Developing microbiological ammunition for robust decolonization of antibiotic resistant bacteria

Supervisory team:
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Project description:

Taking antibiotics is not risk free. For a year after completing a course, there is an increased risk of complex infection from antimicrobial-resistant microbes, and individuals colonized with resistant microbes can transmit them freely to others for extended periods. These resistant bacteria are likely to be gut-dwelling commensals. Commensal bacteria make up most of the highly problematic multi-drug resistant microbes, and tackling the persistence of resistant commensals will be a key part of future antimicrobial stewardship and overall reduction in drug-resistant infections 1.

This project will explore how we might efficiently replace resistant Escherichia coli in the gut with harmless commensals by exploiting selective bacteriophage as phage therapy. Using novel experimental models, such as gut organoids, we aim to optimize these 'decolonization' strategies and develop approaches that are resilient to the evolution of phage resistance. Escherichia coli is a good target for this decolonization since one lineage (the ST 131 clonal complex) is responsible for a large proportion of multi-drug resistant infections, including life-threatening bacteraemia. The supervisors have already developed an efficient pipeline for isolating lineage specific phage as well as techniques (increasing within-species competition) that can make decolonization more effective.

Using this pipeline and an existing phage collection the student will develop diverse phage cocktails with the aim of displacing bacteria without producing widespread phage resistance in target E. coli genotypes. In addition, the student will isolate and sequence phage resistant E. coli in order to better understand the genetic basis of phage resistance to major phage families and test the efficacy of decolonization in simple in vivo models (insects, organoids). We also predict that broad-spectrum phage resistance might have severe fitness consequences for E. coli, especially in complex communities or under the harsher conditions in the gut, so the fitness consequences of phage resistance will also be explored in simple and diverse communities.

This is a multi-disciplinary project providing training in microbiology, evolutionary biology and bioinformatics with significant impacts on how we manage drug resistant and life-threatening infections. A successful student will gain important laboratory and analytical skills with infection models and microbial bioinformatics. The team have expertise in bioinformatics, phage resistance and displacement of antibiotic resistant bacteria 2,3,4 and have a wide range of experience that could match the interests of diverse applicants.

References: (1) Raymond (2019) Evol Appl https://doi.org/10.1111/eva.12808 (2) Watson et al (2021) Cell Host Microbe https://doi.org/10.1016/j.chom.2021.03.018. (3) Mikonranta et al. (2019) Biol Lett https://doi.org/10.1098/rsbl.2018.0895 (4) Cowley et al. (2019) Front Genetics https://doi.org/10.3389/fgene.2019.00763.