Viruses cooperate to overcome immune defences of bacteria

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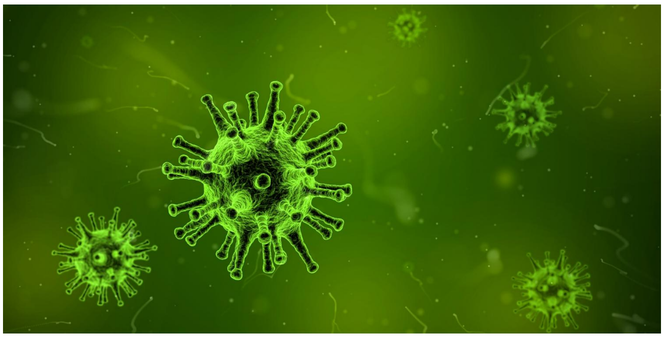

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Virus particles that infect bacteria can work together to overcome antiviral defences, new research shows.

Such viruses are known as phages, and the research shows how particles of a single type of virus can attack in waves—first weakening the bacterial defences, then killing the bacteria.

The findings are a key breakthrough that will help improve phage therapy, which is used to treat life-threatening bacterial infections.

Bacteria have defence systems such as CRISPR-Cas to protect themselves against viruses that infect them.

Like an arms race, phages counteract this defence to keep up with the bacteria and have equipped themselves with molecules termed "anti-CRISPR".

The University of Exeter study shows single virus particles cannot completely counteract CRISPR-Cas on their own—but if enough particles are present together, "teamwork" allows them to overcome it and establish an infection in the bacterial population.

"A high enough number of viral particles can tip an attack in their favour," said first author Dr. Mariann Landsberger, of the Environment and Sustainability Institute on the University of Exeter's Penryn Campus in Cornwall.

"It appears that a strike against bacteria with a viral number below this 'tipping point' leads to extinction of the phage invaders.

"In contrast, a viral amount exceeding the 'tipping point' allows the phages to take over the bacteria together, either by simultaneously or sequentially infecting a given bacterium.

"One explanation of the observed 'tipping point' is that two viruses both possessing anti-CRISPR molecules simultaneously attack the same bacterium, thereby combining forces to inactivate the CRISPR-Cas defences.

"This scenario is more probable at very high numbers of viruses, where the likelihood is higher that two phages infect the same bacterium at the same time."

The researchers found that, given a large enough number of viruses present in the environment, "sequential infections" of bacteria result in the establishment of an epidemic in a bacterial population.

This process involves a first virus invading a bacterium, partially weakening the bacterial immune system with its anti-CRISPR molecules by blocking some of the present CRISPR-Cas defences, but failing to properly infect the cell, and eventually getting destroyed by the remaining active CRISPR-Cas systems.

A second virus is then able to overcome these leftover CRISPR-Cas defences with its anti-CRISPR molecules and successfully infects and kills the bacterium.

Senior author Dr. Stineke van Houte said: "This work shows that phages can work together to disable bacterial immune systems, and this has important implications for using phage to treat human infections, since the dose of phage that is used can determine whether the phage is able to kill the bacteria.

"More generally, it suggests that viruses can work together in unexpected ways where they can cause sudden outbursts of disease when their numbers exceed critical thresholds."

The paper, published in the journal *Cell*, is entitled: "Anti-CRISPR phages cooperate to overcome CRISPR-Cas immunity."

More information: "Anti-CRISPR phages cooperate to overcome CRISPR-Cas immunity," *Cell* (2018). DOI: 10.1016/j.cell.2018.05.058

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