ScienceWatch - Changing Behavior

"The study results are exciting because they show that behavior can be manipulated in social animals using compounds that bring about quick changes in the action of genes."- D. Reinberg

Social insects like ants are famous for their "castes," groups that differ morphologically and behaviorally to perform specialized tasks. For example, Florida carpenter ant workers (*Camponotus floridanus*) are divided into "majors" or soldiers and "minors" or foragers. Although all the workers are sisters sharing the same genome, they look and behave in dramatically different ways. Majors have huge heads and jaws that they use to defend the colony. Minors have small jaws, are half as big and relentlessly search for food to feed the colony.

These differences once thought to be innate can be altered "epigenetically." Epigenetics is the study of stable changes in the gene expression of inherited traits. These changes are caused by external factors that turn genes on or off without changing the DNA sequence in the genes themselves. Epigenetic processes include modifications of histones—proteins that together with DNA make up the structure of chromosomes. The proteins form a core around which the immensely long DNA molecules are coiled. Enzymes that add chemical groups, like acetyl, to histones allow the DNA to locally uncoil and gain access to other proteins that switch on gene expression. Conversely, removal of acetyls from histones causes the DNA to become more tightly compacted and inaccessible, resulting in a shutdown of gene expression.

Such epigenetic processes appear to play key roles in regulating caste morphology and behavior. In honeybees, for example, the "royal jelly" fed to some larva to make queens contains a substance that blocks the addition of acetyl groups to histones—turning a sterile worker into a fertile queen. Now a study examines how epigenetic modifiers directly affect ant caste behavior.

The research team, headed by Daniel Simola and Shelly Berger, University of Pennsylvania, Philadelphia, Pa., and Danny Reinberg, NYU Langone, New York, NY, has been studying epigenetic changes in *C. floridanus* for over eight years. Several years ago they generated an "epigenetic map," showing that particular genes were differently expressed in the two castes. Specifically, they found that genes controlling muscle development were expressed at higher levels in majors, while genes involved in brain development and neurotransmission were more active in minors. Their newest finding, appearing in the January 1, 2016 issue of *Science*, shows they can manipulate ant behavior by changing the balance of acetyl groups in their brains, making one caste behave like the other.

In one experiment the team fed 1-month-old foraging minors valproic acid, a chemical that blocks the removal of acetyl groups from histones. This resulted in more acetyl groups linked to genes for neuronal activity and greatly increased scouting and foraging activity. The same treatment had little or no effect on the behavior of major workers so the team injected a more potent chemical blocker (trichostatin) directly into the brains of 1-day-old majors. Remarkably, delivery of a single dose of trichostatin into young majors' brains caused them to immediately act like minor workers. They began actively scouting and foraging, and continued this behavior for up to two months. The results show that early in adult ant life there is a time, an "epigenetic window of vulnerability," when epigenetic regulators can modify the balance of acetyl groups in the brain to determine subsequent behavior.

These results have important implications for us. Another epigenetic regulator of ant behavior (CPB) adds acetyl groups to histones and also facilitates learning and memory in mice. Moreover, a CPB mutation in humans results in a condition with severe learning disabilities known as Rubenstein-Taybi syndrome.

According to Berger, "Because of the remarkable [epigenetic] window [of vulnerability] we have uncovered, ants also provide an extraordinary opportunity to explore and understand the epigenetic processes that come into play to establish behavioral patterns at a young age. This is a topic of increasing research interest in humans, owing to the growing prevalence of behavioral disorders and diseases …"

The research team is now focusing on the "window" and what controls it. "Understanding the mechanisms of when and how this window is opened and how changes are sustained—and why the window closes as the major ant ages—may have profound implications for explaining human vulnerability to life exposures," said Berger.

Sociobiologists have often compared ant and human behaviors. Now molecular biologists are elucidating the determinants of these complex traits.

Saul Scheinbach