

# Research team finds structure of 'swine flu' virus

March 24 2010

---

A team of scientists from The Scripps Research Institute and other institutions has solved the structure of a key protein from the virus that caused last year's "swine flu" influenza epidemic. The structure reveals that the virus shares many features with influenza viruses common in the early 20th century, helping to explain why, in general, older individuals have been less severely affected by the recent outbreak than younger ones.

The team's findings were published in the March 25, 2010, issue of *Science Express*.

In the study, the team describes the structure of the hemagglutinin (the influenza virus envelope protein) from the H1N1 swine [flu virus](#) that triggered the pandemic in 2009 and is still circulating in the human population. The team then compared the [swine flu](#) hemagglutinin protein with a range of different human H1N1 flu viruses in the past century.

"Parts of the 2009 virus are remarkably similar to human H1N1 viruses circulating in the early 20th century," said Scripps Research Professor Ian Wilson, who was the senior author of the study. "Our findings provide strong evidence that exposure to earlier viruses has helped to provide some people with immunity to the recent [influenza pandemic](#)."

The information should be useful for scientists and public health officials as they respond to current and future pandemics.

## Flu Outbreaks

Influenza is a common viral infection of the lungs that affects millions of people annually and is a leading cause of death in the United States, contributing to around 50,000 deaths per year. Serious influenza outbreaks such as the deadly "Spanish flu" of 1918 have occurred when a virus adapted to birds jumps directly into humans or reassorts and infects another species, such as the pig, and then jumps into humans. Similar outbreaks occurred in 1957 and 1968.

"For a pandemic to occur, there needs to be a naïve population, whose immune systems have not learned to recognize the virus and who can be infected," explained Rui Xu, a research associate in the Scripps Research Wilson lab who was first author of the paper with graduate student Damian Ekiert, also of the Wilson lab. "A pandemic outbreak is different from the seasonal flu, in which existing flu viruses circulate in the human population, gradually mutating as time goes on."

The most recent influenza outbreak, dubbed the "swine flu" by the media due to its recent origin in pigs, was first reported in Mexico in April 2009. The virus has now spread worldwide, and has contributed to at least 16,000 deaths, according to the World Health Organization. A vaccine is now available, but the virus remains a public health concern.

Almost as soon as the outbreak was first reported last April, the Scripps Research team set out to better understand the new influenza virus by examining its structure.

Collaborating with colleagues at Mount Sinai School of Medicine, who provided a clone of the major surface antigen from the emerging virus, A/California/04/2009 (CA04), the scientists called on a technique called x-ray crystallography. In this method, scientists produce quantities of the viral protein and try to crystallize it. This crystal is then placed in

front of a beam of x-rays, which diffract when they strike the atoms in the crystal. Based on the pattern of diffraction, scientists can reconstruct the shape of the original molecule.

The scientists chose to focus on the structure of the virus's hemagglutinin, a protein that is abundantly displayed on the viral surface. In addition to enabling the virus to infect cells of the host organism, hemagglutinin is the main antigenic determinant on the virus—in other words, it is what the immune system primarily recognizes and responds to by making antibodies (a type of immune molecule) and mounting an immune defense. Vulnerability to an individual influenza infection depends on how well a person's immune system recognizes the hemagglutinin.

The scientists' initial experiments went extraordinarily well, and by June, the team was able to reconstruct the structure of the swine flu hemagglutinin. But what did the structure mean?

## **Viral Relatives**

That's when the hard work began.

"One of the interesting aspects of the study to us was that the H1N1 subtype was already circulating in humans," said Xu. "That is the first time that we have seen such a phenomenon. How could the same subtype of influenza virus induce a new pandemic?"

Comparing the 2009 hemagglutinin protein with the hemagglutinin of other influenza samples, including the 1918 flu (a structure that Wilson and colleagues solved six years ago), helped provide answers. For the analysis, the scientists used all known human H1N1 strains between 1918 and 1957, and representative strains since 1977.

The researchers found that while much of the hemagglutinin three-

dimensional structure had been maintained among the different viruses, the amino acids (protein building blocks) on the viral surface were substantially different in the 2009 virus from seasonal strains. This could enable the virus to initially evade detection by the immune system.

Strikingly, the scientists also found that one area of the hemagglutinin, called antigenic site Sa, was highly similar between the 2009 and the 1918 viruses. The similarity of the Sa site for the two viruses suggested that some individuals might be able to mount an immune response that could neutralize either virus.

That would have remained an educated guess if Lady Luck hadn't intervened.

In another flu project ongoing in the Wilson lab, Ekiert was working to determine the structure of an antibody that neutralized the 1918 [influenza virus](#). The antibody had been isolated from a survivor of the 1918 Spanish flu.

"As more information became available, the 1918 antibody suddenly became relevant to the swine flu study," said Ekiert.

Could the particular antibody that Ekiert was working with, called 2D1, not only be effective against the 1918 virus, but also act against the 2009 swine flu?

A study recently published in the *Journal of Virology* with researchers at Vanderbilt University, who are collaborators on this present work, showed that, indeed, mice challenged with the 2009 virus are protected by the administration of the antibody against the 1918 virus. The current [Science Express](#) study provides the structure of the 2D1 antibody in complex with the 1918 [virus](#) and addresses how this protection occurs.

"There is a huge divergence among different influenza viruses," said Ekiert, "so that exposure to one won't confer protection against another. However, this study shows that prior exposure to viruses that were around decades ago can provide some protection against infection against a newly emerging pandemic."

**More information:** In addition to Xu, Ekiert, and Wilson, authors of the paper, "Structural basis of pre-existing immunity to the 2009 H1N1 pandemic influenza virus," are Jens C. Krause and James E. Crowe, Jr. of Vanderbilt University Medical Center and Rong Hai of the Mount Sinai School of Medicine.

Provided by The Scripps Research Institute

Citation: Research team finds structure of 'swine flu' virus (2010, March 24) retrieved 19 April 2024 from <https://medicalxpress.com/news/2010-03-team-swine-flu-virus.html>

|  |
|--|
| <p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p> |
|--|