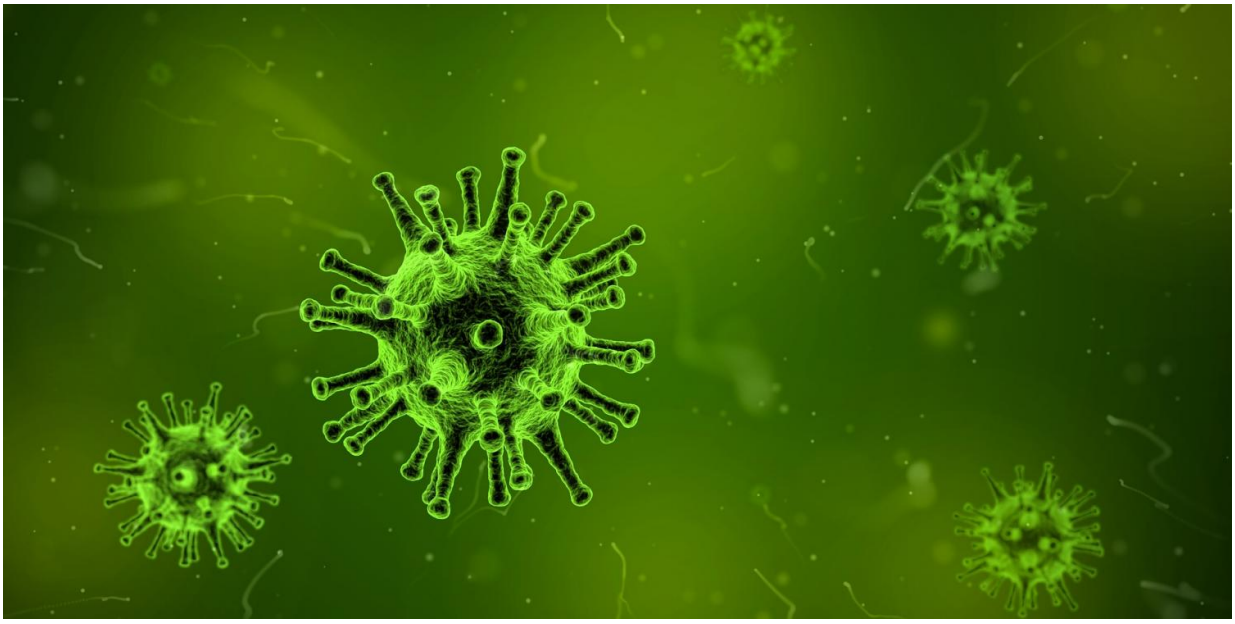
MedicalXpress

Deadly protein duo reveals new drug targets for viral diseases

August 13 2019



Credit: CC0 Public Domain

New research from Cornell University details how two highly lethal viruses have greater pathogenic potential when their proteins are combined.

A research team led by Hector Aguilar-Carreno, associate professor in the Department of Microbiology and Immunology, has found a potentially similar scenario with a pair of viruses, in a study published in

the *Journal of Virology*.

"Co-infections with these two viruses can occur in the same host, but we didn't know what would happen if their proteins combined," Aguilar-Carreno said. "We discovered that not only could they work together, they can work even better than they do separately."

Members of the Aguilar-Carreno research team are experts on how Nipah and Hendra viruses attach to, and fuse with, their hosts' cells. The viruses' natural host is the fruit bat; this relationship was captured in an illustration, chosen for the journal cover, by Aguilar-Carreno's husband, Armando Pacheco, a Cornell Institute of Biotechnology staff member.

The researchers' focus is on the viral fusion proteins (or F proteins) and attachment proteins (G proteins). In previous studies, the team unveiled how the two proteins physically interact to enable viral infections: A G protein attaches to the cell; G then triggers F to flip up and down, triggering fusion between the cellular and viral membranes—the first moment of infection.

Aguilar-Carreno knew this "dance" between G and F was a crucial step in viral infection, but was curious to know how the dance might change if the proteins got new partners. Since both Nipah and Hendra viruses can potentially co-infect fruit bats, a protein partner switch is likely to occur in the wild.

He and his team tested out different Nipah-Hendra protein combinations in the lab, using genetic approaches in human cells. In some pairings, the two gripped each other in a tight, tango-like embrace. But one hybrid—a Hendra F and Nipah G—behaved like Lindy Hoppers, allowing the F protein to perform "aerials" that heightened fusion between the virus and the cell.

"This combination of proteins had a looser interaction," Aguilar-Carreno said. "This looseness actually corresponded to greater fusion capability—and therefore an implied greater" ability to cause disease.

This hybrid protein power-couple has interesting implications.

"I find it fascinating—the tightness of the interaction is so crucial for these two proteins," Aguilar-Carreno said. "If they're too tight, they can't coordinate correctly to get into the cell. And now that we know this, we can leverage that to stop viral-cell fusion."

Aguilar-Carreno said this kind of therapeutic approach might be used to improve vaccine efficacy, or as an alternative to vaccines. His lab is working on vaccine approaches on animal models, as well as therapeutic approaches informed by this new discovery.

Aguilar-Carreno's lab is also working on related research that may lead to vaccine-free therapies or improved vaccines to treat enveloped viruses, which include infectious diseases such as human immunodeficiency virus (HIV) and influenza. Enveloped viruses are wrapped in an outer coat made from a piece of the infected cell's plasma membrane, which may protect the virus and help it infect other cells.

"Our work could lead to drugs," Aguilar-Carreno said, "that enable inventions such as a flu vaccine with broader protection and greater efficacy."

More information: Birgit G. Bradel-Tretheway et al, Nipah and Hendra Virus Glycoproteins Induce Comparable Homologous but Distinct Heterologous Fusion Phenotypes, *Journal of Virology* (2019). DOI: 10.1128/JVI.00577-19