Tackling Zika—using bacteria as a Trojan horse

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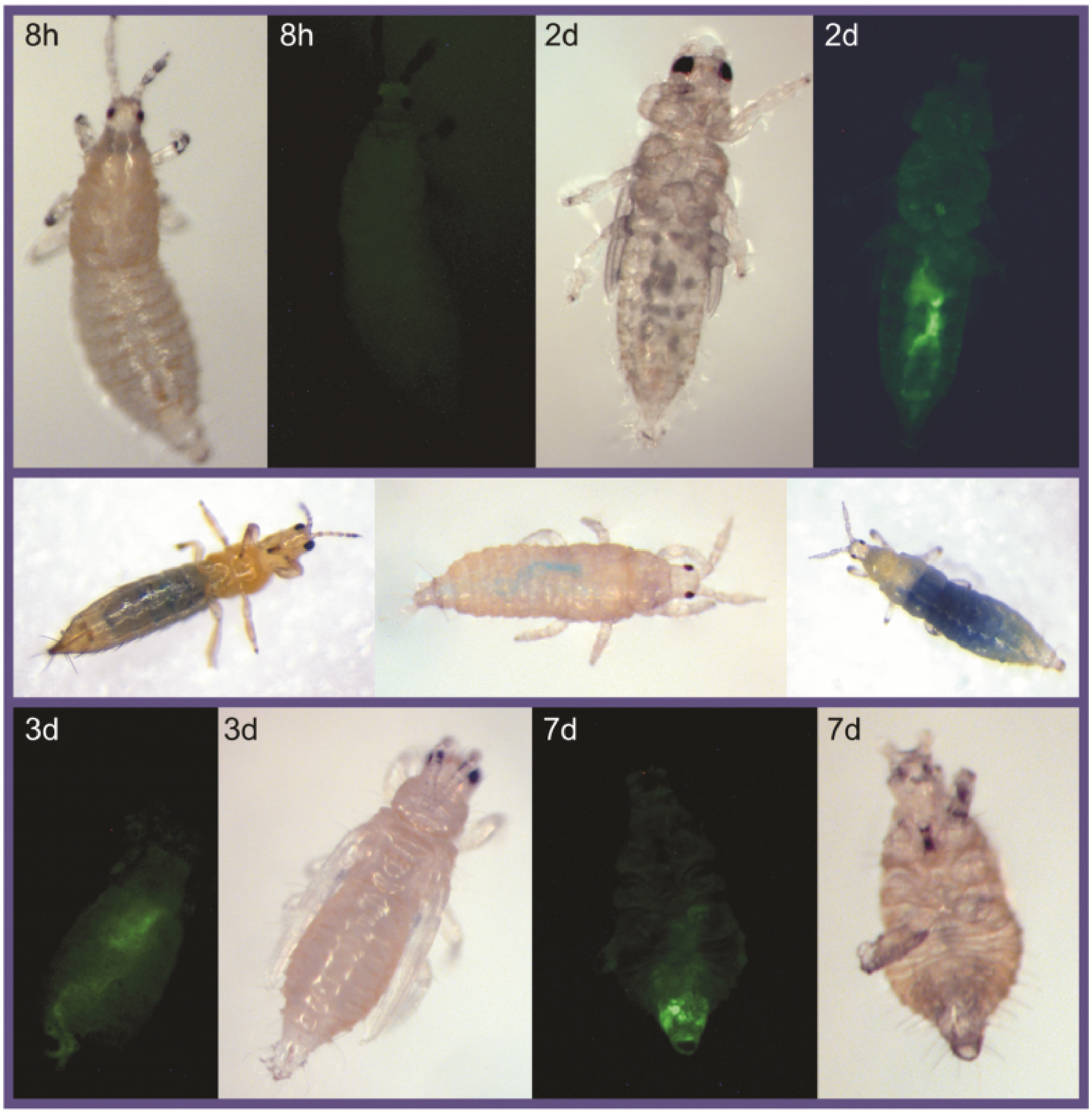


Symbiotic bacteria, here expressing green fluorescent protein, from the gut of the pest insect Western flower thrips (*Frankliniella occidentalis*).This was one of the two species used by researchers at Swansea University for their paper: "Symbiont-mediated RNA interference in insects" Credit: Dr Miranda Whitten, Swansea University

Bacteria in the gut of disease-bearing insects - including the mosquito which carries the Zika virus - can be used as a Trojan horse to help control the insects' population, new research at Swansea University has shown.

