New findings reveal protein structure in rubella virus

December 10 2013, by Emil Venere

(Medical Xpress)—Researchers have determined the structure of the rubella virus capsid protein, which is central to the virus's ability to assemble into an infectious particle and to infect humans.

Although a successful vaccine is available to protect against rubella virus infection, the discovery could aid efforts to develop vaccines and antiviral drugs to treat related infections.

The protein is located on the virus's inner portion of its shell, or capsid, and is an essential structural component as well as a key factor in virus-host interactions. The new findings reveal a protein structure not previously seen in other viruses that is an essential component of infectious rubella virus, said Michael Rossmann, Purdue University's Hanley Distinguished Professor of Biological Sciences.

He led a team of researchers at Purdue that discovered the structure, working with researchers at the University of Alberta who created mutated forms of the virus to validate the structural interpretation.

"What we predicted based on the structure is that if we mutated the virus to change the amino acids in a specific region it would destroy the virus and it wouldn't assemble," said Purdue doctoral student Vidya Mangala-Prasad, who graduates this semester.

The findings were published in November in *Proceedings of the National Academy of Sciences*. The paper was authored by Mangala-Prasad;

University of Alberta graduate student Steven D. Willows; Purdue research scientist Andrei Fokine; Purdue postdoctoral researchers Anthony J. Battisti, Siyang Sun and Pavel Plevka; Tom Hobman, a professor in the Department of Cell Biology at the University of Alberta; and Rossmann.

"These studies may facilitate future vaccine design as well as aid in development of drugs for other RNA viruses for which there are no therapeutic treatments," Hobman said.

RNA viruses include those that cause SARS, influenza or hepatitis C.

The researchers used techniques called cryoelectron tomography, X-ray crystallography and multiple wavelength anomalous dispersion (MAD). Mangala-Prasad crystallized the protein and then used MAD to determine the structure.

"One challenge we had is that the structure we found is not similar to any of the known structures," she said. "So we didn't have any model to go by to solve this particular structure."

Rubella infection leads to severe damage in fetuses when contracted during pregnancy. It is in a class of viruses called togaviruses and causes "German measles," a relatively mild disease characterized by rashes and low-grade fever.

More information: Rubella Virus Capsid Protein Structure and its Role in Virus Assembly and Infection, *PNAS*, www.pnas.org/content/110/50/20105.abstract

Abstract

Rubella virus (RV) is a leading cause of birth defects due to infectious agents. When contracted during pregnancy, RV infection leads to severe

damage in fetuses. Despite its medical importance, compared with the related alphaviruses, very little is known about the structure of RV. The RV capsid protein is an essential structural component of virions as well as a key factor in virus-host interactions. Here we describe three crystal structures of the structural domain of the RV capsid protein. The polypeptide fold of the RV capsid protomer has not been observed previously. Combining the atomic structure of the RV capsid protein with the cryoelectron tomograms of RV particles established a low-resolution structure of the virion. Mutational studies based on this structure confirmed the role of amino acid residues in the capsid that function in the assembly of infectious virions.

Provided by Purdue University

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