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.

Cellular Immunology 353 (2020) 104114

Contents lists available at ScienceDirect

Cellular Immunology

journal homepage: www.elsevier.com/locate/ycimm

Protective immunity after COVID-19 has been questioned: What can we do without SARS-CoV-2-IgG detection?

A B S T R A C T

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induces a severe acute respiratory syndrome that is called COVID-19. Clinical manifestations of COVID-19 include diarrhea, pneumonia, lymphopenia, exhausted lymphocytes, and pro-inflammatory cytokine production. Immunology is part of the process of clinical evolution, but there are some questions around immunity-based protection: (1) why some infected people have only mild symptoms of the disease or are asymptomatic; (2) why delayed and weak antibody responses are associated with severe outcomes; and (3) why positivity in molecular tests does not represent protective antibody IgG. Perhaps T cell responses may be the key to solving those questions. SARS-CoV-2-specific memory T cells persist in peripheral blood and may be capable of providing effective information about protective immunity. The T cells studies can be helpful in elucidating the pathways for development of vaccines, therapies, and diagnostics for COVID-19 and for filling these immunology knowledge gaps.

Currently, the world is experiencing a novel and highly transmissible coronavirus (SARS-CoV-2) outbreak, which also causes high mortality [1,2]. SARS-CoV-2 induces a severe acute respiratory syndrome, termed COVID-19, in which immunology is part of the process of clinical evolution consisting of lung tissue damage induced by an inflammatory response, such as a cytokine storm and macrophage and neutrophil activation [1,2]. A few studies have presented information about the immune response during this infection, which involves antibody production and lymphocyte T cell activation, but the information is restricted to those patients who were hospitalized because they had the virus and were symptomatic. Over the course of the disease in the hospitalized patients who recovered, antibody production was shown to increase after the first week of symptom onset, which is suggestive positive correlation with disease severity [3,4] while T cells were also activated; it seems that memory phenotype also showed an increase after 14 days of hospitalization [5,6]. However, there are some questions around immunity-based protection with respect to who does and does not need hospitalization. The non-hospitalized population is considered a viral host by carrying the virus around and contributing to the spread of the virus. Also, the other barrier in this outbreak is related to asymptomatic cases, mainly in health care professionals in the hospital, which could contribute to the increase in the number of cases. The solution to stopping the viral spread appears to be social distancing and massive testing, mainly for antibody detection. Surprisingly, some people who presented positivity in results from the molecular test did not have detectable levels of protective antibody IgG; furthermore, neutralizing antibodies were low or not at all present even in hospitalized patients [3,4]. This situation raises questions about protective immunity and about the time needed for quarantine. Given that, a few studies have already shown that T cells might be the key to solving this dilemma. Despite the finding that the virus can induce lymphopenia and cause a delay in T cell pathway activation during the first days of infection, after two weeks of symptoms, SARS-CoV-2-specific memory T cell phenotypes (central memory for CD4 and effector memory for CD8 lymphocytes) start to emerge in the peripheral blood. This process is capable of providing useful information about protective immunity [6]. The data that are needed to describe how the memory phenotypes of T cells can differentiate has not been elucidated yet. The minimal amount of information is restricted to preprinted manuscripts, but it is enough to start a discussion about how the immune response should be evaluated. Nowadays, we have some vaccines targeting only T cell activation, thus providing robust memory T cell response, but these studies are still in the preclinical phase. Actually, we have seen a change in the protective immunity status of viral diseases during vaccination in which no antibody detection does not relate to protective status because memory T cells can be activated and protect people from subsequent reinfection [7,8]. Regarding respiratory infections, it also should be noted that viruses are constantly changing via the induction of viral mutations that can contribute to the viral escape of the host immune system. One of our hypotheses concerning the novel coronavirus suggest it has the power to reduce B cell activity. This pathway should be further explored. There is urgent need for solutions addressing the time needed for quarantine in order to prevent shutting the economy down. There may be an answer to this problem in cellular response assays, in which the cost is similar compared to neutralizing antibodies tests. Once we can evaluate a small subpopulation that does not produce IgG antibodies, but has activated T cells after disease, this will be enough to guarantee the immunity protection. Lymphocyte T cell assays have high specificity and sensitivity. There is a lot of information about how to assay T cell immunity after infection, such as proliferation assays using viral particles as stimulators [9,10] and also by optimizing the assays in Biosafety Level 2 labs. The T cell assays could help estimate the population's (hospitalized or not) immunity and will be feasible for countries with specialized immunology laboratories. Adding to that, the cellular assays will provide information that is useful for vaccine development to prevent and control this viral disease.

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.

https://doi.org/10.1016/j.cellimm.2020.104114
Received 23 April 2020; Received in revised form 25 April 2020; Accepted 26 April 2020
Available online 28 April 2020

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cellimm.2020.104114.

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