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Poster abstract submission

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Poster title

Understanding bacterial defence against jumbo phages to evaluate their potential in phage therapy

Poster abstract

The increasing prevalence of multidrug-resistant Pseudomonas aeruginosa (Pae) strains in clinical settings has intensified interest in alternative antibacterial treatments, such as bacteriophage therapy. The Pae jumbo phage PhiKZ is a promising phage therapy candidate because it evades the most prevalent bacterial anti-phage defences, such as restriction- modification and CRISPR–Cas systems, by enclosing the genome first within an early phage infection (EPI) vesicle and subsequently in a proteinaceous phage nucleus. However, alternative bacterial defence mechanisms targeting nucleus-forming jumbo phages could potentially undermine the therapeutic usage of PhiKZ. The two-component jumbo phage killer (Juk) system encoded by the clinical Pae isolate PA14 specifically targets nucleus-forming jumbo phages by stopping early phage infection through disruption of the EPI vesicle. The sensor protein JukA detects phage infection and recruits the effector JukB, resulting in EPI vesicle permeabilisation and clearance of the phage in a non-abortive infection mechanism. Using extensive bioinformatic analyses, we show that JukA is among the most prevalent defence sensors in Gram-negative bacteria and is associated with a wide range of putative effector proteins, including lipases, HNH nucleases, and GTPases, in addition to JukB.
First, we investigate the molecular basis of PhiKZ recognition by the widespread JukA sensor, identifying the phage proteins and additional factors that trigger Juk activation and defining their functional roles during infection. Membrane remodelling caused by the phage infection as well as phage proteins associated with the EPI vesicle influence the efficiency of Juk immunity. These insights help to engineer jumbo phages that evade defences like Juk potentially present in antibiotic-resistant bacteria.
Second, with functional screening for novel JukA-associated systems we aim to better understand the mechanistic diversity of anti-jumbo phage defences and to determine how widespread such systems are among clinically relevant bacteria. This knowledge is essential for understanding the constraints of nucleus-forming phages as alternative to treat antibiotic resistant bacterial infections.

Research topic

Phage or phage products

If you wish to submit a graphic with your abstract you can upload it here.