Auxin Begins to Give Up Its Secrets

Auxin controls the growth of plants and their interactions with their environment, but only now are researchers understanding the basics of this hormone.

Next time you bite into a deliciously juicy strawberry or tomato, thank the seeds. As a fruit forms, its seeds produce a plant hormone called auxin, prompting the fruit to grow and ripen. Without seeds—and without auxin—fruit stays shrunken on the stem.

The wonders auxin works on strawberries and tomatoes are just the start. The hormone controls almost every aspect of plant growth, from putting down roots to determining where to start a new stem or leaf. It allows plants to react to their environment, shaping the response to signals such as light, gravity, and even the presence of bacteria. Auxin is so fundamental that one leading researcher has called it the brains of the plant world. “I got in a fair amount of trouble for saying that” in a radio interview, Ottoline Leyser of the University of York in the United Kingdom ruefully admits, cautioning that the comparison can be taken too far. “But the useful analogy is that it’s an information-processing system.”

Auxin has fascinated and puzzled plant scientists for more than 100 years. In 1880, Charles Darwin and his son Francis wrote in *The Power of Movement in Plants* about a substance that seemed to be produced at the tip of growing plant shoots, prompting them to bend toward light. It was one of the first scientific descriptions of the action of auxin. (There are several closely related hormones known collectively as auxin.) But it wasn’t until the 1930s that scientists identified the chemical structure of the most common plant auxin, indole-3-acetic acid (IAA). Since then, auxins and their synthetic cousins have been used to boost plant growth—and to kill weeds. Too much auxin is actually deadly to plants; the herbicide 2,4-D is a synthetic auxin, and Agent Orange contains a combination of synthetic auxins.

Several recent advances have helped give scientists a better picture of this multitaled hormone. They have finally identified the receptor that senses auxin’s presence, and the transport system that plants use to control levels of the hormone is becoming clearer. Researchers have also found clues to the fundamental mystery of how plants make auxin—still a surprisingly difficult question. They are even unearthing new roles for auxin in plants’ defenses against pathogens. To tackle such complexities, several groups are developing computer models that can keep track of dozens of genes that control or respond to auxin in growing roots or new branches.

All of this is helping to explain how a relatively simple molecule such as auxin can perform such versatile tasks. “It’s a very general signaling system,” says Leyser.

**Target found**

Last year, scientists solved one of the biggest outstanding questions in plant biology when two groups reported that they had finally identified the auxin receptor (*Science*, 27 May 2005, p. 1240). It turns out that the long-sought protein was hidden in plain sight.

In papers published simultaneously in *Nature*, Leyser and her colleagues and Mark Estelle of Indiana University, Bloomington, and his research group showed that auxin binds directly to a protein called TIR1. Scientists already knew that the hormone’s presence in plant cells triggers TIR1 to bind to a class of proteins called Aux/IAA, which repress genes known to be triggered by auxin. But most people assumed that auxin turned on such genes by setting off a long signaling cascade, involving numerous proteins and feedback loops.

In fact, the cascade is just a few steps: Auxin binds to TIR1, which is part of a molecular complex that attaches the cell’s garbage tag, ubiquitin, to proteins destined to be recycled. Auxin, by glomming onto TIR1, helps the complex ubiquitinate Aux/IAA proteins. When the Aux/IAA proteins are broken down, the genes they had repressed turn on. The find “has really simplified things,” Estelle says. Adds Leyser: “I’m just massively relieved that we have a signaling-transduction pathway that starts at auxin and ends at gene expression, and that all the parts are there.”

The find also triggered interest beyond the auxin field. TIR1 is one of roughly 700 so-called F-box proteins already identified in plants and long suspected of playing a role in ubiquitination. The auxin connection suggests that similar small molecules in plants might join with these F-box proteins to direct the breakdown of proteins, Estelle says. Animals, too, have hundreds of F-box proteins.

A deeper look at the auxin-TIR1 interaction has turned up a surprise. Estelle and structural biologist Ning Zheng of the University of Washington, Seattle, have teamed up to solve the crystal structure of TIR1—both with and without auxin. Small molecules that interact with proteins such as TIR1 often change the shape of the target protein. But, as Estelle and Zheng have described at meetings this summer, TIR1 keeps its shape when united with auxin. Auxin, Zheng says, appears to act as “a molecular glue,” helping TIR1 bind to the Aux/IAA proteins. Zheng, who works in a pharmacology department, says this discovery serves as a reminder for drug developers: Instead of just seeking molecules that disrupt binding, it might be useful to also search for those that encourage binding.

Sweet effects. Auxin helps prompt the growth and maturation of strawberries and other fruits.
Transport streams

Before auxin can interact with TIR1 to unleash gene activity, it needs to get to the right place in the right amount. A picture is gradually emerging, says Leyser, of a system of checks and balances that provide stable yet flexible auxin signals for plant growth and development. A plant regulates auxin levels in its cells by manipulating auxin production, making use of specialized transporters that either allow auxin into a cell or pump it out, and adjusting how quickly cells break down the molecule.

