Title

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Journal

Nature Reviews Microbiology, 24(7)

ISSN

1740-1526

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Publication Date

2026-07-01

DOI

10.1038/s41579-026-01309-8

Peer reviewed

Genome watch

https://doi.org/10.1038/s41579-026-01309-8

In search of phage tail-like particles: nature's versatile nanomachines

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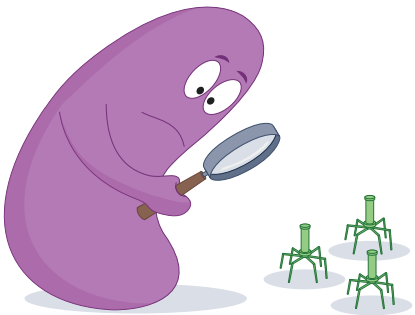
This Genome Watch article highlights the importance of predictive models for identifying and characterizing the roles of phage tail-like particles as a tool for bioengineering and biocontrol.



Phage tail-like particles (PTPs) are structures derived from temperate phages that infect and embed their genomes into their bacterial hosts. There are three major classes of PTPs, all of which have a tail spike, a baseplate and tail fibres: F-type and R-type tailocins, extracellular contractile injection systems (eCISs) and bacterial type VI secretion systems (T6SSs)[1]. Having lost the genes encoding the capsid, they no longer form functional phages but are instead deployed by the producer cell to attack and eliminate neighbouring competitors, scavenge for nutrients, mediate host–microorganism interactions and/or facilitate horizontal gene transfer.

Efforts have been made to identify PTPs in microbial genomes and elucidate how they interact with target cells. However, their rapid rate of evolution, the prevalence of horizontal gene transfer among bacteria and archaea, and the vast structural diversity of these nanomachines pose substantial challenges. Tailocins, for example, are often misidentified due to their similarity to phage tails and the skewed knowledge on their taxonomic distribution. A recent study[2] combined genomics, structural modelling and phylogenetics to predict R-type tailocins in diverse bacterial clades. The authors generated a list of candidate loci that contained phage tail genes but not T6SS marker genes. Subsequent phylogenetic reconstruction using spike and sheath protein sequences allowed the identification of novel putative R-type tailocins in the Morganellaceae and Paenibacillaceae clades.

Tailocin target range is determined by bacterial cell surface lipopolysaccharides, which act as receptors for tailocin tail fibres. A recent study[3] developed a predictive model to understand the determinants of tailocin specificity and to design tailocin-producing commensal bacteria that can protect kiwifruit from pathogens and prevent canker disease. The authors identified and characterized tailocin genes and proteins, and predicted tailocin target specificity using structural genes, hidden Markov model protein profiling and phylogenetic analyses. They hierarchically clustered tailocin killing and sensitivity matrices to successfully predict which tailocin-producing *Pseudomonas syringae* strains would be effective against the kiwifruit pathogen *P. syringae* pv. *actinidiae* by targeting the pathogen's lipopolysaccharides. This highlights the importance of tail fibre genes in target specificity, as well as the potential of tailocin-producing strains to serve as biocontrol agents.

Another study[4] used tail fibre genes in bacterial and archaeal genomes to identify and classify eCISs, providing functional, ecological and evolutionary insights into the roles of their receptor-binding domains. The authors used known eCIS collections to query for candidate tail fibre genes. Hidden Markov model profiles of conserved protein domains in these sequences revealed a shared structure of highly conserved N-terminal domains and variable C-terminal domains. These fibre N-terminal domains, probably responsible for tail fibre attachment to eCIS baseplates, were further classified into five major classes with distinct baseplate attachment and target adherence modules. Furthermore, phylogenetic reconstruction showed that many eCIS sequences nested within metazoan and viral branches, indicating that PTP tail fibres are rapidly evolving genes acquired from other kingdoms of life. Lastly, the authors combined the receptor recognition domain of a tail fibre from *Paenibacillus* sp. with an eCIS construct expressed in *Escherichia coli*. The resulting recombinant protein specifically targeted THP-1 human monocyte-like cells for toxin delivery, probably in a mannose-dependent manner[3]. These results underscore the potential of leveraging tail fibre gene prediction models to engineer systems with specific cell recognition and targeted cargo delivery.

Together, these studies highlight the role of PTPs as essential tools in interbacterial and inter-kingdom warfare, as well as their potential as biocontrol agents. Improvements in sequence annotation and computational models should lead to increasingly reliable characterization and prediction of PTPs, along with better understanding as to how these elements can be utilized in agriculture and other applications.

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Published online: 28 April 2026

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Acknowledgements

The work conducted by the US Department of Energy Joint Genome Institute, a DOE Office of Science User Facility, is supported by the Office of Science of the US Department of Energy operated under contract no. DE-AC02-05CH11231.