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REVIEW
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An Update on Protective Effectiveness of Immune Responses After Recovery From COVID-19

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exhibits variable immunity responses among hosts based on symptom severity. Whether immunity in recovered individuals is effective for avoiding reinfection is poorly understood. Determination of immune memory status against SARS-CoV-2 helps identify reinfection risk and vaccine efficacy. Hence, after recovery from COVID-19, evaluation of protective effectiveness and durable immunity of prior disease could be significant. Recent reports described the dynamics of SARS-CoV-2 -specific humoral and cellular responses for more than six months in convalescent SARS-CoV-2 individuals. Given the current evidence, NK cell subpopulations, especially the memory-like NK cell subset, indicate a significant role in determining COVID-19 severity. Still, the information on the long-term NK cell immunity conferred by SARS-CoV-2 infection is scant. The evidence from vaccine clinical trials and observational studies indicates that hybrid natural/vaccine immunity to SARS-CoV-2 seems to be notably potent protection. We suggested the combination of plasma therapy from recovered donors and vaccination could be effective. This focused review aims to update the current information regarding immune correlates of COVID-19 recovery to understand better the probability of reinfection in COVID-19 infected cases that may serve as guides for ongoing vaccine strategy improvement.

Keywords: recovered, hybrid immunity, vaccination, cellular immunity, COVID-19

INTRODUCTION

About two years after the first identified coronavirus disease 2019 (COVID-19) outbreak, it is still hard to precisely anticipate when the pandemic will finally end, and the protective immunity status in patients after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is a global concern (1, 2). Investigating whether cellular immune response and humoral immunity against SARS-CoV-2 are associated with a decreased risk of reinfection could be a vital issue. In light of determining the future dynamics of SARS-CoV-2 circulation, it is critical to clarify how frequently natural infections with SARS-CoV-2 stimulate that level of protection (3). Evaluating

infection-derived immunity and vaccination prompt multifaceted, functional immune memory; some studies have highlighted that vaccination–derived immune response following natural immunity boosts the immunity, termed hybrid immunity (6, 110). A study carried out by Goldenberg et al. (84) demonstrated that infection by the Delta variant of SARS-CoV-2 has led to a more potent immune response as compared with the BNT162b2 two-dose vaccine-derived immunity, meanwhile; patients who were recovered from SARS-CoV-2, and were then vaccinated by a single dose of the vaccine acquired increased protective response against the Delta variant. There seem to be specific memory lymphocytes, both B cell and T cell components, to hybrid immunity. It is indicated that in the context of reinfection after natural immunity alone or vaccination of naïve individuals, there is a reduction in the level of antibody-mediated immunity against variants of concern (VOCs) (111), but after one dose of vaccination following the previous infection with former VOCs the immunity rises. It should be noted that neutralizing antibody drops are not due to low antigenicity and spike protein mutations of the VOCs. It is exemplified in a study that found in re-infected patients with B.1.351(Beta) variant (previously infected with non-B.1.351), neutralizing antibodies against this variant after vaccination were shown to be 25 times higher than after vaccination (no involved B.1.351 spike) (112, 113). When natural immunity to SARS-CoV-2 is combined with vaccine-induced immunity, it has been found that higher SARS-CoV-2 RBD-specific memory B cells and variant-neutralizing antibodies and a specific population memory SARS-CoV-2 spike-specific CD4+ T cells than previously naive individuals are generated (114). In this line, the production of diverse memory B cells needs T cells and their cytokine profile. Even if the function of antibodies neutralizing is failed against variants, memory T cells can recognize SARS-CoV-2 variants (99), and in hybrid immunity, T cell memory consists of both spike and non-spike T cell memory, unlike the vaccine-induced memory T cell which involves spike –memory T cells. Furthermore, the mutation does not occur in most epitopes of T cells in new variants, demonstrating that the protective role of T cells' immunity is preserved (115).

CONCLUSION

During recovery, the investigation of cellular and humoral immunity among COVID-19 patients with different disease manifestation could run additional insights into the roles of these cell types during natural host immunity. In addition, the clarification of the recovery and immunity process leads to making the proper decisions by policymakers for screening and lockdown, and improved diagnostic assessments of re-infection in individuals. A combined natural/vaccine immune response to SARS-CoV-2 seems to be a notably potent accompanist. According to this concept, more investigation of combinations of SARS-CoV-2 vaccines with different platforms, such as mRNA and adenoviral vectors or mRNA and recombinant protein vaccines, could be appreciated. Moreover, the breadth of recognition of epitopes through T cells, both CD8 and CD4 lymphocytes, may guide ongoing vaccine strategy improvement. In addition, the study of NK cells alongside the evaluation of cytokine profiles (116, 117) in the hybrid immunity can offer information for understanding which vaccines can cross that threshold of hybrid status to confer individual and herd immunity. Since hybrid immunity may be a reproducible way to enhance immunity, the combination of plasma therapy from recovered donors and vaccination could be effective; however, it needs further support from future studies for selecting the best donors to produce off-the-shelf living drugs.

AUTHOR CONTRIBUTIONS

SS devised the main conceptual ideas and designed the figures. SS, NS, and ZGH wrote the manuscript with input from all authors. SS devised the main conceptual ideas and designed the figures. SS, NS, and ZGH wrote the manuscript with input from all authors.

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