The Secret Life of Plants

By tracking the evolution of volatile compounds, researchers hope to understand the past—and map out the future.

THE GARDEN AT JOE NOEL'S SAN DIEGO HOME FEATURES COASTAL SAGE, CALIFORNIA lilacs, and other chaparral plants that once dominated the local landscape. While he appreciates his garden's vibrant colors and water efficiency, like the biochemist he is, Noel sees beyond all that: "There's a tremendous amount of chemistry happening, most evident from the very interesting smells released from the plants throughout the day." ¶ An HHMI investigator at the Salk Institute for Biological Studies, Noel is one of a growing group of scientists fascinated by the extraordinary diversity of volatile and non-volatile compounds found in plants. Plants use these small molecules, which diffuse easily through the membranes of the cells that produce them, to communicate and interact with the outside world.

Often aromatic and almost always highly specialized for a particular ecological niche, volatiles in particular help each plant flourish in its environment, acting as an odiferous language among plants and between plants and other organisms. The chemicals attract pollinators, summon natural predators of pests, or provide protection through their antimicrobial properties.

Scientists have so far identified more than 1,000 plant volatiles. Even closely related plants produce their own unique sets of volatiles—evidence, says Noel, that the pathways giving rise to these chemicals and their biosynthetic precursors (known as secondary metabolism, because their products are not essential for a plant's growth or reproduction) are subject to rapid evolution.

"By evolving new compounds or new ways of making existing compounds, the enzymes in these biosynthetic pathways that produce volatiles and related compounds provide adaptive advantages to organisms," Noel says. "And they're evolving so rapidly that you can begin to piece together a historical record of how these systems originated, what changes they've undergone, and how they're utilized in the present. Ultimately," he adds, "I think we can also learn what changes we are in store for well into the future."

In one system, Noel and his collaborators are comparing enzymes used by members of the nightshade (Solanaceae) family—which includes tobacco, tomatoes, potatoes, and eggplant—to produce compounds closely related to volatile terpene compounds (found throughout the plant kingdom) to ward off fungal infections. In one case, the amino acids that make up two enzyme "cousins" in Egyptian henbane and tobacco plants, which diverged from their common ancestor about 10 million years ago, are 80 percent identical. But a subtle difference in the enzymes' structures means that while one produces a compound that acts against a fungus in Egyptian henbane's habitat, the other produces a chemically distinct natural compound that defends tobacco against its own fungal menace.

The gene sequence of the two enzymes is so similar, Noel says, that "in a traditional sense we would say they're the same enzyme." Yet he and his colleagues have used structural analysis to zero in on nine amino acids, of the nearly 560 comprising each enzyme, that determine which antifungal agent is produced. "When we take these nine positions in the tobacco enzyme and change them to the nine amino acids found in the Egyptian henbane enzyme,

Borrowing from Nature's Chemical Factories

Joe Noel's lab has encoded onto a single gene the entire set of enzymes that grape, peanut, and blueberry plants use to convert the common amino acid tyrosine into resveratrol—a compound particularly abundant in red wine that is known to dramatically enhance muscle tissue's ability to metabolize fat for energy. In collaboration with fellow HHMI investigator Ronald M. Evans, also at the Salk Institute for Biological Studies, Noel plans to create a mouse that expresses this "natural chemical factory" gene only in muscle tissue. Muscle cells in the mouse will then use the enzymes to transform a small amount of the tyrosine in the animal's diet to resveratrol, allowing the scientists to study how the newly produced compound affects muscle without having to feed large amounts of it to the animal. Noel is undertaking a similar project with Salk colleague Fred H. Gage to create mice that express the chemical factory in the brain—overcoming the challenges of getting a compound consumed in the diet across the blood-brain barrier—to learn how resveratrol might slow aging by altering the behavior of neural stem cells. Experiments like these may eventually enable "genetically encoded medicinal chemistry"—allowing scientists to target enzymes to specific tissues and cells in living animals, where they can create chemical variants from materials available in the diet.

"There's a tremendous amount of chemistry happening [in the garden] throughout the day."

JOE NOEL

the enzyme completely alters its characteristics," Noel explains. "It makes the chemical that the Egyptian henbane makes, and it does so with the same efficiency. The reverse experiment also works nicely."

The next step for Noel and his team is to use this information to discern the structure of the enzyme that must have existed millions of years ago in the plants' shared ancestor. "We don't have molecular fossils," he says, "but with the information now available we might be able to re-create what the ancient enzyme looked like and more importantly, how it behaved." They are proceeding by making more than 1,000 specific versions of each of the related enzymes, reflecting every possible combination of the tobacco and Egyptian henbane amino acids in the critical positions identified thus far. "We are also studying each of these variants structurally to see how the shape and dynamics change and assessing the cocktail of chemicals each produces," he says.

Eventually, glimpses like these into the structural and biosynthetic history of enzymes of secondary metabolism may help Noel and other scientists alter biosynthetic pathways to create new pharmaceuticals or other compounds with desirable properties. ■

–JENNIFER MICHALOWSKI

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