

Effective T-Cell Immunity against Various Coronaviruses

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ABSTRACT

The large clinical spectrum of 2019 coronavirus disease (COVID-19) reveals widespread intra-individual variations in host immune response against coronavirus 2, severe acute respiratory syndrome (SARS-CoV-2).

Keywords: SARS-CoV-2, T-Cell Immunity, CD4+

INTRODUCTION

It is possible that the underlying cause of disease heterogeneity is multifactorial. However, before spreading to the lower respiratory tract and the initiation of damaging hyperinflammation, a rapid early host reaction is likely critical to generating control of SARS-CoV-2 viremia [1]. In this respect, there are several examples in the literature where functional T cell responses may provide early control of acute viral infections, including SARS-CoV and Middle East coronavirus respiratory syndrome (MERS-CoV). While several studies have shown that T cells play a role in the early immune response to SARS-CoV-2 and are capable of generating a functional memory pool, the field still has several unanswered questions. Here, we summarise and speculate on a particular collection of questions relating to the immunity of T cells to respiratory viral infections, concentrating on the magnitude, immunity, long-term effects and vaccination of COVID-19 [2]. T cells are important for early control and clearance of many respiratory system viral infections. Recent studies in transgenic mouse models have shown that T cells are also critical for viral clearance after SARS-CoV-2 infection and disease resolution. T cell activation is therefore expected to have emerged as a hallmark of acute COVID-19, perhaps as a result of an early SARS-CoV-2-specific cellular immune response. While early T cell reactions may play a critical role in reducing the severity of the disease, there are also reports describing a pattern of dysregulated and unregulated activation of T cells in severe cases. Increased activation of T cells in extreme cases is likely to indicate increased levels of antigen in the respiratory system, but it remains to be determined if the early T cell response enters a state of exhaustion in individuals with severe hyperinflammation. In addition, because COVID-19 is a respiratory tract disease, it will be necessary to define whether early detection of the activation of T cells in the blood is associated with tissue-specific events. For example, will the later onset of cellular immunity in the respiratory tract indicate the delayed identification of SARS-CoV-2-specific T cells in the blood, or are these two compartments independent of each other in relation to the severity of the disease?

If it would be helpful to dampen COVID-19 intensity if eliciting an early T cell response, then what could be the underlying causes and correlates of an early versus late onset of SARS-CoV-2-specific T cell activity? Old age and male gender are also associated with an increased risk of complications with COVID-19 [3]. After SARS-CoV-2 infection, females tend to have a much stronger T cell activation. T and B cell coordination disruption has been implicated in elderly patients with extreme COVID-19. In hospitalised paediatric patients who have shorter periods of stay compared with their adult counterparts, reduced frequencies of IFN- γ +CD4+ and CD25+CD4+ T cells have been identified at the other end of the age spectrum. Host and viral factors are also likely to play a role in early immune protection and synchronisation of the early SARS-CoV-2-specific T cell response in relation to age and sex. SARS-CoV-2, for example, has mechanisms for antagonising proinflammatory signals, especially interferon type I (IFN-I) signalling. IFN-I proteins are essential inflammatory mediators that initiate antiviral defence, which could lead to delayed clearance of SARS-CoV-2 through viral evasion [4]. This is confirmed by the finding that inborn immunity errors and autoantibodies that decrease IFN-I activity are more frequently found in serious COVID-19 patients. Our scientific understanding of T cell responses to SARS-CoV-2 has been greatly improved by collective efforts, but several unknowns remain to be addressed. Although it is clear that T cells play a central role in generating early control and clearance of many viral infections, their role in the infection of SARS-CoV-2 is only beginning to be revealed. Specific T cells can also have a negative effect on the clinical outcome, contributing to long-term effects of COVID.

CONCLUSION

In order to identify the beneficial versus detrimental aspects of SARS-CoV-2-specific T cells in acute, convalescent, and vaccine settings of COVID-19, there is currently a need for further research using both animal models and longitudinal follow-up studies of large patient cohorts.

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Received: January 28, 2020; **Accepted:** February 12, 2021; **Published:** February 19, 2021

Citation: Zianua F, (2021) Effective T-Cell Immunity against Various Coronaviruses. J Cell Signal. 6:222.

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