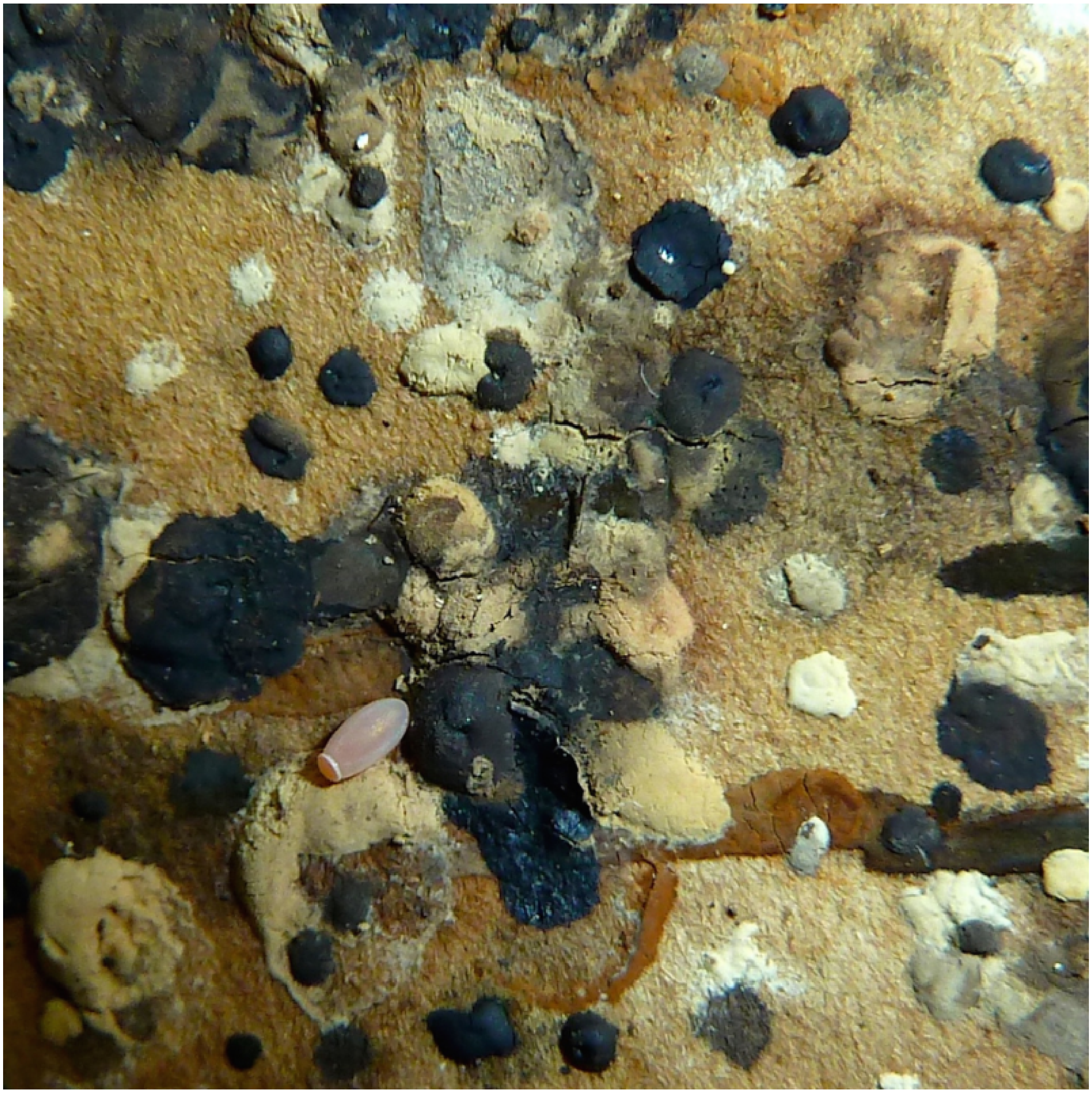
The results showed declines in fertility of up to 100% and an increase of 60% in the mortality rate of larvae, amongst the insects studied.

