

## AMR 2024 conference abstract

Bacterial infections are a growing health concern worldwide and alternative treatment options are urgently needed to combat this new pandemic. Bacteriophages prey on their hosts irrespective of antibiotic-resistance and have been long recognised as an alternative means of combating infections. However, their unreliable performance in vivo despite their high in vitro potency has hindered their adoption as a reliable treatment option. Similarly, the survival of drug-sensitive bacteria to antibiotic treatment has been linked to the presence of non-growing, dormant cells inside patients and evolution of antibiotic resistance. Given the high abundance of non-growing, dormant bacteria in the environment, we wondered how phages interact with dormant bacteria. We found that most phages fail to replicate efficiently on dormant hosts suspend their replication until the host resuscitates ("hibernation"). However, we isolated a new *Pseudomonas aeruginosa* phage named Paride that kills these cells by lytic replication. Furthermore, the combination with Paride enables the carbapenem meropenem to eradicate deep-dormant cultures in vitro and to reduce a resilient bacterial infection of a tissue cage implant in mice. Intriguingly, we also found that efficient replication of Paride on dormant bacteria depends on the same stress responses that drive antibiotic tolerance. We therefore suggest that Paride hijacks weak spots in the dormant bacterial physiology that could be targeted as Achilles' heels to inspire novel strategies to overcome the resilience of persistent bacterial infections.