

Virus that causes COVID-19 puts a plug in cellular defenses

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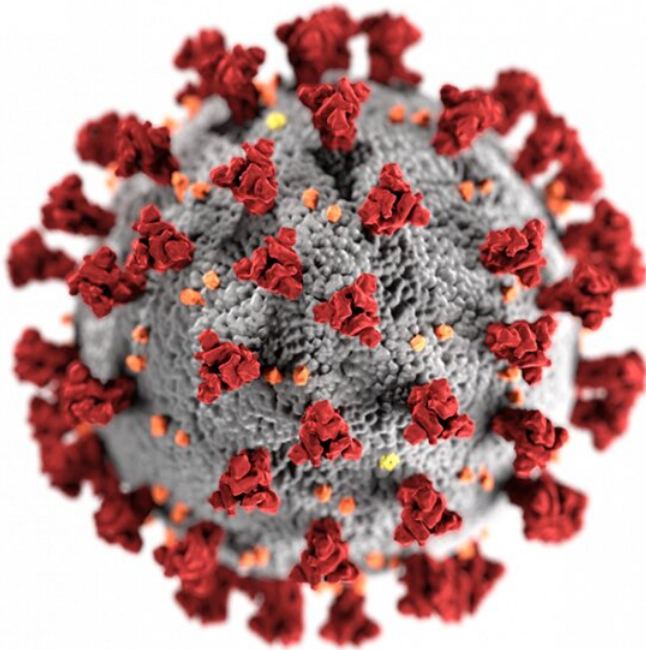


Image of the ultrastructural morphology exhibited by the 2019 Novel Coronavirus (2019-nCoV). Credit: CDC

One of the novel coronavirus' most insidious tricks is that it can block the ability of cells to produce protective proteins without hindering its own ability to replicate.

Now, a multidisciplinary team of Yale researchers has discovered how SARS-CoV-2, the virus that causes COVID-19, accomplishes this trick by blocking production of cellular proteins, including immune molecules, and contributes to severe illness in its host.

"The virus essentially reprograms host cells, and by understanding this mechanism we can hopefully design new therapeutics," said Yong Xiong, professor of molecular biophysics and biochemistry and co-corresponding author of the research published in the journal *Molecular Cell*.

Previous studies had implicated a [viral protein](#), nonstructural protein 1 or Nsp1, in the COVID-19 virus' ability to block cells' ability to produce new proteins. But exactly how Nsp1 works in a cell was not known.

Using advanced genetic screening and [cryogenic electron microscopy](#) (cryo-EM), the Yale team was able to show that Nsp1 is one of SARS-CoV-2's most pathogenic viral proteins. In human lung cells, it can drastically alter [host cell](#) gene expression and essentially form a plug that prevents the ribosome, the cell's protein-making machinery, from receiving genetic instructions for new proteins encoded in messenger RNA.

"This is the entry channel for [genetic material](#), and when it is blocked no protein can be made," Xiong explained. "We didn't understand this mechanism before, but now we know."

This process affects protein production in many parts of the body, and high levels of Nsp1 may help explain why some people fare poorly after infection by the virus, he said.

However, it remains unknown how the [virus](#) is still able to produce its own proteins, using the same ribosome, to replicate in the cell after it disables the cell's ability to make normal proteins, Xiong said.

More information: Shuai Yuan et al, Nonstructural protein 1 of SARS-CoV-2 is a potent pathogenicity factor redirecting host protein synthesis machinery toward viral RNA., *Molecular Cell* (2020). [DOI: 10.1016/j.molcel.2020.10.034](https://doi.org/10.1016/j.molcel.2020.10.034)

Provided by Yale University

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