One key to this tight control of auxin is a family of proteins called PIN-FORMED or PINs, named for the pin-shaped, flowerless shoots grown by Arabidopsis mutants lacking the proteins. In May, Eva Zazimalova of the Institute of Experimental Botany in Prague, Czech Republic, and her colleagues confirmed suspicions that this growth defect was due to an auxin dysfunction. They showed that PIN proteins can transport the hormone between cells and that they are distinct from a second group of well-known auxin transport proteins, called the PGP5 (Science, 12 May, p. 914). In the same issue of Science, Jiri Friml of the University of Tübingen, Germany, and his colleagues report that the specific type and combination of different members of the PIN family, which localize to different sides of a plant cell, determine which direction auxin flows.

Other clues about auxin are coming from computer models that can begin to weave together the effects of dozens of genes. Several groups, including Elliot Meyerowitz of the California Institute of Technology in Pasadena and his colleagues, have developed transgenic Arabidopsis plants in which the PIN genes, among others, glow green during plant growth. The scientists film the plants' growth and use the digitized images to build models of the roles and reactions of key development genes in response to auxin. They can then use such a virtual plant to better understand how changing levels of the hormone affect different cells and tissues.

Illustrating the complexity of the task, Gerd Jürgens and his colleagues at the University of Tübingen have shown in several recent papers that, among other factors, specific combinations of the 29 different Aux/IAA proteins and 22 so-called auxin response factors control a plant cell's response to the hormone.

A strategic defense

Growing evidence suggests that RNA strands also play an important role in the auxin story. In April, for example, Jonathan Jones of the John Innes Centre in Norwich, U.K., and his colleagues revealed that RNAs appear to dampen auxin signaling when a plant is infected with certain bacteria. Plants can sense the presence of bacterial flagella and turn various genes on and off in response. And Jones's team showed that when a plant senses the bacteria, it ramps up production of certain microRNAs (miRNAs), short stretches of RNA that can interfere with the manufacture of specific proteins. They also showed that the miRNAs thwart the production of TIR1 and several related proteins.

Why would a plant interrupt its own auxin response? Perhaps to control plant-dwelling bacteria that also make auxin, says Estelle. Such bacteria, he speculates, use the hormone as part of their colonizing strategy. Extra auxin can trigger growth of new leaves, which might give the bacteria more living space. Indeed, says Estelle, there seems to be a sort of battle to control auxin between plant and pathogen. When the scientists disrupted the miRNA's ability to work, plants more easily succumbed to bacterial infection (Science, 21 April, p. 436).

The microbe-induced response isn't the first to implicate RNA interference in auxin signaling. Bonnie Bartel of Rice University in Houston, Texas, and her colleagues have found that miRNAs interfere with the expression of several auxin-responsive genes. She predicts that such interactions may be a common way plants regulate auxin’s powers. Plant miRNAs “seem to have an over-abundance of auxin-implicated genes in their repertoire of clearer control,” says Bartel.

Although the regulation and effects of auxin are coming into focus, plant biologists also have a somewhat embarrassing problem: They still do not know exactly how plants make the hormone. Researchers have worked out how bacteria produce auxin, but the technique used by plants has remained a mystery because it’s not just complex but also multi-plex. The hormone is so crucial to plant development that a nearly fail-safe system of backup production has evolved. If scientists try to knock out a gene that plays a role in the hormone’s synthesis, another is available to jump in and take its place, thus obscuring the initial gene’s importance.

A recent paper in Genes and Development, however, may have broken the impasse. Yunde Zhao and his colleagues at the University of California, San Diego, showed that a family of genes named after a growth-defective Arabidopsis mutant called yucca seems to play a key role in producing auxin during development. Although knocking out a single member of the gene family left the mustard plant’s growth unperturbed, knocking out three or four at once generated severely misshapen leaves and flowers. Adding auxin back through the stem didn’t rescue the plants, but by inserting a bacterial auxin-producing gene attached to a yucca promoter, the scientists produced nearly normal-looking plants.

The paper “is a huge step forward” in understanding the specific genes involved in auxin production, Estelle says. But Jerry Cohen of the University of Minnesota, Twin Cities, cautions that the story is far from solved: “Nothing has gotten to the point that you can say, ‘This is how it’s made.’”

As scientists sort out the pieces of how auxin is produced, moved, and blocked and broken down, it becomes clearer, says Leyser, that all the processes “interact and intertwine and interreact in horribly complicated feedback mechanisms.” That makes any one part of the auxin system difficult to understand on its own. “It’s necessary to think about it as an integrated system,” she says. “It’s hard science. You have to be moderately obsessed to stick with it. But that’s also why it’s so exciting.”

—GRETCHEN VÖGEL