Scientists discover rare 'gene-for-gene' interaction that helps bacteria kill their host

May 3 2007

Scientists have discovered that a cousin of the plague bacterium uses a single gene to out-fox insect immune defences and kill its host.

In research published in the journal *Proceedings of the National Academy of Science*, scientists have found that Photorhabdus bacteria produce an antibiotic which inhibits the work of an enzyme that insects' immune systems use to defend themselves from attack.

Although such so-called gene-for-gene interactions are thought to be common in diseases, very few examples of a single gene in a pathogen targeting a single gene in an animal or human host have been identified so far.

Photorhabdus is a family of bacteria that in relatively small concentrations can kill insects - between 10-100 cells of it are typically enough – but most are harmless to humans and can be used as a biological control mechanism to replace pesticide use.

The researchers, from the universities of Bath, Bristol and Exeter, all in the UK, used the large caterpillar Manduca sexta (tobacco hornworm) to study the bacteria's so-called virulence genes.

"The beauty of this research is that we have been able to study the whole genome of the bacteria to work out how it kills its host," said Professor Stuart Reynolds from the University of Bath.

"People studying diseases think that the kind of gene-for-gene interaction between pathogen and host that we have found is quite common, but actually rather few are known, which is why this research is so interesting.

"The immune systems of all animals, even relatively simple ones like insects, are all very similar.

"This is particularly true of the innate immune system, which is the fast-acting battery of defences that recognise and kill microbes to prevent infections from occurring.

"Some remarkable discoveries have been made using insects that have subsequently allowed important advances in understanding how the human immune system works."

As part of their innate immune system, insects use an enzyme called phenoloxidase to produce reactive molecules that kill bacteria and then encapsulate them in a dense coat of black pigment called melanin.

The researchers found that Photorhabdus produces a special phenoloxidase inhibitor to protect itself against this particular defence.

They identified the inhibitor as a small molecule called 1,3-dihydroxy-2-(isopropyl)-5-(2-phenylethenyl)benzene, known as ST for short.

This molecule is also an antibiotic and Photorhabdus produces it to kill off other microbes that might grow in the corpse of the dead insect.

To test their findings, the researchers produced a mutant Photorhabdus that is unable to make ST. Without ST, the bacteria were less virulent. The researchers then used a technique known RNA interference to

prevent the insects from producing the phenoloxidase enzyme. These insects were more susceptible to regular Photorhabdus bacteria.

But when the two were combined, it was found that not being able to produce ST made no difference to Photorhabdus when colonising insects unable to produce phenoloxidase.

"This is conclusive evidence for a gene-for-gene interaction between the bacterium and the insect," said Richard ffrench-Constant (correct) of Exeter University.

"Photorhabdus is an important biocontrol organism that is used to control insect pests and reduces pesticide use, so the more we know about it, the more useful it can be.

"Insects are the major players in almost every ecosystem on the planet, so we need to know as much as we can about them."

Source: University of Bath