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

Immunophenotyping of SARS-CoV-2 and vaccine design

Letter to the Editor,

The recent publication of Moghnieh et al. stimulate potentially important and refreshing strategies for the evolution of more completely protective SARS-CoV-2 vaccines [1]. They provided evidence for a more robust immune response after heterologous vaccination. The design of future placebo-controlled human vaccine studies in the current context of variably effective vaccines is likely to stir some controversy. That would not preclude testing of mixtures of infection and vaccination in animal models. Even if currently available vaccines lose efficacy over time or even if variants of concern are associated with a decrease in vaccine efficacy, the current vaccines yet maintain sufficient coverage at least for serious disease and for a considerable proportion of those vaccinated. Regardless, it is inevitable that both nature and human experimentation will truly test hypotheses of heterologous vaccination or combinations of natural infection/vaccination over the next year as exposure mounts to a collective of purposeful vaccines, early virus strains, and emerging variants.

The current strategies of vaccination with few available vaccine candidates will be associated with highly selective immune responses regardless of their potency or number of administrations. It has already become apparent that effective monoclonal antibodies from both animal and human experimentation will lose their efficacy, and hence a polyclonal response is more likely to be efficacious and required over time [2,3]. For previously common endemic human coronaviruses, strain variation has been proposed [4]. Repeat infection among the latter is also recognized [5]. Despite these findings, serious disease is relatively uncommon with past endemic coronaviruses, and it is apparent that a cumulative resistance has evolved over time with multiple natural exposures. The dilemma with SARS-CoV-2 is that any such cumulative immunity is being sought over a much more narrow window and for extremely large populations.

Although variants of SARS-CoV-2 are commonly being characterized through the determination of mutations that vary from the common original strain(s), the extent of impact for these changes is being measured immunologically and clinically. In essence, variants of concern are being categorized both genetically and with a view of their medical impact. For decades, a predominantly immunological categorization of virus strain variation was relied upon through serotyping or serogrouping. Whether among experimental systems or with the aid of post-infectious sera, immunophenotyping methods were utilized to determine the significant variation among many viruses. From animal coronavirology, the definition of disease-relevant serotypes or serogroups has long been a topic of study [6–9]. Similar immunologically-based diversity was proposed in the study of SARS-CoV-1 [10]. Assessments of MERS-CoV did not find strain heterogeneity, but the experience may indeed be relatively limited in comparison to the massive number of infections that have occurred with SARS-CoV-2 or animal coronaviruses to date [11].

Given the size of the coronavirus genome and given the inherent limitation in significantly immunoreactive epitopes, it is quite conceivable that serotypes or serogroups will be defined for SARS-CoV-2. Cele et al. have begun to steer us in that direction with the recognition of what they term serological phenotypes [12]. A comparison to influenza vaccinology and natural infection is quite appropriate. In the long term, repeat exposure to wild-type virus and repeat exposures to vaccines have been met with generalized populace protective efficacy for whatever strength that may be. Equally, the natural or directed experiments for SARS-CoV-2 immunity will be needed to assess protection that evolves after repeat infection and vaccination. As such, post-infection or post-vaccination immunity can be assessed against virus variants as they emerge for whatever genetic mutation(s) that arises. These assessments will best direct the design and use of vaccine variants or their combinations for protective efficacy. The experimentation of human vaccination in these regards should not fear polyclonal responses nor the theoretical risk of immunological imprinting or back-boosting [13]. Rather, the main challenge will be what form of vaccination should be used to make any such assessments, and in this light, the advent of component vaccines will undoubtedly provide some assistance for devising monovalent or polyvalent vaccines. Indeed the availability of monoclonal antibodies and their determination of immunological escapes may go a long way in characterizing clinically relevant immunological phenotypes.

Declaration of Competing Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Keywords:
COVID-19; SARS-CoV-2; Serogroup; Vaccine; Immunization

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