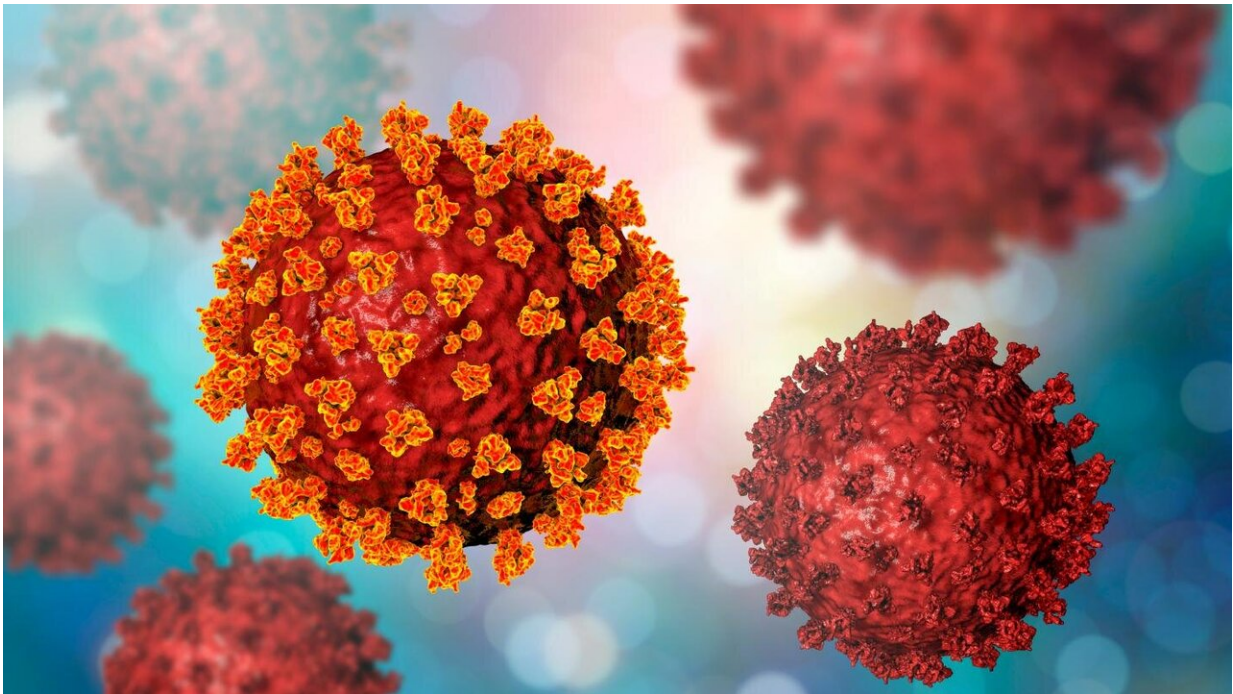


Scientists identify 'immune cop' that detects SARS-CoV-2

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The virus SARS-CoV-2, which causes COVID-19. Credit: Sanford Burnham Prebys Medical Discovery Institute

Scientists at Sanford Burnham Prebys Medical Discovery Institute have identified the sensor in human lungs that detects SARS-CoV-2 and signals that it's time to mount an antiviral response. The study, published today in *Cell Reports*, provides insights into the molecular basis of severe disease and may enable new strategies for the treatment and prevention

of COVID-19.

"Our research has shown that MDA-5 is the immune cop that's tasked to keep an eye out for SARS-CoV-2 and call for back-up," says Sumit Chanda, Ph.D., director of the Immunity and Pathogenesis Program at Sanford Burnham Prebys and senior author of the study. "MDA-5 recognizes replicating viruses in lung cells and activates interferon, the body's own frontline defender against viral invasion. Without a proper interferon response, [viral infections](#) can lead to deadly, out-of-control inflammatory reactions."

The new study surveyed 16 viral RNA binding proteins in human lung [epithelial cells](#) and identified MDA-5 as the predominant sensor responsible for activating interferon. MDA-5 detects double-stranded viral RNA—a form that the SARS-CoV-2 virus takes when it replicates to spread the infection. Prior to this research, it was known that activating interferon is key to a coordinated [immune response](#) to the virus, but the sentinel switch that controls the process was unknown.

"Understanding the biology of a virus and how it is detected is paramount to controlling infection and disease spread," says Chanda. "SARS-CoV-2 appears to disable the innate immune arm of our surveillance system, which, in the case of SARS-CoV-2 is controlled by MDA-5, and prevents the activation of interferon. It's the interferon response that drives the subsequent activation of many genes that exert antiviral activities—and data suggests that we need this activity to control early stages of viral infection and avoid the worst outcomes of COVID-19.

"Whether our bodies can defeat the virus's offensive tactics and activate interferon greatly influences the severity of disease. Past studies have shown that interferon responses are higher in patients with mild-to-moderate cases compared to reduced levels in critically ill patients," adds

Chanda.

According to the World Health Organization, as of January 2020 there have been nearly 87 million confirmed cases of COVID-19, including nearly 1.9 million deaths. Although remdesivir and two antibody treatments have received emergency use authorization by the FDA, cases continue to rise. Newly approved vaccines are rapidly being deployed worldwide to end the crisis, however a handful of people are experiencing severe allergic reactions to the shots.

"There is still a tremendous need to develop effective therapies for COVID-19 and to prepare for future outbreaks," says Chanda. "It's possible that patients who become critically ill are deficient in the interferon signaling pathway. This research opens new avenues toward therapies that enhance the MDA-5 signaling to boost interferon levels early in infection to prevent severe disease.

"It also creates opportunities to develop COVID-19 vaccines that include an adjuvant(s) to enhance MDA-5 signaling. These would be formulations that use less 'vaccine' to minimize toxicity and side effects," adds Chanda.

More information: Xin Yin et al. MDA5 Governs the Innate Immune Response to SARS-CoV-2 in Lung Epithelial Cells. *Cell Reports*. DOI:doi.org/10.1016/j.celrep.2020.108628

Provided by Sanford Burnham Prebys Medical Discovery Institute

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