Researchers use computational modeling to understand why some flu viruses cause more severe infections

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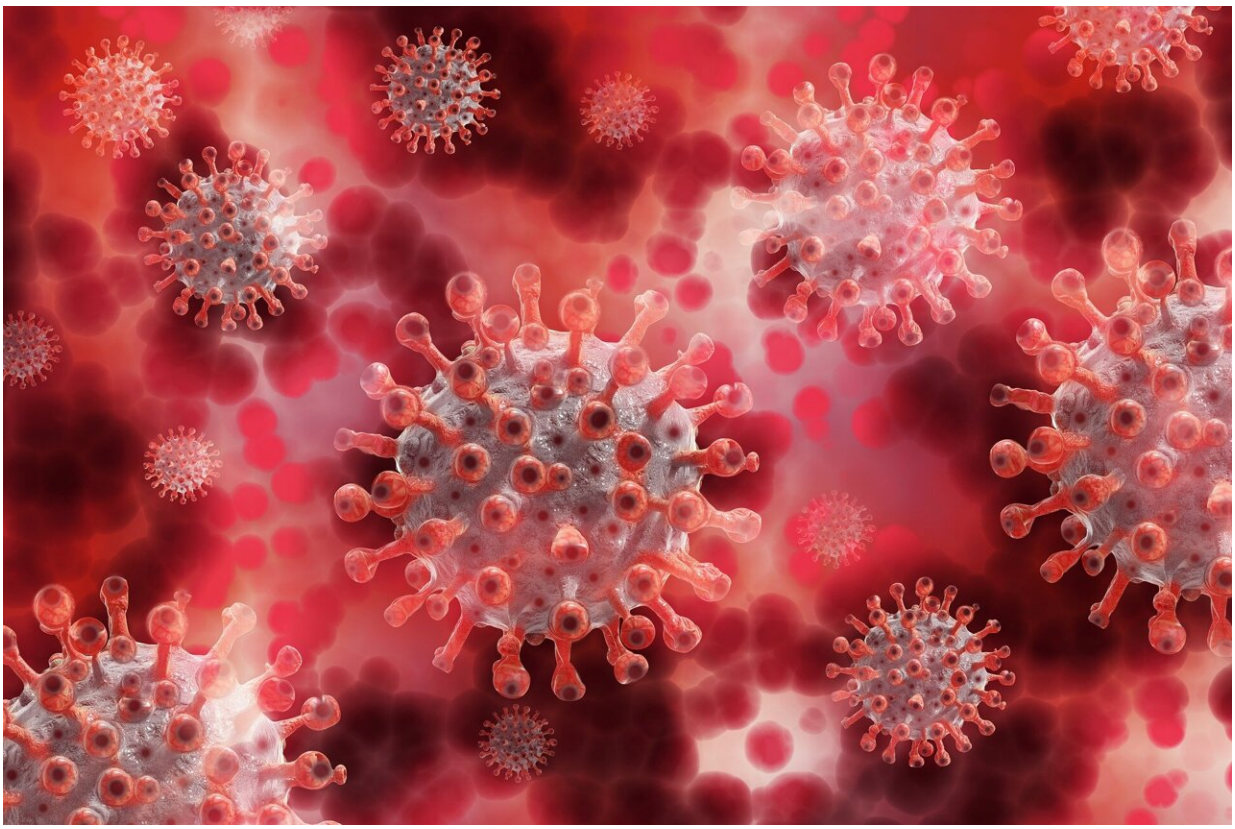

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Avian influenza viruses, or "bird flu," normally infects, well, birds. But when the virus does infect humans, it can cause more severe illness than

other similar influenza viruses.

Research led by the University of Pittsburgh's Jason Shoemaker uses computational modeling to try to understand the body's immune response to avian flu. His latest work, published in the journal Viruses, finds that the levels of interferon may be responsible for its more severe presentation—and may also be the key to treating it.

"It's hard to see what's happening in the human body when it's infected with a virus, but our computational modeling can help us understand the immune system's reaction, and where we might be able to help it do a better job," said Shoemaker, who is an assistant professor of chemical and petroleum engineering at the Swanson School of Engineering. "We need more modeling to really understand what happens to high-risk individuals when they're infected to make them high-risk. Then we can figure out how to better treat them."

Shoemaker and his coauthors Emily Ackerman and Jordan Weaver, graduate students in Shoemaker's ImmunoSystems Lab, used data from mice infected with either H5N1, the high-pathogenic (or disease-causing) avian flu, or H1N1, the low-pathogenic swine flu. They then used an engineering-based approach to model and predict virus replication and key immune responses based on the mice's infections, including the levels of interferon and immune cell activity.

By exploring the different biological responses, the researchers were able to determine that the production rate of interferon drives the strain-specific immune responses observed in the mice. In other words, the high viral load and the resulting interferon production by cells in the lungs after H5N1 infection seems to be the main reason for differing infection outcomes.

"This modeling provides more evidence for the theory that interferon is

induced earlier and more severely by the high-pathogenic H5N1 strain than by other influenza viruses," said Shoemaker. "Interferon then appears to be a main factor in determining how severe the infection will be and explains the distinctive immune response we see in H5N1 infections."

Though the recent paper did not specifically look at SARS-CoV-2, the virus that causes COVID-19, the findings could still give researchers a path to developing better treatments. The group's modeling work has revealed other factors that may be at play, as well. For example, the lab is also using agent-based modeling to understand why women often experience a more severe immune responses to the flu.

More information: Emily E. Ackerman et al, Mathematical Modeling Finds Disparate Interferon Production Rates Drive Strain-Specific Immunodynamics during Deadly Influenza Infection, *Viruses* (2022). DOI: 10.3390/v14050906

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