Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Response to letter to the editor: Immunophenotyping of SARS-CoV-2 and vaccine design

To the Editor,

We thank Dr. Cimolai for the interest in our work and his comments. In this letter, Dr. Cimolai defended the strategy of heterologous vaccination against SARS-CoV-2 and demonstrated its potential benefit from an immunological perspective [1].

Dr. Cimolai elucidated that instead of waiting for several years for communities to develop an immunological memory, mixing different types of COVID-19 vaccines along with the natural infection and hybrid immunity, would tame SARS-CoV-2 and bring it back to the common-cold category, as it has been the case with human coronaviruses causing common cold [1]. This is also what has happened with repeated seasonal infections and annual vaccinations against Influenza virus.

The currently used COVID-19 vaccines produced using epitope-based vaccine design, have so far maintained a high level of protection from severe disease even with the emergence of variants [2].

However, Dr. Cimolai unveils the other side of the coin of such technology [1]. Single epitope-based vaccines would be associated with a strong yet highly selective immune response, which might be the Achilles' tendon of these vaccines. This could parallel the effect of using monoclonal antibodies in pre-emptive COVID-19 therapy. Consequently, deploying multi-epitope based vaccination strategies as with heterologous vaccination would make escape of variants from neutralization less probable. This is analogous to the more effective polyclonal antibody therapy when compared to monoclonal antibodies [3].

In parallel, when looking at heterologous vaccination from a global standpoint, other horizons open up. It was shown that sera from fully vaccinated individuals with 2 doses of BNT162b2, mRNA-1273, and ChAdOx1 neutralized the omicron variant to a much lesser extent than any other SARS-CoV-2 variants, and 3 doses are needed in to achieve acceptable virus neutralisation [4]. So, with the current vaccination strategies, populations that have already received 2 doses still need at least half of what they have already consumed to presumably be fully vaccinated. Nevertheless, disparities in global vaccination progress are large with low-income countries lagging behind, due to the limited access to vaccines, where only 8.9% of people in these countries have received at least one dose [5]. These countries are the ideal "Pandora box" from which variants can emerge. It is ultimately crucial to seal these "Pandora boxes" in order to prevent further emergence of variants which fuel public health crises in the developing world and prolong the pandemic. This can only be achieved through equitable global vaccination. Yet, pursuing vaccine equity is complicated as it is hindered by economic barriers related to the global governance, intellectual property rights, and most importantly vaccine price [6]. In non-vaccine manufacturing low- and middle-income countries, procurement is the major pillar of disease eradication strategy [6]. So far, 6 COVID-19 vaccines are already authorized for human use across the globe. Yet, the vector vaccines have been challenged by major hesitancy due to reported serious side effects [7], and the inactivated whole-cell vaccines are not popular due to the reported low efficacy and effectiveness [8]. Consequently, so far, there is no established fair and price-setting mechanisms for the mRNA vaccines [6].

Making use of different vaccine technologies in heterologous protocols would alleviate the high demand on the mRNA vaccines. Consequently, the need for "difficult-to-get" vaccines would be cut by half in heterologous primary vaccination or by a third in heterologous boosting.

In conclusion, vaccine research based on sound immunological arguments, as provided by Dr. Cimolai, would open up new horizons in vaccine procurement thus contributing to the efforts needed to achieve global vaccine equity for COVID-19.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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