Project title: How does the route of infection affect pathogen host shifts?

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Project keywords: Virus, host shift, emerging infectious disease
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Virus host shifts – where a virus jumps from one host species to another – are a major source of emerging infectious diseases. For example, Ebola, HIV and now SARS-CoV-2 have all jumped into humans from other species. We have a limited understanding about what determines the ability of a virus to infect some groups of hosts but not others, or how viruses will evolve in different hosts. Understanding these processes is vital to predict future diseases emergence.

Viruses are disproportionally responsible for emerging infectious diseases, with RNA viruses that normally infect multiple host species considered the most likely to emerge. Additionally, host shifts appear to occur most often between closely related host species. However, evidence for these hypotheses largely come from correlational data (i.e. observations with no experimental manipulation). Therefore, they point us toward interesting areas for investigation, but cannot tease apart the complex processes explaining the observed patterns.

Experimental studies have highlighted some of the important host-virus interactions that result in successful host shifts but the majority of these studies have been limited to two host in vitro systems, i.e. using cell cultures. Host-virus interactions may differ in whole animals for many reasons, and using only two hosts prevents drawing general conclusions. Therefore, experimental studies using a wide breadth of host species that vary in their relatedness are essential to make broadly applicable conclusions.

Work in our lab uses up to 50 species of Drosophila (fruit flies), and their naturally occurring RNA viruses to examine host shifts (Figure 1 and video here https://youtu.be/ViVHPuPTEZs). These species of Drosophila have equivalent diversity to all mammals and are an established innate-immunity model. By using a large number of different host species we are able to find general patterns that apply across hosts species with varying relatedness. This model offers a unique opportunity to perform experiments that would not be possible in a vertebrate-system. Using this system we have demonstrated the host phylogeny is important for understanding a pathogen's ability to jump between host species, cause virulence and how a virus will evolve in a new host.

Figure 1. Ancestral state reconstruction showing the virulence (harm caused to a host) across the host phylogeny.
**Project description:** Pathogens can be acquired in different ways e.g. ingested, inhaled or by vectors. This project will explore if the route of transmission leads to different outcomes of infection. We will orally infect multiple species of fruit fly with an RNA virus and compare this to data where flies have been systemically injected with the same pathogen. This will allow us to test if species respond in the same or different ways when infected by different routes. The project would suit anyone with an interest in the pathogen evolution. Training will be provided in working with insects, viruses, molecular biology and data analysis in a supportive and friendly lab group.

For informal enquiries, please contact Ben Longdon (b.longdon2@exeter.ac.uk). Dates are flexible (end of June to mid Sept). More info about our group can be found at [https://benlongdon.com/join/](https://benlongdon.com/join/)

**Work schedule at Penryn campus:**

6 weeks: lab work
2 weeks: report, presentation or poster

**Key references**