HHMI
HOWARD HUGHES MEDICAL INSTITUTE

RESEARCH NEWS

JANUARY 12, 2012

Call to Arms

When pathogens invade, growing plants must change their priorities. Growth must be temporarily slowed while the plant turns its attention – and genetic resources – to fortifying its defenses. Now, researchers have discovered a molecular master switch that triggers this genetic overhaul, altering the activity of as many as 3,000 different genes.

Unlike humans, plants don't have an army of specialized immune cells they can mobilize to fend off pathogens. But that doesn't mean plants are defenseless. When microbes attack, plants often instigate what's called the growth-to-defense transition, in which they redirect their resources to self-protection. "Everything involved in growth and development is significantly repressed," says Xinnian Dong, a Howard Hughes Medical Institute-Gordon and Betty Moore Foundation investigator at Duke University. During this change, plants shut down large numbers of genes and switch many others on. For example, they rev up genes that code for pathogen-fighting proteins and the so-called endoplasmic reticulum (ER)-resident genes, which enable cells to fine-tune and secrete defensive proteins.

A decade ago, Dong and her colleagues found that the protein NPR1 teams up with protein partners to activate the genes for anti-pathogen proteins. But it hasn't been clear how NPR1 controls the ER-resident genes, because plants can switch on these genes even if they lack NPR1's partners.

Dong and her team set out to track down the protein that helps NPR1 regulate ER-resident genes. The on-off switches for these genes often carry a characteristic nucleotide sequence called TL1, so the researchers scanned a database of gene activators and repressors to uncover molecules that looked like they could latch onto TL1. They found several candidates that belong to a family of proteins that help plants survive high temperatures. Bacterial attacks prompt plants to increase their production of one of these proteins, suggesting that its job is to guard against disease instead of heat. Dong's team named the protein TL1-binding factor 1(TBF1).

"TBF1 controls so many genes you don't want it around when it's not necessary."

- Xinnian Dong

By studying mutant plants that couldn't make TBF1, the researchers delineated the protein's protective role. Plants bolster their defenses in response to telltale segments of pathogen proteins, known as microbe-associated molecular patterns, or MAMPS. Dong and colleagues found that one kind of MAMP spurred normal plants to curtail their growth, but had a much smaller effect on the TBF1-deficient mutants. After exposure to a specific MAMP, normal plants were able to curb the growth of certain disease-causing bacteria, whereas, the mutants could not keep the bacteria in check.

TBF1 turns out to be a key genetic manager that orchestrates the growth-to-defense transition by activating or silencing around 3,000 genes. That figure, Dong notes, amounts to about 10 percent of the genes in *Arabidopsis thaliana*, a member of the mustard family that the researchers are studying. The list of genes TBF1 shuts off includes some that are necessary for the operation of chloroplasts, the light-capturing organelles that enable the plant to make food through photosynthesis. Despite its family connections, TBF1 doesn't seem to help plants survive heat--mutants lacking TBF1 aren't fazed by high temperatures. Dong and her colleagues reveal their findings in the January 12, 2012, issue of the journal *Current Biology*.

TBF1's widespread effects raise a question--how do plants turn the gene on and off? "TBF1 controls so many genes you don't want it around when it's not necessary," Dong says. The mechanism for keeping the protein under wraps is surprisingly intricate. One factor is NPR1, the protein that inspired the study. It has a reciprocal relationship with TBF1, in which each protein regulates the other's gene.

Dong's team identified another layer of control that involves two sequences known as upstream open reading frames (uORFs) in the messenger RNA that encodes TBF1. Plants use these sequences to inhibit the production of the TBF1 protein. When the researchers exposed plants to bacteria, they found that that TBF1 production switched on, suggesting that pathogens somehow lift inhibition by the uORFs.

Dong and colleagues think they know how. The amino acids encoded by the uORFs include high numbers of phenylalanine, which is a building block for many antimicrobial secondary metabolites. The researchers hypothesize that pathogens starve plants of phenylalanine, and this metabolic change allows plants to activate translation of the TBF1 protein translation. The uORFs "seem to be responsive to specific amino acid changes induced by pathogens," says Dong. She adds that researchers are beginning to recognize

the importance of upstream open reading frames for controlling genes in many different biological processes. “That’s the most exciting part of this work,” she says.