The findings, which are published today in *Proceedings of the Royal Society B*, come as the World Health Organisation calls for all avenues to be explored, including research using genetic technology, in tackling the Zika virus.

The Swansea team's findings offer the prospect of a much more targeted approach to insect control, targeting only the insect in question, and without the significant downsides of chemical pesticides, such as environmental damage, health risks, and insects becoming resistant.

The technology at the heart of the team's work is called RNAi, a natural process that cells use to turn down, or silence, the activity of specific genes, for example the genes that control fertility.

Although RNAi has been investigated previously in relation to insects, the problem has been how to deliver it effectively. Injection into selected insects is one delivery method, but this is time-consuming and expensive, and many insects are simply too small for this to be viable.



A solitary egg surrounded by the symbiont-rich excreta of the blood-sucking bug *Rhodnius prolixus*. This was one of the two species used by Swansea University researchers in their paper: "Symbiont-mediated RNA interference in insects" Credit: Dr Miranda Whitten, Swansea University

The Swansea team's research, which is described as "a significant advance", demonstrates that bacteria can be an effective delivery vehicle for the RNAi.

Their technique, known as symbiont-mediated RNAi, uses friendly (symbiotic) bacteria inhabiting an insect's gut as a Trojan horse to deliver a "switch off" command to chosen target insect genes.

The researchers tested out the technique on two insect species:

- The Kissing bug (*Rhodnius prolixus*) - these long-lived blood-sucking bugs carry the parasites that cause Chagas Disease, which affects up to 8 million people in central and south America. They are known as kissing bugs as they tend to settle on people's faces at night.

  The research showed that the technique suppressed fertility in this bug by up to 100%

- Western Flower Thrips (*Frankliniella occidentalis*) - this is a very invasive agricultural pest affecting many parts of the world, which has developed resistance to pesticides

  The technique resulted in an increase of 60% in the larvae mortality rate of this species

In the light of these findings, the researchers conclude that: "this represents a significant advance in the ability to deliver RNAi, potentially to a large range of non-model insects."

Significantly, the team report that the technique would be transferable to many insect species, including the Aedes mosquitoes, which carry the

Zika virus.

"It is expected that symbiont-mediated RNAi would be effective in other insect species. The unifying prerequisite is that the insects harbor culturable symbionts, a criterion already known to be met by many globally important insect species such as Aedes and Anopheles mosquitoes, tsetse flies, white fly and honeybees."

The method involves identifying an appropriate bacterium in each insect to deliver the RNAi. The bacteria are specific to that particular insect and cannot live outside it.

The technique has various important advantages compared to chemical pesticides:

- It is targeted specifically at the species in question, and does not harm other insects, such as bees and other pollinators
- It does not carry the risk of environmental damage and harm to human health
- Insects do not acquire resistance to it in the way that they do to chemical pesticides

Professor Paul Dyson of Swansea University Medical School and Dr Miranda Whitten of Swansea University College of Science are leading this work. Professor Dyson has just returned from a research visit to Brazil, where the Zika virus is most prevalent. He has also previously used this technology to develop a pesticide-free weapon against insects that cause sleeping sickness and damage crops, research which was funded by the Gates Foundation.

Professor Paul Dyson of Swansea University Medical School said:

New approaches are urgently needed to reduce the global burden of pest insects and to investigate insect biology and disease transmission.

This technology allows us to target insects much more effectively than conventional pesticides, and without their side-effects. Using bacteria as a Trojan horse gets round some of the problems in delivering RNAi to the insect.

It is a significant advance. It can help us to tackle some of the insects and crop pests that have such a devastating impact on human health and the food chain.

Our method could also help in the fight against the Zika virus, as the *Aedes* mosquito that bears the virus has bacteria that would be suitable.

Dr Miranda Whitten of Swansea University College of Science said:

The symbiotic bacteria basically do all the hard work for us - they are programmed to manufacture the RNAi molecules inside the insect's body, for as long as needed, and they do this without being detected by the insect's immune system.

As we can choose which gene - or combination of genes - to target, we now have a highly flexible gene-suppression toolbox. This is combined with an exquisite specificity that shouldn't affect other insect species, even if they share the same habitat.

More information: Symbiont-mediated RNA interference in insects, *Proceedings of the Royal Society B: Biological Sciences*, rspb.royalsocietypublishing.or … .1098/rspb.2016.0042

Provided by Swansea University