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NEWS RELEASE

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Note to Journalists: An electronic copy of the research paper is available from Emil Venere, (765) 494-4709, venere@purdue.edu

Biologists spy close-up view of poliovirus linked to host cell receptor

WEST LAFAYETTE, Ind. - Researchers from Purdue and Stony Brook universities have determined the precise atomic-scale structure of the poliovirus attached to key receptor molecules in human host cells and also have taken a vital snapshot of processes leading to infection.

The virus binds to a receptor on the cell to form a single complex.

"This structure had been predicted, but the predictions were not as accurate as we had thought," said Michael Rossmann, Purdue's Hanley Distinguished Professor of Biological Sciences. "What we have now is the real structure, as opposed to a prediction of the receptor molecule. We also have a much higher resolution view of the complex of the receptor when bound to the virus."

The work was carried out by Ping Zhang, a Purdue doctoral student, and others working in Rossmann's laboratory in collaboration with the group at Stony Brook University in New York.

"These findings show the detailed relationship between atoms in the receptor and atoms in the virus," Rossmann said.

The research, which was funded by the National Institutes of Health, is not immediately geared toward medical applications. However, such findings might one day help scientists design better vaccines for the poliovirus and aid in research into the infection processes of other viruses, Rossmann said.

The findings are detailed in a research paper that appeared on Nov. 25 in the journal Proceedings of the National Academy of Sciences.

The poliovirus has three "serotypes," which cause different effects in people. All three serotypes use the same receptor, and Zhang studied how each serotype binds to the receptor.

The virus is roughly spherical and is made up of 60 triangular facets forming a geometric shape called an icosahedron. Each of the 60 units contains a site that can attach to a host cell's receptor molecules. The receptor molecules are called CD155, for cellular differentiation protein, and are made up of a single protein bound to the membrane that envelops a cell. The part outside the cell is divided into three sections, or domains.

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The virus binds to a specific domain, and the new high-resolution analysis shows the atomic structure at this attachment point.

Zhang used a method called X-ray crystallography to visualize and study the atomic structure of CD155 and electron microscopy to study the combined virus and CD155 receptor molecule.

Though cellular receptors are designed to carry out specific chemical processes for the cell, viruses have developed ways to use them for gaining entry into cells.

"The virus has learned, to the disadvantage of the cell and human beings, to attach itself to this particular receptor molecule in order to enter the cell," Rossmann said.

The researchers also found what happens next by looking at how the virus disintegrates in the cell in order to deliver its genetic material to infect the host.

"These research results provide a detailed analysis of how a virus can enter its host cell," Rossmann said.

Polioviruses cause poliomyelitis, a human disease that affects the central nervous system, injuring or destroying the nerve cells that control the muscles. Though effective vaccines have been developed against polioviruses, scientists do not have a clear understanding of how these viruses attach to receptor molecules on cells to initiate infection.

The authors listed on the paper are Zhang; Steffen Mueller, a postdoctoral research associate at Stony Brook; Marc Morais, a former Purdue postdoctoral research associate; Carol M. Bator, a technical research assistant at Purdue; Purdue electron microscopist Valorie D. Bowman; Susan Hafenstein, a postdoctoral research associate at Purdue; Eckard Wimmer, a distinguished professor of molecular genetics and microbiology at Stony Brook; and Rossmann.

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ABSTRACT

Crystal Structure of CD155 and Electron Microscopic Studies of its Complexes with Polioviruses

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When poliovirus (PV) recognizes its receptor, CD155, the virus changes from a 160S to a 135S particle before releasing its genome into the cytoplasm. CD155 is a transmembrane protein with 3 leg-like extracellular domains, D1-D3, where D1 is recognized by the virus. The crystal structure of D1D2 has been determined to 3.5-Å resolution and fitted into ≈8.5-Å resolution cryoelectron microscopy reconstructions of the virus-receptor complexes for the 3 PV serotypes. These structures show that, compared with human rhinoviruses, the virus-receptor interactions for PVs have a greater dependence on hydrophobic interactions, as might be required for a virus that can inhabit environments of different pH. The pocket factor was shown to remain in the virus during the first recognition stage. The present structures, when combined with earlier mutational investigations, show that in the subsequent entry stage the receptor moves further into the canyon when at physiological temperature, thereby expelling the pocket factor and separating the viral subunits to form 135S particles. These results provide a detailed analysis of how a non-enveloped virus can enter its host cell.