# The tiny, lethal weapon that viruses use to kill bacteria

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(Phys.org) -- It could be the tiniest armor-piercing weapon in the biological universe: EPFL scientists have measured a one-nanometer needle-like tip that viruses use to attack bacteria.

Grouped together under the unassuming name φ92, a family of bacteriophage viruses has perfected its specialty: they attack salmonella and coliform bacteria. The centerpiece of their arsenal is a needle-like tip that pierces its victim's membrane. EPFL scientists have measured this miniscule weapon; at a single nanometer, it's roughly 20 times the diameter of a helium atom. This discovery, published in *Structure*, a Cell Press journal, will allow researchers to better understand the attack strategy used by bacteriophages, which are being intensively studied for their therapeutic potential.

φ92's armor-piercing weapon is made up of three chains of identical proteins. These three long intertwined molecules form an appendage sharp enough to penetrate the bacterial membrane. This molecular needle, discovered recently in EPFL's Laboratory of Structural Biology and Biophysics, led by Petr Leiman, appears to be characteristic of all species belonging to the φ92 family of bacteriophage viruses.

The body of a phage is made up of two main parts. The first, a hollow head called a "capsid," contains the genetic material. The second consists of a tube, a group of appendages resembling feet, and a device designed to penetrate the membrane of its host – the needle-like tip is at the furthest extremity of the virus.

Phages recognize sugars and proteins on the surface of their preferred host bacteria. The virus then attaches its feet to the victim, and a complex process is set in motion. A chain of proteins uncoils, pushing the injection tube and its tip through the victim's membrane like a hypodermic needle. The tip then detaches from the tube and, like an uncorked bottle of champagne, the pressurized genetic material in the capsid is injected into the bacterium. The phage then begins to reproduce inside its victim.

By determining the exact structure of the tip, the EPFL scientists have filled in all the missing details in our understanding of φ92's lethal weapon. To reach this level of detail – at most a dozen or so atoms at the extremity of the tip – they used x-ray crystallography techniques, which are of high enough resolution to determine the shape of individual molecules.

"We managed to determine not only the size, but the complete structure of the tip as well," explains EPFL postdoctoral researcher Christopher Browning, who is first author on the article. In addition, the researchers discovered an iron atom in the appendage. "We still are not sure what it's used for, but to the extent that this element is toxic, we have very good reason to think that it's not there by accident."

This research has implications far beyond simple biological curiosity. Bacteriophages are considered promising weapons in the fight against infectious bacteria, to complement or replace traditional antibiotics. The scientists believe the shape of the needle-like tip determines in part the bacterial species that can be attacked by a phage.

Among the avenues being explored are incomplete bacteriophages called "pyocins," which are naturally produced by some infected bacteria. Pyocins consist of just the injection apparatus of the virus, a kind of mechanical component, but of biological origin. They're of interest to

scientists precisely because they don't have a capsid, and thus don't carry genetic material, explains Browning. "These things can penetrate the bacterial membrane, which can kill the bacterium, but without injecting genetic material. That sidesteps the possibility that the phage could mutate and then attack "good" bacteria. This option is being extensively studied at the moment, but we need to understand the potential of each phage with respect to the various bacteria. The form of the tip is one of those parameters."

**More information:** Christopher Browning, et al., Phage Pierces the Host Cell Membrane with the Iron-Loaded Spike, *Structure* vol.20 issue 2, 2012

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