The evolutionary and mechanistic basis of virus host range

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Project description:
Given the rise in bacteria that are resistant to antibiotics, it is essential to a develop alternative strategies to deal with antimicrobial resistance (AMR). The use of phage (viruses of bacteria) to control bacterial infections offers a promising avenue (https://doi.org/10.1371/journal.pbio.3002119). However, the host range of a phage (which hosts it can infect) can limit its practical use to control infections. There is much to learn about what determines the ability of a phage to infect some groups of hosts but not others, or how phage will evolve in different hosts.

There has been a resurgence in the use of phage to treat bacterial infections due to the rise of antimicrobial resistance. To be effective phage need to have a suitable host range to infect the bacterial strains or species it is targeting and be efficient at replicating in and killing its bacterial host. Host range in phage is highly variable and there is variation in susceptibility across bacterial strains and species.

Our previous work has developed a system of 64 strains of Staphylococcus across 17 species of bacteria, and a broad host range phage called ISP. ISP can infect almost all of the host strains tested and the host phylogeny is an important determinant ISP to infect and replicate across these bacterial hosts (Walsh et al. 2023, https://doi.org/10.1371/journal.ppat.1011433). This suggests host relatedness can be a useful tool in predicting bacterial susceptibility to phage. ISP is currently being used for the treatment of antibiotic resistant Staphylococcus aureus in clinical trials. This project will ask fundamental questions about virus host range using a bacteria-virus system to study the why hosts vary in their susceptibility and the consequences of virus evolution on host range. We will first test how variation in i) the host receptor used by the phage to enter cells and ii) the intracellular defense systems, predict whether the virus can infect a given host. This will allow us to predict optimal characteristics for a broad host range phage with high killing potential. We will use this information, together with experimental evolution of the phage, to optimise its hosts range.

This model offers a unique opportunity to use experimental evolution to ask fundamental questions about virus host shifts with direct relevance for the growing problem of antimicrobial resistance.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.