

# Pathogen persistence

**Drs Helen Hesketh** and **Thomas Jones** discuss the progression of their research into the ecology and evolution of horizontal and vertical transmission strategies in a model insect-virus interaction system



We last spoke with you about your research project in March. Can you begin by briefly recapping the project's key objectives?

Using insects as a model system, our major objective was to explore how ecological conditions influence the methods pathogens use to transmit between their hosts. We know that pathogen transmission is crucial to the persistence of pathogens in the environment and, if it fails, the infected hosts will eventually die or recover, and the pathogen is lost.

Understanding how environmental conditions can alter the rate or occurrence of transmission is critical for understanding how pathogens persist in a constantly changing environment, and what the implications may be for the regulation of natural insect populations.

**What have your recent experiments revealed about how the meal moth *Plodia interpunctella* and its granulovirus, *PiGV*, have evolved?**

We have a complicated dataset from the long-term experiments that have only recently finished – this is one of the most exciting parts of our work as we now get to see how the virus and host have been changing over time. As yet, we don't have a clear picture of how *P. interpunctella* and its virus evolved under the different environmental conditions, but we are gradually piecing together the puzzle using

these data and the detailed molecular results we have obtained.

**Can you clarify the difference between horizontal and vertical virus transmission?**

In our model system, horizontal transmission occurs when a susceptible *P. interpunctella* larva comes into contact with a dead *PiGV* infected larva. If the susceptible larva ingests any virus particles, its gut conditions activate the virus and allow it to pass through the gut wall into the susceptible larvae, where the virus eventually kills the host and perpetuates the cycle. There is therefore an evolutionary pressure for the virus to kill its host, and in so doing, to produce many infectious virus particles.

In contrast, the vertical transmission of *PiGV* occurs between two living hosts, specifically

## A complex conflict

Researchers at the **Centre for Hydrology and Ecology** in Wallingford and the **University of Leeds**, UK, have been investigating the impact of varying ecological conditions and pathogen virulence on different modes of disease transmission

**INFECTIOUS DISEASES ARE** transmitted by one of two mechanisms: horizontally or vertically. Horizontal transmission occurs when an infectious agent is transferred from infected to susceptible individuals, while vertical transmission occurs when a pathogen is passed from mother to embryo, foetus or baby during pregnancy or birth. The two types of transmission operate in clear conflict with one another: the horizontal transmission of a deadly disease that kills the host prevents the vertical transmission of infections further down the line, which depend on host survival and reproduction.

Using an insect model, a Natural Environment Research Council (NERC) project run by the Centre for Hydrology and Ecology in Wallingford and the University of Leeds – respectively led by Drs Helen Hesketh and Steve Sait – has been attempting to understand the conflict between the ecology and evolution of horizontal and vertical transmission strategies. According to Dr Tom Jones, a postdoc who is undertaking the experimental work in Sait's laboratory in Leeds: "There are multiple benefits to understanding how viruses transmit

under different environmental conditions". Hesketh adds: "Natural populations of plants and animals are constantly under threat from emerging and re-emerging diseases and invasive non-native species. A better understanding of the methods by which pathogens transmit between their hosts will help to build a fuller and more informed picture of disease ecology".

### MAPPING THE METHODS

Using their insect-virus model system, the researchers set out to explore the ecological conditions that favour the different modes of transmission and to establish the link between transmission mode and pathogen virulence using the Indian Meal moth (*Plodia interpunctella*) and the *Plodia interpunctella* granulovirus (*PiGV*).

In their studies, the scientists used two main experimental approaches. First, they conducted long-term laboratory experiments that enabled them to maintain multiple lines of host and virus under controlled conditions and, crucially, to determine how the host and virus were affected under different environmental

conditions. In these experiments, they were able to analyse host and virus population dynamics and transmission routes in a relatively natural set-up. Second, the researchers conducted evolution experiments in small microcosms, in which they had a much higher degree of control over the host-pathogen interaction. This allowed them to study the occurrence and evolution of different transmission strategies, along with the associated pathogen traits, at selected host densities.



Bioassay container housing individual test larvae infected with the virus, turning them a milky white colour.

a parent and its offspring. Because vertical transmission requires that an infected individual survives to adulthood and manages to reproduce, there is an evolutionary pressure on the virus to be non-lethal and to do minimum harm to the host while maximising the chance that it is transmitted to any offspring. This presents the virus with a conflict – to be good at horizontal transmission, which requires killing the host, or to be good at vertical transmission, which requires the host to survive.

### Have you opened up any new opportunities for collaboration or identified further research needs as a result of your initial findings?

