Discovery in plant virus may help prevent HIV and similar viruses

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Purdue molecular geneticist Zhixiang Chen is studying a plant virus that causes illness in the same way as human immunodeficiency virus. Cauliflower mosaic virus infected the laboratory plant Arabidopsis on the left. Blocking a gene in the plant on the right prevented infection. Chen's research eventually could lead to new treatments for the plant disease, HIV and other similar illnesses. Credit: Purdue University photo/Alex Turco

In a study that could lead to new ways to prevent infection by human immunodeficiency virus (HIV) and similar organisms, Purdue University researchers have been able to genetically modify a plant to halt reproduction of a related virus.

Cauliflower mosaic virus attacks a group of plants that includes the largest number of agriculturally important plants in the world. The plant virus and HIV, which causes AIDS, use the same process to multiply in their victims' cells and spread disease.

"After HIV infects a person, it must recruit and latch onto particular human proteins so that the virus can replicate throughout the body," said Zhixiang Chen, a Purdue professor of botany and plant pathology. "We found that cauliflower mosaic virus relies on the same protein complex to multiply in plants."

Cauliflower mosaic virus, known as CaMV, attacks a plant group that includes cauliflower, broccoli, cabbages, turnips, canola and many types of mustard.

"We believe that the proteins in these host plants might be particularly important for these types of viruses, such as HIV, because if you block them, then the viruses simply can't replicate."

The retrovirus HIV and the pararetrovirus CaMV both use reverse transcription to recruit the host's proteins in order to reproduce and spread infection. Transcription in cells is the process in which a gene's DNA code is copied into RNA, which, in turn, carries the information to another part of the cell or to another cell. In reverse transcription, used by viruses such as HIV and CaMV, the virus' RNA is copied into DNA after it latches on to a victim's cell. This allows the virus to easily integrate into the host's genome and then reproduce in other cells.

Chen and his colleagues published a report on their study in the most recent issue of the journal *The Plant Cell*.

The researchers found that in the laboratory research plant Arabidopsis, cauliflower mosaic virus recruits a protein complex called CDKC. This is the same protein complex that HIV uses, known in humans as P-TEFb. Since both viruses use this same process to trigger transcription, the scientists now know that this protein complex and its related genes have passed from species to species as organisms evolved over millions of years, Chen said.

"P-TEFb appears to be an evolutionarily conserved target of complex retro- and pararetroviruses for activating transcription," he said. "This must also reflect a fundamental mechanism for transcription inherited by these viruses."

Humans and organisms used for research, such as fruit flies and the tiny wormlike organism Caenorhabditis elegans, have only one gene in the protein complex that retroviruses use to activate transcription. These organisms die if that gene is completely blocked because of its essential role during transcription. This makes it difficult to analyze the function the gene may have in the organisms' growth, development and survival. Unlike those other organisms, the plant protein complex involves two genes.

"In Arabidopsis there are two genes for the CDKC protein complexes that trigger the transcription process," Chen said. "If we knock out one of these genes, the plants become resistant to CaMV and the plant is still growing."

The discovery of these two genes suggests that the mustard plant Arabidopsis is a better organism than others for studying how the proteins regulate gene function and transcription, he said.

However, blocking of one of the plant's genes caused some alteration of leaves, flowers and trichomes (tiny hairlike structures) and delayed flowering on the mutated plants, he said. In addition, mutant plants in which both genes were blocked died in the embryonic stage just as would an organism with only one gene.

Now that Chen knows that Arabidopsis has two genes involved in the transcription process, his research team wants to learn more about genes' possible roles in plant growth and development and where those tasks are performed.

"The two genes each may have specialized functions depending on where they are activated in the plant," he said. "In some tissues the genes appear to be turned on in the same place. But, for example, in the flower, one gene is expressed in one particular place and the other gene is expressed in a different place."

The key question for researchers is how blocking the function of one protein inhibits transcription and replication of the viruses. Discovering the answer could mean major advances for prevention of retroviruses and treatment of the diseases they cause in plants and animals.

Source: Purdue University

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