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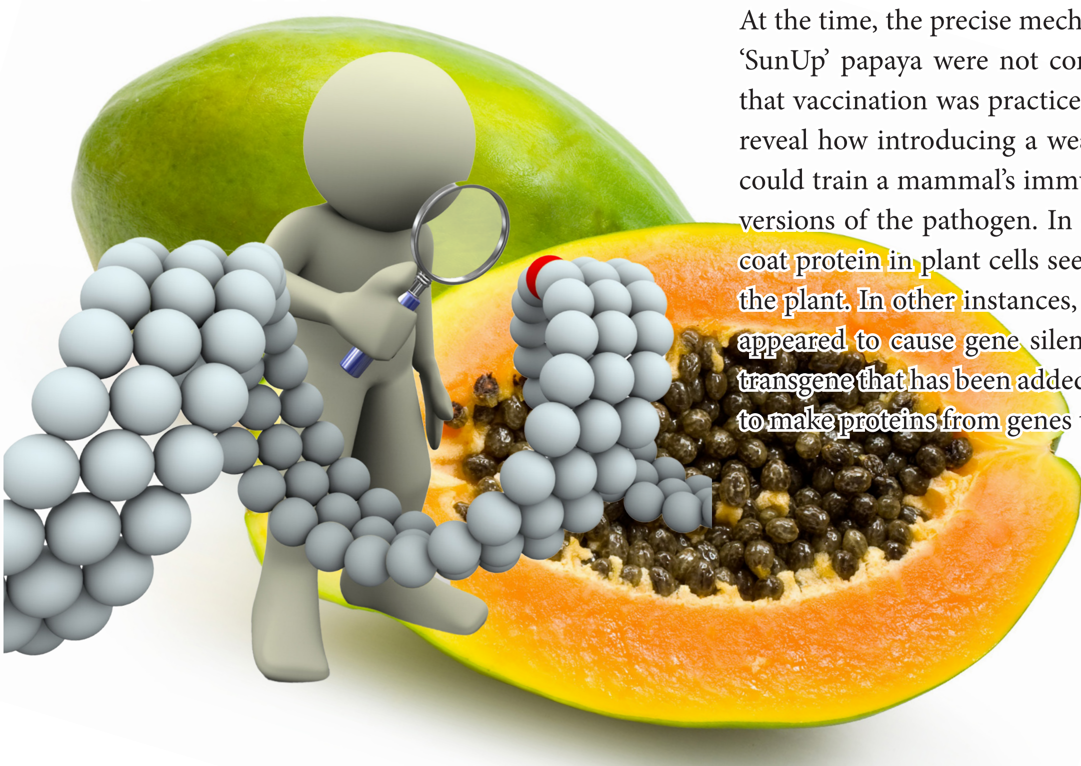
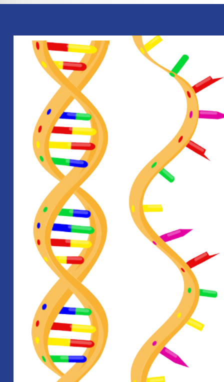
RNAi: New Uses for an Ancient Defense

In 1998, genetically modified (GM) papaya resistant to the Papaya Ringspot Virus (PRSV) entered commercial production in Hawaii. The GM papaya relies on what is called pathogen-derived resistance. A gene from the ringspot virus—the DNA recipe for making the virus's protein coat—was added to the papaya plant's set of genes, or genome, making the virus unable to infect the plant and cause disease. This virus coat protein gene was added to the 21,415 predicted genes in papaya (0.005%).



At the time, the precise mechanisms that protect GM 'Rainbow' and 'SunUp' papaya were not completely understood, in the same way that vaccination was practiced for a century before studies began to reveal how introducing a weak, dead, or partial virus or bacterium could train a mammal's immune system to fend off more dangerous versions of the pathogen. In some cases, the presence of transgenic coat protein in plant cells seemed to interfere with viral behavior in the plant. In other instances, genes from viruses - viral transgenes - appeared to cause gene silencing. This interference occurs when a transgene that has been added to a cell interferes with the cell's ability to make proteins from genes that are similar to the transgene.

In the same year that virus-resistant papaya was introduced, researchers studying a tiny, simple worm were shedding new light on gene silencing. Rather than injecting the worms with genes made from DNA, the scientists used RNAs. We can think of these RNAs as one-sided Xeroxed copies of two-sided DNA. Transcription, the process of copying a single strand of RNA from one of the two paired strands of DNA, is the first step in gene expression, making RNAs or proteins from a gene. RNA copies are the templates on which proteins are built. If RNA copies of a gene aren't available for the cell to translate into protein, the protein isn't produced.



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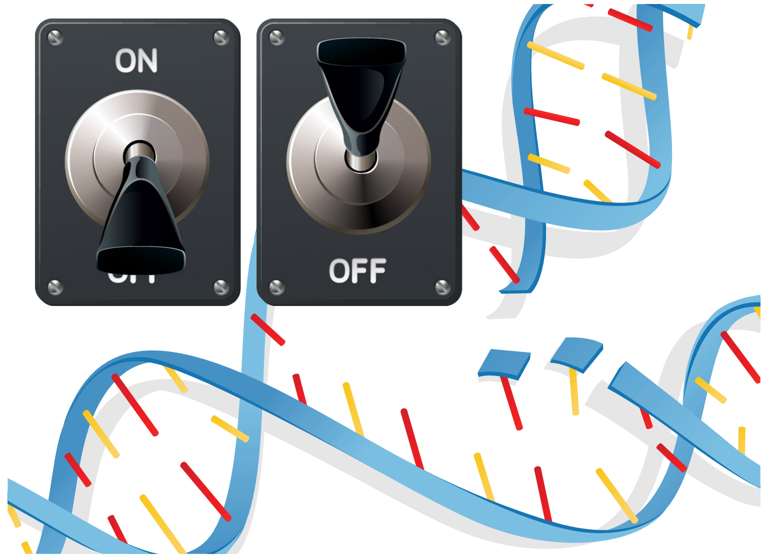
Unexpected Result

Something unexpected happened when researchers injected the worms with single-stranded RNAs copied from each of the paired DNA strands of a worm gene. If these two RNAs were combined before injection or were injected separately within a short time, expression of the worm gene stopped. The two RNAs had paired together, forming double-stranded RNA. For most genes, this silencing effect could be achieved using very small amounts of double-stranded RNA, that suggested that the RNA wasn't physically blocking gene expression, but instead was triggering a response from the plant, by giving an "instruction" to the cells.



Fighting Back

What the researchers had found is a defense mechanism present in most forms of life. Many viruses consist of RNA rather than DNA. These RNA viruses form double-stranded RNAs when they multiply inside a host cell. To fight back against the virus, the cell recognizes these are foreign and chops up the double-stranded RNAs and uses the pieces to identify similar single-stranded RNAs, which the cell also destroys. This gene-silencing mechanism is called RNA interference, or RNAi.

Preventing Virus

GM papaya's resistance to ringspot virus now made sense. The resistant plants already contain RNA copies of the virus's coat protein gene. If invading ringspot virus tries to copy the plant's coat protein RNA, making double-stranded RNA in the process, the plant can target all coat protein RNAs for destruction and prevent the virus from gaining a foothold or reproducing.

Developing A Tool

Biotechnological uses for RNAi are in their infancy. This powerful method for selectively limiting gene expression has been a popular tool in basic research, and there is great interest in developing medical applications.

In our next bulletin, we will discuss how RNAi has been employed in developing new crops, including some that have recently received commercial approval in the United States.

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