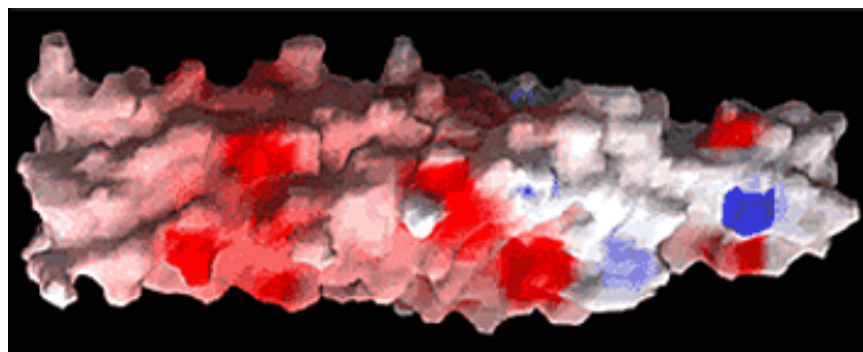


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## Viral Harpoon Reveals Ancestry of Measles, Mumps Viruses



**Image Title:** A computer-enhanced image of the viral harpoon that measles and mumps viruses use to spear host cells. The red color indicates the fusion protein's negatively charged amino acids; blue represents positively charged amino acids. - Robert Lamb/HHMI at Northwestern University

When viruses infect cells, they employ molecular "harpoons" to snare their intended target. Recently, a team of scientists identified and determined the three-dimensional structure of the harpoon protein used by a large family of pathogenic viruses to grab hold of and fuse to host cells. Surprisingly, the protein's structure suggests that viruses that cause measles and mumps may be viral cousins of HIV, influenza and Ebola virus.

The research team, which included Robert Lamb of the Howard Hughes Medical Institute at Northwestern University, believes that its discovery may help lead to the development of drugs that can prevent viral infections by jamming this critical infectious machinery. The researchers reported their findings in the March 26, 1999, issue of the journal *Molecular Cell*.

Lamb and Northwestern University colleagues Theodore Jardetzky, Kent Baker and Rebecca Dutch were studying a member of the paramyxovirus

family, which includes the viruses that cause measles, mumps and respiratory syncytial viral infection (RSV) a leading cause of hospitalization in young children. Other paramyxoviruses cause croup, pneumonia and bronchitis in young children, and members of this family can infect a variety of mammals and birds.

The scientists crystallized the fusion protein of a paramyxovirus that infects monkeys and used x-ray crystallography to determine the proteins three-dimensional structure. This analytical process involves shining an intense x-ray beam through a protein crystal, and then deducing the proteins structure by analyzing the patterns of light that emerge from the crystal.

Although the scientists studied the fusion protein of only one paramyxovirus, they are confident that the structural finding applies to the entire paramyxovirus family. Previous analyses of the basic "primary" structure the order, or sequence, of amino acids that make up a protein of many different paramyxovirus fusion protein molecules revealed that their basic structures are all similar.

But when the scientists analyzed the three-dimensional structure of the simian virus fusion protein, they were surprised to discover close structural similarities to fusion proteins from HIV, influenza and Ebola, said Lamb. Aside from this similarity, he said, "all these viruses have very different strategies for infecting cells and insinuating viral genetic material into the target cells to commandeer their machinery."

According to Lamb, the similarity among such widely varied viruses suggests that they might have had some common ancestor that shared a primitive version of the fusion protein. It is impossible at this point, however, to pinpoint the evolutionary origin of that ancestry, he said.

Regardless, said Lamb, "knowing the structure of this one fusion protein may lead to the development of drugs capable of thwarting the action of the fusion proteins of other members of the paramyxovirus family, and even possibly its distant viral cousins." At the least, he added, these findings will spur further studies involving other medically important viruses.

Specifically, determining the three-dimensional structure of the fusion protein sheds new light on the key event in paramyxovirus infection when the virus unfolds itself to reveal a spikelike protein that is launched into the gel-like outer membrane of the target cell. "It's much like a harpoon going into a target," said Lamb.

He emphasized, however, that more research is needed to answer two important questions: What triggers the harpoon molecule to unfurl, and how does the fusion protein refold itself to draw the virus toward the ensnared target cell? "What happens there is a mystery," he said. "It's like spearing a shark. Its relatively easy to spear it, but getting it onboard the boat is more difficult, and we dont quite know how this kind of process happens in these viruses."