses.

5. CONCLUSION

Coronaviruses share high homology and identity at the genome and protein levels. There is cross-immunity towards coronaviruses. These Immunity features should be invested in the treatment of the current pandemic of SARS-

CoV-2 and future potential emerging corona diseases.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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