Antibody locks up West Nile's infection mechanism

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(PhysOrg.com) -- Researchers have learned the structure that results when an antibody binds to the West Nile virus, neutralizing the virus by locking up its infection mechanism. The information could help scientists develop a vaccine against the mosquito-borne disease.

The findings show precisely how a key part of the antibody, called the antigen binding fragment, or Fab, attaches to two adjacent protein molecules that make up the virus's outer shell. This "crosslinking" attachment between molecules is repeated over the entire shell, interlocking the 30 molecular "rafts" that make up the shell and preventing structural changes needed for the virus to infect host cells, said Michael Rossmann, the Hanley Distinguished Professor of Biological Sciences in Purdue's College of Science.

"The antibody crosslinking causes the virus to become rigid, and this rigidity prevents conformational changes to the virus needed to fuse with host cells," Rossmann said.

Findings are detailed in a research paper that appeared in October in Proceedings of the National Academy of Sciences. The team included postdoctoral researcher Bèrbel Kaufmann, other researchers at Purdue, the Washington University School of Medicine in St. Louis and the biotechnology company Crucell Holland B.V. in The Netherlands.

Learning how antibodies neutralize viruses is important for developing effective vaccines, Rossmann said.

"There are many antibodies that can neutralize West Nile virus," he said. "These findings concern a specific antibody, called CR4354. It uses an unusual approach to neutralize the virus. Normally an antibody binds to a single molecule, but now we see this crosslinking, which is quite clever because it ties everything rigidly together."

The researchers used a process called cryoelectron microscopy to take detailed pictures of the Fab-virus complex. They also used X-ray crystallography to learn the antibody's precise crystalline structure.

West Nile belongs to a family of viruses known as flaviviruses, which includes a number of dangerous insect-borne disease-causing viruses. West Nile virus causes a potentially fatal illness and has infected thousands of people in the United States over the past five years, killing more than 400 people in that time frame, according to the Centers for Disease Control and Prevention. The virus is endemic in parts of Africa, Asia and Europe and in the past decade has spread throughout North America and into Central and South America.

More information: Neutralization of West Nile Virus by Cross-linking of its Surface Proteins with Fab Fragments of the Human Monoclonal Antibody CR4354, by Bärbel Kaufmann et al., *Proceedings of the National Academy of Sciences*.

Provided by Purdue University