No need to catch 'em all: Exploring new worlds of phage-host interactions with handpicked natural isolates

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Résumé

Research on the biology of bacteriophages and their application in clinics and biotechnology is currently booming. However, most work on the molecular mechanisms of phage-host interactions has focused on few model phages, suggesting that natural phage diversity holds a huge untapped potential. We therefore composed a "BASEL collection" of around 80 new isolates that cover all major groups of tailed phages infecting *Escherichia coli*. This collection can serve as a powerful tool to probe a meaningful proportion of phage diversity when exploring any aspect of phage-host interactions, and we freely share these phages with researchers around the world. Our own genomic and phenotypic analyses directly resulted in remarkable discoveries, e.g., regarding the molecular basis of phage receptor specificity or the sensitivity / resistance of different phage groups to bacterial immunity systems. In parallel, we studied how bacteriophages infect slow- or non-growing bacteria that dominate in most ecosystems and are a major cause of chronic or relapsing infections due to their notorious antibiotic tolerance. Intriguingly, most phages failed to productively infect dormant hosts and instead entered an enigmatic state of hibernation previously described as "pseudolysogeny". However, we isolated a new phage called Paride that uniquely wipes out deep-dormant cultures of *Pseudomonas aeruginosa* irrespective of their extreme antibiotic tolerance. We are currently studying the molecular mechanisms underlying this ability. This work will shed new light on the biology of phages in natural environments and might identify Achilles' heels in the resilient physiology of dormant bacteria that could be targeted by new antimicrobials.

Mots-Clés: phage, host interactions

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