New research details parasitic battles

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Scientists at MIT's Department of Civil and Environmental Engineering and the Technion Israel Institute of Technology have for the first time recorded the entire genomic expression of both a host bacterium and an infecting virus over the eight-hour course of infection.

The results of this research likely will encourage scientists in several fields to rethink their approach to the study of host-virus systems, which are believed to play a key evolutionary role by facilitating the transfer of genes between species.

Professors Debbie Lindell of the Technion and Sallie Chisholm of MIT and co-authors report in the Sept. 6 issue of *Nature* that their study of a system involving the marine bacteria, Prochlorococcus, leads them to speculate that viral infection may play a role in shaping the genetic repertoire of families of bacteria, even though individual infected bacteria die.

This could indicate that the meeting between a marine bacterial host and its virus may not be just a battle between two individuals, but an evolutionarily significant exchange that helps both species become more fit for life in the ocean environment.

"The current status of host-virus relations has been influenced by a rich history of interactions," said Lindell. "While we can't definitively pin down the sequence of past co-evolutionary events, our findings suggest a novel means through which the exchange of beneficial genes between host and virus have been triggered."

And, because the pattern of genomic expression in this host-virus system differed significantly from that in the more commonly studied system of intestinal bacteria such as E. coli and a virus called T7, the research will likely lead to increased appreciation for the need to study diverse types of marine bacteria, rather than relying on a single system as a broad model.

“We hope this work will encourage scientists to explore a wide range of host-pathogen systems and thus lead to a significant broadening of our understanding of the diversity of the host-pathogen interactions existing in nature,” said Chisholm, one of the discoverers of Prochlo-rococcus in 1985. “More importantly, these studies will help us understand the role these interactions play in shaping microbial ecosystems.”

Researchers have only in the past few decades begun discovering and studying ecologically relevant ocean bacteria, such as Prochlorococcus, which play a very important role in our lives. These single-celled photosynthetic bacteria use light energy to produce oxygen and organic carbon —supplying a significant portion of the oxygen we breathe—and forming the basis for the ocean food chain.

In previously studied host-virus systems, a virus hijacks the bacterial host cell and shuts down genome expression immediately, preventing the bacterium from conducting its own metabolic processes. The attacking virus redirects expression to its own genome and activates the genes beneficial for its activity, which is to replicate itself quickly at the cost of the host.

But uncharacteristically, in the system of Prochlorococcus and virus P-SSP7, an unprecedented 41 of the bacteria’s 1,717 genes were upregulated. That is, the researchers detected increased quantities of the messenger RNA encoded by these genes in the cell during the infection process. The upregulation of so many host genes during infection is a

phenomenon unseen before in the world of bacteriology.

Moreover, many of the host genes upregulated during infection are among those that are found in genomic islands in the host, variable regions that appear to be hot-spots for genetic exchange between bacterial hosts and viruses. In this case, some of the genes that have been transferred back and forth encode for proteins that affect the bacteria's ability to adapt to changes in environmental factors, such as nutrient deprivation and light stress. The scientists hypothesize that modifications made to the bacterial genes when they were in the virus led to new versions of the proteins that may provide the bacteria with an increased ability to withstand environmental changes. It is also possible that multiple copies of a gene provide some benefit.

Another unusual occurrence is that the viral genome contains genes transferred from bacterial hosts that encode energy-producing proteins, including photosynthesis genes that cyanobacteria need for metabolism and DNA replication. Although these genes are positioned far apart in the viral genome, they are transcribed at the same time during infection rather than in the usual left-to-right order. This leads the researchers to surmise that the virus is trying to keep its host alive longer so that the host continues to provide the energy needed for the virus's own DNA replication.

Lindell and Chisholm believe the most plausible scenario to explain the gene upregulation and gene trading is that the bacterium activates certain genes in response to infection as a means of self-protection. The virus has "learned" to use those genes to its own advantage and so incorporates them into its own genome. Later, when infecting another bacterium, the virus upregulates those genes itself to facilitate its own reproduction within the host bacterium. When a bacterium survives an infection, those viral modified genes are incorporated back into the bacterial DNA in genome islands, making that bacterium and its descendants more likely

to survive in the harsh ocean environment.

“These viral parasites cooperate with their hosts during infection, providing proteins that probably function within host metabolic pathways, to squeeze every bit of energy out them before killing them off,” said Lindell. “Yet on evolutionary scales, such host-pathogen interactions are influencing the evolution of gene content in both host and virus, which in turn is likely impacting their ability to colonize new niches.”

Next steps in the research are to see if the host-like genes in the virus really do confer a fitness advantage to the virus and then to the host bacterium when transferred back.

Source: Massachusetts Institute of Technology