This nearly indestructible lab virus kept sabotaging cultures until researchers found a way to protect against it

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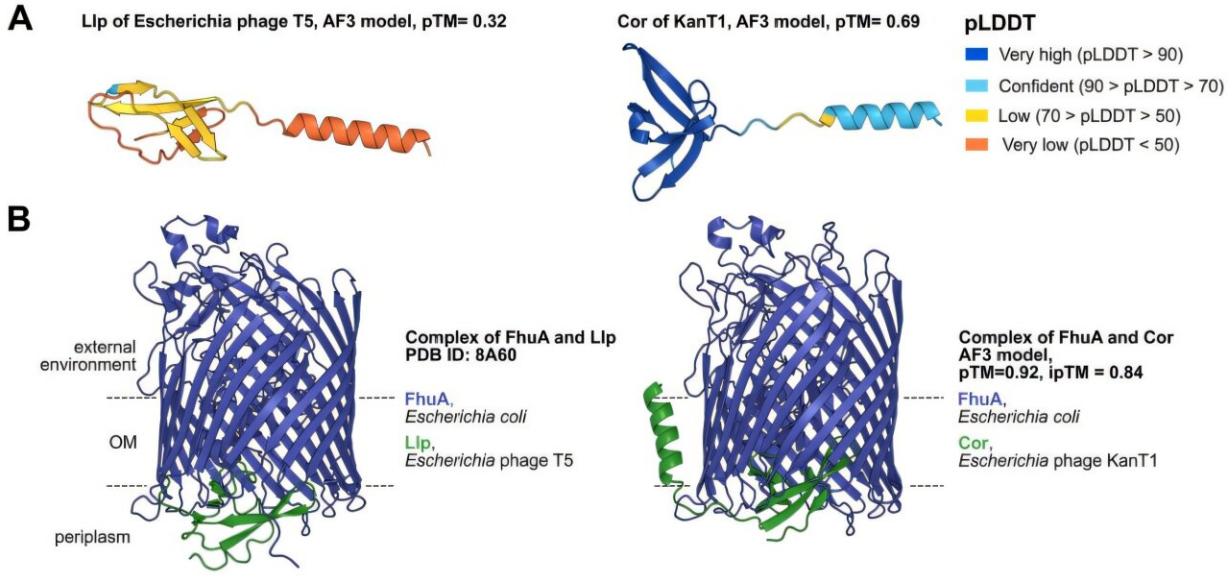

Cor cassette is a consistent feature across BASEL FhuA targeting phages. Credit: *International Journal of Molecular Sciences* (2026). DOI: 10.3390/ijms27093756

Researchers from the VEB.RF Group of Skoltech have uncovered the molecular mechanisms that make one of the most persistent laboratory contaminants—bacteriophage T1—unusually resilient and dangerous to bacterial cultures. The findings could inform the explanation of the nature of contamination in microbiological laboratories and biotech

production facilities, and also offer a protective solution: the use of a resistant bacterial strain that can be implemented in laboratory practice immediately. The work was published in the *International Journal of Molecular Sciences*.

Bacteriophages—viruses that kill bacteria—are indispensable in biotechnology and medicine, but in laboratories they often cause considerable problems. For example, T1 family phages can survive for years on equipment, pass through filters, and destroy an entire bacterial culture overnight, disrupting an experiment or production run. They are difficult to eliminate even with harsh sterilization methods. For a long time, it remained unclear which specific genes and proteins confer such resilience.

A research team led by Artem Isaev, the head of the Laboratory for Metagenome Analysis at the Skoltech Biomed Technologies Center and a recipient of the Russian Federation Presidential Prize in Science and Innovation for Young Scientists in 2025, isolated a new phage from river water in Kaliningrad, naming it KanT1 after Immanuel Kant. It was found to infect a wide range of E. coli strains, including those used in laboratories, and to be resistant to many disinfection methods.

"We discovered that KanT1 was constantly contaminating our samples, and this became the starting point for a systematic study of its genome. To better understand how to fight this 'enemy,' we decided to try to determine what makes this virus so resilient," said Isaev.

"It turned out that standard annotation methods, which compare genes based on sequence, were failing to identify many important proteins in these phages—we managed to detect them and predict their functions through protein structure analysis."

A key novelty of the work was the use of protein structure prediction

methods. Using AlphaFold3—an AI-based system for predicting protein structures—the scientists were able to characterize the functions of proteins previously considered hypothetical, which account for nearly half of the genome. The authors discovered a protein with a particular structure—the so-called SH3 domain.

Previously, such structures had only been found in viruses that infect bacteria with thick, robust cell walls—so-called Gram-positive bacteria. This is the first time such a protein has been found in a virus of E. coli, which has a thin cell wall. It is located near a group of genes responsible for destroying the bacterial cell from within to release new viral particles.

"Finding an SH3 domain in a phage that infects a Gram-negative bacterium came as a surprise to us. We hypothesize that the SH3 protein helps the phage more efficiently destroy the cell from within, which may explain its aggressiveness and ability to spread rapidly through a culture," said Arina Eremina, one of the lead authors of the study, an undergraduate student at HSE University completing her project at the Laboratory for Metagenome Analysis at the Skoltech Biomed Technologies Center.

Comparative analysis of 522 genomes of related phages showed that the SH3 domain is found in more than a third of them, but is far from universal. This suggests its role as an additional evolutionary tool that phages can acquire to enhance their efficiency. The authors also refined the function of another key mechanism—superinfection exclusion—which allows the virus to "take over" a cell and block reinfection by other phages.

"Our study demonstrates that even such a well-studied object as phage T1 contains a significant number of yet uncharacterized genes. The use of protein structure prediction methods allowed us to penetrate this 'dark

matter' of the viral genome and identify functionally significant components. In the long term, understanding such mechanisms will aid in the development of new phage-based antibacterial agents," shared Polina Iarema, one of the lead authors of the study, a Ph.D. student at Skoltech in the Life Sciences program.

The work explains why T1-like phages contaminate laboratory cultures and offers a solution to the problem. The researchers found that the E. coli HS strain—a bacterium normally found in the human gut—is completely resistant to these viruses. This means that in laboratories where contaminating phages are particularly problematic, this strain can be used instead of strains sensitive to phage contamination.

More information: Arina Eremina et al, Analysis of a Novel T1-like Phage KanT1 Reveals a Standalone SH3 Domain as a Widespread Component of Drexlerviridae Cell Lysis Module, *International Journal of Molecular Sciences* (2026). DOI: 10.3390/ijms27093756

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