

Research Project

Phages to the front: Exploiting bacterial viruses to control antibiotic-tolerant infections

Third-party funded project

Project title Phages to the front: Exploiting bacterial viruses to control antibiotic-tolerant infections

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Organisation / Research unit

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Status Completed

Contrary to common perception, chronic or relapsing bacterial infections and antibiotic treatment failure are often not caused by multidrug-resistant pathogens, but rather due to specialized bacterial cells called persisters that have attained phenotypic antibiotic tolerance through entry into a dormant physiological state. Decades of research have implicated a multitude of genetic factors in bacterial persister formation, but no comprehensive understanding or effective treatments have so far been developed. It is therefore time to employ a genuinely new approach that may help to turn the tide against bacterial persistence. The current crisis of antibacterial therapy has recently revived interest in bacterial viruses called bacteriophages for their ability to eliminate multidrug-resistant bacterial pathogens ("phage therapy"). Successful application of phage therapy approaches includes chronic infections that are often linked to bacterial persister cells, indicating that bacteriophages have strategies to overcome their dormancy and kill them. In this project I therefore aim at comprehensively unraveling bacteriophage strategies to overcome the recalcitrance of bacterial persisters. I will therefore identify bacteriophages that are particularly proficient in killing persister cells, determine the genetic basis of this ability, and explore how bacteriophages manipulate the dormant physiology of persisters to their advantage. I anticipate that this research project will uncover true Achilles' heels in the physiology of persister cells that may be shared among different bacterial pathogens. These findings will therefore provide an in-depth molecular view into the essence of the elusive persister state and, consequently, guide the way for future studies aimed at the development of effective treatment options to cure persistent infections.

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