Findings uncover new details about mysterious virus

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(PhysOrg.com) -- An international team of researchers has determined key structural features of the largest known virus, findings that could help scientists studying how the simplest life evolved and whether the unusual virus causes any human diseases.

The mimivirus has been called a possible "missing link" between viruses and living cells. It was discovered accidentally by French scientists in 1992 but wasn't confirmed to be a virus until 2003.

The virus infects amoebas, but it is thought to possibly be a human pathogen because antibodies to the virus have been discovered in pneumonia patients. However, many details about the virus remain unknown, said Michael Rossmann, Purdue University's Hanley Distinguished Professor of Biological Sciences.

Now a team of researchers from Purdue, the University of California at Irvine and the University of the Mediterranean in Marseilles, France, have thrown more light on the mimivirus' makeup.

The scientists have determined the basic design of the virus' outer shell, or capsid, and also of the hundreds of smaller units called capsomeres making up this outer shell. Findings also confirmed the existence of a starfish-shaped structure that covers a "special vertex," an opening in the capsid where genetic material leaves the virus to infect its host, and an indentation in the virus's genetic material itself is positioned opposite this opening, Rossmann said.

"The findings are important in terms of studying the evolution of cells, bacteria and viruses," said Siyang Sun, a postdoctoral research associate working in Rossmann's lab. "The mimivirus is like an intermediate between a cell and a virus. We usually think of cells as being alive and a virus is thought of as being dead because it needs a host cell to complete its life cycle. The mimivirus straddles a middle ground between viruses and living cells, perhaps redefining what a virus is."

The virus approaches the size of bacteria and is about half of a micron in diameter, more than 10 times larger than the virus that causes the common cold and large enough to be seen with a light microscope. Other viruses are too small to be seen with conventional light microscopes.

The findings are detailed in a research paper that will appear online April 28 in the journal *PLoS Biology*, published by the Public Library of Science, a nonprofit organization of scientists and physicians. The paper's lead author was Chuan Xiao, a former Purdue postdoctoral research associate and now an assistant professor in the Department of Chemistry at the University of Texas at El Paso.

Researchers had previously been unable to determine the virus's structure because they had assumed that, like many other viruses, it's capsid possessed a design known as icosahedral symmetry.

Xiao discovered the true structure when he decided to try reconstructing the virus assuming it possessed not standard icosahedral symmetry but another configuration called five-fold symmetry.

"If you start out thinking the object has icosahedral symmetry, then you assume there are 60 identical pieces, and that influences how you reconstruct the virus's structure," Rossmann said.

Researchers took images of the virus using an atomic force microscope, revealing a pattern of holes regularly spaced throughout the virus's outer shell.

"The capsids of most other large, pseudo icosahedral viruses do not contain such holes, and their function is unknown," Rossmann said.

The researchers used a method called cryo-electron microscopy reconstruction to determine the structure details. The reconstruction method enables researchers to produce three-dimensional structures by combining two-dimensional pictures, much like a complete architectural drawing of a house can be assembled with two-dimensional drawings of the sides, the roof and other elements.

Using five-fold symmetry revealed that one side of the virus's capsid is slightly different than the others, whereas all sides are the same in a regular icosahedron.

An icosahegron has a roughly spherical shape containing 20 triangular facets and 60 identical subunits. Like an icosahedron, the mimivirus capsid also has 20 facets. However, unlike an icosohedron, five facets of the capsid are slightly different than the others and surround the special vertex. Icosohedra contain 12 similar vertices, whereas the mimivirus contains eleven such vertices, with the 12th being different than the others.

The new reconstructed picture of the virus matched features seen using the atomic force microscope picture, Rossmann said.

The starfish-shaped feature apparently opens up like a blooming flower when the virus is ready to infect its host amoeba, enabling the virus to eject its DNA for insertion into the host, Rossmann said.

"In addition, we think the indentation of the genetic material has something to do with how the genome comes out of the virus," he said. "There is a relationship between the shape of the genome and the special vertex."

The research, which is funded by the National Institutes of Health, is ongoing, with future work probing additional properties of the virus, particularly the structure of the starfish-shaped feature and how it functions.

The paper was written by Xiao; microscope expert Yurii G. Kuznetsov in the Department of Molecular Biology and Biochemistry at UC Irvine; Sun; postdoctoral research associates Susan L. Hafenstein and Victor A. Kostyuchenko and electron microscopist Paul R. Chipman, from Purdue; research scientist Marie Suzan-Monti and Didier Raoult, a professor of microbiology, both from the University of the Mediterranean; Alexander McPherson, a professor of molecular biology and biochemistry at UC Irvine; and Rossmann.

Source: Purdue University (news : web)