Coronaviruses are masters of mimicry, new study finds

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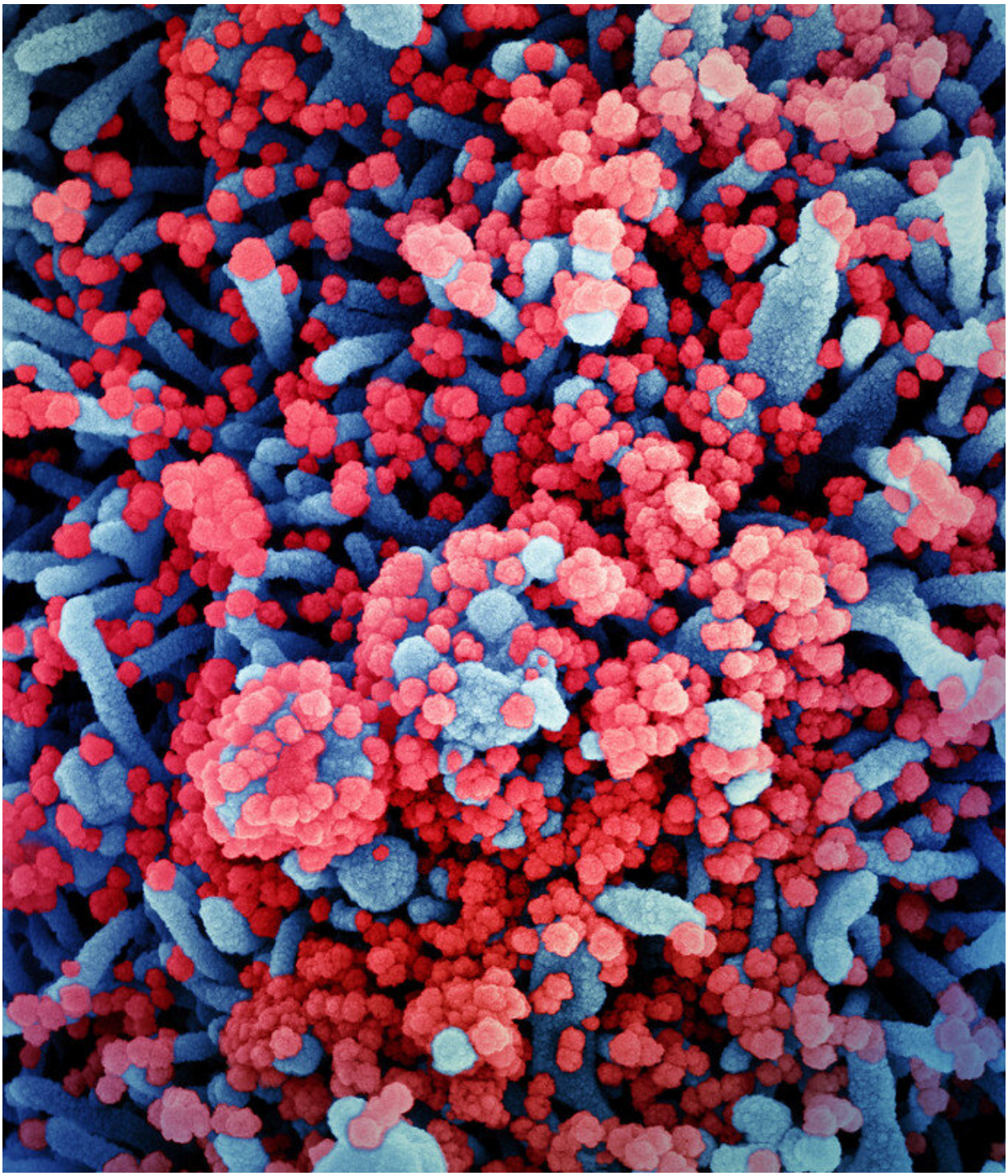

Colorized scanning electron micrograph of a cell (blue) heavily infected with SARS-CoV-2 virus particles (red), isolated from a patient sample. Image captured at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID

Coronaviruses are adept at imitating human immune proteins that have been implicated in severe COVID-19 disease, a study from researchers at Columbia University Vagelos College of Physicians and Surgeons has found.

The study was published online ahead of print in *Cell Systems.*

Many plants and animals use the art of mimicry to trick their prey or predators. Viruses employ a similar strategy: Viral proteins can mimic the three-dimensional shapes of their host's proteins to trick the host into helping the virus complete its life cycle.

"Viruses use mimicry for the same reason as plants and animals—deception," says Sagi Shapira, Ph.D., assistant professor of systems biology at Columbia University Vagelos College of Physicians and Surgeons. "We hypothesized that identifying viral-protein look-alikes would give us clues to the way viruses—including SARS-CoV-2—cause disease."

Coronaviruses Are Masters of Mimicry

In the study, Shapira used supercomputers to search for viral mimics with a program similar to 3-D facial recognition software. They scanned more than 7,000 viruses and over 4,000 hosts across Earth's ecosystems and uncovered 6 million instances of viral mimicry.

"Mimicry is a more pervasive strategy among viruses than we ever imagined," Shapira says. "It's used by all kinds of viruses, regardless of the size of the viral genome, how the virus replicates, or whether the virus infects bacteria, plants, insects or people."

But some types of viruses used mimicry more than others. Papilloma and retroviruses, not so much. Coronaviruses, on the other hand, are particularly good at it and were found to mimic over 150 proteins, including many that control blood coagulation or activate complement—a set of immune proteins that help target pathogens for destruction and increase inflammation in the body.

"We thought that by mimicking the body's immune complement and coagulation proteins, coronaviruses may drive these systems into a hyperactive state and cause the pathology we see in infected patients," Shapira says.

Human Studies Support Role of Viral Mimics in COVID

Over the course of the pandemic, it has become clear that many COVID patients have coagulation problems and some are now treated with anti-coagulants and drugs that limit complement activation.

In a separate paper published in *Nature Medicine*, the Columbia researchers found evidence that functional and genetic dysregulation in immune complement and coagulation proteins are associated with severe COVID-19 disease. They found that people with macular degeneration (which is associated with enhanced complement activation) were more likely to die from COVID-19, that complement and coagulation genes are more active in COVID-19 patients, and that people with certain mutations in complement and coagulation genes are more likely to be hospitalized for COVID-19.

Since that paper first appeared this spring in a preprint, other researchers have also found links between complement and COVID severity and several clinical trials of complement inhibitors have been initiated.

Shapira says the investigation of viral protein functions and mimicry suggests that learning about underlying virus biology could be one way to gain insights into how viruses cause disease and who may be at greatest risk.

"Viruses have already figured out how to exploit their hosts," Shapira says. "By studying viruses we can not only reveal fundamental principles in biology but also how they perturb cellular homeostasis and cause pathology. The hope is that one day we may be able to use this knowledge to fight back.

"Beyond COVID-19, the information we're gathering about how individual viral proteins work—across all viruses on Earth—may one day be leveraged as building blocks in medical and agricultural interventions."

The study, titled "A Sweep of Earth's Virome Reveals Host-Guided Viral Protein Structural Mimicry and Points to Determinants of Disease," was published online in *Cell Systems* on Oct. 13, 2020.

More information: Gorka Lasso et al, A Sweep of Earth's Virome Reveals Host-Guided Viral Protein Structural Mimicry and Points to Determinants of Human Disease, *Cell Systems* (2020). DOI: 10.1016/j.cels.2020.09.006

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