IMMUNOLOGY

Cross-reactive T cells

Cell **181**, 1489–1501 (2020)

Credit: Yulia Reznikov / Moment / Getty

Antibodies are only half of the story of acquired immunity to viral infections. $CD8^+$ T cells recognize and kill infected host cells, while $CD4^+$ T cells instruct and coordinate the host immune response.

Grifoni et al. characterized the $CD4^+$ and $CD8^+$ T cell responses to SARS-CoV-2 peptides in circulating white blood cells (PBMCs) of 20 convalescing patients with COVID-19. All patients had $CD4^+$ T cells, and 70% had $CD8^+$ cells, that responded to the SARS-CoV-2 antigens tested.

More surprisingly, when the authors stimulated PBMCs from 11 healthy control participants collected between 2015 and 2018, approximately half of the samples showed cross-reactive activation of $CD4^+$ T cells by SARS-CoV-2 antigens. The authors also detected cross-reactivity in $CD8^+$ T cells, although this was less strong and less frequent. Pre-existing cross-reactive immunity of both T cells and B cells to SARS-CoV-2 antigens has since been demonstrated by several groups, although its importance, if any, remains unclear. *TC*

https://doi.org/10.1038/s41591-020-01161-0

PEDIATRICS

COVID-19-induced Kawasaki disease

Lancet **395**, 1771–1778 (2020)
Cell https://doi.org/10.1016/j.cell.2020.09.016 (2020)

Children and young adults usually experience a mild form of COVID-19. However, in May, medical doctors in Bergamo, Italy, the city hardest hit by COVID-19, reported a cluster of children with features of the pediatric vascular inflammatory syndrome Kawasaki disease. The absolute number of cases was small — 10 children in a region that had, at that point, seen more than 130,000 cases of COVID-19 — but it represented a 30-fold increase in the local incidence of Kawasaki disease.

The authors noted that five of the ten patients had an acute form of the disease: Kawasaki disease shock syndrome. Affected children were also on average older than the normal age for the diagnosis of Kawasaki disease and showed more cardiovascular involvement. A rare but serious pediatric complication of COVID-19, multisystem inflammatory syndrome in children, has since been described. *TC*

https://doi.org/10.1038/s41591-020-01163-y

VACCINES

Vaccines in the fast lane

https://clinicaltrials.gov/ct2/show/NCT04283461
Lancet **395**, 1845–1854 (2020)

The urgent need to develop a vaccine against SARs-CoV2 compressed the normal vaccine-development timeline to reach in-human clinical trials from several years to just over two months, and a vaccine developed by Moderna was the first to reach this stage in March.

In late May, CanSino Biologics was the first to publish their trial results of a vaccine against COVID-19 in a peer-reviewed journal. CanSino's candidate is an adenoviral construct that expresses the SARS-CoV-2 spike glycoprotein. It was found to be immunogenic, with most of the 108 participants developing specific antibody and T cell responses. Although 81% of the immunized participants reported moderate adverse effects, no serious adverse reactions occurred. So far, no conclusive information on efficacy is available for CanSino's, or any other, vaccine candidate. *TC*

https://doi.org/10.1038/s41591-020-01167-8

TRANSMISSION

Silent spread

J. Am. Med. Assoc. **14**, 1406–1407 (2020).
N. Engl. J. Med. **382**, 970–971 (2020)

Containment of COVID-19 is made difficult because, unlike SARS-CoV and MERS-CoV, SARS-CoV-2 is commonly spread by people showing no symptoms.

Two early reports monitoring contacts of people who traveled from the initial epicenter of the epidemic (Wuhan, China) sounded the alarm. Five family members in Anyang, China, were diagnosed with COVID-19 following the return of a relative from Wuhan. The index case tested positive for SARS-CoV-2 by PCR but did not develop symptons, indicative of asympomatic transmission fom this person. A different cluster, in Germany, was seeded by a traveller from Wuhan who was not symptomatic during her stay in Germany but later developed fever and a cough indicative of presymptomatic transmission.

While the relative role of asymptomatic and presymptomatic transmission in SARS-CoV-2 spread remains contentious, spread by people showing no symptoms is a hallmark of COVID-19. *TC*

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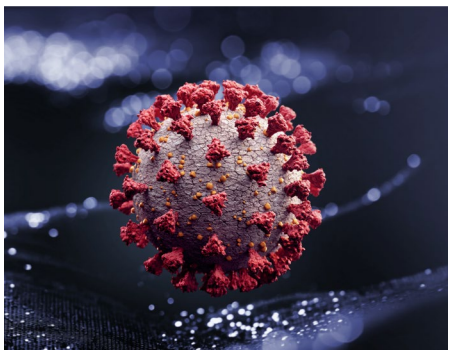
VIRAL ENTRY

ACE2, the viral gateway

Cell **181**, 894–904 (2020)
Cell **181**, 281–292 (2020)



Credit: Radoslav Zilinsky / Moment / Getty

On the basis of sequence information and knowledge of the cellular entry route of other coronaviruses, the host protein angiotensin-converting enzyme 2 (ACE2) was a prime candidate for the binding partner of the SARS-CoV-2 spike protein to enable viral entry.

Walls et al. showed that this spike protein enables SARS-CoV-2 to infect ACE2-expressing cells in vitro, and described a novel enzymatic cleavage site in the SARS-CoV-2 spike protein, which the authors propose may diversify the virus' tissue tropism. The crystal structure of the C-terminal domain of SARS-CoV-2 spike protein bound to human ACE2 generated by Wang et al. predicts that the SARS-CoV-2 spike protein binds its target with greater affinity than that of its relative, SARS-CoV.

The two studies support the development of therapeutic and immunological strategies that target the viral spike protein's ACE2-binding domains, and ACE2 expression in human tissues may explain both pulmonary viral tropism and extrapulmonary viral tropism. *TC*

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