Researchers discover a new way that influenza can infect cells

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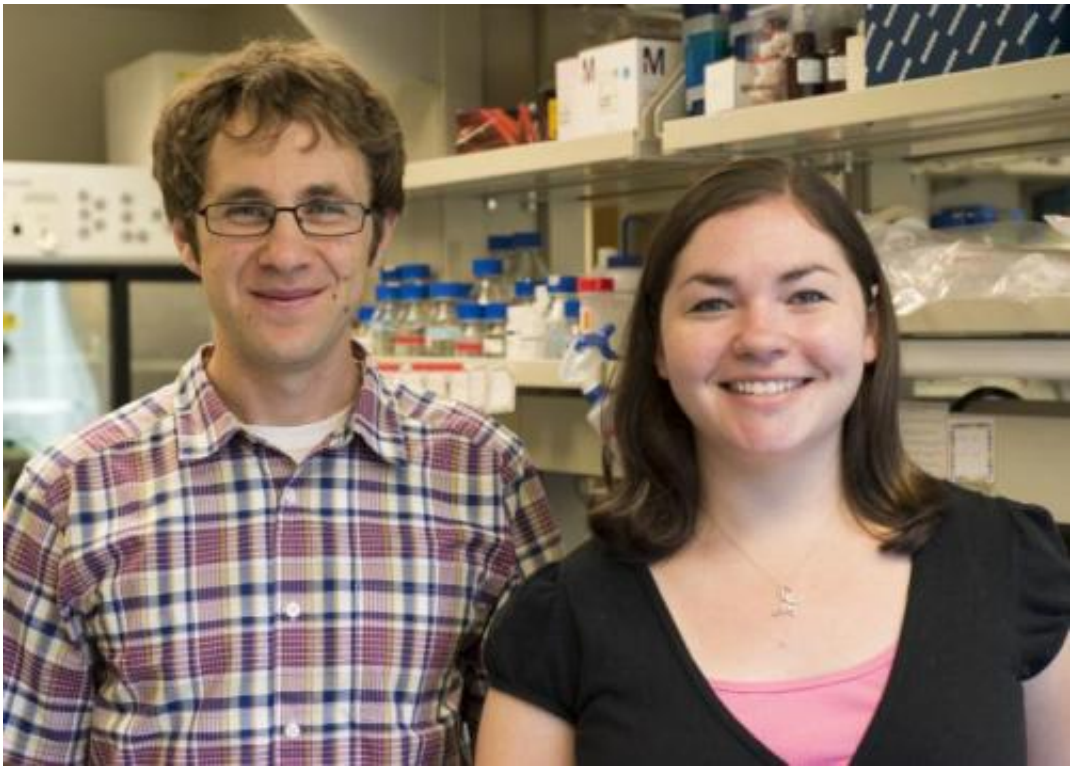

Jesse Bloom, Ph.D., is an assistant member of the Basic Sciences Division and Kathryn Hooper is a graduate research assistant in Bloom's lab at Fred Hutchinson Cancer Research Center. Credit: Fred Hutchinson Cancer Research Center

Scientists at Fred Hutchinson Cancer Research Center have uncovered a new mechanism by which influenza can infect cells – a finding that ultimately may have implications for immunity against the flu.

Influenza viruses have two main proteins on their surface that allow them to do their dirty work: a protein called hemagglutinin allows viruses to infect cells, while a protein called neuraminidase allows viruses to escape from cells.

Now in a paper published online ahead of the December print issue of the *Journal of Virology*, Jesse Bloom, Ph.D., an evolutionary biologist and assistant member of the Fred Hutch Basic Sciences Division, and Kathryn Hooper, a graduate research assistant in the Bloom Lab, describe the discovery of an influenza virus that instead uses neuraminidase to attach to cells.

The researchers discovered the new mechanism of infection after mutating the hemagglutinin of a lab-adapted strain of influenza so that it could no longer attach to cells.

"We expected that viruses with the mutated hemagglutinin wouldn't be able to infect cells," said Bloom, who also is a computational biologist and an assistant member of the Fred Hutch Public Health Sciences Division. "So we were surprised when a virus with this hemagglutinin started to grow. We were even more surprised when we sequenced the virus and discovered that it had evolved a mutation in neuraminidase."

Hooper began characterizing the new virus in detail. She discovered that the mutation allowed neuraminidase to attach the virus to cells. Hemagglutinin's ability to bind to cells – long considered one of the protein's most crucial and conserved properties – was no longer necessary for infection.

What does this finding mean for influenza in humans? That remains an open question, but Bloom and Hooper have already shown that the neuraminidase mutation they discovered is present in some human isolates of influenza.

"This was not a mutation we expected to find in the lab, let alone in viruses that have infected humans over the past few years," Hooper said. "It suggests there is influenza circulating in nature that may be infecting cells by a mechanism that has been overlooked by others in the field."

The researchers are now carefully characterizing human influenza isolates that have the mutation. They are also looking for other mutations that allow neuraminidase to attach viruses to cells.

They say there is a possibility that these types of mutations may have implications for immunity against influenza, since they might enable the virus to escape from antibodies that block the binding of hemagglutinin to cells.

Provided by Fred Hutchinson Cancer Research Center