Mild COVID-19 cases can produce strong T cell response

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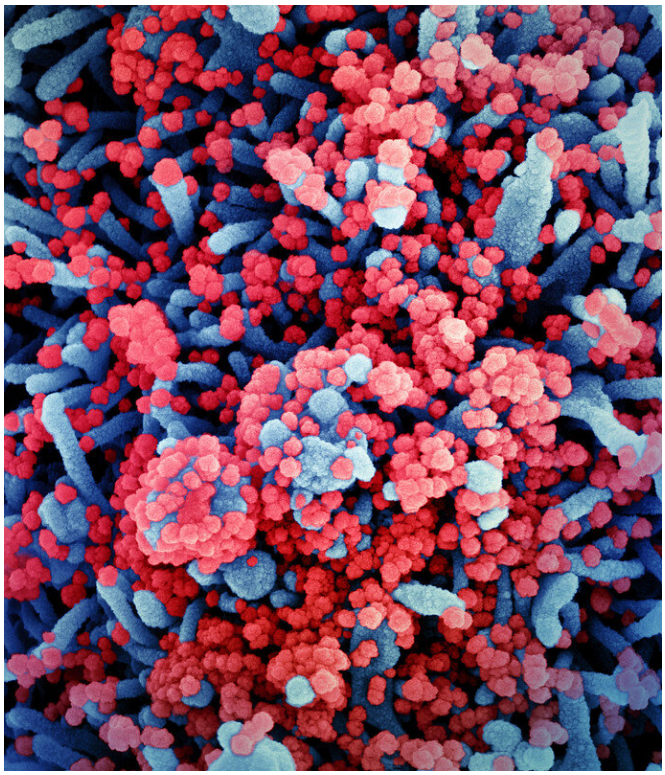

Colorized scanning electron micrograph of a cell (blue) heavily infected with SARS-CoV-2 virus particles (red), isolated from a patient sample. Image captured at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID

Mild cases of coronavirus disease 2019 (COVID-19) can trigger robust memory T cell responses, even in the absence of detectable virus-specific antibody responses, researchers report August 14 in the journal *Cell*. The authors say that memory T cell responses generated by natural exposure to or infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—the virus that causes COVID-19—may be a significant immune component to prevent recurrent episodes of severe disease.

"We are currently facing the biggest global health emergency in decades," says senior author Marcus Buggert of the Karolinska Institutet. "In the absence of a protective vaccine, it is critical to determine if exposed or infected people, especially those with asymptomatic or very mild forms of the disease who likely act inadvertently as the major transmitters, develop robust adaptive immune responses against SARS-CoV-2."

To date, there is limited evidence of reinfection in humans with previously documented COVID-19. Most studies of immune protection against SARS-CoV-2 in humans have focused on the induction of neutralizing antibodies. But antibody responses tend to wane and are not detectable in all patients, especially those with less severe forms of COVID-19. Research in mice has shown that vaccine-induced memory T cell responses, which can persist for many years, protect against the related virus SARS-CoV-1, even in the absence of detectable antibodies. Until now, it was not clear how SARS-CoV-2-specific T cell responses relate to antibody responses or to the clinical course of COVID-19 in humans.

To address this gap in knowledge, Buggert and his collaborators assessed SARS-CoV-2-specific T cell and antibody responses in more than 200 individuals from Sweden across the full spectrum of exposure, infection, and disease. During the acute phase of infection, the T cell responses were associated with various clinical markers of disease severity. After recovery from COVID-19, SARS-CoV-2-specific memory T cell responses were detectable. The strongest T cell responses were present in individuals who recovered from severe COVID-19. Meanwhile, progressively lower T cell responses were observed in individuals who recovered from very mild COVID-19, and family members exposed to the virus.

In line with expectations, all 23 individuals who recovered from severe COVID-19 developed both

SARS-CoV-2-specific antibody and T cell responses. But surprisingly, SARS-CoV-2-specific memory T cell responses were detected months after infection in exposed family members and in most individuals with a history of very mild COVID-19, sometimes in the absence of SARS-CoV-2-specific antibodies. Among the 28 exposed family members, only 17 (a few more than half) had detectable antibody responses, whereas nearly all (26/28) showed T cell responses. Among the 31 individuals who recovered from mild COVID-19, almost all had detectable antibody responses (27/31) and developed T cell responses (30/31).

"Our findings suggest that the reliance on antibody responses may underestimate the extent of population-level immunity against SARS-CoV-2," Buggert says. "The obvious next step is to determine whether robust memory T cell responses in the absence of detectable antibodies can protect against COVID-19 in the long-term."

More information: Takuya Sekine et al, Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19, *Cell* (2020). DOI: 10.1016/j.cell.2020.08.017

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