There is a significant gap in our knowledge in relation to the risks posed to biodiversity by microorganisms in the environment. Studies like ours provide baseline data that build knowledge about invasive non-native pathogens and how they may transmit in the environment. We will be holding a collaborative workshop in 2015 in Wallingford, UK, as part of the COST Action TD1209 'Alien Challenge' funded by the COST Association, to specifically draw together specialists from the UK and the wider EU with research interests in pathogens that affect plants and animals in natural and semi-natural systems.

We are aiming to run an exercise to scan for invasive non-native pathogens that will impact on biodiversity in the EU and highlight where there are research priorities and knowledge gaps in a consensus opinion paper.

### What are the next steps for your research?

The next step is to analyse and synthesise the large datasets that we have generated from our population and evolution experiments. Once we understand the full story, we will write articles that present these results to the scientific community. Beyond that, our initial findings have raised more questions than they have answered – and the connections between simple theory, highly controlled evolutionary microcosm experiments and the more natural population experiments were not always what we expected.

Future directions could involve moving both up and down the scale – upwards to examine some of the processes we have studied in field experiments and natural populations, and downwards to try and understand the differences between vertically and horizontally transmitted viruses at a genetic and molecular level.

## INTELLIGENCE

### THE ECOLOGY AND EVOLUTION OF HORIZONTAL VERSUS VERTICAL TRANSMISSION IN A MODEL INSECT-VIRUS INTERACTION PROJECT

#### OBJECTIVE

To understand the ecological conditions that favour horizontally or vertically transmitted viruses; in particular, the effect of covert infections on host population dynamics and the impact of contrasting transmission strategies on host and pathogen life history traits.

#### KEY COLLABORATORS

Dr Steven M Sait, University of Leeds, UK  
• Professor Rosemary S Hails; Professor Robert D Possee, Centre for Ecology and Hydrology, Wallingford, UK

#### FUNDING

Natural Environment Research Council (NERC) – grant nos. NE/H021256/1 and NE/H021264/1

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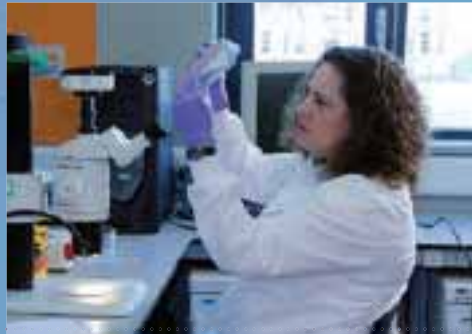
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DR HELEN HESKETH is a higher scientific officer working in the Natural Hazards Science area at the NERC Centre for Ecology and Hydrology. She is an insect pathologist with research interests in the ecology of host-pathogen interactions and developing insect pathogens as biological alternatives to pesticides for controlling agricultural and horticultural pests.

DR THOMAS JONES is a postdoctoral research assistant working in the Department of Biology at the University of Leeds. He is a population biologist with research interests in the ecology of host-pathogen interactions and the role of multispecies interactions structuring ecological communities. Jones' work has mainly focused on insects and their natural enemies, including pathogens and parasitoids.



Dr Helen Hesketh checks for larvae infected with the virus in a microcosm experiment.

### REVEALING THE RESULTS

Having completed the population experiments, the team's analysis of the large and complex datasets is underway. Initial findings demonstrate that environmental conditions have a significant impact on the host-pathogen interaction – but not in the manner originally hypothesised. "The dynamics of the virus produced a major surprise," Jones admits. "We expected that the virus would do well under good environmental conditions and that there would be a lot of horizontal transmission, while in the poor environment we expected that horizontal transmission would be reduced and the virus would rely more on vertical transmission." However, the initial results seem more complex than this, possibly because the environment affects the health and resilience to disease of individual hosts as well population size.

Additionally, the scientists have identified some surprising results from the microcosm experiments. Using molecular probes, they found that the level of vertical transmission in these small and highly controlled populations was significantly less than had been demonstrated in previous experiments using *P. interpunctella*. Indeed, the vertical disease transmission rates responded to disturbances in the host environment in much more flexible ways than had been predicted. "When we performed the controlled selection experiments – which allowed us to look at vertical transmission in isolation from horizontal transmission – we were only able to detect the virus in the next generation of insects," Hesketh discloses. "It therefore appears that vertical transmission alone would not be able to sustain infection in the population as it effectively 'dies out' after one generation."

### JOINING THE DOTS

To date, the researchers have found that the connection between environmental conditions and host-pathogen interactions is subtle and intricate, requiring analysis at the individual, population and evolutionary levels. Looking ahead, they will continue to analyse data in an effort to contribute vital knowledge to disease ecology, helping scientists identify how environmental changes will influence the spread and impact of novel pathogens on natural populations in the future.



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