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Editorial

The COVID-19 Vaccine Development Race Needs a Finishing Line and a Coordinated Utilization of Its Legacy

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The World Health Organization declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant B.1.1.529 as a variant of concern (VOC) named Omicron on November 26, 2021.[1] A few days later, coronavirus disease 2019 (COVID-19) cases attributed to this new VOC were identified in countries other than South Africa (where it was first reported), including Australia, Canada, Israel, the United Kingdom, and several European Union member countries.[1] The alarming spread of the Omicron variant was accompanied by the equally alarming discovery that it bears by far the largest number of mutations among all SARS-CoV-2 variants identified so far; in fact, the SARS-CoV-2 Omicron variant was found to bear approximately 30 mutations in its spike glycoprotein, and half of these mutations were found to be located at the glycoprotein's receptor binding region.[2] These mutations allow for the Omicron variant of SARS-CoV-2 to bind better to the human angiotensin-converting enzyme 2 (ACE2) as well as to animal ACE2 orthologs,[3] but restrict the ability of the virus to transmit via cell fusion through a transmembrane serine protease 2 (TMPRSS2)-dependent process.[4] In practical terms, this means that COVID-19 can spread easier and faster thanks to this new VOC, but the resulting clinical outcome of the infection would be milder due to the inability of the new SARS-CoV-2 variant to transmit in a TMPRSS2-dependent manner throughout the lower respiratory tract, thereby restricting its infection primarily in the upper respiratory tract.[5]

To make things worse, a few months ago, the Omicron sublineages BA.4 and BA.5 emerged,[6] and their rapid spreading was attributed to mutations that enhanced their antibody evading abilities when compared to that of their ancestral Omicron virus.[7]

In this journal, Vidian *et al.* provide an up-to-date and comprehensive account of our understanding of the molecular characteristics of the SARS-CoV-2 Omicron variant, and a good overview of the available prophylactic and treatment options against COVID-19.[8] Although the authors recognise that a continuously evolving SARS-CoV-2 will very likely lead to the emergence of novel VOCs, they also express a balanced view on the efforts that need to be undertaken in order for us (as a scientific community) to better understand how mutations can affect the effectiveness of exposure- and vaccine-induced immune responses.[8]

As we are about to enter the fourth year of the COVID-19 pandemic, the focus has now shifted toward clarifying the most appropriate strategy forward in terms of vaccine updating. The ever-evolving SARS-CoV-2 is likely to become a "new normal" and, as such, COVID-19 vaccines might require regular updates in the same way as the influenza vaccines do.[9] By the time this commentary is published, a new variant might have emerged, in which new mutations might have rendered it more pathogenic and/or antibody-evading, thereby triggering a new racing round for its molecular characterization and the production of updated vaccines. It is hard to predict how the virus will evolve,[10] and as Rita Rubin wrote in an insightful analysis piece published a few months ago in *JAMA*, *"developing variant-based injectable vaccines might seem like a game of whack-a-mole"*.[9]

For many of those not bound by specific interests dictating otherwise, the end in such a vaccine development race might come from the development of a universal vaccine against all SARS-CoV-2 variants; the development of a pan-SARS-CoV-2 vaccine. This perspective should - in my opinion - be prioritized for two reasons.

The first reason is that we have run out of time. We cannot afford the socioeconomic implications of further lockdowns as a time-buying measure for the development of updated vaccines against new VOCs, nor should we expect the willingness of the public to receive boosters on a frequent basis to be unwavering. In light of the profound failure of our public engagement and science communication channels to convince large parts of the general population for the safety and the efficacy of the developed vaccines, a "whack-a-mole" type of gamification of the vaccine development process might prolong the COVID-19 pandemic, direct the SARS-CoV-2 evolution, and further extend the impact of the disease in both its short- and long-term forms.

The second reason is that due to global warming and overpopulation, the infectious disease landscape is expected to be reshaped in an unpredictable fashion over the next decades. New forms of pathogens will emerge, for which confident and immediate responses will be required. The success and the shortcomings of our response to the ongoing COVID-19 pandemic will define our preparedness for these future challenges and, therefore, we need to: (i)

Abbreviations: ACE2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TMPRSS2, transmembrane serine protease 2; VOC, variant of concern.

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focus on delivering a final hit to the disease, (ii) thoroughly understand the implications of our choices so far, and (iii) invest heavily on the technologies developed. The sooner our resources are relieved from the commitment to the fight against an ever-evolving SARS-CoV-2, the sooner we will be able to utilize them against other devastating diseases.

On a final note, Vidian *et al.* need to be praised for underlining the importance of ensuring equal access to approved COVID-19 vaccines for all populations.[8] This is a major issue of moral and epidemiological nature that needs to be more systematically addressed in the future through the channels of science diplomacy.

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Conflict of interest

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Author contributions

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