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Editorial

Adaptive Immune Responses to SARS-CoV-2 in Recovered Severe COVID-19 Patients

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EDITORIAL NOTE

There is an imperative need to determine the durability of adaptive immunity to SARS-CoV-2. We enumerated SARS-CoV-2-reactive CD4+ and CD8+ T cells targeting S1 and M proteins and measured RBD-specific serum IgG over a period of 2-6 months after symptoms onset in a cohort of subjects who had recovered from severe clinical forms of COVID-19.

We recruited 58 patients (38 males and 20 females; median age, 62.5 years), who had been hospitalized with bilateral pneumonia, 60% with one or more comorbidities. IgG antibodies binding to SARS-CoV-2 RBD were measured by ELISA. SARS-CoV-2-reactive CD69+-expressing-IFNγ-producing-CD4+ and CD8+ T cells were enumerated in heparinized whole blood by flow cytometry for ICS. Detectable SARS-CoV-2-S1/M-reactive CD69+-IFN-γ CD4+ and CD8+ T cells were displayed in 17 (29.3%) and 6 (10.3%) subjects respectively, at a median of 84 days after onset of symptoms (range, 58-191 days). Concurrent comorbidities increased the risk (OR, 3.15; 95% CI, 1.03-9.61; P=0.04) of undetectable T-cell responses in models adjusted for age, sex and hospitalization ward. Twenty-one out of the 35 patients (60%) had detectable RBD-specific serum IgGs at a median of 118 days (range, 60 to 145 days) after symptoms onset. SARS-CoV-2 RBD-specific IgG serum levels were found to drop significantly over time.

Several major findings arose from our study. First, SARS-CoV-2-S1/M-reactive-IFN-γ CD4+ and CD8+ T cells were detected in a limited number of recovered patients from severe COVID-19 (around 30% and 10% for CD4+ and CD8+ T cells, respectively). Furthermore, we were unable to document SARS-CoV-2 T-cell reactivity beyond day 130 after COVID-19 diagnosis.

A large body of evidence has accumulated on the features of SARS-CoV-2-specific adaptive immunity in patients who recovered from mild or severe clinical forms of COVID-19. To our knowledge, these studies mostly involved recently recovered patients (up to 3 months from onset of symptoms), of whom a large percentage (45-95%) consistently exhibited both T- and B-cell responses. The dynamics of such immune responses beyond this time point remains largely unexplored.

All 58 patients in this cohort developed severe forms of COVID-19 requiring hospitalization either in the intensive care unit (ICU) (n=21) or in other hospital wards (n=37). All patients presented with bilateral pneumonia and 60% had one or more comorbidities, including diabetes mellitus, asthma, hypertension, dyslipidemia, cancer or chronic lung disease. All ICU patients underwent mechanical ventilation. Median hospitalization of patients was 16 days (range, 6-61 days). Patients in the two groups were matched for age, sex and comorbidities.

A relatively limited number of subjects who developed severe forms of COVID-19 had detectable SARS-CoV-2-S1/M IFNγ CD4+ and CD8+ T cells at midterm after clinical diagnosis. Our data also indicated that serum levels of RBD-specific IgGs decline over time, becoming undetectable in some patients.

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