

# Genes for Queens

Understanding more about bee genetics

By Jay Withgott

If you're a honeybee, you're probably fated to spend your whole life hard at work gathering food and tending the hive. Or—if you're lucky enough to be the queen—you could spend it lazing around, being waited on hand and foot, with nothing to do but produce offspring.

What makes a bee a queen or a worker? Well, it turns out some of it's in the genes, or at least in the way they're expressed. Two University of Arizona researchers have identified genes that express themselves differently in queen bees and worker bees—a finding that gets at the genetic basis for caste determination in social insects. Jay D. Evans, a recent Center for Insect Science postdoctoral fellow now at the USDA Bee Research Lab in Maryland, and Diana E. Wheeler, an associate professor in the Department of Entomology, reported their findings in the May 11, 1999 *Proceedings of the National Academy of Sciences*.

Social insects are those insects such as ants, bees, and termites, that live in complex societies made up of individuals specialized to perform different functions. These different roles are called castes, and commonly include workers and soldiers. At the center of these societies is the queen—the individual female who grows to enormous size, produces all the colony's offspring, and is tended by these offspring so she can produce still more.

For years biologists have asked how individual insects get pigeon-holed into becoming one caste or another. And with the honeybee, *Apis mellifera*, the answer seemed to be in the food they ate. Larvae that were fed “royal jelly” became queens, while those fed only nectar and pollen became workers.

“We know a great deal about the role of nutrition in driving larvae to become queens or workers,” Evans says, “but little attention has been paid, until recently, to the genes involved with initiating a caste switch.”

In their study, Evans and Wheeler located seven stretches of DNA that expressed themselves differently in queen larvae and worker larvae. It is the first direct demonstration of differential gene expression underlying caste determination in a social insect. In fact, writes Dr. H. Frederik Nijhout of Duke University in a commentary accompanying the report,

it “is the first specific information we have on the molecular events that accompany a developmental switch between alternative pathways in insects in general. We now have a proven technique that can be used to delve into the details of what goes on at the molecular level when developmental pathways diverge.”

Evans and Wheeler believe the diet is a switch that turns these genes on or off, so earlier findings with queen and worker diets are not invalidated. The researchers have simply delved one step deeper into the mechanisms of how castes are determined.

“I've always wanted to know more about the switch, the architecture of it,” Wheeler says. “This is the technological breakthrough I've been waiting for.”

To find the genes, the researchers used a new technique called suppressive subtraction, along with more established methods. Basically, they took messenger RNA (which creates proteins from DNA's instructions) and used it to work in reverse, creating copies of the DNA sequences that were expressing themselves. They took such DNA copies from larvae starting down the queen path and larvae starting down the worker path and with the new method teased apart the DNA that was similar among queen larvae and worker larvae from that which was different. Several experimental steps later, they then determined the nucleotide sequences of the seven DNA strands that differed between queen larvae and worker larvae.

Knowing a gene's nucleotide sequence doesn't tell you much unless you can match it up with sequences from other organisms for which the gene functions are already known. Evans and Wheeler did this, and found suggestive evidence for specific functions of their genes.

Ironically, both researchers switched away from their organism of speciality—ants—to conduct this study. Wheeler is widely recognized for extensive work on hormonal control of caste development in ants, and Evans had done work on interactions among queens in ant species with multiple queens.

But, they say, ants would have been intractable for this question, and honeybees were perfect. Among several reasons is the fact that bees keep their larvae in particular cells so that the researchers could identify and keep track of individual



larvae, whereas ants simply throw them together in a “brood pile.”

Keeping track of larvae was important since Evans and Wheeler wanted to determine when exactly in the young bees' development particular genes get turned on. “We thought we were getting really close, temporally, to the start of differentiation,” Evans said, although he added that now they believe there may be genes differentially expressed even earlier than the ones they found. And certainly, they say, many more than seven genes must be involved.

One interesting aspect of their work is that most of the genes that were “turned on” occurred in worker larvae, rather than queen larvae, thus going against the notion that becoming a queen is the special condition that needs explaining. Evans explains that this could imply that workers are more complex and derived than queens, or it could simply be that other genes specifying queen-ness get turned on in later developmental stages they did not test.

Evans and Wheeler see at least two major future applications of their work. First, their data lays the groundwork for comparative research with other social insects. Knowing these seven bee genes will provide a helpful starting point for other researchers hoping to explore the molecular basis of caste determination and—more broadly—the evolution of sociality in insects.

Second, caste determination is only one example of a broader phenomenon common in insects, called polyphenism. Polyphenism refers to the ability of insects with similar genes to express very different phenotypes, that is, different physical forms or behaviors. The ability to attain different phenotypes that match different environmental conditions, Wheeler says, “has contributed a lot to [insects'] success, and this is a technological breakthrough that will allow us to understand how they do that.” ♦