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Antimicrobial Tailocins- Exploring their Role in Plant Bacterial Management

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INTRODUCTION

Tailocins share a common ancestor with phages, but have repurposed the phage machinery for host-cell targeting for their own fitness advantage. Wild-type bacterium is immune to its own tailocin and because of this self-immunity, can release tailocins into the surroundings, while leaving its own genetic lineage unaffected. The targeting of the tailocin is tunable, with single gene additions or gene swaps shifting killing specificity. The production of tailocins is triggered by diverse stresses, including induction of the SOS (Save our souls) responses like UV light, drugs, oxidants, and chemical mutagens. The most commonly used inducers in laboratory practice are UVs and Mitomycin C (Backman *et al*., 2024).

Trade off and constraints on evolution of tailocins

Phage tail-like bacteriocins (tailocins) are protein complexes produced by bacteria with the potential to kill their neighbors. Widespread throughout Gram-negative bacteria, tailocins exhibit extreme specificity in their targets, largely killing closely related strains. Despite their presence in diverse bacteria, the impact of these competitive weapons on the surrounding microbiota is largely unknown. Recent studies revealed the rapid evolution and genetic diversity of tailocins in microbial communities and suggest that there are constraints on the evolution of specificity and resistance. Given the precision of their targeted killing and the ease of engineering new specificities, understanding the evolution and ecological impact of tailocins may enable the design of promising candidates for novel targeted antibiotics ((Woudstra *et al*., 2024).

Tailocins and microbe-microbe competitions

Ishii *et al*. (2024) reported first Alphaproteobacterial F-type tailocin, named rhizoviticin, as a determinant of the biocontrol activity of *Allorhizobium vitis* VAR03-1 against crown gall.

Rhizoviticin is encoded by a chimeric prophage genome, one providing transcriptional regulators (Region B) and the other contributing to tail formation and cell lysis(Region A), but lacking head formation genes. To investigate the genomic organization surrounding the genes responsible for the antagonistic activity of VAR03-1,they performed whole genome sequencing (WGS) of VAR03-1, VAT0-9 (Ti), and *A. vitis* VAR06-30 (VAR06- 30; a nonpathogenic and nonantagonistic strain) for comparison along with deletion mutants created for genes in region A and region B. The expression analysis revealed that Rhizoviticinwas responsible for most of the antagonistic activity in VAR03-1 culture supernatantagainst pathogenic *A. vitis* strain VAT03-9 (Ti), and rhizoviticin deficiency resulted in a significant reduction in the antitumorigenic activity in planta. Expression analysis of region Agenes in relation to deletion mutants of region B, proved that region B genes are essential for region A.

Coevolution of tailocins and their targets maintains genetic diversity

Baltrus *et al*. (2022) pretreated plants with supernatants from a variety of tailocins from *P*. *syringae* strains *Psy*Cit7 (which produces a tailocin that can target strain *Psy*B728a) and *Psy*B728a (which produces a tailocin butdoes not target itself); *P*. *aeruginosa* strain PAO1 (which produces an R-type pyocin that does not target *Psy*B728a) and no supernatant applied. Upon pretreatment no cells of *Psy*B728a recovered by plating from plants treated with supernatants containing *Psy*Cit7 tailocins. Deletion mutant created from strain USA011R i.e (USA011RΔRbp : receptor binding protein(Rbp) of the tailocin deleted, USA011RΔRbp+Rbp:Rbp and chaperone from strain USA011R was replaced for complementation of strain USA011RΔRbp *in cis*) proved the specificity of RBPs and also antagonistic activity of USA011R against *Psy*B728a in an overlay and also inplant experiments. Whereas mutant strainUSA011RΔRbp failed to control the pathogenic strain , both in overlay and in plant experiments.

Whether a tailocin is adaptive depends on the microbial ecology

Beyond the capacity to kill specific bacteria, what is the influence of tailocins on the larger bacterial community? Tailocins are distinguished by a unique set of molecular characteristics that potentially impact their role in microbial ecology. Tailocins are mechanical weapons that are released by cell lysis, enabling them to exert their lethal effects in a contact-independent manner. This is in contrast to T6SS, which requires direct contact between neighboring bacterial cells. Therefore, in principle, tailocins can exert a long-range influence on the configuration of microbial communities. Whether deploying a long-range weapon or short-range weapon is better may depend on the ecology of the producing bacterium

A phage tail–like bacteriocin suppresses competitors in metapopulations of pathogenic bacteria

The presence of a limited set of tailocin haplotypes in the metapopulation could reflect a limited panel of resistance mechanisms. Our findings provide a roadmap for identifying tailocin specificities to different strains and the possibility of determining the mechanism of this specificity. Tailocin therapy, akin to phage therapy, holds promise as an alternative to traditional antibiotics. Initial studies demonstrate its efficacy in suppressing pathogens in various plant and animal models. However, as with any antimicrobial treatment, resistance may arise.

Exploring the Genetics and Mechanisms of 'Bacterial Homing Missiles

A wide variety of bacteria are capable of producing extremely strong protein nanomachines known as tailocins.

Similar to phages but without viral DNA and replication machinery, tailocins spring into action under stressful conditions and cause cell death by poking a hole in the cell membrane, causing the content to ooze out. They appear to be a tool used by bacteria to compete with their rivals, and go after their targets with incredible specificity (Fig 1).

The Tailocin Tale: Peeling off Phage Tails

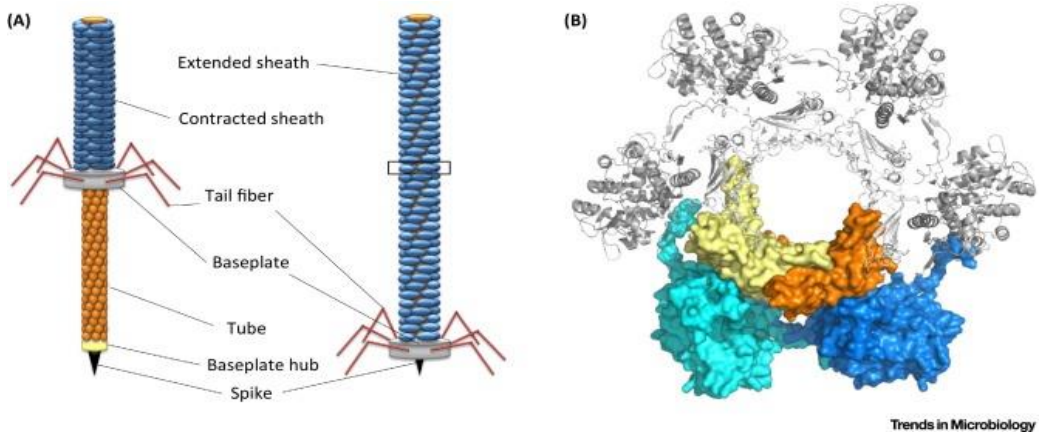

Fig 1- The Tailocin Tale: Peeling off Phage Tails

CONCLUSION

Tailocins have clear potential for the development of novel antibiotics. Synthetic antibiotics largely target broad classes of bacteria resulting in unintended suppression of the whole microbiome. In contrast, tailocin killing can be specific and targeted. The lock-and-key logic of the tail fiber–Lipo Polysaccharide interaction has lent itself to the engineering of newtargets simply by swapping tail fibers between tailocins or adding phage targeting proteins to tailocins. A possibility of engineering tailocins produced by plants may act as an additional layer of resistance against bacterial phytopathogens.

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