Viral gene drives sick gypsy moth caterpillars to climb high and die

September 8 2011

A photo of a Gypsy moth caterpillar 'face.' Credit: James McNeil

For a century, scientists have watched European gypsy moth caterpillars infected with a virus use their last strength to do something that a healthy gypsy moth caterpillar would never do in daylight hours – climb high into a tree and onto a leaf. This behavior in infected caterpillars was so consistent that it inspired the term "Wipfelkrankheit," or "tree top disease," to describe the virus that caused it. For scientists, the question has been how does a virus change its host's behavior?

Gypsy moth caterpillars infected with baculovirus forfeit safety and stay

in the treetops during the day because a virus gene manipulates their hormones to eat continuously and forego molting, according to entomologists. The caterpillars die where they climb and infect other gypsy moth caterpillars. "Normally, gypsy moth caterpillars are active at night," said Kelli Hoover, professor of entomology, Penn State. "They hide during the day in the soil or bark crevices protected from birds. They climb up the foliage at night to feed." Researchers have long known that gypsy moth caterpillars, like nearly all caterpillars, have baculoviruses that infect them and that a gene in the virus, egt, blocks molting in the caterpillar, keeping it in a feeding state. These viruses use most of the tissue of their hosts to reproduce and almost always kill their host.

"Baculoviruses have been known to induce climbing behavior in their caterpillar hosts for over 100 years," the researchers report in today's (Sept 9) issue of *Science*. "Until recently, determining the evolutionary basis for these altered behaviors has proven difficult in the absence of a mechanistic explanation."

The infection was labeled tree top disease 100 years ago, but back then, researchers could not look at either the virus' genetic material or the metabolic pathways in the caterpillar. Hoover and her team looked into the mechanism by which the gypsy moth baculovirus manipulates the behavior of the caterpillars.

They identified a specific viral gene, egt, that codes for an enzyme, EGT --UDP-glycosyltransferase -- that inactivates the hormone that triggers molting. Male gypsy moth caterpillars molt five times during their lives, while females molt six times before they pupate and emerge as moths. But infected caterpillars do not molt again once levels of EGT become high enough. EGT induces the caterpillar to climb to the treetops, hang onto the leaf or bark with their prolegs and die. Then, they liquefy and rain viral particles over the leaves for other caterpillars to ingest and

become infected. Older caterpillars are induced to die on the bark next to their fellow gypsy moths that pupate and emerge to walk over the dead cadavers, picking up virus that can be transmitted to the next generation during egg laying

"One of the best ways to control complex behavior is to manipulate hormones," said Hoover. Genes that influence hormones are perfect targets to change behaviors. The viral gene egt blocks molting by inactivating the molting hormone ecdysone, keeping the insect in a feeding state.

"It is good for the virus because if host spends 24 hours not feeding while they prepare to molt, this is time that the host is not getting bigger to maximize the host's biomass to make into more virus," said Hoover. "In this case we've found that that the gene also somehow induces the caterpillars to go to just the right location to enhance transmission of the virus to new hosts."

The researchers are not completely certain why the caterpillars climb or stay aloft during daylight when they are infected. One possibility is that without the molting cue, the caterpillars simply have an urge to eat continuously and so remain in the treetops.

"Michael Grove, my former technician who initiated this study in my lab, thinks that even when the molting hormone is inactivated, the caterpillars may still be triggered to climb to molt," said Hoover. "They climb, but rather than molt, they stay where they are until they die."

To show that the egt gene is responsible for the climbing, the researchers used tall plastic bottles lined with screens for the caterpillars to climb on. The bottles contained an artificial caterpillar diet for food. The researchers tested six different virus infected groups of caterpillars and one uninfected group. Two groups were infected with different,

naturally occurring virus; two groups were infected with virus that had their egt gene inactivated in different ways; and two groups had the egt gene reinserted in the viral DNA.

The two naturally occurring viruses caused the caterpillars to climb and die at the top of the container, but the caterpillars infected with virus lacking the egt gene died at the bottom of the container. The caterpillars with the restored egt gene also died at elevated positions.

All the infected caterpillars exhibited the same symptoms during the initial phases of the infection, but only those infected with viruses containing egt climbed to die.

Hoover notes that this is one of the first studies to identify the gene of the parasite responsible for altering the behavior of the host animal. Many parasites manipulate their hosts, but in most cases, how this occurs in not known. Other pathogens that control host behavior in mammals include toxoplasmosis and rabies. Toxoplasmosis is a parasitic disease that mostly infects cats, but can infect other mammals. If a mouse becomes infected with toxoplasmosis, they lose their innate fear of cats and become easier for cats to catch. This benefits the infecting protozoa because it more easily spreads to its preferred host.

The rabies virus also alters behavior causing normally nocturnal animals to appear during the day and to become far more aggressive than normal.

Provided by USDA Forest Service