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STUDY REVEALS INTERESTING FACET OF THE NOVEL CORONAVIRUS

Relevant for: Developmental Issues | Topic: Health & Sanitation and related issues

Crown of spikes: The novel coronavirus consists of an RNA genome contained in a capsule which has many proteins, one of which is the spike protein that gives it its characteristic ‘crown’. | Photo Credit: Maksim Tkachenko

Studies of the coronavirus have largely focused on its ‘spike’ protein. A new study from IISER Bhopal has found that other proteins, in particular, the nucleocapsid or ‘N’ protein may also be responsible for the infectivity of the virus.

The SARS-CoV-2, or novel coronavirus, consists of an RNA genome contained in a spherical capsule which has many proteins, one of which is the ‘spike’ protein that gives it its characteristic spiky surface or ‘crown’. These spike proteins are the ones that help the virus penetrate and enter the body of human hosts. This is therefore used as a target by those developing vaccines as well as drugs. In order to test the effect of these formulations on the virus, scientists often use not live virus particles but ‘pseudotype’ them. That is, they use a core which is a different, harmless virus, encapsulate it in a lipid–protein sphere which has spikes on them made by the spike protein. Usually only the spike protein is used in pseudotyping. However, in real situations, the spike protein does not act in isolation but in conjunction with other proteins.

Hence the IISER Bhopal team was curious to study the effect of combinations of proteins on the infectivity of the virus. In their study they used vectors of lentivirus that they had pseudotyped with not only the spike protein but with 24 other proteins in all, including the N protein. “We use lentivirus-derived vectors that have been proven really safe to handle inside the labs to study virus-entry processes,” says Ajit Chande from the Department of Biological Sciences at IISER, Bhopal, who led the study, in an email.

The infectivity of each of pseudoviruses containing the 24 proteins was tested separately, and the group found that the pseudovirus containing the nucleocapsid ‘N’ protein had higher infectivity than the others.

The researchers used an assay where the extent of infectivity can be readily quantified using either enzymatic activity or fluorescence. “For this, we included a pair of reporter genes in the pseudoviruses (lentiviral vectors), which when delivered to the target cells expresses both an enzyme (called “luciferase”) and a green fluorescent protein,” explains Sreepadmanabh, an author of the paper published in *Frontiers in Cellular and Infection Microbiology.*

“After allowing the viral infection to occur, we measured the level of enzyme activity and counted the number of cells showing fluorescence, which gave a quantitative estimation of how infectious the virus would have been,” adds Tarun Mishra, also an author of the paper. The inference was that stronger the signal, higher was the infectivity.

These results were found to hold when they studied the so-called U.K. variant also. “The results which hold true for the original spike protein remain unchanged in the case of this mutant as well – the N protein, when included, leads to the production of more infectious viral particles,” says Dr Chande.

According to him, this discovery opens up exciting possibilities. “Ongoing or planned studies which seek to screen neutralising antibodies or therapeutic drugs could benefit by incorporating the N protein as a part of their experimental setup while using such pseudotyping systems,” says Dr Chande.

“This would help obtain more physiologically relevant infectivity levels and help set a proper threshold for such preliminary screenings which could improve their success rate.”

As Dr Chande says, this work also highlights a new role for the N protein, which is worth further investigation by itself. “It is possible that a more comprehensive understanding of the impact of the N protein on the spike may help identify key portions of these proteins which help mediate this effect. Such segments could then be specifically targeted using drugs to disrupt this process,” he adds.

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Some genes inherited from Neanderthals help defy the virus, others carry a risk of getting critically ill

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