Plant biologists discover unexpected proteins affecting small RNAs

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Now that high school biology students can recite that genes are made of DNA, which is transcribed into messenger RNA (mRNA), which is then translated into protein, along comes a new class of molecules, sending students—and many scientists—scrambling for updated textbooks.

A study by Salk Institute for Biological Studies investigator Joseph Ecker, Ph.D., reported in the May 15, 2008 online issue of *Developmental Cell*, shows that the RNA world is more complex than imagined. Ecker and colleagues tinkered with factors that process mRNAs in the mustard weed Arabidopsis thaliana and observed affects on short, or small RNAs. Their findings could impact fields as diverse as plant pathology and cancer research.

Although they don't fit neatly into the DNA-to-mRNA-to-protein progression, small RNAs or microRNAs are the next big thing in both plant and animal molecular biology. Discovered a decade ago, numerous studies show that small RNAs put the brakes on the mRNA-to-protein step, by latching onto mRNA and blocking its translation into protein or causing its destruction, a phenomenon called RNA silencing.

Ecker, a professor in the Plant Biology Laboratory and director of the Salk Institute Genomic Analysis Laboratory, started by posing a simple genetic question. Researchers knew that eliminating either one of two proteins—one an mRNA-degrading enzyme called EIN5, and another a protein called ABH1 that binds to and protects mRNA from degradation—caused developmental defects in plants. Ecker's group asked what the effects of mutating both simultaneously might be.

Aided by revolutionary “deep-sequencing” technology, which detects rare RNAs at high resolution, the investigators combed through the collection of all small RNAs—known as the “smRNAome”—and found that ein5/abh1 double mutant plants ramped up small RNA levels just enough to reveal something not seen before: the mutant plant cells were churning out small RNAs made from some of their own protein-coding mRNAs.

Investigators already knew that plants defend themselves against invading pathogens like viruses by generating short RNAs that recognize and silence foreign viral RNA. Observing that plants may silence their own RNAs in this manner was unanticipated. “Our study shows that the way plants regulate RNAs produced in viruses is also probably the way they regulate their own genes,” said Ecker. “This has not been shown before in any organism—plant or animal.”

Ecker thinks this type of mRNA silencing is not an aberration of ein5/abh1 mutant plants. “What we are seeing is in these mutants is probably a generic phenomenon that will likely hold true across all systems,” said Ecker.

And why have these types of small RNAs not been observed before" Probably because researchers have not had the tools—namely, the “right” mutants scrutinized by powerful new sequencing technology—to detect them until now.

Brian D. Gregory, Ph.D., a postdoctoral fellow in the Ecker lab and first author of the paper, feels that understanding small RNA activity—whether in a plant or animal cell setting—has implications for cancer research, a connection you might expect a plant biologist who is also recipient of the highly prestigious Damon Runyon fellowship for cancer research to make.

“What we learn about RNA silencing pathways in plants could be applied to cancer chemotherapy,” Gregory explained. “There are genes expressed in tumor cells that protect them from being killed by chemotherapy—we might be able to use small RNAs to antagonize the effect of these genes in cancer cells.”

Ecker also sees the study as particularly timely in terms of ecological change. “If you understand how plants respond normally to pathogens, you can rapidly make changes in that response,” he said. “If climate change occurs there is no doubt that insect pest populations will shift, and insects are what transmit viruses. Those insects will likely move into areas they have not seen before. Since small RNAs evolved to target invading pathogens, manipulating them may combat these effects.”

Source: Salk Institute

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